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

PRODUCT ASSESSMENT REPORT OF A BIOCIDAL PRODUCT FOR NATIONAL AUTHORISATION APPLICATIONS

Product identifier in R4BP	**Ruby Paste**
Product type:	14 (Rodenticide)
Active ingredient(s):	Difenacoum
Case No. in R4BP	BC-YC001264-53
Asset No. in R4BP	IE-0000686-0000
Evaluating Competent Authority	Ireland – Department of Agriculture, Food & the Marine
Internal registration/file no	**IE/BPA 70530**
Date	30.04.2018 (NA-RNL renewal)

Version 2.0

1 Version History

Date	Version	Reason for revision
2011/06/30	Version 1.0	Initial PAR
2016/05/09	Version 1.1	Revised PAR
2018/04/30	Version 2.0	Updated at 1st Renewal of authorisation RNL

2 Overview of applications

Application type	refMS	Case number in the refMS	Decision date	Assessment carried out (i.e. first authorisation / amendment /renewal)	Page
National Authorisation Dir.98/8/EC	IE	n/a	2011/06/30	1st Authorisation	97
NA-RNL	IE	BC-YC001264-53	2018/04/30	Renewal	29

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1st Renewal PAR – April 2018

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

PRODUCT ASSESSMENT REPORT OF A BIOCIDAL PRODUCT FOR THE RENEWAL OF A NATIONAL AUTHORISATION (NA-RNL)

Product identifier in R4BP	**Ruby Paste**
Product type:	14 (Rodenticide)
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1 Conclusion

The Irish CA for the authorisation of biocidal products has processed an application for renewal for the biocidal product Ruby Paste which contains the active substance Difenacoum (0.005 % w/w).
The assessment presented in the Product Assessment Report for the first authorisation showed acceptable efficacy but unacceptable risks for the environment, if the product is used as a rodenticide (product-type 14) for use in and around buildings, by the general public, professionals and trained professionals, and in open areas and waste dumps by professionals and trained professionals.

The conditions for granting an authorisation according to Article 19 (1) of Regulation (EU) No 528/2012[1] (BPR) are not fulfilled.
In consequence the product can only be authorised in accordance with Article 19 (5) BPR, as this Article provides Member States with the legal basis to authorise products in cases where not authorising the product would result in disproportionate negative impacts for society when compared to the risks to human health arising from the use of the biocidal product.

Detailed information on the uses appropriate at the renewal of authorisation are presented in section 2.4.
General directions for use of the product are summarised in section 2.5.

Prior to renewing the approval of anticoagulant active substances and renewing the authorisations of the respective products discussions took place at EU-level to harmonise use instructions and risk mitigation measures to the greatest possible extend. As an outcome of these discussions a set of three standard SPCs (Summary of Product Characteristics) compiling the relevant sentences for the uses that may be authorised for each of the three user categories (general public, professionals and trained professionals) has been produced (for details please refer to document CA-Nov16-Doc.4.1.b – Final).

The specific conditions from Commission Implementing Regulation (EU) 2017/1379[2] for the active substance Difenacoum were considered for the re-assessment.

The Irish CA concludes that the conditions set out in Article 5(2) b) and c) of the BPR are currently met. Anticoagulant rodenticides are considered essential to ensure appropriate rodent control in Ireland by

[1] Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the making available on the market and use of biocidal products, last amended by Regulation (EU) No 334/2014 of the European Parliament and of the Council of 11 March 2014.

[2] Commission Implementing Regulation (EU) 2017/1379 of 25 July 2017 renewing the approval of difenacoum as an active substance for use in biocidal products of product-type 14

efficient pest management and as a consequence, to prevent or control any serious danger to human and animal health in which rodents are involved.
Rodent control in Ireland currently relies largely on the use of anticoagulant rodenticides, the non-renewal of which could lead to insufficient rodent control in Ireland. This may not only cause significant negative impacts on human or animal health or the environment, but may also affect the public's perception of its safety with regard to exposure to rodents or the security of a number of economic activities that could be vulnerable to rodents, resulting in economic and social consequences in Ireland.

The product has been classified according to the 9th ATP of Regulation (EC) No 1272/2008[3]. Detailed information on classification and labelling is provided in Section 2.3.
As a consequence of the new harmonised classification, the active substance Difenacoum meets the criteria for exclusion according to Article 5(1) BPR as well as for substitution according to Article 10 BPR Therefore, in line with Article 23 (1) BPR a comparative assessment for the product Ruby Paste has been conducted (for details see Section 3.10).

Comparative assessment
In line with Article 23 (1) BPR a comparative assessment for the product has been conducted (for details see Section 3.10).
In summary it can be concluded that the criteria according Article 23(3) a), b) BPR are not fulfilled.
According to Article 23 (6) BPR the authorisation of the product will be renewed for 5 years.

Approval of the active substance
The active substance Difenacoum is included in the Union list of approved active substances and the specific provisions laid down there are fulfilled:

The authorisations of biocidal products containing Difenacoum are subject to the conditions listed in the Annex to Commission Implementing Regulation (EU) 2017/1379:

Composition and formulation
The ready-to-use product is a paste bait and contains the active substance Difenacoum.
No substance of concern has been identified.
Please refer to section 5.1 for detailed information.

Physical, chemical and technical properties
No new data was provided nor had new guidance to be taken into account for the renewal evaluation.

[3] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006.

Accordingly, the conclusion from the former assessment regarding physical, chemical and technical properties remains valid.

Physical hazards and respective characteristics

No new data was provided, nor had new guidance to be taken into account for the renewal evaluation. Accordingly, the conclusion from the former assessment regarding physical hazards and respective characteristics remains valid.

Methods for detection and identification

No new data was provided, nor had new guidance to be taken into account for the renewal evaluation. Accordingly, the conclusion from the former assessment regarding methods for detection and identification remains valid.

Efficacy

The IE CA considers that the efficacy data has confirmed that Ruby Paste is effective in the proposed areas for use, at the recommended dose rate when used as per label recommendations. Apart from two studies using 3-year aged bait no new data was provided nor had new guidance to be taken into account for re-assessment.

An evaluation of the studies provided demonstrated that the ready-to-use pasta bait formulation proved to be both palatable to and effective against infestations of rats (*Rattus norvegicus* and *Rattus rattus*) and house mice (*Mus musculus / domesticus*).

Consequently, the conclusion from the former assessment regarding the product's efficacy against target organisms remains valid.

The conclusion of the evaluation is that the product may be authorised.

Risk assessment for human health

The human health risk assessment for this product is based on the active substance.

According to the BPC Opinion the EFSA-Guidance on dermal absorption had been taken into account when reviewing the dermal absorption of the product.

Based on the risk assessment of the active substance, a risk for professional users resulting from the intended use is unlikely.

For risk mitigation measures please refer to section 2.

Due to the new classification (Repr.1B) it is not allowed to grant authorisation for the use by general public (Article 19 (4) and (5) BPR). Therefore the product will not be authorised for the non-professional user.

Based on the risk assessment it is unlikely that the intended use(s) cause any unacceptable acute or chronic risk to professional users, bystanders and residents. Regarding the trained professional users health protection, there are no objections against the intended uses if the directions for use are followed (For details see section 2).

Risk assessment for the environment

No new data was provided. The only area where new guidance was relevant was with respect to the groundwater assessment. Following discussion at the CG-18 meeting and subsequent agreement, Tier II PEC groundwater was calculated using the FOCUS models PEARL or PELMO in the instances where Tier I indicated an exceedance of the relevant trigger value.

According to the risk assessment, the risk for poisoning of non-target predator birds and mammals during primary (acute and long-term exposure) and secondary poisoning is high as the trigger value is exceeded in all cases.

No safe use was established for the Difenacoum product at a concentration of 50 ppm in the ecotoxicology risk assessment.

In consequence the product can only be authorised in accordance with Article 19 (5) BPR.

Overall conclusion

The assessment of the biocidal product Ruby Paste remains valid. However, the authorisation has to be adapted where necessary taking into account the points mentioned above.

The biocidal product will be authorised according to Article 19 (5) BPR in conjunction with Article 23 (6) BPR.

According to Article 23 (6) BPR the authorisation of the product will be renewed for 5 years.

2 Summary of the product assessment

2.1 Administrative information

2.1.1 Identifier in R4BP

Ruby Paste
Additional trade name(s): Roded Paste

2.1.2 Authorisation holder

Name and address of the authorisation holder	**Name**	LODI S.A.S.
	Address	Parc d'Activités des Quatre Routes 35390 Grand Fougeray France
Authorisation number	IE/BPA 70530	
Date of the authorisation	30.04.18	
Expiry date of the authorisation	30.04.23	

2.1.3 Manufacturer(s) of the product

Name of manufacturer	LODI S.A.S.
Address of manufacturer	Parc d'Activités des Quatre Routes 35390 Grand Fougeray France
Location of manufacturing sites	Parc d'Activités des Quatre Routes 35390 Grand Fougeray France

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

Active substance	Difenacoum
Name of manufacturer	PelGar International Limited

Address of manufacturer	Unit 13, Newman Lane Alton Hampshire GU34 2QR UK
Location of manufacturing sites	Prazska 54, 280 02 Kolin, Czech Republic

2.2 Product composition and formulation

2.2.1 Qualitative and quantitative information on the composition

Table 1

Common name	IUPAC name	Function	CAS number	EC number	Content (%)
Difenacoum	**3-(3biphenyl-4-yl-1,2,3,4-tetrahydro-1-naphtyl)-4-hydroxycoumarin**	Active Substance	**56073-07-5**	**259-978-4**	0.005

- The product contains a bittering agent and a dye.
  - ➢ Information on the full composition is provided in the confidential[4] annex (see chapter 4).
- According to the information provided the product contains no nanomaterials as defined in Article 3 paragraph 1 (z) of Regulation No. 528/2012:

2.2.2 Information on the substance(s) of concern

The Product contains 0.15% Butylhydroxytoluene (CAS 128-37-0) as co-formulant. Butylhydroxytoluene is recognised as an SoC for community workspace exposure limits.

2.2.3 Candidate(s) for substitution

The following substance was identified as a candidate for substitution:

- **Difenacoum**

Difenacoum meets the following exclusion criteria according to Article 5(1) BPR:

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

[4] Access level: “Restricted” to applicant and authority

Therefore Difenacoum meets the conditions laid down in Article 10 BPR, and is consequently a candidate for substitution.

2.2.4 Type of formulation

Ready-to-use bait: paste

2.3 Classification and Labelling according to the Regulation (EC) No 1272/2008[5]

Table 2

Classification **Hazard classes, Hazard categories**	**Hazard statements**
STOT RE 2	H373: May cause damage to organs (blood) through prolonged or repeated exposure
Repr. 1B	H360D: May damage the unborn child.

Table 3

Labelling	**Code**	**Pictogram / Wording**
	GHS08	
Signal word		Danger
Hazard statements	STOT RE 2	H373: May cause damage to organs (blood) through prolonged or repeated exposure
	Repr. 1B	H360D: May damage the unborn child.

5 Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006.

Supplemental label elements		
Precautionary statements:	P201	Obtain special instructions before use
	P202	Do not handle until all safety precautions have been read and understood.
	P260	Do not breathe dust.
	P280	Wear protective gloves.
	P308+P313	IF exposed or concerned: Get medical advice/attention.
	P314	Get Medical advice/attention if you feel unwell.
	P405	Store locked up.
	P501	Dispose of contents in accordance with local/regional/national /international regulations
	-	
Note		

2.4 Uses appropriate for further authorisation[6]

Table 4: Summary Table of Uses

No.	Use
1	House mice – professionals – indoor
2	Rats – professionals – indoor
3	House mice and/or rats – professionals – outdoor around buildings
4	House mice and/or rats – trained professionals – indoor
5	House mice and/or rats – trained professionals – outdoor around buildings
6	Rats – trained professionals – Outdoor open areas & waste dumps

2.4.1 Use 1 appropriate after renewal of the authorisation – House mice – professionals – indoor

Product Type(s)	14

6 Member States might refuse to grant an authorisation or adjust the terms and conditions of the authorisation to be granted according to Article 37 BPR.

Where relevant, an exact description of the use	Rodenticide
Target organism(s) (including development stage)	House mouse (*Mus musculus* / *Mus domesticus*) – adults and juveniles
Field(s) of use	Indoors
Application method(s)	Ready-to-use bait to be used in tamper-resistant bait stations
Application rate(s) and frequency	20-30 g of bait per bait station. If more than one bait station is needed, the minimum distance between bait stations should be 3 meters (high infestation). If there is a low infestation the distance between bait stations should be 5 meters.
Category(ies) of users	Professionals
Pack sizes and packaging material	Minimum pack size 2.5 kg **Grams of bait in individual sachet:** 10 **Packaging material and size:** **Bucket: (PP,PE)** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cardboard box with inner PE liner** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cartridge in PP**: 50 g, 100g, 150g, 200g, 250g, 260g , 270g, 280g, 310g, 500g Outer packaging - cardboard box with pack sizes of: 50 cartridges of 50g, 25 cartridges of 100g, 20 cartridges of 150g, 15 cartridges of 200g, 10 cartridges of 250g, 12 cartridges of 250g, 18 cartridges of 250g, 10 cartridges of 260g, 12 cartridges of 260g, 18 cartridges of 260g, 10 cartridges of 270g, 12 cartridges of 270g, 18 cartridges of 270g, 10 cartridges of 280g, 12 cartridges of 280g, 18 cartridges of 280g, 10 cartridges of 310g, 12 cartridges of 310g, 18 cartridges of 310g or 5 cartridges of 500g. **Pre-baited station (PP,PS,PVC)**: 2*10g or 3*10g in cardboard box of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg

2.4.1.1 Use-specific instructions for use

- For mice use 20-30 g securely in tamper-resistant bait stations spaced 5m apart (3m apart in high infestation areas) in areas where mice are active.
- Bait stations should be placed in the immediate vicinity of places where rodent activity has been previously observed (e.g. travel paths, nesting sites, feedlots, holes, burrows etc.).

- Regularly check bait consumption and replace consumed or spoilt bait until consumption has stopped.
- Repeat treatment in situations where there is evidence of new infestation (e.g. fresh tracks or droppings). Mice are very inquisitive and it may help the control program to move baits every 2-3 days at the time when bait points are inspected or topped up. Make frequent inspections of the bait points during the first 10-14 days and replace any bait eaten by rodents or that has been damaged by water or contaminated by dirt. If all the bait has been eaten from certain areas, increase the quantity of bait by placing more bait points. Do not increase the bait point size. Replace any bait eaten by rodents or that has been damaged by water or contaminated by dirt.
- The bait stations should be visited at least every 2 to 3 days at the beginning of the treatment and at least weekly afterwards, in order to check whether the bait is accepted, the bait stations are intact and to remove rodent bodies. Re-fill bait when necessary.
- The resistance status of the target population should be taken into account when considering the choice of rodenticide to be used. In those areas where evidence of resistance to specific active ingredients is suspected, avoid their use. To control the spreading of resistance, it is advisable to alternate baits containing different anticoagulant active ingredients.
- Do not use this product for permanent or pulse-baiting.
- Remove the remaining bait or the bait stations at the end of the treatment period.

2.4.1.2 Use-specific risk mitigation measures

- Products shall not be used beyond 35 days without an evaluation of the state of the infestation and of the efficacy of the treatment.
- Do not use baits containing anticoagulant active substances as permanent baits for the prevention of rodent infestation or monitoring of rodent activities.
- The product information (i.e. label and/or leaflet) shall clearly show that:
  - the product shall not be supplied to the general public (e.g. "for professionals only").
  - the product shall be used in adequate tamper resistant bait stations (e.g. "use in tamper resistant bait stations only").
  - users shall properly label bait stations with the information referred to in section 5.3 of the SPC (e.g. label bait stations according to the product recommendations").
- Using this product should eliminate rodents within 35 days. The product information (i.e. label and/or leaflet) shall clearly recommend that in case of suspected lack of efficacy by the end of the treatment (i.e. rodent activity is still observed), the user should seek advice from the product supplier or call a pest control service.
- Do not wash the bait stations with water between applications.

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

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

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

None

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

None

2.4.2 Use 2 appropriate after renewal of the authorisation – Rats – professionals – indoor

Product Type(s)	14
Where relevant, an exact description of the use	Rodenticide
Target organism(s) (including development stage)	Brown rats (*Rattus norvegicus*) – adults and juveniles Roof rats (*Rattus rattus*) – adults and juveniles
Field(s) of use	Indoors
Application method(s)	Ready-to-use bait to be used in tamper-resistant bait stations
Application rate(s) and frequency	90-100 g of bait per bait station. If more than one bait station is needed, the minimum distance between bait stations should be of 5 meters (high infestation) and 10 meters (low infestation).
Category(ies) of users	Professionals
Pack sizes and packaging material	Minimum pack size 2.5 kg **Grams of bait in individual sachet:** 10 **Packaging material and size:** **Bucket: (PP,PE)**

	10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cardboard box with inner PE liner** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cartridge in PP**: 50 g, 100g, 150g, 200g, 250g, 260g , 270g, 280g, 310g, 500g Outer packaging - cardboard box with pack sizes of: 50 cartridges of 50g, 25 cartridges of 100g, 20 cartridges of 150g, 15 cartridges of 200g, 10 cartridges of 250g, 12 cartridges of 250g, 18 cartridges of 250g, 10 cartridges of 260g, 12 cartridges of 260g, 18 cartridges of 260g, 10 cartridges of 270g, 12 cartridges of 270g, 18 cartridges of 270g, 10 cartridges of 280g, 12 cartridges of 280g, 18 cartridges of 280g, 10 cartridges of 310g, 12 cartridges of 310g, 18 cartridges of 310g or 5 cartridges of 500g. **Pre-baited station (PP,PS,PVC)**: 2*10g or 3*10g in cardboard box of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg

2.4.2.1 Use-specific instructions for use

- For rat infestations use 90-100 g of bait securely in tamper resistant baiting stations spaced 10m apart (5m apart in areas of high infestation).
- Bait stations should be placed in the immediate vicinity of places where rodent activity has been previously observed (e.g. travel paths, nesting sites, feedlots, holes, burrows etc.).
- Regularly check bait consumption and replace consumed or spoilt bait until consumption has stopped. Repeat treatment in situations where there is evidence of new infestation (e.g. fresh tracks or droppings). Do not move or disturb bait points for several days after laying bait. If no signs of rat activity are seen near the bait after 7-10 days, move the bait to an area of higher rat activity.
- The bait stations should be visited only 5 to 7 days after the beginning of the treatment and at least weekly afterwards, in order to check whether the bait is accepted, the bait stations are intact and to remove rodent bodies. Re-fill bait when necessary.
- The resistance status of the target population should be taken into account when considering the choice of rodenticide to be used. In those areas where evidence of resistance to specific active ingredients is suspected, avoid their use. To control the spreading of resistance, it is advisable to alternate baits containing different anticoagulant active ingredients.
- Do not use this product for permanent or pulse-baiting.
- Remove the remaining bait or the bait stations at the end of the treatment period

2.4.2.2 Use-specific risk mitigation measures

- Products shall not be used beyond 35 days without an evaluation of the state of the infestation and of the efficacy of the treatment.
- Do not use baits containing anticoagulant active substances as permanent baits for the prevention of rodent infestation or monitoring of rodent activities.
- The product information (i.e. label and/or leaflet) shall clearly show that:
  - the product shall not be supplied to the general public (e.g. "for professionals only").
  - the product shall be used in adequate tamper resistant bait stations (e.g. "use in tamper resistant bait stations only").
  - users shall properly label bait stations with the information referred to in section 5.3 of the SPC (e.g. label bait stations according to the product recommendations").
- Using this product should eliminate rodents within 35 days. The product information (i.e. label and/or leaflet) shall clearly recommend that in case of suspected lack of efficacy by the end of the treatment (i.e. rodent activity is still observed), the user should seek advice from the product supplier or call a pest control service.
- Do not wash the bait stations with water between applications.

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

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

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

None

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

None

2.4.3 Use 3 appropriate after renewal of the authorisation – House mice and/or rats – professionals – outdoor around buildings

Product Type(s)	14
Where relevant, an exact description of the use	Rodenticide
Target organism(s) (including development stage)	House mouse (*Mus musculus / Mus domesticus*) – adults and juveniles Brown rats (*Rattus norvegicus*) – adults and juveniles Roof rats (*Rattus rattus*) – adults and juveniles
Field(s) of use	Outdoors around buildings
Application method(s)	Ready-to-use bait to be used in tamper-resistant bait stations
Application rate(s) and frequency	Mice : 20-30 g / Rats 90-100 g of bait per bait station. If more than one bait station is needed, the minimum distance between bait stations should be 3 meters for mice and 5 meters for rats (high infestation). If there is a low infestation the distance between bait stations should be 5 meters for mice and 10 meters for rat.
Category(ies) of users	Professionals
Pack sizes and packaging material	Minimum pack size 2.5 kg **Grams of bait in individual sachet:** 10 **Packaging material and size:** **Bucket: (PP,PE)** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cardboard box with inner PE liner** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cartridge in PP**: 50 g, 100g, 150g, 200g, 250g, 260g , 270g, 280g, 310g, 500g Outer packaging - cardboard box with pack sizes of: 50 cartridges of 50g, 25 cartridges of 100g, 20 cartridges of 150g, 15 cartridges of 200g, 10 cartridges of 250g, 12 cartridges of 250g, 18 cartridges of 250g, 10 cartridges of 260g, 12 cartridges of 260g, 18 cartridges of

	260g, 10 cartridges of 270g, 12 cartridges of 270g, 18 cartridges of 270g, 10 cartridges of 280g, 12 cartridges of 280g, 18 cartridges of 280g, 10 cartridges of 310g, 12 cartridges of 310g, 18 cartridges of 310g or 5 cartridges of 500g. **Pre-baited station (PP,PS,PVC)**: 2*10g or 3*10g in cardboard box of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg

2.4.3.1 Use-specific instructions for use

- For mice use 20-30 g in tamper-resistant bait stations.
- Secure 20-30 g of bait in tamper resistant baiting stations spaced 5m apart (3m apart in high infestation areas) in areas where mice are active. Regularly check bait consumption and replace consumed or spoilt bait until consumption has stopped. Repeat treatment in situations where there is evidence of new infestation (e.g. fresh tracks or droppings). Mice are very inquisitive and it may help the control program to move baits every 2-3 days at the time when bait points are inspected or topped up. Make frequent inspections of the bait points during the first 10-14 days and replace any bait eaten by rodents or that has been damaged by water or contaminated by dirt. If all the bait has been eaten from certain areas, increase the quantity of bait by placing more bait points. Do not increase the bait point size.

- For rats up to 90-100 g in tamper-resistant bait stations.
- Secure 90-100 g of bait in tamper resistant baiting stations spaced 10m apart (5m apart in areas of high infestation) in areas where rats are active. Regularly check bait consumption and replace consumed or spoilt bait. Repeat treatment in situations where there is evidence of new infestation (e.g. fresh tracks or droppings). Do not move or disturb bait points for several days after laying bait. If no signs of rat activity are seen near the bait after 7-10 days, move the bait to an area of higher rat activity. If all the bait has been eaten from certain areas, increase the quantity of bait by placing more bait points. Do not increase the bait point size.

- Bait stations should be placed in the immediate vicinity of places where rodent activity has been previously observed (e.g. travel paths, nesting sites, feedlots, holes, burrows etc.).
- Replace any bait eaten by rodents or that has been damaged by water or contaminated by dirt.
- Protect bait from the atmospheric conditions (e.g. rain, snow, etc.). Place the bait stations in areas not liable to flooding.
- Replace any bait in a bait station in which bait has been damaged by water or contaminated by dirt.

- The resistance status of the target population should be taken into account when considering the choice of rodenticide to be used. In those areas where evidence of resistance to specific active ingredients is suspected, avoid their use. To control the spreading of resistance, it is advisable to alternate baits containing different anticoagulant active ingredients.
- Do not use this product for permanent or pulse-baiting.
- Remove the remaining bait or the bait stations at the end of the treatment period

2.4.3.2 Use-specific risk mitigation measures

- Do not apply this product directly in the burrows.
- Products shall not be used beyond 35 days without an evaluation of the state of the infestation and of the efficacy of the treatment.
- Do not use baits containing anticoagulant active substances as permanent baits for the prevention of rodent infestation or monitoring of rodent activities.
- The product information (i.e. label and/or leaflet) shall clearly show that:
  - the product shall not be supplied to the general public (e.g. "for professionals only").
  - the product shall be used in adequate tamper resistant bait stations (e.g. "use in tamper resistant bait stations only").
  - users shall properly label bait stations with the information referred to in section 5.3 of the SPC (e.g. label bait stations according to the product recommendations").
- Using this product should eliminate rodents within 35 days. The product information (i.e. label and/or leaflet) shall clearly recommend that in case of suspected lack of efficacy by the end of the treatment (i.e. rodent activity is still observed), the user should seek advice from the product supplier or call a pest control service.
- Do not wash the bait stations with water between applications.

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

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

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

None

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

None

2.4.4 Use 4 appropriate after renewal of the authorisation – House mice and/or rats – trained professionals – indoor

Product Type(s)	14
Where relevant, an exact description of the use	Rodenticide
Target organism(s) (including development stage)	House mouse (*Mus musculus* / *Mus domesticus*) – adults and juveniles Brown rats (*Rattus norvegicus*) – adults and juveniles Roof rats (*Rattus rattus*) – adults and juveniles
Field(s) of use	Indoors
Application method(s)	Ready-to-use bait to be used in covered bait points or in tamper-resistant bait stations
Application rate(s) and frequency	Mice: 20-30 g / Rats: 90-100 g of bait per bait station. - - Bait products: **Mice** - High infestation: (20-30) g of bait per baiting point every 3 meters - Low infestation: (20-30) g of bait per baiting point every 5 meters **Rats** - High infestation: (90-100) g of bait per baiting point every 5 meters - Low infestation: (90-100) g of bait per baiting point every 10 meters Permanent baiting - **Mice** - High infestation: (20-30) g of bait per baiting point every 3 meters - Low infestation: (20-30) g of bait per baiting point every 5 meters **Rats** - High infestation: (90-100) g of bait per baiting point every 5 meters - Low infestation: (90-100) g of bait per baiting point every 10 meters
Category(ies) of users	Trained Professionals
Pack sizes and packaging material	Minimum pack size 2.5 kg **Grams of bait in individual sachet:** 10 **Packaging material and size:** **Bucket: (PP,PE)**

	10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cardboard box with inner PE liner** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cartridge in PP**: 50 g, 100g, 150g, 200g, 250g, 260g , 270g, 280g, 310g, 500g Outer packaging - cardboard box with pack sizes of: 50 cartridges of 50g, 25 cartridges of 100g, 20 cartridges of 150g, 15 cartridges of 200g, 10 cartridges of 250g, 12 cartridges of 250g, 18 cartridges of 250g, 10 cartridges of 260g, 12 cartridges of 260g, 18 cartridges of 260g, 10 cartridges of 270g, 12 cartridges of 270g, 18 cartridges of 270g, 10 cartridges of 280g, 12 cartridges of 280g, 18 cartridges of 280g, 10 cartridges of 310g, 12 cartridges of 310g, 18 cartridges of 310g or 5 cartridges of 500g. **Pre-baited station (PP,PS,PVC)**: 2*10g or 3*10g in cardboard box of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg

2.4.4.1 Use-specific instructions for use

- For mice use 20-30 g in tamper-resistant bait stations or covered bait points.
- Secure 20-30g of bait in covered tamper resistant baiting stations or covered bait points spaced 5m apart (3m apart in high infestation areas) in areas where mice are active. Regularly check bait consumption and replace consumed or spoilt bait until consumption has stopped. Repeat treatment in situations where there is evidence of new infestation (e.g. fresh tracks or droppings). Mice are very inquisitive and it may help the control program to move baits every 2-3 days at the time when bait points are inspected or topped up. Make frequent inspections of the bait points during the first 10-14 days and replace any bait eaten by rodents or that has been damaged by water or contaminated by dirt. If all the bait has been eaten from certain areas, increase the quantity of bait by placing more bait points. Do not increase the bait point size.

- For rats up to 90-100 g in tamper-resistant bait stations or covered bait points.
- Secure 90-100 g of bait in covered tamper resistant baiting stations or covered bait points spaced 10m apart (5m apart in areas of high infestation) in areas where rats are active. Regularly check bait consumption and replace consumed or spoilt bait. Repeat treatment in situations where there is evidence of new infestation (e.g. fresh tracks or droppings). Do not move or disturb bait points for several days after laying bait. If no signs of rat activity are

seen near the bait after 7-10 days, move the bait to an area of higher rat activity. If all the bait has been eaten from certain areas, increase the quantity of bait by placing more bait points. Do not increase the bait point size.

- The product should be placed in the immediate vicinity of places where rodent activity has been previously observed (e.g. travel paths, nesting sites, feedlots, holes, burrows etc.).
- Regularly check bait consumption and replace consumed or spoilt bait until consumption has stopped. Repeat treatment in situations where there is evidence of new infestation (e.g. fresh tracks or droppings). Make frequent inspections of the bait points during the first 10-14 days.

- The frequency of visits to the treated area should be at the discretion of the operator, in the light of the survey conducted at the outset of the treatment. That frequency should be consistent with the recommendations provided by the relevant code of best practice.
- The resistance status of the target population should be taken into account when considering the choice of rodenticide to be used. In those areas where evidence of resistance to specific active ingredients is suspected, avoid their use. To control the spreading of resistance, it is advisable to alternate baits containing different anticoagulant active ingredients.
- Remove the remaining product at the end of treatment period.
- For Permanent Baiting: Where possible, it is recommended that the treated area is revisited every 4 weeks at the latest in order to avoid any selection of a resistant population. [When available] Follow any additional instructions provided by the relevant code of best practice.

2.4.4.2 Use-specific risk mitigation measures

- The product information (i.e. label and/or leaflet) shall clearly show that the product shall only be supplied to trained professional users holding certification demonstrating compliance with the applicable training requirements (e.g. "for trained professionals only".
- Do not use in areas where resistance to the active substance can be suspected.
- Products shall not be used beyond 35 days without an evaluation of the state of the infestation and of the efficacy of the treatment [unless authorised for permanent baiting treatments].
- Do not rotate the use of different anticoagulants with comparable or weaker potency for resistance management purposes. For rotational use, consider using a non-anticoagulant rodenticide, if available, or a more potent anticoagulant.
- Do not wash the bait stations or utensils used in covered and protected bait points with water between applications.
- Permanent baiting is strictly limited to sites with a high potential for reinvasion when other

methods of control have proven insufficient. • The permanent baiting strategy shall be periodically reviewed in the context of integrated pest management (IPM) and the assessment of the risk for re-infestation.

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

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

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

None

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

None

2.4.5 Use 5 appropriate after renewal of the authorisation – House mice and/or rats – trained professionals – outdoor around buildings

Product Type(s)	14
Where relevant, an exact description of the use	Rodenticide
Target organism(s) (including development stage)	House mouse (*Mus musculus* / *Mus domesticus*) – adults and juveniles Brown rats (*Rattus norvegicus*) – adults and juveniles Roof rats (*Rattus rattus*) – adults and juveniles
Field(s) of use	Outdoors around buildings
Application method(s)	Ready-to-use bait to be used in covered bait points or in tamper-resistant bait stations, or in direct application of ready-to-use bait into the burrow.
Application rate(s) and	Mice: 20-30 g / Rats: 90-100 g of bait per bait station. - -

frequency	Bait products: **Mice** - High infestation: (20-30) g of bait per baiting point every 3 meters - Low infestation: (20-30) g of bait per baiting point every 5 meters **Rats** - High infestation: (90-100) g of bait per baiting point every 5 meters - Low infestation: (90-100) g of bait per baiting point every 10 meters - In burrows: 90-100g of bait per burrow. Permanent baiting - **Mice** - High infestation: (20-30) g of bait per baiting point every 3 meters - Low infestation: (20-30) g of bait per baiting point every 5 meters **Rats** - High infestation: (90-100) g of bait per baiting point every 5 meters - Low infestation: (90-100) g of bait per baiting point every 10 meters
Category(ies) of users	Trained Professionals
Pack sizes and packaging material	Minimum pack size 2.5 kg **Grams of bait in individual sachet:** 10 **Packaging material and size:** **Bucket: (PP,PE)** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cardboard box with inner PE liner** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cartridge in PP**: 50 g, 100g, 150g, 200g, 250g, 260g , 270g, 280g, 310g, 500g Outer packaging - cardboard box with pack sizes of: 50 cartridges of 50g, 25 cartridges of 100g, 20 cartridges of 150g, 15 cartridges of 200g, 10 cartridges of 250g, 12 cartridges of 250g, 18 cartridges of 250g, 10 cartridges of 260g, 12 cartridges of 260g, 18 cartridges of 260g, 10 cartridges of 270g, 12 cartridges of 270g, 18 cartridges of 270g, 10 cartridges of 280g, 12 cartridges of 280g, 18 cartridges of 280g, 10 cartridges of 310g, 12 cartridges of 310g, 18 cartridges of 310g or 5 cartridges of 500g. **Pre-baited station (PP,PS,PVC)**: 2*10g or 3*10g in cardboard box of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg

2.4.5.1 Use-specific instructions for use

- For mice use 20-30 g in tamper-resistant bait stations or covered bait points.
- Secure 20-30g of bait in covered tamper resistant baiting stations or covered bait points spaced 5m apart (3m apart in high infestation areas) in areas where mice are active.

Regularly check bait consumption and replace consumed or spoilt bait until consumption has stopped. Repeat treatment in situations where there is evidence of new infestation (e.g. fresh tracks or droppings). Mice are very inquisitive and it may help the control program to move baits every 2-3 days at the time when bait points are inspected or topped up. Make frequent inspections of the bait points during the first 10-14 days and replace any bait eaten by rodents or that has been damaged by water or contaminated by dirt. If all the bait has been eaten from certain areas, increase the quantity of bait by placing more bait points. Do not increase the bait point size.

- For rats up to 90-100 g in tamper-resistant bait stations or covered bait points, or directly into the burrow.
- Secure 90-100 g of bait in covered tamper resistant baiting stations or covered bait points spaced 10m apart (5m apart in areas of high infestation) in areas where rats are active. Regularly check bait consumption and replace consumed or spoilt bait. Repeat treatment in situations where there is evidence of new infestation (e.g. fresh tracks or droppings). Do not move or disturb bait points for several days after laying bait. If no signs of rat activity are seen near the bait after 7-10 days, move the bait to an area of higher rat activity. If all the bait has been eaten from certain areas, increase the quantity of bait by placing more bait points. Do not increase the bait point size.

- The product should be placed in the immediate vicinity of places where rodent activity has been previously observed (e.g. travel paths, nesting sites, feedlots, holes, burrows etc.).
- For outdoor use, baiting points must be covered and placed in strategic sites to minimise the exposure to non-target species.
- Regularly check bait consumption and replace consumed or spoilt bait until consumption has stopped. Repeat treatment in situations where there is evidence of new infestation (e.g. fresh tracks or droppings). Make frequent inspections of the bait points during the first 10-14 days.
- The bait stations should be visited only 5 to 7 days after the beginning of the treatment and at least weekly afterwards, in order to check whether the bait is accepted, the bait stations are intact and to remove rodent bodies. Re-fill bait when necessary
- The frequency of visits to the treated area should be at the discretion of the operator, in the light of the survey conducted at the outset of the treatment. That frequency should be consistent with the recommendations provided by the relevant code of best practice.
- The resistance status of the target population should be taken into account when considering the choice of rodenticide to be used. In those areas where evidence of resistance to specific active ingredients is suspected, avoid their use. To control the spreading of resistance, it is advisable to alternate baits containing different anticoagulant active ingredients.

- Protect bait from the atmospheric conditions (e.g. rain, snow, etc.). Place the bait stations in areas not liable to flooding.
- Remove the remaining product at the end of treatment period.
- Replace any bait in baiting points in which bait has been damaged by water or contaminated by dirt.
- When used in burrows: Baits must be placed to minimise the exposure to non-target species and children. Cover or block the entrances of baited burrows to reduce the risks of bait being rejected and spilled.
- For Permanent Baiting: Where possible, it is recommended that the treated area is revisited every 4 weeks at the latest in order to avoid any selection of a resistant population. [When available] Follow any additional instructions provided by the relevant code of best practice.

2.4.5.2 Use-specific risk mitigation measures

- Do not use the product as permanent baits for the prevention of rodent infestation or monitoring of rodent activities.
- The product information (i.e. label and/or leaflet) shall clearly show that the product shall only be supplied to trained professional users holding certification demonstrating compliance with the applicable training requirements (e.g. "for trained professionals only".
- Do not use in areas where resistance to the active substance can be suspected.
- Products shall not be used beyond 35 days without an evaluation of the state of the infestation and of the efficacy of the treatment [unless authorised for permanent baiting treatments].
- Do not rotate the use of different anticoagulants with comparable or weaker potency for resistance management purposes. For rotational use, consider using a non-anticoagulant rodenticide, if available, or a more potent anticoagulant.
- Do not wash the bait stations or utensils used in covered and protected bait points with water between applications.
- Permanent baiting is strictly limited to sites with a high potential for reinvasion when other methods of control have proven insufficient.
- The permanent baiting strategy shall be periodically reviewed in the context of integrated pest management (IPM) and the assessment of the risk for re-infestation.

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

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

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

None

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

None

2.4.6 Use 6 appropriate after renewal of the authorisation – Rats – trained professionals – Outdoor open areas & waste dumps

Product Type(s)	14
Where relevant, an exact description of the use	Rodenticide
Target organism(s) (including development stage)	Brown rats (*Rattus norvegicus*) – adults and juveniles Roof rats (*Rattus rattus*) – adults and juveniles
Field(s) of use	Outdoor open areas & waste dumps
Application method(s)	Ready-to-use bait to be used in covered bait points or in tamper-resistant bait stations, or in direct application of ready-to-use bait into the burrow.
Application rate(s) and frequency	Rats 90-100 g of bait per bait station. - - - High infestation: (90-100) g of bait per baiting point every 5 meters - Low infestation: (90-100) g of bait per baiting point every 10 meters - In burrows: 90-100g of bait per burrow. Permanent baiting - Rats - High infestation: (90-100) g of bait per baiting point every 5 meters - Low infestation: (90-100) g of bait per baiting point every 10 meters

Category(ies) of users	Trained Professionals
Pack sizes and packaging material	Minimum pack size 2.5 kg **Grams of bait in individual sachet:** 10 **Packaging material and size:** **Bucket: (PP,PE)** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cardboard box with inner PE liner** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cartridge in PP**: 50 g, 100g, 150g, 200g, 250g, 260g , 270g, 280g, 310g, 500g Outer packaging - cardboard box with pack sizes of: 50 cartridges of 50g, 25 cartridges of 100g, 20 cartridges of 150g, 15 cartridges of 200g, 10 cartridges of 250g, 12 cartridges of 250g, 18 cartridges of 250g, 10 cartridges of 260g, 12 cartridges of 260g, 18 cartridges of 260g, 10 cartridges of 270g, 12 cartridges of 270g, 18 cartridges of 270g, 10 cartridges of 280g, 12 cartridges of 280g, 18 cartridges of 280g, 10 cartridges of 310g, 12 cartridges of 310g, 18 cartridges of 310g or 5 cartridges of 500g. **Pre-baited station (PP,PS,PVC)**: 2*10g or 3*10g in cardboard box of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg

2.4.6.1 Use-specific instructions for use

- For rats use 90-100 g of bait in tamper-resistant bait stations or covered bait points, or directly into the burrow.
- Secure 90-100 g of bait in covered tamper resistant baiting stations or covered bait points spaced 10m apart (5m apart in areas of high infestation) in areas where rats are active. Do not move or disturb bait points for several days after laying bait. If no signs of rat activity are seen near the bait after 7-10 days, move the bait to an area of higher rat activity. If all the bait has been eaten from certain areas, increase the quantity of bait by placing more bait points. Do not increase the bait point size.
- The product should be placed in the immediate vicinity of places where rodent activity has been previously observed (e.g. travel paths, nesting sites, feedlots, holes, burrows etc.).
- For outdoor use, baiting points must be covered and placed in strategic sites to minimise the exposure to non-target species.
- Regularly check bait consumption and replace consumed or spoilt bait until consumption

has stopped. Repeat treatment in situations where there is evidence of new infestation (e.g. fresh tracks or droppings). Make frequent inspections of the bait points during the first 10-14 days.

- The bait stations should be visited only 5 to 7 days after the beginning of the treatment and at least weekly afterwards, in order to check whether the bait is accepted, the bait stations are intact and to remove rodent bodies. Re-fill bait when necessary.
- The frequency of visits to the treated area should be at the discretion of the operator, in the light of the survey conducted at the outset of the treatment. That frequency should be consistent with the recommendations provided by the relevant code of best practice.
- The resistance status of the target population should be taken into account when considering the choice of rodenticide to be used. In those areas where evidence of resistance to specific active ingredients is suspected, avoid their use. To control the spreading of resistance, it is advisable to alternate baits containing different anticoagulant active ingredients.
- Protect bait from the atmospheric conditions (e.g. rain, snow, etc.). Place the bait stations in areas not liable to flooding.
- Remove the remaining product at the end of treatment period.
- Replace any bait in baiting points in which bait has been damaged by water or contaminated by dirt.
- When used in burrows: Baits must be placed to minimise the exposure to non-target species and children. Cover or block the entrances of baited burrows to reduce the risks of bait being rejected and spilled.
- For permanent baiting - - Where possible, it is recommended that the treated area is revisited every 4 weeks at the latest in order to avoid any selection of a resistant population. *[When available]* Follow any additional instructions provided by the relevant code of best practice.

2.4.6.2 Use-specific risk mitigation measures

- Do not use the product as permanent baits for the prevention of rodent infestation or monitoring of rodent activities.
- The product information (i.e. label and/or leaflet) shall clearly show that the product shall only be supplied to trained professional users holding certification demonstrating compliance with the applicable training requirements (e.g. "for trained professionals only".
- Do not use in areas where resistance to the active substance can be suspected.
- Products shall not be used beyond 35 days without an evaluation of the state of the infestation and of the efficacy of the treatment [unless authorised for permanent baiting

treatments].

- Do not rotate the use of different anticoagulants with comparable or weaker potency for resistance management purposes. For rotational use, consider using a non-anticoagulant rodenticide, if available, or a more potent anticoagulant.
- Do not wash the bait stations or utensils used in covered and protected bait points with water between applications.
- Permanent baiting is strictly limited to sites with a high potential for reinvasion when other methods of control have proven insufficient.
  The permanent baiting strategy shall be periodically reviewed in the context of integrated pest management (IPM) and the assessment of the risk for re-infestation.

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

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

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

None

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

None

2.5 General directions for use

2.5.1 Instructions for use

- Read and follow the product information as well as any information accompanying the product or provided at the point of sale before using it.
- *[When available]* Follow any additional instructions provided by the relevant code of best practice.
- Carry out a pre-baiting survey of the infested area and an on-site assessment in order to identify the rodent species, their places of activity and determine the likely cause and the extent of the infestation.
- Remove food which is readily attainable for rodents (e.g. spilled grain or food waste). Apart from this, do not clean up the infested area just before the treatment, as this only disturbs the rodent population and makes bait acceptance more difficult to achieve.
- The product should only be used as part of an integrated pest management (IPM) system, including, amongst others, hygiene measures and, where possible, physical methods of control.
- Consider preventive control measures (e.g. plug holes, remove potential food and drink as far as possible) to improve product intake and reduce the likelihood of reinvasion.
- Where possible, bait stations must be fixed to the ground or other structures.
- Bait stations must be clearly labelled to show they contain rodenticides and that they must not be moved or opened (see section 2.5.3 for the information to be shown on the label).
- [If national policy or legislation require it] When the product is being used in public areas, the areas treated should be marked during the treatment period and a notice explaining the risk of primary or secondary poisoning by the anticoagulant as well as indicating the first measures to be taken in case of poisoning must be made available alongside the baits.
- Bait should be secured so that it cannot be dragged away from the bait station.
- Place the product out of the reach of children, birds, pets, farm animals and other non-target animals.
- Place the product away from food, drink and animal feeding stuffs, as well as from utensils or surfaces that have contact with these.
- If bait uptake is low relative to the apparent size of the infestation, consider the replacement of bait stations to further places and the possibility to change to another bait formulation.
- When using the product do not eat, drink or smoke. Wash hands and directly exposed skin after using the product.
- If after a treatment period of 35 days baits are continued to be consumed and no decline in rodent activity can be observed, the likely cause has to be determined. Where other elements have been excluded, it is likely that there are resistant rodents, so consider the use of a non-

anticoagulant rodenticide, where available, or a more potent anticoagulant rodenticide. Also consider the use of traps as an alternative control measure.

- Bait in sachets: Do not open the sachets containing the bait].
- Wear protective chemical resistant gloves during product handling phase (nitrile gloves EN 374-2).

2.5.2 Risk mitigation measures

- Where possible, prior to the treatment inform any possible bystanders (e.g. users of the treated area and their surroundings) about the rodent control campaign [in accordance with the applicable code of good practice, if any]".
- Do not use Difenacoum-containing products for pulse baiting.
- Dispose of dead rodents in accordance with local requirements [The method of disposal shall be described specifically in the national SPC and be reflected on the product label].
- To reduce risk of secondary poisoning, search for and remove dead rodents at frequent intervals during treatment (e.g. at least twice a week) [Where relevant, specify if more frequent or daily inspection is required], in line with the recommendations provided by the relevant code of best practice.

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

This product contains an anticoagulant substance. If ingested, symptoms, which may be delayed, may include nosebleed and bleeding gums. In severe cases, there may be bruising and blood present in the faeces or urine.
Antidote: Vitamin K1 administered by medical/veterinary personnel only.

In case of: Dermal exposure, wash skin with water and then with water and soap.
Eye exposure, rinse eyes with eyes-rinse liquid or water, keep eyes lids open at least 10 minutes.
Oral exposure, rinse mouth carefully with water. Never give anything by mouth to unconscious person. Do not provoke vomiting. If swallowed, seek medical advice immediately and show the product's container or label. *[insert country specific information].*

Contact a veterinary surgeon in case of ingestion by a pet *[insert country specific information].*

Bait stations must be labelled with the following information: "do not move or open"; "contains a rodenticide"; "product name or authorisation number"; "active substance(s)" and "in case of incident, call a poison centre [insert national phone number]".

Hazardous to wildlife.

2.5.4 Instructions for safe disposal of the product and its packaging

At the end of the treatment, dispose of uneaten bait and the packaging in accordance with local requirements. Use of gloves is recommended.

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

Shelf-life: 24 months

Store in a dry, cool and well ventilated place. Keep the container closed and away from direct sunlight.

Store in places prevented from the access of children, birds, pets and farm animals.

Keep only in original container.

2.5.6 Other information

Because of their delayed mode of action, anticoagulant rodenticides may take from 4 to 10 days to be effective after consumption of the bait.

Rodents can be disease carriers. Do not touch dead rodents with bare hands, use gloves or use tools such as tongs when disposing them.

This product contains a bittering agent and a dye.

2.5.7 Documentation

2.5.7.1 Data submitted in relation to product application

Please see General Annexes section 4.1

2.5.7.2 Access to documentation

The applicant supported the evaluation of the active substance at EU level and has full access to the documents submitted by the taskforce for the EU review programme.

3 Assessment of the product

3.1 Proposed Uses

3.1.1 Use 1 – House mice – professionals – indoor

Product Type(s)	14
Where relevant, an exact description of the use	Rodenticide
Target organism(s) (including development stage)	House mouse (*Mus musculus* / *Mus domesticus*) – adults and juveniles
Field(s) of use	Indoors
Application method(s)	Ready-to-use bait to be used in tamper-resistant bait stations
Application rate(s) and frequency	20-30 g of bait per bait station. If more than one bait station is needed, the minimum distance between bait stations should be 3 meters (high infestation). If there is a low infestation the distance between bait stations should be 5 meters.
Category(ies) of users	Professionals
Pack sizes and packaging material	Minimum pack size 2.5 kg **Grams of bait in individual sachet:** 10 **Packaging material and size:** **Bucket: (PP,PE)** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cardboard box with inner PE liner** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cartridge in PP**: 50 g, 100g, 150g, 200g, 250g, 260g , 270g, 280g, 310g, 500g Outer packaging - cardboard box with pack sizes of: 50 cartridges of 50g, 25 cartridges of 100g, 20 cartridges of 150g, 15 cartridges of 200g, 10 cartridges of 250g, 12 cartridges of 250g, 18 cartridges of 250g, 10 cartridges of 260g, 12 cartridges of 260g, 18 cartridges of 260g, 10 cartridges of 270g, 12 cartridges of 270g, 18 cartridges of 270g, 10 cartridges of 280g, 12 cartridges of 280g, 18 cartridges of 280g, 10 cartridges of 310g, 12 cartridges of 310g, 18 cartridges of 310g or 5 cartridges of 500g. **Pre-baited station (PP,PS,PVC)**: 2*10g or 3*10g in cardboard box of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg

3.1.2 Use 2 – Rats – professionals – indoor

Product Type(s)	14
Where relevant, an exact description of the use	Rodenticide
Target organism(s) (including development stage)	Brown rats (*Rattus norvegicus*) – adults and juveniles Roof rats (*Rattus rattus*) – adults and juveniles
Field(s) of use	Indoors
Application method(s)	Ready-to-use bait to be used in tamper-resistant bait stations
Application rate(s) and frequency	90-100 g of bait per bait station. If more than one bait station is needed, the minimum distance between bait stations should be of 5 meters (high infestation) and 10 meters (low infestation).
Category(ies) of users	Professionals
Pack sizes and packaging material	Minimum pack size 2.5 kg **Grams of bait in individual sachet:** 10 **Packaging material and size:** **Bucket: (PP,PE)** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cardboard box with inner PE liner** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cartridge in PP**: 50 g, 100g, 150g, 200g, 250g, 260g , 270g, 280g, 310g, 500g Outer packaging - cardboard box with pack sizes of: 50 cartridges of 50g, 25 cartridges of 100g, 20 cartridges of 150g, 15 cartridges of 200g, 10 cartridges of 250g, 12 cartridges of 250g, 18 cartridges of 250g, 10 cartridges of 260g, 12 cartridges of 260g, 18 cartridges of 260g, 10 cartridges of 270g, 12 cartridges of 270g, 18 cartridges of 270g, 10 cartridges of 280g, 12 cartridges of 280g, 18 cartridges of 280g, 10 cartridges of 310g, 12 cartridges of 310g, 18 cartridges of 310g or 5 cartridges of 500g. **Pre-baited station (PP,PS,PVC)**: 2*10g or 3*10g in cardboard box of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg

3.1.3 Use 3 - House mice and/or rats – professionals – outdoor around buildings

Product Type(s)	14
Where relevant, an exact description of the use	Rodenticide
Target organism(s) (including development stage)	House mouse (*Mus musculus* / *Mus domesticus*) – adults and juveniles Brown rats (*Rattus norvegicus*) – adults and juveniles Roof rats (*Rattus rattus*) – adults and juveniles
Field(s) of use	Outdoors around buildings
Application method(s)	Ready-to-use bait to be used in tamper-resistant bait stations
Application rate(s) and frequency	Mice : 20-30 g / Rats 90-100 g of bait per bait station. If more than one bait station is needed, the minimum distance between bait stations should be 3 meters for mice and 5 meters for rats (high infestation). If there is a low infestation the distance between bait stations should be 5 meters for mice and 10 meters for rat.
Category(ies) of users	Professionals
Pack sizes and packaging material	Minimum pack size 2.5 kg **Grams of bait in individual sachet:** 10 **Packaging material and size:** **Bucket: (PP,PE)** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cardboard box with inner PE liner** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cartridge in PP**: 50 g, 100g, 150g, 200g, 250g, 260g , 270g, 280g, 310g, 500g Outer packaging - cardboard box with pack sizes of: 50 cartridges of 50g, 25 cartridges of 100g, 20 cartridges of 150g, 15 cartridges of 200g, 10 cartridges of 250g, 12 cartridges of 250g, 18 cartridges of 250g, 10 cartridges of 260g, 12 cartridges of 260g, 18 cartridges of 260g, 10 cartridges of 270g, 12 cartridges of 270g, 18 cartridges of 270g, 10 cartridges of 280g, 12 cartridges of 280g, 18 cartridges of 280g, 10 cartridges of 310g, 12 cartridges of 310g, 18 cartridges of 310g or 5 cartridges of 500g. **Pre-baited station (PP,PS,PVC)**: 2*10g or 3*10g in cardboard box of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg

3.1.4 Use 4 - House mice and/or rats – trained professionals – indoor

Product Type(s)	14
Where relevant, an exact description of the use	Rodenticide
Target organism(s) (including development stage)	House mouse (*Mus musculus* / *Mus domesticus*) – adults and juveniles Brown rats (*Rattus norvegicus*) – adults and juveniles Roof rats (*Rattus rattus*) – adults and juveniles
Field(s) of use	Indoors
Application method(s)	Ready-to-use bait to be used in covered bait points or in tamper-resistant bait stations
Application rate(s) and frequency	Mice: 20-30 g / Rats: 90-100 g of bait per bait station. - - Bait products: **Mice** - High infestation: (20-30) g of bait per baiting point every 3 meters - Low infestation: (20-30) g of bait per baiting point every 5 meters **Rats** - High infestation: (90-100) g of bait per baiting point every 5 meters - Low infestation: (90-100) g of bait per baiting point every 10 meters
Category(ies) of users	Trained Professionals
Pack sizes and packaging material	Minimum pack size 2.5 kg **Grams of bait in individual sachet:** 10 **Packaging material and size:** **Bucket: (PP,PE)** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cardboard box with inner PE liner** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cartridge in PP**: 50 g, 100g, 150g, 200g, 250g, 260g , 270g, 280g, 310g, 500g Outer packaging - cardboard box with pack sizes of: 50 cartridges of 50g, 25 cartridges of 100g, 20 cartridges of 150g, 15 cartridges of 200g, 10 cartridges of 250g, 12 cartridges of 250g, 18 cartridges of 250g, 10 cartridges of 260g, 12 cartridges of 260g, 18 cartridges of 260g, 10 cartridges of 270g, 12 cartridges of 270g, 18 cartridges of 270g, 10 cartridges of 280g, 12 cartridges of 280g, 18 cartridges of 280g, 10 cartridges of 310g, 12 cartridges of 310g, 18 cartridges of 310g or 5 cartridges of 500g. **Pre-baited station (PP,PS,PVC)**: 2*10g or 3*10g in cardboard box of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg

3.1.5 Use 5 - House mice and/or rats – trained professionals – outdoor around buildings

Product Type(s)	14
Where relevant, an exact description of the use	Rodenticide
Target organism(s) (including development stage)	House mouse (*Mus musculus* / *Mus domesticus*) – adults and juveniles Brown rats (*Rattus norvegicus*) – adults and juveniles Roof rats (*Rattus rattus*) – adults and juveniles
Field(s) of use	Outdoors around buildings
Application method(s)	Ready-to-use bait to be used in covered bait points or in tamper-resistant bait stations
Application rate(s) and frequency	Mice: 20-30 g / Rats: 90-100 g of bait per bait station. - - Bait products: **Mice** - High infestation: (20-30) g of bait per baiting point every 3 meters - Low infestation: (20-30) g of bait per baiting point every 5 meters **Rats** - High infestation: (90-100) g of bait per baiting point every 5 meters - Low infestation: (90-100) g of bait per baiting point every 10 meters
Category(ies) of users	Trained Professionals
Pack sizes and packaging material	Minimum pack size 2.5 kg **Grams of bait in individual sachet:** 10 **Packaging material and size:** **Bucket: (PP,PE)** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cardboard box with inner PE liner** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cartridge in PP**: 50 g, 100g, 150g, 200g, 250g, 260g , 270g, 280g, 310g, 500g Outer packaging - cardboard box with pack sizes of: 50 cartridges of 50g, 25 cartridges of 100g, 20 cartridges of 150g, 15 cartridges of 200g, 10 cartridges of 250g, 12 cartridges of 250g, 18 cartridges of 250g, 10 cartridges of 260g, 12 cartridges of 260g, 18 cartridges of 260g, 10 cartridges of 270g, 12 cartridges of 270g, 18 cartridges of 270g, 10 cartridges of 280g, 12 cartridges of 280g, 18 cartridges of 280g, 10 cartridges of 310g, 12 cartridges of 310g, 18 cartridges of 310g or 5 cartridges of 500g. **Pre-baited station (PP,PS,PVC)**: 2*10g or 3*10g in cardboard box of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg

3.1.6 Use 6 - Rats – trained professionals – Outdoor open areas & waste dumps

Product Type(s)	14
Where relevant, an exact description of the use	Rodenticide
Target organism(s) (including development stage)	House mouse (*Mus musculus* / *Mus domesticus*) – adults and juveniles Brown rats (*Rattus norvegicus*) – adults and juveniles Roof rats (*Rattus rattus*) – adults and juveniles
Field(s) of use	Outdoor open areas & waste dumps
Application method(s)	Ready-to-use bait to be used in covered bait points or in tamper-resistant bait stations
Application rate(s) and frequency	Rats 90-100 g of bait per bait station. - - - High infestation: (90-100) g of bait per baiting point every 5 meters - Low infestation: (90-100) g of bait per baiting point every 10 meters
Category(ies) of users	Trained Professionals
Pack sizes and packaging material	Minimum pack size 2.5 kg **Grams of bait in individual sachet:** 10 **Packaging material and size:** **Bucket: (PP,PE)** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cardboard box with inner PE liner** 10 g: 2.5 kg (250*10), 3 kg (300*10), 3.5 kg (350*10), 4 kg (400*10), 4.5 kg (450*10), 5 kg (500*10), 5.5 kg (550*10), 6 kg (600*10), 6.5 kg (650*10), 7 kg (700*10), 7.5 kg (750*10), 8 kg (800*10), 8.5 kg (850*10), 9 kg (900*10), 9.5 kg (950*10), 10 kg (1000*10) **Cartridge in PP**: 50 g, 100g, 150g, 200g, 250g, 260g , 270g, 280g, 310g, 500g Outer packaging - cardboard box with pack sizes of: 50 cartridges of 50g, 25 cartridges of 100g, 20 cartridges of 150g, 15 cartridges of 200g, 10 cartridges of 250g, 12 cartridges of 250g, 18 cartridges of 250g, 10 cartridges of 260g, 12 cartridges of 260g, 18 cartridges of 260g, 10 cartridges of 270g, 12 cartridges of 270g, 18 cartridges of 270g, 10 cartridges of 280g, 12 cartridges of 280g, 18 cartridges of 280g, 10 cartridges of 310g, 12 cartridges of 310g, 18 cartridges of 310g or 5 cartridges of 500g. **Pre-baited station (PP,PS,PVC)**: 2*10g or 3*10g in cardboard box of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg

3.2 Physical, chemical and technical properties

Two new studies have been provided and are evaluated below. All other conclusions from the former assessments (Original PAR and the Addendum to the Product Assessment Report, April 2012) regarding physical, chemical and technical properties remain valid. No new guidance had to be taken into account for the renewal evaluation.

<table>
<tr><th>Property</th><th>Guideline and Method</th><th>Results</th><th>Reference</th></tr>
<tr>
<td>Storage stability test – accelerated storage

35°C for 12 weeks</td>
<td></td>
<td>Metal box with PP cover
<table>
<tr><th>Weight</th><th>T_o (g)</th><th>T_{12week} (g)</th><th>Deviation (%)</th></tr>
<tr><td>Box</td><td>80.60</td><td>80.61</td><td>0.01 %</td></tr>
<tr><td>Cover</td><td>4.36</td><td>4.36</td><td>0.00 %</td></tr>
<tr><td>Sample</td><td>127.11</td><td>125.76</td><td>-1.06 %</td></tr>
<tr><td>Sample 1</td><td>10.11</td><td>9.85</td><td>-1.60 %</td></tr>
<tr><td>Sample 2</td><td>9.42</td><td>9.29</td><td>-1.38 %</td></tr>
<tr><td>Sample 3</td><td>9.73</td><td>9.60</td><td>-1.34 %</td></tr>
<tr><td>Sample 4</td><td>10.03</td><td>9.83</td><td>-1.99 %</td></tr>
<tr><td>Sample 5</td><td>10.15</td><td>9.89</td><td>-2.56 %</td></tr>
<tr><td>Total</td><td>212.07</td><td>210.73</td><td>-0.63 %</td></tr>
</table>
Sample Aspect
T_0: Red paste in individual tea paper sachet. Presence of fat on sachets.
$T_{12weeks}$: Red paste in individual tea paper sachet. Presence of fat on sachets.

Packaging aspect
T_0: Cylindrical metal box, opaque. No porosity. Black cover. All is</td>
<td>‘Compatibility between Difenacoum paste bait and packagings after accelerated storage’.

Lodi 18/2015
S Richerioux
Date: 2015-08-31</td>
</tr>
</table>

clean and dry.
$T_{12weeks}$: Clyindrical metal box, opaque. No porosity. Presence of traces of fat on internal wall of the box. Clean and dry black cover.

Metal box with PP cover + PP bag

Weight	**T_o (g)**	**T_{12week} (g)**	**Deviation (%)**
Box	81.52	81.52	0.00
Cover	4.58	4.57	-0.22
PP bag	3.27	3.29	0.61
Sample	115.46	114.61	-0.74
Sample 1	9.88	9.74	-1.42
Sample 2	9.21	8.98	-2.50
Sample 3	9.63	9.40	-2.39
Sample 4	9.33	9.27	-0.64
Sample 5	9.15	9.05	-1.09
Total weight	204.82	204.01	-0.40

Sample Aspect
T_0: Red paste in individual tea paper sachet. Presence of fat on sachets.
$T_{12weeks}$: Red paste in individual tea paper sachet. Presence of fat on sachets.

Packaging aspect
T_0: Cylindrical metal box, opaque. No porosity. Black cover. All is clean and dry. PP transparent bag. No hole. Clean and dry bag.
$T_{12weeks}$: Cylindrical metal box, opaque. No porosity. Black cover. All is clean and dry. PP transparent bag. No hole. Presence of traces of fat inside the bag.

Storage stability test – **long term storage at ambient temperature**			"Chemical stability after storage at 20 °C ±2°C after 6 months, one year and 2 years of Difenacoum pasta baits 0.005%." S Richerioux Lodi 20/2009

	Conc. (mg/kg)	**Deviation from declared content %**	**Deviation from T_0 %**
T_0	48.79	-2.42	-
$T_{6\ m}$	41.22	-17.56	-15.52
$T_{1\ yr}$	47.09	-5.82	-3.48
$T_{14\ months\ yr}$	41.38	-17.24	-15.19
$T_{2\ years}$	44.59	-10.82	-8.61
$T_{3\ years}$	48.0	-4.00	-1.62
$T_{4\ years}$	49.0	-2.00	0.43

The declared value was 50 ppm.

Aspect

Time	**Aspect**	**Odor**
T_0	Pink malleable paste	Hazelnut
$T_{6months}$	Red malleable paste	Slightly sweety
T_{1year}	Red malleable paste	Slightly sweety
$T_{14months}$	Red malleable paste	Slightly sweety
T_{2years}	Red malleable paste	Slightly sweety
T_{3years}	Red malleable paste	Slightly sweety
T_{4years}	Red malleable paste	Slightly sweety

Conclusion on the physical, chemical and technical properties of the product

Storage stability test at ambient temperature for 2 years (20˚C)

Study performed to GLP. The relative deviation of Difenacoum content from measured value at T_0 to two years is 8.61%. (Relative deviation was found to be < 5% at 3 and 4 years. Shelf life past 2 years is not being sought by the applicant). No significant change was observed concerning the aspect of the sample.

A large variation in results across the time points was observed. Refer to the addendum of the Product Assessment Report for Ruby Block nad Grain, April 2012. This cites that Difenacoum does not degrade over time but becomes bound to the matrix and therefore becomes harder to extract. The results of the study investigating the degradation products of Difenacoum under heat and acid degradation show that Difenacoum does not degrade during storage for two years at ambient temperatures and that the efficacy of the product holds for 2 years (Biolytics Study no. 11-TOX014). The applicant is in the process of developing a new method of analysis.

Please Note: A non GLP study was evaluated previously indicating stability for 2 years at ambient temperature. Deviation from T_0 after 2 years was -0.19%, Report: Biannic, Marie-Laure. 12th November 2009.

Compatibility with packaging at accelerated storage at 35 ˚C for 12 weeks

Study performed to GLP. Deviation weights are less than 3%. No significant changes were observed on the aspect of the packaging and test item. Acceptable.

Compatible packaging: Metal box with PP cover and Metal box with PP cover with PP bag.

Proposed shelf life

The test item is considered stable at ambient temperature for 2 years.

3.3 Physical hazards and respective characteristics

No new data was provided, nor had new guidance to be taken into account for the renewal evaluation. Accordingly, the conclusion from the former assessment regarding physical hazards and respective characteristics remains valid.

3.4 Methods for detection and identification

No new data was provided, nor had new guidance to be taken into account for the renewal evaluation. Accordingly, the conclusion from the former assessment regarding methods for detection and identification remains valid.

3.5 Efficacy against target organisms

The results from laboratory palatability and efficacy studies and field trials previously evaluated demonstrate that the product is both palatable to, and effective in controlling target populations of rats (*Rattus norvegicus* and *Rattus rattus*) and house mice (*Mus musculus / domesticus*) when applied according to the label advice. The pasta bait formulation proved to be both attractive to and effective against infestations of brown rats and house mice in the trials and provided excellent control of the infestations treated based upon census baiting and tracking data. Thus, the previously evaluated laboratory palatability and field studies remain valid.
The results of two new laboratory trials demonstrated that the product is both palatable to, and effective in controlling target populations of brown rats and house mice after storage at ambient temperature for 3 years (36 months) for the brown rat and house mouse. 3-year palatability and efficacy data is required on the roof rat (*Rattus rattus*) to extend the proposed 36 months storage stability claim to all target organisms. In light of the palatability and efficacy demonstrated on brown rats and house mice this information can be generated as a post-authorisation data requirement.

Resistance to the first generation anticoagulants has been widely reported in both *Rattus norvegicus* and *Mus domesticus* since the late 1950's. The incidence of resistance to first generation anticoagulants in areas in which it is established is commonly 25-85%.
The enzyme vitamin K 2, 3 epoxide reductase (VKOR) is the target for anticoagulants. Modifications in the protein structure due to polymorphisms on the gene coding the VKOR may induce anticoagulant resistance. Most resistant strains are characterised by one single nucleotide polymorphism (SNP). These SNPs cause the exchange of one amino acid in the VKOR enzyme. The biochemical mechanism of anticoagulant resistance has been studied in several geographic strains/VKORC1-variants of the

Norway rat. Amino acid substitutions in the VKOR seem to alter its structure and function, resulting in decreased sensitivity to anticoagulant inhibition, depending on strain characteristics.

For house mice, a dominant autosomal warfarin-resistance gene was determined on chromosome 7 in house mice. Three VKORC1 sequence variants mediating resistance to anticoagulants seem to be widely distributed. House Mice carrying the homozygous of one of these variants (Y139C) were found highly resistant to warfarin and bromadiolone.

For roof rats, experiments on warfarin resistant rats indicated considerable instability in the resistance and suggested a multifactorial basis for resistance.

Some degree of resistance to difenacoum has been reported in the UK, Denmark, France and Germany but this is usually found in certain populations of rodents highly resistant to first generation anti-coagulants (Greaves et al., 1982[7]; Lund, 1984[8]; Pelz et al. 1995[9]). The resistance factor tells how much the anticoagulant dose has to be multiplied to kill resistant individuals compared to sensitive ones. The resistant factors for difenacoum in the brown rats ranged from 1.1 to 8.6 (Greaves and Cullen-Ayres 1988[10]). The study included rats resistant to warfarin and difenacoum. Resistance factors for warfarin ranged from approx. 50 to 2300. Greaves et al. (1982) reported a fivefold difenacoum dose needed to kill difenacoum resistant rats. Considerable doubt exists as to the significance of reports in UK of resistance to second-generation anticoagulants and in the UK control failures with the second-generation products are increasingly being attributed to baiting problems rather than physiological resistance (Greaves and Cullen Ayres, 1988; Quy et al. 1992a,b[11]).

Studies carried out in different European countries, in the UK more particularly (Kerins et al, 2001; see annex 1) revealed the occasional occurrence of cross-resistances to second-generation anticoagulants, such as difenacoum and bromadiolone on resistant brown rats populations to coumafene. Moreover, a publication (Baer et al., 2012) has demonstrated that the majority (91%) of warfarin resistant rat trapped in East and West parts of Belgium were also resistant to bromadiolone. The rats trapped in the region of Flanders (Northern Belgium) carried mutation Y139F. This mutation is found extensively in France where it also confers resistance to bromadiolone (Grandemange et al., 2009). The same mutation was also found in UK (Prescott et al., 2011) where applications of bromadiolone had been unsuccessful. Difenacoum is also thought to be partially resisted by rats which carry Y139F.

7 Greaves J. H.; Shepherd D. S.; Gill, J. E. (1982): An investigation of difenacoum resistance in Norway rat populations in Hampshire. *Annals of Applied Biology* 100, 581–587.

8 LUND, M. (1984): Resistance to the second generation anticoagulant rodenticides. *In Proceedings of 11th vertebrate pest conference*, Sacramento, Ca. March 6-8, 1984: 89-94.

9 Pelz H-J, Ha¨nisch D, Lauenstein G (1995) Resistance to anticoagulant rodenticides in Germany and future strategies to control *Rattus norvegicus. Pestic Sci* 43, 61–67

10 Greaves J. H.; Cullen-Ayres P. B. (1988): Genetics of difenacoum resistance in the rat. In: J. W. Suttie (Ed.), Current advances in vitamin K research, Elsevier, N.Y., 381–388.

11 Quy R.J., Shepherd D.S., Inglis I.R. (1992): Bait avoidance and effectiveness of anticoagulant rodenticides against warfarin- and difenacoum-resistant populations of Norway rats (Rattus norvegicus). *Crop Protection*, Volume 11, Issue 1, February 1992, Pages 14-20

House mice carrying the homozygous Y139C sequence variant were found to be highly resistant to warfarin and bromadiolone. It is important to understand that all known resistance mutations, in both rats and mice, are capable of effective control with applications of the most potent second-generation anticoagulants (brodifacoum, difethialone and flocoumafen) and that no practical resistance to any of these active substances is presently known.
So, resistance to second generation anticoagulant rodenticides should not be underestimated.
An exhaustive study carried out at the French and European levels could enable to point-out resistant areas with first generation anticoagulants and potential cross-resistances to second-generation anticoagulants. It is one of the actions undertaken since 2010 in France by a group of scientists (Rodent program “impacts of anticoagulants rodenticides on ecosystems-adaptations of target rodents and effects on their predators”).
The document CropLife International (RRAC 2015) provides guidance to advisors, national authorities, professionals, practitioners and others on the nature of anticoagulant resistance in rodents, the identification of anticoagulant resistance, strategies for rodenticide application that will avoid the development of resistance and the management of resistance where it occurs.
The following are the essential elements of an effective program: survey, use of physical and chemical control techniques, environmental management, record keeping, monitoring and review.
The authorization holder should report any observed resistance incidents to the Competent Authorities or other appointed bodies involved in resistance management at the renewal of the product.
To ensure a satisfactory level of efficacy and avoid the development of resistance, the recommendations proposed in the SPC have to be implemented.

3.6 Risk assessment for human health

A dermal absorption value of 0.1% was used for the risk assessment for difenacoum. The dermal absorption study performed on difenacoum was reinterpreted using EFSA guidance on dermal absorption (2012). This resulted in a dermal absorption of 0.1%, based on integrating the standard deviation into the dermal absorption mean presented in the original study and subsequent rounding of values.
Assessment of effects of the active substance on human health
See section 3.6.3.

3.6.1 Assessment of effects of the product on human health

See section 3.6.3.

3.6.2 Exposure assessment

SA dermal absorption value of 0.1% was used for the risk assessment for difenacoum. The dermal absorption study performed on difenacoum was reinterpreted using EFSA guidance on dermal absorption (2012). This resulted in a dermal absorption of 0.1%, based on integrating the standard deviation into the dermal absorption mean presented in the original study and subsequent rounding of values.

The risk assessment for trained and non-trained professional users used the chronic AEL of 1.1×10^{-6} mg/kg bw/day. The HEEG recommendations 9, 10 and 12 were incorporated into the risk assessment model. The risk assessment for trained and non-trained professional users modelled the loading and cleaning of 100g of bait in 10 g sachets.

For the 'transient mouthing of poison bait' scenario, 10 mg (TNsG, with bittering agent/repellent) of the product is assumed to be swallowed by an infant per poisoning event as stated in: The Human Exposure to Biocidal Products (Technical Notes for Guidance – June 2002). The weight of the infant is assumed to be 10 Kg. The risk assessment for toddlers used the acute AEL of 1.1×10^{-6} mg/kg bw/day. Oral absorption was considered to be 100% for the mouthing scenarios.

Biocidal Exposure Risk assessment for Ruby Paste difenacoum rodenticide (50 ppm) .	
Professional user	
	Paste
Without PPE	259.1% of AEL (0.00000285 mg/kg bw/day)
With PPE	13% of AEL (0.000000143 mg/kg bw/day)
Spatula application required to exceed 100% AEL without PPE	1320 mg
Spatula application required to exceed 100% AEL with PPE	26.4 g
Non-trained professional user (farmer)	
	Paste

Without PPE	23.2% of AEL (0.000000255 mg/kg bw/day)
With PPE	1.2% of AEL (0.0000000128 mg/kg bw/day)
Exposure to children (Toddler)	
	Paste
Oral exposure -treated with repellent	4545.45% AEL (0.00005 mg/kg bw/day)
Oral exposure - without repellent	2272727.27% AEL (0.025 mg/kg bw/day)

Derived values indicated a no safe usage scenario for professional users handling the difenacoum paste product without PPE and a safe usage scenario with PPE. Derived values for professional users handling the paste product without PPE were 0.00000285 mg/kg bw/day (259.1% AEL). Derived values for professional users handling the paste product with PPE were 0.000000143 mg/kg bw/day (13% AEL).

A reverse reference calculation indicated that applying pasta bait to stations using prefilled cartridges and spatula was unlikely to result in an expedience of 100% of the AEL. Application of pasta in pre-filled cartridges without PPE would 1320 mg of product to remain on the trained professionals hands to exceed the AEL. However if PPE are utilised as recommended the amount required to exceed 100% of the AEL would be 26.4 g which is highly unlikely given the amount of product to be applied per day.

Derived values indicated safe usage for non-trained professional users handling the paste product with and without PPE. Derived values for non-trained professional users handling the paste product without PPE were 0.000000255 mg/kg bw/day (23.2% AEL). Derived values for non-trained professional users handling the paste product with PPE were 0.0000000128 mg/kg bw/day (1.2% AEL).

Derived values indicated no safe exposure scenarios for toddlers through oral exposure/transient mouthing of the paste product. Derived values for oral exposures in the toddler found transient mounting of a paste not containing a repellent to result in a dose of 0.025 mg (2272727.27% AEL). Derived values for oral exposures in the toddler found transient mounting of a paste containing a repellent to result in a dose of 0.00005 mg (4545.45% AEL). However, the design of the rat bait boxes will incorporate a tamper-proof seal system to prevent easy access to internal compartments.

As a result of incorporating a tamper proof seal system toddlers are not expected to be able to gain access to the rodenticides and subsequent mouthing scenarios are deemed unlikely.

3.6.3 Risk characterisation for human health

3.6.3.1 Risk for professional users

As shown in section 3.6.2.

3.6.3.2 Risk for the general public

Not relevant.

3.6.3.3 Risk for consumers via residues in food

No new data was provided nor had new guidance to be taken into account for the renewal evaluation. Accordingly, the conclusion from the former assessment regarding risks for consumers via residues in food remain valid.

3.6.3.4 Risk characterisation from combined exposure to several active substances or substances of concern within a biocidal product[12]

The biocidal product does not contain other substances in quantities that would be of toxicological concern in the production formulation.

3.6.3.5 Summary of risk characterisation

Derived values indicated a no safe usage scenario for professional users handling the difenacoum paste product without PPE and a safe usage scenario with PPE. Derived values for professional users handling the paste product without PPE were 0.00000285 mg/kg bw/day (259.1% AEL). Derived values for professional users handling the paste product with PPE were 0.000000143 mg/kg bw/day (13% AEL).

A reverse reference calculation indicated that applying pasta bait to stations using prefilled cartridges and spatula was unlikely to result in an expedience of 100% of the AEL. Application of pasta in pre-filled

cartridges without PPE would 1320 mg of product to remain on the trained professionals hands to exceed the AEL. However if PPE are utilised as recommended the amount required to exceed 100% of the AEL would be 26.4 g which is highly unlikely given the amount of product to be applied per day.

Derived values indicated safe usage for non-trained professional users handling the paste product with and without PPE. Derived values for non-trained professional users handling the paste product without PPE were 0.000000255 mg/kg bw/day (23.2% AEL). Derived values for non-trained professional users handling the paste product with PPE were 0.0000000128 mg/kg bw/day (1.2% AEL).

Derived values indicated no safe exposure scenarios for toddlers through oral exposure/transient mouthing of the paste product. Derived values for oral exposures in the toddler found transient mounting of a paste not containing a repellent to result in a dose of 0.025 mg (2272727.27% AEL). Derived values for oral exposures in the toddler found transient mounting of a paste containing a repellent to result in a dose of 0.00005 mg (4545.45% AEL). However, the design of the rat bait boxes will incorporate a tamper-proof seal system to prevent easy access to internal compartments. As a result of incorporating a tamper proof seal system toddlers are not expected to be able to gain access to the rodenticides and subsequent mouthing scenarios are deemed unlikely.

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3.7 Risk assessment for animal health

No new data was provided, nor had new guidance to be taken into account for the renewal evaluation. Accordingly, the conclusion from the former assessment regarding animal health remains valid.

3.8 Risk assessment for the environment

The exposure assessment carried out for this product in 2013 is still valid. Regarding groundwater, the recent CG decision requires this now be assessed:

Groundwater assessment for rodenticides
As required by Article 31(3) of the BPR and Article 2(1)(f) of Regulation 492/2014, when carrying out their assessment of whether the conclusions of the first authorisation regarding Article 19(1)(iv) remain valid, applicants will have to address the groundwater assessment. Since no new guidance was agreed in the past that could become applicable at the time of the completion of the applications for renewal by 28/02/2017, the guidance of reference are the existing methods that are applied since years as standard tools for the assessment of active substances:

- Tier I according to Vol. IV Part B (the former TGD), as provided in chapter 2.3.8.6 of this guidance document.
- Tier II using the FOCUS models PEARL or PELMO for refinements in case Tier I would lead to an exceedance of the relevant trigger values.

