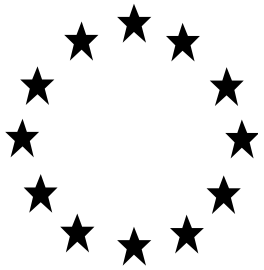
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

PRODUCT ASSESSMENT REPORT OF A BIOCIDAL PRODUCT FOR NATIONAL AUTHORISATION APPLICATIONS



Product identifier in R4BP	**Ruby Block**
Product type:	14 (Rodenticide)
Active ingredient(s):	Difenacoum
Case No. in R4BP	BC-XF000564-43
Asset No. in R4BP	IE-0001152-0000
Evaluating Competent Authority	Ireland – Department of Agriculture, Food & the Marine
Internal registration/file no	**IE/BPA 70528**
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 (plus Addenda, January 2012 & April 2012)
2016/09/07	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	99
NA-RNL	IE	BC-XF000564-43	2018/04/30	Renewal	35

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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 Block**
Product type:	14 (Rodenticide)
Active ingredient(s):	Difenacoum
Case No. in R4BP	BC-XF000564-43
Asset No. in R4BP	IE-0001152-0000
Evaluating Competent Authority	Ireland – Department of Agriculture, Food & the Marine
Internal registration/file no	**IE/BPA 70528**
Date	30.04.2018 (NA-RNL renewal)

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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 Block** 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, and in sewers 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 Block** 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 wax block 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 Block 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 block formulation proved to be both palatable to and effective against infestations of brown rats (*Rattus norvegicus*) and house mice (*Mus musculus/ domesticus*).

No efficacy data using the block formulation was provided for the roof rat (*Rattus rattus*) therefore only claims relating to control of the brown rat (*Rattus norvegicus*) and house mice (*Mus musculus/ domesticus*) are authorised.

Ruby Block is proposed for use in damp or wet conditions such as those encountered in sewer systems and data demonstrating the bait's robust ability to perform in such environments has been previously evaluated and approved.

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 Block** 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 Block
Additional trade name(s): Roded Block

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 70528	
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-(3-biphenyl-4-yl-1,2,3,4- tetrahydro-1-naphthyl)-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

There are no substances of concern.

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

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

- persistent and very persistent, bioaccumulative and toxic

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: block

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.
Supplemental label elements		

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.

Precautionary statements:	P201	Obtain special instructions before use
	P202	Do not handle until all safety precautions have been read and understood.
	P280	Wear protective gloves.
	P308+P313	IF exposed or concerned: Get medical advice/attention.
	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
7	Rats – trained professionals – sewers

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

Product Type(s)	14
Where relevant, an exact description of the use	Rodenticide
Target organism(s) (including development stage)	House mice (*Mus musculus/domesticus*) – adults and juveniles

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.

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 of 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 2.5kg **Grams of bait (individually wrapped in PE or PP sachet or unwrapped)** : 20-30 **Packaging material and size:** **Bucket (PE or PP) :** 20g: 2.5 kg (125*20), 3kg (150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Cardboard box (with inner liner in PE if bait is unwrapped):** 20g: 2.5 kg (125*20), 3kg (150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Pre-baited station (PP, PVC,PS) in cardboard box containing each 1 block of 20 or 30 g:** : - 2.5 kg (125*20 g) or (84*30 g) - 3 kg(150*20g) or (100*30g) - 4 kg (200*20g) or (134*30 g) - 5 kg (250*20g) or (167*30g)

2.4.1.1 Use-specific instructions for use

- 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.
- [When available] Follow any additional instructions provided by the relevant code of best practice.

2.4.1.2 Use-specific risk mitigation measures

None

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
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 5 meters (high infestation). If there is a low infestation the distance between bait stations should be 10

	meters.
Category(ies) of users	Professionals
Pack sizes and packaging material	Minimum pack size 2.5kg **Grams of bait (individually wrapped in PE or PP sachet or unwrapped):** : 20-30 **Packaging material and size:** **Bucket (PE or PP) :** 20g: 2.5 kg (125*20), 3kg (150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20), 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Cardboard box (with inner liner in PE if unwrapped)** 20g: 2.5 kg (125*20), 3kg (150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Pre-baited station (PP, PVC,PS) in cardboard box** of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg: **90g** : 3*30 g **100g:** 5*20 g

2.4.2.1 Use-specific instructions for use

- 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.
- [When available] Follow any additional instructions provided by the relevant code of best practice

2.4.2.2 Use-specific risk mitigation measures

None

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 mice (*Mus musculus/domesticus*) – adults and juveniles Brown rats (*Rattus norvegicus*) – 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 rats
Category(ies) of users	Professionals
Pack sizes and packaging material	Minimum pack size 2.5kg **Grams of bait (individually wrapped in PE or PP sachet or unwrapped):** 20-30

	Packaging material and size: **Bucket (PE or PP) :** 20g: 2.5 kg (125*20), 3 kg(150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Cardboard box (with inner liner in PE if unwrapped):** 20g: 2.5 kg (125*20), 3 kg(150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Pre-baited station (PP, PVC,PS) in cardboard box*of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg:** 90 g: 3*30g (*remove 2) 100g: 5*20g (* remove 4) *If the product is intended to be used against mice, remove the number of sachets/baits corresponding

2.4.3.1 Use-specific instructions for use

- Protect bait from the atmospheric conditions (e.g. rain, snow, etc.). Place the bait stations in areas not liable to flooding.
- The bait stations should be visited [for mice - at least every 2 to 3 days at] [for rats - 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.
- Replace any bait in a bait station in which bait has been damaged by water or contaminated by dirt.
- [*When available]* Follow any additional instructions provided by the relevant code of best practice.

2.4.3.2 Use-specific risk mitigation measures

- Do not apply this product directly in the burrows. .

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

When placing bait 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 mice (*Mus musculus/domesticus*) – adults and juveniles Brown rats (*Rattus norvegicus*) – 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. **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 2.5kg **Grams of bait (individually wrapped in PE or PP sachet or unwrapped):** 20-30 **Packaging material and size:** **Bucket (PE or PP) :** 20g: 2.5 kg (125*20), 3 kg(150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Cardboard box (with inner liner in PE if unwrapped):** 20g: 2.5 kg (125*20), 3 kg(150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Pre-baited station (PP, PVC,PS) in cardboard box* of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg:** 90 g: 3*30g (*remove 2) 100g: 5*20g (* remove 4) *If the product is intended to be used against mice, remove the number of sachets/baits corresponding

2.4.4.1 Use-specific instructions for use

- Remove the remaining product at the end of treatment period.
- *[When available]* Follow any additional instructions provided by the relevant code of best practice.
- 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

- 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]*.
- Consider preventive control measures (e.g. plug holes, remove potential food and drinking as far as possible) to improve product intake and reduce the likelihood of reinvasion.
- To reduce risk of secondary poisoning, search for and remove dead rodents during treatment at frequent intervals, in line with the recommendations provided by the relevant code of best practice
  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.
  Do not use this product in pulsed baiting treatments.

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 mice (*Mus musculus/domesticus*) – adults and juveniles Brown rats (*Rattus norvegicus*) – 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 frequency	Mice : 20-30 g/ Rats 90-100 g of bait per bait station. **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 2.5kg **Grams of bait (individually wrapped in PE or PP sachet or unwrapped):** 20-30 **Packaging material and size:** **Bucket (PE or PP) :** 20g: 2.5 kg (125*20), 3 kg(150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20), 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Cardboard box (with inner liner in PE if unwrapped):**

	20g: 2.5 kg (125*20), 3 kg(150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Pre-baited station (PP, PVC,PS) in cardboard box* of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg:** 90 g: 3*30g (*remove 2) 100g: 5*20g (* remove 4) *If the product is intended to be used against mice, remove the number of sachets/baits corresponding

2.4.5.1 Use-specific instructions for use

- 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 baiting points in which bait has been damaged by water or contaminated by dirt.
- 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.
- *[For outdoor use, baiting points must be covered and placed in strategic sites to minimise the exposure to non-target species]. [When available]* Follow any additional instructions provided by the relevant code of best practice.
- 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.

2.4.5.2 Use-specific risk mitigation measures

- Where possible, prior to the treatment inform any possible bystanders (e.g. users of the treated area and their surroundings) about the rodent control campaign *[in accordance with the applicable code of good practice, if any]*.
- Consider preventive control measures (e.g. plug holes, remove potential food and drinking as far as possible) to improve product intake and reduce the likelihood of reinvasion.
- To reduce risk of secondary poisoning, search for and remove dead rodents during

treatment at frequent intervals, in line with the recommendations provided by the relevant code of best practice • 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. • Do not use this product in pulsed baiting treatments.

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

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. - - **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 – **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 2.5kg **Grams of bait (individually wrapped in PE or PP sachet or unwrapped):** 20-30 **Packaging material and size:** **Bucket (PE or PP) :** 20g: 2.5 kg (125*20), 3 kg(150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Cardboard box (with inner liner in PE if unwrapped):** 20g: 2.5 kg (125*20), 3 kg(150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Pre-baited station (PP, PVC,PS) in cardboard box of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg**: **90 g**: 3*30g **100g:** 5*20g

2.4.6.1 Use-specific instructions for use

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

- Remove the remaining product at the end of treatment period.
- *[When available]* Follow any additional instructions provided by the relevant code of best practice.
- 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.
- *[For outdoor use, baiting points must be covered and placed in strategic sites to minimise the exposure to non-target species]. [When available]* Follow any additional instructions provided by the relevant code of best practice.
- 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.

2.4.6.2 Use-specific risk mitigation measures

- Where possible, prior to the treatment inform any possible bystanders (e.g. users of the treated area and their surroundings) about the rodent control campaign *[in accordance with the applicable code of good practice, if any]*.
- To reduce risk of secondary poisoning, search for and remove dead rodents during treatment at frequent intervals, in line with the recommendations provided by the relevant code of best practice.
- 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.
- Do not use this product for pulsed baiting.

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

2.4.7 Use 7 appropriate after renewal of the authorisation – Rats – trained professionals – sewers

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
Field(s) of use	Sewers
Application method(s)	Ready-to-use bait to be anchored or applied in bait stations preventing the bait from getting into contact with waste water.
Application rate(s) and frequency	Rats: secure 100 g of bait per bait station. 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. - Permanent baiting – **Rats** - High infestation: (100) g of bait per baiting point every 5 meters - Low infestation: (100) g of bait per baiting point every 10 meters
Category(ies) of users	Trained Professionals
Pack sizes and packaging material	Minimum pack size 2.5kg **Grams of bait unwrapped : 100 (with hooker)** **Bucket (PE or PP) :** 100 g: 2.5 kg (25*100), 3 kg (30*100), 3.5 kg (35*100), 4 kg (40*100), 4.5 kg (45*100), 5 kg (50*100), 5.5 kg (55*100), 6 kg (60*100), 6.5 kg (65*100), 7 kg (70*100), 7.5 kg (75*100), 8 kg (80*100), 8.5 kg (85*100), 9 kg (90*100), 9.5 kg (95*100), 10 kg (100*100) **Cardboard box with inner liner in PE:** 100 g: 2.5 kg (25*100), 3 kg (30*100), 3.5 kg (35*100), 4 kg (40*100), 4.5 kg (45*100), 5 kg (50*100), 5.5 kg (55*100), 6 kg (60*100), 6.5 kg

	(65*100), 7 kg (70*100), 7.5 kg (75*100), 8 kg (80*100), 8.5 kg (85*100), 9 kg (90*100), 9.5 kg (95*100), 10 kg (100*100)

2.4.7.1 Use-specific instructions for use

- Baits must be applied in a way so that they do not come into contact with water and are not washed away.
- *[When available]* Follow any additional instructions provided by the relevant code of best practice.
- 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.

2.4.7.2 Use-specific risk mitigation measures

- [If national policy or legislation requires it] Place baits only in sewer systems which are connected to the sewage treatment plant.
- Do not use this product in pulsed baiting treatments.
- 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.

2.4.7.3 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.

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

None

2.4.7.5 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

2.5.1.1 Instructions for Use - Professionals

- Read and follow the product information as well as any information accompanying the product or provided at the point of sale before using it.
- Carry out a pre-baiting survey of the infested area and an on-site assessment in order to identify the rodent species, their places of activity and determine the likely cause and the extent of the infestation.
- Remove food which is readily attainable for rodents (e.g. spilled grain or food waste). Apart from this, do not clean up the infested area just before the treatment, as this only disturbs the rodent population and makes bait acceptance more difficult to achieve.
- The product should only be used as part of an integrated pest management (IPM) system, including, amongst others, hygiene measures and, where possible, physical methods of control.
- 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.
- Bait stations/ points 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.).
- 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.
- Wear protective chemical resistant gloves during product handling phase (glove material to be specified by the authorisation holder within the product information).
- When using the product do not eat, drink or smoke. Wash hands and directly exposed skin after using the product.
- 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.
- 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.
- Remove the remaining bait or the bait stations at the end of the treatment period.
- Bait in sachets: Do not open the sachets containing the bait.

2.5.1.2 Instructions for Use – Trained Professionals

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

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

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

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

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

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

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

- *[If national policy or legislation requires 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 and farm animals and other non-target animals.

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

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

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

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

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

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

Bait in sachets: [For non-emptiable sachets - Do not open the sachets containing the bait].

IE Only: 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.

2.5.2 Risk mitigation measures

2.5.2.1 Risk mitigation measures - Professionals

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

2.5.2.2 Risk mitigation measures – Trained Professionals

- Where possible, prior to the treatment inform any possible bystanders about the rodent control campaign *[in accordance with the applicable code of good practice, if any]*".

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

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

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

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

- Do not wash the bait stations or utensils used in covered and protected bait points with water between applications.

- 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]*.

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 mice (*Mus musculus/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 of 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 2.5kg **Grams of bait (individually wrapped in PE or PP sachet or unwrapped)** : 20-30 **Packaging material and size:** **Bucket (PE or PP) :** 20g: 2.5 kg (125*20), 3kg (150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Cardboard box (with inner liner in PE if bait is unwrapped):** 20g: 2.5 kg (125*20), 3kg (150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Pre-baited station (PP, PVC,PS) in cardboard box containing each 1 block of 20 or 30 g:** : - 2.5 kg (125*20 g) or (84*30 g) - 3 kg(150*20g) or (100*30g) - 4 kg (200*20g) or (134*30 g) - 5 kg (250*20g) or (167*30g)

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
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 5 meters (high infestation). If there is a low infestation the distance between bait stations should be 10 meters.
Category(ies) of users	Professionals
Pack sizes and packaging material	Minimum pack size 2.5kg **Grams of bait (individually wrapped in PE or PP sachet or unwrapped):** : 20-30 **Packaging material and size:** **Bucket (PE or PP) :** 20g: 2.5 kg (125*20), 3kg (150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20), 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Cardboard box (with inner liner in PE if unwrapped)** 20g: 2.5 kg (125*20), 3kg (150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Pre-baited station (PP, PVC,PS) in cardboard box** of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg: **90g** : 3*30 g **100g:** 5*20 g

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 mice (*Mus musculus/domesticus*) – adults and juveniles Brown rats (*Rattus norvegicus*) – 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 rats
Category(ies) of users	Professionals
Pack sizes and packaging material	Minimum pack size 2.5kg **Grams of bait (individually wrapped in PE or PP sachet or unwrapped):** 20-30 **Packaging material and size:** **Bucket (PE or PP) :** 20g: 2.5 kg (125*20), 3 kg(150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Cardboard box (with inner liner in PE if unwrapped):** 20g: 2.5 kg (125*20), 3 kg(150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Pre-baited station (PP, PVC,PS) in cardboard box*of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg:** 90 g: 3*30g (*remove 2) 100g: 5*20g (* remove 4) *If the product is intended to be used against mice, remove the number of sachets/baits corresponding

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 mice (*Mus musculus/domesticus*) – adults and juveniles Brown rats (*Rattus norvegicus*) – 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. **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 2.5kg **Grams of bait (individually wrapped in PE or PP sachet or unwrapped):** 20-30 **Packaging material and size:** **Bucket (PE or PP) :** 20g: 2.5 kg (125*20), 3 kg(150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Cardboard box (with inner liner in PE if unwrapped):** 20g: 2.5 kg (125*20), 3 kg(150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Pre-baited station (PP, PVC,PS) in cardboard box* of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg:** 90 g: 3*30g (*remove 2) 100g: 5*20g (* remove 4) *If the product is intended to be used against mice, remove the number of sachets/baits corresponding

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 mice (*Mus musculus/domesticus*) – adults and juveniles Brown rats (*Rattus norvegicus*) – 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. **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 2.5kg **Grams of bait (individually wrapped in PE or PP sachet or unwrapped):** 20-30 **Packaging material and size:** **Bucket (PE or PP) :** 20g: 2.5 kg (125*20), 3 kg(150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20), 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Cardboard box (with inner liner in PE if unwrapped):** 20g: 2.5 kg (125*20), 3 kg(150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Pre-baited station (PP, PVC,PS) in cardboard box* of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg:** 90 g: 3*30g (*remove 2) 100g: 5*20g (* remove 4) *If the product is intended to be used against mice, remove the number of sachets/baits corresponding

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)	Brown rats (*Rattus norvegicus*) – 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. - - **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 2.5kg **Grams of bait (individually wrapped in PE or PP sachet or unwrapped):** 20-30 **Packaging material and size:** **Bucket (PE or PP) :** 20g: 2.5 kg (125*20), 3 kg(150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Cardboard box (with inner liner in PE if unwrapped):** 20g: 2.5 kg (125*20), 3 kg(150*20), 3.5 kg (175*20), 4 kg (200*20), 4.5 kg (225*20), 5 kg (250 *20), 5.5 kg (275*20), 6 kg (300*20), 6.5 kg (325*20) , 7 kg (350*20), 7.5 kg (375*20), 8 kg (400*20), 8.5 kg (425*20), 9 kg (450*20), 9.5 kg (475*20), 10 kg (500*20) 30g: 2.5 kg (84*30), 3 kg (100*30), 3.5 kg (117*30), 4 kg (134*30), 4.5 kg (150*30), 5 kg (167*30), 5.5 kg (184*30), 6 k g(200*30), 6.5 kg (217*30), 7 kg (234*30), 7.5 kg (250*30), 8 kg (267*30), 8.5 kg (284*30), 9 kg (300*30), 9.5 kg (347*30), 10 kg (334*30) **Pre-baited station (PP, PVC,PS) in cardboard box of 2.5 kg, 3 kg, 3.5 kg, 4 kg, 4.5 kg and 5 kg**: **90 g**: 3*30g **100g:** 5*20g

3.1.7 Use 7 - Rats – trained professionals – sewers

Product Type(s)	14
Where relevant, an exact description of the use	Rodenticide
Target organism(s) (including	Brown rats (*Rattus norvegicus*) – adults and juveniles

development stage)	
Field(s) of use	Sewers
Application method(s)	Ready-to-use bait to be anchored or applied in bait stations preventing the bait from getting into contact with waste water.
Application rate(s) and frequency	Rats: secure 100 g of bait per bait station. 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.
Category(ies) of users	Trained Professionals
Pack sizes and packaging material	Minimum pack size 2.5kg **Grams of bait unwrapped : 100 (with hooker)** **Bucket (PE or PP) :** 100 g: 2.5 kg (25*100), 3 kg (30*100), 3.5 kg (35*100), 4 kg (40*100), 4.5 kg (45*100), 5 kg (50*100), 5.5 kg (55*100), 6 kg (60*100), 6.5 kg (65*100), 7 kg (70*100), 7.5 kg (75*100), 8 kg (80*100), 8.5 kg (85*100), 9 kg (90*100), 9.5 kg (95*100), 10 kg (100*100) **Cardboard box with inner liner in PE:** 100 g: 2.5 kg (25*100), 3 kg (30*100), 3.5 kg (35*100), 4 kg (40*100), 4.5 kg (45*100), 5 kg (50*100), 5.5 kg (55*100), 6 kg (60*100), 6.5 kg (65*100), 7 kg (70*100), 7.5 kg (75*100), 8 kg (80*100), 8.5 kg (85*100), 9 kg (90*100), 9.5 kg (95*100), 10 kg (100*100)

3.2 Physical, chemical and technical properties

Two new studies were 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 remains 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 – long term storage at ambient temperature</td>
<td>GIFAP Monograph No. 17</td>
<td>
<table>
<tr><th>Time</th><th>Conc (ppm)</th><th>Deviation from declared value (%)</th><th>Deviation between T_0 and T_{2year} (%)</th></tr>
<tr><td>T=0</td><td>40.6</td><td>-18.8</td><td>-</td></tr>
<tr><td>T = 2 years</td><td>39.0</td><td>-22.0</td><td>-3.9</td></tr>
</table>
The declared value was 50 ppm.

Aspect

T_0: Red block. Sweet odour.

$T_{2\ years}$: Red block. Sweetish, slightly perceptible odour.
</td>
<td>‘Chemical stability after storage at 20˚C ± 2˚C after 2 years of Difenacoum block baits 0.005%’.

S Richerioux
LODI 24/2009
Version Date: 2011-12-13</td>
</tr>
<tr>
<td>Particle size distribution, content of dust/fines, attrition, friability</td>
<td>Attrition: CIPAC MT 193</td>
<td>The attrition of tablets was 0.4%</td>
<td>‘Attrition of tablets test on RUBIS BLOC’

N Ferron
Report12.912011-003
Date: 12 September 2012</td>
</tr>
</table>

Conclusion on the physical, chemical and technical properties of the product
Storage stability at ambient temperature (2 years) The study was carried out to GLP. The relative deviation of Difenacoum content in block bait after two years at 20˚C is < 10%. No significant change was observed concerning the aspect of the sample. **Proposed shelf life** The test item is considered stable at ambient temperature for 2 years. **Attrition** The attrition of the tablets was carried out to GLP and tested according to CIPAC Method 193 and determined as 0.4%. This is acceptable.

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 brown rats (*Rattus norvegicus*) and house mice (*Mus musculus/ domesticus*) when applied according to the label advice. The block 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. Two newly submitted studies established that the product is attractive to and effective against rats and mice when stored for up to three years (36 months) at ambient temperatures.
No efficacy data using the block formulation was provided for the roof rat (*Rattus rattus*) therefore only claims relating to control of the brown rat (*Rattus norvegicus*) and house mice (*Mus musculus/ domesticus*) are authorised.

Data previously evaluated concluded that Ruby Block is particularly suitable for use in damp or wet conditions such as those encountered in sewer systems and the product's palatability and effectiveness even under adverse environmental conditions has been demonstrated.

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

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

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.

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

No new studies were submitted. 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.

3.6.1 Assessment of effects of the active substance on human health

See section 3.6.3.

3.6.2 Assessment of effects of the product on human health

See section 3.6.3.

3.6.3 Exposure assessment

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.

The risk assessment for trained and non-trained professional users used the chronic AEL (1.1x10-6 mg/kg bw/day) as the endpoint. The HEEG recommendations 9, 10 and 12 were incorporated into the risk assessments. The risk assessment for trained and non-trained professional users modelled the loading of 100g of bait loading as 20g blocks.

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 toddler risk assessment used the acute AEL (1.1 x 10^{-6} mg/kg bw/day). An oral absorption of 100% was assumed for the mouthing scenarios in the toddler risk assessment.

Biocidal Exposure Risk assessment for Ruby Block difenacoum rodenticide (50 ppm).

Professional user

	Block
Without PPE	132.8% of AEL (0.00000146 mg/kg bw/day)
With PPE	6.6% of AEL (0.000000073 mg/kg bw/day)
Sewer application without PPE	25.26%

	(0.000000278 mg/kg bw/day)
Sewer application with PPE	1.26% (0.0000000139 mg/kg bw/day)
Non-trained professional user (farmer)	
	Block
Without PPE	12.7% of AEL (0.000000140 mg/kg bw/day)
With PPE	0.6% of AEL (0.00000000698 mg/kg bw/day)
Exposure to children (Toddler)	
	Block
Oral exposure -treated with repellent	4545% AEL (0.25 mg/kg bw/day)
Oral exposure - without repellent	2272727% AEL (0.00005 mg/kg bw/day)

Derived values indicated a no safe usage scenario for professional users handling the difenacoum block product without PPE and a safe usage scenario with PPE. Derived values for professional users handling the block product without PPE were 0.00000146 mg/kg bw/day (132.8% AEL). Derived values for professional users handling the block product with PPE were 0.000000073 mg/kg bw/day (6.6% AEL).

Derived values indicated safe usage for trained professional users placing the block product in sewer areas both with and without PPE. Derived values for non-trained professional users handling the block product without PPE were 0.000000278 mg/kg bw/day (25.26% AEL). Derived values for non-trained professional users handling the block product with PPE were 0.0000000139 mg/kg bw/day (1.26% AEL).

Derived values indicated safe usage for non-trained professional users handling the block product with and without PPE. Derived values for non-trained professional users handling the block product without PPE were 0.000000140 mg/kg bw/day (12.7% AEL). Derived values for non-trained professional users handling the block product with PPE were 0.00000000698 mg/kg bw/day (0.6% AEL).

Derived values indicated no safe exposure scenarios for toddlerss through oral exposure/transient

mouthing of the block product due its teratogen properties. Derived values for oral exposures in the toddler found transient mounting of a block not containing a repellent to result in a dose of 0.025 mg (4545% AEL). Derived values for oral exposures in the toddler found transient mounting of a block containing a repellent to result in a dose of 0.00005 mg (2272727% 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.

3.6.4 Risk characterisation for human health

3.6.4.1 Risk for professional users

As shown in section 3.6.2.

3.6.4.2 Risk for the general public

Not relevant.

3.6.4.3 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.

3.6.4.4 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.

3.6.4.5 Summary of risk characterisation

Derived values indicated a no safe usage scenario for professional users handling the difenacoum block product without PPE and a safe usage scenario with PPE. Derived values for professional users handling the block product without PPE were 0.00000146 0.003 mµg/kg bw/day (119132.8% AEL).

Derived values for professional users handling the block product with PPE were 0.000000073 0.0003 mµg/kg bw/day (1.196.6% AEL).
Derived values indicated safe usage for trained professional users placing the block product in sewer areas both with and without PPE. Derived values for non-trained professional users handling the block product without PPE were 0.000000278 mg/kg bw/day (25.26% AEL). Derived values for non-trained professional users handling the block product with PPE were 0.0000000139 mg/kg bw/day (1.26% AEL).

Derived values indicated safe usage for non-trained professional users handling the block product with and without PPE. Derived values for non-trained professional users handling the block product without PPE were 0.000000140 0.0001 mµg/kg bw/day (10.612.7% AEL). Derived values for non-trained professional users handling the block product with PPE were 0.00000000698 0.00001 mµg/kg bw/day (1.060.6% AEL).
Derived values indicated no safe exposure scenarios for toddlers through oral exposure/transient mouthing of the block product due its teratogen properties. Derived values for oral exposures in the toddler found transient mounting of a block not containing a repellent to result in a dose of 0.0253 mg (MOE: 0.014545% AEL). Derived values for oral exposures in the toddler found transient mounting of a block containing a repellent to result in a dose of 0.000056 mg (MOE: 5.442272727% 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.

3.7 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***
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 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 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	

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	**PNEC**	**PNEC[1]**	**PEC**	**PEC/PNEC**

Organism	µg/kg food	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)

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

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
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.

[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.

Conclusion

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	DIFEBLOC, containing 0.005% difenacoum	*Mus domesticus*	Laboratory conditions. Test was performed on product stored for 14 days at 54°C. 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.	The study showed that, when freshly manufactured, DIFEBLOC wax block is palatable to Swiss House mice, with a mean palatability against a ground laboratory diet of 66.4%. The formulation also resulted in 100% mortality after a four-day choice between this formulation and challenge diet. It is apparent from this test that the test item, DIFEBLOC wax blocks, when freshly manufactured, should be acceptable for product authorisation.	Prescoot C.V, Efficacy assessment, using the bait choice feeding test, of Difebloc wax blocks (T0) containing 50 mg.kg-1 difenacoum, using CD-1 albino house mouse, Study reference VPU Study Plan Number VPU/10/004, VPU trial No. GB01-10-R009, Project number 153SRI10P, trial code SRIT10-1001-153P. Unpublished
PT14 RODENTICIDE	Belgabloc, containing 0.005% difenacoum	Wild brown rats (*Rattus norvegicus*)	Laboratory housing with rats captured in fields from an external enclosure. Test was performed on product stored for 2 years. 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.	The palatability of BELGABLOC was rated very highly in comparison to safe crushed wheat. In the study BELGABLOC achieved an efficacy specification of 90%.	Latteur G., CRA Gembloux, Efficacy test performed on BELGABLOC, The palatability of BELGABLOC was rated very highly in comparison to safe crushed wheat. In the study BELGABLOC achieved an efficacy specification of 90%. paraffinic bait block containing 0.005% of Difenacoum, against brown rats (*Rattus*

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

					norvegicus Berkenhout), at different storages stages (Appetizing test included), rapport 965, May 1997. Unpublished
PT14 RODENTICIDE	DIFEBLOC, containing 0.005% difenacoum	Wild grey mice (*Mus musculus*)	Field study: experiment conducted in restaurant. 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.	*Block bait/ Field efficacy/ Mice /Product at T0* Very good palatability and acceptance for the paraffin block bait DIFEBLOC. Excellent efficacy (97.1%) achieved.	LODI, Efficacy trial: Rodenticide block containing 0.005% Difenacoum, against house mice (*Mus musculus*), Trial date: 10th April to 6th May, 2007. Unpublished
PT14 RODENTICIDE	Racobloc, containing 0.005% difenacoum	Wild brown rats (*Rattus norvegicus*)	Laboratory conditions. 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.	*Block bait/ Laboratory efficacy/ Rats / Fresh product (T0)* Very good acceptance of the bait RACO BLOCS despite the changing of food type. Excellent efficacy observed, markedly higher to the 90 % (95%) required by the guidelines.	Grolleau G., Panciroli J., Pest Control Assistance (PCA), Experimentation, in nature, of block bait against rats (*Rattus Norvegicus*) 2005. Unpublished
PT14 RODENTICIDE	DIFEBLOC, containing 0.005% difenacoum	*Mus domesticus*	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.	The study showed that, after a storage period of 2 weeks at 54°C, DIFEBLOC wax block is palatable to Swiss House mice, with a mean palatability against the ground laboratory diet of 53.1%. The formulation also resulted in 100% mortality after a four-day choice between this formulation and challenge diet. It is apparent from this test that the test item, DIFEBLOC wax blocks, following storage of 2 weeks at 54°C, should be acceptable for product authorisation.	Prescott C.V., Efficacy assessment, using the bait choice feeding test, of Difebloc wax blocks (T2weeks accelerated) containing 50 mg.kg-1 difenacoum, using CD-1 albino house mouse, Study reference VPU Study Plan Number VPU/10/005, VPU trial No. GB01-10-R010, Project number

					153SRI10P, trial code SRIT10-1002-153P. Unpublished
PT14 RODENTICIDE	Belgabloc, containing 0.005% difenacoum	Albino brown rats (*Rattus norvegicus*)	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.	*Block bait/ Laboratory efficacy/ Rats /Product at T0 and T6* The palatability of BELGABLOC did not decreased after 6 months of storage at ambient temperature (20°C), it's rate of active substance also remained intact. The block bait has an efficacy of 95 % at T0 and 100% at T6.	Latteur G., CRA Gembloux, Efficacy test through different period of time, performed on BELGABLOC, containing 0.005% of Difenacoum, against brown rats (*Rattus norvegicus*), rapport complement 980, April 1998. Unpublished
PT14 RODENTICIDE	Probloc, containing 0.005% difenacoum	Albino brown rats (*Rattus norvegicus*)	Laboratory: household process Test was performed on fresh product and product with a storage of 12 months 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.	*Block bait/ Laboratory efficacy/ Rats /Product at T0 and T12* Palatability of PROBLOC did not decreased during 12 months of storage at ambient temperature (20°C). The block bait has an efficacy of 90 % at T0 and 100% at T12.	De Proft M., CRA Gembloux, Efficacy test through different period of time, performed on PROBLOC, bait ready to use, containing 0.005% of Difenacoum, against brown rats (*Rattus norvegicus*), rapport complement 9547, 1999. Unpublished
PT14 RODENTICIDE	DIFEBLOC, containing 0.005% difenacoum	Wild grey mice (*Mus musculus*)	Field study: experiment conducted in restaurant. Test was performed on product stored for 2 years. 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.	*Block bait/ Field efficacy/ Mice / Product at T2 years* Good acceptance for the two year old paraffin block bait, despite the change of food type. The efficacy almost reached the 90 % required by the guidelines (89.1%).	LODI, Efficacy trial: Rodenticide block containing 0.005% Difenacoum, after 2 years ageing, against house mice (*Mus musculus*), Trial date= 2nd to 29th March, 2009. Unpublished
PT14 RODENTICIDE	DIFEBLOC, containing	Wild brown rats (*Rattus norvegicus*)	Field study: experiment conducted in restaurant.	*Block bait/ Field efficacy/ Rats / Product at T2 years* Good acceptance for the two year old paraffin blocks	LODI, Efficacy trial: Rodenticide block

	0.005% difenacoum		Test was performed on product with a storage of 12 months 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.	bait, despite the changing of food type. Efficacy almost reached the 90 % required by the guidelines (89.6%).	containing 0.005% Difenacoum, after 2 years ageing, against rats (*Rattus norvegicus*), Trial date= 6th April to 13th May, 2009. Unpublished
PT14 RODENTICIDE	Difenacoum Block Bait 0.005% difenacoum	Albino house mice (*Mus musculus*)	Difenacoum block bait (batch No. 09415) (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 9-day testing period, the percentage intake of challenged diet was 51.2±6.4% for female mice and 33.1±9.5% for male mice. The percentage intake of difenacoum block bait was 48.8±6.4% for female mice and 66.9±9.5% for male mice. Globally, mortality occurred in 100% of male and female mice with a mean day to death of 5.7±1.9 days (range 3 to 9 days).	Bureau, M, Choice feeding trials for difenacoum block bait (aged product) against albino house mice, 0LODI13. Unpublished
PT14 RODENTICIDE	Difenacoum Block Bait 0.005% difenacoum	Albino brown rats (*Rattus norvegicus*)	Difenacoum block bait (batch No. 09415) (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 81.6±13.2% for female rats and 91.7±9.6% for male rats. The percentage intake of difenacoum block bait was 18.4±13.2% for female rats and 8.3±9.6% for male rats. Globally, mortality occurred in 90% of male and female rats with a mean day to death of 6.3±1.4 days (range 5 to 9 days), with a surviving male rat (rat M7) at the end of the experiment (D18).	Bureau, M, Choice feeding trials for difenacoum block bait (aged product) against rats, 0LODI23. Unpublished
PT14 RODENTICIDE	Probloc, containing 0.005% difenacoum	Brown rats (*Rattus norvegicus*)	Field: study conducted in sewer The Probloc wax blocks were 150g blocks. Probloc remained stable despite being in a damp environment prone to flooding. Aim of study was to test the resistance of Probloc to the very damp conditions in a sewer system, to monitor the uptake of the blocks by rats in "field" conditions and to monitor the uptake over time. Estimated test population of approximately 42 rats.	Field study – sewer system Good acceptance of the bait was observed. Blocks were assessed 10 and 23 days after placing the bait. There was a markedly lower consumption at the 2nd assessment timing indicating that the population had diminished dramatically (56% blocks eaten vs 12%). No dead rats were found but this is not unusual in an open sewer system. After 23 days most of the blocks remaining were still relatively intact considering the difficult environmental conditions. Efficacy assessment can be calculated as 79%.	Feys JL., Belgagri SA., Massar E., Insectirat sprl, Field trial with Probloc wax baits against sewer rats (*Rattus Norvegicus*) 2010. Belgagri SA,1 rue des Tuielleries B-4480 Engis. *Unpublished*

4.6 Other

None.

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

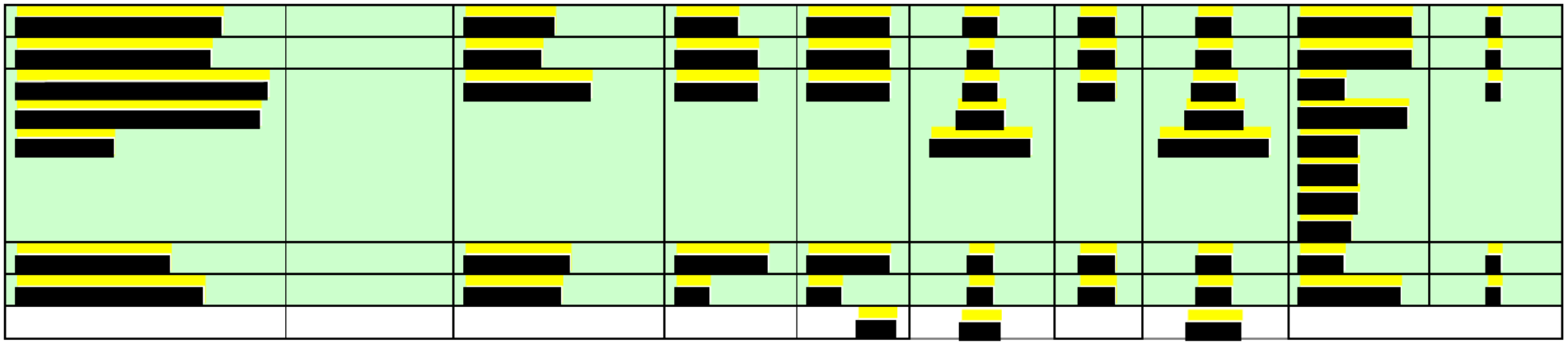
5.1 Full composition of the product

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[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	g/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]									

[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 Block

Active substance:	**Difenacoum**
Product-type:	**PT 14: Rodenticides**
Type of application:	**Authorisation**
Authorisation No:	**IE/BPA 70002 (non-professional product)** **IE/BPA 70025 (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

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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 Block 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 Block
Authorisation No.:	IE/BPA 70002 (non-professional) IE/BPA 70025 (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 Block	IE/BPA 70026	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 Block
Manufacturer's development code no:	N/A
Active substance content (% w/w):	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) Block Bait (BB)
Ready-to-use (RTU) 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 (yes/no); If yes: product name:	Yes (Notified under transitional arrangements with the PRCD) Ruby Block, PCS 94704
Is the biocidal product equivalent to the product assessed for the purpose of Annex I inclusion to 98/8/EC (yes/no):	No.

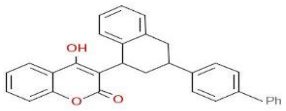
Manufacturer of Formulated Product:	LODI S.A.
Address:	Parc d'activities des quatre routes Grand Fougeray 35390 France
Tel:	[redacted]
E-mail:	[redacted]

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
EC No:	259-978-4
Purity (minimum, g/kg or g/l):	>960 g/kg (96.0% w/w)

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

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:	+44 1420 80744
E-mail:	info@pelgar.co.uk

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

Main Group:	MG02 (Pest control)
Product-type:	PT14 (Rodenticide)
Intended use:	Difenacoum block bait to control rodents indoors, outdoors and in sewers 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, open areas) Sewers (IE/BPA 70025 only)
Directions for use including minimum and maximum application rates, typical size of application area:	Rats: 90-100g of blocks spaced 10m apart (5m apart in high infestation areas). Typical treatment time 6 weeks. Mice: 20-30g of blocks spaced 5m apart (3m apart in high infestation areas). Typical treatment time 6 weeks.
Application method:	Wax bait blocks contained in secured bait stations
Interval between applications:	When required. Regularly check bait consumption and 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 Block containing difenacoum.

Please see the attached reference list in Annex IV.

[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.

According to the Assessment Report (17-09-2009) *'No classification of products containing 50 mg/kg or 75 mg/kg difenacoum would be necessary according to Directive 1999/45/EC. However, specific*

concentration limits of difenacoum have been agreed by the Technical Committee on Classification and Labelling.'

Classification and Labelling of the biocidal product, Ruby Block, 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 Block, 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 70025) 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 Block, as presented by the applicant, 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:	Box container					
Pack size(s):	150g	240g	260g	300g	450g	~~600g~~
Baits per pack:	5x30g 10x15g	8x30g 12x20g 16x15g	13x20g	10x30g 15x20g 20x15g	15x30g 30x15g	~~20x30g~~ ~~30x20g~~ ~~40x15g~~
Pack dimensions (LxWxH):	100x47x155 140x90x100	140x55x180	140x55x180	140x55x180 140x80x210	140x70x210	~~140x80x190~~
Packaging materials:	Cardboard					

Ready-to-use (yes/no)	Yes
Shelf-life:	2 years
Conditions of storage:	Store in dry, cool area. Store in tightly closed packaging. Keep in original containers. Store away from damp or wet conditions. Keep away from children.

Container description:	Bucket container	
Pack size(s):	300g	~~3kg~~
Baits per pack:	10x30g, 15x20g, 20x15g	~~100x30g, 150x20g, 200x15g~~
Pack dimensions (LxWxH):	130x130x130	~~290x200x210~~
Packaging materials:	PP or PE	
Ready-to-use (yes/no)	Yes	
Shelf-life:	2 years	
Conditions of storage:	Store in dry, cool area. Store in tightly closed packaging. Keep in original containers. Store away from damp or wet conditions. Keep away from children.	

Container description:	Pre-baited bait station			
Pack size(s):	20g	30g	50g	100g
Baits per pack:	1x20g	1x30g	1x50g	2x50g
Pack dimensions (LxWxH):	135x42x80	135x42x80	300x130x70 140x80x40	230x190x90 200x150x80
Packaging materials:	PVC, PP, PS or cardboard bait box			
Ready-to-use (yes/no)	Yes			
Shelf-life:	2 years			
Conditions of storage:	Store in dry, cool area. Store in tightly closed packaging. Keep in original containers. Store away from damp or wet conditions. Keep away from children.			

Professional product packaging:

Container description:	Box container
Pack size(s):	10kg

Baits per pack:	125x80g, 334x30g, 500x20g, 667x15g
Pack dimensions (LxWxH):	390x290x240
Packaging materials:	Cardboard
Ready-to-use (yes/no)	Yes
Shelf-life:	2 years
Conditions of storage:	Store in dry, cool area. Store in tightly closed packaging. Keep in original containers. Store away from damp or wet conditions. Keep away from children.

Container description:	Bucket container			
Pack size(s):	3kg	5kg	10kg	10kg (crochet)
Baits per pack:	100x30g, 150x20g, 200x15g	63x80g, 167x30g, 250x20g, 334x15g	125x80g, 334x30g, 500x20g, 667x15g	100x100g, 125x80g
Pack dimensions (LxWxH):	290x200x210	290x200x270	380x290x220	380x290x350
Packaging materials:	PP or PE			
Ready-to-use (yes/no)	Yes			
Shelf-life:	2 years			
Conditions of storage:	Store in dry, cool area. Store in tightly closed packaging. Keep in original containers. Store away from damp or wet conditions. Keep away from children.			

Container description:	Pre-baited bait station			
Pack size(s):	20g	30g	50g	100g
Baits per pack:	1x20g	1x30g	1x50g	2x50g
Pack dimensions (LxWxH):	135x42x80	135x42x80	300x130x70 140x80x40	230x190x90 200x150x80
Packaging materials:	PVC, PP, PS or cardboard bait box			
Ready-to-use (yes/no)	Yes			
Shelf-life:	2 years			
Conditions of storage:	Store in dry, cool area. Store in tightly closed packaging. 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 block bait should be supplied to the amateur market in sachets/wrapped in order to reduce exposure risks to amateur operators during application to bait stations.

Pack size:	IE/BPA 70002 – Maximum pack size of 500g
	Pre-baited stations: 30g (mice) and 100g (rats)
	Refill packs: 150g, 160g, 240g, 260g, 300g, 450g (the bait must be supplied in inner packs or units, each containing enough bait for one point)
	IE/BPA 70025
	Pre-baited stations: 30g (mice) and 100g (rats)
	Refill packs: 3kg, 5kg and 10kg (the bait should be supplied in inner packs or units, each containing enough bait for one point)
Container materials[18]:	Box container – cardboard
	Bucket container – PP or PE
	Pre-baited bait station – PVC, PP, PS or cardboard
Safety features:	Covered bait stations (tamper resistant)
	Wrapped bait (sachets)

[18] PP = polypropylene, PS = polystyrene, PE = polyethylene, HDPE = high-density polyethylene, PVC = polyvinylchloride

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 Block is not explosive, oxidising or flammable and therefore does not classify from a physical/chemical point of view. The test item is stable after storage for two years at ambient temperature. The test item is a ready-to-use block 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 Block 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 Block

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 Block 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 Block 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

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

Section	Study	Method	Results	Comment	Reference
1.1.1	Appearance	Observation.	Appearance: Red solid block. Odour: Slightly waxed.	See 1.7.1b below.	
1.1.1	Appearance	OPPTS 830.6302 OPPTS 830.6303 OPPTS 830.6304	Colour (Munsell code): Red-rose (10 RP4/12) Physical state: blocks Odour: characteristic	Carried out to GLP. Study is acceptable.	NOTOX Project 490521. "Determination of physic-chemical properties of difenacoum block baits". Brekelmans, Ir. M.J.C. 17th September 2010.
1.1.2	Melting point	EEC A1 OECD 102	Melting point: 52.8 - 54.5°C (326 – 328K) Reaction and/or decomposition of the test substance was observed starting at 75°C (348K).	Carried out to GLP. The melting temperature of difenacoum block baits was determined using DSC. Study is acceptable.	NOTOX Project 490521. "Determination of physic-chemical properties of difenacoum block 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 its 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 IE-CA accepts that difenacoum was determined not to be explosive as part of the Annex I inclusion process (expert statement). IE-CA accepts the justification provided by the notifier that Ruby Block is not explosive.	
1.2.1	Explosive properties		A reasoned statement was provided by the Notifier. Difenacoum block bait is not explosive.	The IE-CA accepts the Notifiers justification. Difenacoum block bait is not explosive.	NOTOX Project 490521. "Determination of physic-chemical properties of difenacoum block baits". Brekelmans, Ir. M.J.C. 17th September 2010.

Section	Study	Method	Results	Comment	Reference
1.2.2	Oxidising properties		Neither the active substance nor the solvent present oxidising properties. Examination of the structure establishes 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)*.	The IE-CA accepts that difenacoum was determined not to be oxidising as part of the Annex I inclusion process. IE-CA accepts the justification provided by the notifier that Ruby Block is not oxidising.	
1.2.2	Oxidising properties		A reasoned statement was provided by the Notifier. Difenacoum block bait is not oxidising.	The IE-CA accepts the Notifiers justification. Difenacoum block bait is not oxidising.	NOTOX Project 490521. "Determination of physic-chemical properties of difenacoum block 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		There are no components present in the formulation that present flammability properties.	The IE-CA accepts that difenacoum was determined to be not highly flammable as part of the Annex I inclusion process. A justification is not acceptable in this case, however further information was supplied, see 1.3.2 below to show that the block bait is not highly flammable.	
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 2 seconds and no propagation of combustion was observed. Performance of the main test was not required.	Carried out to GLP. The test substance is considered "not highly flammable". The study is acceptable.	NOTOX Project 490521. "Determination of physic-chemical properties of difenacoum block baits". Brekelmans, Ir. M.J.C. 17th September 2010.

Section	Study	Method	Results	Comment	Reference
1.3.3	Auto-flammability	EEC A.16 (relative self-ignition temperature for solids)	A strong exothermic effect of the test substance was observed. The temperature of the test substance reached 400^{o}C at an oven temperature of 256^{o}C. The self-ignition temperature of the test item is 256^{o}C.	Carried out to GLP. The self-ignition temperature of the test item is 256^{o}C. The study is acceptable.	NOTOX Project 490521. "Determination of physic-chemical properties of difenacoum block baits". Brekelmans, Ir. M.J.C. 17th September 2010.
1.4.1	Free acidity/ Alkalinity		Not applicable, the product is a ready to use block bait, which is a solid block at ambient temperatures.	Accept justification.	
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 during NOTOX project 490522 to be 6.1. Therefore since this pH was within the pH range 4-10 the acidity/alkalinity test was not required and thus not performed.	IE-CA agrees that the acidity/alkalinity test is not required.	NOTOX Project 490521. "Determination of physic-chemical properties of difenacoum block baits". Brekelmans, Ir. M.J.C. 17th September 2010.
1.4.2	pH (1 %)		Not applicable, the product is a ready to use block bait, which is a solid block at ambient temperatures. See comment in 1.4.1.	No data required.	

Section	Study	Method	Results	Comment	Reference
1.5.1	Viscosity		Not applicable, the product is a ready to use block bait.	Accept justification.	
1.5.2	Surface tension		Not applicable, the product is a ready to use block bait.	Accept justification.	
1.6	Relative density		Not applicable, the product is a ready to use block bait, which is a solid block at ambient temperatures.	Accept justification.	
1.6	Density	CIPAC MT 109 (density of liquids and solids) EC. A.3.	Density: 1.28 g/cm^3 Relative density: 1.28	Carried out to GLP. A gas comparison pycnometer was used for the determination of the density and relative density of the test item. The study is acceptable.	NOTOX Project 490521. "Determination of physic-chemical properties of difenacoum block 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 block (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>52.7</td><td>49.6</td><td>44.9</td><td>39.2</td><td>43.0</td></tr>
<tr><td>Deviation from the declared value</td><td>+ 5.4%</td><td>- 0.8%</td><td>- 10.2%</td><td>- 21.6%</td><td>- 14%</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, which would indicate that the block bait will be stable for a minimum of 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. Results indicate that the block bait will be stable for a minimum of 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°C)	GIFAP Monograph No. 17 CIPAC MT 46	<u>Analysis at T0:</u> Aspect: Red block Odour: Slightly waxed Contents: 0.0045% of difenacoum <u>Analysis at T14:</u> Aspect: Red block Odour: Slightly waxed Contents: 0.0042% of difenacoum (-6.66% after accelerated storage)	Carried out to GLP. The results of the study indicate that the test item is stable for 2 weeks at 54°C and 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.15/2009. Study report: Chemical stability after accelerated storage of difenacoum block baits 0.005%. Magnier, Claire. 23rd November 2009.

Section	Study	Method	Results	Comment	Reference
1.7.1c	Storage stability (Accelerated storage – 18 weeks at 30^{o}C)	FAO, SANCO/3030/99 (a.i. content) OPPTS 830.6302 (colour, Munsell code) OPPTS 830.6303 (physical state) OPPTS 830.6304 (odour) CIPAC MT 75.3 (pH (1%))	**Difenacoum content (g/kg):** Before: 0.0462 After: 0.0430 **Appearance:** Before: Red (10 RP4/12), block, characteristic odour. After: Red (10 RP4/12), block, no characteristic odour. **pH (1% in water):** Before: 6.1 After: 6.9	Carried out to GLP. The test item is stable after 18 weeks storage at 30^{o}C, which indicates that the test item will be stable for 2 years at ambient temperatures. The results are acceptable.	NOTOX Project 490522. "Determination of the accelerated storage stability of difenacoum block baits by heating". 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>1.7.2</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 block (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>52.7</td><td>57.1</td><td>43.5</td></tr><tr><td>Deviation from the declared value</td><td>5.40%</td><td>8.35%</td><td>-17.46%</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 block 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 ready to use block bait.</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 block bait.</td><td>Accept justification.</td><td></td></tr>
</table>

Section	Study	Method	Results	Comment	Reference
1.8.3.2	Dispersibility		Not applicable, the product is a ready to use block bait.	No data required.	
1.8.4	Wet/dry sieving test		Not applicable, the product is a ready to use block bait.	Accept justification.	
1.8.5	Particle size distribution in suspension	Only for powders and granules	Not applicable, the product is a ready to use block bait.	Accept justification.	
1.8.6	Water content		Not applicable, the product is a ready to use block bait.	No data required.	
1.8.7	Emulsion stability	Only for ECs and ready for use emulsions	Not applicable, the product is a ready to use block bait.	Accept justification.	
1.8.8	Flowability, pourability and dustability	Flowability only for granular preparations, pourability only for suspensions and dustability only for dustable powders.	Not applicable, the product is a block.	Accept justification.	
1.9	Physical compatibility		Not applicable, the product is a ready-to-use block bait and is not intended to be added or mixed with any other product.	Accept justification.	

Conclusions:

The biocidal product Ruby Block 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 block bait and is not intended to be added or mixed with any other product.

Data requirements/clarifications:

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

3.1.4. Analytical methods

Ruby Block 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>09-902018-005</td></tr>
<tr><td>Title:</td><td>“Analytical method validation for the determination of difenacoum in difenacoum block 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>After a methanol dilution and heating under reflux for 90 minutes the extract was filtered and diluted again in methanol and acetonitrile. Difenacoum was then quantified by liquid chromatography using a reverse phase column and UV detector at 310 nm. The purity of the reference standard difenacoum used was 970 g/kg.</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>0.88</td><td rowspan="2">95</td></tr>
<tr><td>Extract 1 100%</td><td>0.92</td><td>0.87</td></tr>
<tr><td>Extract 2 100%</td><td>0.92</td><td>0.92</td><td rowspan="2">98</td></tr>
<tr><td>Extract 2 100%</td><td>0.92</td><td>0.89</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>0.46</td><td rowspan="2">100</td></tr>
<tr><td>Extract 1 50%</td><td>0.46</td><td>0.46</td></tr>
<tr><td>Extract 2 50%</td><td>0.46</td><td>0.45</td><td rowspan="2">99</td></tr>
<tr><td>Extract 2 50%</td><td>0.46</td><td>0.46</td></tr>
</table>
The recovery results are between 95 - 100%, 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 3.34 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.
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 analytical method described above has been successfully validated for linearity, precision, accuracy and specificity.

Data requirements:

None.

Table 3.1.4.3

Report:	Study No. LODI.17/2009
Title:	"Analytical method validation for determination of difenacoum in difenacoum bait (pasta grain and block)."
Author(s):	Magnier, Claire.
Date:	4th November 2009.
GLP: Yes/No	Yes.
Guideline:	CITAC/EURACHEM
Principle of the Method:	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 09-902018-005 and 05-912011-001.
Linearity:	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 $r^2 > 0.99$.
Precision/repeatability:	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.

<table>
<tr><td></td><td>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>Block bait</td><td>100.43 %</td><td>97.22%</td><td>98.99%</td><td>99.88%</td></tr>
</table></td></tr>
<tr><td>Specificity:</td><td>There was no peak observed in either the block placebo or extraction solution chromatograms. An adjacent peak appeared in the stressed block but the resolution being higher than 2 (R = 2.16), 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 block is a ready-to-use rodenticide block bait containing 0.005% (w/w) difenacoum or 50 ppm difenacoum. The efficacy of the products was assessed against the proposed label claims. Both amateur and professional uses are proposed in and around buildings. Professional users can also use the product in sewers.

The applicant submitted new data in the form of 10 trial reports where both fresh and aged blocks under a wide range of conditions (laboratory and field) were tested and evaluated for their effectiveness. Studies were conducted according to a variety of standards and protocols. Five of the studies were conducted under laboratory conditions with wild strains of mice (2 studies) and rats (3 studies). In two of the studies wild rodents were captured in the field and acclimatized prior to commencing baiting trials. The laboratory studies were all choice tests conducted according to recognised standards. The studies have shown that Ruby Wax block 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 study a mouse infested restaurant (estimated population ~157 mice) was used to establish the effectiveness of fresh block bait. Efficacy following census pre and post-baiting demonstrated a reduction in the mouse population of over 97% after just 7 days of baiting. In the second study the site chosen was also a restaurant with a significant mouse problem estimated at 220 individuals. After a 9-day treatment phase with a 2-year aged bait an efficacy specification approaching 90% was achieved. The third study was a laboratory choice test using 10 house mice and fresh bait. 100% control was achieved within 5 days of using the wax block bait. The next study investigated the palatability and control levels after an accelerated storage study (14 days at 54^{o}C). The bait proved palatable and effective with 100% mortality achieved in just 4 days (10 mice). 10 brown rats were used for the next study with poisoned bait provided for just 2 days. 90% control was achieved in the following days, with the remaining individual having consumed very low levels of block. 22 brown rats were used in the next study again with a short poisoning period using fresh and aged (6 month old) baits. 95% control was achieved with the fresh bait and 100% with the aged with the sole surviving female having consumed very low levels of the block bait. In the next test 22 rats were used in a study on fresh and 12-month aged blocks. 90% control was achieved with the fresh bait and total control achieved with the aged bait. Neophobia was considered by the experiment coordinator as being a factor in the results. A poultry and deer breeding farm was chosen for another study on brown rats. Based on census baiting ~150 rats were estimated as existing on site with free access to significant quantities of alternative animal feed. After a 7-day baiting period the population reduction was calculated at 95%. A rat infested restaurant (~81 rats) was chosen for the next study. Aged bait (2 year old) was used resulting in 89.1% control after a short 5-day baiting period. The final study considered the sewer treatment of a rat infestation in Belgium. Wax blocks in polystyrene containers were hung above the high water point in a sewer. 23 days after the initial baits were hung there was a marked reduction in their consumption indicating a reduction in the test population.

The block bait formulation proved to be highly palatable and effective against both rats and mice in the tests. Both fresh and aged baits (6, 12 and 24 months after manufacture) provided 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 block formulation is particularly suitable for baiting in damp or wet conditions (i.e. sewers), whereby it can be moulded into polystyrene jars and hung above the high water level to attract and bait rats. Results from the study carried out in a sewer demonstrated the products effectiveness and inherent resistance to mould growth.

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 block formulation was provided in the form of laboratory and field studies to verify the proposed label claims.

Product	Codes*	Terms*	GIFAP codes
Block	VIII.3.3	Block-bait	BB

3.2.2. Dose/Mode of action

Blocks 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 block of 30g every 3 to 5 metres
For rats: place 3 blocks of 30g 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 representative 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 have been submitted to the Rapporteur Member State about the distribution and incidence of resistance in the house mouse or black rat in Europe. Resistance was discussed comprehensively 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 Block against the intended target organisms

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
DIFEBLOC, containing 0.005ppm difenacoum	Wild grey mice (*Mus musculus*)	Field study: experiment conducted in restaurant. 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.	*Block bait/ Field efficacy/ Mice /Product at T0* Very good palatability and acceptance for the paraffin block bait DIFEBLOC. Excellent efficacy (97.1%) achieved.	***IIIB5-10_01*** -, LODI, Efficacy trial: Rodenticide block containing 0.005% Difenacoum, against house mice (*Mus musculus*), Trial date: 10th April to 6th May, 2007. Unpublished
DIFEBLOC, containing 0.005ppm difenacoum	Wild grey mice (*Mus musculus*)	Field study: experiment conducted in restaurant. Test was performed on product stored for 2 years.	The method used has been inspired by the French method called "method no. 002 from Biological Trials Commission (C.E.B) ",	*Block bait/ Field efficacy/ Mice / Product at T2 years* Good acceptance for the two year old paraffin block bait, despite the change of food type. The efficacy almost reached the 90 % required by the	***IIIB5-10_02*** -, LODI, Efficacy trial: Rodenticide block containing 0.005% Difenacoum, after 2 years ageing, against

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
			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.	guidelines (89.1%).	house mice (*Mus musculus*), Trial date= 2nd to 29th March, 2009. Unpublished
DIFEBLOC, containing 0.005ppm difenacoum	*Mus domesticus*	Laboratory conditions. Test was performed on product stored for 14 days at 54°C.	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	*10_03_A_Block bait/ Lab efficacy/ Mice / Product at T0.* The study showed that, when freshly manufactured, DIFEBLOC wax block is palatable to Swiss House mice, with a mean palatability against a ground laboratory diet of 66.4%. The formulation also resulted in 100% mortality after a four-day choice between this formulation and challenge diet. It is apparent from this test that the test item, DIFEBLOC wax blocks, when freshly manufactured, should be acceptable for product authorisation.	***IIIB5-10_03a*** Prescoot C.V, Efficacy assessment, using the bait choice feeding test, of Difebloc wax blocks (T0) containing 50 mg.kg-1 difenacoum, using CD-1 albino house mouse, Study reference VPU Study Plan Number VPU/10/004, VPU trial

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
			1980.		No. GB01-10-R009, Project number 153SRI10P, trial code SRIT10-1001-153P. Unpublished
DIFEBLOC, containing 0.005ppm difenacoum	*Mus domesticus*	Laboratory conditions. Test was performed on product stored for 14 days at 54°C.	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.	*10_03_B_Block bait/ Lab efficacy/ Mice / Product at T14days and 54°C* The study showed that, after a storage period of 2 weeks at 54°C, DIFEBLOC wax block is palatable to Swiss House mice, with a mean palatability against the ground laboratory diet of 53.1%. The formulation also resulted in 100% mortality after a four-day choice between this formulation and challenge diet. It is apparent from this test that the test item, DIFEBLOC wax blocks, following storage of 2 weeks at 54°C, should be acceptable for product authorisation.	***IIIB5-10_03b*** Prescott C.V., Efficacy assessment, using the bait choice feeding test, of Difebloc wax blocks (T2weeks accelerated) containing 50 mg.kg-1 difenacoum, using CD-1 albino house mouse, Study reference VPU Study Plan Number VPU/10/005, VPU trial No. GB01-10-R010, Project number 153SRI10P, trial code SRIT10-1002-153P. Unpublished
Belgabloc, containing 0.005ppm difenacoum	Wild brown rats *(Rattus*	Laboratory housing with rats captured in fields from an external enclosure.	The method used has been inspired by the French method called	*Block bait/ Semi field efficacy/ Rats /Fresh product (T0)*	***IIIB5-10_04*** Latteur G., CRA Gembloux, Efficacy

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
	norvegicus)	Test was performed on product stored for 2 years.	"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.	The palatability of BELGABLOC was rated very highly in comparison to safe crushed wheat. In the study BELGABLOC achieved an efficacy specification of 90%.	test performed on BELGABLOC, paraffinic bait block containing 0.005% of Difenacoum, against brown rats (*Rattus norvegicus* Berkenhout), at different storages stages (Appetizing test included), rapport 965, May 1997. Unpublished
Belgabloc, containing 0.005ppm difenacoum	Albinos brown rats *(Rattus norvegicus)*	Laboratory: external enclosure process with species captured in field. Test was performed on fresh product and product stored for 6 months.	The method used has been inspired by the French method called "method no. 002 from Biological Trials Commission (C.E.B) ", Method for practical	*Block bait/ Laboratory efficacy/ Rats /Product at T0 and T6* The palatability of BELGABLOC did not decreased after 6 months of storage at ambient temperature (20°C), it's rate of	***IIIB5-10_05*** Latteur G., CRA Gembloux, Efficacy test through different period of time, performed on BELGABLOC,

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
			efficacy trials of raticides: • Adopted on 1960, derived from the work of Chitty and Dotty in the 1940. • Revised by OEPP in 1980.	active substance also remained intact. The block bait has an efficacy of 95 % at T0 and 100% at T6.	containing 0.005% of Difenacoum, against brown rats (*Rattus norvegicus*), rapport complement 980, April 1998. Unpublished
Probloc, containing 0.005ppm difenacoum	Albinos brown rats *(Rattus norvegicus)*	Laboratory: household process Test was performed on fresh product and product with a storage of 12 months	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.	*Block bait/ Laboratory efficacy/ Rats /Product at T0 and T12* Palatability of PROBLOC did not decreased during 12 months of storage at ambient temperature (20°C). The block bait has an efficacy of 90 % at T0 and 100% at T12.	***IIIB5-10_06*** De Proft M., CRA Gembloux, Efficacy test through different period of time, performed on PROBLOC, bait ready to use, containing 0.005% of Difenacoum, against brown rats (*Rattus norvegicus*), rapport complement 9547,

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
					1999. Unpublished
Racobloc, containing 0.005ppm difenacoum	Wild brown rats *(Rattus norvegicus)*	Laboratory conditions. 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.	*Block bait/ Field efficacy/ Rats / Fresh product (T0)* Very good acceptance of the bait RACO BLOCS despite the changing of food type. Excellent efficacy observed, markedly higher to the 90 % (95%) required by the guidelines.	***IIIB5-10_07*** Grolleau G., Panciroli J., Pest Control Assistance (PCA), Experimentation, in nature, of block bait against rats (*Rattus Norvegicus*) 2005. Unpublished
DIFEBLOC, containing 0.005ppm difenacoum	Wild brown rats *(Rattus norvegicus)*	Field study: experiment conducted in restaurant. Test was performed on product with a storage of	The method used has been inspired by the French method called "method no. 002 from Biological Trials	*Block bait/ Field efficacy/ Rats / Product at T2 years* Good acceptance for the two years old paraffin blocks bait of DIFEBLOC,	***IIIB5-10_08*** -, LODI, Efficacy trial: Rodenticide block containing 0.005%

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
		12 months	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.	despite the changing of food type. Efficacy reaches almost the 90 % required by the guidelines.	Difenacoum, after 2 years ageing, against rats (*Rattus norvegicus*), Trial date= 6th April to 13th May, 2009. Unpublished
Probloc, containing 0.005ppm difenacoum	Sewer rats (*Rattus norvegicus*)	Field: study conducted in sewer The Probloc wax blocks were 150g blocks packed in polystyrene foam jars. Probloc remained stable despite being in a damp environment prone to flooding.	Aim of study was to test the resistance of Probloc to the very damp conditions in a sewer system, to monitor the uptake of the blocks by rats in "field" conditions and to monitor the uptake over time.	*Block bait/ Field efficacy/ Black rat /* Good acceptance of the bait was observed. Blocks were assessed 10 and 23 days after placing the bait. There was a markedly lower consumption at the 2nd assessment timing indicating that the population had diminished dramatically (56% blocks eaten vs 12%). No dead rats were found but this is not unusual in an open sewer system. After 23 days	***IIIB5-10_09*** Field trial with Probloc wax baits against sewer rats, March 1st-23rd 2010. Unpublished.

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
				most of the blocks remaining were still relatively intact considering the difficult environmental conditions.	

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

3.3.1. Description of the intended use(s)

Ruby Block is a rodenticide wax block 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. Use of this product in fields will be covered under the Plant Protection Product Directive. Ruby Block takes the form of a solid waxy block with a strong sweet smell. It contains 0.005 % (w/w) or 50 ppm difenacoum, a second generation 4-hydroxy coumarin, a superwafarin anticoagulant, which causes death due to 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. These are held together with an edible wax such that the block retains its integrity under humid conditions. The blocks are made in a range of shapes and sizes, being typically rectangular, and are available in weights of 20g, 30g and 100g. The blocks are dyed red to make them unattractive to wildlife, birds in particular.