The previous exposure assessment contained a Tier 1 assessment of groundwater PECs. The following is an extract from the report:

Exposure of groundwater may occur as a result of soil exposure which occurs via residues present in sewage sludge after using the bait in sewers and via direct (spillages) and disperse release (urine and faeces) after the use of the product in the scenarios in and around buildings, open areas and waste dumps. As an indication for potential groundwater levels, the concentration in porewater of agricultural soil was taken. It should be noted that this is a worst-case assumption, neglecting transformation and dilution in deeper soil layers. A summary of the PECs obtained are presented in ***Table 3.3.6.4-1****. All concentrations are less than the EU trigger value of 0.1 μg/L.*

Table 3.3.6.4-1. Predicted Environmental Concentration (μg/L) of difenacoum in groundwater

Compartment/Scenario	***ESD realistic worst case scenario***	***ESD realistic worst case scenario with modified input parameters***	***ESD normal use scenario with modified input parameters***
In and around buildings scenario			
Groundwater/porewater	*1.5×10^{-3}*	*1.1×10^{-3}*	*3.2×10^{-4}*
Open areas			
Groundwater/porewater	*5.23×10^{-3}*	*1.05×10^{-2}*	*---*
Waste dump			
Groundwater/porewater	*2.24×10^{-4}*	*2.5×10^{-4}**	*---*

*******For high infestations of rats the blocks are spaced 5 m apart. According to calculations provided by the Reviewer this could potentially result in a maximum of ~441 (21, 100 m lines of 21 blocks, 5 m apart) blocks in a 1 ha area during high infestations. This corresponds to ~44.1 kg of product, which is greater than the quantity considered under realistic worst-case conditions in the ESD. Consequently the notifiers exposure calculation is not sufficient to support this use. The Reviewer generated new exposure calculations for this use*

However, during the 2016 renewal of the active substance difenacoum, the reference value for groundwater according to BPR Annex VI, point 68, was lowered to 0.01 μg/L. As the value for the open areas scenario exceeds the trigger (0.0105μg/L) the eCA has performed a Tier II assessment using FOCUS PEARL v4.4.4. The open areas scenario exceeds the trigger (0.196μg/L) the eCA has performed a Tier II assessment using FOCUS PEARL v4.4.4. The open areas scenario outlined in the PT14 ESD describes placement of the grain bait at the bottom of a cylindrical hole of radius 4cm and depth 30cm. A larger

soil cylinder of radius 28cm is assumed to be exposed to the bait. From the soil exposure performed in the 2013 evaluation, 0.0025g of active substance is deposited each campaign (Elocalsoil). The base of the cylinder has an area of $0.062m^2$ (π x 0.14^2). 0.0025g spread over an area of $0.062m^2$ gives an application rate of $0.0406gm^{-2}$ or $0.406kgha^{-1}$. This application rate assumes the bait is placed uniformly across the field or park. In reality bait is placed in specific burrows at distances of 5m or greater where rodents are active. Therefore the actual use rate will be considerably lower than 0.406kg/ha. The ESD proposes a 6 day campaign during which the rodenticide is applied. This allows for a possibility of approximately 50 campaign per year. Again this is likely to be significantly greater than the actual number of campaigns per year so our assessment is expected to be highly conservative in nature. The input parameters are summarised below:

Input parameter	**Unit**	**Difenacoum**
Physicochemical parameters		
Molecular weight	g mol^{-1}	444.5
Water solubility	mg L^{-1}	0.43 (20°C)
Molar enthalpy of dissolution	kJ mol^{-1}	27 (default)
Saturated vapor pressure	Pa	5.4E-14 (25°C)
Molar enthalpy of vaporisation	kJ mol^{-1}	95 (default)
Diffusion coefficient in water	m^2 d^{-1}	4.3E-05 (default)
Diffusion coefficient in air	m^2 d^{-1}	0.43 (default)
Degradation parameters		
Half-life at reference condition	d	439 (20°C)
Molar activation energy	kJ mol^{-1}	65.4 (default)
Exponent for the effect of liquid	-	0.7 (default)
Sorption parameters		
Kom value (=Koc/1.724)	L kg^{-1}	1.1E06 (QSAR value)
Freundlich exponent 1/n	-	1.0 (worst case assumption)
Method of subroutine	-	pH independent
Crop related parameters		
FOCUS crop	-	Grassland
Crop uptake factor	-	0
Application parameters		
Number of applications per annum	-	50
Application rate	kg ha^{-1}	0.406

Application type	-	Injection at 30 cm
Number of applications per annum	-	50

The 80th percentile PEC_{GW} values are shown below. Based on this assessment it can be concluded that there is no risk to groundwater from use of the product.

PEARL SCENARIO	**$PEC_{groundwater}$ (µg/L)**
Châteaudun	<0.001
Hamburg	<0.001
Jokioinen	<0.001
Kremsmünster	<0.001
Okehampton	<0.001
Piacenza	<0.001
Porto	<0.001
Seville	<0.001
Thiva	<0.001
• Levels above 0.01 µg/L exceed the drinking water limit for difenacoum	

Environmental Risk Assessment

Risk Characterisation for surface water, groundwater and sediment after elimination processes in STP

Difenacoum is very toxic to fish, aquatic invertebrates and algae. Toxicity to fish, the most sensitive species, is based on the inhibition of blood clotting. The mode of action in aquatic invertebrates and algae is unknown. The PNEC value was calculated according to ESD guidelines (Larsen, 2003), applying an Assessment Factor of 1000 to the lowest endpoint from studies on three trophic levels. . in the updated CAR (2016), EC_{50} > 2.3 mg/L for *Pseudomonas putida*. According to the BPR (2015), the $PNEC_{STP}$ is set equal to a NOEC from a test performed with a 'specific bacterial populations' like nitrifying bacteria or *P. putida* while an EC_{50} from this test is divided by an assessment factor of 10. Therefore $PNEC_{STP}$ should be 2.3/10 = 0.23 mg/L or 230µg/L. The risk characterisation for the STP and aquatic compartment including sediment is presented below:

Aquatic PEC/PNEC ratios using realistic worst case scenario with normal use after elimination processes in STP

Exposed Compartment	Endpoint	PNEC	PEC	PEC/PNEC
Surface water	LC_{50} 0.064 mg/l	0.06 µg/l	2.11×10^{-4} µg/l	3.5×10^{-3}
Sediment	-[1]	2.51[1] mg/kg ww	8.61×10^{-3} mg /kg ww	3.4×10^{-3}
STP	EC_{50} > 2.3 mg/L for *Pseudomonas putida*	0.23 µg/l	8.06×10^{-3} µg/l	3.5×10^{-2}

[1]In the absence of any ecotoxicological data for sediment-dwelling organisms and as PECsediment is calculated using EUSES 2.0.3, an aquatic PEC/PNEC ratio is used for sediment risk characterisation increasing it according to BPR Vol. IV Part B (the former TGD) with a factor of 10 as difenacoum has a log Kow > 5. PNEC reported as 2.51mg/kg ww in the Assessment Report (17-09-2009)

The PEC/PNEC ratios were less than 1 in all compartments indicating that difenacoum, following recommended use of Ruby Block, does not cause unacceptable risk to aquatic organisms, sediment-dwelling organisms or biological processes at the sewage treatment plant.

Risk Characterisation for Terrestrial Compartments

In the updated CAR (2016), NOEC = 62.5 mg/kg dw for *Eisenia fetida* (reproductive toxicity test). According to the BPR (2015), if a NOEC for one long-term toxicity test is available, the AF is 100. Therefore the $PNEC_{soil}$ is 62.5/100 = 0.625 mg/kg dw. The risk characterisation for the terrestrial compartment including is presented below:

Terrestrial PEC/PNEC ratios using realistic worst case scenario with normal use

Exposed Compartment		PNEC	PEC	PEC/PNEC
Sewer-application of sewage sludge	Local PEC in agric. soil (total) average over 30 d	0.625 mg/kg ww	3.29×10^{-3} mg/kg ww	5.26×10^{-3}
	Local PEC in agric. soil (total) average over 180 d	0.625 mg/kg ww	3.29×10^{-3} mg/kg ww	5.26×10^{-3}
	Local PEC in grassland. soil (total) average over 180 d	0.625 mg/kg ww	1.31×10^{-3} mg/kg ww	2.09×10^{-3}
In and around buildings	Direct	0.625 mg/kg ww	4.1×10^{-2} mg/kg ww	6.5×10^{-2}
	Indirect	0.625 mg/kg ww	6.0×10^{-3} mg/kg ww	9.6×10^{-3}
	Total	0.625 mg/kg ww	4.7×10^{-2} mg/kg ww	7.5×10^{-2}
Open areas		0.625 mg/kg ww	1.73×10^{-1} mg/kg ww	0.276
Waste dump		0.625 mg/kg ww	8.2×10^{-3} mg/kg ww*	1.3×10^{-2}

* Value calculated by Environmental Fate and Behaviour Reviewer for High infestations of rats.

The PEC/PNEC ratios were less than 1 in all compartments indicating that difenacoum, following recommended use of Ruby Block, does not cause unacceptable risk to organisms in any of the terrestrial compartments assessed.

Primary and Secondary Poisoning

Primary Poisoning

The Tier 1 assessment assumes that there is no bait avoidance by the non-target animals, and that they obtain 100% of their diet in the treated area and have access to the difenacoum product. The worst case Tier 1 PEC_{oral} is 50 mg/kg and is used in quantitative risk assessment for the long-term situation. The LD_{50} values are 56 mg/kg bw for birds (AF 3000) and 1.8 mg/kg bw for mammals (AF 90) (List of Endpoints in the Assessment Report (17-09-2009). The Tier 1 Primary poisoning PEC/PNEC ratios are provided below:

Tier 1 Primary poisoning PEC/PNEC ratios

Exposed Organism	PNEC µg/kg food	PNEC[1] µg/kg bw/d	PEC	PEC/PNEC
Birds	0.5	0.1	50 mg/kg food	500000
Mammals	7	0. 3	50 mg/kg food	166667

[1] Appendix V- Assessment Report (17-09-2009)

Acute risk assessment for primary poisoning of a non-target organism:

Tier 2:

In the refined risk assessment the daily uptake (ETE) is compared to the PNEC for birds and mammals. The PNEC values for each representative animal are compared with the ETE values to provide an indication of the risk to non-target animals ingesting a daily dose of the product.

Tier 2 acute risk assessment: $PEC_{oral}/PNEC_{oral}$ for non-target animals accidentally exposed to bait containing Difenacoum after one meal

Non-target animals	ETE, concentration of Difenacoum after one meal (one day) (mg/kg b.w.)		$PNEC_{oral}$ (dose, mg/kg b.w./d)	PEC/PNEC	
	Step 1	Step 2		Step 1	Step 2
Tree sparrow	17.3	12.44	0.0001	173000	124400

Chaffinch	15.00	10.8	0.0001	150000	108000
Wood pigeon	5.42	3.9	0.0001	54200	39000
Pheasant	5.39	3.9	0.0001	53900	39000
Dog	3.0	2.16	0.0003	10000	7200
Pig	0.375	0.27	0.0003	1250	900
Pig, young	1.2	0.864	0.0003	4000	2880

The ratios PEC/PNEC are above 1 indicating a potential risk even after refinement.

Long-risk assessment for primary poisoning of a non-target organism:

Tier 2:

In the long-term risk assessment, the EC (expected concentration of active substance in the animal) after metabolism and other elimination is calculated and used to calculate the $EC_{oral/}PNEC_{ratio}$after 1-day and 5-day elimination of **Difenacoum**. The $EC_{oral/}PNEC_{ratio}$ are above 1 after 1-day elimination of **Difenacoum** indicating a potential risk (data not shown). The $EC_{oral/}PNEC_{ratio}$ for the 5-day elimination of **Difenacoum** are shown below.

Tier 2 long-term risk assessment: $EC_{oral}/PNEC_{oral}$ ratio after 5-day elimination

Species	**EC_{oral} after 5 days (mg/kg b.w./d) with excretion factor = .4, AV = 1, PT = 1 (mg/kg bw)[a]**	**EC_{oral} after 5 days (mg/kg b.w./d) with excretion factor = 0.4, AV = 0.9, PT = 0.8 (mg/kg bw)[a]**	**$PNEC_{oral}$ (mg/kg b.w./d)**	**Ratio $EC_{oral}/PNEC_{oral}$**
Tree sparrow	23.03	13.8	0.0001	138191
Chaffinch	19.97	11.98	0.0001	119836
Wood pigeon	7.21	4.32	0.0001	43297
Pheasant	7.18	6.30	0.0001	43086
Dog	3.99	2.39	0.0003	7989
Pig	0.499	0.299	0.0003	998
Pig, young	1.59	1.34	0.0003	4491

[a] calculation according to equation 21 in the ESD

The ratios PEC/PNEC are above 1 indicating a potential risk even after refinement.

Conclusion:

Overall, all acute and long-term $PEC_{oral}/PNEC_{oral}$ ratios are still above the trigger value of 1 indicating acute and long-term unacceptable risks.

Secondary Poisoning

Aquatic and terrestrial food chain

Avian and mammalian predators of the aquatic and terrestrial food chains may be at risk for secondary poisoning if they feed on contaminated water or soil organisms such as fish or earthworms. The risk characterisation is carried out for both birds and mammals.

Revised risk assessment for secondary poisoning in aquatic food chain (sewer scenario) and terrestrial food chain (in and around buildings)

	Aquatic PECoral, predator µg/kg fish	**Terrestrial $PEC_{oral, predator}$, µg/kg earthworm**	**$PNEC_{oral}$ µg/kg food**	**PEC/PNEC Aquatic**	**PEC/PNEC Terrestrial**
Scenario	**Sewer**	**In and around buildings**			
Birds	0.245	3.183	0.5	0.49	6.4
Mammals	0.245	3.183	7	0.035	0.45

Conclusion

Even though risk is identified in the terrestrial food chain for birds, the risk via poisoned rodents is considered significantly higher compared to risk via earthworms or other invertebrates.

Rodent-eating birds and mammals

A Tier 1 risk assessment was carried out to assess the risk for poisoning of non-target predator birds and mammals during acute and long-term exposure via rodents poisoned. The $PEC_{oral}/PNEC_{oral}$ values exceeded the trigger value of 1 (data not shown). Therefore, a refined tier 2 assessment was carried out, based on representative species. The refined tier 2 risk assessment considers exposure of relevant species of predators, based on their bodyweights and food intakes. The **Difenacoum** concentrations in non-target mammals and birds consuming contaminated rodents is calculated ($ETE_{oral\ predators}$) and compared to the $PNEC_{oral}$.

Tier 2 risk assessment of secondary poisoning (non-resistant and resistant rodents)

Species	**Exposure**	**$ETE_{oral\ predators}$ (mg a.s./kg/d)**	**$PNEC_{oral}$ (mg a.s./kg/d)**	**Ratio $ETE_{oral\ predators}$ / $PNEC_{oral}$**
Barn owl	Day 5 before the last meal	0.80	0.0001	8058
	Day 5 after the last meal	1.42		14257
	Day 14 after the last meal	1.54		15497

Species	Exposure	ETE $_{oral\ predators}$ (mg a.s./kg/d)	PNEC$_{oral}$ (mg a.s./kg/d)	Ratio ETE $_{oral\ predators}$ / PNEC$_{oral}$
Kestrel	Day 5 before the last meal	1.22	0.0001	12238
	Day 5 after the last meal	2.16		21651
	Day 14 after the last meal	2.35		23534
Little owl	Day 5 before the last meal	0.91	0.0001	9195
	Day 5 after the last meal	1.62		16268
	Day 14 after the last meal	1.76		17682
Tawny owl	Day 5 before the last meal	0.74	0.0001	7407
	Day 5 after the last meal	1.31		13106
	Day 14 after the last meal	1.42		14245
Fox	Day 5 before the last meal	0.29	0.0003	988
	Day 5 after the last meal	0.52		1749
	Day 14 after the last meal	0.57		1901
Polecat	Day 5 before the last meal	0.61	0.0003	2058
	Day 5 after the last meal	1.09		3641
	Day 14 after the last meal	1.18		3958
Stoat	Day 5 before the last meal	0.88	0.0003	2943
	Day 5 after the last meal	1.56		5207
	Day 14 after the last meal	1.69		5660
Weasel	Day 5 before the last meal	1.27	0.0003	4247
	Day 5 after the last meal	2.25		7514
	Day 14 after the last meal	2.45		8167

All ratios ETE$_{oral\ predators}$ / PNEC$_{oral}$ are above the trigger value of 1 indicating an unacceptable risk of secondary poisoning.

Overall conclusion

According to this risk assessment the risk for poisoning of non-target predator birds and mammals during primary (acute and long-term exposure) and secondary poisoning is high as the trigger value is exceeded in all cases.

No safe use was established for the Difenacoum product at a concentration of 50 ppm in the ecotoxicology risk assessment.

3.9 Assessment of a combination of biocidal products

A use with other biocidal products is not intended.

3.10 Comparative assessment

The Irish CA for biocides has processed an application for renewal for this biocidal product which contains the active substance Difenacoum. The active substance Difenacoum meets the criteria for exclusion according to Article 5(1) BPR as well as for substitution according to Article 10 BPR (for details see chapter 2.2.3).
Therefore, in line with Article 23 (1) BPR, a comparative assessment for this product has to be conducted.

At the 60th meeting of representatives of Members States Competent Authorities for the implementation of the BPR held on 20 and 21 May 2015, all Member States submitted to the Commission a number of questions to be addressed at Union level in the context of the comparative assessment to be carried out at the renewal of anticoagulant rodenticide biocidal products ('anticoagulant rodenticides'). The questions submitted were the following:

(a) Is the chemical diversity of the active substances in authorised rodenticides in the Union adequate to minimise the occurrence of resistance in the target harmful organisms?;
(b) For the different uses specified in the applications for renewal, are alternative authorised biocidal products or non-chemical means of control and prevention methods available?;
(c) Do these alternatives present a significantly lower overall risk for human health, animal health and the environment?;
(d) Are these alternatives sufficiently effective?;
(e) Do these alternatives present no other significant economic or practical disadvantages?

The information addressing these questions is provided in the Annex of the Commission Implementing Decision (EU) 2017/1532[13]. In accordance with Article 1 of Commission Implementing Decision (EU) 2017/1532, the Irish CA considered the information in the Annex during the comparative assessment of anticoagulant rodenticide biocidal products.

Conclusion

[13] Commission Implementing Decision (EU) 2017/532 of 7 September 2017 addressing questions regarding the comparative assessment of anticoagulant rodenticides in accordance with Article 23(5) of Regulation (EU) No 528/2012 of the European Parliament and of the Council.

Based on the information provided in the Annex of the Commission Implementing Decision (EU) 2017/1532 the Irish CA came to the conclusion that in the absence of anticoagulant rodenticides, the use of rodenticides containing other active substances would lead to an inadequate chemical diversity to minimize the occurrence of resistance in the target harmful organisms. These products also showed some significant practical or economical disadvantages for the relevant uses.

The Irish CA also considered a number of non-chemical control or prevention methods ("non-chemical alternatives"), which in our view do not provide sufficient alternatives to anticoagulant rodenticides.

In summary it can be concluded that the criteria according Article 23(3) a), b) BPR are not fulfilled. Therefore, the authorisation of this product will be renewed for 5 years.

4 General Annexes

4.1 List of studies for the biocidal product

Author	Year	Title	Publication	Report no.	Legal entity owner	Report date	GLP/ GEP	Data Protection Claimed

4.2 Output tables from exposure assessment tools

None

4.3 New information on the active substance

Under the 9th Adaptation to Technical Progress of the Classification and Labelling regulation (Commission Regulation (EU) 2016/1179), anticoagulant rodenticides were classified as Toxic to Reproduction Category 1A or 1B with a specific concentration limit of 0.003%. Under Article 19 of the Biocidal Products Regulation, biocidal products with such classifications (including anticoagulant rodenticides at this and higher concentrations) shall not be authorised for use by the general public.

4.4 Residue behaviour

No assessment necessary.

4.5 Summaries of the efficacy studies (B.5.10.1-xx)[14]

Function and field of use envisaged	Test substance	Test organism(s)	Test method, test system/concentrations applied/ exposure time	Test results; effects	Reference
PT14 RODENTICIDE	DIFEPASTA, containing 0.005% difenacoum	Wild grey mice (*Mus musculus*)	Laboratory housing for wild mice captured in warehouse. Test was performed on fresh product. *Test was carried out in accordance with Decision criteria edited by the Major Guideline for the Rodenticide efficacy assessment (Lignes Directrices pour l'évaluation de l'Efficacité des Rodenticides).*	*Paste bait/ Semi field efficacy/ Mice/ Fresh product (T0)* DIFEPASTA, rodenticide bait containing 0.005% de Difenacoum, is sufficiently attractive and very efficacious in controlling grey mice (*Mus musculus*). The efficacy is 90% against mice.	Mahaut T., Cavellier M., CRA Gembloux, Efficacy test on DIFEPASTA, bait ready to use, containing 0.005% of Difenacoum, against grey mice (*Mus* musculus L.), ROD 2003-03-Belgagri, 20 October 2003. Unpublished
PT14 RODENTICIDE	PASTA DIFE,, containing 0.005% difenacoum	Wild Brown rats (*Rattus norvegicus*)	Field study: experiment conducted in pigeon farm. Test was performed on fresh product. The method used has been inspired by the French method called "method no. 002 from Biological Trials Commission (C.E.B) ", Method for practical efficacy trials of raticides: • Adopted on 1960, derived from the work of Chitty and Dotty in the 1940. Revised by OEPP in 1980.	*Paste bait/ Field efficacy/ Rats/ Fresh product (T0)* The efficacy reached 95%. We can say that the tested bait, PASTA DIFE, achieved a good level of effectiveness and that complies with the required criteria for licensing.	Grolleau G., Pest Control Assistance (PCA), Effectiveness testing under natural conditions of PASTA DIFE rat killer in paste bait form in sachets on brown rats / Test under natural conditions of a rat killer in paste bait form (PASTA DIFE) containing 0.005% Difenacoum, on Brown rats (Rattus norvegicus) 2002. Unpublished
PT14 RODENTICIDE	NORA PASTA BAITS, containing 0.005% difenacoum	Black rats (*Rattus rattus*)	Field: study conducted in pig stables Test was performed on fresh product (T0) Test was carried out in accordance with Decision criteria edited by the Major Guideline for the Rodenticide efficacy assessment (Lignes Directrices pour l'évaluation de l'Efficacité des Rodenticides)	*Paste bait/ Field efficacy/ Roof rat / Product at T0* DIFENACOUM is said to kill rodents in 5 to 21 days. In these tests the first signs of illness started after 9 days; 3 dead rats were found after 14 days. After twenty days there was	Feys J-L., Field trial with NORA PASTA BAITS against ROOF RATS 21 January 2010_08 February 2010, batch NO 091109. Belgagri. Unpublished

14 If an IUCLID file is not available, please indicate here the summaries of the efficacy studies.

				still some activity, which ended later (unrecorded). These results are consistent with the results expected with difenacoum baits. One can conclude that NORA PASTA Paste Baits is very well suited for the extermination of *Rattus rattus* in stables.	
PT14 RODENTICIDE	PASTA DIFE,, containing 0.005% difenacoum	Albino rats (*Rattus norvegicus*)	Laboratory conditions. Test was performed on different stage of product: • Fresh product. • Product after 12 months • Test was carried out in accordance with Decision criteria edited by the Major Guideline for the Rodenticide efficacy assessment (*Lignes Directrices pour l'évaluation de l'Efficacité des Rodenticides*)	*Paste bait/ Lab choice test/ Rats / Product at T0 and T12* • T0: 19 dead rats at the end of the trial • T12: 18 dead rats at the end of trial. Between fresh product and the 12 months aged product, loss of palatability is not significant.	De Proft M., CRA Gembloux, Study of ageing behavior of ready-to-use baits containing 0.005% of Difenacoum, PART 1: Pasta Bait, report number ROD 2008 11 BIO 6 Unpublished
PT14 RODENTICIDE	DIFEPASTA, containing 0.005% difenacoum	White Mice (*Mus musculus*)	Laboratory conditions. Test was performed with different storage periods of product: • Fresh product. • Product after 24 months • Test was carried out in accordance with Decision criteria edited by the Major Guideline for the Rodenticide efficacy assessment (*Lignes Directrices pour l'évaluation de l'Efficacité des Rodenticides*).	*Paste bait/ Laboratory efficacy/ Mice/ Product at T12 and T24 months* - At T12, all tested mice died. (n=20) - At T24, all tested animals died except 4 mice (n = 20). After 12 months storage, the efficacy of DIFEPASTA reached 100% with mice. After 2 years, the efficacy of DIFEPASTA decreases to 85% with mice.	De Proft M., Galoux M., CRA Gembloux, Efficacy test through different period of time, performed on DIFEPASTA, bait ready to use, containing 0.005% of Difenacoum, rapport number 11 594 ROD 2003-003, June 2006 Unpublished
PT14 RODENTICIDE	PASTA DIFE,, containing 0.005% difenacoum	Wild Brown rats (*Rattus norvegicus*)	Field study: experiment conducted in pigeon farm. Test was performed on fresh product. The method used has been inspired by the French method called "method no. 002 from Biological Trials Commission (C.E.B) ", Method for practical efficacy trials of raticides: • Adopted on 1960, derived from the work	*Paste bait/ Field efficacy/ Rats/ Fresh product (T0)* The efficacy reached 95%. We can say that the tested bait, PASTA DIFE, achieved a good level of effectiveness and that complies with the required criteria for licensing.	Grolleau G., Pest Control Assistance (PCA), Effectiveness testing under natural conditions of PASTA DIFE rat killer in paste bait form in sachets on brown rats / Test under natural conditions of a

			of Chitty and Dotty in the 1940. Revised by OEPP in 1980.		rat killer in paste bait form (PASTA DIFE) containing 0.005% Difenacoum, on Brown rats (Rattus norvegicus) 2002. Unpublished
PT14 RODENTICIDE	PASTA DIFE,, containing 0.005% difenacoum	Wild Brown rats (*Rattus norvegicus*)	Field study: experiment conducted in warehouse. Test was performed on product stored for two years, (T24). The method used has been inspired by the French method called "method no. 002 from Biological Trials Commission (C.E.B) ", Method for practical efficacy trials of raticides: • Adopted on 1960, derived from the work of Chitty and Dotty in the 1940. Revised by OEPP in 1980.	*Paste bait/ Field efficacy/ Rats / Product at T2years* The efficacy trial of PASTA DIFE has been conclusive, with the results permitting the declaration that the product is efficacious against Norway rats. The product achieved 92% efficacy against rats.	Biannic M-L., LODI S.A.S, Efficacy assessment of a rat killer in a field trial –product: PASTA DIFE, July 2009. Unpublished
PT14 RODENTICIDE	Difenacoum paste bait (batch No. LAB20091103) (aged; 3 years at room temperature) 0.005% difenacoum	Albino house mice (*Mus musculus*)	Difenacoum paste bait (aged; 3 years at room temperature) was provided by the Sponsor and stored at Biotrial Pharmacology at room temperature. The test was performed on 3-years aged product in comparison with challenged diet (non-poisoned source).	During the 11-day testing period, the percentage intake of challenged diet was 54.3±7.7% for female mice and 56.6±8.4% for male mice. The percentage intake of difenacoum paste bait was 45.7±7.7% for female mice and 43.4±8.4% for male mice. Globally, mortality occurred in 100% of male and female mice with a mean day to death of 7.0±2.5 days (range 3 to 11 days). Furthermore acceptance of difenacoum paste bait on D7, D8, D9, D10, D11 and D12 was 51% (n=10), 48% (n=10), 43%(n=10), 32% (n=9), 51% (n=7) and 35% (n=6) for male and female mice.	Bureau, M, Choice feeding trial for difenacoum paste bait (aged product) against albino house mice, 0LODI14. Unpublished
PT14 RODENTICIDE	Difenacoum paste bait (batch No. LAB20091103) (aged; 3 years at room temperature) 0.005% difenacoum	Albino brown rats (*Rattus norvegicus*)	Difenacoum paste bait (aged; 3 years at room temperature) was provided by the Sponsor and stored at Biotrial Pharmacology at room temperature. The test was performed on 3-years aged product in comparison with challenged diet (non-poisoned source).	During the 10-day testing period, the percentage intake of challenged diet was 70.4±5.6% for female rats and 77.7±13.7% for male rats. The percentage intake of difenacoum paste bait was	Bureau, M, Choice feeding trial for difenacoum paste bait (aged product) against rats, 0LODI17. Unpublished

				29.6±5.6% for female rats and 22.3±13.7% for male rats. Globally, mortality occurred in 100% of male and female rats with a mean day to death of 6.4±2.0 days (range 4 to 10 days). Furthermore acceptance of difenacoum past bait on D7, D8,D9, D10, D11 and D12, was 26% (n=10), 30% (n=10), 21% (n=10), 19% (n=10), 23% (n=7) and 9% (n=7), for male and female rats.	

4.6 Other

None.

5 Confidential annex (Access level: “Restricted” to applicant and authority)

5.1 Full composition of the product

Active substance(s)				Contents				
Common name	IUPAC name	CAS No.	EC No.	Concentration	Unit [15]	w/w (%)	Minimum purity (% w/w)	Same source as for Annex I inclusion (Y/N)
Difenacoum	3-(3biphenyl-4-yl-1,2,3,4-tetrahydro-1-naphtyl)-4-hydroxycoumarin	56073-07-5	259-978-4	0.05	mg/kg	[redacted]	[redacted]	[redacted]

Co-formulants					Contents				
Common name	IUPAC name	Function	CAS No.	EC No.	Concentration	Unit	w/w (%)	Classification	Substance of concern (Y/N)
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]		[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]		[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]		[redacted]

[15] g/l, g/kg, other. For biological products, the concentration should state the number of activity units/units of potency (as appropriate) per defined unit of formulation (e.g. per gram or per litre).

Annex 1 - Initial PAR – June 2011

Product Assessment Report

Ruby Paste

Active substance:	**Difenacoum**
Product-type:	**PT14: Rodenticides**
Type of application:	**Authorisation**
Authorisation No:	**IE/BPA 70004 (Non-professional product)** **IE/BPA 70033 (Professional product)**
Date:	**30 June 2011**

Biocidal Product Assessment Report (PAR) related to Product Authorisation under Directive 98/8/EC.

Department of Agriculture, Fisheries and Food
An Roinn Talmhaíochta, Iascaigh agus Bia

Pesticide Registration and Control Division
Department of Agriculture, Fisheries & Food
Backweston Campus
Young's Cross
Celbridge
Co. Kildare
Ireland

CONTENTS

1. General information about the product application

An application for authorisation was made to the Pesticide Registration and Control Division of the Department of Agriculture Fisheries and Food by Lodi S.A.S for the biocidal product Ruby Paste on 1st April 2010 in accordance with the provisions set out by Commission Directive 2008/81/EC.

This Product Assessment Report is for:

Trade name:	Ruby Paste
Authorisation No.:	IE/BPA 70004 (Non-professional) IE/BPA 70033 (Professional and Trained Professional)

The following authorisations in Ireland are linked to the above product authorisation:

Trade name	Authorisation No.	Marketing/Distribution Co.	Authorisation Type
Roded Paste	PCS 70034	Hygeia Chemicals Ltd	Supplemental Authorisation (Back-2-Back Authorisation)

1.1 Applicant/Authorization Holder

Company Name:	LODI S.A.
Address:	Parc d'activities des quatre routes Grand Fougeray 35390 France
Tel:	[redacted]
E-mail:	[redacted]

[redacted]

Company Name:	[redacted]
Address:	[redacted]
Tel:	[redacted]

1.3 Marketing/Distributing Company (where applicable)

Company Name:	LODI UK
Address:	Pensnett Trading Estate Building 69 3rd Avenue Kingswinford West Midlands, DY6 7FD UK
Tel:	[redacted]

1.4 General Information on the Biocidal Product

Trade name:	Ruby Paste
Manufacturer's development code number(s):	N/A
Active substance content:	0.005% w/w difenacoum
Main group:	MG3 – Pest control
Product type:	PT14 - Rodenticides
Product Specification:	See Confidential Annex
Site of product formulation:	See Confidential Annex
Formulation type:	Ready-to-use (RB) Paste (PA) Bait
Ready to use product (yes/no):	Yes (Only RTU products to be authorised)
Chemical/micro-organism:	Chemical substance
Contain or consist of GMOs[16] (yes/no):	N/A
Is the product already notified/authorised (Directive 98/8/EC) (yes/no); If yes: product name:	Yes (Notified under transitional arrangements with the PRCD) Ruby Paste, PCS 96004
Is the biocidal product equivalent to the product assessed for the purpose of Annex I inclusion to 98/8/EC (yes/no):	No.

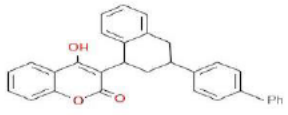
Manufacturer of Formulated Product:	LODI S.A.
Address:	Parc d'activities des quatre routes Grand Fougeray 35390 France
Tel:	[redacted]
E-mail:	[redacted]

1.5 Information on active substance(s)[17]

Active substance chemical name:	Difenacoum
IUPAC name:	3-(3biphenyl-4-yl-1,2,3,4-tetrahydro-1-naphtyl)-4-hydroxycoumarin
CAS No:	56073-07-5

[16] A copy of any written consent(s) of the competent authorities to the deliberate release into the environment of the GMOs for research and development purposes where provided for by Part B of the above-mentioned Directive was provided.

[17] Please insert additional columns as necessary

EC No:	259-978-4
Purity (minimum, g/kg or g/l):	>960 g/kg (96.0% w/w)
Structural Formula:	
Manufacturing site:	See Confidential Annex
Specification of pure active substance:	See Confidential Annex
Is a new active substance data package (source) supplied (yes/no):	No
If yes, Is the active substance equivalent to the active substance listed in Annex I to 98/8/EC (yes/no):	N/A
If no, does the applicant have a LoA to the active substance data packaged used to support Annex I inclusion (yes/no):	Yes (Pelgar International Ltd.)

Manufacturer of active substance(s):	Pelgar International Ltd.
Address:	Unit 13 Newman Lane Alton Hants. GU34 2QR UK
Tel:	[redacted]
[redacted]	[redacted]

1.6 Information on the intended use(s) of the biocidal product

Main Group:	MG03 (Pest control)
Product-type:	PT14 (Rodenticide)
Intended use:	Difenacoum paste bait to control rodents indoors and outdoors for the protection of public health, stored products and materials.
Target organisms:	(I.1) Rodents (I.1.1) Murids (I.1.1.1) Brown rats (*Rattus Norvegicus*) (I.1.1.2) House rat (*Rattus rattus*) (I.1.1.3) House mouse (*Mus musculus*)
Development stage:	(II.1) Juveniles (II.2) Adults
Function:	Rodenticide
Mode of action:	Anticoagulant III.2 long-term action III.2.1 anticoagulant

	III.2.1.1 ingestion toxin III.2.1.1.1 ingestion by eating
Application aim:	Protection of: Public health/hygiene, materials and Stored products
Category of users:	Trained professionals, professionals and non-professional (general public/amateur)
Area of use (indoors/outdoors):	Indoors (warehouses, outbuildings) Outdoors (in and around buildings, waste dumps and open areas)
Directions for use including minimum and maximum application rates, typical size of application area:	Rats: 90-100 g of paste per bait point spaced at 10m (spaced at 5m in high infestation areas). Typical treatment time 6 weeks. Mice: 20-30 g of paste per bait point spaced at 5m (spaced at 3m in high infestation areas). Typical treatment time 6 weeks.
Application method:	Paste baits contained in secured bait stations
Interval between applications:	Inspect baits frequently (particularly during the first 10 to 15 days) and regularly check bait consumption and, when required, replace consumed or spoilt bait until consumption has stopped. Repeat treatment in case of new infestation, new tracks or fresh droppings.
Typical treatment time:	6 weeks for rats and mice
Potential for release into the environment (yes/no):	Yes
Potential for contamination of food/feedingstuff (yes/no):	No

1.7 Documentation

1.7.1 Data submitted in relation to product application

A full new product dossier was submitted by Lodi S.A. in support of the product Ruby Paste containing difenacoum.

Please see the attached reference list in Annex IV.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

2. *Classification, labelling and packaging*

Under this heading the assessment of the classification, labelling and packaging should be summarised. Further, any result of the assessments made under the following headings that require recommendations or restrictions appearing on the label should be summarised here.

2.1. Harmonised classification of the active substance

The current classification of the active substance based on the proposals resulting from the review programme for difenacoum, according to Directive 67/548/EEC, is provided in the table below. Additionally, the extrapolation of these proposals using the BG RCI converter tool (http://www.gischem.de/ghs/konverter) is also provided in the table below in accordance with Regulation (EC) 1272/2008.

Classification of the active substance, difenacoum, according to Directive 67/548/EEC and CLP Regulation (EC) 1272/2008:

Symbol(s):	 	**Pictogram(s):**	
Indication(s) of danger:	Very Toxic Dangerous for the Environment	**Signal word(s):**	Danger
Risk phrases:	R26/27/28: Very Toxic by inhalation, in contact with skin and if swallowed. R48/23/24/25: Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed. R61: May cause harm to the unborn child. R50/53: Very Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.	**Hazard statements:**	H300: Fatal if swallowed. H310: Fatal in contact with skin. H330: Fatal if inhaled. H360D: Suspected of damaging the unborn child. H372: Causes damage to organs through prolonged or repeated exposure through inhalation . H410: Very toxic to aquatic life with long lasting effects.
Safety phrases:	S45: In case of accident or if you feel unwell, seek medical advice immediately (show label where possible). S53: Avoid exposure - obtain special instruction before use. S60: This material and/or its container must be disposed of as hazardous waste. S61: Avoid release to the environment. Refer to special instructions/safety data sheet.	**Precautionary statements:**	P201: Obtain special instructions before use. P273: Avoid release to the environment. P308 + P313: IF exposed or concerned: Get medical advice/attention. P314: Get medical advice/attention if you feel unwell. P501: Dispose of contents/container to hazardous waste facilities in accordance with national regulations.

2.2. Harmonised classification and labelling of the biocidal product

The current classification and labelling according to Directive 99/45/EC and Regulation (EC) 1272/2008, Annex VI, Part 3 are provided in the tables below.

Classification and Labelling of the biocidal product, Ruby Paste, according to Directive 99/45/EC:

Symbol(s):	None
Indication(s) of danger:	None
Risk phrases:	None
Safety phrases:	S1+S2: Keep locked up and out of reach of children S13: Keep away from food, drink and animal feedingstuffs S37: Wear suitable gloves S46: If swallowed, seek medical advice immediately and show this container or label S57: Use appropriate containment to avoid environmental contamination. S35: This material and its container must be disposed of in a safe way.

Classification and Labelling of the biocidal product, Ruby Paste, according to the CLP Regulation (EC) 1272/2008:

Pictogram(s):	None
Signal word(s):	None
Hazard statements:	None
Precautionary statements	P102: Keep out of reach of children. P103: Read label before use. P220: Keep/Store away from food, drink and animal feedingstuffs. P270: Do not eat, drink or smoke when using this product. P273: Avoid release to the environment. P280: Wear protective gloves P301+310: IF SWALLOWED: Immediately call a poison centre or doctor/physician. P404+405: Store locked up in a closed container. P501: Dispose of contents/container in accordance with national regulations.

Further, the content of the label should be updated to comply with the labelling requirements established (for biocidal products) where the labelling requirements in Article 20(3) of Directive 98/8/EC has been implemented. The safety data sheet should comply with the requirements in Regulation (EC) 1907/2006.

Additional Labelling Requirements:

Addition safety Information:	To avoid risks to human health and the environment, comply with the instructions for use. Use bait containers clearly marked “poison” at all surface baiting points. Remove all remains of bait, dead rodents during and after treatment and dispose of safely. Apply only in positions inaccessible to children and pets.
Special labelling provisions for Ireland:	Use Biocides Safely and Sustainably (IE/BPA 70033) Not For Amateur Sale It is illegal to use this product for uses or in a manner other than that prescribed on this label.
If a separate leaflet is attached to or supplied with the product, add the following information to the front label:	Read attached instructions before use

2.3. Packaging

The packaging details for the biocidal product, Ruby Paste, are outlined below for amateur and professional users.

Nomenclature: PP = polypropylene, PS = polystyrene, PE = polyethylene, HDPE = high-density polyethylene, PVC = polyvinylchloride

Amateur product packaging:

Container description:	Sachets		
Pack size(s):	200g	240g	500g
Baits/sachets per pack:	20x10g	24x10g	50x10g
Pack dimensions (LxWxH):	180x50x190	190x50x190	190x50x250
Packaging materials:	PE or PP or PP+PE or PE + Aluminium		
Ready-to-use (yes/no)	Yes		
Shelf-life:	4 years		
Conditions of storage:	Store in dry, cool area. Store in tightly closed packings. Keep in original containers. Store away from damp or wet conditions. Keep away from		

	children.

Container description:	Bucket container	Box container			
Pack size(s):	~~2.5kg~~	200g	240g	400g	500g
Baits/sachets per pack:	~~250x10g~~	20x10g	24x10g	40x10g	50x10g
Pack dimensions (LxWxH):	~~290x200x210~~	140x55x180	40x55x180	140x70x210	140x70x210
Packaging materials:	PP or PE	Cardboard			
Ready-to-use (yes/no)	Yes				
Shelf-life:	4 years				
Conditions of storage:	Store in dry, cool area. Store in tightly closed packings. Keep in original containers. Store away from damp or wet conditions. Keep away from children.				

Container description:	Prebaited tray		Prebaited box container		
Pack size(s):	50g	60g	10g	20g	40g
Baits/sachets per pack:	1x50g	1x60g	1x10g	2x10g	4x10g
Pack dimensions (LxWxH):	150x70x30	150x70x30	135x42x80	135x42x80	220x190x90
Packaging materials:	PS or PVC tray		PP or PS or PVC bait box		
Ready-to-use (yes/no)	Yes				
Shelf-life:	4 years				
Conditions of storage:	Store in dry, cool area. Store in tightly closed packings. Keep in original containers. Store away from damp or wet conditions. Keep away from children.				

Professional product packaging:

Container description:	Bucket container				Box container	
Pack size(s):	2.5kg	4kg	5kg	15kg	10kg	20kg
Baits/sachets per pack:	250x10g	400x10g	500x10g	1500x10g	1000x10g	2000x10g
Pack dimensions	290x20	290x20	290x200x2	380x290x4	390x290x24	400x400x37

(LxWxH):	0x210	0x270	70	50	0	0
Packaging materials:	PP or PE				Cardboard (PE liner)	
Ready-to-use (yes/no)	Yes					
Shelf-life:	4 years					
Conditions of storage:	Store in dry, cool area. Store in tightly closed packings. Keep in original containers. Store away from damp or wet conditions. Keep away from children.					

Container description:	Prebaited tray		Prebaited box container		
Pack size(s):	50g	60g	10g	20g	40g
Baits/sachets per pack:	1x50g	1x60g	1x10g	2x10g	4x10g
Pack dimensions (LxWxH):	150x70x30	150x70x30	135x42x80	135x42x80	220x190x90
Packaging materials:	PS or PVC tray		PP or PVC bait box		
Ready-to-use (yes/no)	Yes				
Shelf-life:	4 years				
Conditions of storage:	Store in dry, cool area. Store in tightly closed packings. Keep in original containers. Store away from damp or wet conditions. Keep away from children.				

Container description:	Cartridge
Pack size(s):	310 ml
Baits/sachets per pack:	1x310ml
Pack dimensions (LxWxH):	230x50
Packaging materials:	PP
Ready-to-use (yes/no)	Yes
Shelf-life:	4 years
Conditions of storage:	Store in dry, cool area. Store in tightly closed packings. Keep in original containers. Store away from damp or wet conditions. Keep away from children.

On the basis of the packaging details presented, it is considered appropriate to limit aspects of the packaging for amateur users as a risk mitigation measure. Packaging restrictions are to be limited to pre-baited bait stations and refill packs with a maximum pack-size of 500g. Additionally, the paste bait should be supplied to the amateur market in sachets in order to reduce exposure risks to amateur operators during application to bait stations.

Packaging details:

Pack size:	IE/BPA 70004 – Maximum pack size of 500g
	Pre-baited stations: 30g (mice) and 100g (rats)
	Refill packs: 200, 240g, 400g and 500g (the bait should be supplied in inner packs or units, each containing enough bait for one point)
	IE/BPA 70033
	Pre-baited stations: 30g (mice) and 100g (rats)
	Refill packs: 2.5kg, 4kg, 5kg, 10kg, 15kg and 20kg (the bait should be supplied in inner packs or units, each containing enough bait for one point)
	Cartridge 310ml
Container materials:	Box (cardboard with PE inner lining)
	Bucket (PP or PE)
	Pre-baited station (PVC, PP, PS, cardboard)
	Cartridge (PP)
Safety features:	Covered bait stations (tamper resistant)
	Wrapped bait (sachets)

3. Summary of the product assessment

3.1. Physical/chemical properties and analytical methods

Active substance (taken from the CAR):
Difenacoum does not exhibit hazardous physical-chemical properties. Difenacoum is a white to off-white powder (off-white to beige, technical grade). It has low vapour pressure; Henry's Law constant (1.75×10^{-6} Pa m^3 mol^{-1} or <0.046 Pa m^3 mol^{-1}) was calculated based on an estimated value of 6.7×10^{-9} Pa at 25°C or on an estimated vapour pressure of less than 5×10^{-5} Pa at 45°C. Difenacoum is a weak acid with a pKa value of 4.84 or with an estimated pKa value of 4.5+1. The water solubility is pH dependent and it increases with increasing pH. At neutral conditions the water solubility of Difenacoum is low, 1.7 mg/l (at pH 7 at 20°C), or in 0.48 mg/l (at 20°C at pH 6.5). Solubility in organic solvents tested ranged from 1 to 20 g/l. The estimated log K_{ow} value is 7.6. The experimental information available on Difenacoum suggests that it may be beyond the performance ranges of the experimental tests for log K_{ow}. The substance is thermally stable up to about 300°C or up to 250°C. No boiling point was detected before start of decomposition. Difenacoum is not highly flammable and it shows no self-ignition at temperatures up to melting point, 211-215°C or 215°C, the maximum temperature in the test. Corrosiveness to containers has not been observed. Difenacoum does not show oxidising or explosive properties.

Biocidal product:
The biocidal product Ruby Paste is not explosive, oxidising or flammable and does not classify from a phys.chem point of view. The test item is stable after storage for two years at ambient temperatures. The test item is a ready-to-use paste bait and is not intended to be added or mixed with any other product.

3.1.1. Identity related issues

The source of active substance used in the biocidal product Ruby Paste is the same source of active substance that is listed in Annex I of 98/8/EC (Pelgar International Ltd.).

Table 3.1.1: Composition of the biocidal product Ruby Paste

Component	% w/w	g/kg	Chemical name	CAS no	Function
Concentrate containing - Difenacoum 2.5% (Purity 96%, Technical 0.005%) + other components which are identified in the Confidential section.	0.20 (0.005 % Technical active substance)	2.00 (0.05 g/kg technical active substance)	3-(3biphenyl-4-yl-1,2,3,4-tetrahydro-1-naphtyl)-4-hydroxycoumarin	56073-07-5	Active substance
Co-formulants	See Confidential Data and Information (Annex I)				

Note: The biocidal product Ruby Paste is not the same as the representative biocidal product accompanying the Annex I inclusion. See confidential information and data for details of composition.

3.1.2. Physical-chemical properties

The source of active substance used in the biocidal product Ruby Paste is the same source of active substance that is listed in Annex I of 98/8/EC (Pelgar International Ltd.). Pelgar International Ltd. provided a letter of access for LODI S.A for their source of active substance.

3.1.3. Physical, Chemical and Technical Properties of the Biocidal Product

General note: sometimes the text says ”pasta” instead of ”paste”

Summary of the Physical and Chemical Properties of the Biocidal Product Ruby Paste

Section	Study	Method	Results	Comment	Reference
1.1.1	Appearance	OPPTS 830.6302 OPPTS 830.6303 OPPTS 830.6304	Colour (munsell code): Red (3.75 R 4/14) Physical state: paste Odour: not characteristic	Carried out to GLP. Observations were carried out at 19.5^{o}C. Study is acceptable.	NOTOX Project 490526. “Determination of physic-chemical properties of difenacoum paste baits”. Brekelmans, Ir. M.J.C. 17th September 2010.
1.1.1	Appearance		Colour: Pink paste Physical state: paste Odour: hazelnut	See 1.7.1b below.	
1.1.2	Melting point	EEC A1 OECD 102	Melting point: -16^{o}C (257 K) Decomposition of the test substance was observed at 100^{o}C (373K).	Carried out to GLP. Study is acceptable.	NOTOX Project 490526. “Determination of physic-chemical properties of difenacoum paste baits”. Brekelmans, Ir. M.J.C. 17th September 2010.

Section	Study	Method	Results	Comment	Reference
1.2.1	Explosive properties		The absence of certain reactive groups in the structural formula of the a.s., difenacoum (CAS 56073-07-5) *{Ref: Brethrick, Handbook of Reactive Chemical Hazards, Butterworths, London 1979}*, and it oxygen balance, establish beyond reasonable doubt that difenacoum is incapable of decompositing, forming gases, or realising heat very rapidly. There are no other components in the formulation which present any explosive properties.	The RefMS accepts the Notifiers justification. Difenacoum paste bait is not explosive.	
1.2.1	Explosive properties		A reasoned statement was provided by the Notifier. Difenacoum paste bait is not explosive.	The RefMS accepts the Notifiers justification. Difenacoum paste bait is not explosive.	NOTOX Project 490526. "Determination of physic-chemical properties of difenacoum paste baits". Brekelmans, Ir. M.J.C. 17th September 2010.

Section	Study	Method	Results	Comment	Reference
1.2.2	Oxidising properties		Nor the a.s. or the solvent present oxidising properties Examination of the structural establish beyond reasonable doubt that the a.s., difenacoum (CAS 56073-07-5) is incapable of reacting exothermically with a combustible material *(refer to Explosive Properties)*. There are no other components in the formulation which present any oxidising properties.	The RefMS accepts the Notifiers justification. Difenacoum paste bait is not oxidising.	
1.2.2	Oxidising properties		A reasoned statement was provided by the Notifier. Difenacoum paste bait is not oxidising.	The RefMS accepts the Notifiers justification. Difenacoum paste bait is not oxidising.	NOTOX Project 490526. "Determination of physic-chemical properties of difenacoum paste baits". Brekelmans, Ir. M.J.C. 17th September 2010.
1.3.1	Flash point		No flash point data is required for solids. See 1.3.2, Flammability below.		

Section	Study	Method	Results	Comment	Reference
1.3.2	Flammability	EEC A.10 (flammability (solids)).	Flammability: Not highly flammable. The flame of the gas burner did ignite the test substance pile. The test substance glowed and burned with a yellow flame and turned into a charred residue. White smoke was observed. After removal of the ignition source, the flame extinguished after 28 seconds and no propagation of combustion was observed. Performance of the main test was not required.	The RefMS accepts that Difenacoum was determined to be not highly flammable as part of the Annex I inclusion process. Carried out to GLP. The test substance is considered "not highly flammable". The study is acceptable.	NOTOX Project 490526. "Determination of physic-chemical properties of difenacoum paste baits". Brekelmans, Ir. M.J.C. 17th September 2010.
1.3.3	Auto-flammability	EEC A.16 (relative self-ignition temperature for solids)	The test item is considered "not self-ignitable"	Carried out to GLP. The test item is not self-ignitable.	NOTOX Project 490526. "Determination of physic-chemical properties of difenacoum paste baits". Brekelmans, Ir. M.J.C. 17th September 2010.
1.4.1	Free acidity/ Alkalinity		The determination of acidity or alkalinity is required if the pH of the 1% (w/v) aqueous test substance dispersion is <4 or >10. The pH of a 1% (w/v) aqueous test substance solution was determined to be 6.4. Therefore since this pH was within the pH range 4-10 the acidity/alkalinity test was not required and thus not performed.	RefMS agrees that the acidity/alkalinity test is not required.	NOTOX Project 490526. "Determination of physic-chemical properties of difenacoum paste baits". Brekelmans, Ir. M.J.C. 17th September 2010.

Section	Study	Method	Results	Comment	Reference
1.4.2	pH (1 %)	CIPAC MT 75.3	pH (1%) = 6.4	Carried out to GLP. The temperature was 20^{o}C. The results are acceptable.	NOTOX Project 490526. "Determination of physic-chemical properties of difenacoum paste baits". Brekelmans, Ir. M.J.C. 17th September 2010.
1.5.1	Viscosity		Not applicable, the product is a paste.	Accept justification.	
1.5.2	Surface tension		Not applicable, the product is a paste.	Accept justification.	
1.6	Relative density	OECD 109 EEC A.3	Density = 1.24 g/cm^{3} Relative density = 1.24	Carried out to GLP. The results are acceptable.	NOTOX Project 490526. "Determination of physic-chemical properties of difenacoum paste baits". Brekelmans, Ir. M.J.C. 17th September 2010.

<table>
<tr><th>Section</th><th>Study</th><th>Method</th><th>Results</th><th>Comment</th><th>Reference</th></tr>
<tr><td>1.7.1a</td><td>Storage stability
(Accelerated storage – up to 5 weeks at 54^{o}C)</td><td>GIFAP Monograph No. 17
CIPAC MT 46.3</td><td>The study examined the Difenacoum content before and after accelerated storage for three different products (paste, block and cereals). Only the Difenacoum paste (0.005%) results are given below:

<table>
<tr><th>Weeks at 54^{o}C</th><th>0</th><th>2</th><th>3</th><th>4</th><th>5</th></tr>
<tr><td>Agent conc. in ppm</td><td>52.9</td><td>49.0</td><td>49.9</td><td>50.4</td><td>49.2</td></tr>
<tr><td>Deviation from the declared value</td><td>+ 5.8%</td><td>-2%</td><td>- 0.2%</td><td>+0.8%</td><td>- 1.6%</td></tr>
<tr><td>Min. Tolerance in ppm</td><td>37.5</td><td>37.5</td><td>37.5</td><td>37.5</td><td>37.5</td></tr>
</table>

The sample was stable during 5 weeks at 54^{o}C, indicating that the paste bait will be stable for up to 2 years at ambient temperature.</td><td>Note that the rat poison was considered stable when less than 25% agent breakdown was observed.
The sample was stable during 5 weeks at 54^{o}C. The result indicates that the paste bait will be stable for up to two years at ambient temperature. The study is acceptable.</td><td>Study report: Stability of Difenacoum baits after accelerated storage procedure. Biannic, Marie-Laure. 7th January 2008.</td></tr>
</table>

Section	Study	Method	Results	Comment	Reference
1.7.1b	Storage stability (Accelerated storage – 14 days at 54^{o}C)	GIFAP Monograph No. 17 CIPAC MT 46	<u>Analysis at T0:</u> Aspect: Pink malleable paste Odour: Hazelnut Contents: 48.79 mg/kg of Difenacoum (-2.42% deviation from the declared value) <u>Analysis at T14:</u> Aspect: Pink crumbly paste Odour: Hazelnut Contents: 50.38 mg/kg of Difenacoum (+0.76 % after accelerated storage)	Carried out to GLP. The only change observed was in the aspect which became crumbly, which did not influence the stability of the difenacoum content in the paste. The results of the study indicate that the test item is stable for 2 weeks at 54^{o}C and would be expected to be stable for up to two years at ambient temperatures. The study is acceptable. Note that the analytical method used was validated in study LODI.17/2009; the LOQ = 0.25 ppm.	Study No: LODI.14/2009. Study report: Chemical stability after accelerated storage of Difenacoum paste baits 0.005%. Meriadec, Elodie. 25th November 2009.

<table>
<tr><th>Section</th><th>Study</th><th>Method</th><th>Results</th><th>Comment</th><th>Reference</th></tr>
<tr><td>1.7.2</td><td>Shelf life (storage ambient temperatures for two years)</td><td></td><td>The study examined the stability of Difenacoum in the test item for three different products (paste, block and cereals). Only the Difenacoum paste (0.005%) results are given below:

<table><tr><th>Time</th><th>0</th><th>6 months</th><th>2 yrs</th></tr><tr><td>Agent conc. in ppm</td><td>52.9</td><td>49.97</td><td>52.8</td></tr><tr><td>Deviation from the declared value</td><td>5.80%</td><td>-5.54%</td><td>-0.19%</td></tr><tr><td>Min. tolerance in ppm</td><td>37.5</td><td>37.5</td><td>37.5</td></tr></table>
The test item is considered stable for two years at ambient temperatures.</td><td>Note that the rat poison was considered stable when less than 25% agent breakdown was observed. The test item is considered stable for two years at ambient temperatures. The study is acceptable.</td><td>Study report: Stability of Difenacoum baits after a storage at ambient temperature. Biannic, Marie-Laure. 12th November 2009.</td></tr>
<tr><td>1.8.1</td><td>Wettability</td><td></td><td>Not applicable, the product is a ready-to-use paste bait.</td><td>Accept justification.</td><td></td></tr>
<tr><td>1.8.2</td><td>Persistent foaming</td><td></td><td>Not applicable, the product is a paste.</td><td>Accept justification.</td><td></td></tr>
<tr><td>1.8.3.1</td><td>Suspensibility</td><td></td><td>Not applicable, the product is a ready-to-use paste bait.</td><td>Accept justification.</td><td></td></tr>
<tr><td>1.8.3.2</td><td>Dispersibility</td><td></td><td>Not applicable, the product is a paste.</td><td>Accept justification.</td><td></td></tr>
</table>

Section	Study	Method	Results	Comment	Reference
1.8.4	Wet/dry sieving test		For WPs, SCs, granules and tablets therefore not applicable in this case as the product is a paste.	Accept justification.	
1.8.5	Particle size distribution in suspension		Only for powders and granules therefore Not applicable, the product is a paste.	Accept justification.	
1.8.6	Water content		Not applicable, the product is a ready to use paste bait.	No data required.	
1.8.7	Emulsion stability		Only for ECs and ready to use emulsions, therefore not applicable in this case as the product is a paste.	Accept justification.	
1.8.8	Flowability, pourability and dustability		Not applicable, the product is a paste.	Accept justification.	
1.9	Physical compatibility		Not applicable, the product is a ready-to-use paste bait and is not intended to be added or mixed with any other product.	Accept justification.	

Conclusions:

The biocidal product Ruby Paste is not explosive, oxidising or flammable and does not classify from a phys.chem. point of view. The test item is stable after storage for two years at ambient temperatures. The test item is a ready-to-use paste bait and is not intended to be added or mixed with any other product.

Data requirements:

Information on the reactivity of the paste bait towards the container material is outstanding.

3.1.4. Analytical methods

Ruby Paste was not assessed as part of the Annex I inclusion process therefore the Notifer has submitted the following methods of analysis to cover the outstanding data gaps.

Table 3.1.4.1

<table>
<tr><td>Report No.:</td><td>09-902018-007</td></tr>
<tr><td>Title:</td><td>“Analytical method validation for the determination of difenacoum in difenacoum pasta bait”</td></tr>
<tr><td>Author(s):</td><td>Ricau, Hélène.</td></tr>
<tr><td>Date:</td><td>19th October 2009</td></tr>
<tr><td>GLP: Yes/No</td><td>Yes.</td></tr>
<tr><td>Guideline study</td><td>CIPAC/3807R</td></tr>
<tr><td>Principle of the Method:</td><td>Difenacoum was extracted from the pasta bait using Methanol and heated under reflux for about 90 minutes at 80°C in an oil bath. Extract was filtered through a Whatman filter N°1 and diluted in Methanol and Acetonitrile before injection. Difenacoum was quantified by liquid chromatography using a reverse phase column and a UV detector at 310 nm.</td></tr>
<tr><td>Linearity:</td><td>See analytical method R05-912011-001 in Table 3.1.4.2.</td></tr>
<tr><td>Precision/repeatability:</td><td>See analytical method R05-912011-001 in Table 3.1.4.2.</td></tr>
<tr><td>Accuracy:</td><td>The method has been validated at 0.92 mg/l (100% level) and at 0.46 mg/l (50% level).
<table>
<tr><th>Item solutions</th><th>Reconstituted (mg/l)</th><th>Conc. found (mg/l)</th><th>Recovery (%)</th></tr>
<tr><td colspan="4">Accuracy determination at a 100% level:</td></tr>
<tr><td>Extract 1 100%</td><td>0.92</td><td>0.84</td><td rowspan="2">91</td></tr>
<tr><td>Extract 1 100%</td><td>0.92</td><td>0.84</td></tr>
<tr><td>Extract 2 100%</td><td>0.92</td><td>0.83</td><td rowspan="2">91</td></tr>
<tr><td>Extract 2 100%</td><td>0.92</td><td>0.84</td></tr>
<tr><td colspan="4">Accuracy determination at a 50% level:</td></tr>
<tr><td>Extract 1 50%</td><td>0.46</td><td>0.43</td><td rowspan="2">92</td></tr>
<tr><td>Extract 1 50%</td><td>0.46</td><td>0.42</td></tr>
<tr><td>Extract 2 50%</td><td>0.46</td><td>0.43</td><td rowspan="2">94</td></tr>
<tr><td>Extract 2 50%</td><td>0.46</td><td>0.44</td></tr>
</table>
The recovery results are between 91 - 94%, which fall within acceptable criteria.</td></tr>
<tr><td>Specificity:</td><td>To define the specificity of the analytical method, the following solutions were analysed: blank solvent, blank formulation, reference item and test item. The specificity was evaluated by the absence of interfering peaks in the area of interest.</td></tr>
</table>

	Results: No peak was observed in the blank solvent or in the blank formulation. In the reference item and in the test item, the peak at the retention time around 3.42 min represents Difenacoum. No other peak was found in the reference item or in the test item.
Interferences	No interfering peak was observed in the blank solvent, in the blank formulation and in the reference item at the retention time of Difenacoum.
Limit of quantification:	-

Conclusion:

The analytical method CIPAC/3807R has been successfully validated for accuracy and specificity. See analytical method R05-912011-001 in Table 3.1.4.2 below for information on linearity and precision.

Data requirements:

None.

Table 3.1.4.2:

<table>
<tr><td>Report No:</td><td>05-912011-001</td></tr>
<tr><td>Title:</td><td>“Quantification of Difenacoum 0.005% m/m in a rat poison bait”</td></tr>
<tr><td>Author(s):</td><td>Ricau, Hélène</td></tr>
<tr><td>Date:</td><td>16th June 2005</td></tr>
<tr><td>GLP: Yes/No</td><td>Yes</td></tr>
<tr><td>Guideline study:</td><td>-</td></tr>
<tr><td>Principle of the Method:</td><td>After a methanol dilution and heating under reflux for 90minutes the extract was filtered and diluted again in methanol and acetonitrile. Difenacoum was quantified by liquid chromatography using a reverse phase column and a UV detector at 310 nm. The purity of the reference standard for Difenacoum was 975 g/kg.
Note: The method is the same as the method outlined in Table 3.1.4.1 above with the exception of a Whatman filter no.40 being used instead of filter no.1.</td></tr>
<tr><td>Linearity:</td><td>The response of Difenacoum is linear within the range of 0.0008 mg/ml to 0.0012 mg/ml (3 concentrations analysed twice). Correlation coefficient r^2 = 1.000. A calibration plot was included and was acceptable.</td></tr>
<tr><td>Precision/repeatability:</td><td>The precision was determined by analysing six samples (in duplicate) for the content of Difenacoum. The concentration of Difenacoum in the test item equalled 0.005% w/w or 0.05 g/kg. The % RSD = 3.40, which is within the acceptable criteria (<20%).</td></tr>
<tr><td>Accuracy:</td><td>The accuracy was determined by analysing two samples in duplicate for the content of Difenacoum. The accuracy results are between 102-105%, which are in line with current guidelines.
<table>
<tr><th>Sample</th><th>Content (% w/w)</th><th>Average (% w/w)</th><th>Recovery (%)</th></tr>
<tr><td>DEF05-0062B</td><td>0.0049</td><td rowspan="2">0.0049</td><td rowspan="2">102</td></tr>
<tr><td>DEF05-0062B</td><td>0.0049</td></tr>
<tr><td>DEF05-0062C</td><td>0.0050</td><td rowspan="2">0.0050</td><td rowspan="2">105</td></tr>
<tr><td>DEF05-0062C</td><td>0.0051</td></tr>
</table></td></tr>
<tr><td>Specificity</td><td>The specificity was determined by injecting the blank solvent, the reference item and the test item. A shift of Difenacoum retention time was observed in the test item due to the presence of waxy co-extracts.</td></tr>
</table>

<table>
<tr><td></td><td>By comparison of the UV spectra at the level of the reference item peak (at 4.20 min) and the test item peak, it was shown that the peak at around 4.60 represents Difenacoum. The retention time of Difenacoum in the test item changes from about 4.60 to 4.80. No peak was observed in the blank solvent.</td></tr>
<tr><td>Active substance concentration</td><td>Two independent analysis of the test item were made.
<table>
<tr><th></th><th>Difenacoum concentration (% w/w)</th><th>Average Difenacoum concentration (% w/w)</th></tr>
<tr><td>DEF05-0062</td><td>0.005</td><td rowspan="2">0.005</td></tr>
<tr><td>DEF05-0062</td><td>0.005</td></tr>
<tr><td>DEF05-0062A</td><td>0.005</td><td rowspan="2">0.005</td></tr>
<tr><td>DEF05-0062A</td><td>0.005</td></tr>
</table></td></tr>
<tr><td>Limit of quantification:</td><td>-</td></tr>
</table>

Conclusion:

The method of analysis presented above was not validated for the paste bait only the block bait and therefore it cannot be used to cover the paste bait. However, the linearity and precision information provided covers the data gaps in study no. 09-902018-007 (see Table 3.1.4.1 above).

Data requirements:

None.

Table 3.1.4.3

<table>
<tr><td>Report No:</td><td>09-912011-004</td></tr>
<tr><td>Title:</td><td>“Quantification of difenacoum in Rattofene (Pasta Bustine)”</td></tr>
<tr><td>Author(s):</td><td>Ricau, Hélène</td></tr>
<tr><td>Date:</td><td>1st April 2009</td></tr>
<tr><td>GLP: Yes/No</td><td>Yes.</td></tr>
<tr><td>Guideline study:</td><td>-</td></tr>
<tr><td>Principle of the Method:</td><td>The objective of the study was to determine the content of difenacoum in the test item. Difenacoum was extracted from the pasta bait using Methanol and ultrasonicated for 15 minutes before analysis. Extract was diluted in Methanol before injection. Difenacoum was quantified by liquid chromatography using a reverse phase column and a UV detector at 310 nm.</td></tr>
<tr><td>Linearity:</td><td>-</td></tr>
<tr><td>Precision/repeatability:</td><td>-</td></tr>
<tr><td>Accuracy:</td><td>-</td></tr>
<tr><td>Specificity</td><td>-</td></tr>
<tr><td>Active substance concentration</td><td>Declared content of Difenacoum: 0.005% w/w
<table>
<tr><th>Test item</th><th>Difenacoum</th><th>Difencoum</th><th>Final result</th><th>Deviation</th></tr>
</table></td></tr>
</table>

		conc. (% w/w)	**mean conc. (% w/w)**	**(% w/w)**	**from declared content (%)**
	09-011A	0.0046	0.0047	0.0050	0
		0.0047			
	09-011B	0.0051	0.0052		
		0.0053			
Limit of quantification:	-				

Conclusion:

The concentration of the active substance is with FAO tolerances (± 15%).

Data requirements:

None.

Table 3.1.4.4

<table>
<tr><td>Report:</td><td>Study No. LODI.17/2009</td></tr>
<tr><td>Title:</td><td>“Analytical method validation for determination of difenacoum in difenacoum bait (pasta grain and paste).”</td></tr>
<tr><td>Author(s):</td><td>Magnier, Claire.</td></tr>
<tr><td>Date:</td><td>4th November 2009.</td></tr>
<tr><td>GLP: Yes/No</td><td>Yes.</td></tr>
<tr><td>Guideline:</td><td>CITAC/EURACHEM</td></tr>
<tr><td>Principle of the Method:</td><td>The test item was quantified by liquid chromatography using a reverse phase column and a UV detector.
Note that no exact information on the principle of the method was provided. The company clarified that the method is similar to the principle of the method used in reports 09-902018-007 and 05-912011-001.</td></tr>
<tr><td>Linearity:</td><td>The response of Difenacoum was linear over the range 80% - 120% of the test item concentration. Five measurements were made in triplicate. The correlation coefficient $r^2 > 0.99$. Calibration curves were provided and were acceptable.</td></tr>
<tr><td>Precision/repeatability:</td><td>Three solutions were prepared of a concentration C (~ 2.367 mg/l) of the product. Three injections of each solution were carried out and the RSD was calculated.
RSD <1.168</td></tr>
<tr><td>Accuracy:</td><td>The method was validated at 50%, 100% and 150% doped placebo. Three injections were carried out per solution and the average recoveries are reported below.

<table>
<tr><th></th><th>50% doped placebo</th><th>100% doped placebo</th><th>150% doped placebo</th><th>Average recovery</th></tr>
<tr><td>Paste bait</td><td>102.90%</td><td>97.78%</td><td>95.11%</td><td>98.60%</td></tr>
</table>
The recovery results are between 95-103%, which fall within acceptable criteria.</td></tr>
<tr><td>Specificity:</td><td>There was no peak observed in the paste placebo or extraction solution chromatograms. An adjacent peak appeared in the stressed paste (R = 2.25) but the resolution being higher than 2, the quantification was considered acceptable.</td></tr>
<tr><td>Limit of quantification:</td><td>0.25 mg/kg (ppm)</td></tr>
<tr><td>Limit of detection:</td><td>0.05 mg/kg (ppm)</td></tr>
</table>

Conclusion:

The method is acceptable. The information provided in this study is considered extra information only, with the exception of the LOD and LOQ information.

Data requirements:

None.

3.1.5. Analytical method for the relevant impurities, isomers and co-formulants in the biocidal product

There are no relevant impurities or isomers in the biocidal product therefore no analytical method is required.

3.2. Efficacy of the Biocidal Product

Ruby paste is a ready-to-use rodenticide paste containing 0.005% (w/w) difenacoum or 50 ppm difenacoum which is contained within a sachet. The efficacy of the product was assessed against the proposed label claims. Both amateur and professional uses are proposed in and around buildings.

The applicant submitted new data in the form of 7 trial reports where both fresh and aged paste baits were used in both laboratory and field situations to assess the palatability and effectiveness of the product. Studies were conducted according to a variety of standards and protocols. Three of the studies were conducted under laboratory conditions with wild strains of mice used in one study. The other two studies used laboratory strains of mice and rats respectively. The laboratory studies were all choice tests conducted according to recognised standards.

The studies have shown that Ruby paste is palatable to the house mouse, brown rat and black rat according to the criteria given in the TNsG on product evaluation. The bait intake was more than 20% of the total food consumption in all of the studies.

In the first laboratory choice test using captured wild mice 90% control was achieved using fresh bait. The surviving mouse ate abnormally large doses of the product but appeared much less sensitized to difenacoum. The second laboratory trial used an albino strain of mice with aged bait (12 and 24 months). All mice died with the 12 month aged bait whilst 85% control was achieved with the 2 year aged paste. The third study was conducted in an infested restaurant with a 2 year aged paste achieving 95% efficacy (based on pre-baiting consumption levels). A pigeon farm where significant quantities of alternative feed was available was chosen for the next study where wild brown rats were baited using a fresh bait product. Again based on pre and post-baiting consumption levels 95% efficacy was achieved. Another field study on brown rats in a warehouse achieved an efficacy specification of 92% with 2 year old product. The next laboratory test using albino rats and a fresh and 12-month aged bait proved no significant loss in acceptance levels/palatability or efficacy.
The final study considered was aimed at the control of an estimated population of 15-25 black rats in a pig production building with fresh bait. Excellent levels of control were achieved. 3 dead rats were found and the pest control operator reported a complete reduction in activity soon after the post-baiting period ended.

The paste bait formulation proved to be sufficiently palatable and effective against both rats and mice in the tests. Both fresh and aged baits (12 and 24 months after manufacture) achieved excellent control of the test animals with the ageing process not adversely affecting the active substance content, palatability or the effectiveness of the product. The product is concluded to be effective against brown rats, black rats and mice.

The paste formulation is not suitable for baiting in damp or wet conditions (i.e. sewers).

3.2.1. Function/Field of use

Main Group (MG):	3 – Pest control
Product-type (PT):	14
Function:	Rodenticide

Difenacoum is intended to be used to control rodent pests, both indoors and outdoors, in and around buildings, sewers, open areas and waste sites. The target species are brown rat (*Rattus norvegicus)*, black rat (*Rattus rattus)* and house mouse (*Mus musculus/domesticus)*. 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 new data on the paste formulation was provided in the form of laboratory and field studies to verify the proposed label claims.

Product	Codes*	Terms*	GIFAP codes
Pasta	VIII.4.1	Paste	RB

3.2.2. Dose/Mode of action

Ruby Paste should be placed in discrete locations within the infested area and placed in secure, (preferably dry) tamper-proof baiting stations, bait boxes or pipe sections.

For mice: place 1 to 3 sachets of 10g every 3 to 5 metres.
For rats: place 3 to 6 sachets of 10g every 5 to 10 metres.
The distance has to be adapted to the infestation level.

Difenacoum is a second generation anticoagulant which prevents blood clotting in the target organisms by inhibiting regeneration of the active form of vitamin K1. Clinical signs are progressive and occur within 2-3 days after ingestion of a toxic dose, ultimately leading to death from 4-5 days later. Effects are reversible by administration of the antidote vitamin K1 which stimulates the regeneration of the clotting factors.

Anticoagulant rodenticides are vitamin K antagonists. The main site of their 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. The anticoagulants accumulate and are 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 antidoting therapy (vitamin K1).

Signs of poisoning in rodents and other mammals are those associated with an increased tendency to bleed leading ultimately to profuse haemorrhage. After feeding on bait containing the active ingredient for 2 – 3 days the animal becomes lethargic and slow moving. Signs of bleeding are often noticeable and blood may be seen around the nose and anus. As symptoms develop the animal will lose its appetite and will remain in its burrow or nest for increasingly long periods of time. Death will usually occur within 4-5 days of ingesting a lethal dose and animals often die out of sight in their nest or burrow.

The standard concentration at which difenacoum is typically used in ready for use baits is 0.005% w/w. This concentration has been standardised over the last 25 years as the optimal concentration to deliver the benefits of the active substance. Difenacoum is inherently not very palatable and at concentrations above 50 ppm there is a risk that it can be detected by the target species. Difenacoum, even at 50 ppm, is a multi-feed product and if this concentration was lower then the time to control the target population would be extended to several weeks or even months, which is unlikely to be acceptable where there is a rodent population that needs to be controlled for public health reasons. A further disadvantage of reducing the concentration is that it takes longer to accumulate a lethal dose in the target species such that moribund rodents containing residues of the anticoagulants will be active above ground over a longer period. Because of the poisoning effects of general lethargy these are likely to be the individuals targeted by predators. Maintaining and perhaps limiting the use rate at 50 ppm ensures a lethal dose is quickly ingested and death also follows quickly.

The assessment of the biocidal activity of difenacoum demonstrates that it has a sufficient level of efficacy against the target organisms in concentration of 50 mg/kg and the evaluation of the summary data provided in support of the efficacy of the accompanying product, establishes that the product may be expected to be efficacious. Difenacoum content in the product is 50 mg/kg.

3.2.3. Organisms to be controlled

Pest organisms to be controlled by the formulated product 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.1.1.2	*Rattus rattus*	Roof rat, House rat
I.1.1.3	*Mus musculus*	House mouse

Developmental stages of target organisms to be controlled

II.1	Juveniles
II.2	Adults

*Application codes for encoding Rodenticides (PT14), edited the 16 January 2009 on website Ex-ECB, in point IVB5-0_01 of the dossier).

3.2.4. Effects on the target organisms (efficacy)

Anticoagulant rodenticides disrupt the normal blood-clotting, mechanisms, resulting in increased bleeding tendency and eventually, and profuse haemorrhage.
Signs of anticoagulant poisoning in rats and mice included lethargy, hunched posture and vain clearing in the ears. Blood around the eyes, mouth and anus, indicating internal haemorrhaging, appears prior to death.

Data requirements: None.

3.2.5. Known limitations (e.g. resistance)

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. No reports were submitted to the Rapporteur Member State about the distribution and incidence of resistance in the house mouse or black rat in Europe. Resistance was comprehensively discussed in the CAR.

Resistance management strategies

The immediate aim of resistance management is to prevent or retard the development of resistance to a given anticoagulant while, as far as is not counterproductive, permitting its continued use. The ultimate aim is to reduce or eliminate the adverse consequences of resistance.

CropLife International has published a strategy for resistant management of rodenticides (RRAC 2003). The habitat management is addressed in the strategy in addition to chemical control. The access of rodents should be restricted by physical barriers and no food should be available for rodents. Rotation between different anticoagulants is not a reliable means of managing the anticoagulant resistance, as all anticoagulants have the same mode of action and the nature of resistance is also similar. The resistant individuals can be identified by conducting a blood clotting response (BCR) test (Gill et al. 1993, RRAC 2003). The problem with the BCR test is that it has proven difficult to standardise and it produces both false positives and negatives (Pelz et al. 2005). In order to follow the

occurrence and spread of difenacoum resistance, wild rats should be continuously monitored for resistance in the rodent controlled area. The recommendations of CropLife International are quoted below.

To avoid the development of resistance in susceptible rodent populations:

- When anticoagulant rodenticide is used, 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 strategies, extend the baiting programme or apply alternative control techniques to eliminate the residual infestation (acute or sub-acute rodenticides, gassing or trapping).
- Ensure that complete elimination of the infestation is achieved.
- As appropriate during the rodenticide treatment, apply effective Integrated 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 advice on the local circumstances.
- Alternatively use an acute or sub-acute but non-anticoagulant rodenticide.
- In both cases it is essential 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 Integrated 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 known resistance and ideally beyond.
- These programmes must be effectively coordinated and should encompass the procedures identified above.

3.2.6. Humaneness

The use of difenacoum as a rodenticide could cause suffering of vertebrate target organisms. The use of anti-coagulant rodenticides is necessary as there are at present no other viable measures available to control the rodent population in the European Union. Rodent control is needed to prevent disease transmission, contamination of food and feeding stuffs and structural damage. It is recognised that such substances do cause pain in rodents but it is considered that this is not in conflict with the requirements of Article 5.1 of Directive 98/8/EC 'to avoid unnecessary pain and suffering of vertebrates', as long as effective, but comparable less painful alternative biocidal substances or biocidal products or even non-biocidal alternatives are not available.