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**

Parameter	Test material	Species	Result	Classification	Ref.
	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 Toxicity	Difenacoum technical, 97.7 % w/w purity	Rat CRL:(WI)BR (Wistar), female / male	Males: LC_{50} = 20.74µg/L/4h Females: LC_{50} = 16.27µg/L/4h	T+; R26 / Acute Tox. 2; H330	[redacted] (1995) 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-coagulent 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] 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):**

Parameter	Test material	Species	Result	Classification	Ref.
					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 % 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 Block

Parameter	Test material	Species	Result	Classification	Ref.
Acute Oral Toxicity	Difenacoum wax block bait.	Rat, female, Sprague-	LD_{50} > 2000 mg/kg bw	none.	[redacted] (2009). study

Parameter	Test material	Species	Result	Classification	Ref.
	Batch: PB090209	Dawley, SPF Caw, 6 in total.			number: TAO423 PH-09/0085
	Acceptable (Y/N): Yes		**Method:** OECD 423 (2002)		**GLP (Y/N): Yes**
	Comments: No mortality occurred during the study at 2000mg/kg. There were no clinical signs observed. 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). Considering the water solubility of the active substance is extremely low, the use of a water vehicle for gavage is questionable because we do not know the content of difenacoum prior to gavage. 2g of wax block was powdered and mixed with 10 ml water and then filtered before use.				
Acute Dermal Toxicity	Difenacoum wax block bait. Batch: PB090209	Rat, male & female, Sprague-Dawley, SPF Caw, 10 in total.	LD_{50} > 2000 mg/kg bw	none.	[redacted] (2009). study number: TAD PH-09/0085
	Acceptable (Y/N): Yes		**Method:** OECD 402 (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 extremely 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 wax block formulation. Active substance has very low volatility and is only present at 0.005% (w/w) in the solid, wax 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 BLOCK BAIT and the label claims, the rodenticide BLOCK BAIT is not intended to be used in a mix with other biocidal products. Company justification accepted.				
Acute Skin Irritation	Difenacoum wax block bait. Batch: PB090209	Rabbit, male, NZW, 3 in total	No irritation	none	[redacted] (2009). study number: IC-OCDE PH-09/0085
	Acceptable (Y/N): Yes		**Method:** OECD 404 (2002)		**GLP (Y/N): Yes**
	Comments: The test item was reduced to a fine powder with a coffee mill. 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.				
Acute Eye Irritation	Difenacoum wax block bait. Batch: PB090209	Rabbit, male, NZW, 3 in total	Slight irritation	none	[redacted] (2009). study number: IO-OCDE PH-09/0085
	Acceptable (Y/N): Yes		**Method:** OECD 405 (2002)		**GLP (Y/N): Yes**
	Comments: The test item was reduced to a fine powder with a coffee mill. The test item was applied at a dose of 0.1 g instilled into the conjunctival sac of one eye in each animal. After 1 hr the treated eyes of animals A9664 and A9665 were rinsed to				

<table>
<tr><th>Parameter</th><th>Test material</th><th>Species</th><th>Result</th><th>Classification</th><th>Ref.</th></tr>
<tr><td></td><td colspan="5">wash out remaining residual material. Ocular conjunctivae reactions observed during the study were slight to moderate and totally reversible by 48 hr in the three animals. Company report accepted. Results (expressed as mean of the 24, 48 and 72 hr time points per animal) do not warrant classification.
<table>
<tr><th>Animal number</th><th>A9650</th><th>A9664</th><th>A9665</th></tr>
<tr><td>Corneal Opacity</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>Iritis</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>Redness</td><td>1.7</td><td>0.7</td><td>0.7</td></tr>
<tr><td>Chemosis</td><td>1.0</td><td>0.3</td><td>0.3</td></tr>
<tr><td>Result</td><td>negative</td><td>negative</td><td>negative</td></tr>
</table></td></tr>
<tr><td>Skin Sensitisation (M&K)</td><td>Difenacoum wax block bait. Batch: PB090209</td><td>Guinea Pig, female, Dunkin-Hartley strain, 5 in negative control, 11 in treated groups.</td><td>negative</td><td>none</td><td>[redacted] (2009). study number: SMK PH-09/0085</td></tr>
<tr><td></td><td colspan="2">Acceptable (Y/N): No</td><td colspan="2">Method: OECD 406 (1992)</td><td>GLP (Y/N): Yes</td></tr>
<tr><td></td><td colspan="5">Comments: The test item was reduced to a fine powder with a coffee mill but then assessed as unsuitable for intradermal injection. Changes made to the protocol of the GPMT included induction by topical application only. This test should have being revised and concluded as a Buehler test instead of an M&K test in order to carefully ascertain the results. In its present form it is similar to a Buehler but with too few animals in the study. Potentiation by injection of test material with Freund's Complete Adjuvant has not been performed; taking all these things into consideration the company report is rejected. Suitable positive controls were reported. In the original CAR, the applicant submitted two sensitisation studies with a 2.5% liquid concentrate of difenacoum, one Magnusson & Kligman test and one Buehler test (see Doc IIIA, CAR). The RMS concluded that the available studies (both negative) provided sufficient evidence for no sensitisation potential by the active substance. It is therefore unlikely that the product ruby wax is a skin sensitiser on the basis of its difenacoum content.</td></tr>
</table>

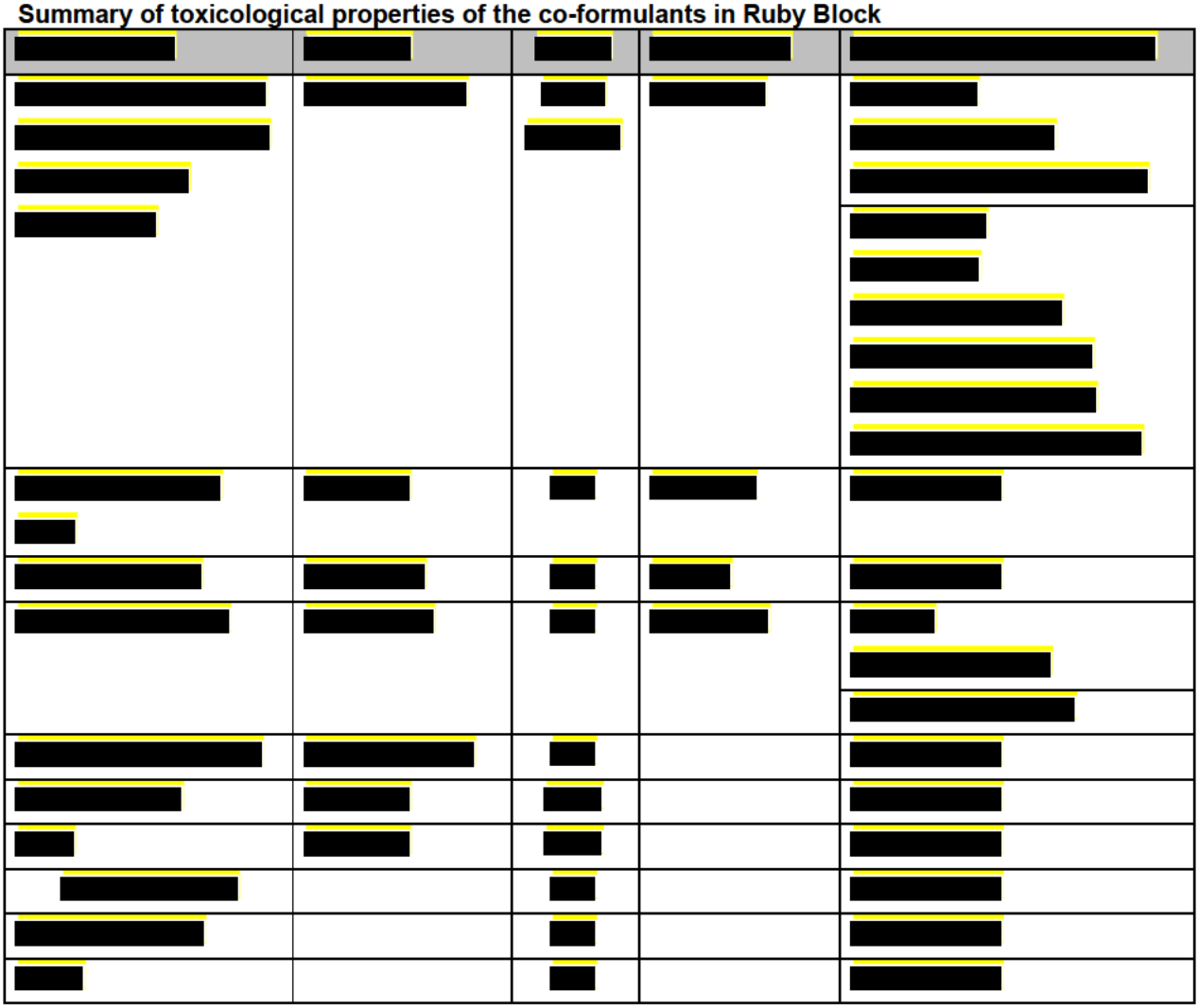
Conclusion:
According to the results of the toxicological studies, Ruby Block (containing 50mg/kg difenacoum) does not classify with respect to Directive 1999/45/EC or Regulation (EC) No 1272/2008. However, safety phrases and precautionary statements are proposed by the Rapporteur. One issue that does not seem to be 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 x 10^{-4} g/l at pH 6.5 or < 0.5mg per litre, 3.72 x 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 Block



3.3.3. Exposure Assessment for Human Health

The most relevant route of exposure to the active substance is the dermal route. For exposure assessment only active substance from wax blocks has been modelled. The block product typically takes the form of a solid waxy block with a strong sweet smell containing 0.005% w/w difenacoum. The 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, inhalation exposure is irrelevant. Inhalation exposure from handling grain bait during loading/application and cleaning is also proposed as negligible. The

only relevant inhalation exposure is assumed to be that from the decanting of loose grain, pellets and granules due to the potential release of airborne dusts.

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, (teratogenicity 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 Block 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

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 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 of 10 blocks. 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 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 – 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 (20g wax block baits, 5 blocks/bait box) 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 x 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 × (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 product to five bait sites 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. 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 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.

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) without 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.

3.3.4.2. Non-professional users

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 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 ecotoxicology 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".*[19]

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 IE-CA 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 IE-CA 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}*

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mg/l, with PNECwater of 0.06 µg/l the risk ratio will be 0.00016[20]. 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 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."[19]

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 IE-CA 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.[21] The IE-CA 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 PNECwater 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 is 480µg/l (the limit of solubility). In the absence of any ecotoxicological data for sediment-dwelling organisms, the PNECsediment was calculated using the equilibrium partitioning method resulting in a value of 2.51 mg/kg (wet weight).

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

21 "*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)

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 PNECsoil of 0.877 mg/kg wet weight was determined.

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

Difenacoum is very toxic to birds, with the $PNEC_{oral}$ of birds determined to be 0.5 µg/kg food or 0.1 µg/kg bw/d. Difenacoum is also very toxic to mammals The PNECoral 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 Blocks 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 Block 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 Block, 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, in sewers, and open areas. The product is applied as a wax block in secured bait stations. The directions for use including minimum and maximum application rates are:

Rats: 90-100 g of blocks spaced 10 m apart (5 m apart in high infestation areas). Typical treatment time 6 weeks.

Mice: 20-30 g of blocks spaced 5 m apart (3 m apart in high infestation areas). Typical treatment time 6 weeks.

3.3.6-1. Aquatic compartment

Ruby Block is used in sewer systems to control rats and mice. Consequently, exposure to the aquatic compartment occurs through the STP route. Based on worst case assumptions [22] 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 to 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 wax blocks 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.

[22] Realistic worst-case: 21 days campaign

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

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 2.41x 10^{-3} mg/kg wwt. The highest concentration of difenacoum in soil from in and around buildings[23] is 0.0348 mg/kg wwt under realistic worst case conditions (200 g of product/bait point, each bait point is 5 m apart).

The notifier also proposes to use the product in open areas. The IE-CA notes no scenario is prescribed in the ESD for the use of wax blocks in open areas. The notifier used the scenario for the outdoor use of impregnated grain in open areas to support the authorisation of the wax block. This approach has been used in the past for other rodenticides and is deemed acceptable by the IE-CA. 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. However, the IE-CA notes the ESD states "Wax blocks are only allowed for use in feeding stations in the Nordic countries; however, in many other countries in the EU wax blocks (100-200 g) may be placed directly inside holes. 20-30 g wax block baits are also commonly used in several countries e.g. in UK." Consequently, the use of 200 g by the notifier in the exposure assessment seems reasonable and is deemed acceptable by the IE-CA. 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[24], the maximum concentration in soil from applications in waste dumps is predicted to be 0.0082 mg/kg wwt.

23 <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 double the proposed amount.

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)

<u>Open areas (Grain scenario used as a surrogate for wax blocks)</u>

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

24 <u>Waste dumps</u>

Amount of product used in control operation per application: For high infestations of rats the blocks are spaced 5 m apart. This could potentially result in a maximum of ~441 blocks (21, 100 m lines of 21 blocks, 5 m apart) in a 1 ha area during high infestations. This would correspond to ~44.1 kg of product

No. of replenishments: 7

Fraction of active ingredient released to soil through excreta and dead bodies 0.9.

Area of waste dump: 1 ha

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.

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 wax blocks 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 □g/L.

Table 3.3.6.4-1. Predicted Environmental Concentration (□g/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 blocks are spaced 5 m apart. According to calculations provided by the IE-CA this could potentially result in a maximum of 441 blocks (21 100 m lines of 21 blocks, 5 m apart) in a 1 ha area during high infestations. This would correspond to ~44.1 kg of product. This is higher than the default value considered in the ESD under realistic worst-case conditions. Consequently the notifiers exposure calculation is not sufficient to support this use. The IE-CA generated new exposure calculations for this use

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 baits. 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 Blocks. 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 Blocks result in unacceptable risks to birds and mammals (see ANNEX VI).

3.3.7. Risk Characterisation for the Environment

Ruby Block is used in sewer systems, in and around buildings, open areas and waste dumps to control rats and mice. Exposure to the aquatic compartment occurs through the STP route. Exposure of soil to the active substance occurs via residues present in sewage sludge after using wax blocks in sewers 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 Blocks 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 Block 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 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 wax blocks 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 Block 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: sewers, in and around buildings, open areas and waste dumps. Therefore, normal use of Ruby Blocks 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 Block bait. One day's consumption of difenacoum 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's 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 Block 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% of the total ingested. 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 Blocks. Due to high food intake in relation to the body weight, 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 Block 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 when 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 Blocks. The derivation of $PNEC_{oral}$ for birds and mammals is outlined in Annex VI. The derivation of PEC values for mammals and birds that consume fish and earthworms is outlined in ANNEX VI. These values assume direct ingestion of Ruby Block by the prey, and rely 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 Block 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 Blocks, 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 Block, 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 with lower residues in other tissues including the fat tissue. 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 carries s 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 should 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.
- For use in sewers where there is no risk to children, companion animals and non-target species blocks should be secured to available structures by wire to ensure the block is not washed away.
- 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:

This product contains paraffin wax, which is combustible and vapours from molten wax are flammable.

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 required, 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

This product contains paraffin wax.

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 Block, 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 Block 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.

From the results of acute toxicology studies presented for the product, Ruby Block (containing 0.0055 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. 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.

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 secured in sealed packs and 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. Additionally, baits should be placed in areas inaccessible to children.

An environmental exposure and effects assessment for the product indicated that difenacoum in Ruby Block 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 Block does not adversely impact non-target organisms in the aquatic or terrestrial compartments when used according to label instructions. However, there is a high potential 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 appropriate and available risk mitigation measures, as outlined in section 3.4.

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 Block 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 Block is for a period of 5-years with an annual renewal.

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

Only ready-to-use Ruby Block 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 rats and mice (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 only 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. The product can also be utilised in sewers. 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 be used for rodent control in tamper resistant, secured bait stations or other secure coverings. However, for use in sewers where there is no risk to children, companion animals and non-target species blocks should be secured to available structures by wire to ensure the block is not washed away.

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

Wax blocks shall be secured to the bait station(s) so that rodents cannot 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.

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 Block, the authorisation holder shall provide statistics to PRCD on the import and export from Ireland and also manufacture statistics where appropriate for Ruby Block 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 - July 2013

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)[25]

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]

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

Study summaries of new data[26] 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. IE-CA accepts France's assessment.

[redacted]

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

[redacted]

[redacted]

[redacted]

[redacted]

Product trade name: Ruby Block

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[27]	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		[redacted]	[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]

[27] 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]	[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[28] 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).

[28] 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 Block

Subsection (Annex Point/TNsG)	Method	Purity/ Specification	Result	Remarks/ Justification	GLP (Y/N)	Reliability	Reference	Official Use only
3.1 Appearance (IIB3.1/Pt. I-B3.1)	Red block							
3.1.1 Physical state and nature	solid							
3.1.2 Colour	red							
3.1.3 Odour	Slightly waxed							
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 that difenacoum is incapable of decomposing,				

				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)*.				
3.4 Flash-point and other indications of flammability or spontaneous ignition (IIB3.4/Pt. I-B3.4)	EPA 830.6315	-	**flammability** : None observed	There are no other components present in the formulation which present flammability properties.				
Flammable properties				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 solid block at ambient temperature.				
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 solid block 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,	Block baits contained	Degradation: < 25% after 5 weeks at	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.	Y	1	Biannic ML., LODI-Group, 2008-01-07	

	CIPAC MT 46.3	0.005% Difenacoum	54°C. (stable)	No significant change was observed in the characteristics of the items, neither in the difenacoum content after the accelerated storage procedures.				
(IV.B3.7.2)	- GIFAP Monography n°17, CIPAC MT 46	Block baits contained 0.005% Difenacoum	< 25% after 14 days at 54°C (stable)	No significant change was observed in the characteristics of the test item neither in the difenacoum content after the accelerated storage procedures. The test items were considered to be stable.	Y	1	Magnier C., LODI-Group, Study report n° LODI15/2009 (2009-11-23)	
(IV.B3.7.3)	- HPLC(UV) and Azur after 6 months and 2 years storage at ambient T°.	Block baits contained 0.005% Difenacoum	<25 % after 2 years at T°N.	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	Biannic ML, LODI-Group, 2009-11-12	
Effects of light				None, see packaging				

Reactivity towards container material				Compliant with ADR, DOT and EPA specifications				
Other	give in months if shelf life is < 2 years							
3.8 Technical characteristics (IIB3.8/Pt. I-B3.8)								
Wettability/ Suspensibility				Not applicable, the product is a ready-to-use block bait.				
Wet sieve analysis				Not applicable, the product is a block.				
Emulsifiability	Only for ECs and ready for use emulsions			Not applicable, the product is a block.				
Disintegration time				Not applicable, the product is a block..				
Attrition/friability of granules; integrity of tablets				Not applicable, the product is is a block.				
Persistence of foaming				Not applicable, the product is a block.				
Flowability/Pourability	Flowability only for granular preparations,			Not applicable, the product is a block.				

	pourability only for suspensions							
Dustability	Only for dustable powders			Not applicable, the product is a block.				
3.9 Compatibility with other products (IIB3.9/Pt. I-B3.9)				Not applicable, the product is a ready-to-use block bait 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 block.				
3.11 Viscosity (Pt. I-B3.10)				Not applicable, the product is a block.				
3.12 Particle size distribution (Pt. I-B3.11)	Only for powders and granules			Not applicable, the product is a block.				

Conclusion:

Ruby block bait is not flammable, explosive or oxidising and does not classify from a physical/chemical point of view. It is stable for two years at ambient temperatures. The test item is a ready-to-use block bait and is not intended to be added or mixed with any other product.

Data requirement:

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

Methods of Analysis:

Doc IIIB Section 4.1		**Analytical Method for Detection and Identification**	
BPD Data Set IIB/ Annex Point III.4		Analytical method validation for the determination of difenacoum in block baits	
		2 Reference: IIIB4.1a	**Official use only**
2.1	***Reference***	Ricau H, Analytical method validation for the determination of Difenacoum in Difenacoum Block Bait, Anadiag group-Defitraces, Study Report n°09-902018-005, 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 grain 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 a mobile phase of methanol.	
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.	
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, 97 and 100%	
4.5.1	**Recovery results**	Between 95% and 100% 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 95 and 100%.	
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 Reference Member State	
Date	10.11.2010	
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		**Analytical Method for Detection and Identification**	
BPD Data Set IIB/ Annex Point III.4		Analytical method validation for the determination of difenacoum in block baits	
		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	
2.2	***Guideline study***	Method was developed in compliance with the Standard Operating Procedures in uses at DEFITRACES.	
2.3	***GLP***	Yes	
2.4	***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	
3.2	***Preliminary treatment***		
3.2.1	**Enrichment**	Difenacoum was extracted from the grain bait using methanol and heated under reflux for about 90 minutes at 80°C.	X
3.2.2	**Cleanup**	Extract was filtered through a Whatman filter N°40 and diluted in methanol and acetonitrile before injection.	
3.3	***Detection***		
3.3.1	**Separation**	HPLC using a Supelcosil LC-8 (25*4.0 ID) column with a flow rate	

	method	of 0.3 ml/min and a mobile phase of methanol.	
3.3.2	**Detector**	UV detection at 310 nm	
3.3.3	**Standard (s)**	Difenacoum standard (Cluzeau Info Labo) for reference item solution preparation	
3.3.4	**Interfering substance(s)**	No peak was observed in the blank solvent, in the blank formulation and in the reference item.	
3.4	***Linearity***		
3.4.1	**Calibration range**	The response of difenacoum is linear within the range of 0.0008mg/ml to 0.0012 mg/ml.	
3.4.2	**Number of measurements**	6	
3.4.3	**Linearity**	Correlation coefficient = 1.000	
3.5	***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.	
3.6	***Recovery rates at different levels***	The method has been validated at 0.005 % (m/m).	
3.6.1	**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.	
3.7	***Limit of determination***		
3.8	***Precision***		
3.8.1	**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%).	X
3.8.2	**Independent laboratory validation**	Not available	

		4. Applicant's summary and conclusion	
4.2	***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.	
4.3	***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%.	
4.3.1	**Reliability**	1	
4.3.2	**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	10.11.2010	
Materials and Methods	The method of analysis presented above is acceptable.	
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 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. The results for linearity, precision, accuracy and specificity are acceptable.	
Conclusion	The method of analysis is acceptable.	
Reliability	1	
Acceptability	Acceptable	
Remarks	None.	

Doc IIIB Section 4.1		**Analytical Method for Detection and Identification**	
BPD Data Set IIB/ Annex Point III.4.		Analytical method validation for the determination of Difenacoum in block baits	
		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	X
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 block placebo. An adjacent peak appeared in the stressed block but the resolution being higher than 2 (R = 2.16), 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 97.22% and 100.43% for block bait. The mean recovery = 98.88% 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 translate 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 09-902018-005 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 09-902018-005 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 BLOCK bait	
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. Place the bait nearby: 1 block of 30g every 3 to 5 metres against ***mice*** and 3 blocks of 30g every 5 to 10 metres against ***rats*** (depending on infestation level). The distance has to be adapted to the infestation. he distance has to be adapted to the infestation. 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 bait, until the consumption has stopped. 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

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. Place the bait nearby: 1 block of 30g every 3 to 5 metres against ***mice*** and 3 block of 30g every 5 to 10 metres against ***rats*** (depending on infestation level). The distance has to be adapted to the infestation. he distance has to be adapted to the infestation. 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 bait, until the consumption has stopped. 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

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, professsional,**	*Include code(s) and term(s) and briefly describe the use conditions*

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

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 I_App 3 (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.

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. Place the bait nearby: 1 block of 30g every 3 to 5 metres against ***mice*** and 3 block of 30g every 5 to 10 metres against ***rats*** (depending on infestation level). The distance has to be adapted to the infestation. he distance has to be adapted to the infestation. 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 bait, until the consumption has stopped. general rodenticide treatment with anticoagulant rodenticides would be expected to achieve control within 35 days. ***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	*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*

(IIB5.10)

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

LODI, Efficacy trial: Rodenticide block containing 0.005% Difenacoum, against house mice (*Mus musculus*), Trial date: 10th April to 6th May, 2007.

Unpublished

5.2 Data protection

Yes

5.2.1 Data owner

LODI S.A.,

Parc d'activité des Quatre Routes,

35390 Grand Fougeray, FRANCE

5.2.2 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

5.3 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.

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 Difebloc

Composition of Product tested 0.005 % of Difenacoum

Physical state and nature Paraffin rodenticide block bait

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 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 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 a period between 7 to 10 days.

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 mice population. For the post-baiting, it does not exceed 5 days in general, in order to avoid eventual recontamination by mice 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

Not mentioned please find details of estimation in table 1.2.

Test system

The experimental site is a restaurant: Le Gavroche (75002 Paris) which is composed of one ground floor which is composed of

- Several storage rooms in cellar
- Equipped kitchen
- Bakery room with cupboard and local for table and chair storage
- Restaurant and reception rooms, a cloakroom for employees and a technical room.

Some specific parts described above were used for baiting and the efficacy test with ageing block.

Application of TS

Determination of initial consumption level: 50g of wheat were placed in rat bait box. Every day each spots were weighed until graph reaches a plateau in the food consumption.

Test conditions

The experimental site is a restaurant: Le Gavroche (75002 Paris) which is composed of several parts grouped in one floor. Please find

in the following tables where exactly baits were placed at each part of the building:

Parts	Baits were place in	Comments
Bar	At 6 spots.	-
Kitchen	Sinks	Droppings onto the shelves in the kitchen.
	Hobs	
	Cooking tables	Infestation seems localised in this room
	shelves	
Separator	Folding screen and shelves	-
Baking flour	Cupboard,	Bakery regularly washed with plenty of water, treatment not feasible there.
	Good lift	
	Mezzanine	Droppings in air conditioning, mezzanine was treatment event if no traces were observed
	Air conditioning system on mezzanine	
Restaurant	Table for buffet	-
	Shelves	
Toilets	At 4 spots.	Bait boxes were placed even there were no trace of mice

Every evening, employees have removed the food, so that mice feed only with the bait dispatched in the all restaurant, in order to quickly reach the initial consumption plateau.

Duration of the test / Exposure time

The experiment was settled down all along the month of march.

- Step 0: Inspection of the trial place and setting up of the baiting map (number and place points)
- Pre-baiting: Determination of initial consumption with wheat= 14 DAYS, initial amount placed 50g of wheat.
- Poisoning bait : Treatment with 1 or 2 blocks for each bait point= 7 DAYS

- Post-baiting: Determination of final consumption= 5 DAYS

Any rest period was observed.

Number of replicates performed

No replicates

Controls

No control.

Examination

Effect investigated

Reduction of mice population by poisoning with paraffin block bait produced in the year.

Method for recording / scoring of the effect

The method is to estimate by indirect observation, the bait consumption, a decrease of population before and after poisoning bait.

Intervals of examination

Daily

Statistics

[Average Pre-btg (grams) – Average Post-btg (grams)] x100/ Average Pre-btg (grams) = Efficacy

Btg= baiting

Post monitoring of the test organism

Yes, X

After the poisoning phase, safe wheat replaced block at same spot. It is called, the post-baiting phase, where the reduction in population is estimated.

7 Results

Efficacy

Pre-baiting consumption (for the last 3 days) : 471.6g X

Post baiting consumption (for the last 7 days): 13.5 g

Based on calculus explained in 2.4.4., we obtain an efficacy of 97.1% efficacy.

X

Dose/Efficacy curve

An important decrease in block consumption was observed at day 19 of the experiment, either Day 5 of the poisoning period.

The changing in food, wheat to poisoned block has seemed create a phenomena of mistrust among mice, which was observed by a low consumption the first days, were a total of block were 131.1 and 291.7 for the day 1 and 2. 288 g were consumed. Generally, the neophobia has been within 2 days, with a consumption of 389 g at the third measurement.

Begin and duration of effects

The consumption of poisoned bait felt on the 5th day of the treatment phase.

Observed effects in the post monitoring phase

1. The post baiting happened normally. The flow of consumption remains as low during the post period than the end of the treatment period.
2. By indirect observation, we suppose the targeted animals are died from the ingestion of poisoning bait.

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

Details for the efficacy calculus:

	Pre-baiting	Post baiting
Consumption	471.6g	13.5g
Average based on the last	3 days	7 days
Efficacy	(471.6-13.5)/471.6 x 100 <=> 97.1%	

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	This experiment is a scaling-up. This experiment is closer to reality than laboratory process. Moreover, restaurant and food storage are exposed to mice invasions. Please note that both conditions are tested in the dossier.
Intended actual scale of biocide application	Not applicable
Relevance compared to field conditions	
Application method	Not applicable, this study is closer to field condition than laboratory process.
Test organism	YES
Observed effect	Not applicable
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.

9 Applicant's Summary and

conclusion

Materials and methods

The experimental site has been chosen to their natural condition opportunities, indeed all food storage room, even regularly washed, represents for rodent an important part of their habitat.

The restaurant, “Le Gavroche”, is located in Paris, 75 002. 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 block 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 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.

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.

Assessment of efficacy, data analysis and interpretation

The post baiting happened normally. The flow of consumption remains as low during the post period than the end of the treatment period.
Some small peaks appear during the first days of the post baiting, then the consumption decreases again at the end of the period.
The maximum consumptions means a phenomenon of recovery (partial fast during, hence compensation. and then a small fall from day 3 to 5. This small fall exists for two reasons:

- A return to normal consumption among the surviving mice and,
- an end of mortality of less sensitive mice
  (13.6+13.9+11.8+12.4+16.2) /5= 13.5 g/day

The efficacy assessment can thus be easily calculated:

[Average Pre-btg (grams) – Average Post-btg (grams)] x100/ Average Pre-btg (grams) = Efficacy

$\Leftrightarrow$ (471.6-13.5) *100 / 471.6 =97.1%

Conclusion

Very good acceptances for the paraffin block bait DIFEBLOC, despite the changing of kind of food and excellent efficacy (97.1%). Moreover, the efficacy guidelines require a efficiency higher to 90 %, which is fill in.

Proposed efficacy specification

According to the point, we can declare the product as very efficiency with the rate of 97.1% find in this experiment, which is compliance with the rodenticide guidelines.

	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	**2.4.5** Post baiting for 5 days after the poisoning period. **3.1** Post baiting (post poisoning) was reportedly conducted for 5 days. **3.1.1** Remove the word “either” to read “day 5 of the poisoning period”.
Summary and conclusion	Excellent acceptances for the paraffin block bait DIFEBLOC was observed, (97.1%) indicating effective control of the mouse population under field test conditions.
	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	DIFEBLOC: paraffin rodenticide block bait. Containing 0.005 % of Difenacoum
Origin	Batch N°: 070307. Manufacturing date: 03/2007.
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 mice, not estimated in the first phase.
Collection / storage of samples	By comparative measure between before and after baiting with placebo (wheat)
Preparation of inoculum for exposure	The measures for the pre-baiting started the 6th May 2009, at the rate of 50g of wheat by station. Fourteen days were necessary to obtain a stabilised consumption of wheat. One or two poisoning block, during the treatment period had to be placed due to the weight difference and the initial consumption. The poison period lasted 7 days. Immediately after the poisoning period, 5 days of post baiting with safe wheat was exposed in the bait station. The weighing process was recorded every day of the 3 phases.

Pretreatment	Any
Active substance determined in the product	Containing 0.005 % of Difenacoum

1.2 Test organism (*if applicable*)

Criteria	Details
Species	Mouse *(Mus musculus)*
Strain	Wild
Source	From the surrounding areas of the restaurant
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	The average consumption of last 3 days of pre-baiting shows: (472+473.8+469)/3= 471.6 grams / day. Based on the average and if we allocate an effective consumption of 3 g per mice, we could estimate the test population to nearly 157 mice.
Method of cultivation	Bait stations were weighted daily.
Pretreatment of test organisms before exposure	Preliminary step was put in place to bring as many mice as possible.
Initial density/number of test	Based on the pre-baiting step and an average of 3g per

organisms in the test system	mouse, the population is estimated to 157 mice.

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	Whole wheat during the pre-baiting and post baiting phase and Block during the poisoning phase
Delivery method	In box mice bait
Dosage rate	Weighted the daily consumption
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_02

Reference

Official use only

Reference

-, LODI, Efficacy trial: Rodenticide block containing 0.005% Difenacoum, after 2 years ageing, against house mice (*Mus musculus*), Trial date= 2nd to 29th March, 2009.

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 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 Difebloc

Composition of Product tested 0.005 % of Difenacoum

Physical state and nature Paraffin rodenticide block bait

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 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 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 a period between 7 to 10 days. 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 mice population. For the post-baiting, it does not exceed 5 days in general, in order to avoid eventual recontamination by mice 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	Not mentioned please find details of estimation in table 1.2.	X
Test system	The experimental site is a restaurant: Le Taillevent (75000 Paris) which is composed of : • Several storage rooms in cellar • Equipped kitchen • Bakery room with cupboard and local for table and chair storage • Restaurant and reception rooms, a cloakroom for employees and a technical room. Some specific parts described above were used for baiting and the efficacy test with ageing block.	
Application of TS	Determination of initial consumption level: 50g of wheat were placed in	

rat bait box. Every day each spots were weighed until graph reaches a plateau in the food consumption.

Test conditions

The experimental site is a restaurant: Le Taillevent (75000 Paris) which is composed of several parts. Please find in the following tables where exactly baits were placed at each part of the building:

Parts	Comments	Baits were place in
Cellars	No traces in cellular except in food storage where some bags were damaged nibbled.	Cheese storage room
		Spices storage room
Kitchen	Kitchen regularly washed with plenty of water, treatment not feasible there. Traces of nibbled wastes and droppings	In goods lift
		Dustbins room
Baking flour	Bakery regularly washed with plenty of water, treatment not feasible there. Droppings in air conditioning, mezzanine was treatment event if no traces were observed	Cupboard,
		Good lift
		Mezzanine
		Air conditioning system on mezzanine
Restaurant		Back room, along the wall (under removable covering)
		Side table
		Toilets
First stage	Any trace of mice	Technical local
		Good lift
		Boiler room
		Storage of crockery

Duration of the test / Exposure

The experiment was settled down all along the month of march.

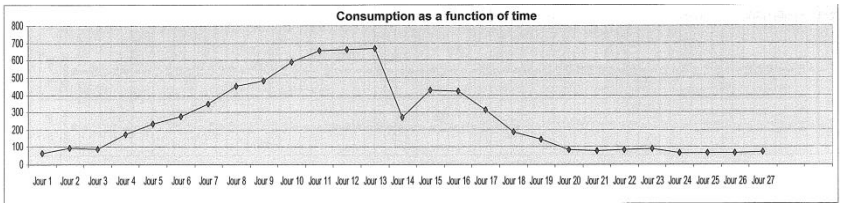
- Step 0: Inspection of the trial place and setting up of the

time	baiting map (number and place points) • Pre-baiting: Determination of initial consumption with wheat= 13 DAYS • Poisoning bait : Treatment with 1 or 2 blocks for each bait point= 9 DAYS • Post-baiting: Determination of final consumption= 5 DAYS Any rest period was observed.
Number of replicates performed	No replicates
Controls	No control.
Examination	
Effect investigated	Reduction of mice population by poisoning with 2 years old paraffin block bait.
Method for recording / scoring of the effect	The method is to estimate by indirect observation, the bait consumption, a decrease of population before and after poisoning bait.
Intervals of examination	Daily
Statistics	[Average Pre-btg (grams) – Average Post-btg (grams)] x100/ Average Pre-btg (grams) = Efficacy Btg= baiting
Post monitoring of the test organism	Yes, After the poisoning phase, safe wheat replaced block at same spot. It is called, the post-baiting phase, where the reduction in population is estimated.