Experimental data on the effectiveness of the biocidal product Ruby Paste against the intended target organisms

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
DIFEPASTA, containing 0.005ppm difenacoum	Wild grey mice (*Mus musculus*)	Laboratory housing for wild mice captured in warehouse. Test was performed on fresh product.	Test was carried out in accordance with Decision criteria edited by the Major Guideline for the Rodenticide efficacy assessment (*Lignes Directrices pour l'évaluation de l'Efficacité des Rodenticides*).	*Paste bait/ Semi field efficacy/ Mice/ Fresh product (T0)* DIFEPASTA, rodenticide bait containing 0.005% de Difenacoum, is sufficiently attractive and very efficacious in controlling grey mice (*Mus musculus*). The efficacy is 90% against mice.	***IIIB5-10_01*** Mahaut T., Cavellier M., CRA Gembloux, Efficacy test on DIFEPASTA, bait ready to use, containing 0.005% of Difenacoum, against grey mice (*Mus* musculus L.), ROD 2003-03-Belgagri, 20 October 2003. Unpublished
DIFEPASTA, containing 0.005ppm difenacoum	White Mice (*Mus musculus*)	Laboratory conditions. Test was performed with different storage periods of product: • Fresh product. • Product after 24	Test was carried out in accordance with Decision criteria edited by the Major Guideline for the Rodenticide efficacy assessment (*Lignes Directrices pour l'évaluation de l'Efficacité des Rodenticides*).	*Paste bait/ Laboratory efficacy/ Mice/ Product at T12 and T24 months* - At T12, all tested mice died. (n=20) - At T24, all tested animals died except 4 mice (n = 20). After 12 months storage, the efficacy of DIFEPASTA reached 100% with mice. After 2 years, the efficacy of DIFEPASTA	***IIIB5-10_02*** De Proft M., Galoux M., CRA Gembloux, Efficacy test through different period of time, performed on

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
		months		decreases to 85% with mice.	DIFEPASTA, bait ready to use, containing 0.005% of Difenacoum, rapport number 11 594 ROD 2003-003, June 2006 Unpublished
PASTA DIFE,, containing 0.005ppm difenacoum	Grey mice (*Mus musculus*)	Field study: experiment conducted in restaurant. Test was performed on fresh product. Test was performed on product stored for two years, (T24).	The method used has been inspired by the French method called "method no. 002 from Biological Trials Commission (C.E.B) ", Method for practical efficacy trials of raticides: • Adopted on 1960, derived from the work of Chitty and Dotty in the 1940. • Revised by OEPP in 1980.	*Paste bait/ Field efficacy/ Mice/ Product at T2y* Based on consumption results, PASTA DIFE achieved 95% efficacy even after 2 years under storage conditions. In the conditions of this trial, the product Pasta Dife, a paste containing 0.005% of Difenacoum as an active substance (and aged 2 years), is very effective, being markedly higher to the 90% required by the guidelines. .	***IIIB5-10_03*** - LODI, Efficacy trial: Pasta Dife/ Mice- Confidential report, LODI property, 12 pages, Feb2009. Unpublished
PASTA DIFE,, containing	Wild Brown rats (*Rattus*	Field study: experiment conducted in pigeon farm.	The method used has been inspired by the French method called "method no. 002 from	*Paste bait/ Field efficacy/ Rats/ Fresh product (T0)*	***IIIB5-10_04*** Grolleau G., Pest

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
0.005ppm difenacoum	*norvegicus*)	Test was performed on fresh product.	Biological Trials Commission (C.E.B) ", Method for practical efficacy trials of raticides: • Adopted on 1960, derived from the work of Chitty and Dotty in the 1940. • Revised by OEPP in 1980.	The efficacy reached 95%. We can say that the tested bait, PASTA DIFE, achieved a good level of effectiveness and that complies with the required criteria for licensing.	Control Assistance (PCA), Effectiveness testing under natural conditions of PASTA DIFE rat killer in paste bait form in sachets on brown rats / Test under natural conditions of a rat killer in paste bait form (PASTA DIFE) containing 0.005% Difenacoum, on Brown rats (*Rattus norvegicus*) 2002. Unpublished
PASTA DIFE,, containing 0.005ppm difenacoum	Wild Brown rats (*Rattus norvegicus*)	Field study: experiment conducted in warehouse. Test was performed on product stored for two years, (T24).	The method used has been inspired by the French method called "method no. 002 from Biological Trials Commission (C.E.B) ", Method for practical efficacy trials of raticides: • Adopted on 1960,	*Paste bait/ Field efficacy/ Rats / Product at T2years* The efficacy trial of PASTA DIFE has been conclusive, with the results permitting the declaration that the product is efficacious against Norway rats.	***IIIB5-10_05*** Biannic M-L., LODI S.A.S, Efficacy assessment of a rat killer in a field trial – product: PASTA

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
			derived from the work of Chitty and Dotty in the 1940. • Revised by OEPP in 1980.	The product achieved 92% efficacy against rats.	DIFE, July 2009. Unpublished
PASTA DIFE,, containing 0.005ppm difenacoum	Albino rats (*Rattus norvegicus*)	Laboratory conditions. Test was performed on different stage of product: • Fresh product. • Product after 12 months	Test was carried out in accordance with Decision criteria edited by the Major Guideline for the Rodenticide efficacy assessment (*Lignes Directrices pour l'évaluation de l'Efficacité des Rodenticides*)	*Paste bait/ Lab choice test/ Rats / Product at T0 and T12* • T0: 19 dead rats at the end of the trial • T12: 18 dead rats at the end of trial. Between fresh product and the 12 months aged product, loss of palatability is not significant.	***IIIB5-10_06*** De Proft M., CRA Gembloux, Study of ageing behavior of ready-to-use baits containing 0.005% of Difenacoum, PART 1: Pasta Bait, report number ROD 2008 11 BIO 6 Unpublished
NORA PASTA BAITS, containing 0.005ppm difenacoum	Black rats (*Rattus rattus*)	Field: study conducted in pig stables Test was performed on fresh product (T0)	Test was carried out in accordance with Decision criteria edited by the Major Guideline for the Rodenticide efficacy assessment (*Lignes Directrices pour*	*Paste bait/ Field efficacy/ Roof rat / Product at T0* DIFENACOUM is said to kill rodents in 5 to 21 days. In these tests the first signs of illness started after 9 days; 3 dead rats were found after 14	***IIIB5-10_07*** Feys J-L., Field trial with NORA PASTA BAITS against ROOF RATS 21 January 2010_08

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
			l'évaluation de l'Efficacité des Rodenticides)	days. After twenty days there was still some activity, which ended later (unrecorded). These results are consistent with the results expected with difenacoum baits. One can conclude that NORA PASTA Paste Baits is very well suited for the extermination of *Rattus rattus* in stables.	February 2010, batch NO 091109. Belgagri. Unpublished

3.3. Biocidal Product Risk Assessment (Human Health and the Environment)

3.3.1. Description of the intended use(s)

Ruby Paste is a rodenticide paste bait for the effective control of rodent species, both indoors and outdoors, in and around a variety of places including but not limited to buildings, sewers, open areas and waste dumps. Ruby Paste takes the form of a ready to use paste bait, packaged in a tea bag & containing 0.005% w/w (50 ppm) difenacoum, a second generation 4-hydroxy coumarin or superwafarin anticoagulant, which causes death due to massive internal haemorrhages after several days of ingestion as a consequence of an accumulated lethal dose. The target species are brown rat (*Rattus norvegicus*), black rat (*Rattus rattus*) and house mouse (*Mus musculus / domesticus*). Other than the active ingredient, the product is composed of food-grade materials forming a bait base.

3.3.2. Hazard Assessment for Human Health

No new exposure studies have been submitted for evaluation. Signs of poisoning in rodents and other mammals are those associated with an increased tendency to bleed, leading ultimately to profuse haemorrhage. Non-target organisms are most at risk from secondary poisoning, i.e. consumption of rodent carcasses by predators such as raptors. Difenacoum is highly lipid soluble and persists with a long half life once ingested. This is in contrast to warfarin and is a characteristic of some of the second generation 4-hydroxy coumarin derivatives that makes them particularly hazardous with repeated exposure because of their ability to bioaccumulate and display very prolonged anticoagulant activity in exposed mammals including humans.

3.3.2.1. 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 for difenacoum prepared by the Rapporteur Member State Finland. The threshold limits and labelling regarding human health risks listed in Annex 4 "Toxicology and metabolism" must be taken into consideration. There are no new studies post annex I that impact on the original toxicological assessment carried out by the RMS.

Summary of acute toxicity data for the active substance Difenacoum

Parameter	Test material	Species	Result	Classification	Ref.
Acute Oral Toxicity	Difenacoum technical, 99.7 % w/w purity	Rat CRL:(WI)BR (Wistar), Female: 3/dose, (two low dose groups)	5 < LD_{50} < 50 mg/kg bw	T+; R28 / Acute Tox. 2; H300	[redacted] (2004) Study Code: 04/904-001P
	Acceptability (Y/N): Y		**Method**: OECD Guidelines 423 (2001)		**GLP (Y/N): Y**
	Comments: No deviations. The method used was not intended to allow the calculation of a precise LD50 value.				
Acute Dermal Toxicity	Difenacoum technical, 99.7 % w/w purity	Rat CRL:(WI)BR (Wistar), female / male: 5/sex/group	LD_{50} = 51.5 mg/kg bw (females)	T+; R27 / Acute Tox. 1; H310	[redacted] (2004) Study Code: 04/904-002P
	Acceptability (Y/N): Yes		**Method:** OECD Guidelines 402		**GLP (Y/N): Yes**
	Comments: Males and females in low dose group (20 mg/kg bw) only. Only females in the other 2 dosing groups (55 & 155 mg/kg bw). 2 out of 5 males died in the low dose group, compared with 3 out of 5 for the mid and 5 out of 5 for the top dose groups. The LD_{50} value was calculated for female rats only (51.5 mg/kg bw) even though males were apparently more sensitive. Due to the overall mortality (both sexes) the risk phrase R27; Very toxic in contact with skin, was warranted by the RMS.				
Acute Inhalation	Difenacoum	Rat	Males: LC_{50} =	T+; R26 / Acute	[redacted] (1995)

Parameter	Test material	Species	Result	Classification	Ref.
Toxicity	technical, 97.7 % w/w purity	CRL:(WI)BR (Wistar), female / male	20.74µg/L/4h Females: LC_{50} = 16.27µg/L/4h	Tox. 2; H330	Report no. MLS/9825
	Acceptability (Y/N): Yes		**Method:** Complies with OECD 403		**GLP (Y/N): Yes**
	Comments: Groups of 5 male and 5 female rats were exposed, nose only for a single four hour period to aerosols of difenacoum technical material. The aerosols had concentrations of 3.28, 7.52 and 20.33µg/L. Two males and four females were killed in extremis following exposure to 20.33µg/l. Clinical signs, delayed deaths and post mortem findings were consistent with anti-coagulant poisoning. Only slight signs of toxicity were seen in animals exposed to the lower concentrations. The LC_{50} value is 20.74µg/L/4h (95% confidence limits 12.03-39.76) for males and 16.27 µg/L/4h (95% confidence limits 10.03-26.24) for females.				
Acute Dermal Irritation	Difenacoum technical, 99.7 % w/w purity. Batch 03652.	Rabbit, male, NZW, 3 in total	No irritation.	none	[redacted] (2004). Study code: 04/904-006N
	Acceptability (Y/N): Yes		**Method:** Complies with OECD 404		**GLP (Y/N): Yes**
	Comments: Pure difenacoum technical was applied in a single dose of 0.5 g to the shaven skin of all experimental animals. After 4 hours test article was removed and animals were examined 1, 24, 48 and 72 hours after patch removal. No irritation symptoms (erythema and oedema) or other signs were recorded (Draize scores of 0, all time points). Difenacoum is not a skin irritant.				
Acute Eye Irritation	Difenacoum technical, 99.7 % w/w purity. Batch 03652.	Rabbit, male, NZW, 3 in total	No irritation.	none	[redacted] (2004). Study code: 04/904-005N
	Acceptability (Y/N): Yes		**Method:** OECD 405 (2002)		**GLP (Y/N): Yes**
	Comments: 0.1 g of difenacoum technical was applied to the left eye of each animal. The untreated right eye served as control. The treated eyes of the test animals were not washed out following the instillation of 0.1g of test item. The eyes were examined at 1, 24, 48, and 72 hours after application. There was no evidence of irritation by the active substance (Draize scores of 0 for 24, 48, & 72 hour time points).. Difenacoum is not an eye irritant.				
Skin Sensitisation (M & K study)	Difenacoum, as a technical concentrate of the a.s. (2.6% w/v) in solvent. Batch SC7396.	Guinea Pig, (Dunkin-Hartley), male & female. Control group: 5 male, 5 female. Test group: 10 male & 10 female.	No sensitisation.	none	[redacted] (1996). Report number CIT/14302
	Acceptability (Y/N): Yes		**Method:** OECD 406		**GLP (Y/N): Yes**
	Comments: Preparation for induction; intradermal injections at day 0, a 1% (w/w) preparation of the technical concentrate in isotonic saline solution and Freund's complete adjuvant. On day 7, sodium laurylsulphate in vaseline (10% w/w) was applied on the test site to induce local irritation. On day 8, this same test site was treated by topical application of the test substance (technical concentrate with 2.6% difenacoum w/v) or the vehicle (control group) and was covered by an occlusive dressing for 48 hours. Challenge was performed on day 22 with undiluted test substance (technical concentrate with 2.6% difenacoum w/v). Test substance and vehicle were maintained under an occlusive dressing for 24 hours. Skin reactions were evaluated at 24 and 48 hours. There were no clinical signs or mortalities during the study. No cutaneous reactions were recorded after the challenge application. Positive controls were acceptable. Dilution of a liquid sample of very low water solubility with isotonic saline solution is highly questionable.				
Skin Sensitisation (Buehler study)	Difenacoum, as a technical concentrate of the a.s. (2.6% w/v) in solvent. Batch TCP 0047/94.	Guinea Pig, (Dunkin-Hartley), male & female. Control group: 5 male, 5 female. Test group: 10 male & 10 female.	No sensitisation.	none	[redacted] No. MLS/10009
	Acceptability (Y/N): Yes		**Method:** OECD 406		**GLP (Y/N): Yes**
	Comments: On day 1 the test site was treated by topical application of the test substance (10				

Parameter	Test material	Species	Result	Classification	Ref.
	% w/v preparation of the formulation in deionised water) or the vehicle (control group) and was covered by an occlusive dressing for 6 hours. This was repeated at 7 day intervals to give a total of three 6 hour exposures over 14 days. The animals were left untreated for 14 days prior to challenge. Challenge consisted of topical application of test substance (10 % and 3% w/v preparation of the formulation in deionised water) and vehicle were maintained under an occlusive dressing for 6 hours. Skin reactions were evaluated at 24 and 48 hours. There were no clinical signs or mortalities during the study. No cutaneous reactions were recorded after the challenge application. Dilution of a liquid sample of very low water solubility with deionised water is highly questionable.				

Difenacoum is acutely very toxic by the oral and inhalation routes. Difenacoum may also be considered very toxic by the dermal route. It is not a skin or eye irritant. Difenacoum is not a skin sensitiser.

Summary of difenacoum subchronic, chronic, mutagenic and reproductive toxicity.

Repeated oral administration of difenacoum to rats in diet at doses up to 0.06 mg/kg bw/day for 90 days gave rise to increased kaolin-cephalin times and histological findings indicative of toxic effects related to anticoagulation only at the highest dose level. No other adverse effects were observed. A suggestive NOAEL value can be established at 0.03 mg/kg bw/day.

Repeated oral exposure to difenacoum results in toxic effects related to anticoagulation giving cause to concern for serious damage to health by prolonged exposure. Furthermore, based on the results of the acute dermal and inhalation toxicity studies and route-to-route extrapolation, it is justified to assume a similar concern for serious damage to health by prolonged exposure through dermal and inhalation routes also. Difenacoum classifies for repeated dose toxicity; T; R48/23/24/25, Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed.

Difenacoum was not mutagenic in bacterial cells, but the mutation frequency and chromosome aberrations were increased in mammalian cells *in vitro*. All *in vivo* genotoxicity tests were negative. It can be concluded that difenacoum does not classify as mutagenic.

Developmental toxicity tests have been performed in two species. In the rabbit, the LOAEL value for maternal toxicity is 0.001 mg/kg bw/day. A higher incidence of foetal effects (skeletal variations) was observed at two dose levels compared to controls, but the incidence was not dose dependent. The NOEL/NOAEL value for developmental toxicity is 0.01 mg/kg bw/day. The NOEL/NOAEL for maternal toxicity in rats is 0.03 mg/kg bw/day. There was no evidence of embryotoxic or teratogenic potential following oral exposure of pregnant rats at 0.09 mg/kg bw/day (=NOEL/NOAEL for developmental toxicity).

Clear developmental toxicity was not observed in rabbits or rats. However, difenacoum should be considered teratogenic to humans because it contains the same chemical moiety responsible for the teratogenicity of warfarin, a known human teratogenic agent, and it has the same mode of action that is a known mechanism of teratogenicity in humans. The possible teratogenic effects of coumarin-related compounds cannot be detected using the standard OECD 414 study design, because the exposure period has to be adjusted to correspond to the critical periods in rat for the observed effects in humans. Furthermore, maternal bleeding has to be prevented, e.g. by vitamin K supplementation, to achieve a biochemical blockade of net extrahepatic vitamin K – dependent processes. Based on read across from warfarin, difenacoum is classified for reproductive toxicity, Repr. Cat. 1; R61, "May cause harm to the unborn child". In addition, specific concentration limits have been set by the RMS due to the very high acute toxicity associated with difenacoum.

Effects on fertility have been studied in a rat multi-generation study. In this study, dose levels had to be lowered twice during the course of the study due to extensive mortality. Regardless of the very low

doses, it can be concluded that difenacoum does not have clear effects on fertility. However, there were indications of disturbed oestrous cycling perhaps due to ovarian hormonal disturbances. Because the main findings related to fertility (irregular oestrous cycles in treated animals in both generations and ovarian cysts at a maternally toxic dose of 0.06 mg/kg bw/day in F0 females) did not affect the fertility index, no severe increase in post-implantation loss (increased spontaneous abortions have been associated with warfarin treatment in humans) were observed, and warfarin is not classified for fertility, it is considered that classification for fertility effects is not necessary for difenacoum. In the literature, there are no indications of adverse fertility effects associated with warfarin or vitamin K recycling blockade. It is considered that the possible effects on ovarian function are adequately covered by the risk phrase R48/23/24/25.

There are no studies on neurotoxicity. Other studies with difenacoum did not reveal any neurotoxic potential and there are no structural alerts evident for this endpoint.

Data requirements: (List if applicable)
None.

3.3.2.2. Toxicology of the biocidal product

The toxicology of the biocidal product 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.

Summary of acute toxicity data for the biocidal product Ruby Paste

Parameter	Test material	Species	Result	Classification	Ref.
Acute Oral Toxicity	Difenacoum pasta bait Batch: LAB290109	Rat, female, Sprague-Dawley, SPF Caw, 6 in total.	LD_{50} > 2000 mg/kg bw	none.	[redacted] (2009). study number: TAO423-PH-09/0086
	Acceptable (Y/N): Yes		**Method:** OECD 423 (24 April 2002)		**GLP (Y/N): Yes**
	Comments: No mortality occurred during the study at 2000mg/kg. There were no clinical signs observed. Macroscopic examination of the animals at the end of the study revealed a thickening of the corpus (5/6 animals) with presence of red spots (3/6 animals). Considering the water solubility of the active substance is extremely low, the use of a water vehicle for gavage is questionable. 2g of paste was mixed with 10 ml water prior to use.				
Acute Dermal Toxicity	Difenacoum paste bait. Batch: LAB290109	Rat, male & female, Sprague-Dawley, SPF Caw, 10 in total.	LD_{50} > 2000 mg/kg bw	none.	[redacted] (2009). study number: TAD-PH-09/0086
	Acceptable (Y/N): Yes		**Method:** OECD 402 (24 Feb 1987)		**GLP (Y/N): Yes**
	Comments: No mortality occurred during the study at 2000mg/kg. No cutaneous reactions or systemic clinical signs related to the administration of the test item were observed. Some slight pink colouration of the test site was observed. Considering the water solubility of the active substance is incredibly low, the use of a water vehicle for dermal application is questionable.				
Acute Inhalation Toxicity	none	none	none	none	none
	Acceptable (Y/N):		**Method:**		**GLP (Y/N):**
	Comments: Inhalation exposure is not appropriate for a wrapped paste formulation. Active substance has very low volatility and is only present at 0.005% (w/w) in the product. Company justification accepted.				
Information on mixture of biocidal products	none	none	none	none	none
	Acceptable (Y/N): Yes		**Method:**		**GLP (Y/N):**
	Not applicable since following the proposed uses of the product and the label claims, the rodenticide is not intended to be used in a mix with other biocidal products. Company justification accepted.				

Parameter	Test material	Species	Result	Classification	Ref.
Acute Skin Irritation	Difenacoum pasta bait Batch: LAB290109	Rabbit, male, NZW, 3 in total	No irritation	none	[redacted] (2009). study number: IC-OCDE-PH-09/0086
	Acceptable (Y/N): Yes		**Method:** OECD 404 (24 April 2002)		**GLP (Y/N): Yes**
	Comments: The test item was applied at a dose of 0.5 g, on an undamaged skin area of one flank of each animal for 4 hours. No cutaneous reactions (erythema and oedema) were observed on the treated areas. Company report accepted. Results do not warrant classification under the conditions of the study.				
Acute Eye Irritation	Difenacoum pasta bait Batch: LAB290109	Rabbit, male, NZW, 3 in total	Slight irritation	none	[redacted] (2009). study number: IC-OCDE-PH-09/0086
	Acceptable (Y/N): Yes		**Method:** OECD 405 (24 April 2002)		**GLP (Y/N): Yes**
	Comments: The test item was applied at a dose of 0.1 g instilled into the conjunctival sac of one eye in each animal. Ocular conjunctivae reactions observed during the study were slight to moderate and totally reversible by 4 days in the three animals. Company report accepted. Results do not warrant classification under the conditions of the study.				

Animal number	A9661	A9678	A9679
Corneal Opacity	0	0	0
Iritis	0	0	0
Redness	1.7	0	0.7
Chemosis	1.7	0.3	0.3
Result	-	-	-

Skin Sensitisation (M&K)	Difenacoum pasta bait Batch: LAB290109	GuineaPig, female, Dunkin-Hartley strain, 5 in negative control, 11 in treated groups.	negative	none	[redacted] (2009). study number: SMK -PH-09/0086
	Acceptable (Y/N): Yes		**Method:** OECD 406 (17 July 1992)		**GLP (Y/N): Yes**

Comments: The study format was a Guinea Pig maximisation method skin sensitization test. The test item was given at 40% at intradermal induction and 70% and 35% at challenge phase. The study used 5 concurrent controls and 11 treated animals.

Animals	70% (MNIC)				35% (1/2 MNIC)			
	24 hours		48 hours		24 hours		48 hours	
	Erythema	Oedema	Erythema	Oedema	Erythema	Oedema	Erythema	Oedema
Negative control group								
1882 F	0 depilation	0	0	0	0	0	0	0
1883 F	0 depilation	0	0	0	0	0	0	0
1884 F	0 depilation	0	0	0	0	0	0	0
1885 F	0 depilation	0	0	0	0	0	0	0
1886 F	0 depilation	0	0	0	0	0	0	0
Treated group								
1887 F	0	0	0	0	0	0	0	0
1888 F	0 depilation	0	0	0	0	0	0	0
1889 F	0 depilation	0	0	0	0	0	0	0
1890 F	0	0	0	0	0 depilation	0	0	0
1891 F	0 depilation	0	0	0	0 depilation	0	0	0
1892 F	0	0	0	0	0	0	0	0
1893 F	0 depilation	0	0	0	0	0	0	0
1894 F	0 depilation	0	0	0	0 depilation	0	0	0
1895 F	0	0	0	0	0	0	0	0
1896 F	0 depilation	0	0	0	0 depilation	0	0	0
1897 F	0 depilation	0	0	0	0 depilation	0	0	0

Parameter	Test material	Species	Result	Classification	Ref.
	Under the condition of the test Difenacoum pasta bait does not require classification for sensitisation.				

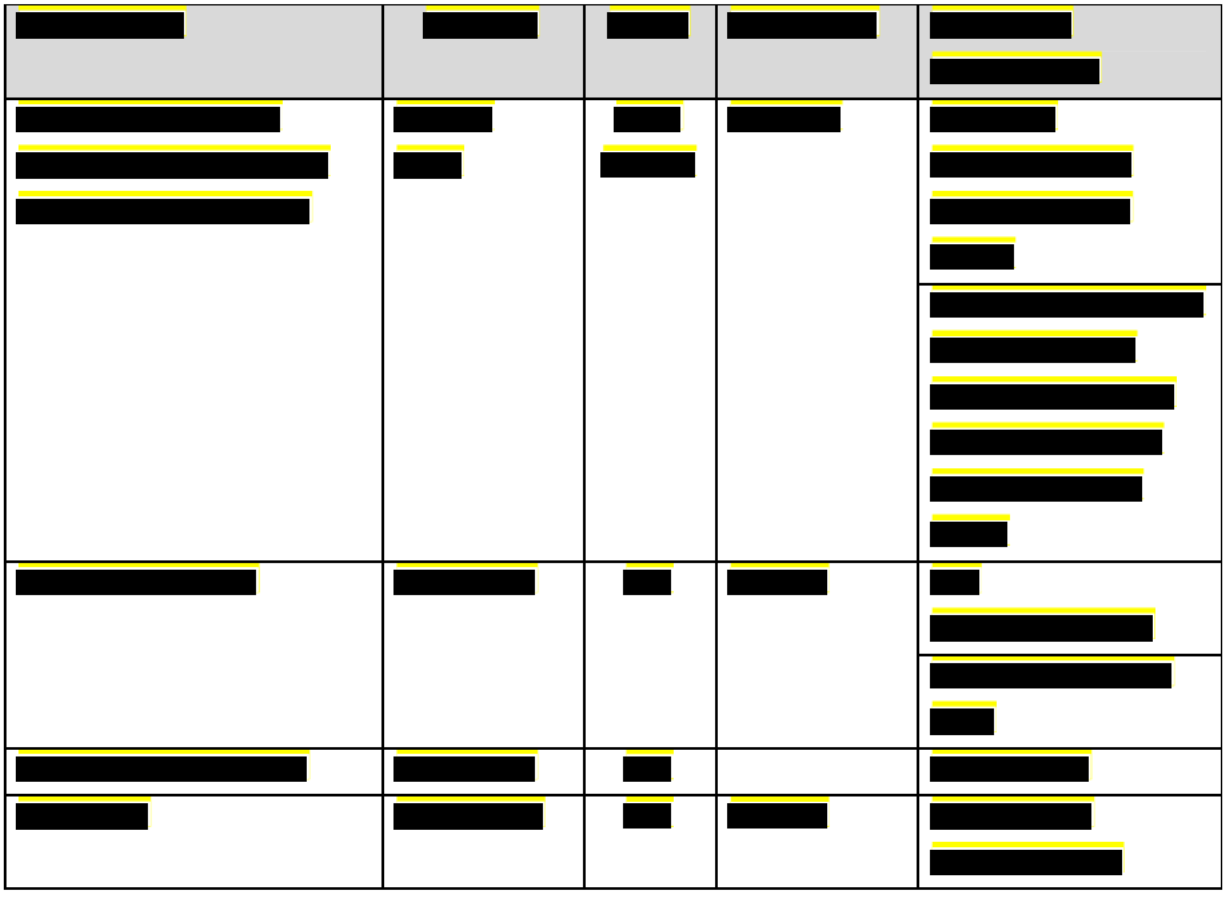
Conclusion:
According to the results of the toxicological studies, Ruby Paste (containing 50mg/kg difenacoum) does not classify with respect to Directive 1999/45/EC or Regulation (EC) No 1272/2008. However, safety phrases and precautionary statements are proposed by the Rapporteur. One issue that seems to be not addressed by the acute studies above is the solubility of difenacoum in aqueous media. According to the physical / chemistry properties of the active substance, difenacoum has extremely low water solubility (4.83×10^{-4} g/l at pH 6.5 or < 0.5mg per litre, 3.72×10^{-3} g/l at pH 8.9). This affects the amount of active substance in a dose such that between 5 – 40% of the expected amount might be present in the acute oral study, there is no way of being certain from the available data.

Data requirements: (List if applicable)
None.

3.3.2.3. Toxicology of the co-formulants (substances of concern)

The biocidal product contains no other substances in quantities that would be of toxicological concern. The majority of these components are food grade materials and are not classified.

Summary of toxicological properties of the co-formulants in Ruby Paste



3.3.3. Exposure Assessment for Human Health

There are no exposure or risk assessment studies based on the paste, the notifier has instead performed exposure and risk modeling using wax blocks and this is accepted by the Rapporteur. In addition, since TM III 06 there has been general agreement to model paste bait in sachet by using the data determined for wax blocks in the Chambers Study. The paste and the blocks are similar in bait composition, additionally, the paste baits are wrapped in a bag or sachet, and thus exposure to humans and the environment is considered to be lower than that expected with the blocks. The most relevant route of exposure to the active substance is the dermal route. The bait product typically takes the form of a semi-solid fatty block with a strong sweet smell containing 0.005% w/w difenacoum. The wax blocks are made in a range of shapes and sizes, being typically rectangular, and weigh 20g (though they can of course be larger in size). The blocks are dyed various bright colours to make them unattractive to wildlife, and birds.

The active substance has a low vapour pressure, therefore the potential for evaporation is low, and hence the potential for inhalation exposure is low. Inhalation exposure is only of concern during the formulation process where the active substance has a potential for becoming airborne when mixed with dry bait ingredients. In the case of wax blocks (and paste), inhalation exposure is irrelevant.

Any potential oral exposure will be indirect exposure via possible release to the environment. Other possible exposure scenarios include dermal contact with dead animals and accidental ingestion of poison baits by children.

In general there is very little data available for use in modelling human exposure to rodenticides. Any calculations must be viewed in the context of the use of many assumptions and extrapolations from only a few studies. The values presented for exposure assessment and risk characterisation must be viewed at best as being crude estimates.

Key Endpoints for Exposure Assessment

The key endpoints for exposure assessment are the No Observed Adverse Effect Level (NOAEL) for Margin of Exposure (MOE) estimates and the Acceptable Exposure Level (AEL). The lowest Low Observed Adverse Effect Level (LOAEL) in a repeated dose study, (developmental toxicity study in rabbits, LOAEL value for maternal toxicity is 0.001 mg/kg bw/day, Difenacoum CAR, 2009), was chosen as the basis to establish the AEL and calculate an NOAEL for MOE. Risk characterisation in the original CAR for difenacoum and in documents supplied by the notifier in support of Ruby Paste state the bioavailability of difenacoum as 68% following oral absorption of a single low dose in bile duct cannulated rats (Swan, 2006, Difenacoum – Metabolism in Rats. Report no. PLG 0005). However, a true measure of bioavailability must also consider enterohepatic circulation because it is important to consider the reabsorption of lipophilic compounds with long half-lives from the gastrointestinal tract such as difenacoum. Bioavailability may be under-estimated in this case but it is taken as 68% for the

purpose of exposure assessment in this document. Details for the derivation of each endpoint are described below.

NOAEL for MOE:

LOAEL value for rabbit maternal toxicity is 0.001 mg/kg bw/day. To extrapolate from LOAEL to NOAEL an assessment factor of 2 is considered justified due to the steep dose response to acute effects such as lethality. Correction for bioavailability of 68% is applied.

$(0.001 \div 2) \times (68/100) =$ **3.4×10^{-4} mg/kg bw/day**

AEL:

LOAEL value for rabbit maternal toxicity is 0.001 mg/kg bw/day. Default assessment factors of 10 for inter-species variability and 10 for inter-individual variability are applied. Furthermore, due to the toxicological significance and uncertainty in the database, an additional safety factor of 3 for teratogenicity is used for all anticoagulant rodenticides. An additional assessment factor of 2 is supported due to concern over the higher potency of the second generation anticoagulants compared to warfarin and the much higher vulnerability of human foetuses to disturbances in vitamin K recycling and availability compared to rodents. Correction for bioavailability of 68% is applied.

$((0.001 \div (10 \times 10 \times 3)) / 2 = 1.67\times10^{-6}$ mg/kg bw/day

taking into account 68% bioavailability...

$(1.67\times10^{-6}) \times (68/100) =$ **1.13×10^{-6} mg/kg bw/day**

3.3.3.1. Exposure to professional users

The paste baits and wax blocks are used in plastic bait boxes or covered/protected bait points or tied to a fixed object. For professional use, the operator is trained in the correct use of the bait, i.e. placement, number of bait points or stations required based on the infestation rate area, the number of bait blocks per bait point and safe handling procedures. The use of PPE, i.e. disposable gloves and a face-mask may be used when loading bait boxes and disposing of remaining bait and carcasses. However, when the block is contained within a bait trap there will be no exposure of the operator to the product. PPE (coverall, boots and gloves) is required as standard when the blocks are used in sewage systems.

For rats each bait point should contain up to a maximum 10 blocks (i.e. 200g of bait). A mouse bait point will only contain 2 bait blocks. Bait points for mice should be placed 5m apart, although this can be reduced to 2m in areas of high infestation and for rats, bait points should be 10m apart or reduced to 5m apart in high infestation areas. Bait points should be checked frequently and carcasses removed. Operators should search for all rodent bodies in and around the baited area for disposal. Bait points should be removed, in a typical campaign, 6 weeks after initial placement. Sites should not be re-baited until a new infestation is observed.

In sewers, blocks are tied or nailed to stable surfaces above the water level. Blocks placed in sewers are not normally removed. Rodent bodies in sewers will not be collected for disposal

During use, professional pest control operators will be exposed to rodenticide product during (1) the mixing and loading phase (not applicable for ready-to-use paste or wax block baits, however it is valid in the case of grain baits), (2) loading of bait boxes/bait points and application of the blocks in sewers, (3) post application activities including the disposal of old bait and carcasses. Exposure will be via the dermal route and principally involve the hands.

Exposure calculations (Wax Blocks) – professionals

The CEFIC/EBPF Rodenticides Data Development Group conducted an operator exposure study using flocoumafen (which may be considered a suitable surrogate for all other second generation anti-coagulants) to determine exposure during simulated use of rodenticide baits (*Chambers* 2004, unpublished, confidential). This study examined exposure to wax blocks and grain bait. Guidance is also taken from a confidential paper entitled "Harmonised Approach for Rodenticides" by the German Competent Authority, Bundesanstalt für Arbeitsschutz und Arbeitsmedizin (BAuA).

The daily exposure frequency and its division between different tasks are based on a survey organised by CEFIC (and based on a questionnaire answered by selected pest control companies in several EU countries), and on an agreement between Member States on the common approach for exposure assessment and ECB guidelines (see CAR September 2009). A dermal absorption of 0.047% is used for all exposure calculations based on the Roban wax block, during 24 h after 8 h exposure in an *in vitro* study with human skin (see CAR September 2009).

The Chambers study determined exposure from the application phase from the following scenario: 5 operators secured 5 compressed wax blocks (each of 20g, in total 100g bait per box) into a bait station by pushing bait mounting pegs in the stations through holes in wax blocks. Three trials were conducted with 1, 5 and 10 times securing of these wax blocks. Since the results of 1, 5 and 10 securing are similar all trials were included in the calculation of the 75th percentile by the RMS. The proposed value of **28mg (of wax bait) per manipulation** is valid for loading of one bait box with 100g of wax blocks (a single manipulation constitutes the placement of a single bait station). Since the recommended amount for rat control is up to 200g bait per bait point, this exposure value is multiplied by a factor of 2 because only 100g was used in the Chambers Study. The proposed value of **56mg (of wax bait) per manipulation** is valid for loading of one bait box with 200g of wax blocks.

For professional operators the potential total daily dermal exposure (assuming the previously agreed number of 60 manipulations from TM III/10 is applied) from the application-phase is **3360mg** wax block product (i.e. 56mg × 60 bait sites).

The Chambers study determined exposure from the disposal or post-application phase from the following scenario: 5 operators emptied a loaded bait station by sliding the wax block off the mounting pegs into a 10 L plastic bucket. This is done 1, 5 and 10 times. The proposed value of **5.75 mg per manipulation (determined by the RMS, Difenacoum CAR 2009)** is valid for cleaning of one bait box. For the resulting potential dermal exposure of post-application-phase the agreed number of 15

manipulations (TM III/10) should be taken into account. For the post-application phase the potential total daily dermal exposure is **86 mg** wax block product (i.e. 5.75mg × 15 disposal manipulations). The size of one bait block is ignored and the figure is valid for different sized blocks (e.g. 10g, 100 g).

The calculation of PCO (pest control operator) and amateur dermal exposure in placing and clean-up of rodenticidal wax blocks, taking into account measured values (75th percentiles), defaults according to ECB guidelines and the common agreement on daily exposure frequencies (TM III/10) is presented in the following table.

Pest Control Operator, No PPE:	
Amount of exposure to product (75th percentile) during securing of 10 wax blocks (200g). Value is for placement of 1 bait station.	56.0 mg
Amount of difenacoum on fingers/hands (0.005% in wax block)	56 mg × (0.005 / 100) = 2.8×10^{-3} mg
Systemic dose per application at 1 bait station: (dermal absorption 0.047%, bw 60kg)	(2.8×10^{-3} mg x (0.047 / 100)) / 60kg = 2.2×10^{-8} mg/kg
Amount of exposure to product (75th percentile) during clean-up and disposal per bait station	5.75 mg
Systemic dose (difenacoum concentration 0.005%, dermal absorption 0.047%, bw 60 kg) per clean-up of one bait station.	2.25×10^{-9} mg/kg
Assuming 'reasonable worst case' scenario of 60 bait sites and 15 clean-ups, systemic dose per day	((2.2×10^{-8} mg/kg × 60) + (2.25×10^{-9} mg/kg × 15)) = **1.35×10^{-6} mg/kg/day**
Expressed as a % of the AEL: AEL = 1.13×10^{-6} mg/kg bw/day	**120%**

Pest Control Operator, With PPE (gloves)	
Default 10-fold reduction of exposure.	**1.35×10^{-7} mg/kg/day**
Expressed as a % of the AEL: AEL = 1.13×10^{-6} mg/kg bw/day	**12%**

Non-Trained Professional (e.g. farmer), No PPE:	
Systemic dose resulting from application of 10 bait blocks into each bait point (200g bait), placement of five bait points plus five bait sites cleaned per day, no PPE (difenacoum concentration 0.005%, dermal absorption 0.047%, bw 60 kg).	((2.2×10^{-8} mg/kg × 5) + (2.25×10^{-9} mg/kg × 5)) = **1.21×10^{-7} mg/kg/day**
Expressed as a % of the AEL: AEL = 1.13×10^{-6} mg/kg bw/day	**11%**

Non-Trained Professional (e.g. farmer), With PPE (gloves):	
Default 10-fold reduction of exposure.	**1.21×10^{-8} mg/kg/day**
Expressed as a % of the AEL:	

AEL = 1.13×10^{-6} mg/kg bw/day **1%**

3.3.3.2. Exposure to non-professional users

Description of tasks and amateur exposure to Difenacoum

Bait boxes for use by the general public may be supplied as sealed units or as lockable, tamper-proof units that may be refilled by the user. Bait may be used in covered/protected bait points, rather than bait boxes, where appropriate.

Calculations for non-professional exposure are presented below; the first scenario assumes no exposure during application phase while the second scenario assumes that the bait boxes would have to be loaded by the user. As for the non-trained professionals, it is assumed that a non-professional user places ten bait blocks per site(200g) on five bait sites and cleans five bait sites per day.

Product type	Exposure scenario	PPE	Inhalation uptake	Dermal uptake
14	Non-professional (amateur)	None	Not relevant	1.1×10^{-8} mg/kg/day[1)]
14	Non- professional (amateur)	None	Not relevant	1.21×10^{-7} mg/kg/day[2)]

1) scenario 1; 2) scenario 2.

Scenario 1: No dermal contact during placing of baits due to sealed bait boxes. Potential exposure is only during clean-up. Default exposure value for cleanup is 5.75mg product per bait site, difenacoum present at a concentration of 0.005% (w/w), 60kg body mass, 0.047% dermal absorption value. The value is calculated from the cleanup exposure per bait station of ((2.25×10^{-9} mg/kg) × 5).

Scenario 2: Assuming that conventional bait boxes are loaded then the exposure is equal to that of the non-trained professional (e.g. farmer) with no PPE. As a worst case scenario, scenario 2 can be taken forward to risk assessment.

3.3.3.3. Exposure to children/workers/general public

Bait points should be covered or protected in such a way to prevent access to the bait. However, the ingestion of wax block bait by infants has been assessed as a potential secondary exposure route associated with the use of difenacoum in rodenticide products. Secondary exposure is anticipated to be acute in nature. The pasta bait has been manufactured to prevent incidental poisoning to both non-target animals and man, i.e. children. The Ruby Paste "tea sachets" are hard plastic and are either locked or sealed shut to prevent access to the bait. If bait sachets 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. The estimated exposure for the 'transient mouthing of poison bait' scenario is either 2.5×10^{-2} mg/kg or 5.0×10^{-5} mg/kg, depending on the default assumptions. This results in Margin of Exposure (MOE) values of 0.01 or 6.8, respectively. It

shows that infants are at significant risk for secondary exposure, i.e. there is no safe use for children.

For the 'transient mouthing of poison bait' scenario, either 5g (User Guidance) or 10 mg (TNsG, with bittering agent) of the product is assumed to be swallowed by an infant per poisoning event.

TNsG Assumptions: Transient mouthing of poison bait (10mg) treated with repellent:
(10mg × 0.00005) / 10kg bw
=
5.0×10^{-5} mg/kg bw.

Relative to the calculated NOAEL for MOE:
3.4×10^{-4} / 5.0×10^{-5} = **6.8**

User Guidance Assumptions: Transient mouthing of poison bait (5000mg) without repellent;
(5000mg × 0.00005) / 10kg bw
=
2.5×10^{-2} mg/kg bw.

Relative to the calculated NOAEL for MOE:
3.4×10^{-4} / 2.5×10^{-2} = **0.01**

The RMS considered that in connection with transient mouthing of poison baits, infants are also exposed via the dermal route while handling the bait. This however is assumed to play a minor role relative to the amount that could be ingested. It is therefore not included in the overall exposure scenario.

3.3.3.4. Exposure to consumers from residues in food

Not applicable

3.3.3.5. Overall Summary

The exposure data based on measurements in simulated use conditions are acceptable and should be used in risk assessment. The models assume that inhalation exposure is of minor importance for wax blocks (paste bait) compared with dermal exposure. The calculations have been made with the assumptions of rat control, and there are no separate calculations to assess exposure in mice control in which smaller bait sizes are used.

3.3.4. Risk Characterisation for Human Health

3.3.4.1. Professional users

The exposure assessment for professional pest control operators (PCOs) under reasonable worst case assumptions (60 loadings and 15 clean-ups/day), as presented in section 3.3.3.1, yielded a potential dermal exposure leading to a systemic dose of 1.35×10^{-6} mg/kg/day for an unprotected operator during bait handling operations. Comparison to calculated NOAEL for MOE shows that the use of rodenticide baits containing 0.005% difenacoum results in a margin of exposure of 252.

Since pest control operators wear protective gloves by default during pest control operations, a refined assessment is conducted. The resulting margin of exposure (MOE = 2519) indicates that the use of rodenticide baits containing 0.005% difenacoum does not cause a risk for PCOs if gloves are worn.

3.3.4.2. Non-professional users

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 1.21×10^{-7} mg/kg/day for an unprotected person. Even without PPE, the resulting margin of exposure (MOE = 2804) indicates that use of rodenticide baits containing 0.005 % difenacoum is not a risk at the stated exposure frequency. A refined assessment was, nevertheless, conducted since wearing of protective gloves is recommended in the instructions for use. The resulting margin of exposure (MOE = 28041) indicates a high level of protection for non-trained professional users when gloves are worn.

The result of the risk assessment concerning use of difenacoum in bait Blocks indicates that the acceptable exposure level is exceeded for trained professionals (PCOs) not using PPE (gloves) and that the AEL is not exceeded for professionals with PPE and non-trained professionals using the product with or without PPE (gloves). The risk is at an acceptable level without gloves for non-trained professionals. However, use of protective gloves is recommended in all cases for hygiene reasons. Exposure during manufacture of the active substance and formulation of products is beyond the scope of BPD and therefore has not been addressed in this document.

Blocks are supplied either in pre-sealed units or as loose blocks for use in covered/protected bait points or refillable bait boxes. An exposure assessment has been performed taking into account potential exposure both from application and post-application tasks as a worst-case scenario. In the calculations, amateurs were assumed to load five bait points and clean five bait points per day without PPE. The estimated daily systemic dose, 1.21×10^{-7} mg/kg/day, results in an MOE value of 2804 showing that there is also little risk to amateurs.

3.3.4.3. Children/Workers/general public

As a potential secondary exposure route, associated with the use of difenacoum in rodenticide products, ingestion of wax block bait by infants has been assessed. 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 indicating that infants are at risk of poisoning. This should be addressed by ensuring all difenacoum products targeted for amateur use are provided in sealed packs and tamper resistant bait boxes with a bittering agent. The potential exposure due to dermal contact with poisoned rodents is not included in the risk assessment because the available scenarios are unrealistic.

3.3.4.4. Consumers from residues in food

Not applicable, product is not used to treat food stuffs.

3.3.4.5. Overall Summary

The calculations presented have been made with the assumptions of rat control, and there are no separate calculations to assess exposure for mice control in which smaller bait sizes are used.

Using both the MOE and AEL approaches for risk assessment indicates 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 with PPE, untrained professionals and amateurs (with and without PPE). The product is deemed suitable for authorisation and appropriate personal protective equipment is advised.

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 in sealed packs and the use of tamper resistant bait boxes are essential to reducing the risk of secondary exposure. Baits should not be placed where food, feeding stuffs or drinking water could be contaminated.

Workplace operation	**PPE**	**Exposure path**	**Dose (mg/kg bw/day)**	**MOE**	**%AEL**
Trained Professional: Placing of wax block baits and clean-up	None	Dermal, hands	1.35×10^{-6}	252	120
Trained Professional: Placing of wax block baits and clean-up	Protective gloves	Dermal, hands	1.35×10^{-7}	2519	12
Non-Trained Professional: Placing of wax block baits and clean-up	None	Dermal, hands	1.21×10^{-7}	2804	11
Non-Trained Professional: Placing of wax block baits and clean-up	Protective gloves	Dermal, hands	1.21×10^{-8}	28041	1
Amateur: Placing of wax block baits and clean-up	None	Dermal, hands	1.21×10^{-8}	28041	1
Secondary Exposure Transient Mouthing of bait by infants	--	Oral	5.0×10^{-5} (TNsG)	7	--
			2.5×10^{-2} (User Guidance)	0.01	--

3.3.5. Hazard Assessment for the Environment

The Finnish Competent Authority evaluated the active substance difenacoum in 2009. No further fate and behaviour studies were identified as necessary to support the authorisation of the active substance. An overview of the EU fate and behaviour and the ecotoxigology of difenacoum in the environment is presented hereunder:

Environmental fate and behaviour

Difenacoum has two stereogenic centres and thus consists of four diastereoisomers (two enantiomer pairs). The methods of analysis used in the available environmental fate and behaviour studies did not resolve the enantiomers, therefore no information is available on the rate of breakdown or transformation of the different individual enantiomers.

Difenacoum is hydrolytically stable at pH 4, 7 and 9 at 25°C (DT_{50} >1 yr). Under aqueous photolysis degradation is rapid (half-life about 8 hours or less). In the photolysis study of Activa/Pelgar two breakdown products above 10% were detected, and a proposal for the identification of structures was made. In the natural aquatic environment photodegradation is regarded to be of minor significance since surface water is normally deeper and muddier compared to conditions in laboratory studies. Therefore the aqueous photolysis metabolites were not considered in the exposure assessment.

Difenacoum has an estimated half-life of approximately 2 hours in air. Consequently, it is predicted to have a negligible effect on stratospheric ozone. Difenacoum shows no absorption in the so-called atmospheric window (800-1,200 nm) and therefore, according to the TGD on risk assessment (Part II, Section 3.7.2) is not a potential greenhouse gas.

Difenacoum is not readily or inherently biodegradable. Difenacoum degrades slowly under aerobic conditions in soil, with a measured DT_{50} of 439 days (20°C). Photolysis may contribute to the degradation in soil. No information is provided on soil metabolites in the CAR. The CA for difenacoum (FI) stated *"due to the low direct exposure and difenacoum being not ready biodegradable and probably absorbed to soil, the ecotoxicological significance of soil metabolites is regarded low".*[18]

Difenacoum has a measured pKa of 4.84 (20°C) and a water solubility that is pH dependent (range <0.05 mg/L at pH 4 to 61 mg/L at pH 9, pH 7 value 1.7 mg/L all at 20°C). Therefore, in the environmentally relevant pH range of soils, adsorption of difenacoum would be expected to be pH dependent, with adsorption being lower in alkaline soils. No batch soil adsorption experiments were provided for difenacoum. The experimentally derived Koc (HPLC method) was considered as unreliable during the Annex I evaluation for difenacoum. A QSAR (Koc value of 1.8×10^6 (EUSES- Predominantly hydrophobic) was used in the EU exposure assessment instead of the experimentally derived value. The Reviewer notes this value is only relevant for the undissociated form of difenacoum, which will not reflect the dissociation state of difenacoum in the normal pH range of most agricultural soils. The Reviewer also notes the value of the Koc strongly influences the distribution of the active substance to water/sediment, water/sludge and water/soil. The CA for difenacoum stated they do *"..not require more data on Koc, because the significance of Koc is low when uses in sewer and in and around buildings are considered. The choice of Koc does not change the conclusions of the risk assessment. See rationale below:-The surface water PEC calculated using measured (OECD 121) Koc of 67 is appr. 10^{-5} mg/l, with PNECwater of 0.06 µg/l the risk ratio will be 0.00016*[19]*. Low Koc will give lower PECs for soil through sewage sludge and thus high Koc is the worst case. In direct soil exposure from bait boxes (1%) only initial PECs without degradation or further*

18 Response to Comments from Member States and Participant on the Draft Competent Authority Report on Difenacoum of the Activa/Pelgar Brodifacoum and Difenacoum Task Force (3.7.08) 34/46

19 The Reviewer notes this is two orders of magnitude higher than the PEC specifed in the CAR (PEClocal water 2.35×10^{-7} mg/L) which was calaucated with the QSAR Koc.

distribution have been calculated and thus the choice of Koc value does not have any impact on the soil risk from direct exposure. The same applies for indirect exposure via faeces and urine. The secondary poisoning risk through earthworm would be higher with low Koc, because of higher porewater concentrations, but there is a secondary poisoning risk also with the high Koc. The applicant does not have access to data in other dossiers."18

In a rat metabolism study 41-71% of the dose administered was excreted according to analysis of rat faeces and urine (7 days after single dosing, low and high dose). Four major metabolites >10 %AR were identified:

Isomers of hydroxylated difenacoum
F7 (11.3 %)
F8 (7.3 %)

Isomers of difenacoum-based structure, which formed glucuronide conjugates
F5 (12.2 %)
F6 (8.0%)

No data on the toxicity of the four major metabolites are available. The 4-hydroxy coumarin moiety is still present and thus the metabolites could be potent as anticoagulants. For the EU risk assessment the metabolites were treated collectively as one and were assumed to have the same toxicity as the parent. The Reviewer notes no PECs for metabolites are provided in the difenacoum CAR. This is presumably because it is covered by the risk assessment for difenacoum based on the assumptions stated in the CAR. To refine the EU exposure assessment for the active substance it was assumed 40% of the excreted amount in urine and faeces is metabolised and that 40 % of the administered total amount is unchanged difenacoum in faeces.[20] The Reviewer notes unchanged difenacoum was present at maximum at 2.9 %applied in faeces. Consequently, assuming that ~40% of the excreted amount in urine and faeces is metabolised is conservative.

Ecotoxicology

No further ecotoxicological studies were identified as necessary to support the authorisation of the active substance and no studies were submitted to support the authorisation of the product. Based on the environmental fate and behaviour of difenacoum, as outlined above, the environmental exposure assessment was conducted.

Difenacoum is very toxic to fish, aquatic invertebrates and algae. Toxicity to fish, the most sensitive species, is based on the inhibition of blood clotting. The mode of action in aquatic invertebrates and algae is unknown. The $PNEC_{water}$ is 0.06 µg/l based on the LC_{50} for Rainbow Trout. Difenacoum did not inhibit growth or respiration of aquatic microbes. The PNEC for sewage treatment plant (STP) micro-organisms 480 µg/l (the limit of solubility). In the absence of any ecotoxicological data for sediment-dwelling organisms, the $PNEC_{sediment}$ was calculated using the equilibrium partitioning method resulting in a value of 2.51 mg/kg (wet weight).

Exposure of soil organisms to difenacoum by direct contamination of soil may occur following use in and around buildings and waste dumps. It is also possible that soil may become exposed following the spreading of sewage sludge from a sewage treatment plant that has been exposed to difenacoum used in sewers. Difenacoum caused no toxic effects in the acute earthworm test and a $PNEC_{soil}$ of 0.877 mg/kg wet weight was determined.

20 "*40% is from the total administered radioactivity, part of the radioactivity remains in the rat (30-60%). Non-identified radioactivity in urine and faeces is minor part and individual unidentified metabolites each account for <4%"* Source: Response to Comments from Member States and Participant on the Draft Competent Authority Report on Difenacoum of the Activa/Pelgar Brodifacoum and Difenacoum Task Force (3.7.08)

No tests on the soil micro-organisms or plants are required, because difenacoum is not expected to be particularly toxic to them on the basis of the mode of action and available data (Activated sludge, respiration inhibition test/Sorex limited).

Difenacoum is very toxic to birds the $PNEC_{oral}$ of birds was determined to be 0.5 µg/kg food or 0.1 µg/kg bw/d. Difenacoum is also very toxic to mammals The $PNEC_{oral}$ for mammals is 7 µg/kg in food or 0.3 µg/kg bw/d. These $PNEC_{oral}$ values were used in risk characterisation of primary and secondary poisoning.

Difenacoum has a considerable bioaccumulation potential in aquatic and terrestrial organisms. One applicant submitted a fish bioconcentration test, but it was not considered as acceptable by the RMS. The waiving of fish bioconcentration test was accepted, because the test was judged not possible to perform technically, and because an estimated BCF value could be used in the risk assessment. The calculated BCFs range from 9010 (aquatic) to 477 729 (terrestrial). As outlined in the Assessment Report for Difenacoum (17-09-2009) the calculated BCFs estimate bioconcentration in the whole animal and not in the fat tissue, so BCF for difenacoum in fat tissue of the non-target vertebrates is unknown. The risk assessment indicates that accumulation of difenacoum in predators results in unacceptable effects when compared with the environmental acceptance criteria given in the Directive and TNsG on Annex I Inclusion. However, as outlined below, the proposed use of Ruby Paste, according to instructions, by professional users, should minimise the impact of such high calculated BCF values.

3.3.6. Exposure Assessment for the Environment

An overview of the environmental exposure assessment for Ruby Paste is presented in this section. Detailed calculations are provided in the Annexes accompanying this Report. The environmental exposure assessed during the review process and the current intended use is similar.

Ruby Paste, contains 50 mg difenacoum per kg of product and is used to control rats and mice. The proposed use of the product is indoors in warehouses and outbuildings and outdoors in and around buildings, waste dumps and open areas. The directions for use for sachets, pre-baited bait box and cartridges are

Rats: 30-60 g of paste spaced 10 m apart (5 m apart in high infestation areas). Typical treatment time 6 weeks.

Mice: 10-30 g of paste spaced 5 m apart (3 m apart in high infestation areas). Typical treatment time 6 weeks.

3.3.6-1. Aquatic compartment

Ruby Paste, whilst not being supported for use in sewers, was assessed in sewer systems to control rats as a worst-case situation for the STP and aquatic compartment. Consequently, exposure to the aquatic compartment occurs when sewage treatment plants make releases to water bodies. Based on

worst case assumptions[21] taking the metabolism of difenacoum into account the maximum predicted environmental concentration (PEC) of the active substance for microorganisms in the STP is 5.91 x 10^{-6} mg/L. The corresponding amount in surface water is 1.55 x 10^{-7} mg/L. The maximum permissible concentration by directive 80/778/EEC (amended by 98/83/EC) of 0.1 µg/L is not exceeded in surface waters. 6.32 x 10^{-3} mg/kg wwt is predicted to occur in sediment during an emission episode. Full details of the calculations are contained in the Annexes.

Exposure of surface water to the active substance following its use in the scenario "in and around buildings" is considered negligible according to the ESD. This argumentation was also accepted for the Annex I inclusion of difenacoum.

3.3.6-2. Atmosphere

The use pattern and means by which difenacoum is deployed together with its low volatility, ensure that exposure of the atmosphere is highly unlikely. Difenacoum has an estimated half-life of approximately 2 hours in air. Consequently, it is predicted to have a negligible effect on stratospheric ozone. Difenacoum shows no absorption in the so-called atmospheric window (800-1,200 nm) and therefore, according to the TGD on risk assessment (Part II, Section 3.7.2) is not a potential greenhouse gas.

3.3.6-3. Terrestrial compartment

Exposure of soil to the active substance occurs via residues present in sewage sludge after using the product in sewers and via direct and disperse release after the use of the product in and around buildings, open areas and waste dumps.

Based on worst-case assumptions of these typical usage patterns and release mechanisms, the maximum concentration in agricultural soil (averaged over 30 d) after 10 years of sludge application from STP is 2.41 x 10^{-3} mg/kg wwt. The highest concentration of difenacoum in soil from in and around buildings[22] is 0.0348 mg/kg wwt under realistic worst case conditions (200 g of product/bait point, each

21 Realistic worst-case: 21 days campaign

Day 0: 300 wax blocks, Day 7: 100 wax blocks replenished Day 14: 50 wax blocks replenished Day 21: 0 wax blocks replen.

Maximum emission during 1st week: 100 blocks

Amount of product used in control operation: 30 kg

Fraction of a.i. (substance) released: 0.66. Difenacoum metabolism data taken into account.

Standard STP scenario (TGD) 200 L/day, 10,000 inhabitants

To refine the EU exposure assessment for the active substance it was assumed 40% of the excreted amount in urine and faeces is metabolised and that 40 % of administered total amount is unchanged difenacoum in faeces. This was also used in the current exposure assessment.

22 <u>In and around buildings</u>

Amount of product used in control operation for each bait box: 0.25 kg (ESD) and 0.2 kg, which is >3 times the proposed amount.

bait point is 5 m apart). The application rate modelled is approximately three times higher than the proposed use rate for rats.

The notifier also proposes to use the product in open areas. The Reviewer notes no scenario is prescribed in the ESD for the use of a paste formulation in open areas. The notifier used the scenario for the outdoor use of impregnated grain in open areas to support the authorisation of Ruby Paste. The Reviewer notes this scenario was used to assess the exposure arising from a paste formulation for the active substance coumatetralyl during the Review process. Consequently, in light of this precedent the Reviewer deems it acceptable to use the impregnated grain open area scenario as a surrogate for the paste formulation. Under realistic worst-case conditions the ESD assumes one application site is treated twice with the product. The fraction released during use and during application is 0.25. The exposed soil area is assumed to be the lower half of the burrow wall surrounding an 8 cm diameter tunnel, with a soil mixing depth of 10 cm and up to 30 cm from the entrance hole. The amount of product used at each refilling in the control operation is not specified by the ESD. 200 g/bait point was used by the notifier in the exposure assessment. This is approximately three times higher than the proposed use rate for rats. The local concentration arising in soil after a campaign is predicted to be 0.346 mg/kg wwt (200 g of product/bait point).

Based on worst case assumptions, usage patterns and release mechanisms[23], the maximum concentration in soil from applications in waste dumps is predicted to be 0.0074 mg/kg wwt under realistic worst case conditions.

According to the Assessment Report (17-09-2009), difenacoum is not readily or inherently biodegradable. Difenacoum degrades slowly under aerobic conditions in soil, with a measured DT_{50} of 439 days. This suggests difenacoum has the potential to accumulate in soil if applications were made in consecutive years to the same area. However, even in the unlikely event of such use soil accumulation would not be expected to pose a problem given the large margins of safety observed for the terrestrial compartment.

Realistic worst-case: 21 day campaign Bait stations: 10 No. of replenishments: 5 Bait stations are 5 m apart.

Fraction released due to spillage: 0.01 Fraction ingested: 0.99

Fraction released of ingested: 0.4 (Difenacoum metabolism data taken into account)

Spillage area: 0.09 m^2 (0.1 m around station) Frequented area: 550 m^2 (10 m around building

Open areas (Grain scenario used as a surrogate for paste formualtion)

Amount of product used at each refilling in the control operation: 200 g

Realistic worst-case: 6 day campaign Bait stations: 1 No. of replenishments: 2

Fraction of product released to soil during application 0.05 Fraction of product released to soil during use 0.2

[23] Waste dumps

Amount of product used in the control operation: 40 kg/ha (ESD default). According to the proposed use 26.46 kg/ha could be used.

No. of replenishments: 7 Fraction of product released to soil 0.9

3.3.6-4. Groundwater

Exposure of groundwater may occur as a result of soil exposure which occurs via residues present in sewage sludge after using the product in sewers and via direct and disperse release after the use of the product in the scenarios in and around buildings, open areas and waste dumps. As an indication for potential groundwater levels, the concentration in porewater of agricultural soil was taken. It should be noted that this is a worst-case assumption, neglecting transformation and dilution in deeper soil layers. A summary of the PECs obtained are presented in **Table 3.3.6.4-1**. All concentrations are less than the EU trigger value of 0.1 μg/L.

Table 3.3.6.4-1. Predicted Environmental Concentration (µg/L) of difenacoum in groundwater

Compartment/Scenario	ESD realistic worst case scenario	ESD realistic worst case scenario with modified input parameters	ESD normal use scenario with modified input parameters
Sewer scenario			
Groundwater/porewater	9.94×10^{-5}	7.29×10^{-5}	
In and around buildings scenario			
Groundwater/porewater	1.5×10^{-3}	1.1×10^{-3}	3.2×10^{-4}
Open areas			
Groundwater/porewater	5.23×10^{-3}	1.05×10^{-2}	---
Waste dump			
Groundwater/porewater	2.24×10^{-4}	2.5×10^{-4}*	---

***For high infestations of rats the baits are spaced 5 m apart. According to calculations provided by the Reviewer this could potentially result in a maximum of 441 bait points (21 100 m lines of 21 baits, 5 m apart) in a 1 ha area during high infestations. This would correspond to ~26.46 kg of product. This is higher than the default value considered in the ESD under realistic worst-case conditions. Consequently the notifiers exposure calculation (22 kg/ha) is not sufficient to support this use. The Reviewer generated new exposure calculations for this use (26.46 kg/ha)

3.3.6-5 Primary and Secondary poisoning

A clear risk exists for primary and secondary poisoning in both the aquatic and terrestrial compartments for birds and mammals. The empirical risk assumes direct or indirect consumption of the deployed bait. For primary poisoning the initial PEC_{oral} values as outlined above (Section 3.3.5) assume that there is no bait avoidance by the non-target animals and that they obtain 100% of their diet in the treated area and have access to Ruby Paste. Even when avoidance and elimination are taken into account the empirical exposure levels result in unacceptable risks to birds and mammals (see ANNEX VI).
The PEC_{oral} values determined for characterising the risk of secondary poisoning to fish, earthworm and rodent eating birds and mammals is unacceptable. The values assume accumulation based on the PEC values determined for each relevant compartment. Even when avoidance and elimination are taken into account the empirical exposure levels to difenacoum from Ruby Paste result in unacceptable risks to birds and mammals (see ANNEX VI).

3.3.7. Risk Characterisation for the Environment

Ruby Paste is used in and around buildings, open areas and waste dumps to control rats and mice. Ruby Paste, whilst not being supported for use in sewers, was assessed in sewer systems to control rats as a worst-case situation for the STP and aquatic compartment. Consequently, exposure to the aquatic compartment occurs through the STP route. Exposure of soil to the active substance occurs via residues present in sewage sludge and via direct (spillages) and disperse release (deposition only by urine and faeces) after the use of the product in the scenarios in and around buildings, open areas and waste dumps. No new data related to the environment fate and behaviour or the ecotoxicology of the active substance has been submitted by the applicant. PECs were calculated in accordance with the ESD for PT14. These calculations are outlined in the previous section.

3.3.7-1 Aquatic compartment

The use of Ruby Paste containing difenacoum in the sewer system may lead to contamination of surface waters and sediment through sewage water and STP. Exposure of surface water to the active substance following its use in the scenario *"in and around buildings"* is considered negligible according to the ESD. The derivation of the PEC and PNEC values is outlined in ANNEX VI. The PEC values, as determined by fate and behaviour, reflect the predicted concentrations of difenacoum in water following the use of Ruby Paste in the relevant scenarios. Aquatic organisms are therefore assessed for effects of difenacoum in their environment for the relevant use scenarios. The PEC/PNEC ratios, for the realistic worst case scenarios with normal use, were less than 1 in all compartments indicating that difenacoum does not cause unacceptable risk to aquatic organisms, sediment-dwelling organisms or biological processes at the sewage treatment plant. As difenacoum is not readily biodegradable, the degradation of difenacoum in sediment is also anticipated to be low. However, according to the PEC calculations, concentrations in sediment would be low (6.32×10^{-3} mg/kg wwt), and below the level that causes unacceptable risk, thus risk for unacceptable accumulation in sediment can be regarded low.

No risk is identified to either groundwater/porewater or surface water used as drinking as in both cases the maximum permissible concentration by directive 80/778/EEC (amended by 98/83/EC) of 0.1 μg/l is not exceeded in the ESD realistic worst case scenarios for uses in sewer, in and around buildings, open areas and waste dumps.

3.3.7-2 Atmospheric compartment

The use pattern and means by which difenacoum is deployed together with its low volatility, ensure that exposure of the atmosphere is highly unlikely. Difenacoum has an estimated half-life of approximately 2 hours in air. Consequently, it is predicted to have a negligible effect on stratospheric ozone. Difenacoum shows no absorption in the so-called atmospheric window (800-1,200 nm) and therefore, according to the TGD on risk assessment (Part II, Section 3.7.2) is not a potential greenhouse gas.

3.3.7-3 Terrestrial compartment

Exposure of soil to the active substance occurs via residues present in sewage sludge after using paste bait in sewers and via direct (spillages) and disperse release (deposition by urine and faeces) after the use of the product in and around buildings, open areas and waste dumps. The derivation of the PEC and PNEC values is outlined in ANNEX VI. The PEC values, as determined by fate and behaviour, reflect the predicted concentration of difenacoum in soil following the use of Ruby Paste in the relevant scenarios. Terrestrial organisms are therefore assessed for effects of difenacoum in their environment for the relevant use scenarios. The PEC/PNEC ratios, for the realistic worst case scenarios with normal use, were less than 1 for all the compartments assessed: sewer, in and around buildings, open areas and waste dumps. Therefore, normal use of Ruby Paste does not cause unacceptable risk to terrestrial organisms.

3.3.7-4 Primary poisoning

Acute risk

For the acute exposure situation, no $PNEC_{oral}$ is determined and no quantitative risk characterisation is performed. Instead a qualitative assessment is done by comparing LD_{50} values to the expected concentration of the active substance in birds and mammals following their direct ingestion of Ruby Paste bait. One day consumption of difenacoum containing baits is not assumed to kill birds and mammals with the exception of foxes. The other animals would suffer from sublethal effects, although

mortality cannot be excluded. The assumption is based on the comparison of expected concentration in animals after one day exposure without elimination. The species specific sensitivity differences are not taken into account in this assumption (i.e. no assessment factor is applied to the LD_{50} values), and hence this description must not be considered as a risk characterisation.

Long-term risk

According to the ESD the comparison of concentration in the non-target animals and the $PNEC_{oral}$ describes the long-term risk for primary poisoning. The PEC values generated for the long-term risk assessment were calculated assuming direct ingestion of Ruby Paste by non-target birds and mammals. The expected concentration in the non-target animals are calculated after five days intake and elimination. The elimination is assumed to be 40%. The Step 2 assumptions are used for the calculation of the expected concentrations (see Annex VI for the calculations). The calculations show that mammals and birds would suffer long-term effects of difenacoum if they ingested Ruby Paste. Due to high food intake in relation to the body weight the birds are at considerably higher risk than mammals.

Primary poisoning incidents can be minimised by preventing the access of non-target animals, including companion animals, to the baits. Ruby Paste contains the bittering agent, denatonium benzoate, as a deterrent (0.195 % w/w) which may further reduce the risk of primary poisoning of non-target birds and mammals. It is assumed in the ESD that if the rodenticide baits are used according to the label instructions, the risk for primary poisoning is negligible. However, it may not be possible to exclude exposure of all non-target animals, as the baits have to be accessible to target rodents, they may as well be accessible to non-target mammals and birds of equal or smaller size than the target rodents.

3.3.7-5 Secondary poisoning

In the terrestrial and aquatic environments birds and mammals may be at risk of secondary poisoning if they feed on contaminated organisms following the use of Ruby Paste. The derivation of $PNEC_{oral}$ for birds and mammals is outlined in Annex VI. The derivation of PEC values for fish eating and earthworm eating birds and mammals is outlined in ANNEX VI. These values assume direct ingestion of Ruby Paste by the prey, and relies on PEC values generated by environmental fate and behaviour for the relevant compartments. The risk assessment for rodent eating birds and mammals applies an estimated concentration in rodent prey based on the assumption of direct ingestion of Ruby Paste by rodents (see ANNEX VI).

Aquatic

For the aquatic food chain, the PEC/PNEC ratios exceed 1 for both fish eating birds and mammals. Despite this calculation, the risk of secondary poisoning via the aquatic food chain is considered insignificant due to low water solubility and high adsorption tendency of difenacoum. It is also assumed that mechanical screening of sewage water reduces the concentration in the recipient water, although this reduction cannot be quantified. The negligible risk of secondary poisoning of fish-eating birds is supported by the monitoring data in the UK where the fish-eating birds, cormorants, herons, goosanders and red-breasted mergansers have not been involved in any of the reported incidents.

Terrestrial

For the terrestrial environment, following the use of Ruby Paste, the PEC/PNEC ratios exceed 1 for earthworm and rodent eating birds and mammals indicating unacceptable risk. Contaminated rodents are the most likely source for difenacoum residues in raptorial birds and mammalian predators.

Acute risk-Rodent eating birds and mammals

A qualitative assessment of the acute secondary poisoning is made by comparing the concentration in the rodents to LD_{50} values from acute oral studies. Rodents are assumed to eat entirely on bait containing difenacoum and the non-target animals are assumed to consume entirely poisoned rodents. The calculations of PEC_{oral} values are outlined in Annex VI. The results indicate that birds are likely to survive and mammals are likely to die if they eat poisoned rats. The species specific sensitivity differences or other aspects normally covered by the assessment factors are not taken into account in the qualitative assessment.

Long-term risk-Rodent eating birds and mammals

The quantitative risk assessment for long-term exposure to Ruby Paste, based on ESD guidance parameters, for susceptible and resistant rodents indicate that difenacoum causes unacceptable risk for non-target vertebrates. In laboratory studies on Barn Owls, fed on contaminated rodents, accumulation of difenacoum was noted. 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 fat 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.

Bioaccumulation of difenacoum in predators has been shown in the measurements of difenacoum residues in the animal carcasses found from the field in the United Kingdom during monitoring campaigns (for details see Annex VI). While the PEC/PNEC ratios based on measured concentration in rats and mice were lower than the respective figures calculated according to the ESD, they were still considerably higher than 1 indicating risk of secondary poisoning of Barn Owls. Population level effects of difenacoum have not been studied and while all available information indicates risk, it does not tell the frequency of secondary poisoning incidents among wildlife. The conclusion, however, is that difenacoum causes a high risk for secondary poisoning.

The risk for secondary poisoning is more difficult to control than that for primary poisoning, as poisoned rodents may be available for predators for several days after intake of difenacoum. The use of difenacoum inside the buildings may reduce the secondary poisoning risk, but does not exclude it as the exposed rodents may move out from the building. The secondary poisoning can be excluded only in fully enclosed spaces where rodents cannot move to outdoor areas or to areas where predators may have access. When using difenacoum as a rodenticide all possible measures have to be taken in order to minimize secondary poisoning of the non-target animals. The measures include use of tamper resistant bait boxes, collection of unconsumed baits after termination of the control campaign and collection of dead rodents during and after the control campaign.

3.4. Measures to protect man, animals and the environment

The information submitted covering the requirements as described in the TNsG on Data Requirements, common core data for the product, section 8, points 8.1 to 8.8 is provided below.

3.4.1. Methods and precautions concerning handling, use, storage, transport or fire

Methods and precautions concerning handling and use:

- Always read the label before use and follow the instructions provided.
- Do not decant product into unlabelled containers.
- Avoid all unnecessary exposure, in particular avoid ingestion.
- Keep away from food, drink and animal feeding stuffs.
- Do not smoke eat or drink while handling this product.
- Baits must be secured in tamper resistant bait boxes to minimise the risk of consumption and poisoning to children, companion animals and other non-target animals.
- Bait boxes must be placed in areas inaccessible to children, companion animals and non-target animals.
- Bait boxes must always be clearly labelled “Do Not Touch” and warn of the contents.
- In public areas (such as business premises, schools, hospitals etc) it must be clearly signed that rodenticide control is in operation. Signage must provide information on the risks of interfering with the product and dead rodents.
- Dead rodent bodies must be collected during all control operations to minimise the risk of consumption and poisoning to children, companion animals and other non-target animals.
- It is illegal to use this product for the intentional poisoning of non-target, beneficial and protected animals.
- Wash hands and face after application and use of the product, and before eating, drinking or smoking.

Methods and precautions concerning storage:

- Store in a cool, dry, well-ventilated place
- Store locked up in the original container
- Store original container tightly closed
- Keep/store out of reach of children and companion animals
- Keep/store away from food, drink and animal feedstuffs.

Methods and precautions concerning transport:

Not classified as dangerous for transport.

Methods and precautions concerning 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.

Specific hazards:

Not applicable

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.

3.4.2. Specific precautions and treatment in case of an accident

Personal precautions

Wear suitable protective clothing, gloves and eye/face protection, if applicable and where appropriate.

- Respiratory Protection: No special respiratory protection equipment is recommended under normal conditions of use with adequate ventilation.
- Hand protection: Wear gloves.
- Skin protection: No special clothing/skin protection equipment is recommended under normal conditions of use.
- Eye protection: Not required.

- Ingestion: When using this product, do not eat, drink or smoke

Personal treatment

- General advice: In the case of accident or if you feel unwell, seek medical advice immediately (show the label where possible and report the authorisation number).
- Skin contact: May cause skin irritation. Remove contaminated clothing Wash off immediately with soap and plenty of water. If irritation persists obtain medical attention Contaminated clothing should be washed and dried before re-use.
- Eye contact: May cause eye irritation. Rinse immediately with plenty of water and seek medical advice.
- Inhalation: Unlikely to present an inhalation hazard unless excessive dust is present. Move to fresh air. Obtain medical advice immediately.
- Ingestion: If swallowed, seek medical advice immediately.

ADVICE FOR DOCTORS:

Difenacoum is an indirect anti-coagulant. Phytomenadione, Vitamin K1, is antidotal. Determine prothrombin times not less than 18 hours after consumption. If elevated, administer Vitamin K1 until prothrombin time normalises. Continue determination of prothrombin time for two weeks after withdrawal of antidote and resume treatment if elevation occurs in that time.

Report all incidents of poisonings to the relevant national poisons centre; include information on the product authorisation number, product trade name and active substance. In Ireland, this is the National Poisons Information Centre, Beaumont Hospital, Dublin (01-8092166)

Environmental precautions

- Prevent accidental exposure of the product to the environment.
- Keep un-used bait locked-up and in secure storage containers
- Bait must be secured in tamper resistant bait boxes in areas away from drains, water courses and non-target organisms.

Environmental treatment

- Clean up accidental spillages promptly by sweeping or vacuum.
- If the product gets into water or soil, it should be removed mechanically.
- Transfer to a suitably labelled container and dispose of to a certified waste disposal operator for incineration and licensed waste disposal site.
- Subsequently, wash the contaminated area with water, taking care to prevent the washings entering sewers or drains.
- For further instructions, see section 3.4.6 below.

3.4.3. Procedures for cleaning application equipment

No application equipment is needed, therefore, no specific cleaning for equipment is required

If necessary, following use, bait boxes should be washed with detergent and water. The bait box should be washed out 3 times (triple rinsed).

3.4.4. Identity of relevant combustion products in cases of fire

Not applicable.

3.4.5. Procedures for waste management of the biocidal product and its packaging

Dispose of packaging, remains of unused product and dead rodents to a certified waste disposal operator for incineration and licensed waste disposal site.

3.4.6. Possibility of destruction or decontamination following accidental release

Air:
Difenacoum has a very low vapour pressure, and decomposes at around 220°C and therefore does not boil. The formulated product is a wax block. The risk of release of the active ingredient or the product to the atmosphere is negligible.

Water (including drinking water):
The octanol-water partition coefficient of difenacoum is high, and hence the active ingredient will remain in the product. The product is know 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, require users **not** to place bait points where water could become contaminated (excepting sewers), 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.

Soil:
Sources for release to the soil compartment include: sludge spreading, transport of bait by rodents, degradation of dead rodent remains hidden in burrows and excretion of the active ingredient by poisoned rodents. Bioremediation will probably prove the most effective method of decontamination, as 30% biodegradation in a 28 day ready biodegradation study suggests.

In the event of spillage of an appreciable amount of product, this material should be collected for incineration.

3.4.7. Undesirable or unintended side-effects

Toxic to mammalian and avian species, including domesticated animals, wildlife and humans. Therefore the risk to these non-target species should be considered when using bait.

3.4.8. Poison control measures

The wax blocks are dyed (e.g. red or blue) to make them unattractive to wildlife, and birds in particular. In addition, in case of accidental ingestion, the presence of a dye may help to confirm that there has been ingestion and thus facilitate antidote treatment.

The product contains a human taste deterrent (adversive agent – Bitrex).

To report human poisoning incidents call the relevant national poison information centre. Include information on the product authorisation number, product trade name and active substance. Where possible provide a copy of the label or safety data sheet (SDS).

In Ireland to report a poisoning incident, call: 01 (8092566 / 8379964) The Poisons Information Centre of Ireland, Beaumont Hospital, Beaumont Road, Dublin 9.

ADVICE FOR DOCTORS:

Difenacoum is an indirect anti-coagulant. Phytomenadione, Vitamin K1, is antidotal. Determine prothrombin times not less than 18 hours after consumption. If elevated, administer Vitamin K1 until prothrombin time normalises. Continue determination of prothrombin time for two weeks after withdrawal of antidote and resume treatment if elevation occurs in that time.

Report all incidents of poisonings to the relevant national poisons centre (include information on the product authorisation number, product trade name and active substance)

4. Proposal for Decision

The assessment presented in this report has shown that the ready-to-use product, Ruby Paste, formulated by Lodi S.A. 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 of rodents (rats and mice).

This authorisation of the product Ruby Paste has duly taken in to consideration the conclusions and recommendations of both the Finnish Assessment Report for the active substance, difenacoum and Commission Directive 2008/81/EC including difenacoum in Annex I of Directive 98/8/EC.

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, in the proposed areas for use at the proposed dose rate. However, paste bait was shown not to be suitable for damp or wet conditions, such as in sewers. Therefore, this use area is not supported by this authorisation.

Acute toxicology studies presented for the product indicated that Ruby Paste (containing 0.005% w/w difenacoum) does not classify with respect to Directive 1999/45/EC or Regulation (EC) No 1272/2008. However, safety phrases and precautionary statements are proposed by the Rapporteur.

A human health exposure and effects assessment for the product was carried out for professionals and amateurs on the product Ruby Block, based on the larger baiting quantities for rats. Using both the MOE and AEL approaches for risk assessment indicates 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 with PPE, untrained professionals and amateurs (with and without PPE). The product is deemed suitable for authorisation and appropriate personal protective equipment is advised.

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 in sealed packs and the use of tamper resistant bait boxes are essential to reducing the risk of secondary exposure. Baits should not be placed where food, feeding stuffs or drinking water could be contaminated.

An environmental exposure and effects assessment for the product indicated that difenacoum in Ruby Paste does not pose a threat to groundwater ($PEC_{GW} < 0.1$ µg/L) and does not infinitely accumulate in soil when used according to label instructions. Difenacoum has an estimated half-life of approximately 2 hours in air. Consequently, it is predicted to have a negligible effect on stratospheric ozone. Difenacoum shows no absorption in the so-called atmospheric window (800-1,200 nm) and therefore, according to the TGD on risk assessment (Part II, Section 3.7.2) is not a potential greenhouse gas.

Difenacoum in Ruby Paste does not adversely impact non-target organisms in the aquatic or terrestrial compartments when used according to label instructions. There is a high risk for primary and secondary poisoning for non-target vertebrates. Additionally, difenacoum is a potential PBT substance (see Difenacoum Assessment Report (17-09-2009)) . These identified risks are minimized by applying all apropriate and available risk mitigation measures.

During the active substance review of difenacoum by Finland, primary and secondary poisoning risks were identified for non-target organisms and for potential accidental incidents involving children. The

assessment of those EU identified risks during the product authorisation evaluation of Ruby Paste have also indicated a potential risk of primary and secondary poisoning to no-target animals and the potential for the accidental primary poisoning of children. As such risk mitigation measures are applied to product authorisation.

Additionally, as the target rodents are vermin and are both direct transmitters of disease (such as through biting or contamination of food/feed by urine or faeces) or indirect carriers of disease (such as disease vectors, where fleas move from rat to humans) to humans and other animals. Transmitted diseases can include leptospirosis (or Weil's disease), trichinosis and salmonella. Authorisation of this product is considered necessary on the basis of public health grounds, since rodent populations are considered to constitute a danger to public health through the transmission of disease.

Conditions of authorisation

Two authorisations should be issued. The first authorisation covers professional and trained professional use product. The second authorisation covers amateur use product.

This authorisation of Ruby Paste is for a period of 5-years with an annual renewal.

The concentration of the active substance, difenacoum, in Ruby Paste shall **not** exceed 0.05 g/kg (0.005% w/w).

Only ready-to-use Ruby Paste product is authorised.

As a poison control measure, the authorisation requires that the product shall contain an aversive, bittering agent.

The authorisation requires that the product be dyed with a colour to make them unattractive to wildlife, and birds in particular.

This product shall **not** be used as a tracking poison.

The product is authorised only for use against rodents (for example brown rats, house rats and house mice). Authorisation of this product does **not** allow use against non-target organisms.

The authorisation of this product for professionals and trained professionals allows for use indoors and outdoors in the following areas: Indoors, including areas such as houses, warehouses, outbuildings and commercial premises. Outdoors uses include areas such as in-and-around buildings, waste dumps and open areas. Difenacoum baits must not be placed where food, feeding stuffs or drinking water can become contaminated.

The authorisation of this product for amateurs allows for use of this product indoors and outdoors in the following areas: Indoors, including only privates houses and outbuildings. Outdoors uses, including only in-and-around private building premises and private gardens. Difenacoum baits should not be placed where food, feeding stuffs or drinking water can become contaminated.

The product should only be used for rodent control in tamper resistant, secured bait stations or other secure coverings.

Bait stations should be clearly marked to show that they contain rodenticides and that they should not be disturbed.

Paste bait sachets shall be secured to the bait station(s) so that rodents can not remove bait from the bait box.

For amateur use products placed on the market in Ireland packaging restrictions are to be limited to pre-baited bait stations and refill packs with a maximum pack-size of 500g. Additionally, the paste bait shall be supplied to the amateur market in sachets and where relevant to professionals in order to reduce exposure risks to amateur operators during application to bait stations.

All product placed on the Irish market after the date of authorisation must be in compliance with the conditions of this authorisation and shall carry the approved label with the IE/BPA authorisation number and be packaged in the approved packaging.

Prior to any amendment relating to this authorised product, such as specification, use, labelling or administrative changes, application must be made to this Authority to do so

Upon annual renewal of the product Ruby Paste, the authorisation holder shall provide statistics to PRCD on the import and export from Ireland and also manufacture statistics where appropriate for Ruby Grain for the given full annual period or part thereof.

Authorisation of the biocidal product may be subject to review, following a detailed assessment of the risks involved, in accordance with the European Communities (Authorisation, Placing on the Market, Use and Control of Biocidal Products) Regulations, 2001, as amended. This review may lead to changes in or revocation of this authorisation.

ANNEXES to Initial PAR – June 2011

ANNEXES

Annex:

1. Confidential Information and Data
2. Summary of the Product Characteristics (SPC)
3. Study Summaries of Studies Reviewed
4. List of Studies Reviewed
5. Toxicology Calculations
6. Environmental Calculations
7. Residue Calculations

ANNEX I: Confidential Information and Data

Manufacturing site(s) of the active substance(s)[24]

Manufacturing site of the active substance(s):	
Company Name:	Pelgar International Ltd.
Address:	Prazska 54, 280 02 Kolin, Czech Republic c/o Pelgar International Ltd. Unit 13, Newman Lane, Alton, Hants. GU34 2QR, UK
Tel:	[redacted]
E-mail:	[redacted]
Contact:	[redacted]

Manufacturing site(s) of the biocidal product

Manufacturing site of the biocidal product:	
Company Name:	LODI S.A.
Address:	Parc d'activities des quatre routes Grand Fougeray 35390 France
Tel:	[redacted]
E-mail:	[redacted]
Contact:	[redacted]

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

Study summaries of new data[25] submitted in support of the evaluation of the active substance (IIIA)

A new 5-batch analysis for Difenacoum was submitted. This information was assessed by France and was found to be acceptable. Ireland accepts France's assessment.

[redacted]

[25] Data which have not been already submitted for the purpose of the Annex I inclusion.

Product trade name: Ruby Paste

Qualitative and quantitative information on the composition/specification of the biocidal product

Active substance(s)				Contents				
Common name	IUPAC name	CAS No.	EC No.	Concentration	Unit[26]	w/w (%)	Minimum purity (% w/w)	Same source as for Annex I inclusion (Y/N)
Difenacoum	3-(3biphenyl-4-yl-1,2,3,4-tetrahydro-1-naphtyl)-4-hydroxycoumarin	56073-07-5	259-978-4	50	mg/kg	[redacted]	[redacted]	[redacted]

Co-formulants					Contents				
Common name	IUPAC name	Function	CAS No.	EC No.	Concentration	Unit	w/w (%)	Classification	Substance of concern (Y/N)
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]		[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]		[redacted]
[redacted]			[redacted]	[redacted]	[redacted]	[redacted]	[redacted]		[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]		
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]		

[26] g/l, g/kg, other. For biological products, the concentration should state the number of activity units/units of potency (as appropriate) per defined unit of formulation (e.g. per gram or per litre).

[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]		[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]		[redacted]
				[redacted]	[redacted]		[redacted]		

Annex II: Summary of the Products Characteristics (SPC)

Annex III: Study Summaries of Studies Reviewed

Study summaries of new data[27] submitted in support of the evaluation of the active substance (IIIA)

Physical Chemical Characteristics

New data was submitted in support of PelGar's Difenacoum source of active substance. This included a study report to demonstrate the appearance of the technical substance. This information was assessed by France and was found to be acceptable. Ireland accepts France's assessment.

Methods of Analysis

New data was submitted in support of PelGar's Difenacoum source of active substance. This included a validated method of analysis for difenacoum in animal and human tissues, validation data for the analytical method for the determination of residues of difenacoum in meat and oil-seed rape (food/feeding stuffs) and validation data for the analytical method for determination of difenacoum in sediment (based on the analysis method for difenacoum in soil). This information was assessed by France and was found to be acceptable. Ireland accepts France's assessment.

Efficacy

Not applicable.

Toxicology

Not applicable

Environment (including Eco-Toxicology)

Not applicable

Confidential Section:

See confidential section (Annex I).

[27] Data which have not been already submitted for the purpose of the Annex I inclusion.

Study summaries of new data submitted in support of the evaluation of the biocidal product (IIIB)

Physical Chemical Characteristics For Ruby Paste

Subsection (Annex Point/TNsG)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.1 Appearance (IIB3.1/Pt. I-B3.1)	Pink pasta							
3.1.1 Physical state and nature	pasta							
3.1.2 Colour	pink							
3.1.3 Odour	hazelnut							
3.2 Explosive properties (IIB3.2/Pt. I-B3.2)				The absence of certain reactive groups in the structural formula of the a.s., difenacoum (CAS 56073-07-5) *{Ref: Brethrick, Handbook of Reactive Chemical Hazards, Butterworths, London 1979}*, and it oxygen balance, establish beyond reasonable doubt				

Subsection (Annex Point/TNsG)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
				that difenacoum is incapable of decompositing, forming gases, or realising heat very rapidly. There are no other components in the formulation which present any explosive properties.				
3.3 Oxidising properties (IIB3.3/Pt. I-B3.3)				Nor the a.s. or the solvent present oxidising properties Examination of the structural establish beyond reasonable doubt that the a.s., difenacoum (CAS 56073-07-5) is incapable of reacting exothermically with a combustible material *(refer to Explosive Properties)*. There are no other components in the				

Subsection (Annex Point/TNsG)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
				formulation which present any oxidising properties.				
3.4 Flash-point and other indications of flammability or spontaneous ignition (IIB3.4/Pt. I-B3.4)	EPA 830.6315	-	**flammability** : None observed when heated to 100°C	There are no other components present in the formulation which present flammability properties.				
Flash point				There are no other components present in the formulation which present flammability properties.				
Autoflammability				There are no other components present in the formulation which present flammability properties.				
Other indications of flammability				Not applicable				
3.5 Acidity/Alkalinity (IIB3.5/Pt. I-B3.5)				Not applicable, the product is a ready to use bait which is a pasta at ambient temperature.				

Subsection (Annex Point/TNsG)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
3.6 Relative density/bulk density (IIB3.6/Pt. I-B3.6)				Not applicable, the product is a ready to use bait which is a pasta at ambient temperature				
3.7 Storage stability - stability and shelf life (IIB3.7/Pt. I-B3.7)								
Effects of temperature (IV.B3.7.1)	- GIFAP Monography n°17, CIPAC MT 46.3	Pasta baits contained 0.005% Difenacoum	Degradation: < 25% after 5 weeks at 54°C. (stable)	The sample is stable during 5 weeks at 54°C that means that the sample is considered to be stable after 5 years at T°N. No significant change was observed in the characteristics of the items, neither in the Difenacoum content after the accelerated storage procedures.	Y	1	Biannic ML., LODI-Group, 2008-01-07	
(IV.B3.7.2)	- GIFAP Monography n°17,	Pasta baits contained 0.005%	< 15% after 14 days at 54°C (stable)		Y	1	Meriadec E., LODI-	

Subsection (Annex Point/TNsG)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
(IV.B3.7.3)	CIPAC MT 46 - HPLC(UV) and Azur after 6 months and 2 years storage at ambient T°.	Difenacoum Pasta baits contained 0.005% Difenacoum	<25 % after 2 years at T°N.	No significant change was observed concerning the characteristics of the test item except the aspect, which become crumbly, but it doesn't influence the stability of the Difenacoum content in the pasta. The test items were considered to be stable. No significant change was observed in the characteristics of the item, neither in the Difenacoum content after the accelerated storage procedures. The test item was considered to be stable	Y	1	Group, Study report n° LODI14/2009 (2009-11-25) Biannic ML, LODI-Group, 2009-11-12	
Effects of light				None, see packaging				
Reactivity towards container material				Compliant with ADR, DOT and EPA specifications				

Subsection (Annex Point/TNsG)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
Other	give in months if shelf life is < 2 years							
3.8 Technical characteristics (IIB3.8/Pt. I-B3.8)								
Wettability/ Suspensibility	Only solid preparations			Not applicable, the product is a ready-to-use pasta bait.				
Wet sieve analysis	for WPs, SCs, granules, tablets			Not applicable, the product is a pasta.				
Emulsifiability	only forECs and ready for use emulsions			Not applicable, the product is a pasta.				
Disintegration time				Not applicable, the product is a pasta..				
Attrition/friability of granules; integrity of tablets				Not applicable, the product is a pasta.				
Persistence of foaming				Not applicable, the product is a pasta.				
Flowability/Pourability				Not applicable, the product is a pasta.				
Dustability	Only for dustable			Not applicable, the product				

Subsection (Annex Point/TNsG)	Method	Purity/ Specification	Results	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official use only
	powders			is a pasta.				
3.9 Compatibility with other products (IIB3.9/Pt. I-B3.9)				Not applicable, the product is a ready-to-use pasta and is not intended to be added or mixed with any other product.				
3.10 Surface tension (Pt. I-B3.10)				Not applicable, the product is a pasta.				
3.11 Viscosity (Pt. I-B3.10)				Not applicable, the product is a pasta.				
3.12 Particle size distribution (Pt. I-B3.11)	Only for powders and granules			Not applicable, the product is a pasta.				

Conclusion:

The biocidal product Ruby Paste is not explosive, oxidising or flammable and does not classify from a phys.chem. point of view. The test item is stable after storage for two years at ambient temperatures. The test item is a ready-to-use paste bait and is not intended to be added or mixed with any other product.

Data requirement:

Information on the reactivity of the paste bait towards the container material is outstanding.

Methods of Analysis

Doc IIIB Section 4.1 **BPD Data Set IIB/** **Annex Point III.4.**		**Analytical Method for Detection and Identification** Analytical method validation for the determination of difenacoum in paste bait.	
		2 Reference: IIIB4.1a	**Official use only**
2.1	***Reference***	Ricau H, Analytical method validation for the determination of Difenacoum in Difenacoum Pasta Bait, Anadiag group-Defitraces, Study Report n°09-902018-007, 19 pages, Bio6. Unpublished	
2.2	***Data protection***	Yes	
2.2.1	**Data owner**	Bio6 s.a.	
2.2.2	**Companies with letter of Access**	PelGar International Ltd	
2.2.3	**Criteria for data protection**	Data on existing [a.s. / b.p.] submitted under national legislation for Post Inclusion of a.s. authorisation Data on existing [a.s./b.p.] submitted for the first time for Post Inclusion of a.s.	
		3 Guidelines and Quality Assurance	
3.1	***Guideline study***	CIPAC/3807R	
3.2	***GLP***	Yes	
3.3	***Deviations***	One deviation was recorded. Due to a presence of an interferent in the test item a second reverse phase column C8 was used. This deviation has not affected the quality or the interpretation of the results obtained.	
		4 MATERIALS AND MethodS	
4.1	***Preliminary treatment***		
4.1.1	**Enrichment**	Difenacoum was extracted from the pasta bait using Methanol and heated under reflux for about 90 minutes at 80°C in an oil bath.	

4.1.2	**Cleanup**	Extract was filtered through a Whatman filter N°1 and diluted in Methanol and Acetonitrile before injection.	
4.2	***Detection***		
4.2.1	**Separation method**	HPLC using a Phenomenex Hyperclone Mos C8 + Luna 5µC8 ((10+25)*(4.6+4.0)ID) column with a flow rate of 0.8 ml/min and Methanol as mobile phase.	
4.2.2	**Detector**	UV detection at 310 nm	
4.2.3	**Standard (s)**	Difenacoum standard (Cluzeau Info Labo) for reference item solution preparation	
4.2.4	**Interfering substance(s)**	No peak was observed in the blank solvent, in the blank formulation and in the reference item at the retention time of Difenacoum.	
4.3	***Linearity***	(Ref IVB.4.1b-R05-912011-001)	
4.3.1	**Calibration range**	The response of difenacoum is linear within the range of 0.0008mg/ml to 0.0012 mg/ml.	
4.3.2	**Number of measurements**	6	
4.3.3	**Linearity**	Correlation coefficient = 1.000	
4.4	***Specificity:*** Interfering substances	The specificity of the method was evaluated by the absence of interfering peaks in the area of interest. When injecting blank samples, no interfering peak shows up at the retention time where the analyte signal was expected. No other peak was found in the reference item and in the test item. The specificity was therefore defined.	
4.5	***Recovery rates at different levels***	The method has been validated at 0.92mg/ml (100%level) and at 0.46mg/ml (50%level). Recovery found respectively, 91 and 94%	
4.5.1	**Recovery results**	Between 80% and 120% in conformity with the CIPAC Guideline requirements which recommend recovery results in the range 80%-120%.	
4.6	***Limit of determination***		
4.7	***Precision***		
4.7.1	**Repeatability**	The concentration of difenacoum in the test item is equal to 0.005% (m/m) or 0.50g/kg. In the case of difenacoum, the	

		precision is acceptable as the RSD is lower than the result of the modified Horwitz equation: 3.40 < 5.95 (C=0.0001%). (Ref IVB.4.1b-R05-912011-001).	
4.7.2	**Independent laboratory validation**	Not available	
		5 Applicant's summary and conclusion	
5.1	***Materials and methods***	After a methanol dilution and heated under reflux during 90 minutes, extract was filtered and diluted again in methanol and acetonitrile. Determination of difenacoum was made by liquid chromatography on a reversed phase analytical column using UV detection at 310nm.	
5.2	***Conclusion***	The analytical method showed a good specificity for difenacoum analysis. The accuracy results of difenacoum were in conformity with the CIPAC Guidelines requirements for formulations containing less than 0.1% of an active substance. Indeed, the recovery results should be in the range 80-120% and they were experimentally between 91 and 94%.	
5.2.1	**Reliability**	1	
5.2.2	**Deficiencies**	No	

	Evaluation by Competent Authorities

	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	Evaluation by Rapporteur Member State
Date	28.3.2011
Materials and Methods	The method of analysis presented above was only validated in terms of its accuracy and specificity. The outstanding validation data is presented in report no: R05-912011-001.
Results and discussion	Accept the results of the Notifier.
Conclusion	Accept the conclusion of the Notifier.
Reliability	1
Acceptability	Acceptable. Note that the outstanding validation data is presented in report no: R05-912011-001.
Remarks	None.

Doc IIIB Section 4.1 BPD Data Set IIB/ Annex Point III.4		**Analytical Method for Detection and Identification** Analytical method validation for the determination of difenacoum	
		1 Reference: IIIB4.1b	**Official use only**
1.1	***Reference***	Ricau H, Quantification of Difenacoum 0.005% m/m in a rat poison bait., Defitraces, Study Report n°05-912011-001, 22 pages, LODI sa. Unpublished	
1.2	***Data protection***	Yes	
1.2.1	**Data owner**	LODI s.a.	
1.2.2	**Companies with letter of Access**	PelGar International Ltd	
1.2.3	**Criteria for data protection**	Data on existing [a.s. / b.p.] submitted under national legislation for Post Inclusion of a.s. authorisation Data on existing [a.s./b.p.] submitted for the first time for Post Inclusion of a.s.	
		2 Guidelines and Quality Assurance	
2.1	***Guideline study***	Method was developed in compliance with the Standard Operating Procedures in uses at DEFITRACES.	
2.2	***GLP***	Yes	
2.3	***Deviations***	One deviation was recorded. Issue of the draft report in March 2005 instead of February 2005 as described in the study plan. This deviation has no adverse effect on the study.	
		3 MATERIALS AND MethodS	
3.1	***Preliminary treatment***		
3.1.1	**Enrichment**	Difenacoum was extracted from the grain bait using Methanol and heated under reflux for about 90 minutes at 80°C.	
3.1.2	**Cleanup**	Extract was filtered through a Whatman filter N°40 and diluted in Methanol and Acetonitrile before injection.	
3.2	***Detection***		
3.2.1	**Separation method**	HPLC using a Supelcosil LC-8 (25*4.0 ID) column with a flow rate of 0.3 ml/min and a mobile phase of Methanol.	

3.2.2	**Detector**	UV detection at 310 nm	
3.2.3	**Standard (s)**	Difenacoum standard (Cluzeau Info Labo) for reference item solution preparation	
3.2.4	**Interfering substance(s)**	No peak was observed in the blank solvent, in the blank formulation and in the reference item.	
3.3	***Linearity***		
3.3.1	**Calibration range**	The response of difenacoum is linear within the range of 0.0008mg/ml to 0.0012 mg/ml.	
3.3.2	**Number of measurements**	6	
3.3.3	**Linearity**	Correlation coefficient = 1.000	
3.4	***Specificity:*** Interfering substances	A shift of difenacoum retention time was always observed in the test item presumably due to the presence of waxy co-extracts. By comparison of the UV spectra at the level of the reference item peak and the test item peak, it was shown that the peak at around 4.60 represents difenacoum. The retention time of difenacoum in the test item changes from about 4.60 to 4.80. It was concluded that the analytical method showed a good specificity.	
3.5	***Recovery rates at different levels***	The method has been validated at 0.005 % (m/m).	
3.5.1	**Recovery results**	Between 102% and 105% in conformity with the CIPAC Guideline requirements which recommend recovery results in the range 102%-105% for formulations containing less than 1% of an active substance.	
3.6	***Limit of determination***		
3.7	***Precision***		
3.7.1	**Repeatability**	The concentration of difenacoum in the test item is equal to 0.005%, m/m or 0.50g/kg. In the case of difenacoum, the precision is acceptable as the RSD is lower than the result of the modified Horwitz equation: 3.40 < 5.95 (C=0.0001%).	
3.7.2	**Independent laboratory validation**	Not available	
		4 Applicant's summary and conclusion	

4.1	***Materials and methods***	After a methanol dilution and heated under reflux during 90 minutes, extract was filtered and diluted again in methanol and acetonitrile. Determination of difenacoum was made by liquid chromatography on a reversed phase analytical column using UV detection at 310nm.	
4.2	***Conclusion***	The analytical method showed a good specificity for difenacoum analysis. The response of difenacoum was linear within the range of 0.0008 mg/ml to 0.0012 mg/ml. The precision was acceptable as the RSD was lower than the modified Horwitz equation. The accuracy results of difenacoum were in conformity with the CIPAC Guidelines requirements for formulations containing less than 1% of an active substance. Indeed, the recovery results should be in the range 95-105% and they were experimentally between 102 and 105%.	
4.2.1	**Reliability**	1	
4.2.2	**Deficiencies**	No	

	Evaluation by Competent Authorities	

	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	Evaluation by Reference Member State	
Date	28.3.2011	
Materials and Methods	The method of analysis presented above was not validated for the paste bait only the block bait and therefore is unacceptable. However, the information on the linearity and precision can be used to cover the lack of linearity and precision data in study 09-90218-003.	
Results and discussion	X Enrichment It states that "Difenacoum was extracted from the grain bait ....". However the study was carried out on a wax block bait. X Linearity The linearity data presented in this study was carried out using standard solutions and the same analytical method as in 09-902018-007 therefore it covers the data requirement for linearity for that method. X Repeatability A correction should be made, the concentration of Difenacoum in the test item is equal to 0.005%, m/m or 0.05 g/kg not 0.50 g/kg as stated in the above text.	
Conclusion	The information on linearity and precision provided in this study is acceptable and covers the data requirements from study 09-902018-007.	
Reliability	2	
Acceptability	Acceptable in terms of the linearity and precision data.	
Remarks	The method of analysis presented above was not validated for the paste bait only the block bait and therefore it cannot be used to cover the paste bait. However, the information on the linearity and precision can be used to cover the lack of linearity or precision data in study 09-90218-007.	

Doc IIIB Section 4.2 BPD Data Set IIB/ Annex Point III.4.		**Analytical Method for Detection and Identification** Analytical method validation for the determination of difenacoum	
		1 Reference: IIIB4.2	**Official use only**
1.1	***Reference***	Ricau H, Quantification of Difenacoum in RATTOFENE (Pasta Bustine), Defitraces, Study Report n°09-912011-004, 14 pages, LODI sa. Unpublished	
1.2	***Data protection***	Yes	
1.2.1	**Data owner**	LODI s.a.	
1.2.2	**Companies with letter of Access**	PelGar International Ltd	
1.2.3	**Criteria for data protection**	Data on existing [a.s. / b.p.] submitted under national legislation for Post Inclusion of a.s. authorisation Data on existing [a.s./b.p.] submitted for the first time for Post Inclusion of a.s.	
		2 Guidelines and Quality Assurance	
2.1	***Guideline study***	Method was developed in compliance with the Standard Operating Procedures in uses at DEFITRACES.	
2.2	***GLP***	Yes	
2.3	***Deviations***	No incident, which could have affected the quality or the interpretation of the results obtained, was observed.	
		3 MATERIALS AND MethodS	
3.1	***Preliminary treatment***		
3.1.1	**Enrichment**	Difenacoum was extracted from the pasta bait using Methanol and ultrasonicated for 15 minutes before analysis	
3.1.2	**Cleanup**	Extract was diluted in Methanol before injection.	
3.2	***Detection***		
3.2.1	**Separation method**	Liquid chromatography using a reverse phase column (Phenomenex-Luna 5µ C8 100A) with a methanol mobile phase flow rate of 1ml/min.	

3.2.2	**Detector**	UV detection at 310nm	
3.2.3	**Standard (s)**	Difenacoum standard (Cluzeau Info Labo) for reference item solution preparation	
3.2.4	**Interfering substance(s)**	No interferences	
3.3	***Linearity***		
3.3.1	**Calibration range**	Not available	
3.3.2	**Number of measurements**	Not available	
3.3.3	**Linearity**	Not available	
3.4	***Specificity:*** Interfering substances	Not available	
3.5	***Recovery rates at different levels***	Not available	
3.5.1	**Recovery results**	Around 100% in conformity with the FAO tolerances of 15%	
3.6	***Limit of determination***	Not available	
3.7	***Precision***	Not available	
3.7.1	**Repeatability**	Not available	
3.7.2	**Independent laboratory validation**	Not available	
		4 Applicant's summary and conclusion	
4.1	***Materials and methods***	After a methanol dilution and ultrasonication during 15 minutes, extract was diluted again in methanol. Determination of difenacoum was made by liquid chromatography on a reversed phase analytical column using UV detection at 310nm.	
4.2	***Conclusion***	The analytical method showed a good recovery for difenacoum analysis in pasta bait in accordance with the FAO tolerance.	
4.2.1	**Reliability**	2	
4.2.2	**Deficiencies**	No	

	Evaluation by Competent Authorities

	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	Evaluation by Rapporteur Member State
Date	28.3.2011
Materials and Methods	Acceptable.
Results and discussion	Accept the results of the Notifier.
Conclusion	Accept the conclusion of the Notifier.
Reliability	2
Acceptability	Acceptable
Remarks	The concentration of the active substance is with FAO tolerances (± 15%).

Doc IIIB Section 4 litt-01 BPD Data Set IIB/ Annex Point III.4		**Analytical Method for Detection and Identification** Analytical method validation for the determination of difenacoum in paste bait.	
		1 Reference: IIIB4 litt-01	**Official use only**
1.1	***Reference***	Magnier C., Analytical method validation for determination of Difenacoum in Difenacoum Bait (pasta, grain and block), LodiGroup, Study Report n°LODI17/2009, 21 pages, LODI sa. Unpublished	
1.2	***Data protection***	Yes	
1.2.1	**Data owner**	LODI s.a.	
1.2.2	**Companies with letter of Access**	PelGar International Ltd	
1.2.3	**Criteria for data protection**	Data on existing [a.s. / b.p.] submitted under national legislation for Post Inclusion of a.s. authorisation Data on existing [a.s./b.p.] submitted for the first time for Post Inclusion of a.s.	
		2 Guidelines and Quality Assurance	
2.1	***Guideline study***	CITAC/EURACHEM	
2.2	***GLP***	Yes	
2.3	***Deviations***	No deviation	
		3 MATERIALS AND MethodS	
3.1	***Preliminary treatment***		
3.1.1	**Enrichment**	Not available	
3.1.2	**Cleanup**	Not available	
3.2	***Detection***		
3.2.1	**Separation method**	HPLC using a reverse phase column and an UV detector	
3.2.2	**Detector**	Not available	
3.2.3	**Standard (s)**	Not available	
3.2.4	**Interfering substance(s)**	Not available	
3.3	***Linearity***		

3.3.1	**Calibration range**	The response of difenacoum is linear within the range of 80% to 120% of the item concentration.	
3.3.2	**Number of measurements**	5*3	
3.3.3	**Linearity**	Correlation coefficient > 0.99	
3.4	***Specificity:*** Interfering substances	No peak was observed in the extraction solution and in the pasta placebo. An adjacent peak appeared in the stressed pasta but the resolution being higher than 2 (R = 2.25), the quantification was not disturbed. The analytical method showed a good specificity.	
3.5	***Recovery rates at different levels***	The method has been validated at several levels: 50 – 100 and 150% doped placebo.	X
3.5.1	**Recovery results**	Between 95.00% and 102.90% for pasta bait. The mean recovery = 98.60% which is in conformity with the requirements which recommend recovery results in the range 95%-105%.	X
3.6	***Limit of determination***	Limit of detection = 0.05ppm Limit of quantification = 0.25ppm	X
3.7	***Precision***		
3.7.1	**Repeatability**	RSD <1.168	
3.7.2	**Independent laboratory validation**	Not available	
		4 Applicant's summary and conclusion	
4.1	***Materials and methods***	Test item was quantified by liquid chromatography on a reversed phase analytical column using an UV detector. Quality criteria applied on the method allowed to validate this analytical method for determination of difenacoum in baits.	
4.2	***Conclusion***	The analytical method showed a good specificity for difenacoum analysis. The response of difenacoum was linear within the range of 80 to 120% of the concentration in the test item. The precision was acceptable as the RSD was lower than the modified Horwitz equation. The accuracy results of difenacoum translates the narrowness between the found value and the value of reference. The recovery results were between 95% and 105%	
4.2.1	**Reliability**	2	

4.2.2 Deficiencies	No	

	Evaluation by Competent Authorities	

	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	Evaluation by Reference Member State	
Date	11.11.2010	
Materials and Methods	X The Notifier gave no information on the principle of the method only that HPLC was used with UV detection. The company clarified (1.3.2011) that the method is similar to the principle of the method used in reports 09-902018-007 and 05-912011-001. X Three injections were carried out at each of the different levels (50, 100 and 150% doped placebo) for the recovery experiment. The mean recovery at each of the fortification levels was 100.43%, 97.22% and 98.99% respectively. The overall mean was 98.88%. X LOD: the operator injected a solution containing 10 ppm of test item to calculate the S/N ratio. The operator divided by 10 then by 2 the concentration of test item until obtaining a ratio lower than 3 (S/N $\geq$ 3). LOQ: The operator injected a solution containing 50 ppm of test item to calculate the S/N ratio. The operator divided by 10 and then by 2 the concentration of test item until obtaining a ratio lower than 10 (S/N $\geq$ 10).	
Results and discussion	The results are acceptable.	
Conclusion	The information provided in this study is considered extra information only, with the exception of the LOD and LOQ information.	
Reliability	2	
Acceptability	Acceptable.	

Remarks	The company clarified that the method is similar to the principle of the method used in reports 09-902018-007 and 05-912011-001. The company also clarified that the units for the concentrations of the solutions used in the precision experiment were mg/l.

Efficacy

Subsection (Annex Point)			Official use only
5.1	**Product type(s) and field(s) of use envisaged (IIB5.1)**		
5.1.1	**Product type(s)**		
	MG03: Pest control Further specification	Product types PT14 - Rodenticides Pasta bait under “tea bag ”package	
5.1.2	**Overall use pattern**	Rodenticidal bait, containing 0.005% difenacoum as the active substance, may be used: • indoors, • around buildings, • away from building; • around waste sites and sewers. The product is used in the manner in all of these situations, the bait is placed in discrete locations within the infested area, and it is not disperses or broadcast within the environment. The products are primarily used to treat existing infestations. Locate rodents’ activity traces (droppings, holes, nests, etc.) and place the bait nearby: 1 to 3 sachets (“tea bags”) of 10g every 3 to 5 metres against ***mice*** and 3 to 6 sachets of 10g every 5 to 10 metres against rats (depending on infestation level). Protect non target animals: preferably use appropriate bait boxes or dispose the bait in a pipe section or under a tile. Check the consumption as frequent as necessary and renew consumed or soiled sachets, until the consumption has stopped. A treatment generally lasts 8 to 10 days; when the treatment is finished, remove the bait and dispose of safely.	

Renew the treatment in case of a new infestation.

An adequate of baits points are placed in dry locations, protected from the weather and in an appropriate positions to help prevent access by non-target animals.

The number of bait point employed and the amount of the product used is dependent on:

- The treatment site
- The size and the severity of the infestations
- The users, and
- The user's requirement and needs.

A large number of bait points would be used on a site where immigrations pressure is high, the existing infestations is heavy, the users is professionally competent and requires maximum control. Conversely, a low number of bait points would be used in domestic premises where the householder had sightings of a rodent pest and considered it necessary to take some action.

The common strategy for best rat control, given that rats generally live outdoors, is to place protected baits between where rats live and feed so that they encounter the bait before encountering alternative foods. Bait points are thus best placed around burrows and living area, along runs where rats habitually travels, at entry points into buildings and around area where rats are known to feed.

As mice are sporadic feeders and more confidents than rats, and they generally live indoors within inaccessible spaces and voids, the strategy for best mouse control is to place many bait points throughout the area where mice are known to feed.

Bait points are inspected frequently and the bait point is filled in when a decrease in bait is observed. When the amount bait is stabilised for more than three days it is considered that control

has been achieved and bait points are removed from the site. It is normally expected that a typical baiting treatment of an infestation will not exceed 35 day duration.

At the conclusions of a rodent control treatment all remains of bait and bait containers are removed from the site and disposal safety, in accordance with the local/national safety regulations into force.

Some Members States have specifics disposal requirement; for example, in the UK non professional users can dispose of their waste direct to landfill sites (via domestic refuse but professional users have to dispose of waste as controlled wastes under EU waste legislation. Rodents bodies must be disposed of using the same way.

5.2 Method of application including description of system used (IIB5.2)

a) Include code(s) and term(s)
b) Give name of substances used for dilution including their concentration in the biocidal product. State any other substance(s) added including purpose and concentration in the product. Describe the application technique(s). Particularly if more than one product type or application method is applicable, you may summarize these data in tabular form (see example Table A5-1 below).

The codes and terms for the Product Type 14 - Rodenticides is:

Product	Codes*	Terms*	GIFAP codes
Block	VIII.3.3	Block-bait	BB
Cereals	VIII.3.1	Granular bait	AB,
Pasta	**VIII.4.1**	**Paste**	-

Application codes for encoding Rodenticides (PT14), edited the 16 January 2009 on website Ex-ECB.* ***In point IVB5-0_01*

of the dossier)

The product is ready to use and contains 50 ppm difenacoum, as the active substance. Other components are added at the production phase of the product, but the product is not intended to be diluted with any other substance or preparation prior to use.

The product is applied but manually placing measured amounts of baits points, at discrete locations throughout a rodent infested area.

5.3 Application rate and if appropriate, the final concentration of the biocidal product and active substance in the system in which the preparation is to be used, e.g. cooling water, surface water, water used for heating purposes (IIB5.3)

For each product type and application technique give the recommended dose of the biocidal product and the active substance per object (e.g. per surface area of the material to be protected or as a concentration in a water system)

Product Type 14 - This product is ready to use and contains 50 ppm difenacoum, as the active substance.

Locate rodents' activity traces (droppings, holes, nests, etc.) and place the bait nearby: 1 to 3 sachets ("tea bags") of 10g every 3 to 5 metres against ***mice*** and 3 to 6 sachets of 10g every 5 to 10 metres against rats (depending on infestation level).

Protect non target animals: preferably use appropriate bait boxes or dispose the bait in a pipe section or under a tile.

Check the consumption as frequent as necessary and renew consumed or soiled sachets, until the consumption has stopped.

A treatment generally lasts 8 to 10 days; when the treatment is finished, remove the bait and dispose of safely.

An adequate of baits points are placed in dry locations, protected from the weather and in an appropriate positions to help prevent access by non-target animals.

Rodenticidal bait can be used indoors, around buildings, away from building, around waste sites and sewers. The amount of product laid is influenced by different factors, including the treatment site, the size and severity of infestation, the user and their requirement and needs.

5.4 Number and timing of applications, and where relevant, any particular information relating to geographical variations, climatic variations, or necessary waiting periods to protect man and animals (IIB5.4)

Indicate the recommended number and timing, i.e. duration of application and possible reapplications as well as waiting periods considered necessary. Where relevant, describe how the application should be varied in different parts of the Community. Particularly if more than one product type or application method is applicable, you may summarize these data in tabular form (see example Table A5-2 below).

Rodent control is undertaken by users in response to a rodent infestation. Rodenticidal products are used in the same manner whatever the geographical are or the climate, as the intended purpose for using the product is the same, *i.e.* to control rodent infestations. Therefore, the number and timings of applications is dependent on the presence of a rodent infestation.

An average rodent treatment should not continue beyond 35 days. (*British Pest control Association, 2001, Guidelines for the use of anticoagulant rodenticide by professional users, PT-958-1225*, ***in point IVB5-0_02 of the dossier****)*

5.5 Function (IIB5.5)

Include code(s) and term(s) for fungicide, rodenticide, insecticide, bactericide or other

The codes and terms for the Product Type 14 - Rodenticides is:

Product	Codes*	Terms*	GIFAP codes
Block	VIII.3.3	Block-bait	BB
Cereals	VIII.3.1	Granular bait	AB,
Pasta	**VIII.4.1**	**Paste**	-

Application codes for encoding Rodenticides (PT14), edited the 16 January 2009 on website Ex-ECB, **in point IVB5-0_01 of the dossier)*

5.6 Pest organism(s) to be controlled and products, organisms or objects to be protected
(IIB5.6)

5.6.1 Pest organism(s) to be controlled

Include code(s) and term(s) and state common name, scientific name, sex, strain and stadia if relevant

Rodents (I.1), Murids (I.1.1):

Codes*	Specific names*	Common English Terms*
I.1.1.1	*Rattus Norvegicus*	Brown rats
I.1.1.2	*Rattus rattus*	Roof rat, House rat
I.1.1.3	*Mus musculus*	House mouse

Application codes for encoding Rodenticides (PT14), edited the 16 January 2009 on website Ex-ECB. **In point IVB5-0_01 of the dossier)*

5.6.2 Products, organisms or objects to be protected

Include code(s) and term(s) for products, organisms or objects to be protected and the application aim

For the purpose of the protection of public health, including:

- Prevention of transmission disease;
- Prevention of the contamination of food and feeding stuffs and other materials, with urine, faeces and rodent hairs, at all stages of their production, storage and use;

- Protection of buildings and structures including pipes, cables and overall integrity;
- Protection of livestock, wild and domestic;
- Social abhorrence and stigma
- Legal requirement, for example, UK Prevention of Damage by Pest Act 1954.

Please find codes and term(s) for products, organisms or objects to be protected and the application aim in the following table:

Codes *	Terms*
VII.1	Stored product protection/food protection
VII.2	Health protection
VII.3	Material protection (i.e. historical buildings, technical objects)

Application codes for encoding Rodenticides (PT14), edited the 16 January 2009 on website Ex-ECB.* ***In point IVB5-0_01 of the dossier**)*

5.7 Effects on target organisms (IIB5.7)

Describe the effects on the target organisms required for the claimed efficacy and specify these for each product type and method of application if appropriate.

Anticoagulant rodenticides disrupt the normal blood-clotting, mechanisms, resulting in increased bleeding tendency and eventually, and profuse haemorrhage.

Signs of anticoagulant poisoning in rats and mice included lethargy, hunched posture and vain clearing in the ears. Blood around the eyes, mouth and anus, indicating internal haemorrhaging, appears prior to death. *(Extract from WHO, 1995. Environmental Health Criteria 175 – Anticoagulant Rodenticides, International Programme on Chemical Safety, pages 22 and 55,* ***in point IVB5-0_03 of the dossier****)*

5.8 Mode of action (including time delay) in so far as not covered by section A5.4 (IIB5.8)

Refer to data given for the active substance or describe here. If appropriate, refer to experimental studies summarized in section 5.10 or any other studies.

Difenacoum is a second generation anticoagulant which prevents blood clotting in the target organisms by inhibiting regeneration of the active form of vitamin K1.

(*Extract Assessment Report – Difenacoum, Product-type 14 (Rodenticides), Directive 98/8/EC concerning the placing of biocidal products on the market. Inclusion of active substances in Annex I or IA to Directive 98/8/EC, 17 September 2009, Annex I – Finland, p9,* ***in point IVB5-0_04 of the dossier***).

Anticoagulant rodenticides are vitamin K antagonists. The main site of their 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 point of action appears to be the inhibition of K1 epoxide reductase.

Anticoagulant rodenticides are easily absorbed from the gastrointestinal tract, and may also be absorbed through the skin and respiratory system. After oral administration, the major route of elimination in various species is through the faeces.

The metabolic degradation of warfarin and indandiones in rats mainly involves hydroxylation. However, the second-generation anticoagulants are mainly eliminated as unchanged compounds. The low urinary excretion precludes isolation of metabolites from the urine.

(Extract from WHO, 1995. Environmental Health Criteria 175 – Anticoagulant Rodenticides, International Programme on Chemical Safety, pages 20, ***in point IVB5-0_03 of the dossier****).*

The liver is the main organ for accumulation and storage of rodenticide anticoagulants. Difenacoum has been found in the liver as both the parent compound and metabolites. The metabolism and elimination of the *trans*-isomer was more rapid than those of the *cis*-isomer.

The elimination from the liver and kidney is biphasic with an initial rapid phase of three days and a slower phase with a half-life of 118-120 days. In the pancreas, the concentration declined more slowly (a half-life of 182 days). No data are available for the kinetics and metabolism of difenacoum in humans.

(*Extract from IPCS International Programme On Chemical Safety, Health and Safety Guide No. 95, Difenacoum Health And Safety Guide, United Nations Environment Programme, International Labour Organisation, World Health Organization, World Health Organization, Geneva 1995,* ***in point IVB5-0_05 of the dossier***)

Accumulation also occurs in the fat.

Clinical signs are progressive and occur within 18 hours after ingestion of a toxic dose, ultimately leading to death from 3 to 10 days later. Effects are reversible by administration of the antidote vitamin K1 which stimulates the regeneration of the clotting factors.

(*Extract Assessment Report – Difenacoum, Product-type 14 (Rodenticides), Directive 98/8/EC concerning the placing of biocidal products on the market. Inclusion of active substances in Annex I or IA to Directive 98/8/EC, 17 September 2009, Annex I – Finland, p9,* ***in point IVB5-0_03 of the dossier****).*

5.9 User: industrial, *Include code(s) and term(s) and briefly describe the use*

professsional, general public (non-professional) (IIB5.9)

conditions

Please find codes and term(s) for products, organisms or objects to be protected and the application aim in the following table:

Codes *	Terms*
V.1	Non professional/general public
V.2	Professional
V.3	Specialised professional

Application codes for encoding Rodenticides (PT14), edited the 16 January 2009 on website Ex-ECB., **in point IVB5-0_01 of the dossier).*

1. Industrial

[The inclusion of further exposure information is possible, see e.g. EASE (LEV, Full containment etc.)]

ormulation of the product requires a number of stages:

he batch process is performed at least once per week, as and when orders and stock level require it. Preparation, i.e. charging the mixer with the formulation components, takes 30minutes with a mixing time of 5 minutes.

ppropriate RPE/PPE is used at each stage. This prevents exposure by inhalation and dermal routes. Routine worker monitoring confirms no exposure.

Please refer to Manufacturing Process description in Doc IVB 1 (Confidential)

Please refer also to DOC I_Appendix 2_ description of packaging

2. Professional

his user group is not exposed to the active substance, except when formulated in a rodenticidal product at the concentration of 50 ppm.

he following tasks are undertaken when using rodenticidal baits.

- Decanting of bait from bulk container may occur;
- Loading of bait point with bait;

- Topping-up bait points when bait has been consumed, and
- Clean-up and disposal of spent baits at the end of the treatment.

oading the bait point with bait and topping up bait points when bait has been consumed are essentially identical tasks.

lthough gloves are not necessary when handling the product they are recommended for protection against exposure to rodent-borne diseases.

is expected that a professional user would undertake a risk assessment to the standard required by chemical Agents Directive 98/24/EC o, order to determine if any exposure controls are required for any specific tasks on specific treatment sites.

Refer to DOC I_Appendix 2_ description of packaging

3. General public

his user group is not exposed to the active substance, except when formulated in a rodenticidal product at the concentration of 50 ppm.

he following tasks are undertaken when using rodenticidal baits.

- Decanting of bait from bulk container may occur;
- Loading of bait point with bait;
- Topping-up bait points when bait has been consumed, and
- Clean-up and disposal of spent baits at the end of the treatment

oading the bait point with bait and topping up bait points when bait has been consumed are essentially identical tasks.

lthough gloves are not necessary when handling the product they are recommended for protection against exposure to rodent-borne diseases.

xposure id indirectly limited by controls on pack sizes available to this user group.

Please refer to DOC I_Appendix 2_ description of packaging

5.10 Efficacy data: The proposed label claims for the product and efficacy data to support these claims, including any available standard protocols used, laboratory tests, or field trials, where appropriate (IIB5.10)

5.10.1 Proposed label claims for the product

or the control of rats and mice by professional and non – professional users.

Locate rodents' activity traces (droppings, holes, nests, etc.) and place the bait nearby: 1 to 3 sachets ("tea bags") of 10g every 3 to 5 metres against ***mice*** and 3 to 6 sachets of 10g every 5 to 10 metres against rats (depending on infestation level).

Protect non target animals: preferably use appropriate bait boxes or dispose the bait in a pipe section or under a tile.

Check the consumption as frequent as necessary and renew consumed or soiled sachets, until the consumption has stopped.

A treatment generally lasts 8 to 10 days; when the treatment is finished, remove the bait and dispose of safely.

general rodenticide treatment with anticoagulant rodenticides would be expected to achieve control within 35 days.

Please refer to DOC I_Appendix 1_ proposed draft label text for this representative product.

5.10.2 Efficacy data

Include efficacy data; use standard format B5_10 to summarize any efficacy tests

All efficacy studies have been summarised using the standard format B5_10.

5.11 Any other known limitations on efficacy including resistance (IIB5.10)

Give information on the occurrence of resistance or possible occurrence of the development of resistance and appropriate management strategies. If appropriate, refer to test results described in section 5.10.2.

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. No reports have been submitted to the Rapporteur Member State about the distribution and incidence of resistance in the house mouse or black rat in Europe.

(*Extract Assessment Report – Difenacoum, Product-type 14 (Rodenticides), Directive 98/8/EC concerning the placing of biocidal products on the market. Inclusion of active substances in Annex I or IA to Directive 98/8/EC, 17 September 2009, Annex I – Finland, p9 and 21,* ***in point IVB5-0_03 of the dossier****).*

Please also refer to efficacy studies summarised in B5_10 of the dossier.

5.11.1 Use-related restrictions

Describe possible restrictions or recommendations concerning the use of the product in specific environmental or other conditions.

It is widely accepted as good general practice of rodent control that removal of alternative food and feedstuffs, clearing up any spillages of possible food sources and containment of stocks of feedstuffs will promote the take of the bait. Also, following a successful rodenticide treatment the removal of vegetation, rubbish and any other potential burrows will help maintain a

rodent free site.

This information is communicated to the user via industry and through product-related literature, in the form of leaflets or web pages.

(*Extract Assessment Report – Difenacoum, Product-type 14 (Rodenticides), Directive 98/8/EC concerning the placing of biocidal products on the market. Inclusion of active substances in Annex I or IA to Directive 98/8/EC, 17 September 2009, Annex I – Finland, p9 and 21,* ***in point IVB5-0_03 of the dossier****).*

5.11.2 Prevention of the development of resistance

Describe and give reasons for possible recommendations concerning the avoidance of the continuous use of the product in order to prevent the development of resistant strains.

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.
- These programmes must be effectively coordinated and should encompass the procedures identified above.

(Extract Anticoagulant resistance management strategy for pest management professionals, central and local government and other competent users of rodenticides. Crop Life International RRAC (Rodenticide Resistance Action Committee) Technical Monograph, Brussels, p. 18 and www.croplife.org, 2003, p11, ***in point IVB5-0_06 of the dossier***)

Resistance Management Strategies:

The important issues here are firstly to identify strategies for avoiding the development of resistance in susceptible rodent populations and secondly to identify strategies for managing resistance to the anticoagulants when it is suspected or

identified.

Remember that the normal strategy used for managing resistance in populations of insects, weeds or other pests is to rotate the control between different groups of pesticide, targeting as they do, different control mechanisms.

Unfortunately, the anticoagulant rodenticides all work in much the same way and the nature of the resistance to the different anticoagulants is so similar that simply rotating between the anticoagulants is not a reliable means of managing anticoagulant resistance. However, using anticoagulants of higher toxicity plays a major part in resistance management. In case of confirmed practical resistance, an anticoagulant rodenticide of higher toxicity compared to that, which is hit by resistance, should be used to eradicate the infestation. In some cases, especially with mice, alternations with non-anticoagulants can be part of the strategy.

(Extract Anticoagulant resistance management strategy for pest management professionals, central and local government and other competent users of rodenticides. CropLife International RRAC (Rodenticide Resistance Action Committee) Technical Monograph, Brussels, p. 18 and www.croplife.org, 2003, p8, ***in point IVB5-0_06 of the dossier***)

5.11.3 Concomittant use with other (biocidal) products

State if the product cannot be mixed with other substances, particularly other biocidal products, or if the use of the product with other biocidal products is recommended.

The product is ready to use and is not intended to be mixed with any other substance or preparation

Section B5.10_01

Official use only

5 Reference

5.1 Reference

Mahaut T., Cavellier M., CRA Gembloux, Efficacy test on DIFEPASTA, bait ready to use, containing 0.005% of Difenacoum, against grey mice (*Mus musculus* L.), ROD 2003-03-Belgagri, 20 October 2003.

CRA (Agronomic Research Center), Phytopharmacological department, Rue du Bordia, 11, 5030 Gembloux Belgium.

Unpublished

5.2 Data protection

Yes

5.2.1 Data owner

BELGAGRI

Industrial Zone of Noville-les-Bois

14, rue du Grand Champ

5380 FERNELMONT, Belgium

5.2.2 Criteria for

Data submitted to the MS before 14 May 2000 on existing [a.s. / b.p.]

data protection	for the purpose of its [entry into Annex I/IA / authorisation] / Post inclusion	
5.3 Guideline study	Decision critters edited by the Major Guideline for the Rodenticide efficacy assessment (*Lignes Directrices pour l'évaluation de l'Efficacité des Rodenticides)*	X
5.4 Deviations	No	

6 Method

Test Substance (Biocidal Product)	as given in section 2 deviating from specification given in section 2 *(Fill in the fields 3.1.2 and 3.1.3)*	
Trade name/ proposed trade name	DIFEPASTA	
Composition of Product tested	0.005 % of Difenacoum	
Physical state and nature	Bait ready to use in small portion (sachet/tea bag) with pink paste of 15g.	
Monitoring of active substance concentration	Yes, The results will be used in appetizing test and chemical evolution of the product through time in rapport 11 594, summarised in IIIB_5-10_02.	
Method of analysis	HPLC	
Reference substance	No.	
Method of analysis for reference	Not applicable	

substance

Testing procedure

Test population / inoculum / test organism

Efficacy test on mice: 10 (*Mus musculus*) capture in enclosure in the warehouse area from Gembloux. The mice population in the enclosure is fed with crushed wheat.

The initial population from this enclosure are renewed every year.

Test system

Rodents are housed in individual cage.

Application of TS

Mice efficacy trials:

- Pre-baiting: 10g of crushed wheat.
- Poisoning bait Vs safe food: 15g of DIFEPASTA and 10g of crushed wheat.
-

The remainders from each rodent are weighed every morning and mangers are refilled.

Test conditions

Minimum three weeks were observed between the first and the last captured rodent, in order to suppress pregnant female and sick animals from the test.

Duration of the test / Exposure time

- Pre-baiting with crushed wheat: 5days
- Poisoning bait Vs safe crushed bait: 21 days

Number of replicates performed

No replicates.

Controls

Yes, 2 rodents were fed with crushed wheat during the entire test

- one male
- one female

Examination

Effect investigated	Efficacy of DIFEPASTA on grey mice NB: The efficacy trials was carried out with the same product sample and it is developed in study summarised in IIIB_5-10_06, report 11594 (stored product on grey mice)
Method for recording / scoring of the effect	The method is to estimate the food consumption, by weighing every day the mangers and compares values obtained from safe food and poisoning bait.
Intervals of examination	Daily
Statistics	The total death in rodents.
Post monitoring of the test organism	Yes, the main and only phase is the poisoning and the post monitoring observations.

7 Results

Efficacy	Every mouse died excepted one animal on 10. The efficacy is 90% in mice.
Dose/Efficacy curve	Mice population died after a bait consumption between 5.0 and 15.1g by animal.
Begin and duration of effects	Mice died without the 21 days of observation settle down in protocol.
Observed effects in the post monitoring phase	All mice died excepted one mouse which survived after the 21 days required for the observation phase, after ingested 38.8 g of DIFEPASTA. This animal seems less sensitized than other to the paste bait rodenticide.

Effects against organisms or objects to be protected Not applicable

Other effects Not applicable

Efficacy of the reference substance Not applicable

Tabular and/or graphical presentation of the summarised results Please find summarised results in the following table:

Timing (months)	Rate in Difenacoum (mg/kg)	Number of (10 animals)	
		death mice	Survived mice
T0	53.5	9	1

Efficacy limiting factors

Occurrences of resistances Not applicable

Other limiting factors Not applicable

8 Relevance of the results compared to field conditions

Reasons for laboratory testing	The laboratory conditions shows the : • Daily amount of food consumed by rodents • Timing needed for the product efficacy after ingestion • Rodent's behaviour in competitive food condition (appetizing behaviour of rodents in presence of product) All these parameters are important when the scaling will be settled down.	
Intended actual scale of biocide application	Not applicable	
Relevance compared to field conditions	The parameters explained in 4.1 are estimated, the individual specification of mice can varied in an open space. Moreover, in nature rodent have access to other kind of food.	
Application method	In this laboratory experiment, rodents have accessed to two types of food. In nature condition, rodents have access to other kind of food, which can run in competition with the poisoned bait. Moreover the change in food can cause mistruth and modify the alimentary behaviour in rodents. It is very interesting to observe and compare their behaviour in the field condition. Moreover, nature trials are closer to real condition of use than a laboratory process.	X
Test organism	YES	X

Observed effect YES X

Relevance for read-across Yes,
We can refer to the study, which regrouped all excellent parameters, as a relevant example of efficacy test for the dossier.

9 Applicant's Summary and conclusion

Materials and methods The aim of the experiment is to observe efficacy results in wild rodents species:

- Grey mice (*Mus musculus*)

Mice (*Mus musculus*) were captured in warehouse.

Initial population from these enclosures are renewed every year. Enclosed rodents were fed entire wheat for mice.

After acclimatization period in their individual cage, where rodent received water and food ad libitum, the experimentation could start. The food portion were weighed and refilled every day:

- 10 g for mice of crushed wheat in manger
- 15g for mice for tested product, DIFEPASTA in manger.

DIFEPASTA, the tested product is a rodenticide containing 0.005 % of Difenacoum, presented as pink paste in small portion of 15g.

This experiment contains only two phases:

- Pre baiting
- Poisoning and monitoring phase grouped together.

Controls were observed during 21 days.

The concentration in active ingredient was also determined before the experiment.

Reliability 1, Study conducted in compliance with agreed protocols. X

Assessment of efficacy, Nine mice died from the absorption of DIFEPASTA after a consumption of bait between 5.0 and 15.1 g by mouse during the 21

data analysis and interpretation	days of observation. Only one mouse survived to the poisoning bait after a huge and abnormal consumption of DIFEPASTA bait (38.8g). This animal seems less sensitized than other mice to the paste bait rodenticide
Conclusion	DIFEPASTA, rodenticide bait containing 0.005% de Difenacoum, is sufficient attractive and very efficient to fight against grey mice (*Mus musculus*). The efficacy is 90% in mice
Proposed efficacy specification	DIFEPASTA can be used to fight against mice.

Evaluation by Competent Authorities	
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	10 Evaluation by Rapporteur Member State
Date	April 2011.
Comments	**1.3** The decision criteria were not attached to the test report. **4.3.1** The word “mistruth” should be changed to “mistrust”. **4.3.2** Test organism – Wild strain of grey mice (*Mus musculus*), trapped in a warehouse. **4.3.3** Observed effect – 90% efficacy. **5.2** Reliability of 2 is more appropriate. Table 1.3: Number of vessels is 10 as singly caged animals tested following capture.

Summary and conclusion	The test is considered to be acceptable although the use of 20 animals is recommended in the TNsG on product evaluation. 90% mortality of mice was observed. One mouse survived consuming what would be considered an abnormally large dose of the poison bait and was considered by the applicant to be “less sensitised” than the other test animals. No further investigations into possible quantifiable resistance were conducted. Notwithstanding the survival of this mouse, the palatability and lethality of the fresh DIFEPASTA are considered valid and acceptable.

11 Comments from ... *(specify)*

Date	*Give date of comments submitted*
Comments	*Discuss if deviating from view of rapporteur member state*
Summary and conclusion	*Discuss if deviating from view of rapporteur member state*

Tables for Method

1.1 (mixed) Population / Inoculum (*if necessary; include separate table for different samples*)

Criteria	Details
Nature	DIFEPASTA: rodenticide bait. Pink paste in small portion of 15g. Containing 0.005 % of Difenacoum
Origin	Production batch / date: 10/2003 Number in the lab: R211003b
Initial biomass	Not applicable
Reference of methods	Not mentioned
Collection / storage of samples	Not mentioned
Preparation of inoculum for exposure	Not mentioned
Pretreatment	Twenty kilos of DIFEPASTA Arrived at lab the 21/10/03. It is considered as fresh and it is dispatched in several sub-samples: • 0.3 kg at -18°C, waiting the fresh product experiment. • 9.6 kg in a storage room, at+20°C for 6, 12 and 24 months, for appetizing test on stored product. • 10.1 kg at 4°C for efficacy trial on grey mice.
~~**Initial density of test population in the test system/**~~ **Active substance determined in the product**	Chemical analyse of Difenacoum in fresh DIFEPASTA is 53.5 mg s.a. /kg (ALBI 2003-06).

1.2 Test organism number 1

Criteria	Details
Species	Grey mice *(Mus musculus)*
Strain	Wild
Source	Captured in warehouse
Laboratory culture	No applicable Mice are captured in enclosure from a warehouse. Every year, enclosures populations are refill in with new mice. Population in enclosure were fed with entire wheat. During the experiment rodents are housed in individually cage in 0.5m x 0.3mx 0.25m. They were acclimatized in their cage with water and fresh crushed wheat.
Stage of life cycle and stage of stadia	No applicable.
Mixed age population	Not mentioned
Other specification	Not applicable due to the test conditions
Number of organisms tested	10 mice
Method of cultivation	Consumed food was weighted and replace daily.
Pretreatment of test	Not mentioned

organisms before exposure	
Initial density/number of test organisms in the test system	10 mice

1.3 Test system

Criteria	Details
Culturing apparatus / test chamber	Not applicable due to the test conditions. Rodents are housed in individual cage at lab.
Number of vessels / concentration	.
Test culture media and/or carrier material	
Nutrient supply	
Measuring equipment	

1.4 Application of test substance

<table>
<tr><th>Criteria</th><th>Details</th></tr>
<tr><td>Application procedure</td><td>During the 5 first days, rodents received of crushed wheat in mangers. Every day, the consumption is measured.

Then, another manger is added which is contained the poisoning bait. Every day, mangers are alternated in their position.
During this period control received their usual crushed wheat.

Consumed food is weighed and replaced every day.</td></tr>
<tr><td>Delivery method</td><td>In mangers</td></tr>
<tr><td>Dosage rate</td><td>- 10g of crushed wheat.
- 15g of DIFEPASTA:

Every day, mangers are alternated in their position.</td></tr>
<tr><td>Carrier</td><td>Not applicable due to the test conditions</td></tr>
<tr><td>Concentration of liquid carrier</td><td>Not applicable due to the test conditions</td></tr>
<tr><td>Liquid carrier control</td><td>Not applicable due to the test conditions</td></tr>
<tr><td>Other procedures</td><td>The product DIFEPASTA was tested at different time in the same lab conditions. The experiments were carried out at:

<table>
<tr><th></th><th>Storage at 20°during</th><th>Code analysis</th><th>Experiment started on</th></tr>
<tr><td>T0</td><td>0 months</td><td>FO-Ch-3000-2003-194</td><td>13/11/03</td></tr>
<tr><td>T12</td><td>12 months</td><td>FO-Ch-3178-2004-183</td><td>10/11/04</td></tr>
<tr><td>T24</td><td>24 months</td><td>FO-Ch3420-2005-A</td><td>09/11/05</td></tr>
</table>
</td></tr>
</table>

1.5 Test conditions

Criteria	Details
Substrate	Not applicable due to the test conditions
Incubation temperature	
Moisture	
Aeration	
Method of exposure	
Aging of samples	
Other conditions	

Section B5.10_02

Reference

Official use only

Reference

De Proft M., Galoux M., CRA Gembloux, Efficacy test through different period of time, performed on DIFEPASTA, bait ready to use, containing 0.005% of Difenacoum, rapport number 11 594 ROD 2003-003, June 2006.

CRA (Agronomic Research Center), Phytopharmacological department, Rue du Bordia, 11, 5030 Gembloux Belgium

Data protection

Yes

Data owner

BELGAGRI

Industrial Zone of Noville-les-Bois

14, rue du Grand Champ

5380 FERNELMONT, Belgium

Criteria for data

Data submitted to the MS before 14 May 2000 on existing [a.s. / b.p.]

protection	for the purpose of its [entry into Annex I/IA / authorisation] / Post inclusion
Guideline study	Decision critters edited by the Major Guideline for the Rodenticide efficacy assessment (*Lignes Directrices pour l'évaluation de l'Efficacité des Rodenticide)*
Deviations	No

12 Method

Test Substance (Biocidal Product)	as given in section 2 deviating from specification given in section 2 *(Fill in the fields 3.1.2 and 3.1.3)*
Trade name/ proposed trade name	DIFEPASTA
Composition of Product tested	0.005 % of Difenacoum
Physical state and nature	Pink paste in small portion of 15g.
Monitoring of active substance concentration	Yes, Before each test, determination in of active substance containing in DIFEPASTA
Method of analysis	HPLC
Reference substance	No.
Method of analysis for reference substance	Not applicable
Testing procedure	

Test population / inoculum / test organism

20 white mice were tested at T12 and T24 months.

- 10 males
- 10 females

Test system

Mice are housed in individual cage.

Application of TS

The product DIFEPASTA was tested at different time in the same lab conditions. The experiments were carried out at:

- T0, fresh product.
- T12, 12 months of storage at 20°C
- T24, 24 months of storage at 20°C

At each experiment, mice received a daily portion of food, composed by:

- A manger with 10g of crushed wheat during the pre bait and bait phase.
- A manger with the tested product, DIFEPASTA during the bait phase.

Consumed food is weighed every day.

Test conditions

Mice are between 10 and 20 weeks at the beginning of each experiment.

Duration of the test / Exposure time

- Pre-baiting with crushed wheat: 5days
- Poisoning bait Vs safe crushed bait: 21 days

Number of replicates performed

No replicates.

Controls

Yes, 2 rodents were fed with crushed wheat during the entire test

- one male
- one female

Examination

Effect investigated

Efficacy of DIFEPASTA on grey mice at different period of storage.

NB: The efficacy trials was carried out with the same product sample and it is developed in study summarised in IIIB_5-10_05, report ROD 2003-03-Begagri; 20 October 2003 (fresh product on grey mice)

Method for recording / scoring of the effect

The method is to estimate the food consumption, by weighing every day the mangers and compares values obtained from safe food and poisoning bait.

Intervals of examination

Daily

Statistics

Total consumption of each kind of food absorbed by rodent population.

Post monitoring of the test organism

Yes, the main and only phase is the poisoning and the post monitoring observations.

13 Results

Efficacy

The efficacy of DIFEPASTA with mice is 90% X

- At T0, all tested animal died excepted one mouse on 10, please see summary in point IIIB-5.10-01.

After 12 months, the efficacy of DIFEPASTA reaches 100% with mice.

- At T12, all tested mice died. (n=20)

After 2 years, the efficacy of DIFEPASTA decreases to 85% with mice.

- At T24, all tested animal died excepted 4 mice on 20.

Dose/Efficacy curve

Please find the results if the chemical analysis and the number of death. X

Timing (months)	Rate in Difenacoum (mg/kg)	Number of death
		Mice/20
T0	53.5	-
T6	55.5	-
T12	53.0	20
T24	47.6	16

According to chemical critters edited by the Major Guideline for the Rodenticide efficacy assessment, DIFEPASTA is conforming.

Begin and duration of effects

At T12, the efficacy is 100 in mice.

At T24, the efficacy in mice is 80%.

X

Observed effects in the post monitoring phase

1) Death of rodent is observed.
2) All the tested animals have absorbed the DIFEPASTA, but some of mice seems less sensitized than other animals in the selected population.

Effects against organisms or objects to be protected

Not applicable

Other effects

-

Efficacy of the reference substance

Not applicable

Tabular and/or graphical presentation of the summarise

Please find results obtained from the chemical analysis and the number of dead in the tested rodents.

d results

Timing (months)	Rate in Difenacoum (mg/kg)	Number of dead mice	Number of survived Mice
T0	53.5	9/10	1/10
T12	53.0	20/20	0/20
T24	47.6	16/20	4/20

Efficacy limiting factors

Occurrences of resistances Not applicable

Other limiting factors Not applicable

14 Relevance of the results compared to field conditions

Reasons for laboratory testing

The laboratory conditions shows the :

- Daily amount of food consumed by rodents
- Timing needed for the product efficacy after ingestion
- Rodent's behaviour in competitive food condition (appetizing behaviour of mice in presence of product)

All these parameters are important when the scaling will be settled down.

Intended actual scale of biocide application

Not applicable

Relevance compared to field conditions

The parameters explained in 4.1 are estimated, the individual specification of mice can varied in an open space. Moreover, in nature rodent have access to other kind of food.

Application method	In this laboratory experiment, rodents have accessed to two types of food. In nature condition, rodents have access to other kind of food, which can run in competition with the poisoned bait. Moreover the change in food can cause mistruth and modify the alimentary behaviour in mice. It is very interesting to observe and compare their behaviour in the field condition. Moreover, nature trials are closer to real condition of use than a laboratory process.	
Test organism	YES	X
Observed effect	YES	X
Relevance for read-across	Yes, We can refer to the study, which regrouped all excellent parameters, as a relevant example of efficacy test for the dossier.	

15 Applicant's Summary and conclusion

Materials and methods	The aim of the experiment is to compare appetizing behaviour of mice with safe food and poisoning product at different stage of storage: T0, T12 and T24 months. DIFEPASTA, the tested product is a rodenticide containing 0.005 % of Difenacoum, presented as Pink paste in small portion of 15g. During the test, rodents received food dispatched as: - 10g of crushed wheat in manger - the tested product, DIFEPASTA in manger Consumed food is weighed every day.	

This experiment contains only two phases:

- Pre baiting
- Poisoning and monitoring phase grouped together.

Controls were observed during 21 days.

The concentration in active ingredient was also determined before the experiment.

Reliability

1, Study conducted in compliance with agreed protocols.

Assessment of efficacy, data analysis and interpretation

The appetizing test performed on white mice with the 12 months stored product killed all the tested mice. After 24 months of storage, the product kills 16 mice on 20, either 4 mice difference with the fresh product. Thus, this result is conforming.

Conclusion

After 12 months, the efficacy of DIFEPASTA reaches 100% with mice. X

- At T12, all tested mice died. (n=20)

After 2 years, the efficacy of DIFEPASTA decreases to 85% with mice.

- At T24, all tested animal died excepted 4 mice on 20.

The conforming delay could be fixed to 24 months.

DIFEPASTA is conforming with the chemical critters edited by the Major Guideline for the Rodenticide efficacy assessment

Proposed efficacy specification

DIFEPASTA can be used to fight against mice.

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted

16 Evaluation by Rapporteur Member State

	Evaluation by Competent Authorities
Date	April 2011.
Comments	**3.1, 3.1.1, 5.4** These results are contradictory. From the study report the results indicate that the fresh bait achieved 4 mice survived consuming the 24-month aged bait (80% efficacy). **3.1.2** At T12, the efficacy is 100% in mice. **4.3.2** Test organism – White mice (*Mus musculus*). **4.3.3** Observed effect – 100% mortality with 12-month aged bait and 80% with 24-month aged bait.
Summary and conclusion	DIFEPASTA (aged bait) performed excellently in the test. The 12-month and 24-month aged pasta bait achieved 100% and 80% control of the mice tested respectively.

	17 Comments from ... *(specify)*
Date	*Give date of comments submitted*
Comments	*Discuss if deviating from view of rapporteur member state*
Summary and conclusion	*Discuss if deviating from view of rapporteur member state*

Tables for Method

1.1 (mixed) Population / Inoculum (*if necessary; include separate table for different samples*)

Criteria	Details
Nature	DIFEPASTA: rodenticide bait. Pink paste in small portion of 15g. Containing 0.005 % of Difenacoum
Origin	Production batch / date: 10/2003 Number in the lab: R211003b
Initial biomass	Not applicable
Reference of methods	Not mentioned
Collection / storage of samples	Not mentioned
Preparation of inoculum for exposure	Not mentioned
Pretreatment	Twenty kilos of DIFEPASTA Arrived at lab the 21/10/03. It is considered as fresh and it is dispatched in several sub-samples: • 0.3 kg at -18°C, waiting the fresh product experiment. • 9.6 kg in a storage room, at+20°C for 6, 12 and 24 months, for appetizing test on stored product. • 10.1 kg at 4°C for efficacy trial on grey mice.
Initial density of test population in the test system	Chemical analyse of Difenacoum in fresh DIFEPASTA is 53.5 mg s.a. /kg (ALBI 2003-06).

1.2 Test organism number 1

Criteria	Details
Species	Mice (*Mus musculus*)
Strain	White
Source	Not mentioned
Laboratory culture	No applicable
Stage of life cycle and stage of stadia	Not applicable due to the test conditions
Mixed age population	Not mentioned
Other specification	Not applicable due to the test conditions
Number of organisms tested	22 mice at T12 and T24 months - 20 for the tested product (half of each sex) - 2 as controls (half of each sex)
Method of cultivation	Consumed food was weighted and replace daily.
Pretreatment of test organisms before exposure	Not mentioned
Initial density/number of test organisms in the test system	20 mice

1.3 Test system

Criteria	Details
Culturing apparatus / test chamber	Not applicable due to the test conditions.
Number of vessels / concentration	
Test culture media and/or carrier material	
Nutrient supply	
Measuring equipment	

1.4 Application of test substance

<table>
<tr><th>Criteria</th><th>Details</th></tr>
<tr><td>Application procedure</td><td>During the 5 first days, mice received 30g of crushed wheat in mangers. Every day, the consumption is measured.

Then, another manger is added which is contained the poisoning bait. During this period control received their usual crushed wheat.

Consumed food is weighed and replaced every day.</td></tr>
<tr><td>Delivery method</td><td>In mangers</td></tr>
<tr><td>Dosage rate</td><td>- 10g of their usual food
- DIFEPASTA: same amount of wheat</td></tr>
<tr><td>Carrier</td><td>Not applicable due to the test conditions</td></tr>
<tr><td>Concentration of liquid carrier</td><td>Not applicable due to the test conditions</td></tr>
<tr><td>Liquid carrier control</td><td>Not applicable due to the test conditions</td></tr>
<tr><td>Other procedures</td><td>The product DIFEPASTA was tested at different time in the same lab conditions. The experiments were carried out at:

<table>
<tr><th></th><th>Storage at 20°during</th><th>Code analysis</th><th>Experiment started on</th></tr>
<tr><td>T0</td><td>0 months</td><td>FO-Ch-3000-2003-194</td><td>13/11/03</td></tr>
<tr><td>T12</td><td>12 months</td><td>FO-Ch-3178-2004-183</td><td>10/11/04</td></tr>
<tr><td>T24</td><td>24 months</td><td>FO-Ch3420-2005-A</td><td>09/11/05</td></tr>
</table>
</td></tr>
</table>

1.5 Test conditions

Criteria	Details
Substrate	Not applicable due to the test conditions
Incubation temperature	
Moisture	
Aeration	
Method of exposure	
Aging of samples	
Other conditions	

Section B5.10_3

Reference

Official use only

17.1 Reference

- LODI, Efficacy trial: Pasta Dife/ Mice- Confidential report, LODI property, 12 pages, Feb2009.

17.2 Data protection

Yes

17.2.1 Data owner

LODI S.A.,

Parc d'activité des Quatre Routes,

35390 Grand Fougeray, FRANCE

17.2.2 Criteria for data protection

Data submitted to the MS before 14 May 2000 on existing [a.s. / b.p.] for the purpose of its [entry into Annex I/IA / authorisation] / Post inclusion

17.3 Guideline study

Yes,

The method used has been inspired by the French method called "method no. 002 from Biological Trials Commission (C.E.B) ", Method

for practical efficacy trials of raticides:

- Adopted on 1960, derived from the work of Chitty and Dotty in the 1940.
- Revised by OEPP in 1980.

17.4 Deviations

No

18 Method

Test Substance (Biocidal Product)

as given in section 2

deviating from specification given in section 2

(Fill in the fields 3.1.2 and 3.1.3)

Trade name/ proposed trade name

PASTA DIFE

Composition of Product tested

0.005 % of Difenacoum

Physical state and nature

Fresh paste bait containing 0.005% of Difenacoum

Monitoring of active substance concentration

No X

Method of analysis

Testing method of practical efficacy of raticides of the CEB, revised by OEPP:

This method has been adapted to anticoagulants. This is a relative method, which consists in the comparison of two stages of consumption of a placebo: one before, one after the phase of poisoning bait.

It is nearly impossible to know the number rodents, it can only be estimated.

The method consisting offering the placebo of the bait, in bait station that permit to carry out consumption measurements, and to daily statements with the placing of new baits, until we obtain a global consuming stabilised over 3 consecutive days. Then an estimation of the whole population can be made on basis of the food consumed.

A graph represents the variation in daily consumption. When a regular plateau is reached on the graph, it means that the number of rats is high. The value of the consumption plateau is taken as a criterion for the population level.

The practical efficacy trial therefore contains 3 consecutive periods:

- 1st period: determination of the consumption plateau of the initial population,
- 2nd period: execution of the raticides treatment,
- 3rd period: establishment of the consumption plateau for the surviving population.

The comparison of obtained plateau in phase 1 and 3 is executed enables the efficacy of the treatment to be calculated as a relative value.

If Ci (= initial consumption) is the average value of the consumption plateau before treatment and Cr is the average value of the residual consumption, the efficacy of the treatment is expressed as follows:

$$E = [(Ci – Cr)/Ci] \times 100$$

The Ci and Cr values are calculated by weighing on at least three consecutive days.

The method is applied for *Mus musculus*.

Reference substance

No

Method of analysis for reference substance

-

Testing procedure

Test population / inoculum / test organism

Mus musculus.

When the wheat consumption reaches a plateau it means that the mice population is the highest.

Test system

The experimental site is a restaurant: “Le Zimmer” (75001 Paris) which is composed at the -1 level:

- 2storage rooms ,2 cloakroom,
- Freezers, 4 cold rooms for food, Kitchen for vegetables
- Boiler room and goods lift

The ground level is composed by a restaurant room. Some bait is placed in the equipped kitchen and in laundry room.

Application of TS

Baits were weighed and filled every morning with 100g of wheat.

Test conditions

The experimental site is a restaurant: Le Zimmer (75001 Paris) which is composed of 2 levels. Please find in the following tables where exactly baits were placed at each part of the building:

level	Parts	Baits are in
-1	Equipment stock 1	4 places (1 to 4)
	Equipment stock 2	2 places (5 and 6)
	Freezer	1 place (7)
	Women cloakroom	2 places (8 and9)
	Dustbins	1 place (10)
	Goods lift	2 places (11 and 12)
	Cold room vegetables	1 place (13)
	Cold room dairy	1 place (14)

	Cold room meats	1 place (15)
	Cold room fishes	1 place (16)
	Electrical panel	2 places (17 and 18)
	Boiler room	2 places (19 and 20)
	Kitchen	1 place (21)
	Kitchen for vegetables	4 places (22, 34 to 36)
	Men cloakroom	5 places(23 to 27)
0	Kitchen	4 places(28 to 31)
	Laundry	2 places(32 and 33)

Bait boxes are placed where there are sign of mice's activity.
Not many droppings have been seen at the level 0, probably because of the frequent cleaning. Nevertheless, a few bait boxes were put there, in cupboards or onto shelves. Clod rooms (refrigerators): hermetic rooms, no mice tracks, no consumption is expected.

Duration of the test / Exposure time

Pre-baiting: 16 days (4th to 20th February)

Poisoning bait: 7 days (21th to 27th February)

Post-baiting: 6 days (28th February to 5th March)

Total 29 days

Number of replicates performed

No replicates

Controls

No control.

Stations without consumption were abandoned.

Examination

Effect investigated

Killing the mice population.

Observing the efficacy with 2 years stored PASTA DIFE.

Method for recording /

The method is to estimate by indirect observation, the bait consumption, and a decrease of population before and after poisoning

scoring of the effect	bait.
Intervals of examination	Daily, every morning
Statistics	If Ci (= initial consumption) is the average value of the consumption plateau before treatment and Cr is the average value of the residual consumption, the efficacy of the treatment is expressed as follows: $E = [(Ci – Cr)/Ci] \times 100$ The Ci and Cr values are calculated by weighing on at least three consecutive days.
Post monitoring of the test organism	Yes, The post-baiting is required to estimate the reduction in mice population.

19 Results

Efficacy

- Average Ci = (164.5 + 167.1 + 166.8) / 3 = 166.1g*
- Average Cr = (8.3 + 8.5 +9.1) / 3 = 8.6g*
- Efficacy = (Average Ci - Average Cr) / Average Ci * 100 = 94.82%

Efficacy of PASTA DIFE reaches 95%

*based on the last 3 days

Dose/Efficacy curve	The changing in food, wheat to poisoned pasta seems created phenomena of mistrust among mice, which was observed by a low consumption the first days. A peak in PASTA DIFE consumption was observed after 3 days, with nearly 120g. After this peak, the consumption decrease to reach 20g at day 21, either 6 days after the poisoning bait.
Begin and duration of effects	The food consumption decreases to 20g 6 days after the poisoning bait.

Observed effects in the post monitoring phase

The post baiting happened normally, with a relatively low consuming which did not exceed 10g by day.