13 Results

Efficacy	Pre-baiting consumption (for the last 3 days) : 662.6g Post baiting consumption (for the last 4 days): 272.9 g Based on calculus explained in 2.4.4., we obtain an efficacy of 89.6% efficacy.

Dose/Efficacy curve	An important decrease in block consumption was observed between 3 and 6 days after the peak of block consumption. Treatment effects were observed between 3 and The changing in food, wheat to poisoned block has created phenomena of mistrust among rat, which was observed by a low consumption the first day, only 288 g were consumed. Generally, the neophobia has been within 2 days, with a consumption of 1762 g at the third measurement.	X
Begin and duration of effects	The consumption of poisoned bait felt between the second and the 6th day of the treatment phase.	
Observed effects in the post monitoring phase	The post baiting happened normally. The flow of consumption remains as low during the post period than the end of the treatment period. Some small peaks appear during the first days of the post baiting, then the consumption decreases again at the end of the period. The maximum consumptions means a phenomenon of recovery (partial fast during, hence compensation. and then a small fall from day 3 to 5. This small fall exists for two reasons: - A return to normal consumption among the surviving mice and, - An end of mortality of less sensitive mice.	
Effects against organisms or objects to be protected	By indirect observation, we suppose the targeted animals are died from the ingestion of poisoning bait.	
Other effects	-	
Efficacy of the reference substance	Not applicable	
Tabular and/or graphical presentation of the summarised results	Total food consumption during the experiment:	



(jour= days)

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 This experiment is a scaling-up. X

This experiment is closer to reality than laboratory process. Moreover, restaurant and food storage are exposed to mice invasions. Please note that both conditions are tested in the dossier.

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 block bait, even with 2 years of storage is efficient against rodent.

Observed effect Not applicable 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.

15 Applicant's Summary and conclusion

Materials and methods The experimental site has been chosen to their natural condition opportunities, indeed all food storage room, even regularly washed, represents for rodent an important part of their habitat.

The restaurant, “Le Taillevent”, is located in Paris, 75 000. 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 block 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.

Rest period:

During 7 days, no food was exposed in the bait station.

Post-baiting:

Placebo was put in place during 5 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.

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.

Assessment of efficacy, data analysis and interpretation

The post baiting happened normally. The flow of consumption remains as low during the post period than the end of the treatment period.
Some small peaks appear during the first days of the post baiting, then the consumption decreases again at the end of the period.
The maximum consumptions means a phenomenon of recovery (partial fast during, hence compensation. and then a small fall from day 3 to 5. This small fall exists for two reasons:

- A return to normal consumption among the surviving mice and,
- an end of mortality of less sensitive mice
  (67+67.5+67.1+71.3) /4= 272.9 /4 ~ 68 g/day

The efficacy assessment can thus be easily calculated:
[Average Pre-btg (grams) – Average Post-btg (grams)] x100/ Average

Pre-btg (grams) = Efficacy

⟺ (662.6-73.12) *100 / 662.6 ~ 89.6%

Conclusion Good acceptances for the two years old paraffin block bait, despite the changing of kind of food and excellent efficacy. However, the efficacy reaches almost the 90 % required by the guidelines.

Proposed efficacy specification According to the point, we can declare period of 2 years for the consumption of the product, which is efficiency at nearly 90%.

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	16 Evaluation by Rapporteur Member State
Date	April 2011.
Comments	**2.3.1** Mouse *(Mus musculus)* with an estimated population based on census baiting of 220 individuals. **3.1.1** Test was conducted on mice and not rats as described. **3.2** It is “implied” that the target animals died as a result of the ingestion of poison. **4.1** Test was not performed in a laboratory. **4.3** Study is relevant as it was conducted in the field. **4.3.1** Application method was by placing wax bait in baiting station. **4.3.2** Test organism was the Mouse *(Mus musculus)*. **4.3.3** Observed effect was reduction in bait consumption indicating death of the target organism.
Summary and conclusion	The aged wax blocks (2 years old) used in the test proved to be palatable to the target organisms and it achieved excellent control of the mouse population in the restaurant obtaining a calculated 89.6% control based on consumption volumes. A marked decrease in block consumption was noted 3-6 days after the peak of block consumption occurred.
	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	DIFEBLOC: paraffin rodenticide block bait. Containing 0.005 % of Difenacoum
Origin	Batch N°: 070307. Manufacturing date: 03/2007. Stored during 2 years.
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 mice, not estimated in the first phase.
Collection / storage of samples	By comparative measure between before and after baiting with placebo (wheat)
Preparation of inoculum for exposure	The measures for the pre-baiting started the 2d March 2009, at the rate of 50g of wheat by station. One or two poisoning block, during the treatment period had to be placed due to the weight difference and the initial consumption. The poison period lasted 9 days. Immediately after the poisoning period, 5 days of post baiting with safe wheat was exposed in the bait station. The weighing process was recorded every day of the 3 phases.
Pretreatment	Any

Initial density of test population in the test system	Containing 0.005 % of Difenacoum

1.2 Test organism (*if applicable*)

Criteria	Details
Species	Mouse *(Mus musculus)*
Strain	Wild
Source	From the surrounding areas of the restaurant
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	The average consumption of last 3 days of pre-baiting shows: (666.8+663.7+657.3)/3= 6626 grams / day. Based on the average and if we allocate an effective consumption of 3 g per mice, we could estimate the test population to nearly 220 mice.
Method of cultivation	Bait stations were weighted daily.
Pretreatment of test organisms before exposure	Preliminary step was put in place to bring as many mice as possible.
Initial density/number of test	220 mice

organisms in the test 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	Whole wheat during the pre-baiting and post baiting phase and Block during the poisoning phase
Delivery method	In station bait
Dosage rate	Weighted the daily consumption
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_03a

Reference

Official use only

Reference	Prescoot C.V, Efficacy assessment, using the bait choice feeding test, of Difebloc wax blocks (T0) containing 50 mg.kg-1 difenacoum, using CD-1 albino house mouse, Study reference VPU Study Plan Number VPU/10/004, VPU trial No. GB01-10-R009, Project number 153SRI10P, trial code SRIT10-1001-153P. The Vertebrate Pests Unit School of Biological Sciences, The University of Reading Whiteknights, Reading RG6AJ, UK 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, X

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 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 Difebloc

Composition of Product tested 0.005 % of Difenacoum

Physical state and nature Wax block bait

Monitoring of active substance concentration No

Method of analysis During the four day conditioning period, the animals had access to Standard EPA Meal from two symmetrically placed food bowls at the front of each cage. The positions of the two food bowls were alternated daily. The contents of the food bowls were made up daily to provide an excess of the animals 'daily (i.e>10g).

The amount of food consumed by each animal wad determined daily to the nearest 1g by the difference method, taking care first to recover spillage and discard contaminants as far as possible. On each day, both food bowls were weighed, replenished and re-weighed. Following any correction of spillage, spoilage and contamination, the bowl weights were recorded on data entry forms. If a food was fouled by urine or faeces, both food were replaced with fresh. If food, especially spillage, was damp, it was dried before weighed.

During the four-day test period the animals had access to the test item and the challenge diet and the positions of the bowls containing the two diets were alternated daily. Bowl markings indicated whether content are Test (T) or Control (C) diet. The procedures for provisioning and weighing the food bowls were the same as in the conditioning period.

At the end of the test period the animals were returned to laboratory diet and the amount eaten was measured during the fourteen-day observation period.

Weighing scales (Fisherbrand DP 600) were used on data to determine the amounts of diets consumed by the individual animals each day.

Any unusual or significant observations were recorded on data entry forms, including excessive bait spillage, signs of toxicity and death. The theoretical end point was on completion of the specified observation period. Animals were humanely killed (by carbon dioxide inhalation) if they showed signs of toxicity that exceed the severity limit, as specified for that procedure in the Home Office Project Licence of the testing facility.

Reference substance

No

Method of analysis for reference substance

-

Testing procedure

X

Test population / inoculum / test organism

5 males and 5 females of Swiss house mice (*Mus domesticus*).

Test system

The animals were individually caged in purpose-built stainless steel cages measuring 38x28x22 cm. The cages were held in a rack over a plastic tray with an absorbent liner so that spillage could be collected.

Application of TS

During the four day conditioning period, the animals had access to Standard EPA Meal from two symmetrically placed food bowls at the front of each cage. The positions of the two food bowls were alternated daily. The contents of the food bowls were made up daily to provide an excess of the animals daily (i.e>10g).

During the four-day test period the animals had access to the test item and the challenge diet and the positions of the bowls containing the two diets were alternated daily. Bowl markings indicated whether content are Test (T) or Control (C) diet. The procedures for provisioning and weighing the food bowls were the same as in the conditioning period.

At the end of the test period the animals were returned to laboratory diet and the amount eaten was measured during the fourteen-day observation period

Test conditions

Ambient conditions in animals rooms were maintained in accordance with normal laboratory requirement; with a temperature range of 18-24°C, a relative humidity range of 30 % to 80%, with between 10 and 25 air changes per hour, and with a 12 hour light dark-cycle.

Individual animals were be identified by cage label. The test item was identified by a unique reference number (VPU Reference 004/137/3).

Duration of the test / Exposure time

The duration of the test was 22 day, comprising:

- 4 days of acclimatisation,
- 4 day test period (period of exposure to the test item) and
- 14 day observation period.

Number of replicates performed	No replicates
Controls	No control.

Examination

Effect investigated	The bait choice feeding is designed to determine the palatability of established rodenticide bait products for the control of commensal rodent, through testing on a domestic strain of the house mouse (*Mus musculus*). The laboratory choice test procedure is intended to reflect a practical situation in rodent control in which pest rodent have unrestricted access to palatable and familiar alternative food.
Method for recording / scoring of the effect	The procedure is used to generate information on efficacy of bait formulations in accordance with the guidance document on efficacy evaluations of rodenticides (Product type 14) from the European Commission (European Commission, 2008). This document indicates that rodenticide product may be considered "to possess a sufficient level efficacy" if the percentage acceptance of test material is equal or greater than 20% of the total food consumed during the test period.
Intervals of examination	Daily
Statistics	Weighing scales (Fisherbrand DP 600) were used on data to determine the amounts of diets consumed by the individual animals each day.
Post monitoring of the test organism	Yes, After the poisoning phase, a period of 14 days is observed. Any unusual or significant observations were recorded on data entry forms, including excessive bait spillage, signs of toxicity and death. The theoretical end point was on completion of the specified observation period. Animals were humanely killed (by carbon dioxide inhalation) if they showed signs of toxicity that exceed the severity

limit, as specified for that procedure in the Home Office Project Licence of the testing facility.

19 Results

Efficacy

The mean initial weight of the test animals was 26g.

All test animals fed consistently from the feeding bowls during the four day conditioning period and there was no oblivious sign of a preference among the animals for one feeding bowl over another. All animals, therefore, continued into the test period.

Acceptance to the DIFEBLOC wax block was very good and there was a marked preference for the test item over the challenge diet among all individual in the test group. The mean quantity of the test item consumed by each animal during the four-day test period was 14.2 g. A mean of 7.1 g of the challenge diet was consumed during the same period. The mean acceptance of the test item was 66.4% (S.D 12.0), showing that DIFEBLOC was highly palatable formulation.

Mortality was complete (100%) in the test group, with a mean day to death of 5.1 days (range 3 to 7 days). The mean final weight of the animal was 24.0g.

Dose/Efficacy curve

The mean quantity of the test item consumed by each animal during the four-day test period was 14.2 g. A mean of 7.1 g of the challenge diet was consumed during the same period. The mean acceptance of the test item was 66.4% (S.D 12.0), showing that DIFEBLOC was highly palatable formulation.

Begin and duration of effects

Mortality was complete (100%) in the test group, with a mean days to death of 5.1 days (range " to 7 days)/ The mean final weight of the animal was 24.0g. X

Observed effects in the post monitoring

Death of mice X

phase

Effects against organisms or objects to be protected -

Other effects -

Efficacy of the reference substance Not applicable

Tabular and/or graphical presentation of the summarised results The results are summarised in the table below:

7	M	
8	M	
9	M	
10	M	
Total		
Average		
Std Deviation		

*animal terminated

Efficacy limiting factors

Occurrences of resistances Not applicable

Other limiting factors Not applicable

20 Relevance of the results compared to field conditions

Reasons for laboratory testing The laboratory choice test procedure is intended to reflect a practical situation in rodent control in which pest rodent have unrestricted access to palatable and familiar alternative food.

Intended actual scale of biocide Not applicable

application		
Relevance compared to field conditions	Not applicable	
Application method	Not applicable. The bait choice feeding is designed to determine the palatability of established rodenticide bait products for the control of commensal rodent, through testing on a domestic strain of the house mouse (*Mus musculus*).	
Test organism	YES, The fresh product is well accepted by rodents.	
Observed effect	Not applicable	X
Relevance for read-across	Yes, The procedure is used to generate information on efficacy of bait formulations in accordance with the guidance document on efficacy evaluations of rodenticides (Product type 14) from the European Commission (European Commission, 2008). This document indicates that rodenticide product may be considered “to possess a sufficient level efficacy” if the percentage acceptance of test material is equal or greater than 20% of the total food consumed during the test period. The laboratory choice test procedure is intended to reflect a practical situation in rodent control in which pest rodent have unrestricted access to palatable and familiar alternative food.	

21 Applicant's Summary and conclusion

Materials and methods

During the four day conditioning period, the animals had access to Standard EPA Meal from two symmetrically placed food bowls at the front of each cage. The positions of the two food bowls were alternated daily. The contents of the food bowls were made up daily to provide an excess of the animals 'daily (i.e>10g).

The amount of food consumed by each animal wad determined daily to the nearest 1g by the difference method, taking care first to recover spillage and discard contaminants as far as possible. On each day, both food bowls were weighed, replenished and re-weighed. Following any correction of spillage, spoilage and contamination, the bowl weights were recorded on data entry forms. If a food was fouled by urine or faeces, both food were replaced with fresh. If food, especially spillage, was damp, it was dried before weighed.

During the four-day test period the animals had access to the test item and the challenge diet and the positions of the bowls containing the two diets were alternated daily. Bowl markings indicated whether content are Test (T) or Control (C) diet. The procedures for provisioning and weighing the food bowls were the same as in the conditioning period.

At the end of the test period the animals were returned to laboratory diet and the amount eaten was measured during the fourteen-day observation period.

Weighing scales (Fisherbrand DP 600) were used on data to determine the amounts of diets consumed by the individual animals each day.

Any unusual or significant observations were recorded on data entry forms, including excessive bait spillage, signs of toxicity and death. The theoretical end point was on completion of the specified observation period. Animals were humanely killed (by carbon dioxide inhalation) if they showed signs of toxicity that exceed the severity limit, as specified for that procedure in the Home Office Project Licence of the testing facility.

Reliability

1, Study conducted in compliance with agreed protocols.

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.

Assessment of efficacy, data analysis and interpretation

The experiment was conducted on fresh, respectively to the protocol guidelines.

Conclusion

The study showed that, when freshly manufactured, DIFEBLOC wax block is palatable to Swiss House mice, with a mean palatability against ground laboratory diet 66.4%. The formulation also resulted in 100% mortality after a four-day choice between this formulation and challenge diet.

It is apparent from this test that the test item, DIFEBLOC wax blocks, when freshly manufactured, should be favourably for product authorization under both the criteria set by the European commission.

Proposed efficacy specification

The European commission document (European commission, 2008) says in section 4.1 entitled “Norms and Criteria”:
“In the bait choice feeding test the percentage of ingested bait containing the product should be normally ≥ 20%. When the results in ≥ 90% mortality, a lower level than 20% of the total food consumption is acceptable”.

The results of this test are relevant to the field conditions in that the choice test is intended to represent a natural situation in which the test animals have unrestricted access to a well-known food. It is feeding on the familiar diet. The observed effects of high consumption of the test item by mice and the complete mortality of the test group are both relevant to field conditions.

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	**1.3** Guideline study protocol is more appropriate for field testing of rodenticides and not laboratory testing in a choice situation. **2.3.1** 20 animals (10 male and 10 female) are required under in the TNsG on product evaluation but in the CEB guidance the number of animals required is not specified. **3.1.2** Line should be amended to read “range 3 to 7 days”. **3.1.3** 100% mortality was observed in the post observation period. **4.3.3** Observed effect was mortality or exceeding the Home Office toxicity severity limit.
Summary and conclusion	Laboratory mice were used instead of wild mice. 20 animals (10 male and 10 female) are required under in the TNsG on product evaluation but in the CEB guidance the number of animals required is not specified. The fresh DIFEBLOC was palatable as the mean acceptance of the bait was 66.4%. The test is acceptable to confirm the palatability of fresh bait with 100% mortality observed in the mice tested.
	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*)

<table>
<tr><th>Criteria</th><th>Details</th></tr>
<tr><td>Nature</td><td>DIFEBLOC: wax block bait.
Containing 0.005 % of Difenacoum</td></tr>
<tr><td>Origin</td><td>Batch N°: DF241209
Manufacturing date: 24/12/2009
Fresh product</td></tr>
<tr><td>Initial biomass</td><td>Not applicable</td></tr>
<tr><td>Reference of methods</td><td>-</td></tr>
<tr><td>Collection / storage of samples</td><td>By comparative measure between food control and poisoning food.</td></tr>
<tr><td>Preparation of inoculum for exposure</td><td>During the four-day test period the animals had access to the test item and the challenge diet and the positions of the bowls containing the two diets were alternated daily. Bowl markings indicated whether content are Test (T) or Control (C) diet. The procedures for provisioning and weighing the food bowls were the same as in the conditioning period.
At the end of the test period the animals were returned to laboratory diet and the amount eaten was measured during the fourteen-day observation period</td></tr>
<tr><td>Pretreatment</td><td>Any</td></tr>
<tr><td>Active substance determined in the product</td><td>Containing 0.005 % of Difenacoum
Analyse certificate: batch DF241209, manufactured 24/12/2009 (fresh product)
<table>
<tr><th></th><th>Specification</th><th>Decision</th></tr>
<tr><td>Aspect</td><td>Red paraffinic block</td><td>OK</td></tr>
<tr><td>Weight</td><td>Block of 30g</td><td>OK</td></tr>
</table>
</td></tr>
</table>

	Composition	Difenacoum 50ppm±25%	40,56 ppm

1.2 Test organism (*if applicable*)

Criteria	Details
Species	Swiss House mice *(Mus domesticus)*
Strain	Albinos
Source	Charles River UK Ltd
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	5 males and 5 females
Method of cultivation	Bowls were weighted daily.
Pretreatment of test organisms before exposure	-
Initial density/number of test organisms in the test system	5 males and 5 females

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	During the four day conditioning period, the animals had access to Standard EPA Meal from two symmetrically placed food bowls at the front of each cage. The positions of the two food bowls were alternated daily. The contents of the food bowls were made up daily to provide an excess of the animals 'daily (i.e>10g). During the four-day test period the animals had access to the test item and the challenge diet and the positions of the bowls containing the two diets were alternated daily. Bowl markings indicated whether content are Test (T) or Control (C) diet. The procedures for provisioning and weighing the food bowls were the same as in the conditioning period. At the end of the test period the animals were returned to laboratory diet and the amount eaten was measured during the fourteen-day observation period
Delivery method	In two bowls, in front of each cage.
Dosage rate	Weighted the daily consumption
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 B5010_03b

Reference

Official use only

Reference

Prescott C.V., Efficacy assessment, using the bait choice feeding test, of Difebloc wax blocks (T2weeks accelerated) containing 50 mg.kg-1 difenacoum, using CD-1 albino house mouse, Study reference VPU Study Plan Number VPU/10/005, VPU trial No. GB01-10-R010, Project number 153SRI10P, trial code SRIT10-1002-153P
The Vertebrate Pests Unit School of Biological Sciences, The

	University of Reading Whiteknights, Reading RG6AJ, UK 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.	X
Deviations	No	

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	Difebloc	
Composition of Product tested	0.005 % of Difenacoum	
Physical state and nature	Wax block bait	

Monitoring of active substance concentration

No

Method of analysis

During the four day conditioning period, the animals had access to Standard EPA Meal from two symmetrically placed food bowls at the front of each cage. The positions of the two food bowls were alternated daily. The contents of the food bowls were made up daily to provide an excess of the animals 'daily (i.e>10g).

The amount of food consumed by each animal wad determined daily to the nearest 1g by the difference method, taking care first to recover spillage and discard contaminants as far as possible. On each day, both food bowls were weighed, replenished and re-weighed. Following any correction of spillage, spoilage and contamination, the bowl weights were recorded on data entry forms. If a food was fouled by urine or faeces, both food were replaced with fresh. If food, especially spillage, was damp, it was dried before weighed.

During the four-day test period the animals had access to the test item and the challenge diet and the positions of the bowls containing the two diets were alternated daily. Bowl markings indicated whether content are Test (T) or Control (C) diet. The procedures for provisioning and weighing the food bowls were the same as in the conditioning period.

At the end of the test period the animals were returned to laboratory diet and the amount eaten was measured during the fourteen-day observation period.

Weighing scales (Fisherbrand DP 600) were used on data to determine the amounts of diets consumed by the individual animals each day.

Any unusual or significant observations were recorded on data entry forms, including excessive bait spillage, signs of toxicity and death. The theoretical end point was on completion of the specified observation period. Animals were humanely killed (by carbon dioxide

	inhalation) if they showed signs of toxicity that exceed the severity limit, as specified for that procedure in the Home Office Project Licence of the testing facility.	
Reference substance	No	
Method of analysis for reference substance	-	
Testing procedure		
Test population / inoculum / test organism	5 males and 5 females of Swiss house mice (*Mus domesticus*).	X
Test system	The animals were individually caged in purpose-built stainless steel cages measuring 38x28x22 cm. The cages were held in a rack over a plastic tray with an absorbent liner so that spillage could be collected.	
Application of TS	During the four day conditioning period, the animals had access to Standard EPA Meal from two symmetrically placed food bowls at the front of each cage. The positions of the two food bowls were alternated daily. The contents of the food bowls were made up daily to provide an excess of the animals 'daily (i.e>10g). During the four-day test period the animals had access to the test item and the challenge diet and the positions of the bowls containing the two diets were alternated daily. Bowl markings indicated whether content are Test (T) or Control (C) diet. The procedures for provisioning and weighing the food bowls were the same as in the conditioning period. At the end of the test period the animals were returned to laboratory diet and the amount eaten was measured during the fourteen-day observation period	
Test conditions	Ambient conditions in animals rooms were maintained in accordance with normal laboratory requirement; with a temperature range of 18-	

	24°C, a relative humidity range of 30 % to 80%, with between 10 and 25 air changes per hour, and with a 12 hour light dark-cycle. Individual animals were be identified by cage label. The test item was identified by a unique reference number (VPU Reference 004/137/3).
Duration of the test / Exposure time	The duration of the test was 22 day, comprising: - 4 days of acclimatisation, - 4 day test period (period of exposure to the test item) and - 14 day observation period.
Number of replicates performed	No replicates
Controls	No control.
Examination	
Effect investigated	The bait choice feeding is designed to determine the palatability of established rodenticide bait products for the control of commensal rodent, through testing on a domestic strain of the house mouse (Mus musculus). The laboratory choice test procedure is intended to reflect a practical situation in rodent control in which pest rodent have unrestricted access tot palatable and familiar alternative food.
Method for recording / scoring of the effect	The procedure is used to generate information on efficacy of bait formulations in accordance with the guidance document on efficacy evaluations of rodenticides (Product type 14) from the European Commission (European Commission, 2008). This document indicates that rodenticide product may be considered “to possess a sufficient level efficacy” if the percentage acceptance of test material is equal or greater than 20% of the total food consumed during the test period.
Intervals of examination	Daily
Statistics	Weighing scales (Fisherbrand DP 600) were used on data to determine the amounts of diets consumed by the individual animals

each day.

Post monitoring of the test organism

Yes,

After the poisoning phase, a period of 14 days is observed.

Any unusual or significant observations were recorded on data entry forms, including excessive bait spillage, signs of toxicity and death. The theoretical end point was on completion of the specified observation period. Animals were humanely killed (by carbon dioxide inhalation) if they showed signs of toxicity that exceed the severity limit, as specified for that procedure in the Home Office Project Licence of the testing facility.

25 Results

Efficacy

The mean initial weight of the test animals was 25.3g.

All test animals fed consistently from the feeding bowls during the four day conditioning period and there was no oblivious sign of a preference among the animals for one feeding bowl over another. All animals, therefore, continued into the test period.

Acceptance to the DIFEBLOC wax block was very good and there was a marked preference for the test item over the challenge diet among all individual in the test group. The mean quantity of the test item consumed by each animal during the four-day test period was 14.8 g. A mean of 5.3 g of the challenge diet was consumed during the same period. The mean acceptance of the test item was 73.8% (S.D 11.6), showing that DIFEBLOC was highly palatable formulation.

Mortality was complete (100%) in the test group, with mean days to death of 4.7 days (range 3 to 6 days)/ The mean final weight of the animal was 23.8g.

Dose/Efficacy curve

The mean quantity of the test item consumed by each animal during the four-day test period was 14.8 g. A mean of 5.3 g of the challenge diet was consumed during the same period. The mean acceptance of the test item was 73.8% (S.D 11.6), showing that DIFEBLOC was highly palatable formulation.

Begin and duration of effects

Mortality was complete (100%) in the test group, with mean days to death of 4.7 days (range 3 to 6 days)/ The mean final weight of the animal was 23.8g.

Observed effects in the post monitoring phase

Death of mice

Effects against organisms or objects to be protected	-
Other effects	-
Efficacy of the reference substance	Not applicable
Tabular and/or graphical presentation of the summarised results	The results are summarised in the table below:

Sta
Devi
*anir

Efficacy limiting factors

Occurrences of resistances	Not applicable
Other limiting factors	Not applicable

26 Relevance of the results compared to field conditions

Reasons for laboratory testing	The laboratory choice test procedure is intended to reflect a practical situation in rodent control in which pest rodent have unrestricted access to palatable and familiar alternative food.	
Intended actual scale of biocide application	Not applicable	
Relevance compared to field conditions	Not applicable	
Application method	Not applicable. The bait choice feeding is designed to determine the palatability of established rodenticide bait products for the control of commensal rodent, through testing on a domestic strain of the house mouse (*Mus musculus*).	
Test organism	YES, The fresh product is well accepted by rodents.	X
Observed effect	Not applicable	X
Relevance for read-across	Yes, The procedure is used to generate information on efficacy of bait formulations in accordance with the guidance document on efficacy evaluations of rodenticides (Product type 14) from the European Commission (European Commission, 2008). This document indicates that rodenticide product may be considered “to possess a sufficient level efficacy” if the percentage acceptance of test material is equal or greater than 20% of the total food consumed during the test period. The laboratory choice test procedure is intended to reflect a practical	

situation in rodent control in which pest rodent have unrestricted access tot palatable and familiar alternative food.

27 Applicant's Summary and conclusion

Materials and methods

During the four day conditioning period, the animals had access to Standard EPA Meal from two symmetrically placed food bowls at the front of each cage. The positions of the two food bowls were alternated daily. The contents of the food bowls were made up daily to provide an excess of the animals 'daily (i.e>10g).

The amount of food consumed by each animal wad determined daily to the nearest 1g by the difference method, taking care first to recover spillage and discard contaminants as far as possible. On each day, both food bowls were weighed, replenished and re-weighed. Following any correction of spillage, spoilage and contamination, the bowl weights were recorded on data entry forms. If a food was fouled by urine or faeces, both food were replaced with fresh. If food, especially spillage, was damp, it was dried before weighed.

During the four-day test period the animals had access to the test item and the challenge diet and the positions of the bowls containing the two diets were alternated daily. Bowl markings indicated whether content are Test (T) or Control (C) diet. The procedures for provisioning and weighing the food bowls were the same as in the conditioning period.

At the end of the test period the animals were returned to laboratory diet and the amount eaten was measured during the fourteen-day observation period.

Weighing scales (Fisherbrand DP 600) were used on data to determine the amounts of diets consumed by the individual animals each day.

Any unusual or significant observations were recorded on data entry forms, including excessive bait spillage, signs of toxicity and death. The theoretical end point was on completion of the specified

observation period. Animals were humanely killed (by carbon dioxide inhalation) if they showed signs of toxicity that exceed the severity limit, as specified for that procedure in the Home Office Project Licence of the testing facility.

Reliability

1, Study conducted in compliance with agreed protocols.

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.

Assessment of efficacy, data analysis and interpretation

The experiment was conducted on stored product during 14 days at 54°C, respectively to the protocol guidelines. X

Conclusion

The study showed that, after storage of 2 weeks at 54°C, DIFEBLOC wax block is palatable to Swiss House mice, with a mean palatability against ground laboratory diet 53.1%. The formulation also resulted in 100% mortality after a four-day choice between this formulation and challenge diet.

It is apparent from this test that the test item, DIFEBLOC wax blocks, following storage of 2 weeks at 54°C, should be favourably for product authorization under both the criteria set by the European commission.

Proposed efficacy specification

The European commission document (European commission, 2008) says in section 4.1 entitled “Norms and Criteria”:
“In the bait choice feeding test the percentage of ingested bait containing the product should be normally ≥ 20%. When the results in ≥ 90% mortality, a lower level than 20% of the total food consumption is acceptable”.

The results of this test are relevant to the field conditions in that the choice test is intended to represent a natural situation in which the test animals have unrestricted access to a well-known food. It is feeding on the familiar diet. The observed effects of high consumption of the test item by mice and the complete mortality of the test group are both relevant to field conditions.

	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	**1.3** Guideline study protocol is more appropriate for field testing of rodenticides and not laboratory testing in a choice situation. **2.3.1** 20 animals (10 male and 10 female) are required under in the TNsG on product evaluation but in the CEB guidance the number of animals required is not specified. **3.1.2** Line should be amended to read “range 3 to 7 days”. **3.1.3** 100% mortality was observed in the post observation period. **4.3.2** Test organism was a domestic strain of the house mouse (*Mus musculus*). **4.3.3** Observed effect was mortality or exceeding the Home Office toxicity severity limit whereby the animal was humanely dispatched. **5.3** The product was stored for 14 days at 54°C prior to use in the study i.e. an accelerated storage stability test.
Summary and conclusion	Laboratory mice were used instead of wild mice. 20 animals (10 male and 10 female) are required under in the TNsG on product evaluation. In the CEB guidance the number of animals required is not specified. The aged DIFEBLOC was palatable as the mean acceptance of the bait was 73.8% versus a mean consumption of the ground laboratory diet of 53.1%. The test is acceptable to confirm the palatability of aged bait and effectiveness resulting in 100% mortality of the mice tested.
	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*)

<table>
<tr><th>Criteria</th><th>Details</th></tr>
<tr><td>Nature</td><td>DIFEBLOC: wax block bait.
Containing 0.005 % of Difenacoum</td></tr>
<tr><td>Origin</td><td>Batch N°: DF241209
Manufacturing date: 24/12/2009
Product stored at 54°C during 14days</td></tr>
<tr><td>Initial biomass</td><td>Not applicable</td></tr>
<tr><td>Reference of methods</td><td>-</td></tr>
<tr><td>Collection / storage of samples</td><td>By comparative measure between food control and poisoning food.</td></tr>
<tr><td>Preparation of inoculum for exposure</td><td>During the four-day test period the animals had access to the test item and the challenge diet and the positions of the bowls containing the two diets were alternated daily. Bowl markings indicated whether content are Test (T) or Control (C) diet. The procedures for provisioning and weighing the food bowls were the same as in the conditioning period.
At the end of the test period the animals were returned to laboratory diet and the amount eaten was measured during the fourteen-day observation period</td></tr>
<tr><td>Pretreatment</td><td>Any</td></tr>
<tr><td>Active substance determined in the product</td><td>Containing 0.005 % of Difenacoum
Analyse certificate: batch DF241209, manufactured 24/12/2009 (fresh product)
<table>
<tr><th></th><th>Specification</th><th>Decision</th></tr>
<tr><td>Aspect</td><td>Red paraffinic block</td><td>OK</td></tr>
<tr><td>Weight</td><td>Block of 30g</td><td>OK</td></tr>
</table>
</td></tr>
</table>

	Composition	Difenacoum 50ppm±25%	40,56 ppm

1.2 Test organism (*if applicable*)

Criteria	Details
Species	Swiss House mice *(Mus domesticus)*
Strain	Albinos
Source	Charles River UK Ltd
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	5 males and 5 females
Method of cultivation	Bowls were weighted daily.
Pretreatment of test organisms before exposure	-
Initial density/number of test organisms in the test system	5 males and 5 females

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	During the four day conditioning period, the animals had access to Standard EPA Meal from two symmetrically placed food bowls at the front of each cage. The positions of the two food bowls were alternated daily. The contents of the food bowls were made up daily to provide an excess of the animals 'daily (i.e>10g). During the four-day test period the animals had access to the test item and the challenge diet and the positions of the bowls containing the two diets were alternated daily. Bowl markings indicated whether content are Test (T) or Control (C) diet. The procedures for provisioning and weighing the food bowls were the same as in the conditioning period. At the end of the test period the animals were returned to laboratory diet and the amount eaten was measured during the fourteen-day observation period
Delivery method	In two bowls, in front of each cage.
Dosage rate	Weighted the daily consumption
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

Official use only

Reference

Reference

Latteur G., CRA Gembloux, Efficacy test performed on BELGABLOC, paraffinic bait block containing 0.005% of Difenacoum, against brown rats (*Rattus norvegicus* Berkenhout), at different storages stages (Appetizing test included), rapport 965, May 1997.