The plateau has been obtained day 26 but several days more have been spent to confirm this plateau

Effects against organisms or objects to be protected

The bait consumption (wheat) before and after the treatment has been reduced by 95%.

In the conditions of this trial, the product Pasta Dife, a paste containing 0.005% of Difenacoum as an active substance (and aged 2 years), is very effective.

Other effects

-

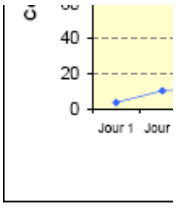
Efficacy of the reference substance

Not applicable

Tabular and/or graphical presentation of the summarised results

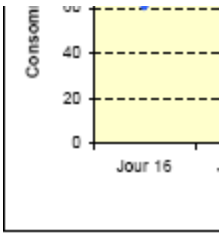
Please different graphs of consumption according time:

Phase 1: pre-baiting with wheat



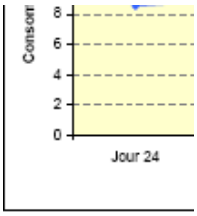
Jour= Days

Phase 2: poison-baiting with PASTA DIFE



Jour= Days

Phase 3: post baiting with wheat



Jour= Days

Efficacy limiting factors

A 2 years stored rodenticide product can:

- lose appetizing aspect towards rodents
- decrease the rate in active substance

Following the results in the experiment, it is not the case.

Occurrences of resistances

Not applicable

Other limiting factors

Not applicable

20 Relevance of the results compared to field conditions

Reasons for laboratory testing	This experiment is a scaling-up. Moreover this experiment is closer to reality than laboratory process.	
Intended actual scale of biocide application	Not applicable	
Relevance compared to field conditions	Not applicable	X
Application method	Not applicable, this study is closer to field condition than laboratory process.	X
Test organism	YES, the pasta bait, even with 2 years of storage is efficient against rodent.	
Observed effect	Killing rodent population	
Relevance for read-across	Yes, This experiment shows results in a specific area with real conditions and constraints related to architecture and uses of the building in process of treatment. Moreover, rodents are very attracted by any food storages, which offer them a huge supply of their needs. We can refer to the study, which regrouped all excellent parameters, as a relevant example of efficacy test for the dossier.	

21 Applicant's Summary and conclusion

Materials and methods

The experimental site has been chosen to their natural condition opportunities, indeed all food storage rooms represent for rodent an important part of their habitat.

The restaurant, “Le Zimmer”, is located in Paris, 75 001. Baits were placed where evident traces of mice were observed and in their possible access used by them.

This method used has been adapted to anticoagulants. This is a relative method, which consists in the comparison of two stages of consumption of a placebo: one before and one after the poisoning bait.

Pre-baiting phase:

It is nearly impossible to know the number of mice, it can only be estimated. The method consisting offering the placebo of the bait, in bait station that permit to carry out consumption measurements, and to daily statements with the placing of new baits, until we obtain a global consuming stabilised what this translated by a plateau on the graph. Then an estimation of the whole population can be made on basis of the food consumed.

Poisoning phase:

After obtaining the estimated population, the placebo is replaced by toxic bait for a week to 10 days.

The changing of food, the passage of whole wheat towards pasta can cause mistrust in mice behaviour. This phenomenon is translated to the field by a low consumption. Generally, this phenomenon is passed within 2 days.

	Post-baiting: Placebo was put in place during 5-7 days but the average consumption. This time corresponds to the surviving mice brings back to the bait stations.
Reliability	1, Study conducted in compliance with agreed protocols.
Assessment of efficacy, data analysis and interpretation	The post baiting happened normally, with a relatively low consuming on the first day, the time that the surviving mice bring back to the bait stations. The plateau has been obtained day 26 but several days more have been spent to confirm this plateau
Conclusion	Based on consumption results, PASTA DIFE reaches 95% of efficacy even after 2 years of storage conditions. In the conditions of this trial, the product Pasta Dife, a paste containing 0.005% of Difenacoum as an active substance (and aged 2 years), is very effective, being markedly higher to 90 % required by the guidelines.
Proposed efficacy specification	According to the point, we can declare as the product as excellent due to the efficacy rate of between 95%.

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	22 Evaluation by Rapporteur Member State
Date	April 2011.
Comments	**2.1.4** Active substance concentration was tested at T0, T6 and T24 (months). **4.3** This study was conducted under field conditions. **4.3.1** Application method is oral.
Summary and conclusion	Although the number of mice present was not estimated based on consumption values recorded prior to and post-baiting with PASTA DIFE indicate a reduction in consumption of 95%. The bait achieved excellent palatability and control of the target organisms after the 2-year storage period.
	23 Comments from ... *(specify)*
Date	*Give date of comments submitted*
Comments	*Discuss if deviating from view of rapporteur member state*
Summary and conclusion	*Discuss if deviating from view of rapporteur member state*

Tables for Method

1.1 (mixed) Population / Inoculum (*if necessary; include separate table for different samples*)

Criteria	Details
Nature	PASTA DIFE: fresh paste rodenticide bait. Containing 0.005 % of Difenacoum.
Origin	Batch N° 020407 Manufacturing date: April 2007
Initial biomass	Not applicable
Reference of methods	Testing method of practical efficacy of raticides of the CEB, revised by OEPP: First step: Pre-baiting: wheat without toxic substance. New baits are put in place daily until the consumption is stabilised over 3 consecutive days. Second step: with the toxic substance Last step: Post-baiting: it does not exceeding 5 days to avoid the arrival of surrounding rodents.
Collection / storage of samples	By comparative measure between before and after baiting with placebo (wheat).
Preparation of inoculum for exposure	- Date of the first visit: 2nd February, 2009 - Beginning of the trial: 4th February, 2009 • Collection of the remaining bait in each bait box, every morning. The non-consumed wheat is collected in small plastic bags. Each plastic bag is numbered with the same number as the bait point. • 100g of "clean" wheat put in each bait box • The collection and the renewing of each bait box is done every morning • The consumed quantities are put in a table and they are presented in a graph. The 1st period stops as soon as a consumption plateau has been reached. It lasted 16 days.
Pretreatment	Not applicable.
~~Initial density of test population in the test system/~~	The product PASTA DIFE was tested at different time in the same lab conditions. The product was stored at room temperature. (Stability , 2009-11-12)

Active substance determined in the product	<table><tr><td></td><td>T0</td><td>6 months</td><td>2 years</td></tr><tr><td>Pasta</td><td>52,9 ppm</td><td>49,97 ppm (-5,54%)**</td><td>52,8 ppm (-0,19%)**</td></tr></table> **Variation of the content after the storage procedure.

1.2 Test organism (*if applicable*)

Criteria	Details
Species	House mice
Strain	*Mus musculus*
Source	From the surrounding areas of the restaurant: "Le Zimmer", 1 place du Chatelet 75001 Paris (France)
Laboratory culture	No, the aim of the study is to be as much as close of the reality.
Stage of life cycle and stage of stadia	Not applicable due to the test conditions
Mixed age population	Not applicable due to the test conditions
Other specification	• Bait boxes placed where there are sign of mice's activity. • Not many droppings seen at the level 0, probably because of the frequent cleaning. Nevertheless, a few bait boxes put there, in cupboards or onto shelves. • Clod rooms (refrigerators): hermetic rooms, no mice tracks, no consumption is expected.
Number of organisms tested	Not mentioned
Method of cultivation	Baits were weighed and filled every morning with 100g of wheat.
Pretreatment of test organisms before exposure	Not mentioned
Initial density/number of test organisms in the test	Not mentioned

system	

1.3 Test system

Criteria	Details
Culturing apparatus / test chamber	Not applicable due to the test conditions
Number of vessels / concentration	Not applicable due to the test conditions
Test culture media and/or carrier material	Not applicable due to the test conditions
Nutrient supply	Not applicable due to the test conditions
Measuring equipment	Not applicable due to the test conditions

1.4 Application of test substance

Criteria	Details
Application procedure	• 1st period: every morning, 100g of wheat put in each bait box • 2nd period: every morning, 100g of product PASTA DIFE on each bait box • 3rd period: every morning, 100g of wheat put in each bait box
Delivery method	In station bait
Dosage rate	1st and last period: Collection of the remaining bait in each bait box, every morning. The non-consumed wheat is collected in small plastic bags. Each plastic bag is numbered with the same number as the bait point. 2nd period: Collection of the remaining Pasta Dife in each bait box, every morning. The non-consumed product is collected in small plastic bags. Each plastic bag is numbered with the same number as the bait point
Carrier	Not applicable due to the test conditions
Concentration of liquid carrier	Not applicable due to the test conditions
Liquid carrier control	Not applicable due to the test conditions
Other procedures	Not applicable due to the test conditions

1.5 Test conditions

Criteria	Details
Substrate	Not applicable due to the test conditions
Incubation temperature	Not applicable due to the test conditions
Moisture	-
Aeration	-
Method of exposure	-
Aging of samples	-
Other conditions	-

Section B5.10_04

Reference

Official use only

Reference

Grolleau G., Pest Control Assistance (PCA), Effectiveness testing under natural conditions of PASTA DIFE rat killer in paste bait form in sachets on brown rats / Test under natural conditions of a rat killer in paste bait form (PASTA DIFE) containing 0.005% Difenacoum, on Brown rats (Rattus norvegicus) 2002.

	PCA, 3 rue Constantin Le Priol 56150 BAUD (France), Unpublished	
Data protection	Yes	
Data owner	LODI S.A., Parc d'activité des Quatre Routes, 35390 Grand Fougeray, FRANCE	
Criteria for data protection	Data submitted to the MS before 14 May 2000 on existing [a.s. / b.p.] for the purpose of its [entry into Annex I/IA / authorisation] / Post inclusion	
Guideline study	Yes, The method used has been inspired by the French method called "method no. 002 from Biological Trials Commission (C.E.B) ", Method for practical efficacy trials of raticides: • Adopted on 1960, derived from the work of Chitty and Dotty in the 1940. • Revised by OEPP in 1980.	
Deviations	Yes, A second treatment was required because the protocol do not mention the case with huge amount of alternative food.	X

24 Method

Test Substance (Biocidal Product)	as given in section 2 deviating from specification given in section 2 *(Fill in the fields 3.1.2 and 3.1.3)*	
Trade name/ proposed trade name	PASTA DIFE	
Composition of Product tested	0.005 % of Difenacoum	
Physical state and nature	Oily paste packaged in 10g sachets (tea bag)	

Monitoring of active substance concentration	No
Method of analysis	Testing method of practical efficacy of raticides of the CEB, revised by OEPP: This method has been adapted to anticoagulants. This is a relative method, which consists in the comparison of two stages of consumption of a placebo: one before, on after bait. It is nearly impossible to know the number rats, it can only be estimated. The method consisting offering the placebo of the bait, in bait station that permit to carry out consumption measurements, and to daily statements with the placing of new baits, until we obtain a global consuming stabilised over 3 consecutive days. Then an estimation of the whole population can be made on basis of the food consumed. After obtaining this stage the placebo is replaced by toxic bait for a week. Regarding the slow mode of action of anticoagulant, one week is needed without toxic bait or placebo, so that death rate we can hope over, and then we go post baiting with the placebo, to establish the second consumption stage. To obtain the first stage, 2 to 3 weeks are necessary depending on the importance of the rats' population. For the post-baiting, it does not exceed 5 days in general, in order to avoid eventual recontamination by rats coming from the surroundings of the site, which would lead to a wrong estimation of consumption.
Reference substance	No
Method of analysis for reference substance	-
Testing	

procedure

Test population / inoculum / test organism

Brown rats (*Rattus norvegicus*)

Exact number in the population: not mentioned in the study.

Test system

The experimental site is a pigeon farm at GUENIN in Morbihan (56, FRANCE).

Application of TS

Daily, the bait stations were measured.

Test conditions

The pigeon farm consists mainly of a slightly raised building, built into a slope and with cage containing pairs of pigeons, with nesting boxes stacked on slats. The Brown rats were mainly livings in burrows dug out of the embankment around the building, coming into it to feed; the presence of a tap at the base of the embankment should be noted, as this enabled them to drink. The maize and wheat grain left by pigeon provided the rats with abundant source of food; in addition, the Brown rats regularly killed and ate the squabs, with a marked effect on the farm's production.

Remarks on the site and meteorological conditions were also recorded.

Duration of the test / Exposure time

- First Pre-baiting: 1 month, from 6th September to 4th October (unfavourable weather conditions).
- First PASTA DIFE baiting: 7 days, from 5th to 12th October 2002.
- First Rest phase: 3 days without food
- First Post bait phase: 7 days, from 15th to 22th October 2002.

Due to the high consumption of wheat in the post bait phase (plateau reached 1250g), it has been decided to carry out a second poison treatment.

- Second PASTA DIFE baiting: 7 days, from 23 October 2002.

- Second Post bait phase: 5 days, from 2d to 6th November.

TOTAL: 59 days

Number of replicates performed No replicates

Controls No control.

Examination

Effect investigated Killing the rat population.

Method for recording / scoring of the effect The method is to estimate by indirect observation, the bait consumption and a decrease of population before and after poisoning bait.

Intervals of examination Daily

Statistics [Average Pre-btg (grams) – Average Post-btg (grams)] x100/ AveragePre-btg(grams) = Efficacy

Btg= baiting

Post monitoring of the test organism Yes,
After the poisoning phases, a rest period without food was observed. Then the post-baiting occurred in order to estimate the reduction in population.
Unfortunately, due to the high consumption of wheat in the post bait phase it has been decided to carry out a second poison treatment.

25 Results

Efficacy

First pre-baiting consumption: 3523.3 g/day*

First post baiting consumption: 1249.7 g/day*

Compared to other studies which the same protocol, the result obtained in post baiting is quite high, this gives also a low efficacy at 64.5%.

Second pre-baiting consumption: 341.3g

⇔(3523.3-341.3) / 3523.3 x 100 = 90.3%

After the second poisoning and post baiting, the efficacy reached 90.3%

Dose/Efficacy curve* *based on the last 3 days*

1st Prebaiting period: Due to food competition, and probably to exacerbated suspicion from the brown rats towards changes in their environment (wheat = new available food), one month was required to obtain the initial consumption plateau.

1st Baiting period: PASTA DIFE consumption decreased between the 2nd and 7th collection, which underlines an increasingly high mortality (last collection = 400g).

1st Postbaiting period: the postbaiting consumption stabilised over the last 3 days at the high level of 1249.7g/day.

The last consumption of the baiting period (around 400g) has probably given a too optimistic view on the efficacy test. Food competition, as well as rats neophobia, should explain these results. It is possible that some of the rats decided to consume the bait late , then died during the postbaiting period.

2nd Baiting period: For these reasons, a second 7-day baiting period was performed. The consumption reached 600g the 2nd day then decreased to stabilise around 220g (average of the 3 last days).

2nd Postbaiting period: The second postbaiting period gave acceptable results. The consumption reached 341.3g/day.

In such an efficacy trial, the aim of the prebaiting period is to feed the whole rodents population. When the initial consumption plateau is reached, it is considered that all the rodents consume the bait. The initial consumption plateau is all the more difficult to reach since the rodent population is large. Considering the high consumption level during the 1st Prebaiting period (more than 3500g/day), we can deduce that the rat population is large; the 1st prebaiting period must have been stopped a bit too early. That's why the trial was performed with 2 baiting periods.

Finally, the calculated efficacy is 90.3% that is an acceptable result according to European requirements.

Begin and duration of effects

During the poisoning bait phase, the consumption was stable, from the 1st to 7th day. Following the results obtained in the first post baiting phase, it seems that rat's population, did not eat the bait.

.

Observed effects in the post monitoring phase

The PASTA DIFE causes death in rat's population from the surrounding area of the pigeon farm. Due to a huge amount of alternative food, the poison treatment should be extended. X

Due to unusual values obtained in the first post baiting phase, a second poison treatment was carried out.

The presence of alternative food has to distort results obtained in the station bait which maybe lead to:

- Under estimate the rat's population.
- Rat's mistruth toward the change food (wheat to paste). At this phase rats could preferred eat wheat, maize and squabs (alternative foods).

The second treatment was more successful.

Effects against organisms or objects to be protected

Not applicable

Other effects

-

Efficacy of the

Not applicable

reference substance		
Tabular and/or graphical presentation of the summarised results	Please find results from the second treatment and post baiting phase in the following table:	

TOTAL CONSUMPTION FROM BAIT STATIONS PER DAY IN GRAMS FROM 23/10/02 TO 06/11/02												
	DAYS 2nd poison treatment								DAYS 2nd poison treatment				
DATES	23-Oct	24 Oct	25 Oct	26 Oct	27 Oct	28 Oct	29 Oct	30 Oct 31 Oct 01 Nov	02 Nov	03 Nov	04 Nov	05 Nov	06 Nov
TOTAL	401	596	152	71	212	235	216		196	259	341	343	340
	←---------- PASTA -DIFE paste bait ----------→								←---------- wheat ----------→				

Efficacy limiting factors	The presence of huge amount and diversified alternative food (wheat and maize for the bird and squabs are killed and eaten by rats).	
Occurrences of resistances	Not applicable	
Other limiting factors	Not applicable	

26 Relevance of the results compared to field conditions

Reasons for laboratory testing	This experiment is a scaling-up. Moreover this experiment is closer to reality than laboratory process.	
Intended actual scale of biocide application	Not applicable	
Relevance compared to field conditions	Not applicable	X
Application method	Not applicable. This study is closer to field condition than laboratory process, rodent have access to plenty alternative food which is in competition with the poison bait.	X
Test organism	YES.	X

Observed effect

Not applicable.
The conclusions have been made from indirect observations: decreased of food consumption)

Relevance for read-across

Yes,
This experiment shows results in a specific area with real conditions and constraints related to architecture and uses of the building in process of treatment.
Moreover, rodents are very attracted by any food storages, which offer them a huge supply of their needs.
We can refer to the study, which regrouped all excellent parameters, as a relevant example of efficacy test for the dossier.

27 Applicant's Summary and conclusion

Materials and methods

The experimental site has been chosen to their natural condition opportunities: a pigeon farm with s squabs

The Brown rats were mainly livings in burrows dug out of the embankment around the building, coming into it to feed; the presence of a tap at the base of the embankment should be noted, as this enabled them to drink. The maize and wheat grain left by pigeon provided the rats with abundant source of food; in addition, the Brown rats regularly killed and ate the squabs, with a marked effect on the farm's production.

This method used has been adapted to anticoagulants. This is a relative method, which consists in the comparison of two stages of consumption of a placebo: one before, on after bait.

Pre-baiting phase:

It is nearly impossible to know the number rats, it can only be estimated. The method consisting offering the placebo of the bait, in bait station that permit to carry out consumption measurements, and

to daily statements with the placing of new baits, until we obtain a global consuming stabilised over 3 consecutive days. Then an estimation of the whole population can be made on basis of the food consumed. For different reasons, it lasted 1 month.

Poisoning phase:

After obtaining the estimated population, the placebo is replaced by toxic bait for a week.

The changing of food, the passage of whole wheat towards paste in station bait causes mistrust in rat behaviour. This phenomenon is translated to the field by a low consumption. Generally, this phenomenon is passed within 2 days.

Rest period:

During 3 days, no food was exposed in the bait station. Generally, this phase lasted 7 days.

Post-baiting:

Placebo was put in place during 5 days but the average consumption was made on 3 days. This time corresponds to the surviving rats brings back to the bait stations.

Unfortunately, the consumption in the last phase was higher than usual. It has been decided to carry out a second poison treatment and post bait, of 7 and 5 days respectively.

Reliability

2, Study conducted in accordance with generally accepted scientific principles, possibly with incomplete reporting or methodological deficiencies, which do not affect the quality of relevant results

The consumption rate established during the poisoning phase corresponds to the expectations, but a comparison with the post baiting values is needed to relatives the all experiment. The plenty of alternative food is not mentioned by the protocol inspired from the French method called “method no. 002 from Biological Trials Commission (C.E.B).

Assessment of efficacy, data analysis and interpretation

The fact is the consumption plateau for the second post bait phase was fully stabilised during the last 3 days of collection indicates that mortality ceased.

On the last day of the first poison treatment, the disappearance – consumption of the bait was 400g, on the second day of the second treatment (10 days later); it was 600g, so 50% higher. Two possibilities:

- A proportion of the population, which did not have access to the bait the first time, came to consume it the second time.
- Young rats, not weaned during the first poison treatment, became consumers during the second. This is possible, bait not really plausible in October- November when breeding levels are low.

The availability of the plenty of alternative food would strengthen the first probability. Nonetheless, the second poison treatment should have led to an overall mortality of over 95%.

Conclusion

The efficacy reached 95%/

We can say that the tested bait, PASTA DIFE, showed an appropriate, even a good level of effectiveness and that complies with the required criteria for licensing.

Proposed efficacy specification

The guidelines required for mortality test the percentage of dead animals should be normally ≥ 90% within normally 20 days. If we cumulated the days of first and the second treatment, it demonstrated an effect at day 9, adding the post baiting monitoring of 5 days, we obtained 14 days, which is under the timing required by the guidelines. According to the point, we can declare as the rodenticide PASTA DIFE, efficient to brown rat with more than 90% of population decreasing.

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	28 Evaluation by Rapporteur Member State
Date	April 2011.
Comments	**1.4** Although the removal of alternative food would have been preferable the deviation from the protocol is acceptable given the conditions on the farm. **3.1.3** Rat's "mistruth" should read "mistrust". **4.3** Study relevant as conducted under field conditions. **4.3.2** Test organism – Brown rats (*Rattus norvegicus*). **4.3.3** Observed effect – decrease in consumption indicating control of the rats.
Summary and conclusion	The reduction in the post baiting consumption was 90.3% on average for the final 3 days indicating good control of the rat population onsite. Neophobia is a likely result of the reason why such a long pre-baiting period was required and additionally a factor in the requirement for a second baiting phase. In addition the availability of an abundance of food sources is a valid reason why the >90% control figure was not achieved within the normal 20-day period. The test is deemed valid for product authorisation as the PASTA DIFE proved both palatable and effective.
	29 Comments from ... *(specify)*
Date	*Give date of comments submitted*
Comments	*Discuss if deviating from view of rapporteur member state*
Summary and conclusion	*Discuss if deviating from view of rapporteur member state*

Tables for Method

1.1 (mixed) Population / Inoculum (*if necessary; include separate table for different samples*)

Criteria	Details
Nature	PASTA DIFE: oily paste bait packaged in sachet (tea bag) Containing 0.005 % of Difenacoum
Origin	Bait was packaged in 10g sachets (tea bag)
Initial biomass	Not applicable
Reference of methods	Testing method of practical efficacy of raticides of the CEB, revised by OEPP: First step: Pre-baiting: wheat without toxic substance. New baits are put in place daily until the consumption is stabilised over 3 consecutive days. Poisoning bait: with the toxic substance Rest phase: phase with no food between poisoning bait and post monitoring phase. Last step: Post-baiting: it does not exceeding 5 days to avoid the arrival of surrounding rodents.
Collection / storage of samples	By comparative measure between before and after baiting with placebo (wheat).
Preparation of inoculum for exposure	First Pre-baiting: These stations were filled with 500g wheat on 6th September and the first collection of the pre-bait was made on 7th September (24 h later). Due to the unfavourable weather conditions, an earth tremor and the availability of plenty of alternative food, the pre-bait phase lasted for 1 month until (finally) a consumption plateau obtained. First PASTA DIFE baiting: On 5th October, the wheat was replaced by 400 to 700 sachets of PASTA DIFE, depending on the station. The poisoning phase lasted 7

	days (5 to 12/10/02). Measurement of consumption was measured of the disappearance of the sachets, the rats having carried them into their burrows, where they might or not consume all of them. First Rest phase: 3 days between the last collection of poisoning bait and the offer of the post bait phase wheat. First Post bait phase: the stations were refilled with wheat on 15/10/02 and for seven consecutive days (last collection on 22/10/02). Due to the high consumption of wheat in the post bait phase (plateau reached 1250g), it has been decided to carry out a second poison treatment. Second PASTA DIFE baiting: this lasted for 7 days, as with the first treatment, from 23 to 29/10/2002. Second Post bait phase with wheat was carried out from 2/11 to 6/11, either during 5 days.
Pretreatment	Following a site study and location of burrows and infested area, 42 bait stations were put in place on 27th August 2002, to habituate rats to their presence.
Initial density of test population in the test system	Not mentioned in the study.

1.2 Test organism (*if applicable*)

Criteria	Details
Species	Brown rats *(Rattus norvegicus)*
Strain	Wild rats
Source	From the surrounding areas of the farm.
Laboratory culture	No, the aim of the study is to be as much as close of the reality.
Stage of life cycle and stage of stadia	Not applicable due to the test conditions
Mixed age population	Not applicable due to the test conditions
Other specification	Not applicable due to the test conditions
Number of organisms tested	Not mentioned in the study.
Method of cultivation	Measurement in bait station every day.
Pretreatment of test organisms before exposure	The installation of bait station on 27th August allowed creating a confident environment for rats.
Initial density/number of test organisms in the test system	Not mentioned in the study.

1.3 Test system

Criteria	Details
Culturing apparatus / test chamber	Not applicable due to the test conditions
Number of vessels / concentration	Not applicable due to the test conditions
Test culture media and/or carrier material	Not applicable due to the test conditions
Nutrient supply	Not applicable due to the test conditions
Measuring equipment	Not applicable due to the test conditions

1.4 Application of test substance

Criteria	Details
Application procedure	Wheat during the pre-baiting and post baiting phase and Paste during the poisoning phase
Delivery method	In station bait
Dosage rate	Measurement of consumption was measured by the disappearance of the sachets, the rats having carried them into their burrows, where they might or not consume all of them.
Carrier	Not applicable due to the test conditions
Concentration of liquid carrier	Not applicable due to the test conditions
Liquid carrier control	Not applicable due to the test conditions
Other procedures	Not applicable due to the test conditions

1.5 Test conditions

Criteria	Details
Substrate	Not applicable due to the test conditions
Incubation temperature	Not applicable due to the test conditions
Moisture	-
Aeration	-
Method of exposure	-
Aging of samples	-
Other conditions	-

Section B5.10_05

Official use only

Reference

Reference

Biannic M-L., LODI S.A.S, Efficacy assessment of a rat killer in a field trial –product: PASTA DIFE, July 2009.

LODI S.A, Parc d'activité des Quatre Routes, 35390 Grand Fougeray, France. Unpublished

Data protection

Yes

Data owner

LODI S.A.,

Parc d'activité des Quatre Routes,

35390 Grand Fougeray, FRANCE

Criteria for data protection

Data submitted to the MS before 14 May 2000 on existing [a.s. / b.p.] for the purpose of its [entry into Annex I/IA / authorisation] / Post inclusion

Guideline study

Yes,

The method used has been inspired by the French method called "method no. 002 from Biological Trials Commission (C.E.B) ", Method for practical efficacy trials of raticides:

- Adopted on 1960, derived from the work of Chitty and Dotty in the 1940.
- Revised by OEPP in 1981, J. Giban.

Deviations

No

30 Method

Test Substance

as given in section 2

(Biocidal Product)	deviating from specification given in section 2 *(Fill in the fields 3.1.2 and 3.1.3)*
Trade name/ proposed trade name	PASTA DIFE
Composition of Product tested	0.005 % of Difenacoum
Physical state and nature	10g sachet (tea bag) of fresh red paste
Monitoring of active substance concentration	No
Method of analysis	Testing method of practical efficacy of raticides of the CEB, revised by OEPP: This method has been adapted to anticoagulants. This is a relative method, which consists in the comparison of two stages of consumption of a placebo: one before, on after bait. It is nearly impossible to know the number rats, it can only be estimated. The method consisting offering the placebo of the bait, in bait station that permit to carry out consumption measurements, and to daily statements with the placing of new baits, until we obtain a global consuming stabilised over 3 consecutive days. Then an estimation of the whole population can be made on basis of the food consumed. After obtaining this stage the placebo is replaced by toxic bait for a week. Regarding the slow mode of action of anticoagulant, one week is needed without toxic bait or placebo, so that death rate we can hope over, and then we go post baiting with the placebo, to establish the

second consumption stage.

To obtain the first stage, 2 to 3 weeks are necessary depending on the importance of the rats' population. For the post-baiting, it does not exceed 5 days in general, in order to avoid eventual recontamination by rats coming from the surroundings of the site, which would lead to a wrong estimation of consumption.

Reference substance

No

Method of analysis for reference substance

-

Testing procedure

Test population / inoculum / test organism

Brown rats/ Norway rats (*Rattus norvegicus*)

Exact number in the population: not mentioned in the study.

Test system

The tested sited is a company named FEROTEC, situated in *« Parc d'activité des Quatre Routes », 35390 Grand Fougeray, France.*

The premises used in the study cover a 2700m² surfaces and are composed of offices in the one hand, and workshop in which machines work 24h a day in the other hand.

Application of TS

Daily, the bait stations were measured.

Test conditions

The FEROTEC site is composed of a part of the workshop and the north and west surrounding of premises. Floor and oil rape constitute food of first class for rats.

Boxes baits were dispatched in the warehouse and its surroundings as follow:

	Bait	Baits are in

	points	
Outdoors	0,1, 2, 3 and 4	Close to the outdoor electrical panel where a dead rat had been seen, and where there were a lot of hole in the soil
	9 and 10	Close to the water, next to the piping entry
	11 and 12	Around the door in the east side of the premises, next to the mixture floor and oil rape.
	5, 6, 7 and 8	Likely way for rats, between burrows, water source and food (flour/oil)
Indoors	13, 14 and 15	Around the mixture flour and oil rape
	28 and 29	Under the metallic sheet where the piping goes through the workshop
	23	Next to the electrical panel
	26 and 27	Above the office where there are regular unpleasant smell
	19and 20	Next to the door at the North side
	31	Next to the air vent (West of the premises)
	16, 16, 18, 21, 22, 24, 25 and 30	Likely way for rats.

Duration of the test / Exposure time

- Pre-baiting: 21 days, from 25th May to 16th June
- PASTA DIFE baiting: 9 days, from 16th to 25th June 2002.
- Rest phase: -
- Post bait phase: 7 days, from 26th June to 2nd July 2002.

TOTAL: 37 days

Number of No replicates

replicates performed

Controls No control.

Examination

Effect investigated Killing the rat population with a 2years storage rodenticide.

Method for recording / scoring of the effect The method is to estimate by indirect observation, the bait consumption and a decrease of population before and after poisoning bait.

Intervals of examination Daily

Statistics If Ci (= initial consumption) is the average value of the consumption plateau before treatment and Cr is the average value of the residual consumption, the efficacy of the treatment is expressed as follows:

$$E = [(Ci – Cr)/Ci] \times 100$$

The Ci and Cr values are calculated by weighing on at least three consecutive days.

Post monitoring of the test organism Yes,
The post-baiting is required to estimate the reduction in rats' population.

31 Results

Efficacy

The efficacy of product PASTA DIFE against Norway rat, in the conditions of the study is 92%

- First pre-baiting consumption (Ci): 461.9 g/day*
- First post baiting consumption (Cr):: 37 g/day*

$$E = [(Ci – Cr)/Ci] \times 100$$

$$\Leftrightarrow (461.9-37) / 461.9 \times 100 = 91.99\%$$

**based on the last 3 days*

Dose/Efficacy curve

The initial consumption plateau (plateau during at least 3 consecutive days) has been reached the 21st day of the experimentation.

Another plateau was observed from the 15th day. The baiting stage has been pursed a few days because the average value of the weekend (day 18, 19 and 20). The results of the 21st day have confirmed the consumption plateau.

The PASTA DIFE consumption reached a peak after day 2 (23of the experiment) and decreased until a plateau in days 25 to 27 and felt under 50g/day the 3 least days.

Begin and duration of effects

The PASTA DIFE consumption reached a peak after day 2 (23of the experiment) and decreased until a plateau in days 25 to 27 and felt under 50g/day the 3 least days.

Observed effects in the post monitoring phase

To day31 to day 34, the food consumption decreased again, around 30g/day, and it is stabilised around the 40g/day.

Effects against organisms or objects to be protected

The PASTA DIFE causes death in rat's population from the surrounding area of warehouse, even after storage of two years.

Other effects

-

Efficacy of the reference substance

Not applicable

Tabular and/or

Please different graphs of consumption according time:

graphical presentation of the summarised results

Phase 1: pre-baiting with wheat during 21 days.

Jour= Days

Phase 2: poison-baiting with PASTA DIFE

Phase 3: post baiting with wheat

Jour= Days

Efficacy limiting factors	The presence of flour and oil rape could be considered as serious competitive food with PASTA DIFE but the result demonstrated that it is not the case.
Occurrences of resistances	Not applicable
Other limiting factors	Not applicable

32 Relevance of the results compared to field conditions

Reasons for laboratory testing	This experiment is a scaling-up. Moreover this experiment is closer to reality than laboratory process.	
Intended actual scale of biocide application	Not applicable	
Relevance compared to field conditions	Not applicable	X
Application method	Not applicable. This study is closer to field condition than laboratory process, rodent have access to plenty alternative food which is in competition with the poison bait.	X
Test organism	YES.	X
Observed effect	Not applicable. The conclusions have been made from indirect observations: decreased of food consumption)	X
Relevance for read-across	Yes, This experiment shows results in a specific area with real conditions and constraints related to architecture and uses of the building in process of treatment. Moreover, rodents are very attracted by any food storages, which offer them a huge supply of their needs. We can refer to the study, which regrouped all excellent parameters, as a relevant example of efficacy test for the dossier.	

33 Applicant's Summary and conclusion

Materials and methods

The experimental site has been chosen to their natural condition opportunities: a warehouse with huge surface with supplies of flour and oil rape which the best class of food for rats. Moreover the building is near to water spot.

Several workers testimonies and traces of rats revealed the Norway rats' presence in the warehouse.

The applied method has been adapted to anticoagulants. This is a relative method, which consists in the comparison of two stages of consumption of a placebo: one before, on after bait.

Pre-baiting phase:

It is nearly impossible to know the number rats, it can only be estimated. The method consisting offering the placebo of the bait, in bait station that permit to carry out consumption measurements, and to daily statements with the placing of new baits, until we obtain a global consuming stabilised over 3 consecutive days. Then an estimation of the whole population can be made on basis of the food consumed. For different reasons, it lasted 1 month.

Poisoning phase:

After obtaining the estimated population, the placebo is replaced by toxic bait for a week.

The changing of food, the passage of whole wheat towards paste in station bait may cause mistrust in rat behaviour. This phenomenon is translated to the field by a low consumption. Generally, this phenomenon is passed within 2 days.

Post-baiting:

Placebo was put in place during 7 days but the average consumption was made on 3 days. This time corresponds to the surviving rats brings back to the bait stations.

Reliability

1, Study conducted in compliance with agreed protocols.

The consumption rate established during the poisoning phase corresponds to the expectations.

Assessment of efficacy, data analysis and interpretation

The wheat consumption by rats, in the tested site FEROTEC, has been decreased of 92%. The efficacy of the product can be deducted from this calculation (92%).

The tested warehouse is situated in an industrial estate, next to a water source. A mixing of wheat and oil rape is used to control the manufacturing in the workshop and it constitutes a source of food for rats. Moreover, this food is available 24h a day. Finally, the underground trench that goes through the warehouse site may be an access to different point: water and food source.

Conclusion

The efficacy trial of PASTA DIFE has been conclusive and the results permit to declare the product efficient against the Norway rats.

The efficacy of the product reaches 92%.

Proposed efficacy

According to rodenticide guidelines, the requirement of an efficacy superior to 90% being reached, we can declare that after two years of

specification	storage the product is still efficient against rodent.

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	34 Evaluation by Rapporteur Member State
Date	April 2011.
Comments	Throughout this study summary reference is made to “floor” which should actually read “flour”. **4.3** Test is applicable as it was conducted under field conditions. **4.3.1** Application method – oral. **4.3.2** Test organism - Brown rats/ Norway rats (*Rattus norvegicus*). **4.3.3** Observed effect – reduction in bait consumption indicating death of the target organism.
Summary and conclusion	The 2-year old PASTA DIFE bait performed excellently in the study achieving 92% efficacy against the rat population based on the reduction in bait consumption levels.
	35 Comments from ... *(specify)*
Date	*Give date of comments submitted*
Comments	*Discuss if deviating from view of rapporteur member state*
Summary and conclusion	*Discuss if deviating from view of rapporteur member state*

Tables for Method

1.1 (mixed) Population / Inoculum (*if necessary; include separate table for different samples*)

Criteria	Details
Nature	PASTA DIFE: 10g sachet (tea bag) of fresh red paste Containing 0.005 % of Difenacoum
Origin	Batch N° 040407 Manufacturing date: April 2007
Initial biomass	Not applicable
Reference of methods	Testing method of practical efficacy of raticides of the CEB, revised by OEPP: First step: Pre-baiting: wheat without toxic substance. New baits are put in place daily until the consumption is stabilised over 3 consecutive days. Poisoning bait: with the toxic substance Last step: Post-baiting: it does not exceeding 5 days to avoid the arrival of surrounding rodents.
Collection / storage of samples	By comparative measure between before and after baiting with placebo (wheat).
Preparation of inoculum for exposure	First Pre-baiting: The bait boxes were filled with 300g wheat, from 26th May to the 15th June 2009. PASTA DIFE baiting: From 16th June to 24th June. Post bait phase: The bait boxes were filled again with wheat, from 25th June to 2nd July.
Pretreatment	A first visit in the tested site, FEROTEC COMPANY, allowed dressing a site map with indirect presence of rat (dropping, worker's testimonies) and determining the exact target: *Rattus norvegicus*.
~~**Initial density of test**~~	The product PASTA DIFE was tested at T0 in the same

~~**population in the test system/**~~ **Active substance determined in the product**	lab conditions. |	Nominal value	Result ppm	Results % w/w | |---|---|---|---| | T0 (2007) | 0,0050 | 50,08 | 0,0050 |

1.2 Test organism (if applicable)

Criteria	Details
Species	Norway rats / Brown rats*(Rattus norvegicus)*
Strain	Wild
Source	From the surrounding areas of the FEROTEC company
Laboratory culture	No, the aim of the study is to be as much as close of the reality.
Stage of life cycle and stage of stadia	Not applicable due to the test conditions
Mixed age population	
Other specification	Bait boxes placed where there are signs of rat's activity, during the preliminary visit: <u>Outdoors observations:</u> - Lots of holes, around the outdoor electrical panel (west surrounding) - A young dead Norway rat (west surrounding) - Water at about 30 meters of the premises (south) - Piping go right through the workshop (east west), making a way for rats (entry where there is water) - Premises are not well closed, rats could enter in the premises, indoor doors, holes in wall, air vent (west of the premises) <u>Indoor observations:</u> - Food (Flour and oil rape) and Norway rats droppings close to this food. - Electrical panel where rats have been seen a couples of time by workers. - Regular unpleasant smells in the office situated behind the electrical panel. - Piping going right through the workshop, access by lifting metallic sheet. <u>Other data and information:</u> - Several workers have told that they have seen, several times rats going through the workshop. - The mixture flour and oil rape constitute a source of food. The numerous rats dropping near this mixture

	confirm that is a source of their food. - The north part of the building is noisy, day and night. Consequently, this part must only be an occasional passage for rats. Probably rats go through this part without stopping here. - The piping goes through the tested site and come out close to water which is constituted a water access for rats. This piping is also a possible access to the workshop.
Number of organisms tested	Not mentioned in the study.
Method of cultivation	Measurement in bait station every day.
Pretreatment of test organisms before exposure	A first visit in the tested site, FEROTEC COMPANY, allowed dressing a site map with indirect presence of rat (dropping, worker's testimonies) and determining the exact target: *Rattus norvegicus*.
Initial density/number of test organisms in the test system	Not mentioned in the study.

1.3 Test system

Criteria	Details
Culturing apparatus / test chamber	Not applicable due to the test conditions. The tested sited is a company named FEROTEC, situated in « Parc d'activité des Quatre Routes », 35390 Grand Fougeray, France. The premises used in the study cover a 2700m² surfaces and are composed of offices in the one hand, and workshop in which machines work 24h a day in the other hand. The study site is composed of a part of the workshop and the north and west surrounding of premises.
Number of vessels / concentration	
Test culture media and/or carrier material	
Nutrient supply	
Measuring equipment	

1.4 Application of test substance

Criteria	Details
Application procedure	Wheat during the pre-baiting and post baiting phase and Paste during the poisoning phase.
Delivery method	Supple plastic (PVC) box have been chosen as bait boxes. They are specially intended to be used as rat bait boxes outdoor and in damp places (bait boxes have been placed indoor and outdoor in the study site). A label, stuck into each bait box, mentioned the bait point number as well as LODI address and phone number.
Dosage rate	Measurement of consumption was measured every day.
Carrier	Not applicable due to the test conditions
Concentration of liquid carrier	Not applicable due to the test conditions
Liquid carrier control	Not applicable due to the test conditions
Other procedures	Not applicable due to the test conditions

1.5 Test conditions

Criteria	Details
Substrate	Not applicable due to the test conditions
Incubation temperature	Not applicable due to the test conditions
Moisture	-
Aeration	-
Method of exposure	-
Aging of samples	-
Other conditions	-

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Reference

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Reference	De Proft M., CRA Gembloux, Study of ageing behavior of ready-to-use baits containing 0.005% of Difenacoum, PART 1: Pasta Bait, report number ROD 2008 11 BIO 6 CRA (Agronomic Research Center), Phytopharmacological department, Rue du Bordia, 11, 5030 Gembloux Belgium	
Data protection	Yes	
Data owner	BIO 6 Industrial Zone of Noville-les-Bois 14, rue du Grand Champ 5380 FERNELMONT, Belgium	
Criteria for data protection	Data submitted to the MS before 14 May 2000 on existing [a.s. / b.p.] for the purpose of its [entry into Annex I/IA / authorisation] / Post inclusion	
Guideline study	Yes, The method used has been inspired by the French method called "method no. 002 from Biological Trials Commission (C.E.B) ", Method for practical efficacy trials of raticides: • Adopted on 1960, derived from the work of Chitty and Dotty in the 1940. • Revised by OEPP in 1981, J. Giban.	
Deviations	No	X

36 Method

Test Substance (Biocidal Product)	as given in section 2 deviating from specification given in section 2 *(Fill in the fields 3.1.2 and 3.1.3)*	
Trade name/ proposed trade name	DIFENACOUM PASTA BAIT (Pasta Dife)	
Composition of	0.005 % of Difenacoum	

Product tested		
Physical state and nature	Little pieces of pasta	X
Monitoring of active substance concentration	No	
Method of analysis	The study protocol included the following : 1) An acceptance of the fresh product with albinos' rats and in individuals cages fresh product. 2) An acceptance of the product aged for 12 months with albinos' rats in individuals 3) An acceptance of the product aged for 24 months with albinos' rats in individuals Acceptance loss is measured by comparing results of several acceptance trials. Each of these trails uses 22 albino rats (11 males and 11 females) 10 to 20 weeks old, from the same origin, the same strain, and the same alimentation story at the trial start. The first trial uses fresh product and the following aged product (respectively 12 and 24 month). Each trials begins when rats have been acclimatized at least 8 days in individual cages in the lab, where they receive as much water and crushed wheat as they want. During the first 5 days, all the rats received 30g crushed wheat in a feeding dish. Daily consumption of each rodent was measure by calculating the difference between weight of the full feeding dish and this one of this dish after 24 hours. In a second time, another dish containing the study bait was added, except for 2 control rodents (one male and one female) which continued to be fed only with crushed wheat. Trials last 20 days.	X
Reference substance	No	
Method of analysis for reference substance	-	
Testing procedure		

Test population / inoculum / test organism	*Rattus norvegicus*
Test system	Rats were housed individually in cages.
Application of TS	Daily, the bait stations were measured.
Test conditions	Each trials begins when rats have been acclimatized at least 8 days in individual cages in the lab, where they receive as much water and crushed wheat as they want.
Duration of the test / Exposure time	Trials last 20 days for each experiment.
Number of replicates performed	No replicates
Controls	Yes: one male and one female. They only received crushed wheat.

Examination

Effect investigated	Determination of bait acceptance by rats.
Method for recording / scoring of the effect	Daily consumption of each rodent was measure by calculating the difference between weight of the full feeding dish and this one of this dish after 24 hours.
Intervals of examination	Daily
Statistics	Calculating the difference between weight of the full feeding dish and this one of this dish after 24 hours.

Post monitoring of the test organism	Yes, The post-baiting is required to estimate the reduction in rats' population.

37 Results

Efficacy	T0: 19 dead rats at the end of the trial T12: 18 dead rats at the end of trial. Between fresh product and the 12 months aged product, acceptance loss is not significant.
Dose/Efficacy curve	Between fresh product and the 12 months aged product, acceptance loss is not significant.
Begin and duration of effects	Not applicable
Observed effects in the post monitoring phase	Not applicable
Effects against organisms or objects to be protected	Not applicable
Other effects	-
Efficacy of the reference substance	Not applicable
Tabular and/or graphical presentation of the summarised results	Between fresh product and the 12 months aged product, acceptance loss is not significant.

Efficacy limiting factors Not applicable

Occurrences of resistances Not applicable

Other limiting factors Not applicable

38 Relevance of the results compared to field conditions

Reasons for laboratory testing

The laboratory conditions shows the :

- Daily amount of food consumed by rodents
- Timing needed for the product efficacy after ingestion
- Rodent's behaviour in competitive food condition (appetizing behaviour of mice in presence of product)

All these parameters are important when the scaling will be settled down.

Intended actual scale of biocide application Not applicable

Relevance compared to field conditions

The parameters explained in 4.1 are estimated, the individual specification of mice can varied in an open space. Moreover, in nature rodent have access to other kind of food.

Application method

In this laboratory experiment, rodents have accessed to two types of food.

In nature condition, rodents have access to other kind of food, which can run in competition with the poisoned bait. Moreover the change in food can cause mistruth and modify the alimentary behaviour in mice.

It is very interesting to observe and compare their behaviour in the field condition.

Moreover, nature trials are closer to real condition of use than a laboratory process.

Test organism YES X

Observed effect YES X

Relevance for read-across Yes,
We can refer to the study, which regrouped all excellent parameters, as a relevant example of efficacy test for the dossier.

39 Applicant's Summary and conclusion

Materials and methods The study protocol included the following :

4) An acceptance of the fresh product with albinos' rats and in individuals cages fresh product.
5) An acceptance of the product aged for 12 months with albinos' rats in individuals
6) An acceptance of the product aged for 24 months with albinos' rats in individuals

Acceptance loss is measured by comparing results of several acceptance trials. Each of these trails uses 22 albino rats (11 males and 11 females) 10 to 20 weeks old, from the same origin, the same strain, and the same alimentation story at the trial start.

The first trial uses fresh product and the following aged product (respectively 12 and 24 month). Each trials begins when rats have been acclimatized at least 8 days in individual cages in the lab, where they receive as much water and crushed wheat as they want.

During the first 5 days, all the rats received 30h crushed wheat in a feeding dish. Daily consumption of each rodent was measure by calculating the difference between weight of the full feeding dish and this one of this dish after 24 hours. In a second time, another dish containing the study bait was added, except for 2 control rodents (one male and one female) which continued to be fed only with crushed wheat. Trials last 20 days.

Reliability 1, Study conducted in compliance with agreed protocols.

Assessment of efficacy, data analysis and interpretation	T0: 19 dead rats at the end of the trial T12: 18 dead rats at the end of trial. Between fresh product and the 12 months aged product, acceptance loss is not significant.
Conclusion	Between fresh product and the 12 months aged product, acceptance loss is not significant.
Proposed efficacy specification	Between fresh product and the 12 months aged product, acceptance loss is not significant.

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	40 Evaluation by Rapporteur Member State
Date	April 2011.
Comments	Firstly, a comprehensive study report was not provided. **2.1.3** Physical state and nature of PASTA DIFE is a soft oily paste packaged in a sachet and not “little pieces of pasta” as described. **1.4, 2.1.5** Study protocol indicated that fresh and aged product (12 & 24 month) was used but results were only provided for the fresh and 12-month aged products. **4.3.2** Test organism – Albino strain of Norway rats / Brown rats*(Rattus norvegicus)*. **4.3.3** Mortality of baited individuals was the observed effect.
Summary and conclusion	**5.2** The study does not appear to have adhered to the agreed protocols and hence a reliability of 2 is more appropriate. The fresh bait achieved 95% control of rats whilst the 12-month aged bait achieved 90% control.
	41 Comments from ... *(specify)*

Date	*Give date of comments submitted*
Comments	*Discuss if deviating from view of rapporteur member state*
Summary and conclusion	*Discuss if deviating from view of rapporteur member state*

Tables for Method

1.1 (mixed) Population / Inoculum (*if necessary; include separate table for different samples*)

Criteria	Details
Nature	DIFENACOUM PASTA BAIT : Containing 0.005 % of Difenacoum
Origin	Batch 090908
Initial biomass	Not applicable
Reference of methods	The study protocol included the following : 1) An acceptance of the fresh product with albinos' rats and in individuals cages fresh product. 2) An acceptance of the product aged for 12 months with albinos' rats in individuals 3) An acceptance of the product aged for 24 months with albinos' rats in individuals Acceptance loss is measured by comparing results of several acceptance trials. Each of these trails uses 22 albino rats (11 males and 11 females) 10 to 20 weeks old, from the same origin, the same strain, and the same alimentation story at the trial start. The first trial uses fresh product and the following aged product (respectively 12 and 24 month). Each trials begins when rats have been acclimatized at least 8 days in individual cages in the lab, where they receive as much water and crushed wheat as they want. During the first 5 days, all the rats received 30h crushed wheat in a feeding dish. Daily consumption of each rodent was measure by calculating the difference between weight of the full feeding dish and this one of this dish after 24 hours. In a second time, another dish containing the study bait was added, except for 2 control rodents (one male and one female) which continued to be fed only with crushed wheat. Trials last 20 days.

Collection / storage of samples	By comparative measure between before and after baiting with placebo (wheat).
Preparation of inoculum for exposure	First Pre-baiting: PASTA DIFE baiting: Post bait phase:

<table>
<tr><td>Pretreatment</td><td>Not applicable</td></tr>
<tr><td><s>Initial density of test population in the test system/</s> Active substance determined in the product</td><td>The product DIFENACOUM PASTA BAIT was tested at different time in the same lab conditions. The product was stored at room temperature.
<table>
<tr><th></th><th>Concentration %</th><th>Deviation of the measured content from the declared value</th><th>Code analysis</th></tr>
<tr><td>Production date (2008/09/08)</td><td>0.00497</td><td>-0,6%</td><td>version date: September 9th, 2008</td></tr>
<tr><td>T0 (start of trial, 2009/01/29)</td><td>0.00501</td><td>+0,2%</td><td>version date: January 30th, 2009</td></tr>
<tr><td>T12 (2009/10/06)</td><td>0.00477</td><td>-4,6%</td><td>version date: October 16th, 2009</td></tr>
</table></td></tr>
</table>

1.2 Test organism (if applicable)

Criteria	Details
Species	Norway rats / Brown rats*(Rattus norvegicus)*
Strain	Albinos
Source	From the same origin, the same strain, and the same alimentation story at the trial start.
Laboratory culture	No, the aim of the study is to be as much as close of the reality.
Stage of life cycle and stage of stadia	10 to 20 weeks old,
Mixed age population	
Other specification	Not applicable
Number of organisms tested	20 tested animal, 10 of each sex.
Method of cultivation	Measurement in bait station every day.
Pretreatment of test organisms before exposure	Not applicable
Initial density/number of test organisms in the test system	Not applicable

1.3 Test system

Criteria	Details
Culturing apparatus / test chamber	Not applicable due to the test conditions.
Number of vessels / concentration	
Test culture media and/or carrier material	
Nutrient supply	
Measuring equipment	

1.4 Application of test substance

Criteria	Details
Application procedure	Wheat during the pre-baiting and post baiting phase and paste during the poisoning phase.
Delivery method	manger
Dosage rate	Measurement of consumption was measured every day.
Carrier	Not applicable due to the test conditions
Concentration of liquid carrier	Not applicable due to the test conditions
Liquid carrier control	Not applicable due to the test conditions
Other procedures	Not applicable due to the test conditions

1.5 Test conditions

Criteria	Details
Substrate	Not applicable due to the test conditions
Incubation temperature	Not applicable due to the test conditions
Moisture	-
Aeration	-
Method of exposure	-
Aging of samples	-
Other conditions	-

Section B5.10_07

Reference

Official use only

Reference	Feys J-L., Field trial with NORA PASTA BAITS against ROOF RATS 21 January 2010_08 February 2010, batch NO 091109. Belgagri. Unpublished
Data protection	Yes
Data owner	BELGAGRI Industrial Zone of Noville-les-Bois 14, rue du Grand Champ 5380 FERNELMONT, Belgium
Criteria for data protection	Data submitted to the MS before 14 May 2000 on existing [a.s. / b.p.] for the purpose of its [entry into Annex I/IA / authorisation] / Post inclusion
Guideline study	Yes, The method used has been inspired by the French method called "method no. 002 from Biological Trials Commission (C.E.B) ", Method for practical efficacy trials of raticides: • Adopted on 1960, derived from the work of Chitty and Dotty in the 1940. • Revised by OEPP in 1981, J. Giban.
Deviations	No

42 Method

Test Substance (Biocidal Product)	as given in section 2 deviating from specification given in section 2 *(Fill in the fields 3.1.2 and 3.1.3)*
Trade name/ proposed trade name	NORA PASTA BAITS
Composition of Product	0.005 % of Difenacoum

tested	
Physical state and nature	paste bait, fresh paste , mixture oils and meal, based on 0.005 % difenacoum
Monitoring of active substance concentration	No
Method of analysis	Field test to control the attractivity, the uptake and the efficacy of NORA PASTA Paste Baits on roof rats (Rattus rattus).
Reference substance	No
Method of analysis for reference substance	-
Testing procedure	
Test population / inoculum / test organism	*Rattus rattus (*Roof rats; Black rats*)* Population estimation: 15-20 rats.
Test system	The field test was performed in one of the pig stables of Mr Herman Van Thillo, Terbeekse straat 73 in Meer, along the E19 and just below the Dutch border, somewhat 20 km to the Northeast of *Antwerp.*
Application of TS	Daily, the bait stations were measured.
Test conditions	The pig stables site is is situated behind the corner of the Terbeeksestraat 73, at Vlamingweg N° 12 in Hoogstraten- Meer (B). It is a big stable, more than 40 metres long and almost as large as long, 36 metres. The entrance door gives access to a central alley with 4 doors to the left and 4 doors to the right. Each door gives access to a separate room, with a central corridor and 7 pig boxes to the right and 7 pig boxes to the left.

So the stable contains 8 x 14 boxes = 112 pig boxes which can contain 8 to10 or even more pigs, depending on their size

The roof of the stable is heavy insulated with very thick polyurethane boards and there is very little access from the floor to the roof, (see picture) so rats have difficulties to attack the insulation panels. This, and the apparently light infestation, explains why in this stable there were only a few holes in the insulation panels. On the other hand al the compartments are separately heated and the heating tubes of the floor heating system all have a control in the central alley.

So between two doors in the central alley there is everywhere an assembly of tubes which disappear under the floor. The heating tubes are protected by an irremovable metal plate and this seemed to be a highway for the roof rats, estimating the number of droppings around these assemblies. Estimating the limited number of holes on one hand and the number of droppings on the other hand, the Pest Controller estimated it to be a limited, early infestation. A small number, somewhere between 15 and 25 rats, was supposed to be the population at the beginning of the test.

Duration of the test / Exposure time

Prebating: 7 days
Poisoning bait: 20 days

Number of replicates performed

No replicates

Controls

No control

Examination

Effect investigated

Killing the rat population with a fresh poisoning bait

Method for recording / scoring of the

The method is to estimate by indirect observation, the bait consumption and a decrease of population before and after poisoning bait.

effect	
Intervals of examination	Daily
Statistics	Observation of the consumed baits and traces of rats in their usual environment.
Post monitoring of the test organism	Yes, The post-baiting is required to estimate the reduction in rats' population.

43 Results

Efficacy	The prebaiting showed a small but active group of Rattus rattus, estimated around 15 - 20 pieces. The tested product NORA PASTA was taken by the roof rats almost as well, be it slightly less, as the placebo bait.
Dose/Efficacy curve	The uptake of NORA PASTA dropped very slowly from the ninth day of the test. Probably, the rats showed first signs of sickness after 9 days. The fourteenth day, 3 dead rats were discovered between the heating tubes in the central alley. The following days the uptake dropped to a very low level, showing most of the rats were eliminated. Pest Controllers use as a standard rule that around 10 % of the dead rats are found, so 3 rats would mean an initial population of 30 rats. The uptake of the placebo bait however indicated more 15 – 20 rats.
Begin and duration of effects	Not applicable
Observed effects in the post monitoring phase	Not applicable
Effects against	Not applicable

organisms or objects to be protected	
Other effects	-
Efficacy of the reference substance	Not applicable
Tabular and/or graphical presentation of the summarised results	Not supplied
Efficacy limiting factors	Not applicable
Occurrences of resistances	Not applicable
Other limiting factors	Not applicable

44 Relevance of the results compared to field conditions

Reasons for laboratory testing	This experiment is a scaling-up. Moreover this experiment is closer to reality than laboratory process.
Intended actual scale of biocide application	Not applicable
Relevance	Not applicable

X

compared to field conditions		
Application method	Not applicable. This study is closer to field condition than laboratory process, rodent have access to plenty alternative food which is in competition with the poison bait.	X
Test organism	YES.	X
Observed effect	Not applicable. The conclusions have been made from indirect observations: decreased of food consumption)	X
Relevance for read-across	Yes, This experiment shows results in a specific area with real conditions and constraints related to architecture and uses of the building in process of treatment. Moreover, rodents are very attracted by any food storages, which offer them a huge supply of their needs. We can refer to the study, which regrouped all excellent parameters, as a relevant example of efficacy test for the dossier	

45 Applicant's Summary and conclusion

Materials and methods	The field test was performed in one of the pig stables of Mr Herman Van Thillo, Terbeekse straat 73 in Meer, along the E19 and just below	

the Dutch border, somewhat 20 km to the Northeast of *Antwerp.*

Before the test started the Pest Control operator, with years of experience in the destruction of Rattus rattus in stables estimated the population in the stable to somewhat 15 to 25 rats.
To control the extension of the population, the uptake of 19 x 100 g placebo bait was monitored during six days.
The test was started and the placebo bait was placed in the bait stations January 21st 2010 After 6 days , January 27th h, the uptake by the rats was steady, around 230 grams per day, and some bait stations were almost empty. See Excel sheet in annex, with the test results.
There was a big variation in uptake between the bait stations; there was a lot more activity at one end than at another. At the entrance door the bait was less taken, there was less activity.
As the rats had also plenty access to the pig food, the uptake of +-230 grams /day can be the result of 15 to 25 rats but is difficult to asses in such field conditions. It certainly showed that there was some uptake in these bait stations at those places and that the uptake was regular. So it was decided to continue the test with the test product placed in the same bait stations and with the same location of the stations.

January 27th the placebo bait was replaced by the test product NORA PASTA.
The bait stations were fitted with the sachets of NORA PASTA, fixed on the metal rod in the station, so the rats could not remove the product. Each station was fitted with 9 to 10 bait doses, approx. 100g NORA PASTA. As there is some slight variation in the doses of NORA PASTA, there was a slight variation in total weight/station, which was recorded.(see results) .
The uptake of the NORA PASTA was measured daily (not the first day after), the bait replaced twice.
The bait was replaced when some bait stations were almost empty. As the uptake was very different, some stations were empty earlier than others, but the bait was replaced at the same time in all the stations.
The first days the uptake of the paste was lower than the uptake of the placebo bait, less than 170 g/day, but from the fifth day on, days 5, 6,

	7 and 8 the uptake was a bit more than 200 grams a day. The eight day, February 2nd, some bait stations were almost empty and the bait was renewed in all the bait stations. The following days the uptake diminished, very little first, then more and more. Day fourteen, February 8th, three dead rats were discovered between the heating tubes in the central alley. The same day the uptake had dropped to a total of 126 g/day and the uptake was null in some bait stations.	
Reliability	2, Study conducted in accordance with generally accepted scientific principles, possibly with incomplete reporting or methodological deficiencies, which do not affect the quality of relevant results	
Assessment of efficacy, data analysis and interpretation		
Conclusion	DIFENACOUM is said to kill rodents in 5 to 21 days. In these test the first signs of illness started after 9 days; 3 dead rats were found after 14 days. After twenty days there was still some activity, which ended later (unrecorded). These results are consistent with the results expected with difenacoum baits. One can conclude that NORA PASTA Paste Baits is very well suited for the extermination of *Rattus rattus* in stables.	X
Proposed efficacy specification	NORA PASTA Paste Baits is very well suited for the extermination of R*attus rattus* in stables.	

Evaluation by Competent Authorities

	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	46 Evaluation by Rapporteur Member State
Date	April 2011.
Comments	**4.3** Study was conducted under field conditions. **4.3.1** Application method was oral. **4.3.2** Test organism - *Rattus rattus* (Wild Roof rats; Black rats). **4.3.3** Dead rodents were discovered post-baiting and consumption levels dropped indicating control of the target organisms. **5.4** The report states that after the recording period of 20 days there was still some activity, which ended later (unrecorded).
Summary and conclusion	Rats had access to pig feed throughout the study but the NORA PASTA bait proved palatable and highly effective against the rat population on the farm. The exact efficacy specification wasn't calculated based on the pre-baiting census was estimated at a population of 15-20 rats. The first signs of illness started after 9 days and 3 dead rats were found at 14 days. Given the difficulties in attracting roof rats in the presence of freely available pig rood the study is acceptable for product authorisation.
	47 Comments from ... *(specify)*
Date	*Give date of comments submitted*
Comments	*Discuss if deviating from view of rapporteur member state*
Summary and conclusion	*Discuss if deviating from view of rapporteur member state*

Tables for Method

1.1 (mixed) Population / Inoculum (*if necessary; include separate table for different samples*)

Criteria	Details
Nature	NORA PASTA BAITS: Containing 0.005 % of Difenacoum
Origin	Batch N°: NO091109 Product manufactured: November 9th 2009
Initial biomass	Not applicable
Reference of methods	Not applicable
Collection / storage of samples	By comparative measure between before and after baiting with placebo (wheat).
Preparation of inoculum for exposure	First Pre-baiting: NORA PASTA BAITS baiting:
Pretreatment	Not applicable
~~**Initial density of test population in the test system/**~~ **Active substance determined in the product**	The product NORA PASTA BAITS was tested at lab conditions, the 16/11/2009.

	Specification	Results	Decision
Aspect	Red paste	Red paste	OK
Composition	Difenacoum 50ppm±12.5 ppm	52.32	OK

1.2 Test organism (if applicable)

Criteria	Details
Species	Roof rats; Black rats *(Rattus rattus)*
Strain	Wild
Source	From the surrounding tested area
Laboratory culture	No, the aim of the study is to be as much as close of the reality.
Stage of life cycle and stage of stadia	Not mentioned
Mixed age population	
Other specification	Not applicable
Number of organisms tested	Not mentioned, only estimation could be performed based on the prebaiting. (Population estimation: 15-20 rats.)
Method of cultivation	Measurement in bait station every day.
Pretreatment of test organisms before exposure	Not applicable
Initial density/number of test organisms in the test system	Not applicable

1.3 Test system

Criteria	Details
Culturing apparatus / test chamber	Not applicable due to the test conditions.
Number of vessels / concentration	
Test culture media and/or carrier material	
Nutrient supply	
Measuring equipment	

1.4 Application of test substance

Criteria	Details
Application procedure	Placebo grain bait during the pre-baiting phase (100g by station) and paste during the poisoning phase.
Delivery method	-
Dosage rate	Measurement of consumption was measured every day.
Carrier	Not applicable due to the test conditions
Concentration of liquid carrier	Not applicable due to the test conditions
Liquid carrier control	Not applicable due to the test conditions
Other procedures	Not applicable due to the test conditions

1.5 Test conditions

Criteria	Details
Substrate	Not applicable due to the test conditions
Incubation temperature	Not applicable due to the test conditions
Moisture	-
Aeration	-
Method of exposure	-
Aging of samples	-
Other conditions	-

Toxicology

Doc IIIB Section 6.1.1 BPD Data Set IIB/ Annex Point VI.6.1.1	**Acute Oral Toxicity**	
	Reference	**Official use only**
Reference	[redacted] Difenacoum pasta bait - Acute Oral Toxicity in the rat - Acute toxic class method, [redacted] study number TAO423-PH-09/0086, 8 December 2009, 40 pages, Bio6. Unpublished	
Data protection	YES	

Data owner	Bio6 S.A,	
Companies with letter of Access	Letter of authorisation from PelGar International (UK) to Bio6 S.A. (Belgium)	
Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing active substance for the purpose of its entry into Annex I.	
	Guidelines and Quality Assurance	
Guideline study	OECD n° 423 (24 April 2002) Test method B.1ter Council regulation No 440/2008	
GLP	YES	
Deviations	Any	
	MATERIALS AND MethodS	
Test material	**Difenacoum pasta bait** It was identified under the code number in the laboratory as **PH-09/0086.**	
Lot/Batch number	LAB290109	
Specification	CAS No: 56073-07-5	
Description	Pasta and red	
Purity	Difenacoum 0.005 % m/m (nominal value). Please see the analysis certificate.	
Stability	2 years	
Test Animals		
Species	Rat	
Strain	Sprague-Dawley, SPF Caw	
Source	[redacted]	
Sex	Female	
Age/weight at study initiation	Females weighed between 196 g and 223 g and were 8 or 9 weeks old	
Number of animals per group	Two groups of three females	
Control animals	No	
Administration/ Exposure	**Oral**	
Post exposure period	14 days	
Type	Administered by gavage	
Concentration	2000 mg/kg	
Vehicle	A suitable syringe graduated fitted with an oesophageal metal canula.	
Concentration in vehicle	2000 mg/kg (2 g of the test item was gradually dissolved in 4 mL of distilled water by manual stirring and the formulation was transferred in a 10 mL volumetric flask, and then completed with distilled water)	X
Total volume applied	10 mL/kg body weight	
Controls	No	
Examinations	Clinical signs (every day), body weights (D0, D2, D7 and D14), and necropsy findings (D14)	

Method of determination of LD_{50}	No mortality occurred during the study. The LD_{50} of the test item Difenacoum pasta bait is higher than 2000 mg/kg body weight by oral route in the rat. In accordance with the OECD guideline n°423, the LD50 cut-off of the test item may be considered higher than 5000 mg/kg body weight by oral route in the rat.	
Further remarks	-*	
	Results and Discussion	
Clinical signs	Daily examinations were carried out to identify any behavioural or toxic effects on the major physiological functions 14 days after administration of the test item. This examination focuses particularly on a list of symptoms, recorded as "present" or "absent" on the observation sheet. These observations were compared to historical control data. Observations and a mortality report were then carried out every day for 14 days. Bodyweight were recorded at the day 0, 2, 7 and 14 (death day). The animal appeared normal for the duration of the study.	
Pathology	This was not investigated during study.	
Other	On D14, the animals were anaesthetised with sodium pentobarbital and administration continued to fatal levels. Macroscopic observations were entered on individual autopsy sheets. Only those organs likely to be modified in cases of acute toxicity were examined. Those presenting macroscopic anomalies can be removed and preserved in view to microscopic examinations.	
LD_{50}	No mortality occurred during the study at 2000mg/kg. The estimated acute LD50, as indicated by the data, was determined to be greater than 5000mg/kg	

	Applicant's Summary and conclusion	
Materials and methods	Six healthy female rats (Sprague Dawley, SPF Caw) originated from Elevage JANVIER were used after an acclimatization period of at least five days. Rats were housed by group of three in solid-bottomed clear polycarbonate cages with a stainless steel mesh lid. Drinking water (tap-water from public distribution system) and foodstuff were supplied freely. Food was removed at D-1 and then redistributed 4 hours after the test item administration. The animals of the treated group, received an effective dose of 2000 mg/kg body weight of the test item Difenacoum pasta bait, prepared extemporaneously in distilled water and administered by gavage under a volume of 10 mL/kg body weight using a suitable syringe graduated fitted with an oesophageal metal canula. 2 g of the test item was gradually dissolved in 4 mL of distilled water by manual stirring and the formulation was transferred in a 10 mL volumetric flask, and then completed with distilled water. The formulation obtained was placed under magnetic stirring up to obtain a homogeneous suspension. Systematic examinations were carried out to identify any behavioural or toxic effects on the major physiological functions 14 days after administration of the test item. This examination focuses particularly on a list of symptoms, recorded as "present" or "absent" on the observation sheet. These observations were compared to historical control data. Observations and a mortality report were then carried out every day for 14 days. On D14, the animals were anaesthetised with sodium pentobarbital and administration continued to fatal levels.	
Results and discussion	No mortality occurred during the study. No clinical signs related to the administration of the test item were observed. The body weight evolution of the animals remained normal throughout the study. The macroscopical examination of the animals at the end of the study revealed a thickening of the corpus (5/6 animals) with presence of red spots (3/6 animals).	
Conclusion	The LD50 of the test item Difenacoum pasta bait is higher than 2000 mg/kg body weight by oral route in the rat. In accordance with the OECD guideline n°423, the LD50 cut-off of the test item may be considered higher than 5000 mg/kg body weight by oral route in the rat. According to the criteria for classification, packaging and labelling of dangerous substances and preparations in accordance with the E.E.C. Directives 67/548, 2001/59 and 99/45, the test item Difenacoum pasta bait must not be classified. No symbol and risk phrase are required. In accordance with the Globally Harmonized System (Regulation (EC) No 1272/2008), the test item must not be classified in category 4. No signal word and hazard statement are required.	

Reliability	1	
Deficiencies	No	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	Evaluation by Rapporteur Member State
Date	*20 April 2010*
Materials and Methods	Adopt applicants version
Results and discussion	Adopt applicants version
Conclusion	Other conclusions: LD50 > 2000mg/kg bw
Reliability	2
Acceptability	acceptable *Difenacoum is lipid soluble. An aqueous extract will not recover all of the active substance from the sample. An emulsion will form and the majority of the difenacoum will partition into the oil phase. Cannot be certain of actual dose.*
Remarks	None
	Comments from ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Doc IIIB Section 6.1.2 BPD Data Set IIB/ Annex Point VI.6.1.2	**Acute Dermal Toxicity**	
	Reference	**Official use only**
Reference	[redacted] Difenacoum pasta bait - Acute Dermal Toxicity in the rat - Acute toxic class method, [redacted] study number TAD-PH-09/0086, 8 December 2009, 39 pages, Bio6. Unpublished	
Data protection	YES	
Data owner	Bio6 S.A,	
Companies with letter of Access	Letter of authorisation from PelGar International (UK) to Bio6 S.A. (Belgium)	
Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing active substance for the purpose of its entry into Annex I.	
	Guidelines and Quality Assurance	
Guideline study	OECD n° 402 (24 February 1987) Test method B.3 Council regulation No 440/2008	
GLP	YES	
Deviations	Any	
	MATERIALS AND MethodS	
Test material	**Difenacoum pasta bait** It was identified under the code number in the laboratory as **PH-09/0086.**	
Lot/Batch number	LAB290109	
Specification	CAS No: 56073-07-5	
Description	Pasta and red	
Purity	Difenacoum 0.005 % m/m (nominal value). Please see the analysis certificate.	
Stability	2 years	
Test Animals		
Species	Rat	
Strain	Sprague-Dawley, SPF Caw	
Source	[redacted]	
Sex	Males and females	
Age/weight at study initiation	Males weighed between 215 g and 244 g and were 7 weeks old Females weighed between 202 g and 214 g and were 8 weeks old	
Number of animals per group	One group of 5 males and the other of 5 females.	
Control animals	No	

Administration/ Exposure	**Dermal**	
Post exposure period	14 days	
Area covered	10% of the total surface area (from the dorsal area of the trunk of the test animals)	
Occlusion	Occlusive	
Vehicle	None.	
Concentration in vehicle	2000mg/kg	
Total volume applied	10ml/kg	
Duration of exposure	24h	
Removal of test substance	The gauze dressings were removed and the treated site was rinsed with distilled water.	
Controls	None.	
Examinations	Clinical signs, body weights, and necropsy findings.	
Method of determination of LD_{50}	There was no mortality during the study. The LD50 of the test item Difenacoum pasta bait is higher than 2000 mg/kg body weight by dermal route in the rat	
Further remarks		
	Results and Discussion	
Clinical signs	Daily examinations were carried out to identify any behavioural or toxic effects on the major physiological functions 14 days after administration of the test item. This examination focuses particularly on a list of symptoms, recorded as "present" or "absent" on the observation sheet. These observations were compared to historical control data. Observations and a mortality report were then carried out every day for 14 days. Bodyweight were recorded at the day 0, 2, 7 and 14 (death day). The animal appeared normal for the duration of the study.	
Pathology	It was not investigated during study.	
Other	On D14, the animals were anaesthetised with sodium pentobarbital and administration continued to fatal levels. Macroscopic observations were entered on individual autopsy sheets. Only those organs likely to be modified in cases of acute toxicity were examined. Those presenting macroscopic anomalies can be removed and preserved in view to microscopic examinations.	
LD_{50}	There was no mortality during the study. The estimated acute LD_{50}, as indicated by the data, was determined to be greater than 2000mg/kg body weight.	

	Applicant's Summary and conclusion	
Materials and methods	During the treatment, the animals were kept in individual cage. On D3, the animals were put into their cage by 2 or 3. The rats were kept in solid-bottomed clear polycarbonate cages with a stainless steel mesh lid. Each cage contains sawdust bedding which was changed at least 2 times a week. Each cage was installed in conventional air conditioned animal husbandry. Drinking water (tap-water from public distribution system) and foodstuff were supplied freely. Approximately 24 hours before the treatment, fur was removed from the dorsal area of the trunk of the test animals by clipping. At least 10 per cent of the body surface area was clear for the application of the test item. The test item was first reduced in fine powder using a coffee mill. Then, 2 g of the test item were weighed in a 10 mL volumetric flask completed with distilled water. The formulation obtained was placed under magnetic stirring up to obtain a homogeneous suspension. Then, the suspension was filtered using a sieve and a pestle. Animals from treated group received by topical application, under porous gauze dressing, an effective dose of 2000 mg/kg body weight of Difenacoum pasta bait, administered under a volume of 10 mL/kg body weight, during 24 hours. After 24-hour exposure period, the gauze dressings were removed and the treatment site was rinsed with distilled water. Systematic examinations were carried out to identify any behavioural or toxic effects on the major physiological functions 14 days after administration of the test item. This examination focuses particularly on a list of symptoms, recorded as "present" or "absent" on the observation sheet. These observations were compared to historical control data. Observations and a mortality report were then carried out every day for 14 days On D14, the animals were anaesthetised with sodium pentobarbital and administration continued to fatal levels.	
Results and discussion	No mortality occurred during the study. Neither cutaneous reactions nor systemic clinical signs related to the administration of the test item were observed. A pink coloration, which did not prevent the observations, was noted on the treatment site on day 1. The body weight evolution of the animals remained normal throughout the study. The macroscopical examination of the animals at the end of the study did not reveal treatment-related changes.	

Conclusion	The LD50 of the test item Difenacoum pasta bait is higher than 2000 mg/kg body weight by dermal route in the rat. According to the criteria for classification, packaging and labelling of dangerous substances and preparations in accordance with the E.E.C. Directives 67/548, 2001/59 and 99/45, the test item Difenacoum pasta bait must not be classified. No symbol and risk phrase are required. In accordance with the Globally Harmonized System (Regulation (EC) No 1272/2008), the test item must not be classified in category 4. No signal word and hazard statement are required.	
Reliability	1	
Deficiencies	No	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	Evaluation by Rapporteur Member State	
Date	20 April 2011	
Materials and Methods	Adopt applicant's version	
Results and discussion	Adopt applicant's version	
Conclusion	Other conclusions: Adopt applicant's version	
Reliability	1	
Acceptability	acceptable *(give reasons if necessary, e.g. if a study is considered acceptable despite a poor reliability indicator. Discuss the relevance of deficiencies and indicate if repeat is necessary.)*	
Remarks	None	
	Comments from ...	
Date	*Give date of comments submitted*	
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*	
Results and discussion	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Reliability	*Discuss if deviating from view of rapporteur member state*	
Acceptability	*Discuss if deviating from view of rapporteur member state*	
Remarks		

III B Section 6.1.3 BPD Data Set IIB Annex Point VI.6.1.3	**INHALATION:** **JUSTIFICATION FOR NON-SUBMISSION OF DATA**	Official use only
	As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. *The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	
Other existing data [ ]	**Technically not feasible [ ] Scientifically unjustified [ ]**	
Limited exposure [ ]	**Other justification [x]**	
Detailed justification:	The active substance and the other co-formulant have low vapor pressures and are present only at low concentration in the product (with the obvious exception of the bait base). For example, difenacoum is present at 0.005% w/W and has a vapor pressure of 6.7 x 10^{-9} – 5.4 x 10^{-14} Pa.	
	According exposure assessment performed on measurements of a surrogate in simulated use conditions and on daily exposure frequencies according to a questionnaire answered by selected pest control companies in several EU countries. In primary exposure, the skin is the main exposure route, and only a small proportion of inhalation exposure to dust from decanting of pellets or grain baits is included in the total exposure. Inhalation exposure is not included for wax block formulation. Oral exposure is not considered relevant in primary exposure. Dermal absorption of 0.047% and body weight of 60 kg for an adult is used for the calculations.	
	Source: *Assessment Report – Difenacoum, Product-type 14 (Rodenticides), Directive 98/8/EC concerning the placing of biocidal products on the market. Inclusion of active substances in Annex I or IA to Directive 98/8/EC, 17 September 2009, Annex I – Finland, p14.*	
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	

Date	20 April 2011
Evaluation of applicant's justification	*Inhalation exposure is not expected to be a factor in exposure scenarios. However, as the active substance is classified regarding inhalation exposure. Information on this endpoint may have been beneficial. The lack of acute toxicity of the product suggests it may have little inhalation toxicity too.*
Conclusion	*The applicant's justification is acceptable.*
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

III B Section 6.1.4 BPD Data Set IIB Annex Point VI.6.1.4	**INFORMATION ON MIXTURE OF BIOCIDAL PRODUCT:** **JUSTIFICATION FOR NON-SUBMISSION OF DATA**	Official use only
	As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. *The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	
Other existing data [ ]	**Technically not feasible [ ] Scientifically unjustified [x]**	
Limited exposure [ ]	**Other justification [ ]**	
Detailed justification:	Not applicable since following the proposed uses of **PASTA BAIT** and the label claims, the rodenticide **PASTA BAIT** is not intended to be used in mix with other Biocidal products.	
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	20 April 2011	
Evaluation of applicant's justification	Bait contained in a sealed wrapper is not available of designed for mixing.	
Conclusion	The applicant's justification is acceptable.	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

IIIB Section 6.2._01 BPD Data Set IIB/ Annex Point VI.6.2	**Acute Dermal Irritation**	
	Reference	**Official use only**
Reference	[redacted] Difenacoum pasta bait – Skin Irritation test in the rabbit, [redacted] study number IC-OCDE-PH-09/0086, 8 December 2009, 36 pages, Bio6. Unpublished	
Data protection	YES	
Data owner	Bio6 S.A,	
Companies with letter of Access	Letter of authorisation from PelGar International (UK) to Bio6 S.A. (Belgium)	
Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing active substance for the purpose of its entry into Annex I.	
	Guidelines and Quality Assurance	
Guideline study	OECD n° 404 (24 April 2002) Test method B.4 Council regulation No 440/2008	
GLP	YES	
Deviations	Any	
	MATERIALS AND MethodS	
Test material	**Difenacoum pasta bait** It was identified under the code number in the laboratory as **PH-09/0086.**	
Lot/Batch number	LAB290109	
Specification	CAS No: 56073-07-5	
Description	Paste and red	
Purity	Difenacoum 0.005 % m/m (nominal value). Please see the analysis certificate.	
Stability	2 years	
Test Animals		
Species	Albino rabbit	
Strain	New Zealand	
Source	[redacted]	
Sex	Male	
Age/weight at study initiation	The animals weighed between 2.81 kg and 3.02 kg. At the beginning of the test, the animals were 13 weeks old.	
Number of animals per group	One group of 3 males	
Control animals	No, but there was for each animal two kind of area, one for the test site and on other for control site.	

Administration/ Exposure	Dermal	
Application		
Preparation of test substance	The test item was applied, as supplied, at a dose of 0.5 g,	
Test site and Preparation of Test Site	The test site was the undamaged skin area of one flank of each animal	
Occlusion	Semi-occlusive dressing, the patch was secured in position with a strip of surgical adhesive tape	
Vehicle	None, application directly on the skin.	
Concentration in vehicle	A dose of 0.5 g	
Total volume applied	Not mentioned	
Removal of test substance	Distilled water	
Duration of exposure	4h	
Postexposure period	If no reaction is observed 72 hours after the treatment, the study is terminated. In case of persistent reactions, additional observations can be carried out from D4 to D14 in order to determine the reversible character of the lesions observed.	
Controls	No specified by the laboratory	
Examinations		
Clinical signs	No	
Dermal examination	Yes	

<table>
<tr><td>Scoring system</td><td>The state scoring system is explained to the fallowing table:

<table>
<tr><td>Score</td><td colspan="2">Evaluation of skins reactions</td></tr>
<tr><td></td><td>Erythema Formation</td><td>Oedema formation</td></tr>
<tr><td>0 (min)</td><td>No erythema</td><td>No oedema</td></tr>
<tr><td>1</td><td>Very slight (Barely perceptible)</td><td>Very slight (Barely perceptible)</td></tr>
<tr><td>2</td><td>Well-defined</td><td>Slight (contour clearly defined)</td></tr>
<tr><td>3</td><td>Moderate to severe</td><td>Moderate (Raised approximately 1mm)</td></tr>
<tr><td>4 (max)</td><td>Severe (beet redness) with eschars formation preventing gradin of erythema</td><td>Severe (raised than 1mm and extending beyond the area of exposure</td></tr>
</table>
</td><td></td></tr>
<tr><td>Examination time points</td><td>The animals were examined at 1, 24, 48 and 72 hours.</td><td></td></tr>
<tr><td>Other examinations</td><td>No other signs of dermal irritation.
A pink or red coloration was noted on the treated area but did not prevent from quotation</td><td></td></tr>
<tr><td>Further remarks</td><td>Initially, a single animal was treated. After consideration of the cutaneous responses produced in the first treated animal, two additional animals were treated during 4 hours.</td><td></td></tr>
<tr><td></td><td>Results and Discussion</td><td></td></tr>
<tr><td>Average score</td><td></td><td></td></tr>
</table>

<table>
<tr><td>Erythema</td><td>The average score for all animals is given at the following table:
<table><tr><td rowspan="2">Animal number</td><td colspan="4">Hours of examination</td></tr><tr><td>1</td><td>24</td><td>48</td><td>72</td></tr><tr><td>A9644
(12 May 09)</td><td>0</td><td>0</td><td>0</td><td>0</td></tr><tr><td>A9647
(19 May 09)</td><td>0</td><td>0</td><td>0</td><td>0</td></tr><tr><td>A9649
(19 May 09)</td><td>0</td><td>0</td><td>0</td><td>0</td></tr></table>0= Non irritating</td><td></td></tr>
<tr><td>Edema</td><td>The average score for all animals is given at the following table:
<table><tr><td rowspan="2">Animal number</td><td colspan="4">Hours of examination</td></tr><tr><td>1</td><td>24</td><td>48</td><td>72</td></tr><tr><td>A9644
(12 May 09)</td><td>0</td><td>0</td><td>0</td><td>0</td></tr><tr><td>A9647
(19 May 09)</td><td>0</td><td>0</td><td>0</td><td>0</td></tr><tr><td>A9649
(19 May 09)</td><td>0</td><td>0</td><td>0</td><td>0</td></tr></table>0= Non irritating</td><td></td></tr>
<tr><td>Reversibility</td><td>Yes</td><td></td></tr>
<tr><td>Other examinations</td><td>No other signs of dermal irritation</td><td></td></tr>
<tr><td>Overall result</td><td>No cutaneous reactions (erythema and oedema) were observed, on the treated area, whatever the examination times (ie 1, 24, 48 and 72 hours).</td><td></td></tr>
</table>

	Applicant's Summary and conclusion	
Materials and methods	Three male albino New Zealand rabbits were used for this experiment. They were kept during minimal 5-day acclimatization. Each animal was kept in an individual box installed in conventional air conditioned animal husbanding. Drinking water (tap-water from public distribution system) and foodstuffs (SDS – C15) were supplied freely. Approximately 24 hours before the test, the rabbit's back and flanks were shorn using electric clippers equipped with a fine comb, so as to expose an area of skin about 6 cm2. The test item was previously reduced in fine powder with a coffee mill. As no tissue destruction was noted after a treatment during 3 minutes and 1 hour, the test item was applied, as supplied, at a dose of 0.5 g, on an undamaged skin area of one flank of each animal, during 4 hours. The patch was secured in position with a strip of surgical adhesive tape under semi-occlusive dressing. After the removal of the patch, the treated area was rinsed with distilled water. On the opposite flank an untreated area was served as the control. Initially, a single animal was treated. After consideration of the cutaneous responses produced in the first treated animal, two additional animals were treated during 4 hours. The irritation scoring was observed at 1, 24, 48 and 72 hours after the substance exposure.	
Results and discussion	No cutaneous reactions (erythema and oedema) were observed, on the treated area, whatever the examination times (ie 1, 24, 48 and 72 hours).	
Conclusion	The results obtained, under these experimental conditions, enable to conclude that the test item Difenacoum pasta bait, according to the scales of interpretation retained: - is non irritant to skin (PSi = 0.0) according to the classification established in the Journal Officiel de la République Française dated February 21st, 1982, - and, must not be classified, according to the criteria for classification, packaging and labelling of dangerous substances and preparations in compliance with the E.E.C. Directives 67/548, 2001/59 and 99/45. No symbol and risk phrase are required. In accordance with the Globally Harmonized System (Regulation (EC) No 1272/2008), the test item must not be classified in category 2. No signal word and hazard statement are required.	
Reliability	1	
Deficiencies	No	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	

	Evaluation by Rapporteur Member State
Date	20 April 2011
Materials and Methods	Adopt applicant's version.
Results and discussion	Adopt applicant's version
Conclusion	Other conclusions: Adopt applicant's version
Reliability	1
Acceptability	Acceptable *(give reasons if necessary, e.g. if a study is considered acceptable despite a poor reliability indicator. Discuss the relevance of deficiencies and indicate if repeat is necessary.)*
Remarks	None

	Comments from ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

IIIB Section 6.2_02 BPD Data Set IIB/ Annex Point VI.6.2	**Acute Eye Irritation**	
	Reference	**Official use only**
Reference	[redacted] Difenacoum pasta bait – Skin Irritation test in the rabbit, [redacted] study number IC-OCDE-PH-09/0086, 8 December 2009, 39 pages, Bio6. Unpublished	
Data protection	YES	
Data owner	Bio6 S.A,	
Companies with letter of Access	Letter of authorisation from PelGar International (UK) to Bio6 S.A. (Belgium)	
Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing active substance for the purpose of its entry into Annex I.	
	Guidelines and Quality Assurance	
Guideline study	OECD n° 405 (24 April 2002) Test method B.5 Council regulation No 440/2008	
GLP	YES	
Deviations	Any	
	MATERIALS AND MethodS	
Test material	**Difenacoum pasta bait** It was identified under the code number in the laboratory as **PH-09/0086.**	
Lot/Batch number	LAB290109	
Specification	CAS No: 56073-07-5	
Description	Paste and red	
Purity	Difenacoum 0.005 % m/m (nominal value). Please see the analysis certificate.	
Stability	2 years	

Test Animals		
Species	Albino rabbit	
Strain	New Zealand	
Source	[redacted]	
Sex	Female	
Age/weight at study initiation	The animals weighed between 2.39 kg and 3.38 kg. At the beginning of the test, the animals were 11 and 13 weeks old.	
Number of animals per group	One group of 3 females	
Control animals	No, but one yes received the test item, the second is used as control.	
Administration/ Exposure		
Preparation of test substance	The test item was previously reduced in fine powder with a coffee-mill.	
Amount of active substance instilled	0.1 g of the test item	
Exposure period	24h	
Postexposure period	If no reaction is observed 72 hours after instillation, the study is terminated. In case of persistent reactions, additional observations can be carried out from D4 to D21 in order to determine the reversible character of the lesions observed	

Examinations		
Ophthalmoscopic examination	Yes	

Scoring system

Chemosis (A)	
No swelling	0
Slight swelling, including the nictitating membrane	1
Swelling with eversion of the eyelid	2
Swelling with eyelid half-closed	3
Swelling with eyelid more than half-closed	4
Discharge (B)	
No discharge	0
Slight discharge (normal slight secretions in the inner corner not to be taken into account	1
Discharge with moistening of the eyelids and neighbouring hairs	2
Discharge with moistening of the eyelids and large areas around the eye	3
Redness (C)	
Blood vessels normal	0
Vessels significantly more prominent than normal	1
Vessels individually distinguishable with difficulty	-
• Generalised red coloration	2
• Generalised deep red coloration	3
Iris (D)	
Normal	0
Iris significantly more wrinkled than normal, congestion, swelling of the iris which continues to react to light, even slowly	1
No reaction to light, haemorrhage, significant damage (any or all of these characteristics	2
Cornea: Degree of opacity (E)	
No modification visible either directly or after instillation of fluorescein (no loss of glint or polish)	0
Translucent areas (diffuse or disseminated), iris details clearly visible	1
Easily identifiable translucent area, iris details slightly obscured	2
Opalescent area, no iris details visible, pupil outline scarcely distinguishable	3
Total corneal opacity, completely obscuring the iris and pupil	4
Cornea: Extent of opacity (F)	
Opaque area present but covering one quarter or less	1
Between one quarter and half	2
Between half and three quarters	3
Between three quarters and the entire surface	4

<table>
<tr><td></td><td>The calculs for the total maximum score for:
<table>
<tr><td></td><td></td><td>Maximum score</td></tr>
<tr><td>CONJUNCTIVAE</td><td>(A+B+C)x2 = X</td><td>20</td></tr>
<tr><td>IRIS</td><td>Dx5 =Y</td><td>10</td></tr>
<tr><td>CORNEA</td><td>ExFx5= Z</td><td>80</td></tr>
<tr><td colspan="2">TOTAL</td><td>110</td></tr>
</table></td><td></td></tr>
<tr><td>Examination time points</td><td>60min, 24h, 48h, 72h</td><td></td></tr>
<tr><td>Other investigations</td><td>None</td><td></td></tr>
<tr><td>Further remarks</td><td>Initially, a single animal was treated. After consideration of the ocular responses produced in the first treated animal at D1, two additional animals were treated.
At the reading time 1 hour, for the animals A9678 and A9679, residual test item was still noted. Therefore, the treated eye was rinse with a physiological saline solution</td><td></td></tr>
<tr><td></td><td>Results and Discussion</td><td></td></tr>
<tr><td>Clinical signs</td><td>No effects</td><td></td></tr>
<tr><td>Average score</td><td></td><td></td></tr>
<tr><td>Cornea</td><td>The average score for the cornea is given at the following table:
<table>
<tr><td>Animal number</td><td colspan="3">A9661</td><td colspan="3">A9678</td><td colspan="3">A9679</td></tr>
<tr><td>Hours of examination</td><td>24</td><td>48</td><td>72</td><td>24</td><td>48</td><td>72</td><td>24</td><td>48</td><td>72</td></tr>
<tr><td>Opacity (E)</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>TOTAL</td><td colspan="3">0</td><td colspan="3">0</td><td colspan="3">0</td></tr>
<tr><td>MEAN</td><td colspan="3">0.0</td><td colspan="3">0.0</td><td colspan="3">0.0</td></tr>
</table></td><td></td></tr>
</table>

Iris

The average score for the iris is given at the following table:

Animal number	**A9661**			**A9678**			**A9679**		
Hours of examination	24	48	72	24	48	72	24	48	72
Opacity (E)	0	0	0	0	0	0	0	0	0
TOTAL	0			0			0		
MEAN	0.0			0.0			0.0		

Conjunctiva

Redness

The average score for the redness is given at the following table:

Animal number	**A9661**			**A9678**			**A9679**		
Hours of examination	24	48	72	24	48	72	24	48	72
Opacity (E)	2	2	1	0	0	0	1	1	0
TOTAL	5			0			2		
MEAN	1.7			0.0			0.7		

Chemosis

The average score for the chemosis is given at the following table:

Animal number	**A9661**			**A9678**			**A9679**		
Hours of examination	24	48	72	24	48	72	24	48	72
Chemosis (A)	2	2	1	1	0	0	1	0	0
TOTAL	5			1			1		
MEAN	1.7			0.3			0.3		

Reversibility

Yes, the redness and the chemosis disappeared after 72 hours.

Other	None	
Overall result	According to the calculated means and the European regulation, the calculated means, the item must not be classified. According to the calculated means and the GHS regulation, the item must not be classified	
	Applicant's Summary and conclusion	
Materials and methods	Three female albino New Zealand rabbits were used for this experiment. They were kept during minimal 5-day acclimatization. Each animal was kept in an individual box installed in conventional air conditioned animal husbanding. Drinking water (tap-water from public distribution system) and foodstuffs (SDS – C15) were supplied freely. The test item was previously reduced in fine powder with a coffee-mill. 0.1 g of the test item was instilled into the conjunctival sac of one eye; the other eye remained untreated serving as control. Initially, a single animal was treated. After consideration of the ocular responses produced in the first treated animal at D1, two additional animals were treated. Ocular examinations were performed on both right and left eyes 1 hour, 24, 48 and 72 hours following treatment,	
Results and discussion	The ocular conjunctivae reactions observed during the study have been slight to moderate and totally reversible in the three animals; a slight to moderate redness, noted 1 hour after the test item instillation and totally reversible between day 1 and day 4, associated with a slight to moderate chemosis, noted 1 hour after the test item instillation and totally reversible between day 2 and day 4.	
Conclusion	The results obtained, under these experimental conditions, enable to conclude that the test item Difenacoum pasta bait: - is slightly irritant for the eye (Max. O.I = 8.7) according to the classification established in the Journal Officiel de la République Française dated July 10th, 1992. - and, must not be classified according to the criteria for the classification, packaging and labelling of dangerous substances and preparations in compliance with the E.E.C. Directives n° 67/548, n°2001/59 and n°99/45. No symbol and risk phrase are required. In accordance with the Globally Harmonized System (Regulation (EC) No 1272/2008), the test item must not be classified in category 2. No signal word and hazard statement are required.	
Reliability	1	

Deficiencies	No	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	

	Evaluation by Rapporteur Member State
Date	20 April 2011
Materials and Methods	Adopt applicant's version.
Results and discussion	Adopt applicant's version.
Conclusion	Other conclusions: Adopt applicant's version.
Reliability	1
Acceptability	Acceptable
Remarks	None

	Comments from ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub) heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

IIIB Section 6.3 BPD Data Set IIB/ Annex Point VI.6.3	**Skin sensitisation**	
	Reference	**Official use only**
Reference	[redacted] Difenacoum pasta bait – Skin sensitisation in the guinea pig - Magnusson and Kligman maximisation method, [redacted] study number SMK-PH-09/0086, 8 December 2009, 43 pages, Bio6. Unpublished	
Data protection	YES	
Data owner	Bio6 S.A,	
Companies with letter of Access	Letter of authorisation from PelGar International (UK) to Bio6 S.A. (Belgium)	
Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing active substance for the purpose of its entry into Annex I.	
	Guidelines and Quality Assurance	
Guideline study	OECD n° 406 (17 July 1992) Test method B.6 Council regulation No.440/2008	
GLP	YES	
Deviations	Any	
	MATERIALS AND MethodS	
Test material	**Difenacoum pasta bait** It was identified under the code number in the laboratory as **PH-09/0086.**	
Lot/Batch number	LAB290109	
Specification	CAS No: 56073-07-5	
Description	Paste and red	
Purity	Difenacoum 0.005 % m/m (nominal value). Please see the analysis certificate.	
Stability	2 years	
Preparation of test substance for application	The following table shows the dose for the induction and for the challenge for the test substance and for the positive control substance:	

		Preparation of the test substance
		Difenacoum pasta bait
Concentration administrated	Induction	50% in distilled water
	Challenge	50% in distilled water

<table>
<tr><td></td><td><table><tr><td></td><td></td><td>25% in distilled water</td></tr></table></td><td></td></tr>
<tr><td>Pretest performed on irritant effects</td><td>Yes, preliminary tests were performed:
The MNNC test was conducted for the purpose of defining a MNNC which, by intradermic injection of the test item, during the induction phase, does not risk causing too great a lesion (non-necrotizing concentration), should be well-tolerated systemically and should be the highest to cause mild-tomoderate skin irritation.
The Pre-Maximal Non Irritant Concentration test (Pre- MNIC), by topical application, which allowed evaluating the irritant potential of the test item, defined whether an application of sodium lauryl sulfate would be needed during topical induction phase.
The MNIC test was carried out for the purpose of determining the of the test item without risk of an irritant effect during the challenge phase</td><td></td></tr>
<tr><td>Test Animals</td><td></td><td></td></tr>
<tr><td>Species</td><td>Guinea pigs</td><td></td></tr>
<tr><td>Strain</td><td>Dunkin-Hartley strain</td><td></td></tr>
<tr><td>Source</td><td>[redacted]</td><td></td></tr>
<tr><td>Sex</td><td>Female</td><td></td></tr>
<tr><td>Age/weight at study initiation</td><td>The animals weighed between 256 g and 278 g at the beginning of the test and were 4 weeks old.</td><td></td></tr>
<tr><td>Number of animals per group</td><td><table><tr><td></td><td>GROUP 1
negative control</td><td>GROUP 2
treated</td></tr><tr><td>Female/group</td><td>5
n° C1882 to C1886</td><td>11
n° C1887 to C1897</td></tr></table></td><td></td></tr>
<tr><td>Control animals</td><td>Negative control (5 for the group)</td><td></td></tr>
<tr><td>Administration/</td><td>The aim of the study was to evaluate the possible allergenic activity</td><td></td></tr>
</table>

<table>
<tr><td>Exposure</td><td>of the test item after topical administration in guinea pigs.</td><td></td></tr>
<tr><td>Induction schedule</td><td>Day 1 – Day 7 – Day 8</td><td></td></tr>
<tr><td>Way of Induction</td><td>Topical</td><td></td></tr>
<tr><td></td><td>Occlusive</td><td></td></tr>
<tr><td>Concentrations used for induction</td><td>The concentration used for the induction was 50% of the test item in distilled water.
<table>
<tr><td></td><td></td><td>Preparation of the test substance</td></tr>
<tr><td></td><td></td><td>Difenacoum pasta bait</td></tr>
<tr><td rowspan="2">Concentration administrated</td><td>Induction</td><td>50% in distilled water</td></tr>
<tr><td rowspan="2">Challenge</td><td>50% in distilled water</td></tr>
<tr><td>25% in distilled water</td></tr>
</table></td><td></td></tr>
<tr><td>Concentration Freunds Complete Adjuvant (FCA)</td><td>50 % FCA in isotonic sodium chloride</td><td></td></tr>
<tr><td>Challenge schedule</td><td>Day 21</td><td></td></tr>
<tr><td>Concentrations used for challenge</td><td>The concentrations used for challenge were 70% (MNIC) and 35% (1/2 MNIC) of the test item in distilled water.</td><td></td></tr>
<tr><td>Rechallenge</td><td>No</td><td></td></tr>
<tr><td>Scoring schedule</td><td>24h, 48h after challenge</td><td></td></tr>
<tr><td>Removal of the test substance</td><td>Not specified.</td><td></td></tr>
<tr><td>Positive control substance</td><td>α-Hexylcinnamaldehyde</td><td></td></tr>
<tr><td>Examinations</td><td></td><td></td></tr>
</table>

Pilot study	Yes	
Further remarks	-	
	Results and Discussion	
Results of pilot studies	- MNNC determination: No necrosis has been observed, at the concentration of 40% in the two animals. The first induction of the Group 2 has been carried out by intradermal injection at the same concentration of 40% (table 1, page 12). - Pre MNIC determination: 24 hours after the removal of the occlusive dressings, no cutaneous reaction was recorded whatever the tested concentration (70% diluted at 35%, 17.5% and 8.75% in distilled water, after being reduced in fine powder with a coffee mill.). In view of these results, the concentration selected was 70% for the 2nd induction of the Group 2 and the MNIC determination began at this concentration of 70%. - MNIC determination: 24 hours after removal of the occlusive dressings, no cutaneous reaction was recorded whatever the tested concentration. In view of this result, the concentrations selected were 70% (MNIC) and 35% (1/2 MNIC) for the challenge phase	

Results of test

24h after challenge

No macroscopic cutaneous reactions was recorded during the examination following the removal of the occlusive dressing (challenge phase) from the animals of the treated group with the test item at 70% and 35%.

It was only noted a depilation at the reading time 24 hours on the treated area at 70% in seven animals (7/11) and on the treated area at 35% in five animals (5/11).

48h after challenge

No macroscopic cutaneous reactions was recorded during the examination following the removal of the occlusive dressing (challenge phase) from the animals of the treated group with the test item at 70% and 35%.

Other findings

No cutaneous intolerance reaction was recorded in animals from the negative control group after the challenge phase, on the treated area with the test item at 70% and 35%. It was only noted a depilation at the reading time 24 hours on the treated area at 70% in all animals (5/5).

Overall result

The following tables show the macroscopic evaluation at 24 and 48 hours after the challenge with the test substance:

Groups	Reading time	Conc	Quotations				% of positive responses ≥1	% of animal sensitized
Negative control group	24	70 %	0	1	2	3or >		
	48	35 %	0	0	0	0	0%	

		24	70 %	0	0	0	0	0%	
		48	35 %	0	0	0	0	0%	
	Treated Group	24	70 %	0	0	0	0	0%	0%
		48	35 %	0	0	0	0	0%	0%
		24	70 %	0	0	0	0	0%	0%
		48	35 %	0	0	0	0	0%	0%

0: No reaction.

	Applicant's Summary and conclusion	
Materials and methods	Sixteen female albino pigs of Dunkin-Hartley strain, supplied by Charles River (F-69592 L'ARBRESLE) were exposed to the test item after an acclimatisation period of at least five days. For the main study, the animals weighed between 256 g and 278 g at the beginning of the test and were 4 weeks old. Prior to the test, the animals were kept for a minimum acclimatization period of 5 days, under stabling and nutritional conditions identical to those of the test. Before the experimentation process, they were identified individually by marking with picric acid and a tattoo placed on their ear. The animals were carefully shorn before each test item application: - On the inter-scapular zone for the induction phase, - On the dorso-lumbar zone for the challenge phase. At least 3 hours before the first reading (challenge phase) they were	

shorn a second time in this dorsolumbar zone.

The animals were weighed at the beginning and at the end of the study.

Preliminary tests were performed to determine the dose in the main study:

- The Maximal Non Necrotizing Concentration (MNNC) was performed on intradermic injection during the induction phase. It does not risk causing too great a lesion.

Two animals received on both sides of the spine, a volume of 0.1 ml of the test item, at 6 concentrations: diluted at 40%, 20%, 10%, 5%, 2.5% and 1.25% in distilled water in view to determine the MNNC.

A macroscopic evaluation of the cutaneous reactions was conducted 24 hours later and 48 hours later if necessary.

- As the test item was not administrable by the intradermal route, the induction in the main study was performed by topical route and no MNNC (Maximal Non Necrotizing Concentration) determination was performed.

- The Maximal Non Irritant Concentration test, was determine with several concentration (70% diluted at 35%, 17.5% and 8.75% in distilled water, after being reduced in fine powder with a coffee mill) applied on the dorso-lumbar zone of two guinea pigs shorn beforehand, with occlusive dressing for 24 hours.

Animals were split in two groups for the main study:

	GROUP 1	GROUP 2
	negative control	treated
Female/group	5 n° C1866 to C1870	11 n° C1871 to C1881

Calendar of the main study		
Day 0	**Intradermal induction** After shearing the scapular zone, three (3) pairs of intradermal injections (ID) of 0.1 ml were performed on the scapular zone in such a way as an injection on each pair is placed to either side of the spine as follows: **GROUP 1 (Negative control):** • 2 ID: Freund's Complete Adjuvant diluted at 50 % in isotonic sodium chloride. • 2 ID: isotonic sodium chloride • 2 ID: a mixture with equal volumes v/v : - Freund's Complete Adjuvant at 50% and isotonic sodium chloride, **GROUP 2 (Treated):** • 2 ID: Freund's Complete Adjuvant diluted by 50 % in isotonic sodium chloride, • 2 ID: test item at 40%, • 2 ID a test mixture in equal volumes v/v : - Freund's Complete Adjuvant at 50% and the test item at 40%.	
Day 7	**Topical induction** The scapular zone of all the animals in each group, shorn beforehand, was brushed with a solution of sodium lauryl sulfate at 10% in thick vaseline, in order to create a local irritation.	
Day 8	**Topical induction** A topical application under occlusive dressing for 48 hours was performed on the injection sites of each animal. GROUP 1 (Negative control): 0.5 ml of distilled water GROUP 2 (treated): 0.5 ml of the test item at 70%	
Rest period		
Day 21	**Challenge phase** The experimental procedure of this phase was	

	identical for both groups GROUP 1 (Negative control) and GROUP 2 (Treated) submitted to this experimentation: on the previously shorn dorso-lumbar zone, an application on either side of the spine, under occlusive dressing, was performed during 24 hours: - 1 sample cup containing the test item at 70% (MNIC) and at 35% (1/2 MNIC).	
Results and discussion	No macroscopic cutaneous reactions was recorded during the examination following the removal of the occlusive dressing (challenge phase) from the animals of the treated group with the test item at 70% and 35%. It was only noted a depilation at the reading time 24 hours on the treated area at 70% in seven animals (7/11) and on the treated area at 35% in five animals (5/11). No cutaneous intolerance reaction was recorded in animals from the negative control group after the challenge phase, on the treated area with the test item at 70% and 35%. It was only noted a depilation at the reading time 24 hours on the treated area at 70% in all animals (5/5).	
Conclusion	In view of these results, under these experimental conditions, the test item Difenacoum pasta bait must not be classified, in accordance with the criteria for classification, packaging and labelling of dangerous substances and preparations of the E.E.C. Directives 67/548, 2001/59 and 99/45. No symbol and risk phrase are required. In accordance with the Globally Harmonized System (Regulation (EC) No 1272/2008), the test item must not be classified in category 1. No signal word and hazard statement are required	
Reliability	1	
Deficiencies	No	

	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	

	Evaluation by Rapporteur Member State
Date	23 May 2011
Materials and Methods	Adopt applicant's version
Results and discussion	Adopt applicant's version
Conclusion	Other conclusions: Adopt applicant's version
Reliability	1
Acceptability	acceptable *(give reasons if necessary, e.g. if a study is considered acceptable despite a poor reliability indicator. Discuss the relevance of deficiencies and indicate if repeat is necessary.)*
Remarks	

	Comments from ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A6_1_5-1. Detailed information including induction/challenge/scoring schedule for skin sensitisation test

State test applied, delete other (modify if necessary, i.e. day of treatment)

Inductions	**GPMT (No applied)**		**Buehler**	**Observations/Remarks** *Give information on irritation effects*
	Day of treatment	Application	Day of treatment	
Induction 1	0	Intradermal	/	No sign of irritation effect
Pre-treatment for non-irritating substances	None	/	/	/
Induction 2	7	Topical	/	Slight to well defined erythema was recorded after the first induction phase in 10 animals (10/11).
Induction 3	8	Topical	/	A slight dryness to dryness was noted in 10 animals (10/11),24 hours after the removal of occlusive dressing of the second induction
Challenge	21	/	/	No sign of irritation effect
(Rechallenge)	None	/	/	/
Scoring 1	Not applicable	/	/	/
Scoring 2	Not applicable	/	/	/

Table A6_1_5-2. Result of skin sensitisation test (modify if necessary)

	Number of animals with signs of allergic reactions / number of animals in group		
	Negative control	**Test group**	**Positive control**
Scored after 24h	0/5	0/11	100% (with the 50% of α-Hexylcinnamaldehyde)
			90% (with the 25% of α-Hexylcinnamaldehyde)
Scored after 48h	0/5	0/11	50% (with the 50% of α-Hexylcinnamaldehyde)
			Between 50% and 90% (with the 25% of α-Hexylcinnamaldehyde)

III B Section 6.4 BPD Data Set IIB Annex Point VI.6.4	**INFORMATION ON DERMAL ABSORPTION**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
	As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. *The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	
Other existing data [ ]	**Technically not feasible [ ] Scientifically unjustified [ ]**	
Limited exposure [ ]	**Other justification [x]**	
Detailed justification:	More details are explained in the Risk Assessment for the human and environmental exposure, where each step of the process was evaluated.	
	According exposure assessment performed on measurements of a surrogate in simulated use conditions and on daily exposure frequencies according to a questionnaire answered by selected pest control companies in several EU countries. In primary exposure, the skin is the main exposure route, and only a small proportion of inhalation exposure to dust from decanting of pellets or grain baits is included in the total exposure. Inhalation exposure is not included for wax block formulation. Oral exposure is not considered relevant in primary exposure. Dermal absorption of 3% (pellets and grain baits) or 0.047% (wax block bait) and body weight of 60 kg for an adult is used for the calculations. The dermal absorption value of 3 % used in the CAR may overestimate the exposure taking into account that the dermal absorption value was much lower (0.047%) for the wax block formulation containing 50 mg/kg difenacoum. Calculations using a product specific dermal absorption value are expected to indicate acceptable risks.	
	Source: *Assessment Report – Difenacoum, Product-type 14 (Rodenticides), Directive 98/8/EC concerning the placing of biocidal products on the market. Inclusion of active substances in Annex I or IA to Directive 98/8/EC, 17 September 2009, Annex I – Finland, p14.*	
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	

	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	*30 May 2011*	
Evaluation of applicant's justification	*Applicant's justification is acceptable*	
Conclusion	*Applicant's justification is acceptable.*	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

III B Section 6.5 BPD Data Set IIB Annex Point VI. 6.5	**AVAILABLE TOXICOLOGICAL DATA RELATING TO TOXICOLOGICALLY RELEVANT NON-ACTIVE SUBSTANCES (I.E. SUBSTANCES OF CONCERN)**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
	As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. *The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	
Other existing data [ ]	**Technically not feasible [ ] Scientifically unjustified [ ]**	
Limited exposure [ ]	**Other justification [x]**	

Detailed justification:	In the formulated product, PASTA BAIT, containing 0.005% difenacoum, there is no presence of co-formulant of toxicological concern. The only substances of concern could be Sorbic acid (CAS 110-44-1) and Butyl hydroxyl toluene (CAS 128-37-0), used as antioxidant: • Sorbic Acid: R 36/37/38: Irritating to eyes, respiratory system and skin. • Butyl hydroxyl toluene R53: May cause long-term adverse effects in the aquatic environment. Due to the low level of Sorbic acid Butyl hydroxyl toluene, respectively 0.02 and 0.15%, we can consider the substance has no influenced on the formulated product. No other studies have been deemed necessary	
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	

	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	*30 May 2011*	
Evaluation of applicant's justification	*Applicant's justification is acceptable.*	
Conclusion	*Applicant's justification is acceptable.*	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

III B Section 6.6 BPD Data Set IIB Annex Point VI.6.6	**INFORMATION RELATED TO THE EXPOSURE OF THE BIOCIDAL PRODUCT**	

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
	As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. *The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	
Other existing data [ ]	**Technically not feasible [ ] Scientifically unjustified [ ]**	
Limited exposure [ ]	**Other justification [x]**	
Detailed justification:	In competent authority reports, exposure and risk from the use of the representative products are calculated based on the dossiers submitted by the relevant applicants. Due to different data base (different repeated dose toxicity NOAEL/LOAEL-values and different bioavailability), different AOEL-values were set in competent authority reports. In this assessment report, the exposure to the products is compared to the lowest relevant repeated dose NOAEL/LOAEL- and AOEL-values identified in competent authority reports. This leads to higher risks for the products which were evaluated using a higher repeated dose NOAEL- and AOEL-values in competent authority reports. In most cases, gloves must be used to reduce the exposure below the AOEL-value for trained professionals. For non-trained professionals and amateurs, the use is generally acceptable also without gloves. Exposure from use of pellets or grain baits to a trained professional, covering daily application and post-application tasks (79 daily exposures), results in $1.0x10^{-6}$ mg/kg bw/day systemic dose with protective gloves. The exposure is approx. 91% of the AOEL (0.0000011 mg/kg bw/day). Because non-trained-professionals (e.g. farmers) and amateurs are expected to handle much smaller amounts of baits daily, the exposure is at lower level than for the pest control operators. The calculated systemic dose (for 10 daily exposure) is $1.0x10^{-6}$ without protective gloves which is below the AOEL-value (91% of the AOEL). Thus, it is concluded that non-trained professional/amateur use of pellet or grain baits does not result in unacceptable health risk. Exposure for a trained professional covering daily application and post-application tasks (75 daily exposures, 60 loadings and 15 clean-ups) from use of wax block bait, results in 1.3x10-7 mg/kg bw/day systemic dose with protective gloves. If protective gloves are worn, the risk is at acceptable level for wax block, bait (12% of the AOEL-value of 0.0000011 mg/kg bw/day). Non-trained-professionals (e.g. farmers) and amateurs are expected to handle much smaller amounts of baits daily, and the exposure is at lower level than for the pest control operators. The calculated systemic dose for wax blocks and 10 daily exposure is 1.2x10-7 without protective gloves which is below the AOEL-value (11% of the	

	AOEL). It is concluded that non-trained professional/amateur use of wax block baits does not result in unacceptable health risk. and clean-up, non-trained professional Placing of pellet or grain bait and clean-up, non-trained professional Placing of pellet or grain bait and clean-up, amateur Information related to the toxicity of the BPD to human is presented in documents IIB and IIC of the present application. A description and an assessment of the intended use for Professional, non trained professionals and amateurs were carried out in doc IIB. Calculations were then compared against the relevant end points in doc IIC. Results of the risk characterization show that worker wearing appropriate PPE, as recommended on the label, are not at potential risk. <u>Source:</u> *Assessment Report – Difenacoum, Product-type 14 (Rodenticides), Directive 98/8/EC concerning the placing of biocidal products on the market. Inclusion of active substances in Annex I or IA to Directive 98/8/EC, 17 September 2009, Annex I – Finland, p14-15 and 40.* *Documents IIB and IIC of the present application.*	
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	

	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	

Date	*30 May 2011*
Evaluation of applicant's justification	*Applicant's justification is acceptable.*
Conclusion	*Applicant's justification is acceptable.*
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Environment (including Eco-Toxicology)

III B Section 7.1 **BPD Data Set IIB** **Annex Point VII.7.1**	**Foreseeable routes of entry into the environment on the basis of the use envisaged**

	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements.* *The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	Official use only
Other existing data	**[Technically not feasible [ ] Scientifically unjustified [ ]**	

] **Limited exposure** [**Other justification [x]**]		
Detailed justification:	Route of entry in the environment have been assessed in documents IIB and IIC. Following the results of the risk assessment carried out and the nature of the molecule, physico-chemical properties and the relation structure/function, there is no foreseen route of entry in the environment that are of concern. Following results on the a.s., nature of the molecule, physico-chemical properties and the relation structure/function, there is no foreseen route of entry in the environment that are of concern. <u>Water justifications:</u> Difenacoum is only slightly soluble in water in neutral conditions, and it is hydrolytically stable. Difenacoum undergoes rapid phototransformation in water (half-life about 8 hours or less). Two applicants did not identify transformation products, because individual transformation products were formed less than 10% of the active substance added. In the photolysis study of Activa/Pelgar Brodifacoum and Difenacoum Task Force two breakdown products above 10% were detected, but not chemically identified. Because the photodegradation is regarded as a minor removal process for difenacoum and the exposure to water is low no further characterization of metabolites was deemed necessary. PEC surface water were calculated and compared against the relevant end points in Doc IIC. PEC surface water were calculated for the representative uses, i.e. sewer systems, in and around buildings, open areas and landfills/dump. No concern has been raised. <u>Air justifications:</u> Difenacoum has a low vapour pressure (< 5 x 10^{-5} Pa) and	

Henry's Law constant (0.046 - 0.0129 x 10^{-2} Pa.$m^3$$mol^{-1}$). Release to air via water is expected to be negligible. This is also supported by calculations using the TGD on risk assessment for percent release to air from a sewage treatment plant (section 3.3.2) where no release to air is predicted. Releases to air from use of wax blocks within bait boxes are considered to be negligible. The manufacture of the active substance is in a closed system. There are no releases to air of difenacoum from manufacturing, formulating, use or disposal phases

Soil justifications:

Difenacoum is not readily or inherently biodegradable. Difenacoum degrades slowly under aerobic conditions in soil, with a measured DT50 of 439 days. Photolysis may contribute to the degradation in soil, but in the lack of experimental evidence, soil photolysis cannot be taken into account.

PEC soil were calculated and compared against the relevant end points in Doc IIC. PEC soil were calculated for the representative uses, i.e. sewer systems, in and around buildings, open areas and landfills/dump. No concern has been raised.

Groundwater justifications:

The QSAR Koc value of 1.8 x 10^6 is used in the risk assessment instead of the experimentally derived Koc values, because they were regarded unreliable. The Koc values were determined with the HPLC method and although the studies *per se* were regarded valid, the test method appeared to be unsuitable for difenacoum.

The HPLC method (OECD 121) is not an actual study with measurements in real soil, but only an estimation based on the comparison of test substance to reference substances under artificial system, and hence there may be more uncertainties than in the adsorption/desorption batch-test (OECD 106).

The experimentally derived Koc values were inversely related to pH, so that high values were obtained in acidic conditions (Koc of 426 579 at pH 3-4) and low values in neutral or alkaline conditions

	(17-165 at pH 7-8.5). The experimentally derived Koc values are not supported by the physical and chemical properties of difenacoum. Difenacoum is a large aromatic molecule with two polar groups which can potentially ionize at environmental relevant pH. Difenacoum has also low water solubility and a high log Kow. The HLPC-method gives quite low Koc value suggesting that ionized form of difenacoum will not have great affinity to organic matter. Although difenacoum is a weak acid with probably two dissociable sites, it might not be in ionized form with low adsorption in natural environment, or ionizable form might behave like a neutral form if the charge is shielded by the large molecule size. Also comparison to similar anticoagulant molecules supports the expert view that due to the intrinsic properties of these molecules the adsorption to particles is probable. One applicant has also experimental data which show that difenacoum is not mobile in soil, as concentrations in leachate from column leaching studies conducted with both the active substance and the product were non-determinable. Difenacoum is therefore not expected to contaminate groundwater. Calculated PECgw leads to concentration far below the EU trigger value for drinking water of 0.1 µg/l <u>Source:</u> *Assessment Report – Difenacoum, Product-type 14 (Rodenticides), Directive 98/8/EC concerning the placing of biocidal products on the market. Inclusion of active substances in Annex I or IA to Directive 98/8/EC, 17 September 2009, Annex I – Finland, p15-16.* *Documents IIB and IIC of the present application.*	
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	04-02-11
Evaluation of applicant's justification	The applicant's justification is acceptable. Foreseeable routes of entry into the environment on the basis of the use envisaged are assessed in the environmental exposure and risk assessment (please see the PAR for further details). The rest of the justification is largely taken from the difenacoum assessment report (17-09-2009) section 2.2.2.1 except where reference is made to PEC calculations.
Conclusion	Applicant's justification is acceptable.
Remarks	
	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

III B Section 7.2 **BPD Data Set IIB** **Annex Point VII.7.2**	**Information on the ecotoxicology of the active substance in the product, where this cannot be extrapolated from the information on the active substance itself**

	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only

	As outlined in the TNsG on data requirements, the applicant must always be able to justify the suggested exemptions from the data requirements. *The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ] Scientifically unjustified [ ]** **Other justification [x]**	
Detailed justification:	Information on the a.s., regarding ecotoxicology, could easily be extrapolated from active substance difenacoum. Indeed, co-formulants used in the final product do not have an impact on the toxicology, ecotoxicology or e-fate. No other studies have been deemed necessary	
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	26/01/11	

Evaluation of applicant's justification	According to the Final AR (Sept 2009) on Difenacoum, Difenacoum classifies as R50/53 under Directive 67/548/EEC. However, it is stated that no classification of products containing 50 mg/kg or 75 mg/kg would be necessary according to Directive 1999/45/EC and GHS Regulation (EC) No 1272/2008. Similarly, according to Directive 67/548/EEC, the co-formulant, Denatonium Benzoate, which is a bittering agent added as a safety measure to protect non-target organisms classifies as R52/53 (MSDS PelGar). However, according to Directive 1999/45/EC and GHS Regulation (EC) No 1272/2008, since the concentration of this co-formulant in the product is only 0.195% w/w, it does not classify. Similarly, according to Directive 67/548/EEC, the co-formulant, Butylhydroxytoluene, which is a antioxydant classifies as 53 (MSDS Vitablend). However, according to Directive 1999/45/EC and GHS Regulation (EC) No 1272/2008, since the concentration of this co-formulant in the product is only 0.15% w/w, it does not classify. Therefore Applicant's justification is acceptable assuming the test material is used according to the supported GAP.
Conclusion	C.A. considers applicant's justification to be acceptable.
Remarks	No further remarks.

	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

III B Section 7.3 **BPD Data Set IIB Annex Point VII.7.3**	**Available ecotoxicological information relating to exotoxicological relevant non-active substances (i.e substances of concern), such as information from safety data sheet.**

	JUSTIFICATION FOR NON-SUBMISSION OF DATA *As outlined in the TNsG on data requirements, the applicant must*	Official use only

	always be able to justify the suggested exemptions from the data requirements. *The justifications are to be included in the respective location (section) of the dossier.* *If one of the following reasons is marked, detailed justification has to be given below. General arguments are not acceptable*	
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ] Scientifically unjustified [ ]** **Other justification [x]**	
Detailed justification:	Information on the a.s., regarding toxicology, could easily be extrapolated from active substance difenacoum. Indeed, co-formulants used in the final product do not have an impact on the toxicology, ecotoxicology or e-fate. No other studies have been deemed necessary	
Undertaking of intended data submission [ ]	*Give date on which the data will be handed in later (Only acceptable if test or study is already being conducted and the responsible CA has agreed on the delayed data submission.)*	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	*26/01/11*	

Evaluation of applicant's justification	According to the Final AR (Sept 2009) on Difenacoum, Difenacoum classifies as R50/53 under Directive 67/548/EEC. However, it is stated that no classification of products containing 50 mg/kg or 75 mg/kg would be necessary according to Directive 1999/45/EC and GHS Regulation (EC) No 1272/2008. Similarly, according to Directive 67/548/EEC, the co-formulant, Denatonium Benzoate, which is a bittering agent added as a safety measure to protect non-target organisms classifies as R52/53 (MSDS PelGar). However, according to Directive 1999/45/EC and GHS Regulation (EC) No 1272/2008, since the concentration of this co-formulant in the product is only 0.195% w/w, it does not classify. Similarly, according to Directive 67/548/EEC, the co-formulant, Butylhydroxytoluene, which is a antioxydant classifies as 53 (MSDS Vitablend). However, according to Directive 1999/45/EC and GHS Regulation (EC) No 1272/2008, since the concentration of this co-formulant in the product is only 0.15% w/w, it does not classify. Therefore Applicant's justification is acceptable assuming the test material is used according to the supported GAP.
Conclusion	C.A. considers applicant's justification to be acceptable.
Remarks	No further remarks.

	COMMENTS FROM OTHER MEMBER STATE *(specify)*
Date	*Give date of comments submitted*
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Annex IV: List of studies reviewed

List of new data[28] submitted in support of the evaluation of the active substance (IIIA)

Not applicable

List of new data submitted in support of the evaluation of the biocidal product (IIIB)

Identity:

Ref No	Author	Year	Title Source Company, Report No. GLP (where relevant)/ (Un)Published	Data owner	LoA# (Y/N)	DPC* (Y/N)
B1	-	-	Statement confidential data Manufacturing process.	Bio6		Y
B2.1_0	-	-	Difenacoum Paste: composition	Bio6		Y
B2.1_1	Porte P., Denny O.	2009	Analytical Certificate Product name: Difenacoum pasta bait Batch number: LAB290109, date of analysis: 5 May 2009. Defitraces, 69126 Brindas, France, 19th October 2009. GLP. Unpublished.	Bio6		Y
B2.1_2	Porte P., Anding C.	2009	Analytical Certificate Product name: Rattofene (Pasta Bustine) Batch number: LAB 220109, date of analysis: February 20, 2009. Defitraces, 69126 Brindas, France, February 27, 2009. GLP. Unpublished.	Bio6		Y
B2.2_1	Anonym	2010	Saftey Data Sheet_Component 1: Difenacoum concentrate 2.5% (Red) Denatonium Benzoate. PELGAR International, UK. Not GLP, Published	Pelgar		Y
B2.2_2	Anonym	-	[redacted]	[redacted]		Y
B2.2_3	Anonym	2010	[redacted]	[redacted]S		Y

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

Ref No	Author	Year	Title Source Company, Report No. GLP (where relevant)/ (Un)Published	Data owner	LoA# (Y/N)	DPC* (Y/N)
B2.2_4	Anonym	2010	[redacted]	[redacted]		Y
B2.2_5	Anonym	2008	[redacted]	[redacted]		Y
B2.2_6	Anonym	-	[redacted]	[redacted]		Y
B2.2_7	Anonym	-	[redacted]	[redacted]		Y
B2.2_8	Anonym	-	[redacted]	[redacted]		Y

Letter of Access
* Data Protection Claimed

Physical/Chemical Properties:

Ref No	Author	Year	Title Source Company, Report No. GLP (where relevant)/ (Un)Published	Data owner	LoA# (Y/N)	DPC* (Y/N)
B.3.7_1	Biannic M-L., Magnier C.	2008	Study report – Stability of Difenacoum baits after accelerated storage procedure. Test item: Baits containing 0.005% of Difenacoum: pasta, block and cereals. LODI Group, Parc d'activité des Quartre Routes, 35390 Grand Fougeray, FRANCE. Version date: 2008-01-07 Unpublished	LODI		Y
B.3.7_2	Meriadec E	2009	Study Report – Chemical stability after accelerated storage of Difenacoum pasta baits 0.005%. LODI Group, Parc d'activité des Quartre Routes, 35390 Grand Fougeray, FRANCE. Study no 14/2009. Version date: 2009-11-25 Unpublished	LODI		Y
B.3.7_3	Biannic M-L., Magnier C.	2009	Study Report –stability of Difenacoum baits after storage at ambient temperature. Test item: Baits containing 0.005% of Difenacoum: baits, block and cereals. LODI Group, Parc d'activité des Quartre Routes, 35390 Grand Fougeray, FRANCE. Version date: 2009-11-12 Unpublished	LODI		Y

Ref No	Author	Year	Title Source Company, Report No. GLP (where relevant)/ (Un)Published	Data owner	LoA# (Y/N)	DPC* (Y/N)
B.3.7_04	Brekelmans, Ir. M.J.C.	2010	Study Report –Determination of physic-chemical properties of difenacoum pasta baits. NOTOX B.V., Hambakenwetering 7, 5231 DD ’s-Hertogenbosch, The Netherlands. Version date: 17th September 2010 Project no: 490526. Unpublished	Bio6		Y

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Methods of Analysis:

Ref No	Author	Year	Title Source Company, Report No. GLP (where relevant)/ (Un)Published	Data owner	LoA# (Y/N)	DPC* (Y/N)
B4_01a	Ricau, H.	2009	Analytical method validation for the determination of difenacoum in Difenacoum pasta bait, in compliance with CIPAC/3807R. Anadiag Group - Defitraces, 69126 Brindas, France. Report No. 09-902018-007, of 19 October 2009. GLP. Unpublished	Bio6		Y
B4_1b	Ricau, H.	2009	Quantification of difenacoum 0.005% m/m in a rat poison bait. Anadiag Group - Defitraces, 69126 Brindas, France. Report No. 05-912011-001, 16 June 2005. GLP. Unpublished	Bio6		Y
B4_2	Ricau H	2009	Quantification of Difenacoum in Rattofene (PASTA BUSTINE) Anadiag Group - Defitraces, 69126 Brindas, France, Report no. 09-912011-004. 1st April 2009 GLP. Unpublished.	LODI		Y
B4_Litt-01	Magnier C., Biannic ML.	2009	Analytical method validation for the determination of difenacoum in Difenacoum bait (pasta, grain and block). LODI Group, Parc d’activité des Quartre Routes, 35390 Grand Fougeray, FRANCE. Study No. LODI 17/2009_Version date 2009-11-04. Unpublished	LODI		Y

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Efficacy

Ref No	Author	Year	Title Source Company, Report No. GLP (where relevant)/ (Un)Published	DPC* (Y/N)	Data owner

Ref No	Author	Year	Title Source Company, Report No. GLP (where relevant)/ (Un)Published	DPC* (Y/N)	Data owner
B5.0_01	Anonym	2004	Application Codes fo Encoding Rodenticides (PT14) No GLP, Published	N	E.U
B5.0_02	Anonym	2001	Guidelines fort he safe use of Anticogulant Rodenticodes by professional BPCA: Bristih Pest Control Association No GLP, Published	N	BPCA
B5.0_03	Anonym	1995	Anticoagulant rodentices (EHC 175, 1995) International Programme on Chemical Safety No GLP, Published	N	INCHEM
B5.0_04	Anonym	2009	Assessment report Difenacoum Product type 14 17th September 2009 No GLP, Published	N	Finland RMS
B5.0_05	Anonym	1995	IPCS INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY: Health and Safety Guide No. 95 DIFENACOUM - HEALTH AND SAFETY GUIDE No GLP, Published	N	IPCS
B5.0_06	Anonym	2003	Technical Monograph 2003 Anticoagulant Resistance Management Strategy For Pest Management Professionals, Central And Local Government and Other Competent Users Of Rodenticides, No GLP, Published	N	CropLife International
B5.10.01a	Mahaut T., Cavellier M	2003	Efficacy test on DIFEPASTA, bait ready to use, containing 0.005% of Difenacoum, against grey mice (*Mus musculus* L.),/ *Evaluation de l'efficacité du DIFEPASTA, appât rodenticide contenant 0.005% de*	Y	Belgagri

Ref No	Author	Year	Title Source Company, Report No. GLP (where relevant)/ (Un)Published	DPC* (Y/N)	Data owner
			difenacoum envers la souris grise (Mus musculus L.) ROD 2003-03-Belgagri, 20 October 2003. *Paste bait/ Semi field efficacy/ Mice/ Fresh product (T0)* *CRA Gembloux,* Belgium GLP, Unpublished		
B5.10.01b	-	2003	Effi 2003-10 (raw data ROD 2003-03)	Y	Belgagri
B5.10.02a	De Proft M., Galoux	2006	Efficacy test through different period of time, performed on DIFEPASTA, bait ready to use, containing 0.005% of Difenacoum/ *Comportement en cours de vieillissement du DIFEPASTA, appât prêt à l'emploi, contenant 0,005% difenacoum*, rapport number 11 594 ROD 2003-003, June 2006 Paste bait/ Laboratory efficacy/ Mice/ Product at T12 and T24 CRA Gembloux, Belgium *GLP, Unpublished*	Y	Belgagri
B5.10.02b	-	2006	Albi 2005-05 (raw data 11594) Certificate of analysis n° Belgagri FO-Ch3420-2005-A_12Oct2005 Analyse on stored Item (T24 months) CRA Gembloux, Belgium *GLP, Unpublished*	Y	Belgagri
B5.10.02c	Ryckel (de). B, Meeus P.	2003	Certificate of analysis n° Belgagri FO-Ch-3000-2003-194, 23Dec2003 Analyse on Fresh Item (T0) CRA Gembloux, Belgium *GLP, Unpublished*	Y	Belgagri
B5.10.02d	Ryckel (de). B,	2004	Certificate of analysis n° Belgagri FO-Ch-3178-2004-183_09Dec2004	Y	Belgagri

Ref No	Author	Year	Title Source Company, Report No. GLP (where relevant)/ (Un)Published	DPC* (Y/N)	Data owner
	Meeus P.		Analyse on stored Item (T12 months) CRA Gembloux, Belgium *GLP, Unpublished*		
B5.10.03a	-		- LODI, Efficacy trial: Pasta Dife/ Mice- Confidential report, LODI property, 12 pages, Feb2009. *Paste bait/ Field efficacy/ Mice/ Product at T2y* LODI S.A, FRANCE No GLP, Unpublished	Y	LODI
B5.10.03b	Biannic M-L., Magnier C.	2009	Difenacoum analyses in Pasta T2years Study Report- stability of Difenacoum baits after a storage at ambient temperature. Test item: Baits containing 0.005% of Difenacoum: pasta, block and cereals. LODI GROUP, Parc d'activité des Quatre Routes, 35390 Grand Fougeray, FRANCE, Version date 2009-11-12. Unpublished	Y	LODI
B5.10.04	Grolleau G	2002	Effectiveness testing under natural conditions of PASTA DIFE rat killer in paste bait form in sachets on brown rats / Test under natural conditions of a rat killer in paste bait form (PASTA DIFE) containing 0.005% Difenacoum, on Brown rats (Rattus norvegicus) 2002. *Paste bait/ Field efficacy/ Rats/ Fresh product (T0)* Pest Control Assistance (PCA), France GLP, Unpublished	Y	Belgagri
B5.10.05a	Biannic M-	2009	Efficacy assessment of a rat killer in a field	Y	LODI

Ref No	Author	Year	Title Source Company, Report No. GLP (where relevant)/ (Un)Published	DPC* (Y/N)	Data owner
	L		trial –product: PASTA DIFE, July 2009. *Paste bait/ Field efficacy/ Rats / Product at T2years* LODI S.A, FRANCE GLP, Unpublished		
B5.10.05b	Magnier C.	2007	Analytical certificate Pasta dife, batch 040407, manufacturing 05/2007, expiry 04/2009 October 11th 2007	Y	LODI
B5.10.05c	-	2009	Analyse : pasta dife lot040407 echantillon1 1st December 2009	Y	LODI
B5.10.05d	-	2009	Analyse : pasta dife lot040407 echantillon1 2 1st December 2009	Y	LODI
B5.10.05e	-	2009	Analyse : pasta dife lot040407 echantillon2 1st December 2009	Y	LODI
B5.10.05f	-	2009	Analyse : pasta dife lot040407 echantillon2 2 1st December 2009	Y	LODI
B5.10.06a	De Proft M	2008	Study of ageing behavior of ready-to-use baits containing 0.005% of Difenacoum, PART 1: Pasta Bait, report number ROD 2008 11 BIO 6 *Paste bait/ Lab choice test/ Rats / Product at T0 and T12* CRA Gembloux, Belgium GLP, Unpublished	Y	Bio6
B5.10.06b	Biannic M-L	2008	Intermediate report – Quantification of Difenacoum in Pasta Bait, version date: September 9th, 2008. Test item at production date, batch 090908. LODI S.A, FRANCE	Y	LODI

Ref No	Author	Year	Title Source Company, Report No. GLP (where relevant)/ (Un)Published	DPC* (Y/N)	Data owner
			No GLP, Unpublished		
B5.10.06c	Biannic M-L	2009	Intermediate report – Quantification of Difenacoum in Pasta Bait, version date: January 30th, 2009. Test item at the start of the trial assay, batch 090908. LODI S.A, FRANCE No GLP, Unpublished	Y	LODI
B5.10.06d	Biannic M-L	2009	Intermediate report – Quantification of Difenacoum in Pasta Bait, version date: October 16th, 2009. Test item after 12 months, batch 090908 LODI S.A, FRANCE No GLP, Unpublished	Y	LODI
B5.10.07a	Feys J-L.	2009	Field trial with NORA PASTA BAITS against ROOF RATS 21 January 2010_08 February 2010, batch NO 091109 *Paste bait/ Field efficacy/ Roof Rats /Product at T0* Belgagri. Unpublished	Y	Belgagri
B5.10.07b	Feys J-L.	2009	Nora Pasta/ Company VARLO-Van Thillo Herman: scheme	Y	Belgagri
B5.10.07c	Feys J-L.	2009	Field trial NORA PASTA on ROOF Rats (21/01/2010) test results	Y	Belgagri
B5.10.07d	Feys J-L.	2009	Field trial with NORA PASTA BAITS against ROOF RATS 21 January 2010_08 February 2010, batch NO 091109 _Summary	Y	Belgagri
B5.10.07e	Magnier C	2009	Analyse certificate, batch batch NO 091109	Y	LODI

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Toxicology

Ref No	Author	Year	Title	Data owner	LoA# (Y/N)	DPC* (Y/N)

Ref No	Author	Year	Title	Data owner	LoA# (Y/N)	DPC* (Y/N)
B6.1.1	[redacted]	2009	Difenacoum pasta bait - Acute Oral Toxicity in the rat - Acute toxic class method	Bio6 S.A.	Y	Y
B6.1.2	[redacted]	2009	Difenacoum pasta bait - Acute Dermal Toxicity in the rat - Acute toxic class method	Bio6 S.A.	Y	Y
B6.2	[redacted]	2009	Difenacoum pasta bait bait – Skin Irritation test in the rabbit	Bio6 S.A.	Y	Y
B6.2	[redacted]	2009	Difenacoum pasta bait – Eye Irritation test in the rabbit	Bio6 S.A.	Y	Y
B6.3	[redacted]	2009	Difenacoum pasta bait – Skin sensitisation in the guinea pig - Magnusson and Kligman maximisation method	Bio6 S.A.	Y	Y

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ANNEX V: Toxicology Calculations

Insert relevant exposure/effect calculations undertaken, if applicable.

ANNEX VI: Environmental Calculations

The Notifier submitted the same assessment that was used to support Annex I inclusion.

A summary of the Environmental exposure assessment

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

Using the scenarios outlined in the ESD for rodenticides and the TGD on risk assessment, and the calculations and assumptions presented in the previous sections above, the following PEC locals presented below have been derived for the aquatic compartment. No risk to ground water ($PEC_{groundwater}$ < 0.1 µg/L) was identified when the product is used in accordance with the assumptions made in the exposure assessment. The maximum permissible concentration by directive 80/778/EEC (amended by 98/83/EC) of 0.1 µg/L is not exceeded in surface waters.

PEC in surface water, sewage treatment plant, groundwater and sediment

Compartment/Scenario	**ESD realistic worst case scenario**	**ESD realistic worst case scenario with modified input parameters**	**ESD normal use scenario with modified input parameters**
Sewer scenario (30 kg of product used in control operation)			
PEC for microorganism in the STP	8.06×10^{-6} mg/L	5.91×10^{-6} mg/L	---
Local PEC in surface water during emission an episode (dissolved)	2.11×10^{-7} mg/L	1.55×10^{-7} mg/L	---
Local PEC in freshwater sediment during an emission episode	8.61×10^{-3} mg/kg wwt	6.32×10^{-3} mg/kg wwt	---
Groundwater/porewater	9.94×10^{-5} µg/L	7.29×10^{-5} µg/L	
In and around buildings scenario			
Groundwater/porewater	1.5×10^{-3} µg/L	1.1×10^{-3} µg/L	3.2×10^{-4} µg/L
Open areas			
Groundwater/porewater	0.00523 µg/L	0.0105 µg/L	---
Waste dump			
Groundwater/porewater	0.000224 µg/L	~0.00025 µg/L*	

*****For high infestations of rats the blocks are spaced 5 m apart. According to calculations provided by the Reviewer this could potentially result in a maximum of ~441 (21, 100 m lines of 21 blocks, 5 m apart) blocks in a 1 ha area during high infestations. This corresponds to ~44.1 kg of product, which is greater than the quantity considered under realistic worst-case conditions in the ESD. Consequently the notifiers exposure calculation is not sufficient to support this use. The Reviewer generated new exposure calculations for this use

PEC in air

Difenacoum is not expected to partition to the atmosphere to any significant extent due to low vapour pressure and Henry's Law constant. Difenacoum has athe potential for rapid photo-oxidative degradation in the air (half-life about two hours). Difenacoum is not expected to have a the potential for long-range atmospheric transport or contribute to global warming, ozone depletion or acidification on the basis of its physical and chemical properties.

PEC in soil

A summary of the soil exposure assessment is presented below:

PEC in soil

Compartment/Scenario	ESD realistic worst case scenario	ESD realistic worst case scenario with modified input parameters	ESD normal use scenario with modified input parameters
Sewer scenario (sludge application)			
Local PEC in agric. Soil (total) average over 30 d	3.29 x 10^{-3} mg/kg wwt	2.41 x10^{-3} mg/kg wwt	---
Local PEC in agric. Soil (total) average over 180 d	3.29 x 10^{-3} mg/kg wwt	2.41 x 10^{-3} mg/kg wwt	---
Local PEC in grassland. Soil (total) average over 180 d	1.31 x 10^{-3} mg/kg wwt	9.64 x 10^{-4} mg/kg wwt	---
In and around buildings scenario			
Total concentration in soil	0.047 mg/kg wwt	0.0348 mg/kg wwt	0.01 mg/kg wwt
Open areas			
Local concentration in soil after a Campaign	0.173 mg/kg wwt	0.346 mg/kg wwt	---
Waste dump			
Local concentration in soil after a Campaign	0.0074 mg/kg wwt	0.0082 mg/kg wwt*	---

*****For high infestations of rats the blocks are spaced 5 m apart. According to calculations provided by the Reviewer this could potentially result in a maximum of ~441 (21, 100 m lines of 21 blocks, 5 m apart) blocks in a 1 ha area during high infestations. This corresponds to ~44.1 kg of product, which is greater than the quantity considered under realistic worst-case conditions in the ESD. Consequently the notifiers exposure calculation is not sufficient to support this use. The Reviewer generated new exposure calculations for this use

Environmental Risk Assessment

Risk Characterisation for surface water, groundwater and sediment after elimination processes in STP

Difenacoum is very toxic to fish, aquatic invertebrates and algae. Toxicity to fish, the most sensitive species, is based on the inhibition of blood clotting. The mode of action in aquatic invertebrates and algae is unknown. The PNEC value was calculated according to ESD guidelines (Larsen, 2003), applying an Assessment Factor of 1000 to the lowest endpoint from studies on three trophic levels. According to the Assessment Report (17-09-2009), the limit of solubility was the PNEC for STP (480 µg/l). The risk characterisation for the STP and aquatic compartment including sediment is presented below:

Aquatic PEC/PNEC ratios using realistic worst case scenario with normal use after elimination processes in STP

Exposed Compartment	Endpoint	PNEC	PEC	PEC/PNEC
Surface water	LC_{50} 0.064 mg/l	0.06 µg/l	2.11 x 10^{-4} µg/l	3.5 x 10^{-3}
Sediment	-[1]	2.51[1] mg/kg ww	8.61 x 10^{-3} mg /kg ww	3.4 x 10^{-3}

STP	Solubility limit	480 µg/l	8.06×10^{-3} µg/l	1.6×10^{-5}

[1]In the absence of any ecotoxicological data for sediment-dwelling organisms and as PECsediment is calculated using EUSES 2.0.3, an aquatic PEC/PNEC ratio is used for sediment risk characterisation increasing it according to TGD (Part II, Section 3.5.2) with a factor of 10 as difenacoum has a log Kow > 5. PNEC reported as 2.51mg/kg ww in the Assessment Report (17-09-2009)

The PEC/PNEC ratios were less than 1 in all compartments indicating that difenacoum, following recommended use of Ruby Block, does not cause unacceptable risk to aquatic organisms, sediment-dwelling organisms or biological processes at the sewage treatment plant. As difenacoum is not readily biodegradable, the degradation of difenacoum in sediment is also anticipated to be low. However, according to the PEC calculations, concentrations in sediment would be low (8.61×10^{-3} mg /kg ww) and below the level that causes unacceptable risk, thus risk for unacceptable accumulation in sediment can be regarded as low. No risk is identified to either groundwater/porewater or surface water used as drinking as in both cases the maximum permissible concentration by directive 80/778/EEC (amended by 98/83/EC) of 0.1 µg/l is not exceeded in the ESD realistic worst case scenarios for uses in sewer, in and around buildings, open areas and waste dumps.

Risk Characterisation for Terrestrial Compartments

The PNEC applied in the risk characterisation for soil is one derived from the endpoint of an acute toxicity study on earthworms with an Assessment Factor of 1000. The risk characterisation for the terrestrial compartment including is presented below:

Terrestrial PEC/PNEC ratios using realistic worst case scenario with normal use

Exposed Compartment		PNEC	PEC	PEC/PNEC
Sewer-application of sewage sludge	Local PEC in agric. soil (total) average over 30 d	0.877 mg/kg ww	3.29×10^{-3} mg/kg ww	3.38×10^{-3}
	Local PEC in agric. soil (total) average over 180 d	0.877 mg/kg ww	3.29×10^{-3} mg/kg ww	3.38×10^{-3}
	Local PEC in grassland. soil (total) average over 180 d	0.877 mg/kg ww	1.31×10^{-3} mg/kg ww	1.5×10^{-3}
In and around buildings	Direct	0.877 mg/kg ww	4.1×10^{-2} mg/kg ww	4.7×10^{-2}
	Indirect	0.877 mg/kg ww	6.0×10^{-3} mg/kg ww	6.8×10^{-3}
	Total	0.877 mg/kg ww	4.7×10^{-2} mg/kg ww	5.4×10^{-2}
Open areas		0.877 mg/kg ww	1.73×10^{-1} mg/kg ww	0.197
Waste dump		0.877 mg/kg ww	8.2×10^{-3} mg/kg ww*	9.4×10^{-3}

* Value calculated by Environmental Fate and Behaviour Reviewer for High infestations of rats.

The PEC/PNEC ratios were less than 1 in all compartments indicating that difenacoum, following recommended use of Ruby Block, does not cause unacceptable risk to organisms in any of the terrestrial compartments assessed.

Primary poisoning

The Tier 1 assessment assumes that there is no bait avoidance by the non-target animals, and that they obtain 100% of their diet in the treated area and have access to the difenacoum product. The worst case Tier 1 PEC_{oral} is 50 mg/kg (difenacoum present at 0.005% w/w in Ruby Block) and is used in quantitative risk assessment for the long-term situation. The LD_{50} values are 56 mg/kg bw for birds (AF 3000) and 1.8 mg/kg bw for mammals (AF 90) (List of Endpoints in the Assessment Report (17-09-2009). The Tier 1 Primary poisoning PEC/PNEC ratios are provided below:

Tier 1 Primary poisoning PEC/PNEC ratios

Exposed Organism	PNEC µg/kg food	PNEC[1]	PEC	PEC/PNEC

		µg/kg bw/d		
Birds	0.5	0.1	50 mg/kg food	500000
Mammals	7	0. 3	50 mg/kg food	166667

[1] Appendix V- Assessment Report (17-09-2009)

According to ESD (Larsen, 2003) a Tier 2 evaluation assessment can be done estimating daily uptake of a compound (ETE) by non-target animals according to the equation 19 of ESD (ETE = (FIR/BW) * C * AV * PT * PD (mg/kg bw/day);

FIR: food intake rate of the indicator species,
BW: indicator species body weight,
C: concentration of the active substance in fresh diet,
AV: avoidance factor,
PT: fraction of diet obtained in treated area and
PD: the fraction of the food type in the diet.

In Tier 2 Step 1 (worst case) AV, PT and PD are all set at 1, in Step 2 (realistic worst case) these AV and PT are refined to 0.9 and 0.8, respectively.

When elimination of active substance is taken into account the expected concentration of active substance (EC) in animals is calculated with equation 20 (ESD), EC = ETE x (1-El), where El is fraction of daily uptake eliminated (number between 0 and 1, default 0.3). According to the toxicokinetic study[9], average level of radioactivity in excreta of rats was 23% of total administered radioactivity during the first day after single dose and daily average 25% during 7 consecutive daily dosing. Difenacoum is also eliminated in the rat body through metabolism, average proportion of difenacoum in extract of liver was 30% on day 168 (and thus metabolites can be assumed to account for 70%). 24.3% of total administered radioactivity was found in liver, so 17% of total administered dose is (liver) metabolites (metabolites in other tissues were not studied and thus not taken into account). Thus the total daily elimination in rats taking into account excretion through faeces and metabolism of difenacoum in rat liver, is approximately 40% (**elimination factor 0.4**), which is also used in calculations for non-target animals as there are no other data available.

For the acute exposure situation, no $PNEC_{oral}$ is determined and no quantitative risk characterisation is performed. Instead a qualitative assessment is done by comparing LD_{50} values to the expected contents of the active substances in birds and mammals. According to the guidance agreed at 23rd CA, these values are used for qualitative risk assessment of **acute primary poisoning**. The values obtained are provided below:

Table 1.

Table 2. Tier 2 Expected concentrations of difenacoum in non-target animals in the worst case (Step 1) and realistic worst case (Step 2) for acute situations with and without elimination

Species		**Body weigh t (g)**	**Daily mean food intake (dw) (g)**	**Rodentic ide consum ption (g)**	**Estimated daily uptake of difenacoum (ETE) after single meal (mg/kg bw)**		**Expected concentration (EC) of a.i. in the animal after one day elimination (mg/kg bw)**	
					Step 1 [1]	Step [2]	Step 1[1]	Step 2[2]
Dog	*Canis*	10000	456	600	2.28	1.64	1.37	0.98

	familiaris							
Pig	*Sus scrofa*	80000	25203 (600)[4]	600	0.4	0.27	0.23	0.16
Pig, young	*Sus scrofa*	25000	969[3] (600)[4]	600	1.2	0.86	0.72	0.52
Fox Representing General non-target mammal	*Vulpes vulpes*	5700 5700	520 [5] 287[3]	520 287	4.56 2.5	3.28 1.8	2.74 1.5	1.97 1.08
Tree sparrow	*Passer montanus*	22	7.6	7.6	17.3	12.44	10.36	7.46
Chaffinch	*Fringilla coelebs*	21.4	6.42	6.42	15.0	10.8	9.0	6.48
Wood pigeon	*Columba palumbus*	490	53.1	53.1	5.4	3.9	3.25	2.34
Pheasant	*Phasianus colchicus*	953	102.7	102.7	5.4	3.9	3.23	2.33

[1] avoidance (AV), Fraction of diet from treated area (PT) and Fraction of food type in diet (PD) are set at 1.

[2] according to ESD AV to 0.9 and PT 0.8.

[3] according to ESD 3.2.1. logFIR = 0.822 logBW – 0.629.

[4] according to ESD 600g is maximum for rodenticide consumption in one daily meal.

[5] ESD table 3.5.

The qualitative assessment of acute primary poisoning is presented below:

Qualitative assessment of acute primary poisoning. The expected concentrations (EC) in the non-target animals after one day exposure with and without elimination. The EC have been calculated with the Step 2 assumptions, i.e, PT=0.8 and AV=0.9

Species		**EC after one day exposure without elimination mg/kg bw**	**EC after one day exposure and elimination mg/kg bw**	**LD_{50}**
Dog	*Canis familiaris*	1.64	0.98	1.8
Pig	*Sus scrofa*	0.27	0.16	1.8
Pig, young	*Sus scrofa*	0.86	0.52	1.8
Fox	*Vulpes vulpes*	3.28	1.97	1.8
Fox, representing general non-target		1.8	1.08	1.8

mammal				
Tree sparrow	*Passer montanus*	12.44	7.46	56
Chaffinch	*Fringilla coelebs*	10.8	6.48	56
Wood pigeon	*Columba palumbus*	3.9	2.34	56
Pheasant	*Phasianus colchicus*	3.9	2.33	56

According to the ESD the comparison of concentration in the non-target animals and the $PNEC_{oral}$ describes the **long-term risk for primary poisoning**. Calculations of the expected concentrations (EC) for 5 days exposure considering elimination are calculated according to ESD equation 21[1]. The Tier 1 calculations represent the a worst case i.e. AV, PT and PD are set to 1. In the Tier 2 calculations, the PT and AV have been modified according to the ESD to the realistic worst case values of 0.8 and 0.9 respectively According to the guidance agreed at 23rd CA meeting, EC_5 values are used for quantitative risk assessment of primary poisoning in the long-term situation. EC_5 values represent the expected concentration of the difenacoum after 5 days of exposure with elimination over the five day period (including the fifth day after exposure). The values obtained are provided below:

Table 3.

Table 4. Expected concentrations of difenacoum (EC_5) in non-target animals for the long-term situations

Species		**Body weight(g)**	**Daily mean food intake (dw) (g)**	**Rodenticide consumption (g)**	**Expected concentration (EC_5) of a.i. in the animal after 5 days exposure, elimination taken into account (mg/kg bw)**	
					Tier 1	Tier 2
Dog	*Canis familiaris*	10000	456[2]	456	3.15	2.27
Pig	*Sus scrofa*	80000	2520[2] (600)[3]	600	0.52	0.37
Pig, young	*Sus scrofa*	25000	969[2] (600)[3]	600	1.66	1.19

Fox Representing General non-target mammal	*Vulpes vulpes*	5700 5700	520[4] 287[2]	520 287	6.31 3.48	4.54 2.51
Tree sparrow	*Passer montanus*	22	7.6	7.6	23.89	17.2
Chaffinch	*Fringilla coelebs*	21.4	6.42	6.42	20.75	14.94
Wood pigeon	*Columba palumbus*	490	53.1	53.1	7.49	5.39
Pheasant	*Phasianus colchicus*	953	102.7	102.7	7.45	5.37

[1]$ECn = \sum_{n=1}^{n-1} ETE * (1\ EL)^n$.

[2] according to ESD3.2.1. logFIR = 0.822 logBW – 0.629.
[3] according to ESD 600g is maximum for rodenticide consumption in one daily meal.

[4] ESD table 3.5.

The results of the risk assessment for long-term primary poisoning are provided below:

Table 5. Tier 2 risk characterisation of primary poisoning. The expected concentrations (EC) in the non-target animals after five days exposure have been calculated with the Step 2 assumptions, i.e, PT=0.8 and AV=0.9. The $PNEC_{oral}$ is expressed as the daily dose

Species		PEC EC_5 µg/kg bw	$PNEC_{oral}$ µg/kg bw/d	PEC/PNEC
Dog	*Canis familiaris*	2270	0.3	7567
Pig	*Sus scrofa*	370	0.3	1233
Pig, young	*Sus scrofa*	1190	0.3	3967
Fox	*Vulpes vulpes*	4540	0.3	15133
Fox, representing general non-target mammal		2510	0.3	11 100
Tree sparrow	*Passer montanus*	17200	0.1	172000
Chaffinch	*Fringilla coelebs*	14940	0.1	149400
Wood pigeon	*Columba palumbus*	5390	0.1	53900
Pheasant	*Phasianus colchicus*	5370	0.1	53700

Secondary poisoning

Calculations of the PEC_{oral} predator for the possible exposure routes are shown below with the relevant re-calculated values from the Environmental Fate and Behaviour section. The waiving of fish bioconcentration test was accepted, because the test was judged not possible to perform technically, and because an estimated BCF value could be used in the risk assessment. The calculated BCFs range from 9010 (aquatic) to 477 729 (terrestrial).These are based on the estimated log P_{ow} of 7.6 (EPIWIN v. 3.1.2) in the absence of valid measured log P_{ow}.

Fish-eating birds and mammals

$PEC_{oral,\ predator}$ = PEC_{water} * BCF_{fish} * BMF (eq 76, TGD,2003):
= 2.11 x 10^{-7} mg/l * 9010 $l/kg_{wetfish}$ * 10 = 0.02 $mg/kg_{wet\ fish}$ (concentration in fish)

The PEC_{water} applied here is the ESD realistic worst case scenario. According to TGD (p. 127) the most appropriate scenario is that 50% of the diet comes from the local area and 50% comes from the regional area, thus when the PEC_{local} water is used in calculation, the PEC_{oral},predator to be used in risk assessment is 0.02 $mg/kg_{wet\ fish}$ *0.5 = **0.01 $mg/kg_{wet\ fish}$.**

Earthworm-eating birds and mammals

The Reviewer has recalculated the PEC_{oral} values by applying the revised exposure estimates provided by Environmental Fate and Behaviour.

PEC $oral,_{predator}$ = $C_{earthworm}$ (eq 80, TGD, 2003)

$C_{earthworm}$ = ($BCF_{earthworm}$*$C_{porewater}$+ C_{soil}*F_{gut}*$CONV_{soil}$)/ (1+$Fg_{ut\ kgdwt/kgwwt}$*$CONV_{soil\ kgwwt/kgdwt}$) (eq 82c, TGD 2003).

No measured BCF for earthworm is available and the calculated BCF of 4.80 x 10^5 $l/kg_{wetearthworm}$ (see Assessment Report, 2009) is used in calculations. The $C_{earthworm}$ is different for each compartment and the equations are given below for ESD realistic worst case scenarios.
According to the TGD (p. 131) the most appropriate scenario is that 50% of the diet comes from a local area and 50% comes from the regional area, thus when the PEClocal,soil is used in calculation, the PECoral, Predator to be used in risk assessment is 50% of the calculated $C_{earthworm}$.