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

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 inclustion	
Guideline study	Guideline for the Rodenticide assessment edited by Ministry for the Middle-classes and Agriculture (*Lignes Directrices du Ministère des Classes Moyennes et de l'Agriculture pour l'évaluation des Rodenticides)*	X
Deviations	No	

30 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	Belgabloc	
Composition of Product tested	0.005 % of Difenacoum	
Physical state and nature	Paraffin blocks rodenticide bait, with wheat flour, crushed wheat, flavour and dye.	
Monitoring of active	Yes,	

substance concentration	Chemical analyse of the BELGABLOC was used to determine the concentration on fresh product.	
Method of analysis	HPLC	
Reference substance	No	
Method of analysis for reference substance	Not applicable	
Testing procedure		
Test population / inoculum / test organism	10 rats (*Rattus norvegicus*) captured in field either a total of : • 7 males • 3 females	X
Test system	Rats are housed in individual cage.	
Application of TS	Rats received a portion of crushed wheat or poisoning block in their mangers. Every day, mangers were weighed in order to estimate the consumption.	
Test conditions	Minimum three weeks were observed between the first and the last captured rats, in order to suppress pregnant female.	
Duration of the test / Exposure time	Please find the duration by phase: • Pre-baiting with crushed wheat: 5 days • Poisoning bait with block: 2 days • Rest period: none • Post-baiting with crushed wheat: 18 days	X
Number of replicates performed	No replicates	
Controls	No.	
Examination		

Effect investigated

Assessment of rats appetizing toward fresh product BELGABLOC compares to crushed wheat.

Method for recording / scoring of the effect

The method is to estimate the food consumption, by weighing every day the mangers and compares values obtains with crushed wheat and poisoning block.

Intervals of examination

Daily

Statistics

Total and average amount eaten by the rat population.

Post monitoring of the test organism

Yes,

After the poisoning phases, a period with crushed wheat was observed (post baiting), to observe the food behaviour before death.

31 Results

Efficacy

All animals died except animal number 2, either an efficacy of 90% for the rodenticide. X

The appetizing assessment in time is based on the amount of food consumed.

Please find in the following table result from fresh product (T0).

Product	T0				
	Total consumed food for all rats at different period			Average consumption (g) by rats and by days	
Phases	Pre baiting	Poison	Post baiting*	Wheat	Block
Days	5	2	18	Until death	2
Rats (n=10)	872.3	422.0	710**	**15.26**	**21.1**

**Tested animals died before the indicated days

Dose/Efficacy curve

The total consumption of fresh product was for the different phase was:

- 872,3 g for crushed wheat during the pre-baiting phase
- 422,0g for the block during the poisoning phase
- 710,0g for crushed wheat during the post-baiting phase

Begin and duration of effects

Despite the total amount consumed, if we take the average consumed calculated with living days where rats received crushed safe wheat, we can observe that the block are good level of consumption.

Observed effects in the post monitoring phase

1. Despite the total amount consumed, if we take the average consumed calculated with living days where rats received crushed safe wheat, we can observe that the block are good level of consumption
2. Based on the average consumption in wheat (pre-baiting and post baiting), by the number of living days for each rats, we obtain nearly the same rage in consumption for wheat and poisoning bait. Please see table in 3.1.
3. After the return of crushed wheat, we observed a decrease in the rat population between day 3 and 7 for product at T0.
4. Moreover, fewer days before death, rats did not eat the wheat crushed.

Effects against organisms or objects to be protected

Not applicable

Other effects

1. Some animals are less sensitized to the block bait rodenticide than the principal population, indeed at T0, male number 2 had consumed a very low amount of block.
2. At the poisoning bait period, we can observe that animal ate less than other previous days. This phenomenon can be result to neophobia behaviour caused by the change of food, wheat to block.

Efficacy of the reference substance

Not applicable

Tabular and/or graphical presentation of the summarised results

Product	T0	
	Total consumed food for all rats at different period	Average consumption (g) by rats and by days

Phases	Pre baiting	Poison	Post baiting*	Wheat	Block
Days	5	2	18	Until death	2
Rats (n=10)	872.3	422.0	710**	**15.26**	**21.1**

**Tested animals died before the indicated days

Efficacy limiting factors

Occurrences of resistances Not applicable

Other limiting factors Not applicable

32 Relevance of the results compared to field conditions

Reasons for laboratory testing

The laboratory conditions shows the :

- Daily amount of food consumed by one rat
- Timing needed for the product efficacy after ingestion
- Rat's behaviour with changing food.

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 rat can varied in an open space. Moreover, in nature rats have access to other kind of food.

Application method In this laboratory experiment, rats only access of one kind of food, following the phase of experiment.

In nature condition, rats have access to other kind of food, which can

run in competition with the poisoned block.

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,
This experiment demonstrated that stored and fresh products are both accepted by rats. Despite the difference in time and their chemical variation in active ingredient.
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 aim of the experiment is to test the appetizing behaviour of rat on fresh product.

BELGABLOC, the tested product is paraffin blocks rodenticide baits containing 0.005 % of Difenacoum.

Rats (*Rattus norvegicus)* used in these experiment were captured in fields:

During the test, rats received a portion of crushed wheat or blocks in their mangers, which was weighed in order to estimate the consumption.

The process is established by this following steps:

- Pre-baiting with crushed wheat: 5 days
- Poisoning bait with block: 2 days
- Rest period: none
- Post-baiting with crushed wheat:
  - Until death.

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

Reliability	1, Study conducted in compliance with agreed protocols.	X
Assessment of efficacy, data analysis and interpretation	Rats ate in same amount crushed wheat and poisoning block.	
Conclusion	Rat appetizing for BELGABLOC is very high compares to safe crushed wheat and BELGABLOC has an efficacy of 90%.	
Proposed efficacy specification	BELGABLOC is appropriate to fight against *Rattus norvegicus.*	

	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	**1.3** The guidelines used in the study were not provided. **2.3.1** The TNsG on product evaluation recommend that 20 animals (10 males and 10 females) should be used. **2.3.5** The poisoning phase used in the study was 2 days but should have been 4 days. The post-baiting period should be 14 days. **3.1** The surviving rat was not tested for resistance despite having consumed 12g of poisoned bait block. The baiting period at just 2 days was too short to conclude whether this individual would have consumed more bait and died as a consequence. **4.3.2** Test organism - *Rattus norvegicus*. **4.3.3** Observed effect was mortality. **5.2** Reliability of 2 is appropriate.
Summary and conclusion	Despite the baiting period being prohibitively short (just 2 days) one rat survived the baiting treatment despite consuming what would be considered a potentially lethal quantity of bait. No resistance testing was conducted on this individual to confirm whether resistance was present. Whilst the applicant claims that this individual rat ate very little of the bait it ate more than the rat number 10 which died as a result of bait consumption. Despite this the bait block proved highly palatable and controlled the remaining 9 rats, thereby achieving 90% efficacy.

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	BELGABLOC: rodenticide blocks bait. Containing 0.005 % of Difenacoum
Origin	Lot 9702301, made in January 1997
Initial biomass	Not applicable
Reference of methods	Director Lines from Authorisation Committee
Collection / storage of samples	By comparative measure between results obtained with safe crushed wheat and poisoning bait on fresh product.
Preparation of inoculum for exposure	Not mentioned
Pretreatment	-
Active substance determined in the product	Chemical analyse in Difenacoum on fresh product : 47.2 ppm (Analyze number 8659lCh.1241/1997/ 21)

1.2 Test organism (*if applicable*)

Criteria	Details
Species	Browns rats *(Rattus norvegicus)*
Strain	wild
Source	Captured in fields
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 mentioned
Other specification	Not applicable due to the test conditions
Number of organisms tested	10 rats
Method of cultivation	Mangers were weighted daily.
Pretreatment of test organisms before exposure	Not mentioned
Initial density/number of test organisms in the test system	10 rats

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	Crushed wheat during the pre-baiting and post baiting phase and Block during the poisoning phase
Delivery method	In mangers
Dosage rate	Not mentioned
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

Reference

Official use only

Reference

Latteur G., CRA Gembloux, Efficacy test through different period of time, performed on BELGABLOC, containing 0.005% of Difenacoum, against brown rats (*Rattus norvegicus*), rapport complement 980, April 1998.

	CRA (Agronomic Research Center), Phytopharmacological department, Rue du Bordia, 11, 5030 Gembloux Belgium. 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	Decision critters edited by the Major Guideline for the Rodenticide efficacy assessment (*Lignes Directrices pour l'évaluation de l'Efficacité des Rodenticides)*	X
Deviations	No	

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	Belgabloc	
Composition of Product tested	0.005 % of Difenacoum	
Physical state and nature	Paraffin blocks rodenticide bait, with wheat flour, crushed wheat, flavour and dye.	

Monitoring of active substance concentration	Yes, Chemical analyse of the BLEGABLOC was used to determine the concentration on fresh product and product stored during 6 months.
Method of analysis	HPLC
Reference substance	No.
Method of analysis for reference substance	Not applicable

Testing procedure

Test population / inoculum / test organism	22 rats (*Rattus norvegicus*) by test. • 11 males • 11 females
Test system	Rats are housed in individual cage.
Application of TS	Rats received a portion of 50 g of crushed wheat in their mangers. Every day, mangers were weighed in order to estimate the consumption.
Test conditions	Minimum three weeks were observed between the first and the last captured rats, in order to suppress pregnant female.
Duration of the test / Exposure time	Please find the duration by phase: • Pre-baiting with crushed wheat: 5 days • Poisoning bait with block: 2 days • Rest period: none • Post-baiting with crushed wheat: 18 days
Number of replicates performed	No replicates
Controls	Yes, two controls by experiment: One male and one female were fed with crushed wheat, like the pre bating phase of the experiment.

Examination

Effect investigated

Assessment of rats appetizing toward fresh product BELGABLOC compares to crushed wheat.

Assessment of rats appetizing toward product BELGABLOC at different period of time: T0 and T6 months.

Method for recording / scoring of the effect

The method is to estimate the food consumption, by weighing every day the mangers and compares values obtains with crushed wheat and poisoning block.

Intervals of examination

Daily

Statistics

Total and average amount ate by the rat population.

Post monitoring of the test organism

Yes,

After the poisoning phases, a period with crushed wheat was observed (post baiting), to determine the time requires to cause rat death and to observe the food behaviour before death.

37 Results

Efficacy

All tested rat died except one female at T0, either an efficacy of: X

- 95% at T0,
- 100% at T6.

The appetizing assessment in time is based on the amount of food consumed. Please find in the following table result from fresh product (T0) and stored product (T6 months)

Average (g) consumption by rats and by days.			
	Wheat	Block	Equivalent in wheat for the control
T0: HPLC results: 47.2 mg/kg of active substance in the fresh product.			
Male	**17.26**	**17.68**	-

Control	21.45	-	22.45
Female	**14.56**	**11.18**	-
Control	18.58	-	14.60
T6: HPLC results: 50.4 mg/kg of active substance in the stored product.			
Male	**22.99**	**20.96**	-
Control	19.3	-	18.65
Female	**16.98**	**17.86**	-
Control	16.5	-	15.50

In order to compare block and wheat consumption, we take the wheat consumption during the pre-baiting and post baiting, the days of living are also take in account.

Dose/Efficacy curve

In general, we observe females eat less than males:

1. The total consumption of fresh product is in:
- Pre-baiting: 1101.8g for male and 831.8g for female with crushed wheat.
- Poison: 345.1g for male and 223.6g for female with block.
- Post-baiting: 383.9g for male and 1082.1g for female with crushed wheat.

2. The total consumption of stored product is in:
- Pre-baiting: 1075.6g for male and 828.1g for female with crushed wheat.
- Poison: 419.2 for male and 357.2g for female with block.
- Post-baiting: 453.6g for male and 395.9g for female with crushed wheat.

Begin and duration of effects

Despite the total amount consumed, if we take the average consumed calculated with living days where rats received crushed safe wheat, we can observe that the block are good level of consumption.

The low block consumption for female at T0 can be easily explained by raw data, indeed, females 7 and 10 ate few amount of block.

Observed effects in the post monitoring phase

5. Despite the total amount consumed, if we take the average consumed calculated with living days where rats received crushed safe wheat, we can observe that the block are good level of consumption
6. Based on the average consumption in wheat (pre-baiting and post baiting), by the number of living days for each rats, we obtain nearly the same range in consumption for wheat and poisoning

bait. Please see table in 3.1.

7. After the return of crushed wheat, we observed a decrease in the rat population between day 3 and 7 for product at T0 and T6.
8. Moreover, fewer days before death, rats did not eat the wheat crushed.

Effects against organisms or objects to be protected

Not applicable.

Other effects

3. Some animals are less sensitized to the block bait rodenticide than the principal population, indeed at T0. Indeed, female 2 took more days to die than the other and 3 animals (female number 2, 7 and 9) survived to the test.
4. At the poisoning bait period, we can observe that animals consume less food than other previous days. This phenomenon can be result to neophobia behaviour caused by the change of food, wheat to block.
5. Moreover, female 7 and 9 survived to the test, it can be explain by their low block consumption

Efficacy of the reference substance

Not applicable

Tabular and/or graphical presentation of the summarised results

Average (g) consumption by rats and by days.			
	Wheat	Block	Equivalent in wheat for the control
T0: HPLC results: 47.2 mg/kg of active substance in the fresh product.			
Male	**17.26**	**17.68**	-
Control	21.45	-	22.45
Female	**14.56**	**11.18**	-
Control	18.58	-	14.60
T6: HPLC results: 50.4 mg/kg of active substance in the stored product.			
Male	**22.99**	**20.96**	-
Control	19.3	-	18.65
Female	**16.98**	**17.86**	-
Control	16.5	-	15.50

Total consumed food (g) by group on different period of day.						
Product	T0			T12		
Phases	Pre baiting	Poison	Post baiting*	Pre baiting	Poison	Post baiting*
Days	5	2	18	5	2	9
Male (n=10)	1101.8	345.1	383.9	1075.6	419.2	453.6
Control (n=1) (wheat)	101.4	44.9	156	95.8	37.3	136.4
Female (n=10)	831.8	223.6	1082.1	828.1	357.2	395.9
Control (n=1) (wheat)	78.1	29.9	349.2	93.9	31	105.7

Efficacy limiting factors

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 one rat
- Timing needed for the product efficacy after ingestion
- Rat's behaviour with changing food.
- Rat's behaviour with an older product stored in realistic conditions.

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 rat can varied in an open space. Moreover, in nature rats have access to other kind of food.	
Application method	In this laboratory experiment, rats only access of one kind of food, following the phase of experiment. In nature condition, rats have access to other kind of food, which can run in competition with the poisoned block. 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, This experiment demonstrated that stored and fresh products are both accepted by rats. Despite the difference in time and their chemical variation in active ingredient. 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 aim of the experiment is to compare appetizing behaviour of rat with fresh and stored product. BELGABLOC, the tested product is paraffin blocks rodenticide baits containing 0.005 % of Difenacoum.	X

	Rats (*Rattus norvegicus)* used in these experiment were captured in fields: During the test, rats received a portion of crushed wheat or blocks in their mangers, which was weighed in order to estimate the consumption. The process is established by this following steps: • Pre-baiting with crushed wheat: 5 days • Poisoning bait with block: 2 days • Rest period: none • Post-baiting with crushed wheat: ○ Until death. The concentration in active ingredient was also determined before the experiment.	
Reliability	1, Study conducted in compliance with agreed protocols.	X
Assessment of efficacy, data analysis and interpretation	The experiment was conducted on fresh and stored product. The laboratory conditions were identical.	
Conclusion	Rat appetizing for BELGABLOC has not decreased during the last 6 months of storage at ambient temperature (20°C), as its rate in active substance. The block bait has an efficacy of 95 % at T0 and 100% at T6.	X
Proposed efficacy specification	BELGABLOC is appropriate to fight against *Rattus norvegicus.*	

	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	**1.3** Wording should be amended to read “Decision criteria”. **2.3.5 & 5.1** The poisoning phase used in the study was 2 days but should have been 4 days. The post-baiting period should be 14 days. **3.1 & 5.4** Two female rats survived the TO treatment albeit with low bait consumption rates. This gives and efficacy of 90% at T0. **4.3.2** Test organism - *Rattus norvegicus*. **4.3.3** Observed effect was mortality. **5.2** Reliability should be 2.
Summary and conclusion	On average both fresh and aged (6 month old) bait blocks proved palatable to the test animals. 90% control of rats was achieved with the fresh bait (two female rats survived the bait treatment consumption albeit at very low consumption (0.9g & 10.4g)). 100% of rats were controlled in the test using the aged bait blocks.
	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	BELGABLOC: rodenticide blocks bait. Containing 0.005 % of Difenacoum
Origin	Lot 9702301, made in January 1997
Initial biomass	Not applicable
Reference of methods	Director Lines from Authorisation Committee
Collection / storage of samples	By comparative measure between results obtained with safe crushed wheat and poisoning bait on fresh product.
Preparation of inoculum for exposure	Not mentioned
Pretreatment	-
Active substance determined in the product	Chemical analyse in Difenacoum on fresh product (T0) : 47.2 ppm (Analyze number 8659lCh.1241/1997/ 21) Chemical analyse in Difenacoum at T6 month : 50,4 ppm (Analyze number 8882/Ch1440/1997/195)

1.2 Test organism (*if applicable*)

Criteria	Details
Species	Browns rats *(Rattus norvegicus)*
Strain	Albinos
Source	Same breeding
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 mentioned
Other specification	Not applicable due to the test conditions
Number of organisms tested	20 rats and 2 controls, by experiment (T0 and T6 months)
Method of cultivation	Mangers were weighted daily.
Pretreatment of test organisms before exposure	Not mentioned
Initial density/number of test organisms in the test system	22 rats by experiment (T0 and T6 months)

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	Crushed wheat during the pre-baiting and post baiting phase and Block during the poisoning phase
Delivery method	In mangers
Dosage rate	Not mentioned
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 B45.10_06

Reference

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Reference

De Proft M., CRA Gembloux, Efficacy test through different period of time, performed on PROBLOC, bait ready to use, containing 0.005% of Difenacoum, against brown rats (*Rattus norvegicus*), rapport complement 9547, 1999.

	CRA (Agronomic Research Center), Phytopharmacological department, Rue du Bordia, 11, 5030 Gembloux Belgium. 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	Decision critters edited by the Major Guideline for the Rodenticide efficacy assessment (*Lignes Directrices pour l'évaluation de l'Efficacité des Rodenticides)*	X
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	Probloc.	
Composition of Product tested	0.005 % of Difenacoum	
Physical state and nature	Red paraffin blocks rodenticide bait. Weight: 45g, sectile at the half	

	Wrapped with transparent plastic.	
Monitoring of active substance concentration	Yes, Chemical analyse of the PROBLOC was used to determine the concentration on the fresh product and after a storage at ambient temperature (20°C) during 12 months.	
Method of analysis	HPLC	
Reference substance	No	
Method of analysis for reference substance	Not applicable	
Testing procedure		
Test population / inoculum / test organism	20 rats (*Rattus norvegicus*) by test. • 10 males • 10 females	
Test system	Before each experiment, rats were housed in individual cage.	
Application of TS	Rats received a portion of 40 g of wheat in their mangers. Every day, mangers were weighed in order to estimate the consumption.	
Test conditions	Rats were acclimated in their individual cage during 8 days before the test. During the acclimatization, they received water and fresh crushed wheat *ad libitum*.	

Duration of the test / Exposure time	The process for fresh and stored product stay more or less the same:
	• Pre-baiting with crushed wheat: 5 days
	• Poisoning bait with block: 2 days
	• Rest period: none
	• Post-baiting with crushed wheat:
	  ○ 18 days with the fresh product, in 1999
	  ○ 7 days with the twelve months stored product, in 2000.
		X

Number of replicates performed No replicates

Controls Yes

One male and one female were fed with crushed wheat, like the pre bating phase of the experiment.

Examination

Effect investigated Assessment of rats appetizing toward product PROBLOC at different period of time: T0 and T12 months.

Method for recording / scoring of the effect The method is to estimate the food consumption, by weighing every day the mangers and compares values obtains with crushed wheat and poisoning block.

Intervals of examination Daily

Statistics Total and average amount eaten by the rat population.

Post monitoring of the test organism Yes,
After the poisoning phases, a period with crushed wheat was observed (post baiting), to observe the food behaviour before death.

43 Results

Efficacy

All tested animals died at T0 except one male and one female, either an efficacy of 90%.

All tested animals died at T12, either an efficacy of 100%.

The appetizing assessment in time is based on the amount of food consumed. Please find in the following table result from fresh product (T0) and stored product (T12 months);

Average (g) consumption by rats and by days.

	Wheat	Block	Equivalent in wheat for the control
T0			
Male	**15.32**	**16**	
Control	21.93	-	21.35
Female	**13.83**	**14**	
Control	14.88	-	14.40
T12			
Male	**20.36**	**19.98**	
Control	24.5	-	21.85
Female	**14.01**	**15.38**	
Control	18.3	-	17.05

Dose/Efficacy curve

In general, we observe females eat less than males.

The total consumption of fresh product was 334.4g for 10 males and 279.9g for 10 females. The twelve month stored product consumption was 379.6g for males and 307.6 for females.

Begin and duration of effects

Maybe, the changing in food, wheat to poisoned block has created phenomena of mistrust among rat, which was observed by a low consumption of block. Moreover, we can observe at T0 that rats seem more confident when the crushed wheat was back, despite the number of dead, the consumption is better in post bait than is poison bait.

Observed effects in the post monitoring phase

9. Despite the storage and the small difference in active ingredient, product seems always attractive to rats and efficient.
10. Based on the average consumption in wheat (pre-baiting and post baiting), by the number of living days for each rats, we obtain nearly the same rage in consumption for wheat and poisoning bait. Please see table in 3.1.
11. After the return of crushed wheat, we observed a decrease in the rat population between:
    - Day 5 and 11 for product at T0.
    - Day 4 and 8 for product at T12.
12. Moreover, fewer days before death, rats did not eat the wheat crushed.

Effects against organisms or

Not applicable

objects to be protected

Other effects

6. Some animals are less sensitized to the block bait rodenticide than the principal population, indeed at T0 indeed, one male and one female, despite their considerable block consumption, survived during the 18 days scheduled for observation in controls.
7. At the poisoning bait period, we can observed that control ate more than the tested animal for the same period, this phenomena can be result to neophobia behaviour caused by the change of food, wheat to block.

Efficacy of the reference substance

Not applicable

Tabular and/or graphical presentation of the summarised results

Table 1: Average consumption (g) by rats and by days.

Average consumption (g) by rats and by days.			
	Wheat (Pre and post baiting)	Block	Equivalent in wheat for the control
T0			
Male	**15.32**	**16**	
Control	21.93	-	21.35
Female	**13.83**	**14**	
Control	14.88	-	14.40
T12			
Male	**20.36**	**19.98**	
Control	24.5	-	21.85
Female	**14.01**	**15.38**	
Control	18.3	-	17.05

Table 2: Total food consumption (g) consumption in rats by period.

Total consumed food (g) by group on different period of day.						
Product	T0			T12		
Phases	Pre baiting	Poison	Post baiting*	Pre baiting	Poison	Post baiting*
Days	5	2	18	5	2	6 for male 7 for female
Male (n=10)	967	334.4	638.1**	1001.9	379.6	343.7**
Control (n=1) (wheat)	97.1	42.7	407.3	114.7	43.7	135
Female (n=10)	827.4	279.9	647.7**	697.2	307.6	450.4**
Control (n=1) (wheat)	77.2	28.8	265.0	84.1	34.1	119.8

*control animals were fed during:

- 18 days for T0 but tested animals died between day 5 and 11.
- 9 days for T12 but tested animals died between day 4 and 8.

**Tested animals died before the indicated days

At T0, two animals survived to the test.

Efficacy limiting factors

Occurrences of resistances Not applicable

Other limiting factors Deference in active substance did not seem affected the issue if the experiment.

44 Relevance of the results compared to field conditions

Reasons for laboratory testing	The laboratory conditions shows the : • Daily amount of food consumed by one rat • Timing needed for the product efficacy after ingestion • Rat's behaviour with changing food. 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 rat can varied in an open space. Moreover, in nature rats have access to other kind of food.	
Application method	In this laboratory experiment, rats only access of one kind of food, following the phase of experiment. In nature condition, rats have access to other kind of food, which can run in competition with the poisoned block. 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, This experiment demonstrated that stored and fresh products are both accepted by rats. Despite the difference in time and their chemical variation in active ingredient. 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 aim of the experiment is to test the appetizing behaviour of rat with a product at two states: fresh and stored during 12 months at ambient temperature (20°C).

PROBLOC, the tested product is red paraffin blocks rodenticide baits containing 0.005 % of Difenacoum, weighted 45g, sectile at the half, wrapped with transparent plastic.

For each state block, rats (*Rattus norvegicus*) are grouped as follows:

- 10 males and 10 females for the tested product
- 1 male and 1female for used as controls; they were fed with crushed wheat.

Animals were acclimated in their individual cage during 8 days before the test. During the acclimatization, they received water and fresh crushed wheat *ad libitum*.

During the test, rats received a portion of 40 g of wheat in their mangers, which was weighed in order to estimate the consumption.

The process for fresh and stored product stay more or less the same:

- Pre-baiting with crushed wheat: 5 days
- Poisoning bait with block: 2 days
- Rest period: none
- Post-baiting with crushed wheat:
  - 18 days with the fresh product, in 1999
  - 6 to7 days with the twelve months stored product, in 2000.

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

Reliability

1, Study conducted in compliance with agreed protocols.

The experiment was conducted on fresh and stored product. The laboratory conditions were identical.

	Appetizing status of product can be modified through time and be avoided by rodents, which is linked to an efficacy loss because the product is anymore absorbed.
Assessment of efficacy, data analysis and interpretation	The consumption of stored product is equivalent to the consumption of fresh product.
Conclusion	Rat appetizing for PROBLOC has not decreased during the last 12 months of storage at ambient temperature (20°C). The block bait has an efficacy of 90 % at T0 and 100% at T12.
Proposed efficacy specification	The conformity time for PROBLOC, ready to use bait containing 0.005% Difenacoum, can easily be 12 months starting from the date of manufacture.

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	**1.3** Wording should be amended to read “Decision criteria”. **2.3.5** The poisoning phase used in the study was 2 days but should have been 4 days. The post-baiting period should be 14 days. **4.3.2** Test organism - *Rattus norvegicus*. **4.3.3** Observed effect – mortality.
Summary and conclusion	Both fresh and aged (12 month) PROBLOC bait blocks proved highly palatable and achieved 90% control of rats using the fresh bait and 100% control with the 12-month old bait. Rats consumed similar levels of bait to the control wheat diet.
	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	PROBLOC: red rodenticide blocks bait. Containing 0.005 % of Difenacoum
Origin	Authorisation number R051099
Initial biomass	Not applicable
Reference of methods	Director Lines from Authorisation Committee
Collection / storage of samples	By comparative measure between results obtained at T0 and T12 months stored product. From the same origin.
Preparation of inoculum for exposure	The measures on fresh product started on 27/10/1999 and on stored product on 11/10/2000.
Pretreatment	The product when it arrived at lab was considered as fresh, then samples were prepared: • 200g stored at -18°C for the chemical analyse on fresh product. • 5kg placed at 4°C, for the experiment with fresh product. • 200g is stored at 20°C for the chemical analyse 12 months later. • 5kg, stored for the appetizing experiment 12 months later. Products were always stored in dark conditions
Active substance determined in the product	Chemical analyze in Difenacoum on fresh product : 47.2ppm (Analyze number Ch.1943/1999) Chemical analyze in Difenacoum at T12 month : 38.3 ppm (Analyze number FO/Ch.2251/2000/209)

1.2 Test organism (*if applicable*)

Criteria	Details
Species	Browns rats *(Rattus norvegicus)*
Strain	Albinos
Source	From the same breeding
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	Between 10 and 20 weeks old.
Other specification	Not applicable due to the test conditions
Number of organisms tested	At each state of product: 11 male and 11 female.
Method of cultivation	New baits were weighted daily.
Pretreatment of test organisms before exposure	Acclimatizing in individual cage during 8 days with water and crushed wheat *ad libitum*.
Initial density/number of test organisms in the test system	22 rats at each experiment (T0 and T6)

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	Whole wheat during the pre-baiting and post baiting phase and Block during the poisoning phase
Delivery method	In mangers
Dosage rate	Wheat with 40g and blocks of 45g
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

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Reference

Grolleau G., Panciroli J., Pest Control Assistance (PCA), Experimentation, in nature, of block bait against rats (*Rattus Norvegicus*) 2005.

PCA, 3 rue Constantin Le Priol 56150 BAUD (France), Organization approved for the carrying out the tests: Cabinet Barrieux, Cabinet Conseil en Agro Technologies, 92100 Boulogne Billancourt France.

Unpublished

Data protection

Yes

Data owner

LODI S.A.,

Parc d'activité des Quatre Routes,

35390 Grand Fougeray, France

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	Yes, The method used has been inspired by the Frenc method called "method no. 002 from Biological Trials Commission (C.E.B) ", Method for pratical efficacy trials of raticides: • Adopted on 1960, derived from the work of Chitty and Dotty in the 1940. • Revised by OEPP in 1980.
Deviations	No

48 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	Raco Blocs
Composition of Product tested	0.005 % of difenacoum
Physical state and nature	Block rodenticide bait
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 a toxic bait for a week. Regarding the slow mode of action of anticoagulant, one week is needed without toxic bait nor 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	Not mentioned please find details of estimation in table 1.2.	X
Test system	The experimental site is a poultry breeding and birds game, that site includes a fold for bucks. In addition to this farming, there is a manufacture of poultry food.	X
Application of TS	Daily, the bait stations were filled in.	

Test conditions	The experimental site is a poultry breeding and birds game, that site includes a fold for bucks. In addition to this farming, there is a manufacture of poultry food. The farming is located in Le Sourn (Morbihan, 56) A close examination of the site has permitted to notice the presence of various hole and traces of rats, which justify the choice of this site for the experimentation. Meteorological conditions were recorded each day.	X
Duration of the test / Exposure time	Preliminary period: 15 days Pre-baiting: 12 days Poisoning bait: 7 days Rest period: 7 days without food Post-baiting: 5 days	
Number of replicates performed	No replicates	
Controls	No control. Stations without consumption success were abandoned, and stations with high rate of consumption were filled in with more wheat until 700g wheat.	
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, 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

49 Results

Efficacy

Pre-baiting consumption: 2972g

Post baiting consumption: 156.5 g

Either an efficacy of 95% efficacy.

Dose/Efficacy curve

The changing in food, wheat to poisoned block has created phenomena of mistrust among rat, which was observed by a low consumption the first day, only 288 g were consumed. Generally, the neophobia has been within 2 days, with a consumption of 1762 g at the third measurement.

Begin and duration of effects

The consumption of poisoned bait felt on the sixth day, after the intoxication and poisoning rats. This part had to be relatives with the post baiting phase.

Observed effects in the post monitoring phase

The post baiting happened normally, with a relatively low consuming on the first day, the time that the surviving rats brings back to the bait stations. A maximum consumptions of the third day, by a phenomenon of recovery (partial fast during, hence compensation. and then a small fall from day 3 to 5. This small fall exists for two reasons:

- A return to normal consumption among the surviving rats and,
- an end of mortality of less sensitive rats (some of them can die only 15 or 18 days after)

Effects against organisms or objects to be

Due to effect observed in 3.1.3, the average for the post baiting is only based on 4 days.

protected

Other effects

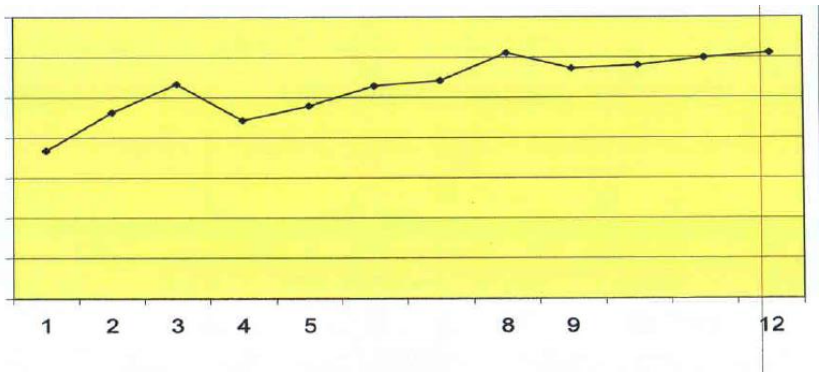
-

Efficacy of the reference substance

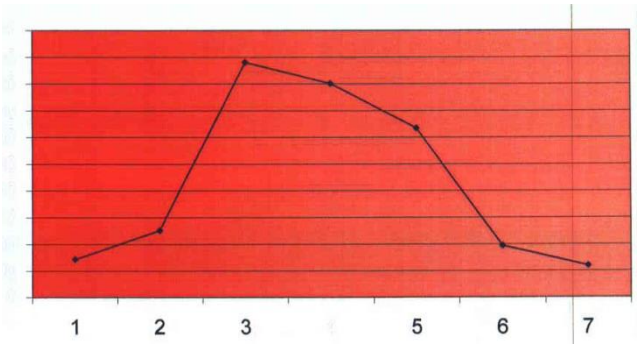
Not applicable

Tabular and/or graphical presentation of the summarised results

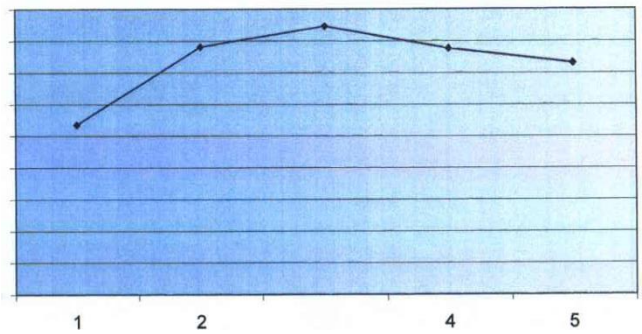
Pre baiting consumption (total by day)



Baiting consumption (total by day)



Post baiting consumption (average by day)



Efficacy limiting

factors		
Occurrences of resistances	Not applicable	
Other limiting factors	Not applicable	

50 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.	
Test organism	YES, the block bait, even with 2 years of storage is efficient against rodent.	
Observed effect	Not applicable	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.	