Sewer Scenario

$C_{earthworm}$ = (4.80 x 10^5 $l/kg_{wetearthworm}$ x 9.94 x 10^{-8} mg/l (max $C_{porewater}$) + 3.29 x 10^{-3} mg/kg (max C_{soil}) x $0.1_{kgdwt/kgwwt}$ x 1.13 $_{kgwwt/kgdwt}$)/(1+0.1 *1.13) = 0.043 $mg/kg_{wetearthworm}$ x 0.5 = **0.022 $mg/kg_{wetearthworm}$.**

In and around buildings scenario

$C_{earthworm}$ = (4.80 x 10^5 $l/kg_{wetearthworm}$ x 1.5 x 10^{-6} mg/l (max $C_{porewater}$) + 0.047 mg/kg (max C_{soil}) x $0.1_{kgdwt/kgwwt}$ x 1.13 $_{kgwwt/kgdwt}$)/(1+0.1 *1.13) = 0.652 $mg/kg_{wetearthworm}$ x 0.5 = **0.326 $mg/kg_{wetearthworm}$.**

Open areas

$C_{earthworm}$ = (4.80 x 10^5 $l/kg_{wetearthworm}$ x 5.23 x 10^{-6} mg/l (max $C_{porewater}$) + 0.173 mg/kg (max C_{soil}) x $0.1_{kgdwt/kgwwt}$ x 1.13 $_{kgwwt/kgdwt}$)/(1+0.1 *1.13) = 2.273 $mg/kg_{wetearthworm}$ x 0.5 = **1.137 $mg/kg_{wetearthworm}$.**

Waste dump

$C_{earthworm}$ = (4.80 x 10^5 $l/kg_{wetearthworm}$ x 2.25 x 10^{-7} mg/l (max $C_{porewater}$) + 0.0082mg/kg (max C_{soil}) x $0.1_{kgdwt/kgwwt}$ x 1.13 $_{kgwwt/kgdwt}$)/(1+0.1 *1.13) = 0.098 $mg/kg_{wetearthworm}$ x 0.5 = **0.049 $mg/kg_{wetearthworm}$.**

The results of the quantitative assessment of acute secondary poisoning for birds and mammals via the aquatic food chain are provided below. The Reviewer has revised the $PNEC_{oral}$ to the daily dose as recommended by SANCO/4145/2000 (Sept 2002).

Table 6.

Table 7. Secondary poisoning via aquatic food chain

	Aquatic $PEC_{oral,\ predator}$, µg/kg wet fish	**$PNEC_{oral}$ µg/kg bw/day**	**Aquatic PEC/PNEC**
Birds	10	0.1	100
Mammals	10	0.3	33

The results of the quantitative assessment of acute secondary poisoning for birds and mammals via the terrestrial food chain are provided below. The Reviewer has revised the $PNEC_{oral}$ to the daily dose as recommended by SANCO/4145/2000 (Sept 2002).

Table 6.5.3.2-2. Secondary poisoning via terrestrial food chain

	Terrestrial compartment	**Terrestrial $PEC_{oral,\ predator}$, µg/kg wet earthworm**	**$PNEC_{oral}$ µg/kg bw/day**	**Terrestrial PEC/PNEC**
Birds	Sewer	22	0.1	220
	In and around buildings scenario	326	0.1	3260
	Open areas	1137	0.1	11370
	Waste dump	49	0.1	490
Mammals	Sewer	22	0.3	73
	In and around buildings scenario	326	0.3	1087
	Open areas	1137	0.3	3790
	Waste dump	49	0.3	490

Rodent-eating birds and mammals

For estimation of secondary poisoning risk through poisoned rats, the amount of difenacoum in rats is estimated according to equations 19 and 21 in ESD (ETE = (FIR/BW) * C * AV * PT * PD (mg/kg bw/day), $EC_n = \sum^{n-1}_{n=1} ETE * (1 - EL)^n$. In calculations AV and PT for rodent are set to 1 and PD values to 1 and 0.5 and 0.2. The daily elimination is assumed to be 40% (see Section 6.5.2). Tier 1 PEC_{oral} for short term situation is calculated according to the equation 22 in ESD (Larsen, 2003); $PEC_{oral,\ predator} = (ECn + ETE) \times F_{rodent}$) using value 1 for F_{rodent} (non-target animal consume 100% of their daily intake on poisoned rodents).

F_{rodent}; fraction of poisoned rodents in predator's diet
EC_n: expected concentration of a.s. in the rodent on day 'n' before the last meal

n; the number of days the rodent is eating rodenticide until caught, default 5.

Results are provided below. These values are used for qualitative risk assessment of **secondary poisoning in acute situation.**
Table 8.

Table 9. Estimated concentration (EC) of difenacoum in target rodents (rats) in mg a.s./kg bw at different times during a control operation

	Residues of rodenticide in target rodent, mg/kg		
	Worst case 100% bait consumption by rodent (PD 1)	**Normal case 50% bait consumption by rodent (PD 0.5)**	**ESD minimum 20% bait consumption by rodent (PD 0.2)**
normal non-resistant target rodent which stops eating on day 5			
Day 1 after 1st meal	5.0	2.5	1.0
Day 2 before new meal	3.0	1.5	0.6
Day 5 before meal	6.53	3.26	1.31
Day 5 after last meal	11.53	5.76	2.31
Day 6*	6.92	3.46	1.38
Day 7 (mean time to death)*	4.15	2.08	0.83
Extreme case – rodent continues eating due to resistance			
Day 14 after the meal	12.49	6.25	2.5

* - The feeding period has been set to a default value of 5 days until the onset of symptoms after which it eats nothing until its death.

A qualitative assessment of the acute secondary poisoning is made by comparing the concentration in the rodents to LD_{50} values from acute oral studies. Rodents are assumed to feed entirely on bait containing difenacoum and the non-target animals are assumed to consume only poisoned rodents. The results of the qualitative assessment are provided below**.**

Table 10. Qualitative assessment of acute secondary poisoning for rodent-eating birds and mammals

	EC in rat on day 5 after last meal mg/kg	**Birds LD_{50} mg/kg bw**	**Mammals LD50 mg/kg bw**

PD=1	11.53	56	1.8
PD=0.5	5.76	56	1.8
PD=0.2	2.31	56	1.8

Tier 1 quantitative assessment of secondary poisoning

The Tier 1 assessment of secondary poisoning for the long term situation is calculated in the way outlined for acute situations but is based on the concentration in the predator's or scavenger's food, i.e. poisoned rodents. The rodents are assumed to consume only bait (PD = 1), while half of the predator's or scavenger's daily food intake is poisoned rodents (F_{rodent} = 0.5). The rodents are assumed to eat the bait over five or fourteen successive days, whereas the predator or the scavenger is assumed to eat the poisoned rodents during one day. The predator is assumed to have caught the rodent after the last meal on day 5 or day 14. Only resistant rodents are assumed to eat bait over 14 days. The results are provided below:

Table 11. Estimated concentration (EC) of difenacoum in target rodents (rats) in mg a.s./kg bw for acute and long term situations

$PEC_{oral,predato}$,mg/kg			
	Worst case 100% bait consumption by rodent (PD 1)	**Normal case 50% bait consumption by rodent (PD 0.5)**	**ESD minimum 20% bait consumption by rodent (PD 0.2)**
Normal non-resistant target rodent which stops eating on day 5			
PEC_{oral} on day 5 for 'acute situation'	11.53	5.76	2.31
PEC_{oral} on day 5 for 'long term situation'	5.76	2.88	1.15
Extreme case – rodent continues eating due to resistance			
$PEC_{oral,predator}$ on day 14 'acute'[1]	12.49	6.25	2.5
$PEC_{oral,predator}$ on day 14 'chronic'	6.25	3.13	1.25

[1] Day 14 after the meal, from Table 6.5.3.2-3. This is different to the figure presented in the CAR.

The results of the Tier 1 assessment of secondary poisoning are provided below**.**

Table 12. Tier 1 risk characterisation of secondary poisoning. Expected concentration in target rodents is compared to the $PNEC_{oral}$ expressed as concentration in food. Rodents

are assumed to consume only bait (PD=1). Half of the predator's diet is poisoned rodents (F_{rodent}=0.5 equivalent to PD=0.5)

	PEC EC in rodent µg/kg	$PNEC_{oral}$ µg/kg bw/day	PEC/PNEC
Rodents caught on day 5 after meal			
Birds	5760	0.1	57600
Mammals	5760	0.3	19200
Rodents caught on day 14 after meal			
Birds	6250	0.1	62500
Mammals	6250	0.3	20833

Tier 2 assessment of secondary poisoning

Tier 2 for long-term exposure:

According to guidance agreed by the CA the PEC_{oral} is the concentration in non-target animals after a single day of exposure (mg/kg bw) using values PD of 1 (100% bait consumption by rodent) and F_{rodent} of 0.5. PEC_{oral} values are presented in below are used for Tier 2 quantitative risk assessment of secondary poisoning in the long-term situation (supporting information from Table 3.5 ESD).

Table 13.
Table 14.
Table 15.
Table 16.
Table 17.
Table 18.
Table 19.
Table 20.

Table 21. Expected concentrations of difenacoum in non-target animals due to secondary poisoning after a single day exposure (concentration of difenacoum in rodenticide bait 0.005 %); rodents caught by predators on day 5 and 14 (after feeding), PD 1, F_{rodent} 0.5

Species		Body wt [g]	Daily FIR [g]	Rodent caught on day 5 after feeding mg ai/kg predator	Rodent caught on day 14 after feeding mg ai/kg predator
Barn owl	*Tyto alba*	294	72.9	1.43	1.55
Kestrel	*Falco tinnunculus*	209	78.7	2.17	2.35
Little owl	*Athene noctua*	164	46.4	1.63	1.77
Tawny owl	*Strix aluco*	426	97.1	1.31	1.42
Fox	*Vulpes vulpes*	5700	520.2	0.53	0.57
Polecat	*Mustela putorius*	689	130.9	1.10	1.19

Stoat	*Mustela erminea*	205	55.7	1.57	1.70
Weasel	*Mustela nivalis*	63	24.7	2.26	2.45

In applying the predicted difenacoum concentrations in predatory birds and mammals, the Tier 2 risk characterisation was conducted and the results of which are provided below.
Table 22.

Table 23. Tier 2 risk characterisation of secondary poisoning. The expected concentrations in predatory birds and mammals are compared to the $PNEC_{oral}$ expressed as daily dose

Species		**PEC EC in predator µg/kg bw Rodent caught on day 5**	**PEC EC in predator µg/kg bw Rodent caught on day 14**	**$PNEC_{oral}$ µg/kg bw/d**	**PEC/PNEC Rodent caught on day 5**	**PEC/PNEC Rodent caught on day 14**
Barn owl	*Tyto alba*	1430	1550	0.1	14 300	15 500
Kestrel	*Falco tinnunculus*	2170	2350	0.1	21 700	23 500
Little owl	*Athene noctua*	1603	1770	0.1	16 030	17 700
Tawny owl	*Strix aluco*	1310	1420	0.1	13 100	14 200
Fox	*Vulpes vulpes*	530	570	0.3	1 767	1 900
Polecat	*Mustela putorius*	1100	1190	0.3	3 667	3 967
Stoat	*Mustela erminea*	1570	1700	0.3	5 233	5 667
Weasel	*Mustela nivalis*	2260	2450	0.3	7 533	8 167

In conclusion, the PEC/PNEC ratios based from the Annex I inclusion CAR on the measured concentration in rats and mice were lower than the respective figures calculated according to the ESD, but still considerably higher than 1 indicating risk for secondary poisoning. Risk mitigation measures need to be applied.

ANNEX VII: Residue Calculations

No residue calculations are required as Ruby Paste is a ready to use bait, which is used to kill rats and mice. Ruby Paste will not come into contact with the human food chain. The bait may be used indoors, around buildings, away from buildings and around waste sites and sewers. The bait will be placed at protected bait points in dry locations, protected from the weather to help prevent access by non target animals.

Annex 2 – Revised PAR – May 2016

Product Assessment Report

Ruby Paste

Active substance:	**Difenacoum**
Product-type:	**PT14: Rodenticides**
Type of application:	**Authorisation**
Authorisation No:	**IE/BPA 70004 (Non-professional product)** **IE/BPA 70033 (Professional product)**
Date:	**09 May 2016**

Biocidal Product Assessment Report (PAR) related to Product Authorisation under Directive 98/8/EC.

Department of Agriculture, Fisheries and Food
An Roinn Talmhaíochta, Iascaigh agus Bia

Pesticide Registration and Control Division
Department of Agriculture, Fisheries & Food
Backweston Campus
Young's Cross
Celbridge
Co. Kildare
Ireland

CONTENTS

2. General information about the product application

An application for authorisation was made to the Pesticide Registration and Control Division of the Department of Agriculture Fisheries and Food by Lodi S.A.S for the biocidal product Ruby Paste on 1st April 2010 in accordance with the provisions set out by Commission Directive 2008/81/EC.

This Product Assessment Report is for:

Trade name:	Ruby Paste
Authorisation No.:	IE/BPA 70004 (Non-professional) IE/BPA 70033 (Professional and Trained Professional)

The following authorisations in Ireland are linked to the above product authorisation:

Trade name	Authorisation No.	Marketing/Distribution Co.	Authorisation Type
Roded Paste	PCS 70034	Hygeia Chemicals Ltd	Supplemental Authorisation (Back-2-Back Authorisation)

47.1 Applicant/Authorization Holder

Company Name:	LODI S.A.
Address:	Parc d'activities des quatre routes Grand Fougeray 35390 France
Tel:	+ [redacted]
[redacted]	[redacted]

[redacted]

Company Name:	[redacted]
Address:	[redacted] A [redacted]
[redacted]	[redacted]

47.3 Marketing/Distributing Company (where applicable)

Company Name:	LODI UK
Address:	Pensnett Trading Estate Building 69 3rd Avenue Kingswinford West Midlands, DY6 7FD UK
Tel:	[redacted]

47.4 General Information on the Biocidal Product

Trade name:	Ruby Paste
Manufacturer's development code number(s):	N/A
Active substance content:	0.005% w/w difenacoum
Main group:	MG3 – Pest control
Product type:	PT14 - Rodenticides
Product Specification:	See Confidential Annex
Site of product formulation:	See Confidential Annex
Formulation type:	Ready-to-use (RB) Paste (PA) Bait
Ready to use product (yes/no):	Yes (Only RTU products to be authorised)
Chemical/micro-organism:	Chemical substance
Contain or consist of GMOs[29] (yes/no):	N/A
Is the product already notified/authorised (Directive 98/8/EC) (yes/no); If yes: product name:	Yes (Notified under transitional arrangements with the PRCD) Ruby Paste, PCS 96004
Is the biocidal product equivalent to the product assessed for the purpose of Annex I inclusion to 98/8/EC (yes/no):	No.

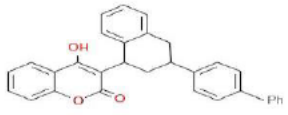
Manufacturer of Formulated Product:	LODI S.A.
Address:	Parc d'activities des quatre routes Grand Fougeray 35390 France
Tel:	[redacted]
E-mail:	[redacted]

47.5 Information on active substance(s)[30]

Active substance chemical name:	Difenacoum
IUPAC name:	3-(3biphenyl-4-yl-1,2,3,4-tetrahydro-1-naphtyl)-4-hydroxycoumarin
CAS No:	56073-07-5

29 A copy of any written consent(s) of the competent authorities to the deliberate release into the environment of the GMOs for research and development purposes where provided for by Part B of the above-mentioned Directive was provided.

30 Please insert additional columns as necessary

EC No:	259-978-4
Purity (minimum, g/kg or g/l):	>960 g/kg (96.0% w/w)
Structural Formula:	
Manufacturing site:	See Confidential Annex
Specification of pure active substance:	See Confidential Annex
Is a new active substance data package (source) supplied (yes/no):	No
If yes, Is the active substance equivalent to the active substance listed in Annex I to 98/8/EC (yes/no):	N/A
If no, does the applicant have a LoA to the active substance data packaged used to support Annex I inclusion (yes/no):	Yes (Pelgar International Ltd.)

Manufacturer of active substance(s):	Pelgar International Ltd.
Address:	Unit 13 Newman Lane Alton Hants. GU34 2QR UK
Tel:	[redacted]
E-mail:	[redacted]

47.6 Information on the intended use(s) of the biocidal product

Main Group:	MG03 (Pest control)
Product-type:	PT14 (Rodenticide)
Intended use:	Difenacoum paste bait to control rodents indoors and outdoors for the protection of public health, stored products and materials.
Target organisms:	(I.1) Rodents (I.1.1) Murids (I.1.1.1) Brown rats (*Rattus Norvegicus*) (I.1.1.2) House rat (*Rattus rattus*) (I.1.1.3) House mouse (*Mus musculus*)
Development stage:	(II.1) Juveniles (II.2) Adults
Function:	Rodenticide
Mode of action:	Anticoagulant III.2 long-term action III.2.1 anticoagulant

	III.2.1.1 ingestion toxin III.2.1.1.1 ingestion by eating
Application aim:	Protection of: Public health/hygiene, materials and Stored products
Category of users:	Trained professionals, professionals and non-professional (general public/amateur)
Area of use (indoors/outdoors):	Indoors (warehouses, outbuildings) Outdoors (in and around buildings, waste dumps and open areas)
Directions for use including minimum and maximum application rates, typical size of application area:	Rats: 90-100 g of paste per bait point spaced at 10m (spaced at 5m in high infestation areas). Typical treatment time 6 weeks. Mice: 20-30 g of paste per bait point spaced at 5m (spaced at 3m in high infestation areas). Typical treatment time 6 weeks.
Application method:	Paste baits contained in secured bait stations
Interval between applications:	Inspect baits frequently (particularly during the first 10 to 15 days) and regularly check bait consumption and, when required, replace consumed or spoilt bait until consumption has stopped. Repeat treatment in case of new infestation, new tracks or fresh droppings.
Typical treatment time:	6 weeks for rats and mice
Potential for release into the environment (yes/no):	Yes
Potential for contamination of food/feedingstuff (yes/no):	No

47.7 Documentation

47.7.1 Data submitted in relation to product application

A full new product dossier was submitted by Lodi S.A. in support of the product Ruby Paste containing difenacoum.

Please see the attached reference list in Annex IV.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

5. *Classification, labelling and packaging*

Under this heading the assessment of the classification, labelling and packaging should be summarised. Further, any result of the assessments made under the following headings that require recommendations or restrictions appearing on the label should be summarised here.

5.1. Harmonised classification of the active substance

The current classification of the active substance based on the proposals resulting from the review programme for difenacoum, according to Directive 67/548/EEC, is provided in the table below. Additionally, the extrapolation of these proposals using the BG RCI converter tool (http://www.gischem.de/ghs/konverter) is also provided in the table below in accordance with Regulation (EC) 1272/2008.

Classification of the active substance, difenacoum, according to Directive 67/548/EEC and CLP Regulation (EC) 1272/2008:

Symbol(s):	 	**Pictogram(s):**	
Indication(s) of danger:	Very Toxic Dangerous for the Environment	**Signal word(s):**	Danger
Risk phrases:	R26/27/28: Very Toxic by inhalation, in contact with skin and if swallowed. R48/23/24/25: Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed. R61: May cause harm to the unborn child. R50/53: Very Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.	**Hazard statements:**	H300: Fatal if swallowed. H310: Fatal in contact with skin. H330: Fatal if inhaled. H360D: Suspected of damaging the unborn child. H372: Causes damage to organs through prolonged or repeated exposure through inhalation . H410: Very toxic to aquatic life with long lasting effects.
Safety phrases:	S45: In case of accident or if you feel unwell, seek medical advice immediately (show label where possible). S53: Avoid exposure - obtain special instruction before use. S60: This material and/or its container must be disposed of as hazardous waste. S61: Avoid release to the environment. Refer to special instructions/safety data sheet.	**Precautionary statements:**	P201: Obtain special instructions before use. P273: Avoid release to the environment. P308 + P313: IF exposed or concerned: Get medical advice/attention. P314: Get medical advice/attention if you feel unwell. P501: Dispose of contents/container to hazardous waste facilities in accordance with national regulations.

5.2. Harmonised classification and labelling of the biocidal product

The current classification and labelling according to Directive 99/45/EC and Regulation (EC) 1272/2008, Annex VI, Part 3 are provided in the tables below.

Classification and Labelling of the biocidal product, Ruby Paste, according to Directive 99/45/EC:

Symbol(s):	None
Indication(s) of danger:	None
Risk phrases:	None
Safety phrases:	S1+S2: Keep locked up and out of reach of children S13: Keep away from food, drink and animal feedingstuffs S37: Wear suitable gloves S46: If swallowed, seek medical advice immediately and show this container or label S57: Use appropriate containment to avoid environmental contamination. S35: This material and its container must be disposed of in a safe way.

Classification and Labelling of the biocidal product, Ruby Paste, according to the CLP Regulation (EC) 1272/2008:

Pictogram(s):	None
Signal word(s):	None
Hazard statements:	None
Precautionary statements	P102: Keep out of reach of children. P103: Read label before use. P220: Keep/Store away from food, drink and animal feedingstuffs. P270: Do not eat, drink or smoke when using this product. P273: Avoid release to the environment. P280: Wear protective gloves P301+310: IF SWALLOWED: Immediately call a poison centre or doctor/physician. P404+405: Store locked up in a closed container. P501: Dispose of contents/container in accordance with national regulations.

Further, the content of the label should be updated to comply with the labelling requirements established (for biocidal products) where the labelling requirements in Article 20(3) of Directive 98/8/EC has been implemented. The safety data sheet should comply with the requirements in Regulation (EC) 1907/2006.

Additional Labelling Requirements:

Addition safety Information:	To avoid risks to human health and the environment, comply with the instructions for use. Use bait containers clearly marked “poison” at all surface baiting points. Remove all remains of bait, dead rodents during and after treatment and dispose of safely. Apply only in positions inaccessible to children and pets.
Special labelling provisions for Ireland:	Use Biocides Safely and Sustainably (IE/BPA 70033) Not For Amateur Sale It is illegal to use this product for uses or in a manner other than that prescribed on this label.
If a separate leaflet is attached to or supplied with the product, add the following information to the front label:	Read attached instructions before use

5.3. Packaging

The packaging details for the biocidal product, Ruby Paste, are outlined below for amateur and professional users.

Nomenclature: PP = polypropylene, PS = polystyrene, PE = polyethylene, HDPE = high-density polyethylene, PVC = polyvinylchloride

Amateur product packaging:

Container description:	Sachets		
Pack size(s):	200g	240g	500g
Baits/sachets per pack:	20x10g	24x10g	50x10g
Pack dimensions (LxWxH):	180x50x190	190x50x190	190x50x250
Packaging materials:	PE or PP or PP+PE or PE + Aluminium		
Ready-to-use (yes/no)	Yes		
Shelf-life:	4 years		
Conditions of storage:	Store in dry, cool area. Store in tightly closed packings. Keep in original containers. Store away from damp or wet conditions. Keep away from		

	children.

Container description:	Bucket container	Box container			
Pack size(s):	~~2.5kg~~	200g	240g	400g	500g
Baits/sachets per pack:	~~250x10g~~	20x10g	24x10g	40x10g	50x10g
Pack dimensions (LxWxH):	~~290x200x210~~	140x55x180	40x55x180	140x70x210	140x70x210
Packaging materials:	PP or PE	Cardboard			
Ready-to-use (yes/no)	Yes				
Shelf-life:	4 years				
Conditions of storage:	Store in dry, cool area. Store in tightly closed packings. Keep in original containers. Store away from damp or wet conditions. Keep away from children.				

Container description:	Prebaited tray		Prebaited box container		
Pack size(s):	50g	60g	10g	20g	40g
Baits/sachets per pack:	1x50g	1x60g	1x10g	2x10g	4x10g
Pack dimensions (LxWxH):	150x70x30	150x70x30	135x42x80	135x42x80	220x190x90
Packaging materials:	PS or PVC tray		PP or PS or PVC bait box		
Ready-to-use (yes/no)	Yes				
Shelf-life:	4 years				
Conditions of storage:	Store in dry, cool area. Store in tightly closed packings. Keep in original containers. Store away from damp or wet conditions. Keep away from children.				

Professional product packaging:

Container description:	Bucket container				Box container	
Pack size(s):	2.5kg	4kg	5kg	15kg	10kg	20kg
Baits/sachets per pack:	250x10g	400x10g	500x10g	1500x10g	1000x10g	2000x10g
Pack dimensions	290x20	290x20	290x200x2	380x290x4	390x290x24	400x400x37

(LxWxH):	0x210	0x270	70	50	0	0
Packaging materials:	PP or PE				Cardboard (PE liner)	
Ready-to-use (yes/no)	Yes					
Shelf-life:	4 years					
Conditions of storage:	Store in dry, cool area. Store in tightly closed packings. Keep in original containers. Store away from damp or wet conditions. Keep away from children.					

Container description:	Prebaited tray		Prebaited box container		
Pack size(s):	50g	60g	10g	20g	40g
Baits/sachets per pack:	1x50g	1x60g	1x10g	2x10g	4x10g
Pack dimensions (LxWxH):	150x70x30	150x70x30	135x42x80	135x42x80	220x190x90
Packaging materials:	PS or PVC tray		PP or PVC bait box		
Ready-to-use (yes/no)	Yes				
Shelf-life:	4 years				
Conditions of storage:	Store in dry, cool area. Store in tightly closed packings. Keep in original containers. Store away from damp or wet conditions. Keep away from children.				

Container description:	Cartridge
Pack size(s):	310 ml
Baits/sachets per pack:	1x310ml
Pack dimensions (LxWxH):	230x50
Packaging materials:	PP
Ready-to-use (yes/no)	Yes
Shelf-life:	4 years
Conditions of storage:	Store in dry, cool area. Store in tightly closed packings. Keep in original containers. Store away from damp or wet conditions. Keep away from children.

On the basis of the packaging details presented, it is considered appropriate to limit aspects of the packaging for amateur users as a risk mitigation measure. Packaging restrictions are to be limited to pre-baited bait stations and refill packs with a maximum pack-size of 500g. Additionally, the paste bait should be supplied to the amateur market in sachets in order to reduce exposure risks to amateur operators during application to bait stations.

Packaging details:

Pack size:	IE/BPA 70004 – Maximum pack size of 500g
	Pre-baited stations: 30g (mice) and 100g (rats)
	Refill packs: 200, 240g, 400g and 500g (the bait should be supplied in inner packs or units, each containing enough bait for one point)
	IE/BPA 70033
	Pre-baited stations: 30g (mice) and 100g (rats)
	Refill packs: 2.5kg, 4kg, 5kg, 10kg, 15kg and 20kg (the bait should be supplied in inner packs or units, each containing enough bait for one point)
	Cartridge 310ml
Container materials:	Box (cardboard with PE inner lining)
	Bucket (PP or PE)
	Pre-baited station (PVC, PP, PS, cardboard)
	Cartridge (PP)
Safety features:	Covered bait stations (tamper resistant)
	Wrapped bait (sachets)

4. Summary of the product assessment

4.1. Physical/chemical properties and analytical methods

Active substance (taken from the CAR):
Difenacoum does not exhibit hazardous physical-chemical properties. Difenacoum is a white to off-white powder (off-white to beige, technical grade). It has low vapour pressure; Henry's Law constant (1.75×10^{-6} Pa m^3 mol^{-1} or <0.046 Pa m^3 mol^{-1}) was calculated based on an estimated value of 6.7×10^{-9} Pa at 25°C or on an estimated vapour pressure of less than 5×10^{-5} Pa at 45°C. Difenacoum is a weak acid with a pKa value of 4.84 or with an estimated pKa value of 4.5+1. The water solubility is pH dependent and it increases with increasing pH. At neutral conditions the water solubility of Difenacoum is low, 1.7 mg/l (at pH 7 at 20°C), or in 0.48 mg/l (at 20°C at pH 6.5). Solubility in organic solvents tested ranged from 1 to 20 g/l. The estimated log K_{ow} value is 7.6. The experimental information available on Difenacoum suggests that it may be beyond the performance ranges of the experimental tests for log K_{ow}. The substance is thermally stable up to about 300°C or up to 250°C. No boiling point was detected before start of decomposition. Difenacoum is not highly flammable and it shows no self-ignition at temperatures up to melting point, 211-215°C or 215°C, the maximum temperature in the test. Corrosiveness to containers has not been observed. Difenacoum does not show oxidising or explosive properties.

Biocidal product:
The biocidal product Ruby Paste is not explosive, oxidising or flammable and does not classify from a phys.chem point of view. The test item is stable after storage for two years at ambient temperatures. The test item is a ready-to-use paste bait and is not intended to be added or mixed with any other product.

3.1.1. Identity related issues

The source of active substance used in the biocidal product Ruby Paste is the same source of active substance that is listed in Annex I of 98/8/EC (Pelgar International Ltd.).

Table 3.1.1: Composition of the biocidal product Ruby Paste

Component	% w/w	g/kg	Chemical name	CAS no	Function
Concentrate containing - Difenacoum 2.5% (Purity 96%, Technical 0.005%) + other components which are identified in the Confidential section.	0.20 (0.005 % Technical active substance)	2.00 (0.05 g/kg technical active substance)	3-(3biphenyl-4-yl-1,2,3,4-tetrahydro-1-naphtyl)-4-hydroxycoumarin	56073-07-5	Active substance
Co-formulants	See Confidential Data and Information (Annex I)				

Note: The biocidal product Ruby Paste is not the same as the representative biocidal product accompanying the Annex I inclusion. See confidential information and data for details of composition.

3.1.2. Physical-chemical properties

The source of active substance used in the biocidal product Ruby Paste is the same source of active substance that is listed in Annex I of 98/8/EC (Pelgar International Ltd.). Pelgar International Ltd. provided a letter of access for LODI S.A for their source of active substance.

3.1.3. Physical, Chemical and Technical Properties of the Biocidal Product

General note: sometimes the text says ”pasta” instead of ”paste”

Summary of the Physical and Chemical Properties of the Biocidal Product Ruby Paste

Section	Study	Method	Results	Comment	Reference
1.1.1	Appearance	OPPTS 830.6302 OPPTS 830.6303 OPPTS 830.6304	Colour (munsell code): Red (3.75 R 4/14) Physical state: paste Odour: not characteristic	Carried out to GLP. Observations were carried out at 19.5^{o}C. Study is acceptable.	NOTOX Project 490526. “Determination of physic-chemical properties of difenacoum paste baits”. Brekelmans, Ir. M.J.C. 17th September 2010.
1.1.1	Appearance		Colour: Pink paste Physical state: paste Odour: hazelnut	See 1.7.1b below.	
1.1.2	Melting point	EEC A1 OECD 102	Melting point: -16^{o}C (257 K) Decomposition of the test substance was observed at 100^{o}C (373K).	Carried out to GLP. Study is acceptable.	NOTOX Project 490526. “Determination of physic-chemical properties of difenacoum paste baits”. Brekelmans, Ir. M.J.C. 17th September 2010.
1.2.1	Explosive properties		The absence of certain reactive groups in the structural formula of the a.s., difenacoum (CAS 56073-07-5) *{Ref: Brethrick, Handbook of Reactive Chemical Hazards, Butterworths, London 1979}*, and it oxygen balance, establish beyond reasonable doubt that difenacoum is incapable of decompositing,	The RefMS accepts the Notifiers justification. Difenacoum paste bait is not explosive.	

Section	Study	Method	Results	Comment	Reference
			forming gases, or realising heat very rapidly. There are no other components in the formulation which present any explosive properties.		
1.2.1	Explosive properties		A reasoned statement was provided by the Notifier. Difenacoum paste bait is not explosive.	The RefMS accepts the Notifiers justification. Difenacoum paste bait is not explosive.	NOTOX Project 490526. "Determination of physic-chemical properties of difenacoum paste baits". Brekelmans, Ir. M.J.C. 17th September 2010.
1.2.2	Oxidising properties		Nor the a.s. or the solvent present oxidising properties Examination of the structural establish beyond reasonable doubt that the a.s., difenacoum (CAS 56073-07-5) is incapable of reacting exothermically with a combustible material *(refer to Explosive Properties)*. There are no other components in the formulation which present any oxidising properties.	The RefMS accepts the Notifiers justification. Difenacoum paste bait is not oxidising.	
1.2.2	Oxidising properties		A reasoned statement was provided by the Notifier. Difenacoum paste bait is not oxidising.	The RefMS accepts the Notifiers justification. Difenacoum paste bait is not oxidising.	NOTOX Project 490526. "Determination of physic-chemical properties of difenacoum paste baits". Brekelmans, Ir. M.J.C. 17th September 2010.
1.3.1	Flash point		No flash point data is required for solids. See 1.3.2, Flammability below.		

Section	Study	Method	Results	Comment	Reference
1.3.2	Flammability	EEC A.10 (flammability (solids)).	Flammability: Not highly flammable. The flame of the gas burner did ignite the test substance pile. The test substance glowed and burned with a yellow flame and turned into a charred residue. White smoke was observed. After removal of the ignition source, the flame extinguished after 28 seconds and no propagation of combustion was observed. Performance of the main test was not required.	The RefMS accepts that Difenacoum was determined to be not highly flammable as part of the Annex I inclusion process. Carried out to GLP. The test substance is considered "not highly flammable". The study is acceptable.	NOTOX Project 490526. "Determination of physic-chemical properties of difenacoum paste baits". Brekelmans, Ir. M.J.C. 17th September 2010.
1.3.3	Auto-flammability	EEC A.16 (relative self-ignition temperature for solids)	The test item is considered "not self-ignitable"	Carried out to GLP. The test item is not self-ignitable.	NOTOX Project 490526. "Determination of physic-chemical properties of difenacoum paste baits". Brekelmans, Ir. M.J.C. 17th September 2010.
1.4.1	Free acidity/ Alkalinity		The determination of acidity or alkalinity is required if the pH of the 1% (w/v) aqueous test substance dispersion is <4 or >10. The pH of a 1% (w/v) aqueous test substance solution was determined to be 6.4. Therefore since this pH was within the pH range 4-10 the acidity/alkalinity test was not required and thus not performed.	RefMS agrees that the acidity/alkalinity test is not required.	NOTOX Project 490526. "Determination of physic-chemical properties of difenacoum paste baits". Brekelmans, Ir. M.J.C. 17th September 2010.
1.4.2	pH (1 %)	CIPAC MT 75.3	pH (1%) = 6.4	Carried out to GLP. The temperature was 20°C. The	NOTOX Project 490526. "Determination of physic-chemical properties of

<table>
<tr><th>Section</th><th>Study</th><th>Method</th><th>Results</th><th>Comment</th><th>Reference</th></tr>
<tr><td></td><td></td><td></td><td></td><td>results are acceptable.</td><td>difenacoum paste baits”. Brekelmans, Ir. M.J.C. 17th September 2010.</td></tr>
<tr><td>1.5.1</td><td>Viscosity</td><td></td><td>Not applicable, the product is a paste.</td><td>Accept justification.</td><td></td></tr>
<tr><td>1.5.2</td><td>Surface tension</td><td></td><td>Not applicable, the product is a paste.</td><td>Accept justification.</td><td></td></tr>
<tr><td>1.6</td><td>Relative density</td><td>OECD 109
EEC A.3</td><td>Density = 1.24 g/cm^3
Relative density = 1.24</td><td>Carried out to GLP. The results are acceptable.</td><td>NOTOX Project 490526. “Determination of physic-chemical properties of difenacoum paste baits”. Brekelmans, Ir. M.J.C. 17th September 2010.</td></tr>
<tr><td>1.7.1a</td><td>Storage stability
(Accelerated storage – up to 5 weeks at 54°C)</td><td>GIFAP Monograph No. 17
CIPAC MT 46.3</td><td>The study examined the Difenacoum content before and after accelerated storage for three different products (paste, block and cereals). Only the Difenacoum paste (0.005%) results are given below:
<table>
<tr><th>Weeks at 54°C</th><th>0</th><th>2</th><th>3</th><th>4</th><th>5</th></tr>
<tr><td>Agent conc. in ppm</td><td>52.9</td><td>49.0</td><td>49.9</td><td>50.4</td><td>49.2</td></tr>
<tr><td>Deviation from the declared value</td><td>+ 5.8%</td><td>-2%</td><td>- 0.2%</td><td>+0.8%</td><td>- 1.6%</td></tr>
<tr><td>Min. Tolerance in ppm</td><td>37.5</td><td>37.5</td><td>37.5</td><td>37.5</td><td>37.5</td></tr>
</table></td><td>Note that the rat poison was considered stable when less than 25% agent breakdown was observed.
The sample was stable during 5 weeks at 54°C. The result indicates that the paste bait will be stable for up to two years at ambient temperature. The study is acceptable.</td><td>Study report: Stability of Difenacoum baits after accelerated storage procedure. Biannic, Marie-Laure. 7th January 2008.</td></tr>
</table>

Section	Study	Method	Results	Comment	Reference
			The sample was stable during 5 weeks at 54°C, indicating that the paste bait will be stable for up to 2 years at ambient temperature.		
1.7.1b	Storage stability (Accelerated storage – 14 days at 54°C)	GIFAP Monograph No. 17 CIPAC MT 46	<u>Analysis at T0:</u> Aspect: Pink malleable paste Odour: Hazelnut Contents: 48.79 mg/kg of Difenacoum (-2.42% deviation from the declared value) <u>Analysis at T14:</u> Aspect: Pink crumbly paste Odour: Hazelnut Contents: 50.38 mg/kg of Difenacoum (+0.76 % after accelerated storage)	Carried out to GLP. The only change observed was in the aspect which became crumbly, which did not influence the stability of the difenacoum content in the paste. The results of the study indicate that the test item is stable for 2 weeks at 54°C and would be expected to be stable for up to two years at ambient temperatures. The study is acceptable. Note that the analytical method used was validated in study LODI.17/2009; the LOQ = 0.25 ppm.	Study No: LODI.14/2009. Study report: Chemical stability after accelerated storage of Difenacoum paste baits 0.005%. Meriadec, Elodie. 25th November 2009.
1.7.2	Shelf life (storage ambient temperatures for two years)		The study examined the stability of Difenacoum in the test item for three different products (paste, block and cereals). Only the Difenacoum paste (0.005%) results are given below:	Note that the rat poison was considered stable when less than 25% agent breakdown was observed. The test item	Study report: Stability of Difenacoum baits after a storage at ambient temperature. Biannic,

<table>
<tr><th>Section</th><th>Study</th><th>Method</th><th>Results</th><th>Comment</th><th>Reference</th></tr>
<tr><td></td><td></td><td></td><td>
<table>
<tr><th>Time</th><th>0</th><th>6 months</th><th>2 yrs</th></tr>
<tr><td>Agent conc. in ppm</td><td>52.9</td><td>49.97</td><td>52.8</td></tr>
<tr><td>Deviation from the declared value</td><td>5.80%</td><td>-5.54%</td><td>-0.19%</td></tr>
<tr><td>Min. tolerance in ppm</td><td>37.5</td><td>37.5</td><td>37.5</td></tr>
</table>

The test item is considered stable for two years at ambient temperatures.</td><td>is considered stable for two years at ambient temperatures. The study is acceptable.</td><td>Marie-Laure. 12th November 2009.</td></tr>
<tr><td>1.7.3</td><td>Packaging stability (20°C)</td><td></td><td>PP Bucket (individual tea paper sachet):
<table>
<tr><th></th><th colspan="3">Weight</th></tr>
<tr><th></th><th>Bucket (g)</th><th>Test item (g)</th><th>Total (g)</th></tr>
<tr><td>T_0</td><td>32.066</td><td>85.888</td><td>117.93</td></tr>
<tr><td>$T_{6months}$</td><td>32.073</td><td>85.987</td><td>117.86</td></tr>
<tr><td>Deviation</td><td>+0.02%</td><td>+0.12%</td><td>-0.06%</td></tr>
<tr><td>T_{1year}</td><td>32.078</td><td>85.516</td><td>117.61</td></tr>
<tr><td>Deviation</td><td>+0.04%</td><td>-0.43%</td><td>-0.27%</td></tr>
<tr><td>$T_{18\ months}$</td><td>32.078</td><td>85.490</td><td>117.59</td></tr>
<tr><td>Deviation</td><td>+0.04%</td><td>-0.46%</td><td>-0.29%</td></tr>
<tr><td>T_{2years}</td><td>32.081</td><td>85.454</td><td>117.55</td></tr>
<tr><td>Deviation</td><td>+0.05%</td><td>-0.51%</td><td>-0.32%</td></tr>
</table>
T_0 = White bucket with smooth and clean internal wall. Malleable red paste. Presence of grease on individual tea paper sachet.
$T_{6months}$ = White bucket with smooth and fatty internal wall. Malleable red paste. Presence of grease on individual tea paper sachet.</td><td>Carried out to GLP.
Deviation weights (packaging weights and test item weights) after 2 years at 20 ± 2°C are lower than 5% for all the packaging. Moreover, no significant changes were observed on the packaging and on the test item.
The packaging is stable for 2 years at ambient temperature.
The results are acceptable.

Note:
The results for the 3-year time point have not been</td><td>Richerioux, Sandra. LODI-Group. 19th April 2016. “Compatibility between difenacoum paste bait and packagings after 3 years of storage at 20°C”. Study No. LODI.01/2014</td></tr>
</table>

<table>
<tr><th>Section</th><th>Study</th><th>Method</th><th>Results</th><th>Comment</th><th>Reference</th></tr>
<tr><td></td><td></td><td></td><td>
T_{1year} = White bucket with smooth and fatty internal wall. Malleable red paste. Presence of grease on individual tea paper sachet.
$T_{18\ months}$ = White bucket with smooth and fatty internal wall. Malleable red paste. Presence of grease on individual tea paper sachet.
$T_{2\ years}$ = White bucket with smooth and fatty internal wall. Malleable red paste. Presence of grease on individual tea paper sachet.

PP + PE Bag (PP inner layer and PE outer layer; individual tea paper sachet):
<table>
<tr><th rowspan="2"></th><th colspan="3">Weight</th></tr>
<tr><th>Bag (g)</th><th>Test item (g)</th><th>Total (g)</th></tr>
<tr><td>T_0</td><td>9.410</td><td>205.63</td><td>215.04</td></tr>
<tr><td>$T_{6months}$</td><td>9.327</td><td>203.80</td><td>213.56</td></tr>
<tr><td>Deviation</td><td>-0.88%</td><td>-0.89%</td><td>-0.69%</td></tr>
<tr><td>T_{1year}</td><td>9.358</td><td>199.60</td><td>209.15</td></tr>
<tr><td>Deviation</td><td>-0.55%</td><td>-2.93%</td><td>-2.74%</td></tr>
<tr><td>$T_{18\ months}$</td><td>9.347</td><td>202.28</td><td>211.66</td></tr>
<tr><td>Deviation</td><td>-0.67%</td><td>-1.63%</td><td>-1.57%</td></tr>
<tr><td>T_{2years}</td><td>9.363</td><td>200.25</td><td>209.81</td></tr>
<tr><td>Deviation</td><td>-0.50%</td><td>-2.62%</td><td>-2.43%</td></tr>
</table>
T_0 = Thick and opaque bag. Clean and dry internal wall. Malleable red paste. Presence of grease on individual tea paper sachet.
$T_{6months}$ = Thick and opaque bag. Presence of grease on internal wall of the bag. Malleable red paste. Presence of grease on individual tea paper sachet.
T_{1year} = Thick and opaque bag. Presence of grease on internal wall of the bag. Malleable red paste. Presence of grease on individual tea paper sachet.
$T_{18\ months}$ = Thick and opaque bag. Presence of grease
</td><td>submitted as the study is still on-going.</td><td></td></tr>
</table>

<table>
<tr><th>Section</th><th>Study</th><th>Method</th><th>Results</th><th>Comment</th><th>Reference</th></tr>
<tr><td></td><td></td><td></td><td>
on internal wall of the bag. Malleable red paste. Presence of grease on individual tea paper sachet.
$T_{2\ years}$ = Thick and opaque bag. Presence of grease on internal wall of the bag. Malleable red paste. Presence of grease on individual tea paper sachet.

PP bag with cardboard box (individual tea paper sachet):
<table>
<tr><th></th><th colspan="4">Weight</th></tr>
<tr><th></th><th>PP bag (g)</th><th>Cardboard box(g)</th><th>Test item (g)</th><th>Total (g)</th></tr>
<tr><td>T_0</td><td>3.277</td><td>42.853</td><td>149.83</td><td>195.93</td></tr>
<tr><td>$T_{6months}$</td><td>3.319</td><td>43.086</td><td>148.46</td><td>195.03</td></tr>
<tr><td>Deviation</td><td>+1.28%</td><td>+0.54%</td><td>-0.91%</td><td>-0.46%</td></tr>
<tr><td>T_{1year}</td><td>3.332</td><td>42.369</td><td>145.99</td><td>192.09</td></tr>
<tr><td>Deviation</td><td>+1.68%</td><td>-1.13%</td><td>-2.56%</td><td>-1.96%</td></tr>
<tr><td>$T_{18\ months}$</td><td>3.335</td><td>43.048</td><td>147.18</td><td>193.96</td></tr>
<tr><td>Deviation</td><td>+1.77%</td><td>+0.46%</td><td>-1.77%</td><td>-1.01%</td></tr>
<tr><td>T_{2years}</td><td>3.342</td><td>42.422</td><td>145.79</td><td>191.96</td></tr>
<tr><td>Deviation</td><td>-1.98%</td><td>-1.01%</td><td>-2.70%</td><td>-2.03%</td></tr>
</table>
T_0 = Dry and clean transparent bag – rectangular cardboard box with clean, grey and dry internal wall. Malleable red paste. Presence of grease on individual tea paper sachet.
$T_{6months}$ = Transparent bag. Presence of grease on internal wall of the bag – rectangular cardboard box with clean, grey and dry internal wall. Malleable red paste. Presence of grease on individual tea paper sachet.
T_{1year} = Transparent bag. Presence of grease on internal wall of the bag – rectangular cardboard box with clean, grey and dry internal wall. Malleable red paste. Presence of grease on individual tea paper
</td><td></td><td></td></tr>
</table>

<table>
<tr><th>Section</th><th>Study</th><th>Method</th><th>Results</th><th>Comment</th><th>Reference</th></tr>
<tr><td></td><td></td><td></td><td>sachet.
$T_{18\ months}$ = Transparent bag. Presence of grease on internal wall of the bag – rectangular cardboard box with clean, grey and dry internal wall. Malleable red paste. Presence of grease on individual tea paper sachet.
$T_{2\ years}$ = Transparent bag. Presence of grease on internal wall of the bag – rectangular cardboard box with clean, grey and dry internal wall. Malleable red paste. Presence of grease on individual tea paper sachet.

PP bait station and cardboard box (individual tea paper sachet):
<table>
<tr><th rowspan="2"></th><th colspan="4">Weight</th></tr>
<tr><th>Bait station(g)</th><th>Cardboard box (g)</th><th>Test item (g)</th><th>Total (g)</th></tr>
<tr><td>T_0</td><td>48.948</td><td>39.153</td><td>22.210</td><td>110.31</td></tr>
<tr><td>$T_{6months}$</td><td>48.958</td><td>39.470</td><td>21.967</td><td>110.39</td></tr>
<tr><td>Deviation</td><td>+0.02%</td><td>+0.81%</td><td>+1.09%</td><td>+0.07%</td></tr>
<tr><td>T_{1year}</td><td>48.954</td><td>38.822</td><td>21.523</td><td>109.31</td></tr>
<tr><td>Deviation</td><td>+0.012%</td><td>-0.85%</td><td>-3.09%</td><td>-0.91%</td></tr>
<tr><td>$T_{18\ months}$</td><td>48.960</td><td>39.431</td><td>21.815</td><td>110.20</td></tr>
<tr><td>Deviation</td><td>+0.02%</td><td>+0.71%</td><td>-1.78%</td><td>-0.10%</td></tr>
<tr><td>T_{2years}</td><td>48.958</td><td>38.886</td><td>21.498</td><td>109.34</td></tr>
<tr><td>Deviation</td><td>+0.02%</td><td>-0.68%</td><td>-3.21%</td><td>-0.88%</td></tr>
</table>
T_0 = Black box with smooth and clean internal wall – Cardboard box with clean, grey and dry internal wall. Malleable red paste. Presence of grease on individual tea paper sachet.
$T_{6months}$ = Black box with smooth internal wall. Presence of grease at the location of the paste. Dry cardboard box - no trace of grease. Malleable red</td><td></td><td></td></tr>
</table>

<table>
<tr><th>Section</th><th>Study</th><th>Method</th><th>Results</th><th>Comment</th><th>Reference</th></tr>
<tr><td></td><td></td><td></td><td>paste. Presence of grease on individual tea paper sachet.
T_{1year} = Black box with smooth internal wall. Presence of grease at the location of the paste. Dry cardboard box - no trace of grease. Malleable red paste. Presence of grease on individual tea paper sachet.
$T_{18\ months}$ = Black box with smooth internal wall. Presence of grease at the location of the paste. Dry cardboard box - no trace of grease. Malleable red paste. Presence of grease on individual tea paper sachet.
$T_{2\ years}$ = Black box with smooth internal wall. Presence of grease at the location of the paste. Dry cardboard box - no trace of grease. Malleable red paste. Presence of grease on individual tea paper sachet.

PET bait station and cardboard box (individual tea paper sachet):
<table><tr><th></th><th colspan="4">Weight</th></tr><tr><th></th><th>Bait station(g)</th><th>Cardboard box (g)</th><th>Test item (g)</th><th>Total (g)</th></tr><tr><td>T_0</td><td>14.637</td><td>24.203</td><td>11.311</td><td>50.154</td></tr><tr><td>$T_{6months}$</td><td>14.649</td><td>24.379</td><td>11.182</td><td>50.211</td></tr><tr><td>Deviation</td><td>+0.08%</td><td>+0.73%</td><td>-1.14%</td><td>+0.11%</td></tr><tr><td>T_{1year}</td><td>14.835</td><td>23.940</td><td>10.957</td><td>49.519</td></tr><tr><td>Deviation</td><td>-1.35%</td><td>-1.09%</td><td>-3.13%</td><td>-127%</td></tr><tr><td>$T_{18\ months}$</td><td>14.654</td><td>24.349</td><td>11.101</td><td>50.103</td></tr><tr><td>Deviation</td><td>+0.12%</td><td>+0.60%</td><td>-1.86%</td><td>-0.10%</td></tr><tr><td>T_{2years}</td><td>14.638</td><td>23.978</td><td>10.940</td><td>49.546</td></tr><tr><td>Deviation</td><td>+0.007%</td><td>-0.93%</td><td>-3.28%</td><td>-1.21%</td></tr></table>T_0 = Shiny black box with clean and dry internal wall – Cardboard box with clean, grey and dry internal wall.</td><td></td><td></td></tr>
</table>

<table>
<tr><th>Section</th><th>Study</th><th>Method</th><th>Results</th><th>Comment</th><th>Reference</th></tr>
<tr><td></td><td></td><td></td><td>
Malleable red paste. Presence of grease on individual tea paper sachet.

$T_{6months}$ = Shiny black box. Presence of grease at the location of the paste. Cardboard box with clean, grey and dry internal wall. Malleable red paste. Presence of grease on individual tea paper sachet.

T_{1year} = Shiny black box. Presence of grease at the location of the paste. Clean and dry cardboard box. Grey and dry internal wall. Malleable red paste. Presence of grease on individual tea paper sachet.

$T_{18\ months}$ = Shiny black box. Presence of grease at the location of the paste. Clean and dry cardboard box. Grey and dry internal wall. Malleable red paste. Presence of grease on individual tea paper sachet.

$T_{2\ years}$ = Shiny black box. Presence of grease at the location of the paste. Clean and dry cardboard box. Grey and dry internal wall. Malleable red paste. Presence of grease on individual tea paper sachet.

PP cartridge:

<table>
<tr><th></th><th>Weight
Total (g)</th></tr>
<tr><td>T_0</td><td>371.91</td></tr>
<tr><td>$T_{6months}$</td><td>371.92</td></tr>
<tr><td>Deviation</td><td>+0.003%</td></tr>
<tr><td>T_{1year}</td><td>371.85</td></tr>
<tr><td>Deviation</td><td>-0.016%</td></tr>
<tr><td>$T_{18\ months}$</td><td>371.87</td></tr>
<tr><td>Deviation</td><td>-0.01%</td></tr>
<tr><td>T_{2years}</td><td>371.81</td></tr>
<tr><td>Deviation</td><td>-0.03%</td></tr>
</table>
T_0 = White opaque cartridge. No leak at stopper. No deformation.
</td><td></td><td></td></tr>
</table>

Section	Study	Method	Results	Comment	Reference
			$T_{6months}$ = White opaque cartridge. No leak at stopper. No deformation. T_{1year} = White opaque cartridge. No leak at stopper. No deformation. $T_{18\ months}$ = White opaque cartridge. No leak at stopper. No deformation. $T_{2\ years}$ = White opaque cartridge. No leak at stopper. No deformation.		
1.8.1	Wettability		Not applicable, the product is a ready-to-use paste bait.	Accept justification.	
1.8.2	Persistent foaming		Not applicable, the product is a paste.	Accept justification.	
1.8.3.1	Suspensibility		Not applicable, the product is a ready-to-use paste bait.	Accept justification.	
1.8.3.2	Dispersibility		Not applicable, the product is a paste.	Accept justification.	
1.8.4	Wet/dry sieving test		For WPs, SCs, granules and tablets therefore not applicable in this case as the product is a paste.	Accept justification.	
1.8.5	Particle size distribution in suspension		Only for powders and granules therefore Not applicable, the product is a paste.	Accept justification.	
1.8.6	Water content		Not applicable, the product is a ready to use paste bait.	No data required.	
1.8.7	Emulsion stability		Only for ECs and ready to use emulsions, therefore not applicable in this case as the product is a paste.	Accept justification.	

Section	Study	Method	Results	Comment	Reference
1.8.8	Flowability, pourability and dustability		Not applicable, the product is a paste.	Accept justification.	
1.9	Physical compatibility		Not applicable, the product is a ready-to-use paste bait and is not intended to be added or mixed with any other product.	Accept justification.	

Conclusions:

The biocidal product Ruby Paste is not explosive, oxidising or flammable and does not classify from a phys.chem. point of view. The test item is stable after storage for two years at ambient temperatures. The test item is a ready-to-use paste bait and is not intended to be added or mixed with any other product.

Compatibility with packaging material:

The test item is compatible with the following packaging for two years at ambient temperatures (20^{o}C):

PP bucket (individual tea paper sachet)
PP + PE Bag (PP inner layer and PE outer layer; individual tea paper sachet)
PP bag with cardboard box (individual tea paper sachet)
PP bait station and cardboard box (individual tea paper sachet)
PET bait station and cardboard box (individual tea paper sachet)
PP cartridge

Data requirements:

None.

3.1.4. Analytical methods

Ruby Paste was not assessed as part of the Annex I inclusion process therefore the Notifer has submitted the following methods of analysis to cover the outstanding data gaps.

Table 3.1.4.1

<table>
<tr><td>Report No.:</td><td>09-902018-007</td></tr>
<tr><td>Title:</td><td>“Analytical method validation for the determination of difenacoum in difenacoum pasta bait”</td></tr>
<tr><td>Author(s):</td><td>Ricau, Hélène.</td></tr>
<tr><td>Date:</td><td>19th October 2009</td></tr>
<tr><td>GLP: Yes/No</td><td>Yes.</td></tr>
<tr><td>Guideline study</td><td>CIPAC/3807R</td></tr>
<tr><td>Principle of the Method:</td><td>Difenacoum was extracted from the pasta bait using Methanol and heated under reflux for about 90 minutes at 80°C in an oil bath. Extract was filtered through a Whatman filter N°1 and diluted in Methanol and Acetonitrile before injection. Difenacoum was quantified by liquid chromatography using a reverse phase column and a UV detector at 310 nm.</td></tr>
<tr><td>Linearity:</td><td>See analytical method R05-912011-001 in Table 3.1.4.2.</td></tr>
<tr><td>Precision/repeatability:</td><td>See analytical method R05-912011-001 in Table 3.1.4.2.</td></tr>
<tr><td>Accuracy:</td><td>The method has been validated at 0.92 mg/l (100% level) and at 0.46 mg/l (50% level).
<table>
<tr><th>Item solutions</th><th>Reconstituted (mg/l)</th><th>Conc. found (mg/l)</th><th>Recovery (%)</th></tr>
<tr><td colspan="4">Accuracy determination at a 100% level:</td></tr>
<tr><td>Extract 1 100%</td><td>0.92</td><td>0.84</td><td rowspan="2">91</td></tr>
<tr><td>Extract 1 100%</td><td>0.92</td><td>0.84</td></tr>
<tr><td>Extract 2 100%</td><td>0.92</td><td>0.83</td><td rowspan="2">91</td></tr>
<tr><td>Extract 2 100%</td><td>0.92</td><td>0.84</td></tr>
<tr><td colspan="4">Accuracy determination at a 50% level:</td></tr>
<tr><td>Extract 1 50%</td><td>0.46</td><td>0.43</td><td rowspan="2">92</td></tr>
<tr><td>Extract 1 50%</td><td>0.46</td><td>0.42</td></tr>
<tr><td>Extract 2 50%</td><td>0.46</td><td>0.43</td><td rowspan="2">94</td></tr>
<tr><td>Extract 2 50%</td><td>0.46</td><td>0.44</td></tr>
</table>
The recovery results are between 91 - 94%, which fall within acceptable criteria.</td></tr>
<tr><td>Specificity:</td><td>To define the specificity of the analytical method, the following solutions were analysed: blank solvent, blank formulation, reference item and test item. The specificity was evaluated by the absence of interfering peaks in the area of interest.</td></tr>
</table>

	Results: No peak was observed in the blank solvent or in the blank formulation. In the reference item and in the test item, the peak at the retention time around 3.42 min represents Difenacoum. No other peak was found in the reference item or in the test item.
Interferences	No interfering peak was observed in the blank solvent, in the blank formulation and in the reference item at the retention time of Difenacoum.
Limit of quantification:	-

Conclusion:

The analytical method CIPAC/3807R has been successfully validated for accuracy and specificity. See analytical method R05-912011-001 in Table 3.1.4.2 below for information on linearity and precision.

Data requirements:

None.

Table 3.1.4.2:

Report No:	05-912011-001
Title:	"Quantification of Difenacoum 0.005% m/m in a rat poison bait"
Author(s):	Ricau, Hélène
Date:	16th June 2005
GLP: Yes/No	Yes
Guideline study:	-
Principle of the Method:	After a methanol dilution and heating under reflux for 90minutes the extract was filtered and diluted again in methanol and acetonitrile. Difenacoum was quantified by liquid chromatography using a reverse phase column and a UV detector at 310 nm. The purity of the reference standard for Difenacoum was 975 g/kg. Note: The method is the same as the method outlined in Table 3.1.4.1 above with the exception of a Whatman filter no.40 being used instead of filter no.1.
Linearity:	The response of Difenacoum is linear within the range of 0.0008 mg/ml to 0.0012 mg/ml (3 concentrations analysed twice). Correlation coefficient r^2 = 1.000. A calibration plot was included and was acceptable.
Precision/repeatability:	The precision was determined by analysing six samples (in duplicate) for the content of Difenacoum. The concentration of Difenacoum in the test item equalled 0.005% w/w or 0.05 g/kg. The % RSD = 3.40, which is within the acceptable criteria (<20%).
Accuracy:	The accuracy was determined by analysing two samples in duplicate for the content of Difenacoum. The accuracy results are between 102-105%, which are in line with current guidelines.

Sample	**Content (% w/w)**	**Average (% w/w)**	**Recovery (%)**
DEF05-0062B	0.0049	0.0049	102
DEF05-0062B	0.0049		
DEF05-0062C	0.0050	0.0050	105
DEF05-0062C	0.0051		

Specificity	The specificity was determined by injecting the blank solvent, the reference item and the test item. A shift of Difenacoum retention time was observed in the test item due to the presence of waxy co-extracts.

<table>
<tr><td></td><td>By comparison of the UV spectra at the level of the reference item peak (at 4.20 min) and the test item peak, it was shown that the peak at around 4.60 represents Difenacoum. The retention time of Difenacoum in the test item changes from about 4.60 to 4.80. No peak was observed in the blank solvent.</td></tr>
<tr><td>Active substance concentration</td><td>Two independent analysis of the test item were made.
<table>
<tr><th></th><th>Difenacoum concentration (% w/w)</th><th>Average Difenacoum concentration (% w/w)</th></tr>
<tr><td>DEF05-0062</td><td>0.005</td><td rowspan="2">0.005</td></tr>
<tr><td>DEF05-0062</td><td>0.005</td></tr>
<tr><td>DEF05-0062A</td><td>0.005</td><td rowspan="2">0.005</td></tr>
<tr><td>DEF05-0062A</td><td>0.005</td></tr>
</table></td></tr>
<tr><td>Limit of quantification:</td><td>-</td></tr>
</table>

Conclusion:

The method of analysis presented above was not validated for the paste bait only the block bait and therefore it cannot be used to cover the paste bait. However, the linearity and precision information provided covers the data gaps in study no. 09-902018-007 (see Table 3.1.4.1 above).

Data requirements:

None.

Table 3.1.4.3

<table>
<tr><td>Report No:</td><td>09-912011-004</td></tr>
<tr><td>Title:</td><td>“Quantification of difenacoum in Rattofene (Pasta Bustine)”</td></tr>
<tr><td>Author(s):</td><td>Ricau, Hélène</td></tr>
<tr><td>Date:</td><td>1st April 2009</td></tr>
<tr><td>GLP: Yes/No</td><td>Yes.</td></tr>
<tr><td>Guideline study:</td><td>-</td></tr>
<tr><td>Principle of the Method:</td><td>The objective of the study was to determine the content of difenacoum in the test item. Difenacoum was extracted from the pasta bait using Methanol and ultrasonicated for 15 minutes before analysis. Extract was diluted in Methanol before injection. Difenacoum was quantified by liquid chromatography using a reverse phase column and a UV detector at 310 nm.</td></tr>
<tr><td>Linearity:</td><td>-</td></tr>
<tr><td>Precision/repeatability:</td><td>-</td></tr>
<tr><td>Accuracy:</td><td>-</td></tr>
<tr><td>Specificity</td><td>-</td></tr>
<tr><td>Active substance concentration</td><td>Declared content of Difenacoum: 0.005% w/w
<table>
<tr><th>Test item</th><th>Difenacoum</th><th>Difencoum</th><th>Final result</th><th>Deviation</th></tr>
</table></td></tr>
</table>

		conc. (% w/w)	**mean conc. (% w/w)**	**(% w/w)**	**from declared content (%)**
	09-011A	0.0046	0.0047	0.0050	0
		0.0047			
	09-011B	0.0051	0.0052		
		0.0053			
Limit of quantification:	-				

Conclusion:

The concentration of the active substance is with FAO tolerances (± 15%).

Data requirements:

None.

Table 3.1.4.4

<table>
<tr><td>Report:</td><td>Study No. LODI.17/2009</td></tr>
<tr><td>Title:</td><td>“Analytical method validation for determination of difenacoum in difenacoum bait (pasta grain and paste).”</td></tr>
<tr><td>Author(s):</td><td>Magnier, Claire.</td></tr>
<tr><td>Date:</td><td>4th November 2009.</td></tr>
<tr><td>GLP: Yes/No</td><td>Yes.</td></tr>
<tr><td>Guideline:</td><td>CITAC/EURACHEM</td></tr>
<tr><td>Principle of the Method:</td><td>The test item was quantified by liquid chromatography using a reverse phase column and a UV detector.
Note that no exact information on the principle of the method was provided. The company clarified that the method is similar to the principle of the method used in reports 09-902018-007 and 05-912011-001.</td></tr>
<tr><td>Linearity:</td><td>The response of Difenacoum was linear over the range 80% - 120% of the test item concentration. Five measurements were made in triplicate. The correlation coefficient $r^2 > 0.99$. Calibration curves were provided and were acceptable.</td></tr>
<tr><td>Precision/repeatability:</td><td>Three solutions were prepared of a concentration C (~ 2.367 mg/l) of the product. Three injections of each solution were carried out and the RSD was calculated.
RSD <1.168</td></tr>
<tr><td>Accuracy:</td><td>The method was validated at 50%, 100% and 150% doped placebo. Three injections were carried out per solution and the average recoveries are reported below.

<table>
<tr><th></th><th>50% doped placebo</th><th>100% doped placebo</th><th>150% doped placebo</th><th>Average recovery</th></tr>
<tr><td>Paste bait</td><td>102.90%</td><td>97.78%</td><td>95.11%</td><td>98.60%</td></tr>
</table>
The recovery results are between 95-103%, which fall within acceptable criteria.</td></tr>
<tr><td>Specificity:</td><td>There was no peak observed in the paste placebo or extraction solution chromatograms. An adjacent peak appeared in the stressed paste (R = 2.25) but the resolution being higher than 2, the quantification was considered acceptable.</td></tr>
<tr><td>Limit of quantification:</td><td>0.25 mg/kg (ppm)</td></tr>
<tr><td>Limit of detection:</td><td>0.05 mg/kg (ppm)</td></tr>
</table>

Conclusion:

The method is acceptable. The information provided in this study is considered extra information only, with the exception of the LOD and LOQ information.

Data requirements:

None.

3.1.5. Analytical method for the relevant impurities, isomers and co-formulants in the biocidal product

There are no relevant impurities or isomers in the biocidal product therefore no analytical method is required.

3.4. Efficacy of the Biocidal Product

Ruby paste is a ready-to-use rodenticide paste containing 0.005% (w/w) difenacoum or 50 ppm difenacoum which is contained within a sachet. The efficacy of the product was assessed against the proposed label claims. Both amateur and professional uses are proposed in and around buildings.

The applicant submitted new data in the form of 7 trial reports where both fresh and aged paste baits were used in both laboratory and field situations to assess the palatability and effectiveness of the product. Studies were conducted according to a variety of standards and protocols. Three of the studies were conducted under laboratory conditions with wild strains of mice used in one study. The other two studies used laboratory strains of mice and rats respectively. The laboratory studies were all choice tests conducted according to recognised standards.

The studies have shown that Ruby paste is palatable to the house mouse, brown rat and black rat according to the criteria given in the TNsG on product evaluation. The bait intake was more than 20% of the total food consumption in all of the studies.

In the first laboratory choice test using captured wild mice 90% control was achieved using fresh bait. The surviving mouse ate abnormally large doses of the product but appeared much less sensitized to difenacoum. The second laboratory trial used an albino strain of mice with aged bait (12 and 24 months). All mice died with the 12 month aged bait whilst 85% control was achieved with the 2 year aged paste. The third study was conducted in an infested restaurant with a 2 year aged paste achieving 95% efficacy (based on pre-baiting consumption levels). A pigeon farm where significant quantities of alternative feed was available was chosen for the next study where wild brown rats were baited using a fresh bait product. Again based on pre and post-baiting consumption levels 95% efficacy was achieved. Another field study on brown rats in a warehouse achieved an efficacy specification of 92% with 2 year old product. The next laboratory test using albino rats and a fresh and 12-month aged bait proved no significant loss in acceptance levels/palatability or efficacy.
The final study considered was aimed at the control of an estimated population of 15-25 black rats in a pig production building with fresh bait. Excellent levels of control were achieved. 3 dead rats were found and the pest control operator reported a complete reduction in activity soon after the post-baiting period ended.

The paste bait formulation proved to be sufficiently palatable and effective against both rats and mice in the tests. Both fresh and aged baits (12 and 24 months after manufacture) achieved excellent control of the test animals with the ageing process not adversely affecting the active substance content, palatability or the effectiveness of the product. The product is concluded to be effective against brown rats, black rats and mice.

The paste formulation is not suitable for baiting in damp or wet conditions (i.e. sewers).

3.4.1. Function/Field of use

Main Group (MG):	3 – Pest control
Product-type (PT):	14
Function:	Rodenticide

Difenacoum is intended to be used to control rodent pests, both indoors and outdoors, in and around buildings, sewers, open areas and waste sites. The target species are brown rat (*Rattus norvegicus)*, black rat (*Rattus rattus)* and house mouse (*Mus musculus/domesticus)*. 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 new data on the paste formulation was provided in the form of laboratory and field studies to verify the proposed label claims.

Product	Codes*	Terms*	GIFAP codes
Pasta	VIII.4.1	Paste	RB

3.4.2. Dose/Mode of action

Ruby Paste should be placed in discrete locations within the infested area and placed in secure, (preferably dry) tamper-proof baiting stations, bait boxes or pipe sections.

For mice: place 1 to 3 sachets of 10g every 3 to 5 metres.
For rats: place 3 to 6 sachets of 10g every 5 to 10 metres.
The distance has to be adapted to the infestation level.

Difenacoum is a second generation anticoagulant which prevents blood clotting in the target organisms by inhibiting regeneration of the active form of vitamin K1. Clinical signs are progressive and occur within 2-3 days after ingestion of a toxic dose, ultimately leading to death from 4-5 days later. Effects are reversible by administration of the antidote vitamin K1 which stimulates the regeneration of the clotting factors.

Anticoagulant rodenticides are vitamin K antagonists. The main site of their 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. The anticoagulants accumulate and are 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 antidoting therapy (vitamin K1).

Signs of poisoning in rodents and other mammals are those associated with an increased tendency to bleed leading ultimately to profuse haemorrhage. After feeding on bait containing the active ingredient for 2 – 3 days the animal becomes lethargic and slow moving. Signs of bleeding are often noticeable and blood may be seen around the nose and anus. As symptoms develop the animal will lose its appetite and will remain in its burrow or nest for increasingly long periods of time. Death will usually occur within 4-5 days of ingesting a lethal dose and animals often die out of sight in their nest or burrow.

The standard concentration at which difenacoum is typically used in ready for use baits is 0.005% w/w. This concentration has been standardised over the last 25 years as the optimal concentration to deliver the benefits of the active substance. Difenacoum is inherently not very palatable and at concentrations above 50 ppm there is a risk that it can be detected by the target species. Difenacoum, even at 50 ppm, is a multi-feed product and if this concentration was lower then the time to control the target population would be extended to several weeks or even months, which is unlikely to be acceptable where there is a rodent population that needs to be controlled for public health reasons. A further disadvantage of reducing the concentration is that it takes longer to accumulate a lethal dose in the target species such that moribund rodents containing residues of the anticoagulants will be active above ground over a longer period. Because of the poisoning effects of general lethargy these are likely to be the individuals targeted by predators. Maintaining and perhaps limiting the use rate at 50 ppm ensures a lethal dose is quickly ingested and death also follows quickly.

The assessment of the biocidal activity of difenacoum demonstrates that it has a sufficient level of efficacy against the target organisms in concentration of 50 mg/kg and the evaluation of the summary data provided in support of the efficacy of the accompanying product, establishes that the product may be expected to be efficacious. Difenacoum content in the product is 50 mg/kg.

3.4.3. Organisms to be controlled

Pest organisms to be controlled by the formulated product 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.1.1.2	*Rattus rattus*	Roof rat, House rat
I.1.1.3	*Mus musculus*	House mouse

Developmental stages of target organisms to be controlled

II.1	Juveniles
II.2	Adults

*Application codes for encoding Rodenticides (PT14), edited the 16 January 2009 on website Ex-ECB, in point IVB5-0_01 of the dossier).

3.4.4. Effects on the target organisms (efficacy)

Anticoagulant rodenticides disrupt the normal blood-clotting, mechanisms, resulting in increased bleeding tendency and eventually, and profuse haemorrhage.
Signs of anticoagulant poisoning in rats and mice included lethargy, hunched posture and vain clearing in the ears. Blood around the eyes, mouth and anus, indicating internal haemorrhaging, appears prior to death.

Data requirements: None.

3.4.5. Known limitations (e.g. resistance)

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. No reports were submitted to the Rapporteur Member State about the distribution and incidence of resistance in the house mouse or black rat in Europe. Resistance was comprehensively discussed in the CAR.

Resistance management strategies

The immediate aim of resistance management is to prevent or retard the development of resistance to a given anticoagulant while, as far as is not counterproductive, permitting its continued use. The ultimate aim is to reduce or eliminate the adverse consequences of resistance.

CropLife International has published a strategy for resistant management of rodenticides (RRAC 2003). The habitat management is addressed in the strategy in addition to chemical control. The access of rodents should be restricted by physical barriers and no food should be available for rodents. Rotation between different anticoagulants is not a reliable means of managing the anticoagulant resistance, as all anticoagulants have the same mode of action and the nature of resistance is also similar. The resistant individuals can be identified by conducting a blood clotting response (BCR) test (Gill et al. 1993, RRAC 2003). The problem with the BCR test is that it has proven difficult to standardise and it produces both false positives and negatives (Pelz et al. 2005). In order to follow the

occurrence and spread of difenacoum resistance, wild rats should be continuously monitored for resistance in the rodent controlled area. The recommendations of CropLife International are quoted below.

To avoid the development of resistance in susceptible rodent populations:

- When anticoagulant rodenticide is used, 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 strategies, extend the baiting programme or apply alternative control techniques to eliminate the residual infestation (acute or sub-acute rodenticides, gassing or trapping).
- Ensure that complete elimination of the infestation is achieved.
- As appropriate during the rodenticide treatment, apply effective Integrated 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 advice on the local circumstances.
- Alternatively use an acute or sub-acute but non-anticoagulant rodenticide.
- In both cases it is essential 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 Integrated 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 known resistance and ideally beyond.
- These programmes must be effectively coordinated and should encompass the procedures identified above.

3.4.6. Humaneness

The use of difenacoum as a rodenticide could cause suffering of vertebrate target organisms. The use of anti-coagulant rodenticides is necessary as there are at present no other viable measures available to control the rodent population in the European Union. Rodent control is needed to prevent disease transmission, contamination of food and feeding stuffs and structural damage. It is recognised that such substances do cause pain in rodents but it is considered that this is not in conflict with the requirements of Article 5.1 of Directive 98/8/EC 'to avoid unnecessary pain and suffering of vertebrates', as long as effective, but comparable less painful alternative biocidal substances or biocidal products or even non-biocidal alternatives are not available.

Experimental data on the effectiveness of the biocidal product Ruby Paste against the intended target organisms

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
DIFEPASTA, containing 0.005ppm difenacoum	Wild grey mice (*Mus musculus*)	Laboratory housing for wild mice captured in warehouse. Test was performed on fresh product.	Test was carried out in accordance with Decision criteria edited by the Major Guideline for the Rodenticide efficacy assessment (*Lignes Directrices pour l'évaluation de l'Efficacité des Rodenticides*).	*Paste bait/ Semi field efficacy/ Mice/ Fresh product (T0)* DIFEPASTA, rodenticide bait containing 0.005% de Difenacoum, is sufficiently attractive and very efficacious in controlling grey mice (*Mus musculus*). The efficacy is 90% against mice.	***IIIB5-10_01*** Mahaut T., Cavellier M., CRA Gembloux, Efficacy test on DIFEPASTA, bait ready to use, containing 0.005% of Difenacoum, against grey mice (*Mus* musculus L.), ROD 2003-03-Belgagri, 20 October 2003. Unpublished
DIFEPASTA, containing 0.005ppm difenacoum	White Mice (*Mus musculus*)	Laboratory conditions. Test was performed with different storage periods of product: • Fresh product. • Product after 24	Test was carried out in accordance with Decision criteria edited by the Major Guideline for the Rodenticide efficacy assessment (*Lignes Directrices pour l'évaluation de l'Efficacité des Rodenticides*).	*Paste bait/ Laboratory efficacy/ Mice/ Product at T12 and T24 months* - At T12, all tested mice died. (n=20) - At T24, all tested animals died except 4 mice (n = 20). After 12 months storage, the efficacy of DIFEPASTA reached 100% with mice. After 2 years, the efficacy of DIFEPASTA	***IIIB5-10_02*** De Proft M., Galoux M., CRA Gembloux, Efficacy test through different period of time, performed on

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
		months		decreases to 85% with mice.	DIFEPASTA, bait ready to use, containing 0.005% of Difenacoum, rapport number 11 594 ROD 2003-003, June 2006 Unpublished
PASTA DIFE,, containing 0.005ppm difenacoum	Grey mice (*Mus musculus*)	Field study: experiment conducted in restaurant. Test was performed on fresh product. Test was performed on product stored for two years, (T24).	The method used has been inspired by the French method called "method no. 002 from Biological Trials Commission (C.E.B) ", Method for practical efficacy trials of raticides: • Adopted on 1960, derived from the work of Chitty and Dotty in the 1940. • Revised by OEPP in 1980.	*Paste bait/ Field efficacy/ Mice/ Product at T2y* Based on consumption results, PASTA DIFE achieved 95% efficacy even after 2 years under storage conditions. In the conditions of this trial, the product Pasta Dife, a paste containing 0.005% of Difenacoum as an active substance (and aged 2 years), is very effective, being markedly higher to the 90% required by the guidelines. .	***IIIB5-10_03*** - LODI, Efficacy trial: Pasta Dife/ Mice- Confidential report, LODI property, 12 pages, Feb2009. Unpublished
PASTA DIFE,, containing	Wild Brown rats (*Rattus*	Field study: experiment conducted in pigeon farm.	The method used has been inspired by the French method called "method no. 002 from	*Paste bait/ Field efficacy/ Rats/ Fresh product (T0)*	***IIIB5-10_04*** Grolleau G., Pest

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
0.005ppm difenacoum	*norvegicus*)	Test was performed on fresh product.	Biological Trials Commission (C.E.B) ", Method for practical efficacy trials of raticides: • Adopted on 1960, derived from the work of Chitty and Dotty in the 1940. • Revised by OEPP in 1980.	The efficacy reached 95%. We can say that the tested bait, PASTA DIFE, achieved a good level of effectiveness and that complies with the required criteria for licensing.	Control Assistance (PCA), Effectiveness testing under natural conditions of PASTA DIFE rat killer in paste bait form in sachets on brown rats / Test under natural conditions of a rat killer in paste bait form (PASTA DIFE) containing 0.005% Difenacoum, on Brown rats (*Rattus norvegicus*) 2002. Unpublished
PASTA DIFE,, containing 0.005ppm difenacoum	Wild Brown rats (*Rattus norvegicus*)	Field study: experiment conducted in warehouse. Test was performed on product stored for two years, (T24).	The method used has been inspired by the French method called "method no. 002 from Biological Trials Commission (C.E.B) ", Method for practical efficacy trials of raticides: • Adopted on 1960,	*Paste bait/ Field efficacy/ Rats / Product at T2years* The efficacy trial of PASTA DIFE has been conclusive, with the results permitting the declaration that the product is efficacious against Norway rats.	***IIIB5-10_05*** Biannic M-L., LODI S.A.S, Efficacy assessment of a rat killer in a field trial – product: PASTA

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
			derived from the work of Chitty and Dotty in the 1940. • Revised by OEPP in 1980.	The product achieved 92% efficacy against rats.	DIFE, July 2009. Unpublished
PASTA DIFE,, containing 0.005ppm difenacoum	Albino rats (*Rattus norvegicus*)	Laboratory conditions. Test was performed on different stage of product: • Fresh product. • Product after 12 months	Test was carried out in accordance with Decision criteria edited by the Major Guideline for the Rodenticide efficacy assessment (*Lignes Directrices pour l'évaluation de l'Efficacité des Rodenticides*)	*Paste bait/ Lab choice test/ Rats / Product at T0 and T12* • T0: 19 dead rats at the end of the trial • T12: 18 dead rats at the end of trial. Between fresh product and the 12 months aged product, loss of palatability is not significant.	***IIIB5-10_06*** De Proft M., CRA Gembloux, Study of ageing behavior of ready-to-use baits containing 0.005% of Difenacoum, PART 1: Pasta Bait, report number ROD 2008 11 BIO 6 Unpublished
NORA PASTA BAITS, containing 0.005ppm difenacoum	Black rats (*Rattus rattus*)	Field: study conducted in pig stables Test was performed on fresh product (T0)	Test was carried out in accordance with Decision criteria edited by the Major Guideline for the Rodenticide efficacy assessment (*Lignes Directrices pour*	*Paste bait/ Field efficacy/ Roof rat / Product at T0* DIFENACOUM is said to kill rodents in 5 to 21 days. In these tests the first signs of illness started after 9 days; 3 dead rats were found after 14	***IIIB5-10_07*** Feys J-L., Field trial with NORA PASTA BAITS against ROOF RATS 21 January 2010_08

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
			l'évaluation de l'Efficacité des Rodenticides)	days. After twenty days there was still some activity, which ended later (unrecorded). These results are consistent with the results expected with difenacoum baits. One can conclude that NORA PASTA Paste Baits is very well suited for the extermination of *Rattus rattus* in stables.	February 2010, batch NO 091109. Belgagri. Unpublished

3.5. Biocidal Product Risk Assessment (Human Health and the Environment)

3.5.1. Description of the intended use(s)

Ruby Paste is a rodenticide paste bait for the effective control of rodent species, both indoors and outdoors, in and around a variety of places including but not limited to buildings, sewers, open areas and waste dumps. Ruby Paste takes the form of a ready to use paste bait, packaged in a tea bag & containing 0.005% w/w (50 ppm) difenacoum, a second generation 4-hydroxy coumarin or superwafarin anticoagulant, which causes death due to massive internal haemorrhages after several days of ingestion as a consequence of an accumulated lethal dose. The target species are brown rat (*Rattus norvegicus*), black rat (*Rattus rattus*) and house mouse (*Mus musculus / domesticus*). Other than the active ingredient, the product is composed of food-grade materials forming a bait base.

3.5.2. Hazard Assessment for Human Health

No new exposure studies have been submitted for evaluation. Signs of poisoning in rodents and other mammals are those associated with an increased tendency to bleed, leading ultimately to profuse haemorrhage. Non-target organisms are most at risk from secondary poisoning, i.e. consumption of rodent carcasses by predators such as raptors. Difenacoum is highly lipid soluble and persists with a long half life once ingested. This is in contrast to warfarin and is a characteristic of some of the second generation 4-hydroxy coumarin derivatives that makes them particularly hazardous with repeated exposure because of their ability to bioaccumulate and display very prolonged anticoagulant activity in exposed mammals including humans.

3.5.2.1. 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 for difenacoum prepared by the Rapporteur Member State Finland. The threshold limits and labelling regarding human health risks listed in Annex 4 "Toxicology and metabolism" must be taken into consideration. There are no new studies post annex I that impact on the original toxicological assessment carried out by the RMS.

Summary of acute toxicity data for the active substance Difenacoum

Parameter	Test material	Species	Result	Classification	Ref.
Acute Oral Toxicity	Difenacoum technical, 99.7 % w/w purity	Rat CRL:(WI)BR (Wistar), Female: 3/dose, (two low dose groups)	$5 < LD_{50} < 50$ mg/kg bw	T+; R28 / Acute Tox. 2; H300	[redacted] (2004) Study Code: 04/904-001P
	Acceptability (Y/N): Y		**Method**: OECD Guidelines 423 (2001)		**GLP (Y/N): Y**
	Comments: No deviations. The method used was not intended to allow the calculation of a precise LD50 value.				
Acute Dermal Toxicity	Difenacoum technical, 99.7 % w/w purity	Rat CRL:(WI)BR (Wistar), female / male: 5/sex/group	LD_{50} = 51.5 mg/kg bw (females)	T+; R27 / Acute Tox. 1; H310	[redacted] (2004) Study Code: 04/904-002P
	Acceptability (Y/N): Yes		**Method:** OECD Guidelines 402		**GLP (Y/N): Yes**
	Comments: Males and females in low dose group (20 mg/kg bw) only. Only females in the other 2 dosing groups (55 & 155 mg/kg bw). 2 out of 5 males died in the low dose group, compared with 3 out of 5 for the mid and 5 out of 5 for the top dose groups. The LD_{50} value was calculated for female rats only (51.5 mg/kg bw) even though males were apparently more sensitive. Due to the overall mortality (both sexes) the risk phrase R27; Very toxic in contact with skin, was warranted by the RMS.				
Acute Inhalation	Difenacoum	Rat	Males: LC_{50} =	T+; R26 / Acute	[redacted] (1995)

Parameter	Test material	Species	Result	Classification	Ref.
Toxicity	technical, 97.7 % w/w purity	CRL:(WI)BR (Wistar), female / male	20.74µg/L/4h Females: LC_{50} = 16.27µg/L/4h	Tox. 2; H330	Report no. MLS/9825
	Acceptability (Y/N): Yes		**Method:** Complies with OECD 403		**GLP (Y/N): Yes**
	Comments: Groups of 5 male and 5 female rats were exposed, nose only for a single four hour period to aerosols of difenacoum technical material. The aerosols had concentrations of 3.28, 7.52 and 20.33µg/L. Two males and four females were killed in extremis following exposure to 20.33µg/l. Clinical signs, delayed deaths and post mortem findings were consistent with anti-coagulant poisoning. Only slight signs of toxicity were seen in animals exposed to the lower concentrations. The LC_{50} value is 20.74µg/L/4h (95% confidence limits 12.03-39.76) for males and 16.27 µg/L/4h (95% confidence limits 10.03-26.24) for females.				
Acute Dermal Irritation	Difenacoum technical, 99.7 % w/w purity. Batch 03652.	Rabbit, male, NZW, 3 in total	No irritation.	none	[redacted] (2004). Study code: 04/904-006N
	Acceptability (Y/N): Yes		**Method:** Complies with OECD 404		**GLP (Y/N): Yes**
	Comments: Pure difenacoum technical was applied in a single dose of 0.5 g to the shaven skin of all experimental animals. After 4 hours test article was removed and animals were examined 1, 24, 48 and 72 hours after patch removal. No irritation symptoms (erythema and oedema) or other signs were recorded (Draize scores of 0, all time points). Difenacoum is not a skin irritant.				
Acute Eye Irritation	Difenacoum technical, 99.7 % w/w purity. Batch 03652.	Rabbit, male, NZW, 3 in total	No irritation.	none	[redacted] (2004). Study code: 04/904-005N
	Acceptability (Y/N): Yes		**Method:** OECD 405 (2002)		**GLP (Y/N): Yes**
	Comments: 0.1 g of difenacoum technical was applied to the left eye of each animal. The untreated right eye served as control. The treated eyes of the test animals were not washed out following the instillation of 0.1g of test item. The eyes were examined at 1, 24, 48, and 72 hours after application. There was no evidence of irritation by the active substance (Draize scores of 0 for 24, 48, & 72 hour time points).. Difenacoum is not an eye irritant.				
Skin Sensitisation (M & K study)	Difenacoum, as a technical concentrate of the a.s. (2.6% w/v) in solvent. Batch SC7396.	Guinea Pig, (Dunkin-Hartley), male & female. Control group: 5 male, 5 female. Test group: 10 male & 10 female.	No sensitisation.	none	[redacted]y (1996). Report number CIT/14302
	Acceptability (Y/N): Yes		**Method:** OECD 406		**GLP (Y/N): Yes**
	Comments: Preparation for induction; intradermal injections at day 0, a 1% (w/w) preparation of the technical concentrate in isotonic saline solution and Freund's complete adjuvant. On day 7, sodium laurylsulphate in vaseline (10% w/w) was applied on the test site to induce local irritation. On day 8, this same test site was treated by topical application of the test substance (technical concentrate with 2.6% difenacoum w/v) or the vehicle (control group) and was covered by an occlusive dressing for 48 hours. Challenge was performed on day 22 with undiluted test substance (technical concentrate with 2.6% difenacoum w/v). Test substance and vehicle were maintained under an occlusive dressing for 24 hours. Skin reactions were evaluated at 24 and 48 hours. There were no clinical signs or mortalities during the study. No cutaneous reactions were recorded after the challenge application. Positive controls were acceptable. Dilution of a liquid sample of very low water solubility with isotonic saline solution is highly questionable.				
Skin Sensitisation (Buehler study)	Difenacoum, as a technical concentrate of the a.s. (2.6% w/v) in solvent. Batch TCP 0047/94.	Guinea Pig, (Dunkin-Hartley), male & female. Control group: 5 male, 5 female. Test group: 10 male & 10 female.	No sensitisation.	none	[redacted] (1995) Report No. MLS/10009
	Acceptability (Y/N): Yes		**Method:** OECD 406		**GLP (Y/N): Yes**
	Comments: On day 1 the test site was treated by topical application of the test substance (10				

Parameter	Test material	Species	Result	Classification	Ref.
	% w/v preparation of the formulation in deionised water) or the vehicle (control group) and was covered by an occlusive dressing for 6 hours. This was repeated at 7 day intervals to give a total of three 6 hour exposures over 14 days. The animals were left untreated for 14 days prior to challenge. Challenge consisted of topical application of test substance (10 % and 3% w/v preparation of the formulation in deionised water) and vehicle were maintained under an occlusive dressing for 6 hours. Skin reactions were evaluated at 24 and 48 hours. There were no clinical signs or mortalities during the study. No cutaneous reactions were recorded after the challenge application. Dilution of a liquid sample of very low water solubility with deionised water is highly questionable.				

Difenacoum is acutely very toxic by the oral and inhalation routes. Difenacoum may also be considered very toxic by the dermal route. It is not a skin or eye irritant. Difenacoum is not a skin sensitiser.

Summary of difenacoum subchronic, chronic, mutagenic and reproductive toxicity.

Repeated oral administration of difenacoum to rats in diet at doses up to 0.06 mg/kg bw/day for 90 days gave rise to increased kaolin-cephalin times and histological findings indicative of toxic effects related to anticoagulation only at the highest dose level. No other adverse effects were observed. A suggestive NOAEL value can be established at 0.03 mg/kg bw/day.

Repeated oral exposure to difenacoum results in toxic effects related to anticoagulation giving cause to concern for serious damage to health by prolonged exposure. Furthermore, based on the results of the acute dermal and inhalation toxicity studies and route-to-route extrapolation, it is justified to assume a similar concern for serious damage to health by prolonged exposure through dermal and inhalation routes also. Difenacoum classifies for repeated dose toxicity; T; R48/23/24/25, Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed.

Difenacoum was not mutagenic in bacterial cells, but the mutation frequency and chromosome aberrations were increased in mammalian cells *in vitro*. All *in vivo* genotoxicity tests were negative. It can be concluded that difenacoum does not classify as mutagenic.

Developmental toxicity tests have been performed in two species. In the rabbit, the LOAEL value for maternal toxicity is 0.001 mg/kg bw/day. A higher incidence of foetal effects (skeletal variations) was observed at two dose levels compared to controls, but the incidence was not dose dependent. The NOEL/NOAEL value for developmental toxicity is 0.01 mg/kg bw/day. The NOEL/NOAEL for maternal toxicity in rats is 0.03 mg/kg bw/day. There was no evidence of embryotoxic or teratogenic potential following oral exposure of pregnant rats at 0.09 mg/kg bw/day (=NOEL/NOAEL for developmental toxicity).

Clear developmental toxicity was not observed in rabbits or rats. However, difenacoum should be considered teratogenic to humans because it contains the same chemical moiety responsible for the teratogenicity of warfarin, a known human teratogenic agent, and it has the same mode of action that is a known mechanism of teratogenicity in humans. The possible teratogenic effects of coumarin-related compounds cannot be detected using the standard OECD 414 study design, because the exposure period has to be adjusted to correspond to the critical periods in rat for the observed effects in humans. Furthermore, maternal bleeding has to be prevented, e.g. by vitamin K supplementation, to achieve a biochemical blockade of net extrahepatic vitamin K – dependent processes. Based on read across from warfarin, difenacoum is classified for reproductive toxicity, Repr. Cat. 1; R61, "May cause harm to the unborn child". In addition, specific concentration limits have been set by the RMS due to the very high acute toxicity associated with difenacoum.

Effects on fertility have been studied in a rat multi-generation study. In this study, dose levels had to be lowered twice during the course of the study due to extensive mortality. Regardless of the very low

doses, it can be concluded that difenacoum does not have clear effects on fertility. However, there were indications of disturbed oestrous cycling perhaps due to ovarian hormonal disturbances. Because the main findings related to fertility (irregular oestrous cycles in treated animals in both generations and ovarian cysts at a maternally toxic dose of 0.06 mg/kg bw/day in F0 females) did not affect the fertility index, no severe increase in post-implantation loss (increased spontaneous abortions have been associated with warfarin treatment in humans) were observed, and warfarin is not classified for fertility, it is considered that classification for fertility effects is not necessary for difenacoum. In the literature, there are no indications of adverse fertility effects associated with warfarin or vitamin K recycling blockade. It is considered that the possible effects on ovarian function are adequately covered by the risk phrase R48/23/24/25.

There are no studies on neurotoxicity. Other studies with difenacoum did not reveal any neurotoxic potential and there are no structural alerts evident for this endpoint.

Data requirements: (List if applicable)
None.

3.5.2.2. Toxicology of the biocidal product

The toxicology of the biocidal product 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.

Summary of acute toxicity data for the biocidal product Ruby Paste

Parameter	Test material	Species	Result	Classification	Ref.
Acute Oral Toxicity	Difenacoum pasta bait Batch: LAB290109	Rat, female, Sprague-Dawley, SPF Caw, 6 in total.	LD_{50} > 2000 mg/kg bw	none.	[redacted] (2009). study number: TAO423-PH-09/0086
	Acceptable (Y/N): Yes		**Method:** OECD 423 (24 April 2002)		**GLP (Y/N): Yes**
	Comments: No mortality occurred during the study at 2000mg/kg. There were no clinical signs observed. Macroscopic examination of the animals at the end of the study revealed a thickening of the corpus (5/6 animals) with presence of red spots (3/6 animals). Considering the water solubility of the active substance is extremely low, the use of a water vehicle for gavage is questionable. 2g of paste was mixed with 10 ml water prior to use.				
Acute Dermal Toxicity	Difenacoum paste bait. Batch: LAB290109	Rat, male & female, Sprague-Dawley, SPF Caw, 10 in total.	LD_{50} > 2000 mg/kg bw	none.	[redacted] (2009). study number: TAD-PH-09/0086
	Acceptable (Y/N): Yes		**Method:** OECD 402 (24 Feb 1987)		**GLP (Y/N): Yes**
	Comments: No mortality occurred during the study at 2000mg/kg. No cutaneous reactions or systemic clinical signs related to the administration of the test item were observed. Some slight pink colouration of the test site was observed. Considering the water solubility of the active substance is incredibly low, the use of a water vehicle for dermal application is questionable.				
Acute Inhalation Toxicity	none	none	none	none	none
	Acceptable (Y/N):		**Method:**		**GLP (Y/N):**
	Comments: Inhalation exposure is not appropriate for a wrapped paste formulation. Active substance has very low volatility and is only present at 0.005% (w/w) in the product. Company justification accepted.				
Information on mixture of biocidal products	none	none	none	none	none
	Acceptable (Y/N): Yes		**Method:**		**GLP (Y/N):**
	Not applicable since following the proposed uses of the product and the label claims, the rodenticide is not intended to be used in a mix with other biocidal products. Company justification accepted.				

Parameter	Test material	Species	Result	Classification	Ref.
Acute Skin Irritation	Difenacoum pasta bait Batch: LAB290109	Rabbit, male, NZW, 3 in total	No irritation	none	[redacted] (2009). study number: IC-OCDE-PH-09/0086
	Acceptable (Y/N): Yes		**Method:** OECD 404 (24 April 2002)		**GLP (Y/N): Yes**
	Comments: The test item was applied at a dose of 0.5 g, on an undamaged skin area of one flank of each animal for 4 hours. No cutaneous reactions (erythema and oedema) were observed on the treated areas. Company report accepted. Results do not warrant classification under the conditions of the study.				
Acute Eye Irritation	Difenacoum pasta bait Batch: LAB290109	Rabbit, male, NZW, 3 in total	Slight irritation	none	[redacted] 2009). study number: IC-OCDE-PH-09/0086
	Acceptable (Y/N): Yes		**Method:** OECD 405 (24 April 2002)		**GLP (Y/N): Yes**
	Comments: The test item was applied at a dose of 0.1 g instilled into the conjunctival sac of one eye in each animal. Ocular conjunctivae reactions observed during the study were slight to moderate and totally reversible by 4 days in the three animals. Company report accepted. Results do not warrant classification under the conditions of the study.				

Animal number	A9661	A9678	A9679
Corneal Opacity	0	0	0
Iritis	0	0	0
Redness	1.7	0	0.7
Chemosis	1.7	0.3	0.3
Result	-	-	-

Parameter	Test material	Species	Result	Classification	Ref.
Skin Sensitisation (M&K)	Difenacoum pasta bait Batch: LAB290109	GuineaPig, female, Dunkin-Hartley strain, 5 in negative control, 11 in treated groups.	negative	none	[redacted] 2009). study number: SMK -PH-09/0086
	Acceptable (Y/N): Yes		**Method:** OECD 406 (17 July 1992)		**GLP (Y/N): Yes**
	Comments: The study format was a Guinea Pig maximisation method skin sensitization test. The test item was given at 40% at intradermal induction and 70% and 35% at challenge phase. The study used 5 concurrent controls and 11 treated animals.				

Animals	70% (MNIC)				35% (1/2 MNIC)			
	24 hours		48 hours		24 hours		48 hours	
	Erythema	Oedema	Erythema	Oedema	Erythema	Oedema	Erythema	Oedema
Negative control group								
1882 F	0 depilation	0	0	0	0	0	0	0
1883 F	0 depilation	0	0	0	0	0	0	0
1884 F	0 depilation	0	0	0	0	0	0	0
1885 F	0 depilation	0	0	0	0	0	0	0
1886 F	0 depilation	0	0	0	0	0	0	0
Treated group								
1887 F	0	0	0	0	0	0	0	0
1888 F	0 depilation	0	0	0	0	0	0	0
1889 F	0 depilation	0	0	0	0	0	0	0
1890 F	0	0	0	0	0 depilation	0	0	0
1891 F	0 depilation	0	0	0	0 depilation	0	0	0
1892 F	0	0	0	0	0	0	0	0
1893 F	0 depilation	0	0	0	0	0	0	0
1894 F	0 depilation	0	0	0	0 depilation	0	0	0
1895 F	0	0	0	0	0	0	0	0
1896 F	0 depilation	0	0	0	0 depilation	0	0	0
1897 F	0 depilation	0	0	0	0 depilation	0	0	0

Parameter	Test material	Species	Result	Classification	Ref.
	Under the condition of the test Difenacoum pasta bait does not require classification for sensitisation.				

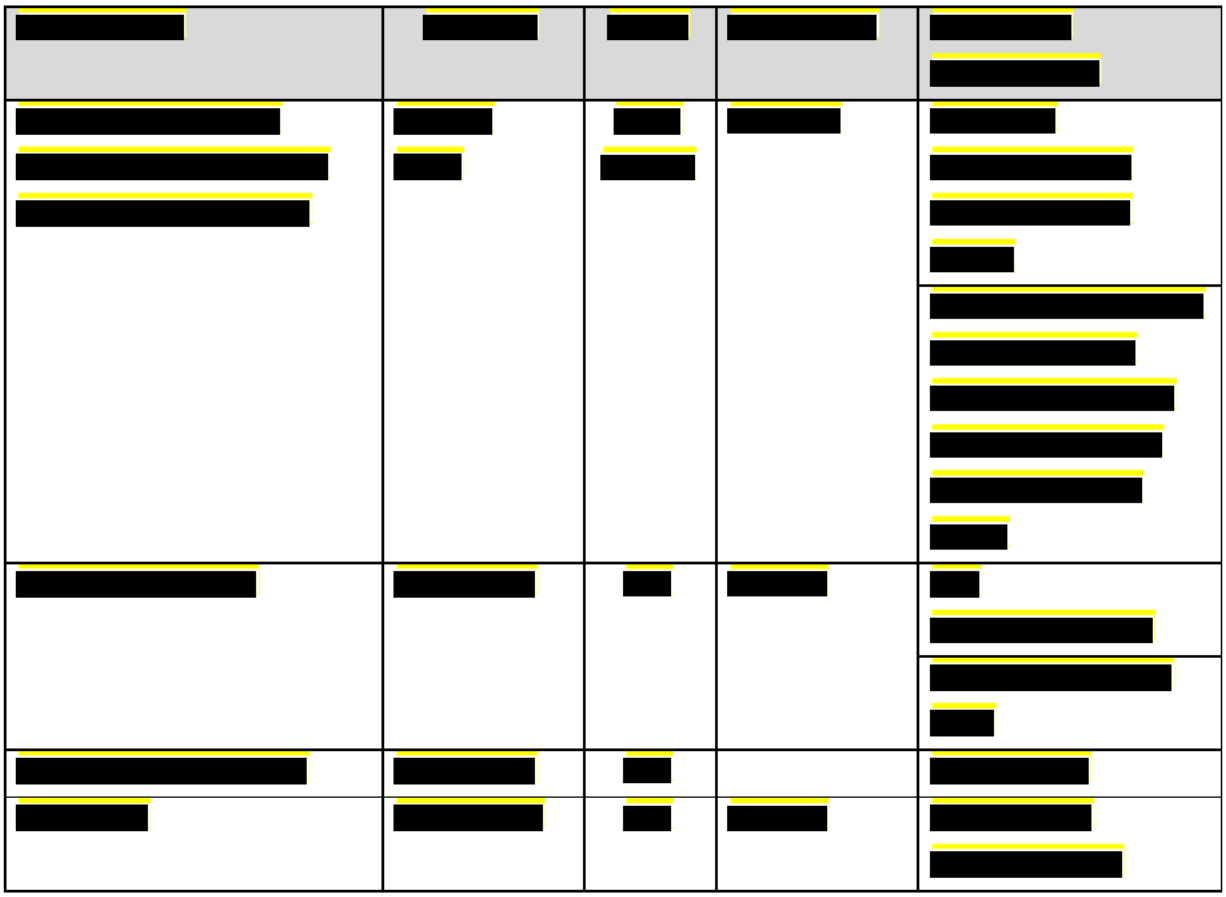
Conclusion:
According to the results of the toxicological studies, Ruby Paste (containing 50mg/kg difenacoum) does not classify with respect to Directive 1999/45/EC or Regulation (EC) No 1272/2008. However, safety phrases and precautionary statements are proposed by the Rapporteur. One issue that seems to be not addressed by the acute studies above is the solubility of difenacoum in aqueous media. According to the physical / chemistry properties of the active substance, difenacoum has extremely low water solubility (4.83×10^{-4} g/l at pH 6.5 or < 0.5mg per litre, 3.72×10^{-3} g/l at pH 8.9). This affects the amount of active substance in a dose such that between 5 – 40% of the expected amount might be present in the acute oral study, there is no way of being certain from the available data.

Data requirements: (List if applicable)
None.

3.5.2.3. Toxicology of the co-formulants (substances of concern)

The biocidal product contains no other substances in quantities that would be of toxicological concern. The majority of these components are food grade materials and are not classified.

Summary of toxicological properties of the co-formulants in Ruby Paste



				[redacted]
[redacted]	[redacted]	[redacted]		[redacted]
[redacted]		[redacted]		[redacted]
[redacted]	[redacted]	[redacted]		[redacted]
[redacted]	[redacted]	[redacted]		[redacted]

3.5.3. Exposure Assessment for Human Health

There are no exposure or risk assessment studies based on the paste, the notifier has instead performed exposure and risk modeling using wax blocks and this is accepted by the Rapporteur. In addition, since TM III 06 there has been general agreement to model paste bait in sachet by using the data determined for wax blocks in the Chambers Study. The paste and the blocks are similar in bait composition, additionally, the paste baits are wrapped in a bag or sachet, and thus exposure to humans and the environment is considered to be lower than that expected with the blocks. The most relevant route of exposure to the active substance is the dermal route. The bait product typically takes the form of a semi-solid fatty block with a strong sweet smell containing 0.005% w/w difenacoum. The wax blocks are made in a range of shapes and sizes, being typically rectangular, and weigh 20g (though they can of course be larger in size). The blocks are dyed various bright colours to make them unattractive to wildlife, and birds.

The active substance has a low vapour pressure, therefore the potential for evaporation is low, and hence the potential for inhalation exposure is low. Inhalation exposure is only of concern during the formulation process where the active substance has a potential for becoming airborne when mixed with dry bait ingredients. In the case of wax blocks (and paste), inhalation exposure is irrelevant.

Any potential oral exposure will be indirect exposure via possible release to the environment. Other possible exposure scenarios include dermal contact with dead animals and accidental ingestion of poison baits by children.

In general there is very little data available for use in modelling human exposure to rodenticides. Any calculations must be viewed in the context of the use of many assumptions and extrapolations from only a few studies. The values presented for exposure assessment and risk characterisation must be viewed at best as being crude estimates.

Key Endpoints for Exposure Assessment

The key endpoints for exposure assessment are the No Observed Adverse Effect Level (NOAEL) for Margin of Exposure (MOE) estimates and the Acceptable Exposure Level (AEL). The lowest Low Observed Adverse Effect Level (LOAEL) in a repeated dose study, (developmental toxicity study in rabbits, LOAEL value for maternal toxicity is 0.001 mg/kg bw/day, Difenacoum CAR, 2009), was chosen as the basis to establish the AEL and calculate an NOAEL for MOE. Risk characterisation in the original CAR for difenacoum and in documents supplied by the notifier in support of Ruby Paste state the bioavailability of difenacoum as 68% following oral absorption of a single low dose in bile duct cannulated rats (Swan, 2006, Difenacoum – Metabolism in Rats. Report no. PLG 0005). However, a true measure of bioavailability must also consider enterohepatic circulation because it is important to consider the reabsorption of lipophilic compounds with long half-lives from the gastrointestinal tract such as difenacoum. Bioavailability may be under-estimated in this case but it is taken as 68% for the

purpose of exposure assessment in this document. Details for the derivation of each endpoint are described below.

NOAEL for MOE:

LOAEL value for rabbit maternal toxicity is 0.001 mg/kg bw/day. To extrapolate from LOAEL to NOAEL an assessment factor of 2 is considered justified due to the steep dose response to acute effects such as lethality. Correction for bioavailability of 68% is applied.

(0.001 ÷ 2) × (68/100) = **3.4×10^{-4} mg/kg bw/day**

AEL:

LOAEL value for rabbit maternal toxicity is 0.001 mg/kg bw/day. Default assessment factors of 10 for inter-species variability and 10 for inter-individual variability are applied. Furthermore, due to the toxicological significance and uncertainty in the database, an additional safety factor of 3 for teratogenicity is used for all anticoagulant rodenticides. An additional assessment factor of 2 is supported due to concern over the higher potency of the second generation anticoagulants compared to warfarin and the much higher vulnerability of human foetuses to disturbances in vitamin K recycling and availability compared to rodents. Correction for bioavailability of 68% is applied.

((0.001 ÷ (10 × 10 × 3)) / 2 = 1.67×10^{-6} mg/kg bw/day

taking into account 68% bioavailability...

(1.67×10^{-6}) × (68/100) = **1.13×10^{-6} mg/kg bw/day**

3.5.3.1. Exposure to professional users

The paste baits and wax blocks are used in plastic bait boxes or covered/protected bait points or tied to a fixed object. For professional use, the operator is trained in the correct use of the bait, i.e. placement, number of bait points or stations required based on the infestation rate area, the number of bait blocks per bait point and safe handling procedures. The use of PPE, i.e. disposable gloves and a face-mask may be used when loading bait boxes and disposing of remaining bait and carcasses. However, when the block is contained within a bait trap there will be no exposure of the operator to the product. PPE (coverall, boots and gloves) is required as standard when the blocks are used in sewage systems.

For rats each bait point should contain up to a maximum 10 blocks (i.e. 200g of bait). A mouse bait point will only contain 2 bait blocks. Bait points for mice should be placed 5m apart, although this can be reduced to 2m in areas of high infestation and for rats, bait points should be 10m apart or reduced to 5m apart in high infestation areas. Bait points should be checked frequently and carcasses removed. Operators should search for all rodent bodies in and around the baited area for disposal. Bait points should be removed, in a typical campaign, 6 weeks after initial placement. Sites should not be re-baited until a new infestation is observed.

In sewers, blocks are tied or nailed to stable surfaces above the water level. Blocks placed in sewers are not normally removed. Rodent bodies in sewers will not be collected for disposal

During use, professional pest control operators will be exposed to rodenticide product during (1) the mixing and loading phase (not applicable for ready-to-use paste or wax block baits, however it is valid in the case of grain baits), (2) loading of bait boxes/bait points and application of the blocks in sewers, (3) post application activities including the disposal of old bait and carcasses. Exposure will be via the dermal route and principally involve the hands.

Exposure calculations (Wax Blocks) – professionals

The CEFIC/EBPF Rodenticides Data Development Group conducted an operator exposure study using flocoumafen (which may be considered a suitable surrogate for all other second generation anti-coagulants) to determine exposure during simulated use of rodenticide baits (*Chambers* 2004, unpublished, confidential). This study examined exposure to wax blocks and grain bait. Guidance is also taken from a confidential paper entitled "Harmonised Approach for Rodenticides" by the German Competent Authority, Bundesanstalt für Arbeitsschutz und Arbeitsmedizin (BAuA).

The daily exposure frequency and its division between different tasks are based on a survey organised by CEFIC (and based on a questionnaire answered by selected pest control companies in several EU countries), and on an agreement between Member States on the common approach for exposure assessment and ECB guidelines (see CAR September 2009). A dermal absorption of 0.047% is used for all exposure calculations based on the Roban wax block, during 24 h after 8 h exposure in an *in vitro* study with human skin (see CAR September 2009).

The Chambers study determined exposure from the application phase from the following scenario: 5 operators secured 5 compressed wax blocks (each of 20g, in total 100g bait per box) into a bait station by pushing bait mounting pegs in the stations through holes in wax blocks. Three trials were conducted with 1, 5 and 10 times securing of these wax blocks. Since the results of 1, 5 and 10 securing are similar all trials were included in the calculation of the 75th percentile by the RMS. The proposed value of **28mg (of wax bait) per manipulation** is valid for loading of one bait box with 100g of wax blocks (a single manipulation constitutes the placement of a single bait station). Since the recommended amount for rat control is up to 200g bait per bait point, this exposure value is multiplied by a factor of 2 because only 100g was used in the Chambers Study. The proposed value of **56mg (of wax bait) per manipulation** is valid for loading of one bait box with 200g of wax blocks.

For professional operators the potential total daily dermal exposure (assuming the previously agreed number of 60 manipulations from TM III/10 is applied) from the application-phase is **3360mg** wax block product (i.e. 56mg × 60 bait sites).

The Chambers study determined exposure from the disposal or post-application phase from the following scenario: 5 operators emptied a loaded bait station by sliding the wax block off the mounting pegs into a 10 L plastic bucket. This is done 1, 5 and 10 times. The proposed value of **5.75 mg per manipulation (determined by the RMS, Difenacoum CAR 2009)** is valid for cleaning of one bait box. For the resulting potential dermal exposure of post-application-phase the agreed number of 15

manipulations (TM III/10) should be taken into account. For the post-application phase the potential total daily dermal exposure is **86 mg** wax block product (i.e. 5.75mg × 15 disposal manipulations). The size of one bait block is ignored and the figure is valid for different sized blocks (e.g. 10g, 100 g).

The calculation of PCO (pest control operator) and amateur dermal exposure in placing and clean-up of rodenticidal wax blocks, taking into account measured values (75th percentiles), defaults according to ECB guidelines and the common agreement on daily exposure frequencies (TM III/10) is presented in the following table.

Pest Control Operator, No PPE:	
Amount of exposure to product (75th percentile) during securing of 10 wax blocks (200g). Value is for placement of 1 bait station.	56.0 mg
Amount of difenacoum on fingers/hands (0.005% in wax block)	56 mg × (0.005 / 100) = 2.8×10^{-3} mg
Systemic dose per application at 1 bait station: (dermal absorption 0.047%, bw 60kg)	(2.8×10^{-3} mg x (0.047 / 100)) / 60kg = 2.2×10^{-8} mg/kg
Amount of exposure to product (75th percentile) during clean-up and disposal per bait station	5.75 mg
Systemic dose (difenacoum concentration 0.005%, dermal absorption 0.047%, bw 60 kg) per clean-up of one bait station.	2.25×10^{-9} mg/kg
Assuming 'reasonable worst case' scenario of 60 bait sites and 15 clean-ups, systemic dose per day	((2.2×10^{-8} mg/kg × 60) + (2.25×10^{-9} mg/kg × 15)) = **1.35×10^{-6} mg/kg/day**
<u>Expressed as a % of the AEL:</u> AEL = 1.13×10^{-6} mg/kg bw/day	**120%**

Pest Control Operator, With PPE (gloves)	
Default 10-fold reduction of exposure.	**1.35×10^{-7} mg/kg/day**
<u>Expressed as a % of the AEL:</u> AEL = 1.13×10^{-6} mg/kg bw/day	**12%**

Non-Trained Professional (e.g. farmer), No PPE:	
Systemic dose resulting from application of 10 bait blocks into each bait point (200g bait), placement of five bait points plus five bait sites cleaned per day, no PPE (difenacoum concentration 0.005%, dermal absorption 0.047%, bw 60 kg).	((2.2×10^{-8} mg/kg × 5) + (2.25×10^{-9} mg/kg × 5)) = **1.21×10^{-7} mg/kg/day**
<u>Expressed as a % of the AEL:</u> AEL = 1.13×10^{-6} mg/kg bw/day	**11%**

Non-Trained Professional (e.g. farmer), With PPE (gloves):	
Default 10-fold reduction of exposure.	**1.21×10^{-8} mg/kg/day**
<u>Expressed as a % of the AEL:</u>	

AEL = 1.13×10^{-6} mg/kg bw/day **1%**

3.5.3.2. Exposure to non-professional users

Description of tasks and amateur exposure to Difenacoum

Bait boxes for use by the general public may be supplied as sealed units or as lockable, tamper-proof units that may be refilled by the user. Bait may be used in covered/protected bait points, rather than bait boxes, where appropriate.

Calculations for non-professional exposure are presented below; the first scenario assumes no exposure during application phase while the second scenario assumes that the bait boxes would have to be loaded by the user. As for the non-trained professionals, it is assumed that a non-professional user places ten bait blocks per site(200g) on five bait sites and cleans five bait sites per day.

Product type	Exposure scenario	PPE	Inhalation uptake	Dermal uptake
14	Non-professional (amateur)	None	Not relevant	1.1×10^{-8} mg/kg/day[1)]
14	Non- professional (amateur)	None	Not relevant	1.21×10^{-7} mg/kg/day[2)]

1) scenario 1; 2) scenario 2.

Scenario 1: No dermal contact during placing of baits due to sealed bait boxes. Potential exposure is only during clean-up. Default exposure value for cleanup is 5.75mg product per bait site, difenacoum present at a concentration of 0.005% (w/w), 60kg body mass, 0.047% dermal absorption value. The value is calculated from the cleanup exposure per bait station of ((2.25×10^{-9} mg/kg) × 5).

Scenario 2: Assuming that conventional bait boxes are loaded then the exposure is equal to that of the non-trained professional (e.g. farmer) with no PPE. As a worst case scenario, scenario 2 can be taken forward to risk assessment.

3.5.3.3. Exposure to children/workers/general public

Bait points should be covered or protected in such a way to prevent access to the bait. However, the ingestion of wax block bait by infants has been assessed as a potential secondary exposure route associated with the use of difenacoum in rodenticide products. Secondary exposure is anticipated to be acute in nature. The pasta bait has been manufactured to prevent incidental poisoning to both non-target animals and man, i.e. children. The Ruby Paste "tea sachets" are hard plastic and are either locked or sealed shut to prevent access to the bait. If bait sachets 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. The estimated exposure for the 'transient mouthing of poison bait' scenario is either 2.5×10^{-2} mg/kg or 5.0×10^{-5} mg/kg, depending on the default assumptions. This results in Margin of Exposure (MOE) values of 0.01 or 6.8, respectively. It

shows that infants are at significant risk for secondary exposure, i.e. there is no safe use for children.

For the 'transient mouthing of poison bait' scenario, either 5g (User Guidance) or 10 mg (TNsG, with bittering agent) of the product is assumed to be swallowed by an infant per poisoning event.

TNsG Assumptions: Transient mouthing of poison bait (10mg) treated with repellent:
(10mg × 0.00005) / 10kg bw
=
5.0×10^{-5} mg/kg bw.

Relative to the calculated NOAEL for MOE:
3.4×10^{-4} / 5.0×10^{-5} = **6.8**

User Guidance Assumptions: Transient mouthing of poison bait (5000mg) without repellent;
(5000mg × 0.00005) / 10kg bw
=
2.5×10^{-2} mg/kg bw.

Relative to the calculated NOAEL for MOE:
3.4×10^{-4} / 2.5×10^{-2} = **0.01**

The RMS considered that in connection with transient mouthing of poison baits, infants are also exposed via the dermal route while handling the bait. This however is assumed to play a minor role relative to the amount that could be ingested. It is therefore not included in the overall exposure scenario.

3.5.3.4. Exposure to consumers from residues in food

Not applicable

3.5.3.5. Overall Summary

The exposure data based on measurements in simulated use conditions are acceptable and should be used in risk assessment. The models assume that inhalation exposure is of minor importance for wax blocks (paste bait) compared with dermal exposure. The calculations have been made with the assumptions of rat control, and there are no separate calculations to assess exposure in mice control in which smaller bait sizes are used.

3.5.4. Risk Characterisation for Human Health

3.5.4.1. Professional users

The exposure assessment for professional pest control operators (PCOs) under reasonable worst case assumptions (60 loadings and 15 clean-ups/day), as presented in section 3.3.3.1, yielded a potential dermal exposure leading to a systemic dose of 1.35×10^{-6} mg/kg/day for an unprotected operator during bait handling operations. Comparison to calculated NOAEL for MOE shows that the use of rodenticide baits containing 0.005% difenacoum results in a margin of exposure of 252.

Since pest control operators wear protective gloves by default during pest control operations, a refined assessment is conducted. The resulting margin of exposure (MOE = 2519) indicates that the use of rodenticide baits containing 0.005% difenacoum does not cause a risk for PCOs if gloves are worn.

3.5.4.2. Non-professional users

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 1.21×10^{-7} mg/kg/day for an unprotected person. Even without PPE, the resulting margin of exposure (MOE = 2804) indicates that use of rodenticide baits containing 0.005 % difenacoum is not a risk at the stated exposure frequency. A refined assessment was, nevertheless, conducted since wearing of protective gloves is recommended in the instructions for use. The resulting margin of exposure (MOE = 28041) indicates a high level of protection for non-trained professional users when gloves are worn.

The result of the risk assessment concerning use of difenacoum in bait Blocks indicates that the acceptable exposure level is exceeded for trained professionals (PCOs) not using PPE (gloves) and that the AEL is not exceeded for professionals with PPE and non-trained professionals using the product with or without PPE (gloves). The risk is at an acceptable level without gloves for non-trained professionals. However, use of protective gloves is recommended in all cases for hygiene reasons. Exposure during manufacture of the active substance and formulation of products is beyond the scope of BPD and therefore has not been addressed in this document.

Blocks are supplied either in pre-sealed units or as loose blocks for use in covered/protected bait points or refillable bait boxes. An exposure assessment has been performed taking into account potential exposure both from application and post-application tasks as a worst-case scenario. In the calculations, amateurs were assumed to load five bait points and clean five bait points per day without PPE. The estimated daily systemic dose, 1.21×10^{-7} mg/kg/day, results in an MOE value of 2804 showing that there is also little risk to amateurs.

3.5.4.3. Children/Workers/general public

As a potential secondary exposure route, associated with the use of difenacoum in rodenticide products, ingestion of wax block bait by infants has been assessed. 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 indicating that infants are at risk of poisoning. This should be addressed by ensuring all difenacoum products targeted for amateur use are provided in sealed packs and tamper resistant bait boxes with a bittering agent. The potential exposure due to dermal contact with poisoned rodents is not included in the risk assessment because the available scenarios are unrealistic.

3.5.4.4. Consumers from residues in food

Not applicable, product is not used to treat food stuffs.

3.5.4.5. Overall Summary

The calculations presented have been made with the assumptions of rat control, and there are no separate calculations to assess exposure for mice control in which smaller bait sizes are used.

Using both the MOE and AEL approaches for risk assessment indicates 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 with PPE, untrained professionals and amateurs (with and without PPE). The product is deemed suitable for authorisation and appropriate personal protective equipment is advised.

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 in sealed packs and the use of tamper resistant bait boxes are essential to reducing the risk of secondary exposure. Baits should not be placed where food, feeding stuffs or drinking water could be contaminated.

Workplace operation	**PPE**	**Exposure path**	**Dose (mg/kg bw/day)**	**MOE**	**%AEL**
Trained Professional: Placing of wax block baits and clean-up	None	Dermal, hands	1.35×10^{-6}	252	120
Trained Professional: Placing of wax block baits and clean-up	Protective gloves	Dermal, hands	1.35×10^{-7}	2519	12
Non-Trained Professional: Placing of wax block baits and clean-up	None	Dermal, hands	1.21×10^{-7}	2804	11
Non-Trained Professional: Placing of wax block baits and clean-up	Protective gloves	Dermal, hands	1.21×10^{-8}	28041	1
Amateur: Placing of wax block baits and clean-up	None	Dermal, hands	1.21×10^{-8}	28041	1
Secondary Exposure Transient Mouthing of bait by infants	--	Oral	5.0×10^{-5} (TNsG)	7	--
			2.5×10^{-2} (User Guidance)	0.01	--

3.3.5. Hazard Assessment for the Environment

The Finnish Competent Authority evaluated the active substance difenacoum in 2009. No further fate and behaviour studies were identified as necessary to support the authorisation of the active substance. An overview of the EU fate and behaviour and the ecotoxigology of difenacoum in the environment is presented hereunder:

Environmental fate and behaviour

Difenacoum has two stereogenic centres and thus consists of four diastereoisomers (two enantiomer pairs). The methods of analysis used in the available environmental fate and behaviour studies did not resolve the enantiomers, therefore no information is available on the rate of breakdown or transformation of the different individual enantiomers.

Difenacoum is hydrolytically stable at pH 4, 7 and 9 at 25°C (DT_{50} >1 yr). Under aqueous photolysis degradation is rapid (half-life about 8 hours or less). In the photolysis study of Activa/Pelgar two breakdown products above 10% were detected, and a proposal for the identification of structures was made. In the natural aquatic environment photodegradation is regarded to be of minor significance since surface water is normally deeper and muddier compared to conditions in laboratory studies. Therefore the aqueous photolysis metabolites were not considered in the exposure assessment.

Difenacoum has an estimated half-life of approximately 2 hours in air. Consequently, it is predicted to have a negligible effect on stratospheric ozone. Difenacoum shows no absorption in the so-called atmospheric window (800-1,200 nm) and therefore, according to the TGD on risk assessment (Part II, Section 3.7.2) is not a potential greenhouse gas.

Difenacoum is not readily or inherently biodegradable. Difenacoum degrades slowly under aerobic conditions in soil, with a measured DT_{50} of 439 days (20°C). Photolysis may contribute to the degradation in soil. No information is provided on soil metabolites in the CAR. The CA for difenacoum (FI) stated *"due to the low direct exposure and difenacoum being not ready biodegradable and probably absorbed to soil, the ecotoxicological significance of soil metabolites is regarded low".*[31]

Difenacoum has a measured pKa of 4.84 (20°C) and a water solubility that is pH dependent (range <0.05 mg/L at pH 4 to 61 mg/L at pH 9, pH 7 value 1.7 mg/L all at 20°C). Therefore, in the environmentally relevant pH range of soils, adsorption of difenacoum would be expected to be pH dependent, with adsorption being lower in alkaline soils. No batch soil adsorption experiments were provided for difenacoum. The experimentally derived Koc (HPLC method) was considered as unreliable during the Annex I evaluation for difenacoum. A QSAR (Koc value of 1.8×10^6 (EUSES- Predominantly hydrophobic) was used in the EU exposure assessment instead of the experimentally derived value. The Reviewer notes this value is only relevant for the undissociated form of difenacoum, which will not reflect the dissociation state of difenacoum in the normal pH range of most agricultural soils. The Reviewer also notes the value of the Koc strongly influences the distribution of the active substance to water/sediment, water/sludge and water/soil. The CA for difenacoum stated they do *"..not require more data on Koc, because the significance of Koc is low when uses in sewer and in and around buildings are considered. The choice of Koc does not change the conclusions of the risk assessment. See rationale below:-The surface water PEC calculated using measured (OECD 121) Koc of 67 is appr. 10^{-5} mg/l, with PNECwater of 0.06 µg/l the risk ratio will be 0.00016*[32]*. Low Koc will give lower PECs for soil through sewage sludge and thus high Koc is the worst case. In direct soil exposure from bait boxes (1%) only initial PECs without degradation or further*

31 Response to Comments from Member States and Participant on the Draft Competent Authority Report on Difenacoum of the Activa/Pelgar Brodifacoum and Difenacoum Task Force (3.7.08) 34/46

32 The Reviewer notes this is two orders of magnitude higher than the PEC specifed in the CAR (PEClocal water 2.35×10^{-7} mg/L) which was calaucated with the QSAR Koc.

distribution have been calculated and thus the choice of Koc value does not have any impact on the soil risk from direct exposure. The same applies for indirect exposure via faeces and urine. The secondary poisoning risk through earthworm would be higher with low Koc, because of higher porewater concentrations, but there is a secondary poisoning risk also with the high Koc. The applicant does not have access to data in other dossiers."18

In a rat metabolism study 41-71% of the dose administered was excreted according to analysis of rat faeces and urine (7 days after single dosing, low and high dose). Four major metabolites >10 %AR were identified:

Isomers of hydroxylated difenacoum
F7 (11.3 %)
F8 (7.3 %)

Isomers of difenacoum-based structure, which formed glucuronide conjugates
F5 (12.2 %)
F6 (8.0%)

No data on the toxicity of the four major metabolites are available. The 4-hydroxy coumarin moiety is still present and thus the metabolites could be potent as anticoagulants. For the EU risk assessment the metabolites were treated collectively as one and were assumed to have the same toxicity as the parent. The Reviewer notes no PECs for metabolites are provided in the difenacoum CAR. This is presumably because it is covered by the risk assessment for difenacoum based on the assumptions stated in the CAR. To refine the EU exposure assessment for the active substance it was assumed 40% of the excreted amount in urine and faeces is metabolised and that 40 % of the administered total amount is unchanged difenacoum in faeces.[33] The Reviewer notes unchanged difenacoum was present at maximum at 2.9 %applied in faeces. Consequently, assuming that ~40% of the excreted amount in urine and faeces is metabolised is conservative.

Ecotoxicology

No further ecotoxicological studies were identified as necessary to support the authorisation of the active substance and no studies were submitted to support the authorisation of the product. Based on the environmental fate and behaviour of difenacoum, as outlined above, the environmental exposure assessment was conducted.

Difenacoum is very toxic to fish, aquatic invertebrates and algae. Toxicity to fish, the most sensitive species, is based on the inhibition of blood clotting. The mode of action in aquatic invertebrates and algae is unknown. The $PNEC_{water}$ is 0.06 µg/l based on the LC_{50} for Rainbow Trout. Difenacoum did not inhibit growth or respiration of aquatic microbes. The PNEC for sewage treatment plant (STP) micro-organisms 480 µg/l (the limit of solubility). In the absence of any ecotoxicological data for sediment-dwelling organisms, the $PNEC_{sediment}$ was calculated using the equilibrium partitioning method resulting in a value of 2.51 mg/kg (wet weight).

Exposure of soil organisms to difenacoum by direct contamination of soil may occur following use in and around buildings and waste dumps. It is also possible that soil may become exposed following the spreading of sewage sludge from a sewage treatment plant that has been exposed to difenacoum used in sewers. Difenacoum caused no toxic effects in the acute earthworm test and a $PNEC_{soil}$ of 0.877 mg/kg wet weight was determined.

33 "*40% is from the total administered radioactivity, part of the radioactivity remains in the rat (30-60%). Non-identified radioactivity in urine and faeces is minor part and individual unidentified metabolites each account for <4%"* Source: Response to Comments from Member States and Participant on the Draft Competent Authority Report on Difenacoum of the Activa/Pelgar Brodifacoum and Difenacoum Task Force (3.7.08)

No tests on the soil micro-organisms or plants are required, because difenacoum is not expected to be particularly toxic to them on the basis of the mode of action and available data (Activated sludge, respiration inhibition test/Sorex limited).

Difenacoum is very toxic to birds the $PNEC_{oral}$ of birds was determined to be 0.5 µg/kg food or 0.1 µg/kg bw/d. Difenacoum is also very toxic to mammals The $PNEC_{oral}$ for mammals is 7 µg/kg in food or 0.3 µg/kg bw/d. These $PNEC_{oral}$ values were used in risk characterisation of primary and secondary poisoning.

Difenacoum has a considerable bioaccumulation potential in aquatic and terrestrial organisms. One applicant submitted a fish bioconcentration test, but it was not considered as acceptable by the RMS. The waiving of fish bioconcentration test was accepted, because the test was judged not possible to perform technically, and because an estimated BCF value could be used in the risk assessment. The calculated BCFs range from 9010 (aquatic) to 477 729 (terrestrial). As outlined in the Assessment Report for Difenacoum (17-09-2009) the calculated BCFs estimate bioconcentration in the whole animal and not in the fat tissue, so BCF for difenacoum in fat tissue of the non-target vertebrates is unknown. The risk assessment indicates that accumulation of difenacoum in predators results in unacceptable effects when compared with the environmental acceptance criteria given in the Directive and TNsG on Annex I Inclusion. However, as outlined below, the proposed use of Ruby Paste, according to instructions, by professional users, should minimise the impact of such high calculated BCF values.

3.3.6. Exposure Assessment for the Environment

An overview of the environmental exposure assessment for Ruby Paste is presented in this section. Detailed calculations are provided in the Annexes accompanying this Report. The environmental exposure assessed during the review process and the current intended use is similar.

Ruby Paste, contains 50 mg difenacoum per kg of product and is used to control rats and mice. The proposed use of the product is indoors in warehouses and outbuildings and outdoors in and around buildings, waste dumps and open areas. The directions for use for sachets, pre-baited bait box and cartridges are

Rats: 30-60 g of paste spaced 10 m apart (5 m apart in high infestation areas). Typical treatment time 6 weeks.

Mice: 10-30 g of paste spaced 5 m apart (3 m apart in high infestation areas). Typical treatment time 6 weeks.

3.3.6-1. Aquatic compartment

Ruby Paste, whilst not being supported for use in sewers, was assessed in sewer systems to control rats as a worst-case situation for the STP and aquatic compartment. Consequently, exposure to the aquatic compartment occurs when sewage treatment plants make releases to water bodies. Based on

worst case assumptions[34] taking the metabolism of difenacoum into account the maximum predicted environmental concentration (PEC) of the active substance for microorganisms in the STP is 5.91 x 10^{-6} mg/L. The corresponding amount in surface water is 1.55 x 10^{-7} mg/L. The maximum permissible concentration by directive 80/778/EEC (amended by 98/83/EC) of 0.1 µg/L is not exceeded in surface waters. 6.32 x 10^{-3} mg/kg wwt is predicted to occur in sediment during an emission episode. Full details of the calculations are contained in the Annexes.

Exposure of surface water to the active substance following its use in the scenario "in and around buildings" is considered negligible according to the ESD. This argumentation was also accepted for the Annex I inclusion of difenacoum.

3.3.6-2. Atmosphere

The use pattern and means by which difenacoum is deployed together with its low volatility, ensure that exposure of the atmosphere is highly unlikely. Difenacoum has an estimated half-life of approximately 2 hours in air. Consequently, it is predicted to have a negligible effect on stratospheric ozone. Difenacoum shows no absorption in the so-called atmospheric window (800-1,200 nm) and therefore, according to the TGD on risk assessment (Part II, Section 3.7.2) is not a potential greenhouse gas.

3.3.6-3. Terrestrial compartment

Exposure of soil to the active substance occurs via residues present in sewage sludge after using the product in sewers and via direct and disperse release after the use of the product in and around buildings, open areas and waste dumps.

Based on worst-case assumptions of these typical usage patterns and release mechanisms, the maximum concentration in agricultural soil (averaged over 30 d) after 10 years of sludge application from STP is 2.41 x 10^{-3} mg/kg wwt. The highest concentration of difenacoum in soil from in and around buildings[35] is 0.0348 mg/kg wwt under realistic worst case conditions (200 g of product/bait point, each

[34] Realistic worst-case: 21 days campaign

Day 0: 300 wax blocks, Day 7: 100 wax blocks replenished Day 14: 50 wax blocks replenished Day 21: 0 wax blocks replen.

Maximum emission during 1st week: 100 blocks

Amount of product used in control operation: 30 kg

Fraction of a.i. (substance) released: 0.66. Difenacoum metabolism data taken into account.

Standard STP scenario (TGD) 200 L/day, 10,000 inhabitants

To refine the EU exposure assessment for the active substance it was assumed 40% of the excreted amount in urine and faeces is metabolised and that 40 % of administered total amount is unchanged difenacoum in faeces. This was also used in the current exposure assessment.

[35] In and around buildings

Amount of product used in control operation for each bait box: 0.25 kg (ESD) and 0.2 kg, which is >3 times the proposed amount.

bait point is 5 m apart). The application rate modelled is approximately three times higher than the proposed use rate for rats.

The notifier also proposes to use the product in open areas. The Reviewer notes no scenario is prescribed in the ESD for the use of a paste formulation in open areas. The notifier used the scenario for the outdoor use of impregnated grain in open areas to support the authorisation of Ruby Paste. The Reviewer notes this scenario was used to assess the exposure arising from a paste formulation for the active substance coumatetralyl during the Review process. Consequently, in light of this precedent the Reviewer deems it acceptable to use the impregnated grain open area scenario as a surrogate for the paste formulation. Under realistic worst-case conditions the ESD assumes one application site is treated twice with the product. The fraction released during use and during application is 0.25. The exposed soil area is assumed to be the lower half of the burrow wall surrounding an 8 cm diameter tunnel, with a soil mixing depth of 10 cm and up to 30 cm from the entrance hole. The amount of product used at each refilling in the control operation is not specified by the ESD. 200 g/bait point was used by the notifier in the exposure assessment. This is approximately three times higher than the proposed use rate for rats. The local concentration arising in soil after a campaign is predicted to be 0.346 mg/kg wwt (200 g of product/bait point).

Based on worst case assumptions, usage patterns and release mechanisms[36], the maximum concentration in soil from applications in waste dumps is predicted to be 0.0074 mg/kg wwt under realistic worst case conditions.

According to the Assessment Report (17-09-2009), difenacoum is not readily or inherently biodegradable. Difenacoum degrades slowly under aerobic conditions in soil, with a measured DT_{50} of 439 days. This suggests difenacoum has the potential to accumulate in soil if applications were made in consecutive years to the same area. However, even in the unlikely event of such use soil accumulation would not be expected to pose a problem given the large margins of safety observed for the terrestrial compartment.

Realistic worst-case: 21 day campaign Bait stations: 10 No. of replenishments: 5 Bait stations are 5 m apart.

Fraction released due to spillage: 0.01 Fraction ingested: 0.99

Fraction released of ingested: 0.4 (Difenacoum metabolism data taken into account)

Spillage area: 0.09 m^2 (0.1 m around station) Frequented area: 550 m^2 (10 m around building

Open areas (Grain scenario used as a surrogate for paste formualtion)

Amount of product used at each refilling in the control operation: 200 g

Realistic worst-case: 6 day campaign Bait stations: 1 No. of replenishments: 2

Fraction of product released to soil during application 0.05 Fraction of product released to soil during use 0.2

[36] Waste dumps

Amount of product used in the control operation: 40 kg/ha (ESD default). According to the proposed use 26.46 kg/ha could be used.

No. of replenishments: 7 Fraction of product released to soil 0.9

3.3.6-4. Groundwater

Exposure of groundwater may occur as a result of soil exposure which occurs via residues present in sewage sludge after using the product in sewers and via direct and disperse release after the use of the product in the scenarios in and around buildings, open areas and waste dumps. As an indication for potential groundwater levels, the concentration in porewater of agricultural soil was taken. It should be noted that this is a worst-case assumption, neglecting transformation and dilution in deeper soil layers. A summary of the PECs obtained are presented in **Table 3.3.6.4-1**. All concentrations are less than the EU trigger value of 0.1 μg/L.

Table 3.3.6.4-1. Predicted Environmental Concentration (μg/L) of difenacoum in groundwater

Compartment/Scenario	ESD realistic worst case scenario	ESD realistic worst case scenario with modified input parameters	ESD normal use scenario with modified input parameters
Sewer scenario			
Groundwater/porewater	9.94×10^{-5}	7.29×10^{-5}	
In and around buildings scenario			
Groundwater/porewater	1.5×10^{-3}	1.1×10^{-3}	3.2×10^{-4}
Open areas			
Groundwater/porewater	5.23×10^{-3}	1.05×10^{-2}	---
Waste dump			
Groundwater/porewater	2.24×10^{-4}	2.5×10^{-4}*	---

*****For high infestations of rats the baits are spaced 5 m apart. According to calculations provided by the Reviewer this could potentially result in a maximum of 441 bait points (21 100 m lines of 21 baits, 5 m apart) in a 1 ha area during high infestations. This would correspond to ~26.46 kg of product. This is higher than the default value considered in the ESD under realistic worst-case conditions. Consequently the notifiers exposure calculation (22 kg/ha) is not sufficient to support this use. The Reviewer generated new exposure calculations for this use (26.46 kg/ha)

3.3.6-5 Primary and Secondary poisoning

A clear risk exists for primary and secondary poisoning in both the aquatic and terrestrial compartments for birds and mammals. The empirical risk assumes direct or indirect consumption of the deployed bait. For primary poisoning the initial PEC_{oral} values as outlined above (Section 3.3.5) assume that there is no bait avoidance by the non-target animals and that they obtain 100% of their diet in the treated area and have access to Ruby Paste. Even when avoidance and elimination are taken into account the empirical exposure levels result in unacceptable risks to birds and mammals (see ANNEX VI).
The PEC_{oral} values determined for characterising the risk of secondary poisoning to fish, earthworm and rodent eating birds and mammals is unacceptable. The values assume accumulation based on the PEC values determined for each relevant compartment. Even when avoidance and elimination are taken into account the empirical exposure levels to difenacoum from Ruby Paste result in unacceptable risks to birds and mammals (see ANNEX VI).

3.3.7. Risk Characterisation for the Environment

Ruby Paste is used in and around buildings, open areas and waste dumps to control rats and mice. Ruby Paste, whilst not being supported for use in sewers, was assessed in sewer systems to control rats as a worst-case situation for the STP and aquatic compartment. Consequently, exposure to the aquatic compartment occurs through the STP route. Exposure of soil to the active substance occurs via residues present in sewage sludge and via direct (spillages) and disperse release (deposition only by urine and faeces) after the use of the product in the scenarios in and around buildings, open areas and waste dumps. No new data related to the environment fate and behaviour or the ecotoxicology of the active substance has been submitted by the applicant. PECs were calculated in accordance with the ESD for PT14. These calculations are outlined in the previous section.

3.3.7-1 Aquatic compartment

The use of Ruby Paste containing difenacoum in the sewer system may lead to contamination of surface waters and sediment through sewage water and STP. Exposure of surface water to the active substance following its use in the scenario *"in and around buildings"* is considered negligible according to the ESD. The derivation of the PEC and PNEC values is outlined in ANNEX VI. The PEC values, as determined by fate and behaviour, reflect the predicted concentrations of difenacoum in water following the use of Ruby Paste in the relevant scenarios. Aquatic organisms are therefore assessed for effects of difenacoum in their environment for the relevant use scenarios. The PEC/PNEC ratios, for the realistic worst case scenarios with normal use, were less than 1 in all compartments indicating that difenacoum does not cause unacceptable risk to aquatic organisms, sediment-dwelling organisms or biological processes at the sewage treatment plant. As difenacoum is not readily biodegradable, the degradation of difenacoum in sediment is also anticipated to be low. However, according to the PEC calculations, concentrations in sediment would be low (6.32×10^{-3} mg/kg wwt), and below the level that causes unacceptable risk, thus risk for unacceptable accumulation in sediment can be regarded low.

No risk is identified to either groundwater/porewater or surface water used as drinking as in both cases the maximum permissible concentration by directive 80/778/EEC (amended by 98/83/EC) of 0.1 μg/l is not exceeded in the ESD realistic worst case scenarios for uses in sewer, in and around buildings, open areas and waste dumps.

3.3.7-2 Atmospheric compartment

The use pattern and means by which difenacoum is deployed together with its low volatility, ensure that exposure of the atmosphere is highly unlikely. Difenacoum has an estimated half-life of approximately 2 hours in air. Consequently, it is predicted to have a negligible effect on stratospheric ozone. Difenacoum shows no absorption in the so-called atmospheric window (800-1,200 nm) and therefore, according to the TGD on risk assessment (Part II, Section 3.7.2) is not a potential greenhouse gas.

3.3.7-3 Terrestrial compartment

Exposure of soil to the active substance occurs via residues present in sewage sludge after using paste bait in sewers and via direct (spillages) and disperse release (deposition by urine and faeces) after the use of the product in and around buildings, open areas and waste dumps. The derivation of the PEC and PNEC values is outlined in ANNEX VI. The PEC values, as determined by fate and behaviour, reflect the predicted concentration of difenacoum in soil following the use of Ruby Paste in the relevant scenarios. Terrestrial organisms are therefore assessed for effects of difenacoum in their environment for the relevant use scenarios. The PEC/PNEC ratios, for the realistic worst case scenarios with normal use, were less than 1 for all the compartments assessed: sewer, in and around buildings, open areas and waste dumps. Therefore, normal use of Ruby Paste does not cause unacceptable risk to terrestrial organisms.

3.3.7-4 Primary poisoning

Acute risk

For the acute exposure situation, no $PNEC_{oral}$ is determined and no quantitative risk characterisation is performed. Instead a qualitative assessment is done by comparing LD_{50} values to the expected concentration of the active substance in birds and mammals following their direct ingestion of Ruby Paste bait. One day consumption of difenacoum containing baits is not assumed to kill birds and mammals with the exception of foxes. The other animals would suffer from sublethal effects, although

mortality cannot be excluded. The assumption is based on the comparison of expected concentration in animals after one day exposure without elimination. The species specific sensitivity differences are not taken into account in this assumption (i.e. no assessment factor is applied to the LD_{50} values), and hence this description must not be considered as a risk characterisation.

Long-term risk

According to the ESD the comparison of concentration in the non-target animals and the $PNEC_{oral}$ describes the long-term risk for primary poisoning. The PEC values generated for the long-term risk assessment were calculated assuming direct ingestion of Ruby Paste by non-target birds and mammals. The expected concentration in the non-target animals are calculated after five days intake and elimination. The elimination is assumed to be 40%. The Step 2 assumptions are used for the calculation of the expected concentrations (see Annex VI for the calculations). The calculations show that mammals and birds would suffer long-term effects of difenacoum if they ingested Ruby Paste. Due to high food intake in relation to the body weight the birds are at considerably higher risk than mammals.

Primary poisoning incidents can be minimised by preventing the access of non-target animals, including companion animals, to the baits. Ruby Paste contains the bittering agent, denatonium benzoate, as a deterrent (0.195 % w/w) which may further reduce the risk of primary poisoning of non-target birds and mammals. It is assumed in the ESD that if the rodenticide baits are used according to the label instructions, the risk for primary poisoning is negligible. However, it may not be possible to exclude exposure of all non-target animals, as the baits have to be accessible to target rodents, they may as well be accessible to non-target mammals and birds of equal or smaller size than the target rodents.

3.3.7-5 Secondary poisoning

In the terrestrial and aquatic environments birds and mammals may be at risk of secondary poisoning if they feed on contaminated organisms following the use of Ruby Paste. The derivation of $PNEC_{oral}$ for birds and mammals is outlined in Annex VI. The derivation of PEC values for fish eating and earthworm eating birds and mammals is outlined in ANNEX VI. These values assume direct ingestion of Ruby Paste by the prey, and relies on PEC values generated by environmental fate and behaviour for the relevant compartments. The risk assessment for rodent eating birds and mammals applies an estimated concentration in rodent prey based on the assumption of direct ingestion of Ruby Paste by rodents (see ANNEX VI).

Aquatic

For the aquatic food chain, the PEC/PNEC ratios exceed 1 for both fish eating birds and mammals. Despite this calculation, the risk of secondary poisoning via the aquatic food chain is considered insignificant due to low water solubility and high adsorption tendency of difenacoum. It is also assumed that mechanical screening of sewage water reduces the concentration in the recipient water, although this reduction cannot be quantified. The negligible risk of secondary poisoning of fish-eating birds is supported by the monitoring data in the UK where the fish-eating birds, cormorants, herons, goosanders and red-breasted mergansers have not been involved in any of the reported incidents.

Terrestrial

For the terrestrial environment, following the use of Ruby Paste, the PEC/PNEC ratios exceed 1 for earthworm and rodent eating birds and mammals indicating unacceptable risk. Contaminated rodents are the most likely source for difenacoum residues in raptorial birds and mammalian predators.

Acute risk-Rodent eating birds and mammals

A qualitative assessment of the acute secondary poisoning is made by comparing the concentration in the rodents to LD_{50} values from acute oral studies. Rodents are assumed to eat entirely on bait containing difenacoum and the non-target animals are assumed to consume entirely poisoned rodents. The calculations of PEC_{oral} values are outlined in Annex VI. The results indicate that birds are likely to survive and mammals are likely to die if they eat poisoned rats. The species specific sensitivity differences or other aspects normally covered by the assessment factors are not taken into account in the qualitative assessment.

Long-term risk-Rodent eating birds and mammals

The quantitative risk assessment for long-term exposure to Ruby Paste, based on ESD guidance parameters, for susceptible and resistant rodents indicate that difenacoum causes unacceptable risk for non-target vertebrates. In laboratory studies on Barn Owls, fed on contaminated rodents, accumulation of difenacoum was noted. 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 fat 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.

Bioaccumulation of difenacoum in predators has been shown in the measurements of difenacoum residues in the animal carcasses found from the field in the United Kingdom during monitoring campaigns (for details see Annex VI). While the PEC/PNEC ratios based on measured concentration in rats and mice were lower than the respective figures calculated according to the ESD, they were still considerably higher than 1 indicating risk of secondary poisoning of Barn Owls. Population level effects of difenacoum have not been studied and while all available information indicates risk, it does not tell the frequency of secondary poisoning incidents among wildlife. The conclusion, however, is that difenacoum causes a high risk for secondary poisoning.

The risk for secondary poisoning is more difficult to control than that for primary poisoning, as poisoned rodents may be available for predators for several days after intake of difenacoum. The use of difenacoum inside the buildings may reduce the secondary poisoning risk, but does not exclude it as the exposed rodents may move out from the building. The secondary poisoning can be excluded only in fully enclosed spaces where rodents cannot move to outdoor areas or to areas where predators may have access. When using difenacoum as a rodenticide all possible measures have to be taken in order to minimize secondary poisoning of the non-target animals. The measures include use of tamper resistant bait boxes, collection of unconsumed baits after termination of the control campaign and collection of dead rodents during and after the control campaign.

6.4. Measures to protect man, animals and the environment

The information submitted covering the requirements as described in the TNsG on Data Requirements, common core data for the product, section 8, points 8.1 to 8.8 is provided below.

6.4.1. Methods and precautions concerning handling, use, storage, transport or fire

Methods and precautions concerning handling and use:

- Always read the label before use and follow the instructions provided.
- Do not decant product into unlabelled containers.
- Avoid all unnecessary exposure, in particular avoid ingestion.
- Keep away from food, drink and animal feeding stuffs.
- Do not smoke eat or drink while handling this product.
- Baits must be secured in tamper resistant bait boxes to minimise the risk of consumption and poisoning to children, companion animals and other non-target animals.
- Bait boxes must be placed in areas inaccessible to children, companion animals and non-target animals.
- Bait boxes must always be clearly labelled “Do Not Touch” and warn of the contents.
- In public areas (such as business premises, schools, hospitals etc) it must be clearly signed that rodenticide control is in operation. Signage must provide information on the risks of interfering with the product and dead rodents.
- Dead rodent bodies must be collected during all control operations to minimise the risk of consumption and poisoning to children, companion animals and other non-target animals.
- It is illegal to use this product for the intentional poisoning of non-target, beneficial and protected animals.
- Wash hands and face after application and use of the product, and before eating, drinking or smoking.

Methods and precautions concerning storage:

- Store in a cool, dry, well-ventilated place
- Store locked up in the original container
- Store original container tightly closed
- Keep/store out of reach of children and companion animals
- Keep/store away from food, drink and animal feedstuffs.

Methods and precautions concerning transport:

Not classified as dangerous for transport.

Methods and precautions concerning 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.

Specific hazards:

Not applicable

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.

6.4.2. Specific precautions and treatment in case of an accident

Personal precautions

Wear suitable protective clothing, gloves and eye/face protection, if applicable and where appropriate.

- Respiratory Protection: No special respiratory protection equipment is recommended under normal conditions of use with adequate ventilation.
- Hand protection: Wear gloves.
- Skin protection: No special clothing/skin protection equipment is recommended under normal conditions of use.
- Eye protection: Not required.

- Ingestion: When using this product, do not eat, drink or smoke

Personal treatment

- General advice: In the case of accident or if you feel unwell, seek medical advice immediately (show the label where possible and report the authorisation number).
- Skin contact: May cause skin irritation. Remove contaminated clothing Wash off immediately with soap and plenty of water. If irritation persists obtain medical attention Contaminated clothing should be washed and dried before re-use.
- Eye contact: May cause eye irritation. Rinse immediately with plenty of water and seek medical advice.
- Inhalation: Unlikely to present an inhalation hazard unless excessive dust is present. Move to fresh air. Obtain medical advice immediately.
- Ingestion: If swallowed, seek medical advice immediately.

ADVICE FOR DOCTORS:

Difenacoum is an indirect anti-coagulant. Phytomenadione, Vitamin K1, is antidotal. Determine prothrombin times not less than 18 hours after consumption. If elevated, administer Vitamin K1 until prothrombin time normalises. Continue determination of prothrombin time for two weeks after withdrawal of antidote and resume treatment if elevation occurs in that time.

Report all incidents of poisonings to the relevant national poisons centre; include information on the product authorisation number, product trade name and active substance. In Ireland, this is the National Poisons Information Centre, Beaumont Hospital, Dublin (01-8092166)

Environmental precautions

- Prevent accidental exposure of the product to the environment.
- Keep un-used bait locked-up and in secure storage containers
- Bait must be secured in tamper resistant bait boxes in areas away from drains, water courses and non-target organisms.

Environmental treatment

- Clean up accidental spillages promptly by sweeping or vacuum.
- If the product gets into water or soil, it should be removed mechanically.
- Transfer to a suitably labelled container and dispose of to a certified waste disposal operator for incineration and licensed waste disposal site.
- Subsequently, wash the contaminated area with water, taking care to prevent the washings entering sewers or drains.
- For further instructions, see section 3.4.6 below.

6.4.3. Procedures for cleaning application equipment

No application equipment is needed, therefore, no specific cleaning for equipment is required

If necessary, following use, bait boxes should be washed with detergent and water. The bait box should be washed out 3 times (triple rinsed).

6.4.4. Identity of relevant combustion products in cases of fire

Not applicable.

6.4.5. Procedures for waste management of the biocidal product and its packaging

Dispose of packaging, remains of unused product and dead rodents to a certified waste disposal operator for incineration and licensed waste disposal site.

6.4.6. Possibility of destruction or decontamination following accidental release

Air:
Difenacoum has a very low vapour pressure, and decomposes at around 220°C and therefore does not boil. The formulated product is a wax block. The risk of release of the active ingredient or the product to the atmosphere is negligible.

Water (including drinking water):
The octanol-water partition coefficient of difenacoum is high, and hence the active ingredient will remain in the product. The product is know 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, require users **not** to place bait points where water could become contaminated (excepting sewers), 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.

Soil:
Sources for release to the soil compartment include: sludge spreading, transport of bait by rodents, degradation of dead rodent remains hidden in burrows and excretion of the active ingredient by poisoned rodents. Bioremediation will probably prove the most effective method of decontamination, as 30% biodegradation in a 28 day ready biodegradation study suggests.

In the event of spillage of an appreciable amount of product, this material should be collected for incineration.

6.4.7. Undesirable or unintended side-effects

Toxic to mammalian and avian species, including domesticated animals, wildlife and humans. Therefore the risk to these non-target species should be considered when using bait.

6.4.8. Poison control measures

The wax blocks are dyed (e.g. red or blue) to make them unattractive to wildlife, and birds in particular. In addition, in case of accidental ingestion, the presence of a dye may help to confirm that there has been ingestion and thus facilitate antidote treatment.

The product contains a human taste deterrent (adversive agent – Bitrex).

To report human poisoning incidents call the relevant national poison information centre. Include information on the product authorisation number, product trade name and active substance. Where possible provide a copy of the label or safety data sheet (SDS).

In Ireland to report a poisoning incident, call: 01 (8092566 / 8379964) The Poisons Information Centre of Ireland, Beaumont Hospital, Beaumont Road, Dublin 9.

ADVICE FOR DOCTORS:

Difenacoum is an indirect anti-coagulant. Phytomenadione, Vitamin K1, is antidotal. Determine prothrombin times not less than 18 hours after consumption. If elevated, administer Vitamin K1 until prothrombin time normalises. Continue determination of prothrombin time for two weeks after withdrawal of antidote and resume treatment if elevation occurs in that time.

Report all incidents of poisonings to the relevant national poisons centre (include information on the product authorisation number, product trade name and active substance)

7. Proposal for Decision

The assessment presented in this report has shown that the ready-to-use product, Ruby Paste, formulated by Lodi S.A. 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 of rodents (rats and mice).

This authorisation of the product Ruby Paste has duly taken in to consideration the conclusions and recommendations of both the Finnish Assessment Report for the active substance, difenacoum and Commission Directive 2008/81/EC including difenacoum in Annex I of Directive 98/8/EC.

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, in the proposed areas for use at the proposed dose rate. However, paste bait was shown not to be suitable for damp or wet conditions, such as in sewers. Therefore, this use area is not supported by this authorisation.

Acute toxicology studies presented for the product indicated that Ruby Paste (containing 0.005% w/w difenacoum) does not classify with respect to Directive 1999/45/EC or Regulation (EC) No 1272/2008. However, safety phrases and precautionary statements are proposed by the Rapporteur.

A human health exposure and effects assessment for the product was carried out for professionals and amateurs on the product Ruby Block, based on the larger baiting quantities for rats. Using both the MOE and AEL approaches for risk assessment indicates 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 with PPE, untrained professionals and amateurs (with and without PPE). The product is deemed suitable for authorisation and appropriate personal protective equipment is advised.

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 in sealed packs and the use of tamper resistant bait boxes are essential to reducing the risk of secondary exposure. Baits should not be placed where food, feeding stuffs or drinking water could be contaminated.

An environmental exposure and effects assessment for the product indicated that difenacoum in Ruby Paste does not pose a threat to groundwater (PEC_{GW} < 0.1 µg/L) and does not infinitely accumulate in soil when used according to label instructions. Difenacoum has an estimated half-life of approximately 2 hours in air. Consequently, it is predicted to have a negligible effect on stratospheric ozone. Difenacoum shows no absorption in the so-called atmospheric window (800-1,200 nm) and therefore, according to the TGD on risk assessment (Part II, Section 3.7.2) is not a potential greenhouse gas.

Difenacoum in Ruby Paste does not adversely impact non-target organisms in the aquatic or terrestrial compartments when used according to label instructions. There is a high risk for primary and secondary poisoning for non-target vertebrates. Additionally, difenacoum is a potential PBT substance (see Difenacoum Assessment Report (17-09-2009)) . These identified risks are minimized by applying all apropriate and available risk mitigation measures.

During the active substance review of difenacoum by Finland, primary and secondary poisoning risks were identified for non-target organisms and for potential accidental incidents involving children. The

assessment of those EU identified risks during the product authorisation evaluation of Ruby Paste have also indicated a potential risk of primary and secondary poisoning to no-target animals and the potential for the accidental primary poisoning of children. As such risk mitigation measures are applied to product authorisation.

Additionally, as the target rodents are vermin and are both direct transmitters of disease (such as through biting or contamination of food/feed by urine or faeces) or indirect carriers of disease (such as disease vectors, where fleas move from rat to humans) to humans and other animals. Transmitted diseases can include leptospirosis (or Weil's disease), trichinosis and salmonella. Authorisation of this product is considered necessary on the basis of public health grounds, since rodent populations are considered to constitute a danger to public health through the transmission of disease.

Conditions of authorisation

Two authorisations should be issued. The first authorisation covers professional and trained professional use product. The second authorisation covers amateur use product.

This authorisation of Ruby Paste is for a period of 5-years with an annual renewal.

The concentration of the active substance, difenacoum, in Ruby Paste shall **not** exceed 0.05 g/kg (0.005% w/w).

Only ready-to-use Ruby Paste product is authorised.

As a poison control measure, the authorisation requires that the product shall contain an aversive, bittering agent.

The authorisation requires that the product be dyed with a colour to make them unattractive to wildlife, and birds in particular.

This product shall **not** be used as a tracking poison.

The product is authorised only for use against rodents (for example brown rats, house rats and house mice). Authorisation of this product does **not** allow use against non-target organisms.

The authorisation of this product for professionals and trained professionals allows for use indoors and outdoors in the following areas: Indoors, including areas such as houses, warehouses, outbuildings and commercial premises. Outdoors uses include areas such as in-and-around buildings, waste dumps and open areas. Difenacoum baits must not be placed where food, feeding stuffs or drinking water can become contaminated.

The authorisation of this product for amateurs allows for use of this product indoors and outdoors in the following areas: Indoors, including only privates houses and outbuildings. Outdoors uses, including only in-and-around private building premises and private gardens. Difenacoum baits should not be placed where food, feeding stuffs or drinking water can become contaminated.

The product should only be used for rodent control in tamper resistant, secured bait stations or other secure coverings.

Bait stations should be clearly marked to show that they contain rodenticides and that they should not be disturbed.

Paste bait sachets shall be secured to the bait station(s) so that rodents can not remove bait from the bait box.

For amateur use products placed on the market in Ireland packaging restrictions are to be limited to pre-baited bait stations and refill packs with a maximum pack-size of 500g. Additionally, the paste bait shall be supplied to the amateur market in sachets and where relevant to professionals in order to reduce exposure risks to amateur operators during application to bait stations.

All product placed on the Irish market after the date of authorisation must be in compliance with the conditions of this authorisation and shall carry the approved label with the IE/BPA authorisation number and be packaged in the approved packaging.

Prior to any amendment relating to this authorised product, such as specification, use, labelling or administrative changes, application must be made to this Authority to do so

Upon annual renewal of the product Ruby Paste, the authorisation holder shall provide statistics to PRCD on the import and export from Ireland and also manufacture statistics where appropriate for Ruby Grain for the given full annual period or part thereof.

Authorisation of the biocidal product may be subject to review, following a detailed assessment of the risks involved, in accordance with the European Communities (Authorisation, Placing on the Market, Use and Control of Biocidal Products) Regulations, 2001, as amended. This review may lead to changes in or revocation of this authorisation.