51 Applicant's Summary and conclusion

Materials and methods

The experimental site has been chosen to their natural condition opportunities:

- a poultry breeding and birds game, that site includes a fold for bucks. In addition to this farming, there is a manufacture of poultry food. The farming is located in Le Sourn (Morbihan, 56)

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.

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 block 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 7 days, no food was exposed in the bait station.

Post-baiting:

Placebo was put in place during 5 days but the average consumption was made on 4 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, but a comparison with the post baiting values is needed to relatives the all experiment.

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 rats brings back to the bait stations. A maximum consumptions of the third day, by a phenomenon of recovery (partial fast during, hence compensation. and then a small fall from day 3 to 5. This small fall exists for two reasons:

- A return to normal consumption among the surviving rats and,
- an end of mortality of less sensitive rats (some of them can die only 15 or 18 days after).

It is the reasons why the consumption in post-baiting is calculated with the last 4 days:

(156+169+155+146)/4 = 156.5 g/day

The efficacy assessment can thus be easily calculated:

[Average Pre-btg (grams) – Average Post-btg (grams)] x100/

AveragePre-btg(grams) = Efficacy

⟺ (2972-156.5) *100 / 2972 = 95%

Conclusion

Very good acceptance of the bait RACO BLOCS despite the changing of kind of food and excellent efficacy, being markedly higher to 90 % (95%) required by the guidelines.

Proposed efficacy specification

According to the point, we can declare as the product as excellent due to the rate of efficacy , between 95 and 99%.

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	52 Evaluation by Rapporteur Member State
Date	April 2011.
Comments	**2.3.1** Calculated test population was approximately 150 rats based on consumption levels recorded. (i.e. 2972 g of pre-bait consumed at an allowance of 20g per rat). **2.3.2 & 2.3.4** The experimental site was poorly described. **4.3** Study is relevant as it was conducted under field conditions. **4.3.3** Observed effect – reduction in consumption indicating mortality of the target pests.
Summary and conclusion	Comparing pre-baiting to post-baiting consumption would indicate a 95% control of the target organisms by the use of 2-year old RACO BLOCs.
	53 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	RACO BLOCS: block rodenticide bait. Containing 0.005 % of Difenacoum
Origin	Batch N° 0501.4- R 1102 A.
Initial biomass	Not applicable
Reference of methods	Testing method of pratical 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 rats, not estimated in the first phase.
Collection / storage of samples	By comparative measure between before and after baiting with placebo (wheat)
Preparation of inoculum for exposure	The measures for the pre-baiting started the 7 January, at the rate of 500g of wheat by station. Several block, during the phase with poison, had to be placed due to the weight difference. The poison period lasted 7 days. A period of rest was observed, during 7 days no food was exposed in the bait station. Then 8 days after the poisoning phase, the station were filled in with 350 g of wheat, as post-baiting step. It lasted 5 days.
Pretreatment	Preliminary period is needed to bring as many rats as possible towards the bait station placed on 3 January. During this period, the stations were filled with wheat, but without measuring consumption. This process has

	permitted to reduce the pre-baiting to a week.
Active substance determined in the product	Containing 0.005 % of Difenacoum

1.2 Test organism (*if applicable*)

Criteria	Details
Species	Browns rats *(Rattus norvegicus)*
Strain	Wild
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	The average consumption of 5 days of pre-baiting shows: (3054+2862+2898+2994+3052)/5= 2972 grams / day. Based on the average and if we allocate an effective consumption of 20 g per rats, we could estimate the test population to nearly 150 rats.
Method of cultivation	New baiting were filled in daily.
Pretreatment of test organisms before exposure	Preliminary step was put in place to bring as many rat as possible.
Initial density/number of test	150 rats.

organisms in the test 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	Whole wheat during the pre-baiting and post baiting phase and Block during the poisoning phase
Delivery method	In station bait
Dosage rate	Weighted the daily consumption
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_08

Official use only

Reference

Reference

-, LODI, Efficacy trial: Rodenticide block containing 0.005% Difenacoum, after 2 years ageing, against rats (*Rattus norvegicus*), Trial date= 6th April to 13th May, 2009.

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 No

54 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 Difebloc

Composition of Product tested 0.005 % of difenacoum

Physical state and nature Block rodenticide bait

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	Not mentioned please find details of estimation in table 1.2.	X
Test system	The experimental site is a restaurant: Le Benjamin (75001 Paris) which is composed of : • Cellar with 2 storage rooms, washing machine and dustbins local. • Equipped kitchen at -1 • Restaurant at ground floor with box room and cloakroom for employees. Some specific parts described above were used for baiting and the efficacy test with 2 years old block.	
Application of TS	Daily, the bait stations were filled in.	
Test conditions	The experimental site is a restaurant: Le Benjamin (75001 Paris) which is composed of several parts. Please find in the following tables where exactly baits were placed at each part of the building:	

Parts	Comments	Baits were place in
Cellars	Lots of dropping at this level. Rats are often seen at this level. Ten bait stations were added fewer days later.	Two Reserves Dustbins
Kitchen (Floor -1)	According to the employees, rats are at this level. Dropping in cellar access, cloakroom, around cooking tables. Impossible to set bait on the kitchen floor due to the frequent cleaning. Baits are put in box room and cloakroom.	Cloak room Box room
Restaurant (ground floor)	No trace o f rats at the level. The food is stored is refrigerator, it is no available to rodent. 2 bait stations are place in order to see their presence or not.	Box room - cloakroom

Duration of the test / Exposure time

Preliminary period: 15 days

Pre-baiting: 9 days

Poisoning bait: 5 days

Rest period: 0

Post-baiting: 7 days

X

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, a decrease of population before and after poisoning bait.	
Intervals of examination	Daily	
Statistics	[Average Pre-btg (grams) – Average Post-btg (grams)] x100/ Average Pre-btg (grams) = Efficacy Btg= baiting	
Post monitoring of the test organism	Yes, After the poisoning phase, safe wheat replaced block at same spot. It is called, the post-baiting phase, where the reduction in population is estimated	

55 Results

Efficacy	Pre-baiting consumption: 1624g (estimation based on the last 3 days) Post baiting consumption: 177 g Either an efficacy of 89.1% efficacy.	
Dose/Efficacy curve	The changing in food, wheat to poisoned block has created phenomena of mistrust among rat, which was observed by a low consumption the first day, only 288 g were consumed. Generally, the neophobia has been within 2 days.	
Begin and duration of effects	The consumption of poisoned bait felt on the sixth day, after the intoxication and poisoning rats. This part had to be relatives with the post baiting phase.	
Observed effects in the post monitoring phase	The post baiting happened normally, with a relatively low consuming on the first day, the time that the surviving rats brings back to the bait stations. A maximum consumptions of the third day, by a phenomenon of recovery (partial fast during, hence compensation. and then a small	X

fall from day 3 to 5. This small fall exists for two reasons:

- A return to normal consumption among the surviving rats and,
- an end of mortality of less sensitive rats (some of them can die only 15 or 18 days after)

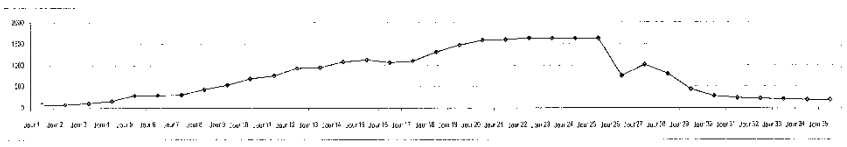
For this reason, the the average for the post baiting is only based on 4 days.

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 Total food consumption during the experiment:



(jour= days)

Efficacy limiting factors

Occurrences of resistances Not mentioned/ Not applicable

Other limiting factors Not applicable

56 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. Please note that both conditions are tested in the dossier.	
Intended actual scale of biocide application	Not applicable	
Relevance compared to field conditions		
Application method	Not applicable, this study is closer to field condition than laboratory process.	
Test organism	YES	X
Observed effect	YES	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.	

57 Applicant's Summary and conclusion

Materials and methods	The experimental site has been chosen to their natural condition opportunities, indeed all food storage room, even regularly washed, represents for rodent an important part of their habitat. The restaurant, “Le Benjamin”, 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, 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.

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 block causes 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 4 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, but a comparison with the post baiting values is needed to relatives the all experiment.

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 rats brings back to the bait stations. A maximum consumptions of the third day, by a phenomenon of recovery (partial fast during, hence compensation. and then a small fall from day 3 to 5. This small fall exists for two reasons:

- A return to normal consumption among the surviving rats and,
- An end of mortality of less sensitive rats (some of them can die only 15 or 18 days after).

It is the reasons why the consumption in post-baiting is calculated with the last 4 days:

(156+169+155+146)/4 = 156.5 g/day

The efficacy assessment can thus be easily calculated:

[Average Pre-btg (grams) – Average Post-btg (grams)] x100/ AveragePre-btg(grams) = Efficacy

⟺ (1624-177) *100 / 1624 = 89.1%

Conclusion

Good acceptances for the two years old paraffin block bait of DIFEBLOC, despite the changing of kind of food and excellent efficacy. However, the efficacy reaches almost the 90 % required by the guidelines.

Proposed efficacy specification

According to the point, we can declare period of 2 years for the consumption of the product, which is efficiency at 89.1%, either little below to the higher 90% efficacy required by the guidelines. X

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	58 Evaluation by Rapporteur Member State
Date	April 2011.
Comments	**2.3.1** Estimated population of 81 rats (*Rattus norvegicus*) based on pre-baiting consumption levels. **2.3.5** The post-baiting phase used was prohibitively short at just 7 days. **3.1.3** If the assumption is made that some rats can die later than the average post-baiting period used (i.e. 4 days) then assessments should have been made to see if indeed consumption levels continued to decrease. **4.3.2** Test organism - *Rattus norvegicus*. **4.3.3** Observed effect – mortality.

Summary and conclusion	**5.5** The efficacy value achieved through the use of 2-year aged DIFEBLOC at 89.1% is just slightly below the required level of 90% control. However, had the post-baiting period been extended it is likely that additional decreases in the post-baiting consumption levels would have resulted indicating sufficient efficacy of the product.

59 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	DIFEBLOC: paraffin rodenticide block bait. Containing 0.005 % of Difenacoum
Origin	Batch N°: 070307. Manufacturing date: 03/2007. Stored during 2 years.
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 rats, not estimated in the first phase.
Collection / storage of samples	By comparative measure between before and after baiting with placebo (wheat)
Preparation of inoculum for exposure	The measures for the pre-baiting started the 7 April, at the rate of 100g of wheat by station. Several block, during the phase with poison, had to be placed due to the weight difference. The poison period lasted 5 days. Then 5 days after the poisoning phase, the station were filled in with 100 g of wheat, as post-baiting step. It lasted 5 days.
Pretreatment	Preliminary period is needed to bring as many rats as possible towards the bait station placed on 3 January. During this period, the stations were filled with wheat,

	but without measuring consumption. This process has permitted to reduce the pre-baiting to a week.
Active substance determined in the product	Containing 0.005 % of Difenacoum

1.2 Test organism (*if applicable*)

Criteria	Details
Species	Browns rats *(Rattus norvegicus)*
Strain	Wild
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	The average consumption of 3 days of pre-baiting shows: (1624.7+1627.5+1624)/3= 1624 grams / day. Based on the average and if we allocate an effective consumption of 20 g per rats, we could estimate the test population to nearly 81 rats.
Method of cultivation	Baits were weighed every day.
Pretreatment of test organisms before exposure	Preliminary step was put in place to bring as many rats as possible.
Initial density/number of test	81 rats.

organisms in the test 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	Whole wheat during the pre-baiting and post baiting phase and Block during the poisoning phase
Delivery method	In station bait
Dosage rate	Weighted the daily consumption
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_10 **Efficacy Data**

Annex Point IIB5.10_10 *Field trial into sewer systems*

TNsG: Pt. I-B5.10, Pt. III-Ch. 6 **Block bait/ Field efficacy/ Rats / Fresh product (T0)/Sewer systems**

		Official use only
60 Reference		
60.1 Reference	Feys JL., Belgagri SA., Massar E., Insectirat sprl, Field trial with Probloc wax baits against sewer rats (*Rattus Norvegicus*) 2010. Belgagri SA,1 rue des Tuielleries B-4480 Engis. Unpublished	
60.2 Data protection	Yes	
60.2.1 Data owner	Belgagri SA,1 rue des Tuielleries B-4480 Engis	
60.2.2 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	
60.3 Guideline study	Guidelines don't exist for damp conditions. So that the trial is a field trial conducted in realistic conditions	X
60.4 Deviations	NA	
61 Method		
Test Substance (Biocidal Product)		
Trade name/ proposed trade name	PROBLOC	
Composition of Product	0.005 % of difenacoum	

Section B5.10_10	**Efficacy Data**
Annex Point IIB5.10_10	*Field trial into sewer systems*
TNsG: Pt. I-B5.10, Pt. III-Ch. 6	**Block bait/ Field efficacy/ Rats / Fresh product (T0)/Sewer systems**

tested	
Physical state and nature	Block rodenticide bait
Monitoring of active substance concentration	Yes
Method of analysis	Dosage by HPLC
Reference substance	No
Method of analysis for reference substance	-
Testing procedure	
Test population / inoculum / test organism	The aim of the study is to test the resistance of PROBLOC to the very damp conditions in a sewer system, to monitor the uptake of the blocks by rats (*Rattus norvergicus*) in 'field' conditions and to monitor the uptake in time.
Test system	The experimental site is situated in the sewer system of the Rue de la tour in the city of Namur, 60 km south of Brussels.
Application of TS	The method consisting offering the blocs on the most appropriate places (accessible for rats, not permanently in contact with water), to control the behaviour of the blocs in damp conditions (mould, disintegration) and the uptake by rats.
Test conditions	The experimental site is sewage system in an urban environment in damp conditions located at 60km south of Brussels. There is a limited access to the sewer system, only under the supervision of a civil servant of the municipality (Ville de Namur). The sewer at this place is

	also flooded by a local, nameless, brook. In winter months and early spring the flow of this brook is so heavy, access to the sewer is too dangerous. The limited access to the sewer system, needing the presence of the pest controller and the civil servant, limits the control of the study object, a daily control being not realistic. One can only asses the uptake the bait and increase/decrease of the uptake. The toxicity of the active for *Rattus norvegicus* is well known and a good uptake of the product can be translated to a good reduction the population.
Duration of the test / Exposure time	Knowing the bait shyness of rats, only 10 days later a first control was performed and product replaced or added when necessary. Another two weeks later a second control was performed and the results assessed. First poisoning bait: March 1st Control and re-baiting: March 10th, 10 days Second control : March 23th, 13 days after control and rebaiting
Number of replicates performed	No replicates
Controls	No control.
Examination	
Effect investigated	Behaviour of the bait (mould, disintegration) and the uptake by rats.
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.

Section B5.10_10	**Efficacy Data**
Annex Point IIB5.10_10	*Field trial into sewer systems*
TNsG: Pt. I-B5.10, Pt. III-Ch. 6	**Block bait/ Field efficacy/ Rats / Fresh product (T0)/Sewer systems**

Intervals of examination	Observation is done at 10 days then 23 days	
Statistics	The effects has been done by an assessment: scores of 0, 3, 5 or 8 were given as followed: SCORE 0 : blocs untouched or not more eaten then 29% SCORE 3 : blocs seriously eaten, not more than 49% SCORE 5 : blocs more than half eaten, less than 79% SCORE 8 : blocs more than 80% eaten	
Post monitoring of the test organism	Yes After the first poisoning phase, a second period with re baiting was observed. Then this second phase is considered to be post-baiting in order to estimate the reduction in population	

62 Results

Efficacy	First-baiting consumption: score of 359 Second-baiting consumption: score of 79 The efficacy assessment can be calculated as [SCORE first phase – SCORE second phase] x100/ SCORE first phase = ⟺ (359-76) *100 / 359 = 79%	X
Dose/Efficacy curve	The condition of the remaining product after three weeks in very damp conditions was fairly good to excellent. Only a few mould spots appeared on some blocs, without affecting the attractivity of the whole bloc. Aged blocks are not less eaten than the fresh ones. Although the complete extermination of *Rattus norvegicus* populations by placement of baits in the sewer system is impossible, the uptake of	

Section B5.10_10	**Efficacy Data**
Annex Point IIB5.10_10	*Field trial into sewer systems*
TNsG: Pt. I-B5.10, Pt. III-Ch. 6	**Block bait/ Field efficacy/ Rats / Fresh product (T0)/Sewer systems**

	the bait gives an idea of the infestation and reduces considerably by the population in the case of mild infestations. If a very heavy infestation appears, a combined treatment of underground sewer systems and the above surface installations must be considered. 10 days after their placement, baits were clearly attacked by rats, 25% of the blocs were almost completely eaten, other blocs showed clearly the marks of the rat teeth, 32% of them were more than half eaten and 29% were considered to be seriously eaten. Only 14% of the blocs remained untouched or not more eaten than 29%. On a possible maximum score of 640, the damage score was 359 (56% of acceptance).
Begin and duration of effects	The consumption of poisoned bait felt on the 10 to 23 days, after the intoxication and poisoning rats.
Observed effects in the post monitoring phase	20 of 80 blocs were renewed at the end of the first stage (10 days) and a second control took place 13 days later. The new damage score was 76, indicating that the activity and the population had already strongly diminished. Most of the blocs remained in good condition, indicating a good resistance to damp conditions.
Effects against organisms or objects to be protected	The toxicity of the bait for *Rattus norvegicus* is well known and a good uptake of the product can be translated to a good reduction of the population. Difenacoum is said to kill rodents in 5 to 21 days. In this test, the first control was performed after 10 days. The uptake of the product was obvious, the condition of the product excellent. The lower uptake after 23 days of the start of the test indicates the diminished population. The results are consistent with the results expected with difenacoum baits.
Other effects	-

Section B5.10_10	**Efficacy Data**
Annex Point IIB5.10_10	*Field trial into sewer systems*
TNsG: Pt. I-B5.10, Pt. III-Ch. 6	**Block bait/ Field efficacy/ Rats / Fresh product (T0)/Sewer systems**

Efficacy of the reference substance	Not applicable
Tabular and/or graphical presentation of the summarised results	No
Efficacy limiting factors	
Occurrences of resistances	Not applicable
Other limiting factors	Not applicable

63 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.	
Test organism	YES, the block bait, even with damp conditions of storage is efficient against rodent.	X
Observed effect	Not applicable	X
Relevance for read-across	Yes, This experiment shows results in a specific area with real conditions and constraints related to architecture of a sewer system. We can refer to the study, which regrouped all excellent parameters (very high level of humidity), as a relevant example of efficacy test in the damp condition of sewer systems.	

64 Applicant's Summary and conclusion

Materials and methods

The experimental site has been chosen to their natural condition opportunities:

- a sewer system in an urban environment with some high water pressure.

The aim of the study is to test the resistance of the product PROBLOC to the very damp conditions in a sewer system and to monitor the uptake of the bait by rats in these field conditions.

It is nearly impossible to know the number rats, it can only be estimated. The method consisting offering the bait and control by an assessment: scores of 0,3, 5 or 8 at two periods: 10 days after the first day of poisoning and 23 days after.

SCORE 0 : blocs untouched or not more eaten then 29%
SCORE 3 : blocs seriously eaten, not more than 49%
SCORE 5 : blocs more than half eaten, less than 79%
SCORE 8 : blocs more than 80% eaten

Then an estimation of the whole population can be made on basis of the food consumed.

Reliability

1, Study conducted in compliance with agreed protocols. X

The consumption rate given by scores and established during the poisoning phase corresponds to the expectations, it gives a good idea of the acceptance of the bait in damp conditions. Observation of the bait is also very important to estimate the preservation of the bait in such extreme conditions.

A comparison between the first phase of poisoning and the second one gives an estimation of the decrease of the population.

Assessment of efficacy, data analysis and interpretation

The efficacy assessment can be calculated as

[SCORE first phase – SCORE second phase] x100/ SCORE first phase

⟺ (359-76) *100 / 359 = 79%

Conclusion

More than efficacy, the observation and acceptance of the bait in very damp conditions are observed in this test. Efficacy is extrapolated from SCORE at the beginning of the test compared with SCORE at the end of the test.

Proposed efficacy specification

According to the point, we can declare that PROBLOC wax baits are very suitable for the treatment of sewer systems. They resist in very damp conditions, last, if not completed eaten, for at last 23 days and are well taken by sewer rats (*Rattus norvegicus*).

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	65 Evaluation by Rapporteur Member State
Date	June 2011.
Comments	**1.3** Guidelines don't exist for testing the effectiveness of rodenticides under the conditions encountered in a sewer system. **4.3** Test was conducted under field conditions. **4.3.2** Test organism: *Rattus norvegicus*. **4.3.3** Observed effect – acceptance of the bait and a reduction in consumption indicating control of the target population. **5.2** Reliability of 2 is more appropriate as the experiment was conducted in a very short period. Difficulties in accessing the site hindered a more thorough monitoring phase. Although applicant claims test was conducted to protocols there are no guidelines to adhere to.
Summary and conclusion	Based on the limited data available from the first and second bait consumption scores, the applicant estimated an efficacy assessment of 79%. The palatability of the block formulation, even under very damp conditions did not lead to the formation of mould or affect the perceived palatability of the bait.
	66 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	PROBLOC: block rodenticide bait. Containing 0.005 % of Difenacoum
Origin	Batch N° NO091109
Initial biomass	Not applicable
Reference of methods	Field trial (real conditions)
Collection / storage of samples	NA
Preparation of inoculum for exposure	NA
Pretreatment	NA
Active substance determined in the product	Containing 0.005 % of Difenacoum

1.2 Test organism (*if applicable*)

Criteria	Details
Species	Browns rats *(Rattus norvegicus)*
Strain	Wild
Source	From the surrounding areas of the sewer system.
Laboratory culture	No
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	The average consumption of 10 days of first-baiting shows: [(150*20*100/100) + (150*26*79/100) + (150*23*49/100) + (150*11*29/100)] /10= 8250/10=825 grams / day. Based on the average and if we allocate an effective consumption of 20 g per rats, we could estimate the test population to nearly 42 rats.
Method of cultivation	New baiting were filled 10 days after the first one.
Pretreatment of test organisms before	Not applicable

exposure	
Initial density/number of test organisms in the test system	42 rats.

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	BLOCS with hook were hanged on different locations in the sewer system; the product did not hang in the water but was easily accessible by the rats
Delivery method	Manual, by a pest controller
Dosage rate	80 blocks of 150g along the sewers system
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 block bait - Acute Oral Toxicity in the rat - Acute toxic class method, [redacted] study number TAO423-PH-09/0085, 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 block bait** It was identified under the code number in the laboratory as **PH-09/0085.**	
Lot/Batch number	PB090209	
Specification	CAS No: 56073-07-5	
Description	Solid and red	
Purity	Difenacoum 0.005 % m/m (nominal value). Please see the analysis certificate.	
Stability	Not provided by applicant	
Test Animals		
Species	Rat	
Strain	Sprague-Dawley, SPF Caw	
Source	[redacted]	
Sex	Female	
Age/weight at study initiation	Females weighed between 182 g and 224 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 were weighed in a 10 ml volumetric flask 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 LD50 of the test item Difenacoum block 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	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}	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 block 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. 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. 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 block 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 block 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	*30 May 2011*
Materials and Methods	*Adopt applicant's version.*
Results and discussion	*Adopt applicant's 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	
	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 block bait - Acute Dermal Toxicity in the rat - Acute toxic class method, [redacted] study number TAD-PH-09/0085, 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° 402 (24 February 1987) Test method B.3 Council regulation No 440/2008	
GLP	YES	
Deviations	Any	
	MATERIALS AND MethodS	
Test material	**Difenacoum block bait** It was identified under the code number in the laboratory as **PH-09/0085.**	
Lot/Batch number	PB090209	
Specification	CAS No: 56073-07-5	
Description	Solid and red	
Purity	Difenacoum 0.005 % m/m (nominal value). Please see the analysis certificate.	
Stability	Not provided by applicant	
Test Animals		
Species	Rat	
Strain	Sprague-Dawley, SPF Caw	
Source	[redacted]	
Sex	Males and females	
Age/weight at study initiation	Males weighed between 217 g and 234 g and were 7 weeks old Females weighed between 206 g and 225 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 block 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 block 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. It was only noted a depilation and a pink coloration, which did not prevent the observations, after rinsing of the remaining test item. 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-relatedchanges. It was only noted a pink coloration of the treated site	
Conclusion	The LD50 of the test item Difenacoum block 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 block 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	*30 May 2011*	
Materials and Methods	*Adopt applicant's version*	
Results and discussion	*Adopt applicant's version*	
Conclusion	*Adopt applicant's version*	
Reliability	*1*	
Acceptability	acceptable	
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		

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 6.7×10^{-9} – 5.4×10^{-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	*30 May 2011*	
Evaluation of applicant's justification	*Accept applicant's justification*	
Conclusion	*Accept applicant's justification*	
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 **BLOCK BAIT** and the label claims, the rodenticide **BLOCK 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	*30 May 2011*	
Evaluation of applicant's justification	*Accept applicant's justification*	
Conclusion	*Accept applicant's justification*	
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 block bait – Skin Irritation test in the rabbit, [redacted] study number IC-OCDE-PH-09/0085, 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 block bait** It was identified under the code number in the laboratory as **PH-09/0085.**	
Lot/Batch number	PB090209	
Specification	CAS No: 56073-07-5	
Description	Solid and red	
Purity	Difenacoum 0.005 % m/m (nominal value). Please see the analysis certificate.	
Stability	Please refer to Section 3 of the dossier	
Test Animals		
Species	Albino rabbit	
Strain	New Zealand	
Source	[redacted]	
Sex	Male	
Age/weight at study initiation	The animals weighed between 2.89 kg and 3.41 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 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.	
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	0.5g	
Removal of test substance	Distilled water	X
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.	

<table>
<tr><td>Controls</td><td>No specified by the laboratory</td><td></td></tr>
<tr><td>Examinations</td><td></td><td></td></tr>
<tr><td>Clinical signs</td><td>No</td><td></td></tr>
<tr><td>Dermal examination</td><td>Yes</td><td></td></tr>
<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>
</table>

<table>
<tr><td></td><td>Results and Discussion</td><td></td></tr>
<tr><td>Average score</td><td></td><td></td></tr>
<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>A9643 (12 May 09)</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>A9645 (19 May 09)</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>A9646 (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>
</table>

Edema	The average score for all animals is given at the following table*:* Animal number / Hours of examination: 1 / 24 / 48 / 72 A9643 *(12 May 09)*: 0 / 0 / 0 / 0 A9645 *(19 May 09)*: 0 / 0 / 0 / 0 A9646 *(19 May 09)*: 0 / 0 / 0 / 0 0= Non irritating	
Reversibility	Yes	
Other examinations	No other signs of dermal irritation	
Overall result	No cutaneous reactions (erythema and oedema) were observed, on the treated area, whatever the examination times (ie 1, 24, 48 and 72 hours).	

	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 cm^2. 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 block bait, according to the scales of interpretation retained: - is non irritant to skin (PSi = 0.00) 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	*30 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 *Difenacoum is water insoluble. Cleaning of the site with an aqueous medium is not suitable to ensure complete removal of product.*	
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		

IIIB Section 6.2_02 BPD Data Set IIB/ Annex Point VI.6.2	**Acute Eye Irritation**	
	Reference	**Official use only**
Reference	[redacted] Difenacoum block bait – Skin Irritation test in the rabbit, [redacted] study number IC-OCDE-PH-09/0085, 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 block bait** It was identified under the code number in the laboratory as **PH-09/0085.**	
Lot/Batch number	PB090209	
Specification	CAS No: 56073-07-5	
Description	Solid and red	
Purity	Difenacoum 0.005 % m/m (nominal value). Please see the analysis certificate.	
Stability	Please refer to Section 3 of the dossier	
Test Animals		
Species	Albino rabbit	
Strain	New Zealand	
Source	[redacted]	
Sex	Male	
Age/weight at study initiation	The animals weighed between 2.34 kg and 2.97 kg. At the beginning of the test, the animals were 11 or 13 weeks old.	
Number of animals per group	One group of 3 males	
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 A9664 and A9665, residual test item was still noted. Therefore, the treated eye was rinse with a physiological saline solution</td><td></td></tr>
</table>

<table>
<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">A9650</td><td colspan="3">A9664</td><td colspan="3">A9665</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>
<tr><td>Iris</td><td>The average score for the iris is given at the following table:
<table>
<tr><td>Animal number</td><td colspan="3">A9650</td><td colspan="3">A9664</td><td colspan="3">A9665</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>
<tr><td>Conjunctiva</td><td></td><td></td></tr>
<tr><td>Redness</td><td>The average score for the redness is given at the following table:
<table>
<tr><td>Animal number</td><td colspan="3">A9650</td><td colspan="3">A9664</td><td colspan="3">A9665</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>2</td><td>2</td><td>1</td><td>1</td><td>1</td><td>0</td><td>1</td><td>1</td><td>0</td></tr>
<tr><td>TOTAL</td><td colspan="3">5</td><td colspan="3">2</td><td colspan="3">2</td></tr>
<tr><td>MEAN</td><td colspan="3">1.7</td><td colspan="3">0.7</td><td colspan="3">0.7</td></tr>
</table></td><td></td></tr>
</table>

<table>
<tr><td>Chemosis</td><td>The average score for the chemosis is given at the following table:
<table>
<tr><td>Animal number</td><td colspan="3">A9650</td><td colspan="3">A9664</td><td colspan="3">A9665</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>Chemosis (A)</td><td>2</td><td>1</td><td>0</td><td>1</td><td>0</td><td>0</td><td>1</td><td>0</td><td>0</td></tr>
<tr><td>TOTAL</td><td colspan="3">3</td><td colspan="3">1</td><td colspan="3">1</td></tr>
<tr><td>MEAN</td><td colspan="3">1.0</td><td colspan="3">0.3</td><td colspan="3">0.3</td></tr>
</table></td><td></td></tr>
<tr><td>Reversibility</td><td>Yes, the redness and the chemosis disappeared after 48 hours.</td><td></td></tr>
<tr><td>Other</td><td>None</td><td></td></tr>
<tr><td>Overall result</td><td>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</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. 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 3 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 3.	
Conclusion	The results obtained, under these experimental conditions, enable to conclude that the test item Difenacoum block bait: - is slightly irritant for the eye (Max. O.I = 10.7) 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	*30 May 2011*	
Materials and Methods	*Adopt applicant's version.*	
Results and discussion	*Adopt applicant's version.*	
Conclusion	*Adopt applicant's version*	
Reliability	*1*	
Acceptability	acceptable	
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		

IIIB Section 6.3 BPD Data Set IIB/ Annex Point VI.6.3	**Skin Sensitisation**	
	Reference	**Official use only**
Reference	[redacted] Difenacoum block bait – Skin sensitisation in the guinea pig - Magnusson and Kligman maximisation method, [redacted] study number SMK-PH-09/0085, 8 December 2009, 42 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	X
GLP	YES	
Deviations	Any	X
	MATERIALS AND MethodS	
Test material	**Difenacoum block bait** It was identified under the code number in the laboratory as **PH-09/0085.**	
Lot/Batch number	PB090209	
Specification	CAS No: 56073-07-5	
Description	Solid and red	
Purity	Difenacoum 0.005 % m/m (nominal value). Please see the analysis certificate.	
Stability	-	

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	

	<table><tr><td></td><td></td><td>Difenacoum block bait</td></tr><tr><td rowspan="3">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>	
Pretest performed on irritant effects	Yes, preliminary tests were performed in order to determine, by topical application the Pre-Maximal Non Irritant Concentration (Pre-MNIC), which allowed to evaluate 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	
Test Animals		
Species	Guinea pigs	
Strain	Dunkin-Hartley strain	
Source	[redacted]	
Sex	Female	
Age/weight at study initiation	The animals weighed between 272 g and 315 g at the beginning of the test and were 4 weeks old.	
Number of animals per group	<table><tr><td></td><td>GROUP 1 negative control</td><td>GROUP 2 treated</td></tr><tr><td>Female/group</td><td>5 n° C1866 to C1870</td><td>11 n° C1871 to C1881</td></tr></table>	
Control animals	Negative control (5 for the group)	
Administration/ Exposure	The aim of the study was to evaluate the possible allergenic activity of the test item after topical administration in guinea pigs.	
Induction schedule	Day 1 – Day 6 – Day 7	

<table>
<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 colspan="2"></td><td>Preparation of the test substance</td></tr><tr><td colspan="2"></td><td>Difenacoum block bait</td></tr><tr><td rowspan="3">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>X</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 20</td><td></td></tr>
<tr><td>Concentrations used for challenge</td><td>The concentrations used for challenge were 50% (MNIC) and 25% (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>
<tr><td>Pilot study</td><td>Yes</td><td></td></tr>
<tr><td>Further remarks</td><td>-</td><td></td></tr>
</table>

	Results and Discussion	
Results of pilot studies	- <u>Pre MNIC determination:</u> 24 hours after the removal of the occlusive dressings, no cutaneous reaction was recorded whatever the tested concentration (50% diluted at 25%, 12.5% and 6.25% in distilled water, after being reduced in fine powder with a coffee mill.). In view of these results, the concentration selected was 50% for the 2nd induction of the Group 2 and the MNIC determination began at this concentration of 50%. - <u>MNIC determination:</u> 24 hours after removal of the occlusive dressings, no cutaneous reaction was recorded whatever the tested concentration (table 2, page 12). In view of this result, the concentrations selected were 50% (MNIC) and 25% (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 50% and 25%. It was only noted a depilation at the reading time 24 hours on the treated area at 50% in three animals (3/11) and on the treated area at 25 % in five animals (5/11). A slight pink coloration, not preventing from scoring, was also noted on the treated areas.	
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 50% and 25%.	

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 50% and 25%. It was only noted a depilation at the reading time 24 hours on the treated area at 25% in two animals (2/5). A slight pink coloration, not preventing from scoring, was also noted on the treated areas.	

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
			0	1	2	3or >		
Negative control group	24	50 %	0	1	2	3or >		
	48	25 %	0	0	0	0	0%	
	24	50 %	0	0	0	0	0%	
	48	25 %	0	0	0	0	0%	
Treated Group	24	50 %	0	0	0	0	0%	0%
	48	25 %	0	0	0	0	0%	0%
	24	50 %	0	0	0	0	0%	0%
	48	25 %	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 272 g and 315 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:

- 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 (50% diluted at 25%, 12.5% and 6.25% 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, two (2) pairs of intradermal injections (ID) of 0.1 ml of Freund's Complete Adjuvant diluted at 50 % in isotonic sodium chloride were performed on the scarified scapular zone in such a way as an injection on each pair is placed to either side of the spine. A topical application under occlusive dressing for 48 hours was performed on the injection sites of each animal.
Day 6	**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 7	**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 50%
Rest period	
Day 20	**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 50% (MNIC) and at 25% (1/2 MNIC).

Results and discussion	An answer over at least 30% of animals is regarded as positive. 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 50% and 25%. It was only noted a depilation at the reading time 24 hours on the treated area at 50% in three animals (3/11) and on the treated area at 25 % in five animals (5/11). A slight pink coloration, not preventing from scoring, was also noted on the treated areas. 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 50% and 25%. It was only noted a depilation at the reading time 24 hours on the treated area at 25% in two animals (2/5). A slight pink coloration, not preventing from scoring, was also noted on the treated areas.	
Conclusion	In view of these results, under these experimental conditions, the test item Difenacoum block bait must not be classified as a skin sensitiser, 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	30 May 2011	
Materials and Methods	Applicants version is not acceptable.	
Results and discussion	Applicants version is not acceptable.	
Conclusion	Other conclusions:	
Reliability	4	
Acceptability	not acceptable - The test substance is finely ground and then diluted with distilled water. However, the test material contains an active substance that is not water soluble that is bound up in a wax matrix that is also not water soluble. At best a fine suspension is created that is unsuitable for intradermal injection. - This procedure cannot be identified as a Guinea Pig Maximisation Test, no intradermal induction can occur as outlined in the materials and methods. - Changes were made to the procedure so that it no longer conforms to the OECD 406 guidelines. - At best this might be described as a modified type of Buehler test, primary induction is by way of topical application over FCA injection sites. - too few animals to consider results in a meaningful way. - no requirement to repeat this study, the results of a GPMT and Buehler study carried out on the active substance difenacoum and submitted in support of the CAR provide no evidence of sensitising potential.	
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		

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.)*	

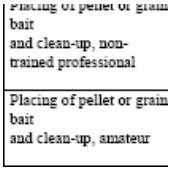
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	*30 May 2011*	
Evaluation of applicant's justification	*Applicant's justification is acceptable*	
Conclusion	*Applicant's 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, **BLOCK BAIT**, containing 0.005% difenacoum, there is no presence of co-formulant of toxicological concern.	
	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.	
	 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.	
	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, p14-15 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 [ ] **Limited exposure [ ]**	**Technically not feasible [ ] Scientifically unjustified [ ]** **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	

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**

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.

Water justifications:

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 was calculated and compared against the relevant end points in Doc IIC. PEC surface water was calculated for the representative uses, i.e. sewer systems, in and around buildings, open areas and landfills/dump. No concern has been raised.

Air justifications:

Difenacoum has a low vapour pressure (< 5 x 10^{-5} Pa) and Henry's Law constant (0.046 - 0.0129 x 10^{-2} $Pa.m^3mol^{-1}$). Release to air via water is expected to be negligible. This is also supported by calculations using the TGD on risk assessment for percent

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**

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 valueswere calculated and compared against the relevant end points in Doc IIC. PEC soilwere 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 1.8×10^6 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

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**	
	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 the 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.)*	

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**

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	19-01-11
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 *As outlined in the TNsG on data requirements, the applicant must*	Official use only

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**	
	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	
Date	**EVALUATION BY RAPPORTEUR MEMBER STATE** 26/01/11	

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**
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. Therefore Applicant's justification is acceptable assuming the test material is used according to the supported GAP.
Conclusion	IE-CA 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 always be able to justify the suggested exemptions from the data requirements.* *The justifications are to be included in the respective location*	Official use only

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.**	
	(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	
Date	**EVALUATION BY RAPPORTEUR MEMBER STATE** *26/01/11*	

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.**
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. 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[29] submitted in support of the evaluation of the active substance (IIIA)

Not Applicable

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

List of <u>new data</u> 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	Y
B2.1_0	-	-	Difenacoum Block: composition	Bio6	Y	Y
B2.1_1	Porte P., Denny O.	2009	Analytical Certificate Product name: Difenacoum block bait Batch number: PB090209, date of analysis: 5 May 2009. Defitraces, 69126 Brindas, France, 19th October 2009. GLP. Unpublished.	Bio6	Y	Y
B2.2_01	Anonym	2003	Saftey Data Sheet_Component 1: Difenacoum concentrate 2.5% (Red) Denatonium Benzoate. PELGAR International, UK. Not GLP, Published	Pelgar	Y	Y
B2.2_02	Anonym	2010	[redacted]	Colorey SAS	-	Y
B2.2_03	Anonym	2006	[redacted]	Quaron	-	Y
B2.2_04	Anonym	2005	[redacted]	Brenntag SA	-	Y
B2.2_05	Anonym	-	[redacted]	EUSA Colors	-	Y
B2.2_06	Anonym	2008	[redacted]	Sasol Wax GmbH	-	Y
B2.2_07	Anonym	-	[redacted]	Bio6	Y	Y
B2.2_08	Anonym	-	[redacted]	Bio6	Y	Y
B2.2_09	Anonym	-	[redacted]	Bio6	Y	Y
B2.2_10	Anonym	-	[redacted]	Bio6	Y	Y

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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	Biannic M-L., Magnier C.	2009	Study Report – Chemical stability after accelerated storage of Difenacoum block baits 0.005%. LODI Group, Parc d'activité des Quartre Routes, 35390 Grand Fougeray, FRANCE. Version date: 2009-11-23 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
B.3.7_04	Brekelmans, Ir. M.J.C.	2010	Study Report –Determination of physic-chemical properties of difenacoum block baits. NOTOX B.V., Hambakenwetering 7, 5231 DD 's-Hertogenbosch, The Netherlands. Version date: 17th September 2010 Project no: 490521. Unpublished	Bio6	Y	Y

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* Data Protection Claimed

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 block bait, in compliance with CIPAC/3807R. Defitraces, 69126 Brindas, France. Report No. 09-902018-005, of 19 October 2009. GLP. Unpublished	Bio6	Y	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, 22 pages, LODI sa. GLP. Unpublished	LODI	Y	Y

Ref No	Author	Year	Title Source Company, Report No. GLP (where relevant)/ (Un)Published	Data owner	LoA# (Y/N)	DPC* (Y/N)
B4_1c	Porte P., Denny O.	2009	Analytical Certificate – Product name: Difenacoum block bait, batch number: 600300, date of analysis: 5th May 2009. Anadiag Group - Defitraces, 69126 Brindas, France, belong to study 09-902018-005. GLP. Unpublished.	Bio6	Y	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	Y

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* Data Protection Claimed

Efficacy

Ref No	Author	Year	Title Source Company, Report No. GLP (where relevant)/ (Un)Published	DPC* (Y/N)	Data owner
B5.10.01	-	2007	Efficacy trial: Rodenticide block containing 0.005% Difenacoum, against house mice (Mus musculus), Trial date: 10th April to 6th May, 2007. Block bait/ Field efficacy/ Mice /Product at T0 LODI S.A., Parc d'activité des Quatre Routes, 35390 Grand Fougeray, FRANCE. Unpublished	Y	Lodi
B5.10.03	-	2009	Efficacy trial: Rodenticide block containing 0.005% Difenacoum, after 2 years ageing, against house mice (Mus musculus), Trial date= 2nd to 29th March, 2009. Block bait/ Field efficacy/ Mice / Product at T2 years LODI S.A., Parc d'activité des Quatre Routes, 35390 Grand Fougeray, FRANCE. Unpublished	Y	Lodi
B5.10.03a	Prescott	2010	Efficacy assessment, using the bait choice feeding test, of Difebloc wax blocks (T0) containing 50 mg.kg-1 difenacoum, using CD-1 albino house mouse, Study reference VPU Study Plan Number VPU/10/004, VPU trial No. GB01-10-R009, Project number 153SRI10P, trial code SRIT10-1001-153P Block bait/ Labo/ Mice / Product at T0 The Vertebrate Pests Unit School of Biological Sciences, The University of Reading Whiteknights, Reading RG6AJ, UK Unpublished	Y	Lodi

Ref No	Author	Year	Title Source Company, Report No. GLP (where relevant)/ (Un)Published	DPC* (Y/N)	Data owner
B5.10.03b	Prescott	2010	FINAL REPORT- Efficacy assessment, using the bait choice feeding test, of Difebloc wax blocks (T2weeks accelerated) containing 50 mg.kg-1 difenacoum, using CD-1 albino house mouse, Study reference VPU Study Plan Number VPU/10/005, VPU trial No. GB01-10-R010, Project number 153SRI10P, trial code SRIT10-1002-153P Block bait/ Labo/ Mice / Product at T14 days accelerated The Vertebrate Pests Unit School of Biological Sciences, The University of Reading Whiteknights, Reading RG6AJ, UK , Unpublished	Y	Lodi
B5.10.03b	Prescott	2010	Efficacy assessment, using the bait choice feeding test, of Difebloc wax blocks (T2weeks accelerated) containing 50 mg.kg-1 difenacoum, using CD-1 albino house mouse, Study reference VPU Study Plan Number VPU/10/005, VPU trial No. GB01-10-R010, Project number 153SRI10P, trial code SRIT10-1002-153P Block bait/ Labo/ Mice / Product at T14 days accelerated The Vertebrate Pests Unit School of Biological Sciences, The University of Reading Whiteknights, Reading RG6AJ, UK , Unpublished	Y	Lodi
B5.10.04a,	Latteur G	1997	Efficacy and Appetizing test performed on BELGABLOC, paraffinic bait block containing 0.005% of Difenacoum, against brown rats (*Rattus norvegicus* Berkenhout), at different storages stages (Appetizing test included). *Efficacité du Belgabloc, bloc paraffine à base de 0,005% de Difenacoum, contre le surmulot (Rattus norvegicus Berkenhout).* Block bait/ Semi field efficacy/ Rats /Fresh product (T0) CRA (Agronomic Research Center), Phytopharmacological department, Rue du Bordia, 11, 5030 Gembloux, Belgium, Report 965, May 1997. GLP, Unpublished	Y	Belgagri
B5.10.05 a	Latteur G	1998	Appetizing test through different period of time,	Y	Belgagri

Ref No	Author	Year	Title Source Company, Report No. GLP (where relevant)/ (Un)Published	DPC* (Y/N)	Data owner
			performed on BELGABLOC, containing 0.005% of Difenacoum, against brown rats (*Rattus norvegicus*). *Evaluation de la perte d'efficacité au cours du vieillissement du BELGABLOC, rotendicide à base de 0.005% de Difenacoum pour lutter contre le surmulot (Rattus norvegicus Berkenhout).* *Block bait/ Laboratory efficacy/ Rats /Product at T0 and T6* CRA (Agronomic Research Center), Phytopharmacological department, Rue du Bordia, 11, 5030 Gembloux Belgium, rapport complement 980, April 1998. GLP, Unpublished		
B5.10.05b	Meeus P., de Ryckel B.	1997	Analyse certificate N°8882Ch.1440/1997, Personnalité Juridique De La Station De Phytopharmacie, Rue du Bordia, ll B - 5030 - GEMBLOUX – Belgique, N°8882Ch.1440/1997 GLP, Unpublished	Y	Belgagri
B5.10.06a	De Proft M.,	1999	Appetizing test through different period of time, performed on PROBLOC, bait ready to use, containing 0.005% of Difenacoum, against brown rats (*Rattus norvegicus*). *Etude du comportement de PROBLOC, appât prêt à l'emploi contenant 0.005% de difénacoum, destiné à lutter contre le rat brun (Rattus norvegicus).* *Block bait/ Laboratory efficacy/ Rats /Product at T0 and T12* CRA (Agronomic Research Center), Phytopharmacological department, Rue du Bordia, 11, 5030 Gembloux Belgium, rapport complement 9547, 1999. GLP, Unpublished	Y	Belgagri
B5.10.06b	Meeus P., de Ryckel B.	1999	Analyse certificate N°Ch. 1943I 1999, Personnalité Juridique De La Station De Phytopharmacie, Rue du Bordia, ll B - 5030 - GEMBLOUX – Belgique*, N°Ch. 1943I 1999*	Y	Belgagri

Ref No	Author	Year	Title Source Company, Report No. GLP (where relevant)/ (Un)Published	DPC* (Y/N)	Data owner
			GLP, Unpublished		
B5.10.07	Grolleau G., Panciroli J.	2005	Experimentation, in nature, of block bait against rats (Rattus Norvegicus). Expérimentation, en nature, d'un appât bloc contre le surmulot (Rattus Norvegicus). Pest Control Assistance (PCA), 3 rue Constantin Le Priol 56150 BAUD (France), Organization approved for the carrying out the tests: Cabinet Barrieux, Cabinet Conseil en Agro Technologies, 92100 Boulogne Billancourt France, 2005. Block bait/ Field efficacy/ Rats / Fresh product (T0) GLP, Unpublished	Y	Lodi
B5.10.08	-	2009	Efficacy trial: Rodenticide block containing 0.005% Difenacoum, after 2 years ageing, against house mice (Rattus norvegicus), Trial date= 6th April to 13th May, 2009. Block bait/ Field efficacy/ Rats / Product at T2 years LODI S.A., Parc d'activité des Quatre Routes, 35390 Grand Fougeray, FRANCE. Unpublished	Y	Lodi
B5.10.09			STUDY ONGOING Statement IVB and IIIB will be supplied to you as soon as we will received the final version		

* Data Protection Claimed

Toxicology

Ref No	Author	Year	Title	Data owner	LoA# (Y/N)	DPC* (Y/N)
B6.1.1	[redacted]	2009	Difenacoum block bait - Acute Oral Toxicity in the rat - Acute toxic class method	Bio6 S.A.	Y	Y
B6.1.2	[redacted]	2009	Difenacoum block bait - Acute Dermal Toxicity in the rat - Acute toxic class method	Bio6 S.A.	Y	Y
B6.2	[redacted]	2009	Difenacoum block bait – Skin Irritation test in the rabbit	Bio6 S.A.	Y	Y
B6.2	[redacted]	2009	Difenacoum block bait – Eye Irritation test in the rabbit	Bio6 S.A.	Y	Y
B6.3	[redacted]	2009	Difenacoum block bait – Skin sensitisation in the guinea pig - Magnusson and Kligman maximisation method	Bio6 S.A.	Y	Y

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* Data Protection Claimed

Environment (including Eco-Toxicology)

Not applicable

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 block is a ready to use bait, which is used to kill rats and mice. Ruby block 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.

Addendum to PAR - January 2012

Addendum

to the Product Assessment Report

Ruby block (IE/BPA 70025; IE/BPA 70002), Probloc (IE/BPA 70037; IE/BPA 70098)
Ruby grain (IE/BPA 70027; IE/BPA 70003), Raco (IE/BPA 70036; IE/BPA 70097)
Ruby paste (IE/BPA 70033; IE/BPA 70004), Nora pasta (IE/BPA 70038; IE/BPA 70099)

Active substance:	**Difenacoum**
Product-type:	**PT14: Rodenticides**
Type of application:	**Authorisation**
Authorisation No:	**See above.**
Date:	**17 January 2012**

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

Department of Agriculture, Food and the Marine
An Roinn Talmhaíochta, Bia agus Mara

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

Background:

The applicant was asked to address the concern that the active ingredient content appears to decrease over storage time in the block bait and grain bait formulations. The block formation when analysed at manufacture contained 52.7 mg/kg (0.0527 g/kg) of active ingredient but at 24 months the active ingredient content was 43.5 mg/kg (0.0435 g/kg), representing a 17.5% decrease {Study report: Stability of Difenacoum baits after a storage at ambient temperature. Biannic, Marie-Laure. 12th November 2009}. The grain formation when analysed at manufacture contained 48.8 mg/kg (0.0488 g/kg) of active ingredient but at 24 months the active ingredient content was 38.2 mg/kg (0.0382 g/kg), representing a 22% decrease {Biannic, Marie-Laure. LODI-Group. 12th November 2009}.

The applicant has stated that for heterogeneous formulations the active substance content can vary by ± 25% when the declared content of active substance is up to 25 g/kg. The active substance concentration for both the block and grain bait is within the ± 25% specification which is in compliance with the FAO's requirement (50 mg/kg ± 25%, therefore between 37.5 – 62.5 mg/kg). The paste bait shows no sign of degradation over the two year period.

Efficacy data presented in the PAR show that the block and grain formulations are effective following storage for up to 24 months.

Block bait: After a 9-day treatment phase with a 2-year aged bait an efficacy specification approaching 90% was achieved (for mice). 22 brown rats were used in a study, with a short poisoning period using fresh and aged (6 month old) baits. 95% control was achieved with the fresh bait and 100% with the aged bait with the sole surviving female having consumed very low levels of the block bait. In the next test 22 rats were used in a study on fresh and 12-month aged blocks. 90% control was achieved with the fresh bait and total control achieved with the aged bait. A rat infested restaurant (~81 rats) was chosen for the next study. Aged bait (2 year old) was used resulting in 89.1% control after a short 5-day baiting period. The block bait formulation proved to be highly palatable and effective against both rats and mice in the tests. Both fresh and aged baits (6, 12 and 24 months after manufacture) provided 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.

Grain bait: A private dwelling house with a mouse infestation estimated at approximately 100 individuals was used for a study in which 2-year old bait was used. 98% efficacy was achieved after what could be considered a relatively short baiting and post-baiting monitoring period. An aviary for wildfowl breeding was chosen for a study on the control of brown rats with aged bait (2 years). The report confirmed that the farm contained a plentiful supply of food and water with nearby harbourage for the rats. Population tracking estimated that there were ~124 rats onsite. A 98% reduction in consumption levels/efficacy was achieved after a 13 day baiting phase. The grain 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) also provided 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.

This information suggests that the observed reduction in Difenacoum content is due to factors other than active substance degradation since Difenacoum must remain in the bait in order for the observed level of mortality.

Below is further information supplied by the Notifier to address the storage stability issues with respect to the block and grain baits (Tables 3.1.3.1 and 3.1.3.2). Paste bait information was also provided and was evaluated below (Table 3.1.3.3).

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

Table 3.1.3.1: Summary of the Physical and Chemical Properties of the Biocidal Product Block Bait

Section	Study	Method	Results	Comment	Reference
1.7.1a	Storage stability (Accelerated storage – 14 days at 54°C)	GIFAP Monograph No. 17 CIPAC MT 46	**Cardboard box:** <u>Analysis at T0:</u> Physical properties: Red block. Cardboard box: Grey with dry internal walls. Cardboard box: 23.462g. Test item: 185.70g Total weight: 209.16g <u>Analysis at T14:</u> Physical properties: Red block – colour more intense than t=0. Cardboard box: Presence of grease on internal and external walls. Cardboard box: 26.429g (12.65%) Test item: 174.80g (-5.875) Total weight: 201.22g (-3.80%) **PE bag with cardboard box:** <u>Analysis at T0:</u> Physical properties: Red block. PE bag with cardboard box: Transparent bag – cardboard box with grey with dry internal wall.	Carried out to GLP. For cardboard box, deviation in weights after accelerated storage is higher than 5%. For all other packaging, deviation of packaging and sample weights after accelerated storage for 2 weeks at 54°C are lower than 5%. No significant changes of characteristics of test item or packaging were observed. The study is acceptable.	"Packing stability used for Difenacoum block bait after accelerated storage". Richerioux, S. Report no.: LODI.57/2011. 2011-11-10.

Section	Study	Method	Results	Comment	Reference
			PE bag: 3.415g Cardboard box: 23.464g Test item: 182.75g Total weight: 209.63g <u>Analysis at T14:</u> Physical properties: Red block – colour more intense than t=0. PE bag with cardboard box: Transparent bag with presence of block dust – cardboard box with grey with dry internal wall. PE bag: 3.472g (1.67%) Cardboard box: 23.414g (-0.21%) Test item: 175.99g (-3.70%) Total weight: 202.89g (-3.22%) **PP Bucket:** <u>Analysis at T0:</u> Physical properties: Red block. PP bucket: white and non-porous internal wall. PP bucket: 44.121g. Test item: 365.34g Total weight: 409.46g		

Section	Study	Method	Results	Comment	Reference
			Analysis at T14: Physical properties: Red block – colour more intense than t=0. PP bucket: white and non-porous internal wall – presence of dust block. PP bucket: 44.457g (0.76%). Test item: 362.34g (-0.82%) Total weight: 406.80g (-0.65%) **PP prebaited baitbox:** Analysis at T0: Physical properties: Red block. Prebaited baitbox: Black box with non-porous internal wall. Prebaited baitbox: 47.483g. Test item: 31.012g Total: 78.495g. Analysis at T14: Physical properties: Red block – colour more intense than t=0. Prebaited baitbox: Black box with non-porous internal wall – presence of block dust at the site of the block. Prebaited baitbox: 47.756g (0.57%). Test item: 29.600g (-4.55%). Total: 77.354g (-1.45%).		

Section	Study	Method	Results	Comment	Reference
			PS prebaited baitbox: Analysis at T0: Physical properties: Red block. Prebaited baitbox: Black box with non-porous internal wall. Prebaited baitbox: 12.525g. Test item: 29.894g. Total: 42.419g. Analysis at T14: Physical properties: Red block – colour more intense than t=0. Prebaited baitbox: Black box with non-porous internal wall – presence of block dust at the site of the block. Prebaited baitbox: 12.784g (2.07%). Test item: 28.779g (-3.73%). Total: 41.563g (-2.02%) **Cardboard prebaited baitbox:** Analysis at T0: Physical properties: Red block. Prebaited baitbox: Dry cardboard. Prebaited baitbox: 18.765g.		

<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>Test item: 30.672g.
Total: 49.737g.

<u>Analysis at T14:</u>
Physical properties: Red block – colour more intense than t=0.
Prebaited baitbox: Presence of a ring at the site of the block.
Prebaited baitbox: 18.860g (0.51%).
Test item: 29.635g (-3.38%).
Total: 48.499g (-1.90%)</td><td></td><td></td></tr>
<tr><td>1.7.2a</td><td>Shelf life (storage ambient temperatures for two years)</td><td>In compliance with GIFAP Monograph No. 17.

pH (CIPAC Handbook J – MT 75.3 Method (2000))</td><td>Physical & Chemical properties:
<table>
<tr><th>Time</th><th>0</th><th>6 months</th><th>12 months</th><th>2 yrs</th></tr>
<tr><td>Appearance</td><td>Bright pink block</td><td>Bright pink block</td><td>Bright pink block</td><td>Bright pink block</td></tr>
<tr><td>Packaging</td><td>White opaque plastic box with red opaque plastic cover</td><td>White opaque plastic box with red opaque plastic cover</td><td>White opaque plastic box with red opaque plastic cover</td><td>White opaque plastic box with red opaque plastic cover</td></tr>
<tr><td>Packaging weight</td><td>756g</td><td>754.5g (-0.20%)</td><td>690.0 (-0.40%)</td><td>625.4g (-0.49%)</td></tr>
</table></td><td>Carried out to GLP. The test item is considered stable for 2 years at ambient temperatures.

The pH at T0 was not given.

The study is acceptable.</td><td>“Chemical stability and physico-chemical tests after a storage procedure for 2 years at 20 ± 2°C on Difenacoum Block Bait”. Demangel, Benjamin. Report no.: 09-902018-004.</td></tr>
</table>

Section	Study	Method	Results	Comment	Reference

		692.8g after sampling	628.5g after sampling	

The appearance of the test item is considered to be stable after the storage procedure for 2 years at 20 ± 2°C, no significant change of weight was observed.

The packaging material is considered to be stable after the storage procedure for 2 years at 20 ± 2°C.

Time	**0**	**6 months**	**12 months**	**2 yrs**
Difenacoum content (% w/w)	0.0047	0.0048	0.0049	0.0050
Deviation from the declared value (%) * deviation from T0 value (%)	-6.0	+2.1	+4.3	+6.4*

The test item is considered to be stable after a storage procedure for 2 years at 20 ± 2°C.

Note that the declared content was 0.005% w/w.

Time	**2 yrs**
pH at 1% w/v in standard water D (at 21.7°C and 21.8°C respectively)	5.89 after 1 min 6.00 after 10 min

The pH at T0 was not given.

<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></td><td></td></tr>
<tr><td>1.7.2b</td><td>Shelf life (storage ambient temperatures for two years)</td><td>In compliance with GIFAP Monograph No. 17.

pH (CIPAC Handbook J – MT 75.3 Method (2000))</td><td>Physical & Chemical properties:
<table>
<tr><th>Time</th><th>Aspect</th><th>Concentration (ppm)</th><th>Deviation with declared value (%)</th><th>Deviation between t_0 and t_{2year} (%)</th></tr>
<tr><td>T=0</td><td>Red block
Sweet odour.</td><td>40.6</td><td>-18.8</td><td>/</td></tr>
<tr><td>T = 2 years</td><td>Red block
Sweetish, slightly perceptible odour.</td><td>39.0</td><td>-22.0</td><td>-3.9</td></tr>
<tr><td colspan="5">The test item is considered to be stable after a storage period of 2 years at 20 ± 2°C.
The declared value was 50 ppm.</td></tr>
</table></td><td>Carried out to GLP. The test item is considered stable for 2 years at ambient temperatures.</td><td>“Chemical stability after storage at 20°C ± 2°C after 2 years of Difenacoum block baits 0.005%”.
Richerioux, Sandra.</td></tr>
</table>

Conclusion:

The packaging material is stable after accelerated storage (14 days at 54°C) with all deviations in packaging and sample weights being below 5%. The values for the cardboard box were slightly higher than the 5% criteria however (deviation of 12.65% for the cardboard box and -5.875% for the test item). There were no significant changes of characteristics of the test item or packaging observed. The Difenacoum block bait is considered compatible with all the packaging tested with the exception of the cardboard box. The appearance, the weight of the test item and the packaging material are considered to be stable after 2 years storage at ambient

temperatures. The deviation in the active substance content was much lower in both these studies at 6.4% (0.0003 mg/kg increase) and at -3.9% (0.0016 mg/kg decrease) than the one submitted in the PAR {17.5% decrease (0.0092 mg/kg decrease)}.

Based on the result above, the cardboard box packaging in contact with unwrapped bait blocks is considered incompatible as a packaging medium in direct contact with the difenacoum block bait. As such product should not be placed on the market under these conditions. However, it is acceptable to continue with the pack size using cardboard where the bait is contained in a inner PE bag, since the above data indicates this packaging situation is acceptable and meets the criteria for packing stability with the difenacoum block bait.

Table 3.1.3.2: Summary of the Physical and Chemical Properties of the Biocidal Product Grain bait

Section	Study	Method	Results	Comment	Reference
1.7.1a	Storage stability (Accelerated storage – 14 days at 54°C)	GIFAP Monograph No. 17 CIPAC MT 46	**HDPE Bottle:** Analysis at T0: Physical properties: Red whole wheat. Bottle: Red and non-porous internal wall. Bottle: 53.456g. Test item: 344.08g Total weight: 397.53g Analysis at T14: Physical properties: Red whole wheat. Bottle: Red and non-porous internal wall – presence of wheat dust. Bottle: 53.913g (0.85%) Test item: 343.53g (-0.16%) Total weight: 397.47g (-0.02%) **PE bag with cardboard box:** Analysis at T0: Physical properties: Red whole wheat. PE bag with cardboard box: Transparent bag – cardboard box with grey and dry internal wall. PE bag: 3.420g, 3.502g and 3.529g.	Carried out to GLP. Differences of packaging and sample weights after accelerated storage during 2 weeks at 54°C are lower than 5% for HDPE bottle, PP bag with cardboard box, PP bucket and Doypack. No significant changes of characteristics of test item or packaging were observed. For the PE bag with cardboard box, the mean deviation on the three studies is lower than 5% and no significant changes of characteristics of test item or packaging were observed. For the PP woven bag, the weight deviation between the initial time and after	"Packaging stability used for Difenacoum grain bait after accelerated storage". Richerioux, S. Report no.: LODI.56/2011. 2011-11-10.

Section	Study	Method	Results	Comment	Reference
			Cardboard box: 23.430g, 23.517g and 23.415g. Test item: 243.98g, 215.98g and 205.10g Total: 270.83g, 242.98g and 232.03g. <u>Analysis at T14:</u> Physical properties: Red whole wheat. PE bag with cardboard box: Transparent bag with presence of wheat dust – cardboard box with grey and dry internal wall. PE bag: 3.483g (1.84%), 3.554g (1.48%) and 3.593g (1.81%). Cardboard box: 23.092g (-1.44%), 22.579g (-3.99%), 23.571g (-3.60%). Test item: 230.92g (-5.35%), 206.73g (-4.28%), 195.51g (-4.68%) Total: 257.48g (-4.93%), 232.86g (-4.16%), 221.68g (-4.46%). **PP bag with cardboard box:** <u>Analysis at T0:</u> Physical properties: Red whole wheat. PP bag with cardboard box: Transparent bag - cardboard box with grey and dry internal wall. PP bag: 6.836g. Cardboard box: 23.530g. Test item: 210.15g. Total: 240.45g.	two weeks accelerated storage was over 5%. The study is acceptable.	

Section	Study	Method	Results	Comment	Reference
			Analysis at T14: Physical properties: Red whole wheat. PP bag with cardboard box: Transparent bag with presence of wheat dust - cardboard box with grey and dry internal wall. PP bag: 7.019g (2.68%). Cardboard box: 23.114g (-1.77%). Test item: 204.68g (-2.60%). Total: 234.80g (-2.35%). **PP bucket:** Analysis at T0: Physical properties: Red whole wheat. PP bucket: White and non-porous internal wall. PP bucket: 44.136g. Test item: 346.54g. Total: 390.68g. Analysis at T14: Physical properties: Red whole wheat. PP bucket: White and non-porous internal wall with presence of wheat dust. PP bucket: 44.587g (1.02%). Test item: 340.06g (-1.87%).		

Section	Study	Method	Results	Comment	Reference
			Total: 384.64g (-1.55%). **Doypack:** <u>Analysis at T0:</u> Physical properties: Red whole wheat. Doypack: Deformable bag with internal wall in aluminium, non-porous. Doypack: 11.709g Test item: 223.07g Total weight: 234.77g <u>Analysis at T14:</u> Physical properties: Red whole wheat. Doypack: Deformable bag with internal wall in aluminium, non-porous – presence of wheat dust. Doypack: 12.015g (2.61%) Test item: 222.99g (-0.04%) Total weight: 235.00g (0.098%) **PP bag:** <u>Analysis at T0:</u> Physical properties: Red whole wheat. PP bag: White woven bag.		

<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>PP bag: 4.967g.
Test item: 186.27g.
Total: 191.24g.

<u>Analysis at T14:</u>
Physical properties: Red whole wheat.
PP bag: White woven bag – presence of wheat dust.
PP bag: 5.664g (14.03%).
Test item: 173.79g (-6.70%).
Total: 179.47g (-6.15%).</td><td></td><td></td></tr>
<tr><td>1.7.2</td><td>Shelf life (storage ambient temperatures for two years)</td><td>In compliance with GIFAP Monograph No. 17.

pH (CIPAC Handbook J – MT 75.3 Method (2000))</td><td>Physical & Chemical properties:
<table>
<tr><th>Time</th><th>0</th><th>6 months</th><th>12 months</th><th>2 yrs</th></tr>
<tr><td>Appearance</td><td>Dark red seeds</td><td>Dark red seeds</td><td>Dark red seeds</td><td>Dark red seeds</td></tr>
<tr><td>Packaging</td><td>Transparent plastic bag</td><td>Transparent plastic bag</td><td>Transparent plastic bag</td><td>Transparent plastic bag</td></tr>
<tr><td rowspan="2">Packaging weight</td><td>Bag 12: 53.2g</td><td>52.4g (-1.5%)</td><td></td><td></td></tr>
<tr><td>Bag 13: 54.1</td><td></td><td>51.1</td><td></td></tr>
</table></td><td>Carried out to GLP. The test item is considered stable for 2 years at ambient temperatures.

The pH at T0 was not given.

The study is acceptable.</td><td>“Chemical stability and physico-chemical tests after a storage procedure for 2 years at 20 ± 2^{o}C on Difenacoum grain bait”.
Demangel, Benjamin. Report no.: 09-902018-002. 11th August 2011.</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>
<table>
<tr><td></td><td></td><td></td><td>(-3.7%)</td><td></td></tr>
<tr><td></td><td>Bags 14 & 15:
54.2g
53.7g</td><td></td><td></td><td>51.8g
51.3g
(-4.4% mean)</td></tr>
</table>
The appearance of the test item is considered to be stable after the storage procedure for 2 years at 20 ± 2°C, no significant change of weight was observed.
The packaging material is considered to be stable after the storage procedure for 2 years at 20 ± 2°C.

<table>
<tr><th>Time</th><th>0</th><th>6 months</th><th>12 months</th><th>2 yrs</th></tr>
<tr><td>Difenacoum content (% w/w)</td><td>0.0052</td><td>0.0043</td><td>0.0046</td><td>0.0044</td></tr>
<tr><td>Deviation from the declared value (%)
* deviation from T0 value (%)</td><td>+4.0</td><td>-17.3*</td><td>-11.5*</td><td>-15.4*</td></tr>
</table>
The test item is considered to be stable after a storage procedure for 2 years at 20 ± 2°C.
Note that the declared content was 0.005% w/w.
</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>
<table>
<tr><th>Time</th><th>2 yrs</th></tr>
<tr><td>pH at 1% w/v in standard water D
(at 21.4^{o}C and 21.5^{o}C respectively)</td><td>6.19 after 1 min
6.24 after 10 min</td></tr>
<tr><td colspan="2">The pH at T0 was not given.</td></tr>
</table>
</td><td></td><td></td></tr>
</table>

Conclusion:

The packaging material is stable after accelerated storage (14 days at 54^{o}C) with all deviations in packaging and sample weights being below 5%. For the PP woven bag, the weight deviation between the initial time and after two weeks accelerated storage was over 5% (deviation of 14.03% for the PP woven bag and -6.70% for the test item). The Difenacoum grain bait is considered compatible with all the packaging tested with the exception of the PP woven bag. There were no significant changes of characteristics of the test item or packaging observed. The appearance, the weight of the test item and the packaging material are considered to be stable after 2 years storage at ambient temperatures. The deviation in the active substance content was lower in this study at -15.4% (0.0008 mg/kg decrease) than the one submitted in the PAR {22% decrease (0.0106 mg/kg decrease)}.

Based on the result above, the PP woven bag packaging in contact with unwrapped grain bait is considered incompatible as a packaging medium in direct contact with the difenacoum block bait. As such product should not be placed on the market under these conditions. However, it is acceptable to continue with the pack size using a PP woven bag where the grain bait or PP woven bag is contained in an inner or outer PP bag, respectively, since the above data indicates that a PP airproof lining bag is acceptable and meets the criteria for packing stability with the difenacoum grain bait.

Table 3.1.3.3: Summary of the Physical and Chemical Properties of the Biocidal Product Paste/Pasta bait

Section	Study	Method	Results	Comment	Reference
1.7.1a	Storage stability (Accelerated storage – 14 days at 54°C)	GIFAP Monograph No. 17 CIPAC MT 46	**PP Bucket:** <u>Analysis at T0:</u> Physical properties: Red and greasy paste in individual sachet Bucket: White and non-porous internal wall. Bucket: 44.034g. Test item: 208.47g Total weight: 252.13g <u>Analysis at T14:</u> Physical properties: Red and greasy paste in individual sachet Bucket: White and non-porous internal wall with presence of grease. Bucket: 44.440g (0.92%) Test item: 207.69g (-0.37%) Total weight: 252.13g (-0.15%) **Doypack:** <u>Analysis at T0:</u> Physical properties: Red and greasy paste in individual sachet Doypack: Bag with internal wall in aluminium, non-porous. Doypack: 11.809g	Carried out to GLP. Differences of packaging and sample weights after accelerated storage during 2 weeks are lower than 5%. No significant changes of characteristics of test item or packaging were observed. The Difenacoum paste bait is considered compatible with all the packaging tested. The study is acceptable.	"Packaging stability used for Difenacoum paste bait after accelerated storage". Richerioux, S. Report no.: LODI.55-2011. 2011-11-10.

Section	Study	Method	Results	Comment	Reference
			Test item: 148.48g Total weight: 160.29g <u>Analysis at T14:</u> Physical properties: Red and greasy paste in individual sachet Doypack: Bag with internal wall in aluminium, non-porous with presence of grease. Doypack: 12.119g (2.63%) Test item: 148.37g (-0.07%) Total weight: 160.49g (0.12%) **PP prebaited baitbox:** <u>Analysis at T0:</u> Physical properties: Red and greasy paste in individual sachet. Prebaited baitbox: Black box with non-porous internal wall. Prebaited baitbox: 50.156g. Test item: 18.011g Total: 68.167g. <u>Analysis at T14:</u> Physical properties: Red and greasy paste in individual sachet. Prebaited baitbox: Black box with non-porous internal wall, presence of grease at the site of the paste.		

Section	Study	Method	Results	Comment	Reference
			Prebaited baitbox: 50.395g (0.48%). Test item: 17.766g (-1.36%) Total: 68.162g (-0.01%). **PS prebaited baitbox:** <u>Analysis at T0:</u> Physical properties: Red and greasy paste in individual sachet. Prebaited baitbox: Black box with non-porous internal wall. Prebaited baitbox: 12.205g. Test item: 19.330g Total: 31.534g. <u>Analysis at T14:</u> Physical properties: Red and greasy paste in individual sachet. Prebaited baitbox: Black box with non-porous internal wall – presence of grease at the site of the paste. Prebaited baitbox: 12.471g (2.18%). Test item: 18.561g (-3.98%). Total: 31.032g (-1.59%). **PE bag with cardboard box:** <u>Analysis at T0:</u>		

Section	Study	Method	Results	Comment	Reference
			Physical properties: Red and greasy paste in individual sachet. PE bag with cardboard box: Transparent bag - cardboard box with grey and dry internal wall. PE bag: 3.420g. Cardboard box: 23.568g Test item: 136.64g. Total: 163.63 g. <u>Analysis at T14:</u> Physical properties: Red and greasy paste in individual sachet. PE bag with cardboard box: Transparent bag with presence of grease-cardboard box with grey and dry internal wall. PE bag: 3.547g (3.71%). Cardboard box: 22.924g (-2.73%) Test item: 130.14g (-4.76%). Total: 156.61 (-4.29%) **PP bag with cardboard box:** <u>Analysis at T0:</u> Physical properties: Red and greasy paste in individual sachet. PP bag with cardboard box: Transparent bag - cardboard box with grey and dry internal wall. PE bag: 6.923g.		

Section	Study	Method	Results	Comment	Reference
			Cardboard box: 23.509g. Test item: 140.78g. Total: 171.21g. <u>Analysis at T14:</u> Physical properties: Red and greasy paste in individual sachet. PP bag with cardboard box: Transparent bag - cardboard box with grey and dry internal wall. PE bag: 7.074g (2.18%). Cardboard box: 22.954g (-2.36%). Test item: 135.36g (-3.85%). Total: 165.38g (-3.41%). **PE bag:** <u>Analysis at T0:</u> Physical properties: Red and greasy paste in individual sachet. PE bag: Transparent bag. PE bag: 3.410g. Test item: 137.42g. Total: 140.84g. <u>Analysis at T14:</u>		

Section	Study	Method	Results	Comment	Reference
			Physical properties: Red and greasy paste in individual sachet. PE bag: Transparent bag with presence of grease. PE bag: 3.556g (4.28%). Test item: 131.03g (-4.65%). Total: 134.59g (-4.44%). **PP bag:** <u>Analysis at T0:</u> Physical properties: Red and greasy paste in individual sachet. PP bag: Transparent bag. PP bag: 6.916g. Test item: 134.70g. Total: 141.62g. <u>Analysis at T14:</u> Physical properties: Red and greasy paste in individual sachet. PP bag: Transparent bag with presence of grease. PP bag: 7.239g (4.67%). Test item: 129.59g (-3.79%). Total: 136.83g (-3.38%). **Coextruded bag:**		

Section	Study	Method	Results	Comment	Reference
			Analysis at T0: Physical properties: Red and greasy paste in individual sachet. Coextruded bag: Transparent bag (with print on external wall). Coextruded bag: 5.556g. Test item: 97.464g. Total: 103.03g. Analysis at T14: Physical properties: Red and greasy paste in individual sachet. Coextruded bag: Transparent bag with presence of grease. Coextruded bag: 5.799g (4.37%). Test item: 96.343g (-1.15%). Total: 102.14g (-0.86%). **PE bag with cardboard box:** Analysis at T0: Physical properties: Red and greasy paste. PE bag with cardboard box: Transparent bag – cardboard box with grey and dry internal wall. PE bag + test item: 233.202g. Cardboard box: 23.393g. Total: 256.59g.		

Section	Study	Method	Results	Comment	Reference
			Analysis at T14: Physical properties: Red and greasy paste. PE bag with cardboard box: Transparent bag with presence of paste – cardboard box with grey and dry internal wall. PE bag + test item: 226.59g (-2.83%). Cardboard box: 23.021g (-1.59%). Total: 249.61g (-2.72%). **PP bucket as cartridge:** Analysis at T0: Physical properties: Red and greasy paste. PP bucket: White and non-porous internal wall. PP bucket: 44.086g. Test item: 376.08g. Total: 420.17g. Analysis at T14: Physical properties: Red and greasy paste. PP bucket: White and non-porous internal wall with presence of paste and grease. PP bucket: 44.533g (1.01%). Test item: 373.74g (-0.62%).		

<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>Total: 418.33g (-0.44%).</td><td></td><td></td></tr>
<tr><td>1.7.2</td><td>Shelf life (storage ambient temperatures for two years)</td><td>In compliance with GIFAP Monograph No. 17.

pH (CIPAC Handbook J – MT 75.3 Method (2000))</td><td>Physical & Chemical properties:
<table>
<tr><th>Time</th><th>0</th><th>6 months</th><th>12 months</th><th>2 yrs</th></tr>
<tr><td>Appearance</td><td>Pink paste</td><td>Pink paste</td><td>Pink paste</td><td>Pink paste</td></tr>
<tr><td>Packaging</td><td>White opaque plastic box with transparent paper bag containing the paste</td><td>White opaque plastic box with transparent paper bag containing the paste</td><td>White opaque plastic box with transparent paper bag containing the paste</td><td>White opaque plastic box with transparent paper bag containing the paste</td></tr>
<tr><td>Packaging weight</td><td>371.5g</td><td>370.9g (-0.16%)
309.9g after sampling</td><td>308.8g (-0.35%)
252.1g after sampling</td><td>251.1g (-0.40%)</td></tr>
<tr><td colspan="5">The appearance of the test item is considered to be stable after the storage procedure for 2 years at 20 ± 2°C, no significant change of weight was observed.
The packaging material is considered to be stable after the storage</td></tr>
</table></td><td>Carried out to GLP. The test item is considered stable for 2 years at ambient temperatures.

The pH at T0 was not given.

The study is acceptable.</td><td>“Chemical stability and physico-chemical tests after a storage procedure for 2 years at 20 ± 2°C on Difenacoum Pasta Bait”. Demangel, Benjamin. Report no.: 09-902018-006. 11th August 2011.</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>
procedure for 2 years at 20 ± 2°C.

<table>
<tr><th>Time</th><th>0</th><th>6 months</th><th>12 months</th><th>2 yrs</th></tr>
<tr><td>Difenacoum content (% w/w).</td><td>0.0052</td><td>0.0048</td><td>0.0052</td><td>0.0047</td></tr>
<tr><td>Deviation from the declared value (%)
* deviation from T0 value</td><td>+4.0</td><td>-7.7*</td><td>0*</td><td>-9.6*</td></tr>
<tr><td colspan="5">No significant change was observed in the content after the storage procedure for 2 years at 20 ± 2°C.
Note that the declared content was 0.005% w/w.</td></tr>
</table>

<table>
<tr><th>Time</th><th>2 yrs</th></tr>
<tr><td>pH at 1% w/v in standard water D (at 22°C)</td><td>5.82 after 1 min
5.91 after 10 min</td></tr>
<tr><td colspan="2">The pH at T0 was not given.</td></tr>
</table>
</td><td></td><td></td></tr>
</table>

Conclusion:

The packaging material is stable after accelerated storage (14 days at 54°C) with all deviations in packaging and sample weights being below 5%. There were no significant changes of characteristics of the test item or packaging observed. The Difenacoum paste bait is considered compatible with all the packaging tested. The

appearance, the weight of the test item and the packaging material are considered to be stable after 2 years storage at ambient temperatures. The deviation in the active substance content in this study was higher at -9.6% (0.0005 mg/kg decrease) than the one submitted in the PAR {0.19% decrease (0.0001 mg/kg decrease)}.

Expert opinions:

Author	Date	Problem	Expert opinion	Conclusion
Dr. Suren Husinec, University of Belgrade, Institute of Chemistry, Technology and Metallurgy, Department of Chemistry. E-mail: depchem@chem.bg.ac.yu Scientific Councillor of the Institute, expert in the field of synthesis, analysis and formulations of biocides. Signed off by: Dr. Vlatka Vajs (Director)	15th December 2011.	Significant decrease in active substance content of between 17.5 and 21% in the block and grain baits in the study report of the stability of Difenacoum baits after storage at ambient temperatures.	The grain formulation of Difenacoum bait presents a heterogeneous mixture of grain, flavouring, attractant, dye and a solution of the active ingredient. Due to the anatomy of the wheat grain the fruit coat and the grain are united and cannot be separated while grain is not too old. The outer coat of the grain is made up of several layers and they protect the main, nutritious part of the grain. Over the time protective layers tend to crack thus enabling molecules from the formulation to penetrate deep into the grain itself. The analytical method used for the determination of Difenacoum active ingredient consists in the first stage to extract Difenacoum from the formulation. Difenacoum on itself has a very poor solubility in organic solvents and the usually present an obstacle in quantitative determination. On the other side incorporation of molecules of Difenacoum into cracks of the protective layer of the grain makes molecules almost being binded to the matrix thus making their extraction almost impossible. With block formulation the situation is slightly different. A large proportion in mass of the block is paraffin which acts almost as a solvent of molecules of Difenacoum. Over the time intermolecular bonds between the molecule of Difenacoum which in large proportion is made up of aromatic hydrocarbon blocks and components of paraffin,	RMS accepts the expert opinion.

<table>
<tr><th>Author</th><th>Date</th><th>Problem</th><th>Expert opinion</th><th>Conclusion</th></tr>
<tr><td></td><td></td><td></td><td>hydrocarbons become stronger. As a result, as in previous case, extracting Difenacoum from paraffin formulation over the time is becoming more and more difficult.

In both cases, grain formulation and block formulation over the time give lower results in concentration of Difencoaum but field studies do not show the decrease in efficacy – this is a clear indication that the concentration of the active ingredient does not change although looking only at analytical results it does not seem so.

In both cases analytical results after two years are within the tolerance limit, almost at the edge in case of grain but still within the limit.</td><td></td></tr>
<tr><td>Dr.ir O. Pigeon,
FAO/WHO JMPS Member.</td><td>December 14th 2011.</td><td>Tolerances of content of active substance.</td><td>The tolerances for formulated products refer to the average result obtained and take into account of manufacturing, sampling and analytical variations; lower is the content of active substance and higher are these variations.

The tolerances proposed in the general FAO/WHO specifications are the following:
<table><tr><th>Declared content in g/kg or g/l at 20°C ± 2°C</th><th>Tolerance</th></tr><tr><td>Up to 25</td><td>± 15% of the declared content for</td></tr></table></td><td>RMS accepts the expert opinion.</td></tr>
</table>

<table>
<tr><th>Author</th><th>Date</th><th>Problem</th><th>Expert opinion</th><th>Conclusion</th></tr>
<tr><td></td><td></td><td></td><td>
<table>
<tr><td></td><td>“homogeneous” formulations (EC, SL etc)
or
± 25% of the declared content for “heterogeneous” formulations (GR, WG etc)</td></tr>
<tr><td>Above 25 up to 100</td><td>± 10% of the declared content</td></tr>
<tr><td>Above 100 up to 250</td><td>± 6% of the declared content</td></tr>
<tr><td>Above 250 up to 500</td><td>± 5% of the declared content</td></tr>
<tr><td>Above 500</td><td>± 25 g/kg or g/l</td></tr>
<tr><td colspan="2">Note: In each range the upper limit is included</td></tr>
</table>

We can consider that the formulated products as block bait (BB), granular bait (GB), ...are heterogeneous formulations and that the tolerance of ± 25% can be applied for this kind of product containing <25 g/kg active substance.</td><td></td></tr>
<tr><td>Dr. Romain Lasseur,
Fundamental and Applied Toxicology (PhD),
Habilitation in Research</td><td>4th January 2012</td><td>Statement regarding the difficulties to extract Difenacoum from wheat used as rodenticides bait.</td><td>Wheat is an important food source for commercial rodent as rats (Rattus sp) and mice (Mus sp). It enters as a major component in their daily intake. This is the main reason explain rodent living around farms, cereals storage or around cereal processing industry. As a consequence, wheat based bait is palatable for rodent as it contain wheat in the</td><td>RMS accepts the expert opinion.</td></tr>
</table>

Author	Date	Problem	Expert opinion	Conclusion
Project Management (HDR), Toxinnov. 8 Rue d'Aquitaine 69210 BULLY. Email: lasseur@free.fr Anticoagulant toxicity, Anticoagulant resistance, Rodent field management Expert.			formulation. Wheat bait mixed with anticoagulant used as rodenticides is excellent bait as it contains only the added anticoagulant to the formulation, know not to affect palatability of wheat in rodent. Difenacoum is a high effective anticoagulant widely used in rodent control in the field as in house. Efficacy was proved in different rodent as rats (*Rattus* sp) and mice (*Mus* sp). Difenacoum active ingredient is formulated in different type of bait (blocks, soft bait, grain...). This active ingredient is known, regarding bibliography, to have a slow degradation rate in different matrix, as the soil, in formulation bait or in live organisms. Focused on bait based products, Difenacoum is known to degrade slowly and this degradation is not as function as bait type containing Difenacoum (blocks, soft bait or grain). Moreover, it is well known that, regarding analytical methods, extraction efficacy of anticoagulant from bait is different from a formulation to another. Extraction efficacy of anticoagulant from block bait is better than extraction efficacy from grain bait and in particular from wheat bait based. Due to possible irreversible migration (and not degradation) of active ingredient (Difenacoum) inside the wheat grain, extraction process not allows to recover the entire Difenacoum dose injected in the initial	

Author	Date	Problem	Expert opinion	Conclusion
			formulation. This problem is observed with a minor importance in other bait than grain bait (wheat bait) due to usuage of wheat flour instead of wheat. Moreover, it is ask to wheat based bait containing Difenacoum to respect 5% variation index after 2 years storage. 5% corresponds to variability index of the analytical method cited as the reference (HPLC/UV detector). To conclude, it seems, to answer this technical problem of difficulty and variation of extraction index of Difenacoum from wheat based bait, WHO guidelines have to be considered as the reference where it indicates that a tolerance of a maximum of 25% of variability in active ingredient can be acceptable. In parallel, what is important for the end-user of the wheat based bait containing Difenacoum, is that bait work effectively as rodenticides after 2 years storage (maximum delay between industrial production and usage of the bait by end-user). In case of difficulty of active ingredient extraction from wheat bait, such studies (bait fresh produced and bait after 2 years storage) have to be conducted to show similarity in term of efficacy in targeted rodent.	

Overall conclusion:

The Irish CA considers that the storage stability information provided in the PAR and in this Addendum, supports a shelf life for the block bait, grain bait and paste bait of two years (24 months), based on the efficacy of the products being maintained over a two year period and the nominal content of active substance (0.05 g/kg) remaining within the FAO requirement of ± 25% specified limits. The product was 90-100% efficacious when stored for 24 months. In the interests of animal welfare the Irish CA does not believe further efficacy testing is necessary on these products.

The packaging material is stable after accelerated storage (14 days at 54^{o}C) with all deviations in packaging and sample weights being below 5% with the exceptions of the cardboard box for the block bait and the PP woven bag for the grain bait which had deviations above 5%. There were no significant changes of characteristics of the test item or packaging observed. The Difenacoum block, grain and paste baits are considered compatible with all the packaging tested (with the exceptions noted above).

The appearance, the weight of the test item and the packaging material are considered to be stable after 2 years storage at ambient temperatures. The deviation in the active substance content for the block bait was much lower in the new studies provided, at 6.4% (0.0003 mg/kg increase) and -3.9% (0.0016 mg/kg decrease) than the one submitted in the PAR {17.5% decrease (0.0092 mg/kg decrease)}. The deviation in the active substance content for the grain bait was lower in the new study at -15.4% (0.0008 mg/kg decrease) than the one submitted in the PAR {22% decrease (0.0106 mg/kg decrease)}. The deviation in the active substance content for the paste bait in the new study was higher at -9.6% (0.0005 mg/kg decrease) than the one submitted in the PAR {0.19% decrease (0.0001 mg/kg decrease)}.

The expert opinions provided support the theory that Difenacoum does not degrade over time but becomes bound to the grain and therefore becomes harder to extract.

Shelf life:

2-year shelf life proposed for Difenacoum block bait, grain bait and paste/pasta bait.

Addendum to PAR - April 2012

Addendum

to the Product Assessment Report

Ruby block (IE/BPA 70025; IE/BPA 70002), Probloc (IE/BPA 70037; IE/BPA 70098)
Ruby grain (IE/BPA 70027; IE/BPA 70003), Raco (IE/BPA 70036; IE/BPA 70097)
Ruby paste (IE/BPA 70033; IE/BPA 70004), Nora pasta (IE/BPA 70038; IE/BPA 70099)

Active substance:	**Difenacoum**
Product-type:	**PT14: Rodenticides**
Type of application:	**Authorisation**
Authorisation No:	**See above.**
Date:	**02 April 2012**

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

Department of Agriculture, Food and the Marine
An Roinn Talmhaíochta, Bia agus Mara

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

Background:

The applicant was asked to address the concern that the active ingredient content appears to decrease over storage time in the block bait and grain bait formulations. The block formation when analysed at manufacture contained 52.7 mg/kg (0.0527 g/kg) of active ingredient but at 24 months the active ingredient content was 43.5 mg/kg (0.0435 g/kg), representing a 17.5% decrease {Study report: Stability of Difenacoum baits after a storage at ambient temperature. Biannic, Marie-Laure. 12th November 2009}. The grain formation when analysed at manufacture contained 48.8 mg/kg (0.0488 g/kg) of active ingredient but at 24 months the active ingredient content was 38.2 mg/kg (0.0382 g/kg), representing a 22% decrease {Biannic, Marie-Laure. LODI-Group. 12th November 2009}.

The applicant has stated that for heterogeneous formulations the active substance content can vary by ± 25% when the declared content of active substance is up to 25 g/kg. The active substance concentration for both the block and grain bait is within the ± 25% specification which is in compliance with the FAO's requirement (50 mg/kg ± 25%, therefore between 37.5 – 62.5 mg/kg). The paste bait shows no sign of degradation over the two year period.

Efficacy data presented in the PAR show that the block and grain formulations are effective following storage for up to 24 months.

Block bait: After a 9-day treatment phase with a 2-year aged bait an efficacy specification approaching 90% was achieved (for mice). 22 brown rats were used in a study, with a short poisoning period using fresh and aged (6 month old) baits. 95% control was achieved with the fresh bait and 100% with the aged bait with the sole surviving female having consumed very low levels of the block bait. In the next test 22 rats were used in a study on fresh and 12-month aged blocks. 90% control was achieved with the fresh bait and total control achieved with the aged bait. A rat infested restaurant (~81 rats) was chosen for the next study. Aged bait (2 year old) was used resulting in 89.1% control after a short 5-day baiting period. The block bait formulation proved to be highly palatable and effective against both rats and mice in the tests. Both fresh and aged baits (6, 12 and 24 months after manufacture) provided 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.

Grain bait: A private dwelling house with a mouse infestation estimated at approximately 100 individuals was used for a study in which 2-year old bait was used. 98% efficacy was achieved after what could be considered a relatively short baiting and post-baiting monitoring period. An aviary for wildfowl breeding was chosen for a study on the control of brown rats with aged bait (2 years). The report confirmed that the farm contained a plentiful supply of food and water with nearby harbourage for the rats. Population tracking estimated that there were ~124 rats onsite. A 98% reduction in consumption levels/efficacy was achieved after a 13 day baiting phase. The grain 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) also provided 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.

This information suggests that the observed reduction in Difenacoum content is due to factors other than active substance degradation since Difenacoum must remain in the bait in order for the observed level of mortality.

Below is further information supplied by the Notifier to address the storage stability issues with respect to the block and grain baits (Tables 3.1.3.1 and 3.1.3.2). Paste bait information was also provided and was evaluated below (Table 3.1.3.3).

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

Table 3.1.3.1: Summary of the Physical and Chemical Properties of the Biocidal Product Block Bait

Section	Study	Method	Results	Comment	Reference
1.7.1a	Storage stability (Accelerated storage – 14 days at 54°C)	GIFAP Monograph No. 17 CIPAC MT 46	**Cardboard box:** Analysis at T0: Physical properties: Red block. Cardboard box: Grey with dry internal walls. Cardboard box: 23.462g. Test item: 185.70g Total weight: 209.16g Analysis at T14: Physical properties: Red block – colour more intense than t=0. Cardboard box: Presence of grease on internal and external walls. Cardboard box: 26.429g (12.65%) Test item: 174.80g (-5.875) Total weight: 201.22g (-3.80%) **PE bag with cardboard box:** Analysis at T0: Physical properties: Red block. PE bag with cardboard box: Transparent bag – cardboard box with grey with dry internal wall.	Carried out to GLP. For cardboard box, deviation in weights after accelerated storage is higher than 5%. For all other packaging, deviation of packaging and sample weights after accelerated storage for 2 weeks at 54°C are lower than 5%. No significant changes of characteristics of test item or packaging were observed. The study is acceptable.	"Packing stability used for Difenacoum block bait after accelerated storage". Richerioux, S. Report no.: LODI.57/2011. 2011-11-10.

Section	Study	Method	Results	Comment	Reference
			PE bag: 3.415g Cardboard box: 23.464g Test item: 182.75g Total weight: 209.63g <u>Analysis at T14:</u> Physical properties: Red block – colour more intense than t=0. PE bag with cardboard box: Transparent bag with presence of block dust – cardboard box with grey with dry internal wall. PE bag: 3.472g (1.67%) Cardboard box: 23.414g (-0.21%) Test item: 175.99g (-3.70%) Total weight: 202.89g (-3.22%) **PP Bucket:** <u>Analysis at T0:</u> Physical properties: Red block. PP bucket: white and non-porous internal wall. PP bucket: 44.121g. Test item: 365.34g Total weight: 409.46g <u>Analysis at T14:</u>		

Section	Study	Method	Results	Comment	Reference
			Physical properties: Red block – colour more intense than t=0. PP bucket: white and non-porous internal wall – presence of dust block. PP bucket: 44.457g (0.76%). Test item: 362.34g (-0.82%) Total weight: 406.80g (-0.65%) **PP prebaited baitbox:** <u>Analysis at T0:</u> Physical properties: Red block. Prebaited baitbox: Black box with non-porous internal wall. Prebaited baitbox: 47.483g. Test item: 31.012g Total: 78.495g. <u>Analysis at T14:</u> Physical properties: Red block – colour more intense than t=0. Prebaited baitbox: Black box with non-porous internal wall – presence of block dust at the site of the block. Prebaited baitbox: 47.756g (0.57%). Test item: 29.600g (-4.55%). Total: 77.354g (-1.45%). **PS prebaited baitbox:**		

Section	Study	Method	Results	Comment	Reference
			Analysis at T0: Physical properties: Red block. Prebaited baitbox: Black box with non-porous internal wall. Prebaited baitbox: 12.525g. Test item: 29.894g. Total: 42.419g. Analysis at T14: Physical properties: Red block – colour more intense than t=0. Prebaited baitbox: Black box with non-porous internal wall – presence of block dust at the site of the block. Prebaited baitbox: 12.784g (2.07%). Test item: 28.779g (-3.73%). Total: 41.563g (-2.02%) **Cardboard prebaited baitbox:** Analysis at T0: Physical properties: Red block. Prebaited baitbox: Dry cardboard. Prebaited baitbox: 18.765g. Test item: 30.672g. Total: 49.737g.		

<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><u>Analysis at T14:</u>
Physical properties: Red block – colour more intense than t=0.
Prebaited baitbox: Presence of a ring at the site of the block.
Prebaited baitbox: 18.860g (0.51%).
Test item: 29.635g (-3.38%).
Total: 48.499g (-1.90%)</td><td></td><td></td></tr>
<tr><td>1.7.2a</td><td>Shelf life (storage ambient temperatures for two years)</td><td>In compliance with GIFAP Monograph No. 17.

pH (CIPAC Handbook J – MT 75.3 Method (2000))</td><td>Physical & Chemical properties:
<table>
<tr><th>Time</th><th>0</th><th>6 months</th><th>12 months</th><th>2 yrs</th></tr>
<tr><td>Appearance</td><td>Bright pink block</td><td>Bright pink block</td><td>Bright pink block</td><td>Bright pink block</td></tr>
<tr><td>Packaging</td><td>White opaque plastic box with red opaque plastic cover</td><td>White opaque plastic box with red opaque plastic cover</td><td>White opaque plastic box with red opaque plastic cover</td><td>White opaque plastic box with red opaque plastic cover</td></tr>
<tr><td>Packaging weight</td><td>756g</td><td>754.5g (-0.20%)
692.8g after sampling</td><td>690.0 (-0.40%)
628.5g after sampling</td><td>625.4g (-0.49%)</td></tr>
<tr><td colspan="5">The appearance of the test item is considered to be stable after the storage procedure for 2 years at 20 ± 2°C, no significant change of weight was observed.</td></tr>
</table></td><td>Carried out to GLP. The test item is considered stable for 2 years at ambient temperatures.

The pH at T0 was not given.

The study is acceptable.</td><td>“Chemical stability and physico-chemical tests after a storage procedure for 2 years at 20 ± 2°C on Difenacoum Block Bait”. Demangel, Benjamin. Report no.: 09-902018-004.</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>
The packaging material is considered to be stable after the storage procedure for 2 years at 20 ± 2°C.

<table>
<tr><th>Time</th><th>0</th><th>6 months</th><th>12 months</th><th>2 yrs</th></tr>
<tr><td>Difenacoum content (% w/w)</td><td>0.0047</td><td>0.0048</td><td>0.0049</td><td>0.0050</td></tr>
<tr><td>Deviation from the declared value (%)
* deviation from T0 value (%)</td><td>-6.0</td><td>+2.1</td><td>+4.3</td><td>+6.4*</td></tr>
</table>
The test item is considered to be stable after a storage procedure for 2 years at 20 ± 2°C.

Note that the declared content was 0.005% w/w.

<table>
<tr><th>Time</th><th>2 yrs</th></tr>
<tr><td>pH at 1% w/v in standard water D
(at 21.7°C and 21.8°C respectively)</td><td>5.89 after 1 min
6.00 after 10 min</td></tr>
</table>
The pH at T0 was not given.
</td><td></td><td></td></tr>
<tr><td>1.7.2b</td><td>Shelf life (storage ambient temperatures for</td><td>In compliance with GIFAP Monograph</td><td>
Physical & Chemical properties:
<table>
<tr><th>Time</th><th>Aspect</th><th>Concentration</th><th>Deviation</th><th>Deviation</th></tr>
</table>
</td><td>Carried out to GLP. The test item is considered stable for 2 years at</td><td>“Chemical stability after storage at 20°C ± 2°C after 2 years of</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>two years)</td>
<td>No. 17.

pH (CIPAC Handbook J – MT 75.3 Method (2000))</td>
<td>
<table>
<tr><th></th><th></th><th>(ppm)</th><th>with declared value (%)</th><th>between t_0 and t_{2year} (%)</th></tr>
<tr><td>T=0</td><td>Red block
Sweet odour.</td><td>40.6</td><td>-18.8</td><td>/</td></tr>
<tr><td>T = 2 years</td><td>Red block
Sweetish, slightly perceptible odour.</td><td>39.0</td><td>-22.0</td><td>-3.9</td></tr>
<tr><td colspan="5">The test item is considered to be stable after a storage period of 2 years at 20 ± 2°C.
The declared value was 50 ppm.</td></tr>
</table>
</td>
<td>ambient temperatures.</td>
<td>Difenacoum block baits 0.005%”.
Richerioux, Sandra.</td>
</tr>
</table>

Conclusion:

The packaging material is stable after accelerated storage (14 days at 54°C) with all deviations in packaging and sample weights being below 5%. The values for the cardboard box were slightly higher than the 5% criteria however (deviation of 12.65% for the cardboard box and -5.875% for the test item). There were no significant changes of characteristics of the test item or packaging observed. The Difenacoum block bait is considered compatible with all the packaging tested with the exception of the cardboard box. The appearance, the weight of the test item and the packaging material are considered to be stable after 2 years storage at ambient temperatures. The deviation in the active substance content was much lower in both these studies at 6.4% (0.0003 mg/kg increase) and at -3.9% (0.0016 mg/kg decrease) than the one submitted in the PAR {17.5% decrease (0.0092 mg/kg decrease)}.

Based on the result above, the cardboard box packaging in contact with unwrapped bait blocks is considered incompatible as a packaging medium in direct contact with the difenacoum block bait. As such product should not be placed on the market under these conditions. However, it is acceptable to continue with the pack size using cardboard

where the bait is contained in a inner PE bag, since the above data indicates this packaging situation is acceptable and meets the criteria for packing stability with the difenacoum block bait.

Table 3.1.3.2: Summary of the Physical and Chemical Properties of the Biocidal Product Grain bait

Section	Study	Method	Results	Comment	Reference
1.7.1a	Storage stability (Accelerated storage – 14 days at 54°C)	GIFAP Monograph No. 17 CIPAC MT 46	**HDPE Bottle:** Analysis at T0: Physical properties: Red whole wheat. Bottle: Red and non-porous internal wall. Bottle: 53.456g. Test item: 344.08g Total weight: 397.53g Analysis at T14: Physical properties: Red whole wheat. Bottle: Red and non-porous internal wall – presence of wheat dust. Bottle: 53.913g (0.85%) Test item: 343.53g (-0.16%) Total weight: 397.47g (-0.02%) **PE bag with cardboard box:** Analysis at T0: Physical properties: Red whole wheat. PE bag with cardboard box: Transparent bag – cardboard box with grey and dry internal wall. PE bag: 3.420g, 3.502g and 3.529g. Cardboard box: 23.430g, 23.517g and 23.415g.	Carried out to GLP. Differences of packaging and sample weights after accelerated storage during 2 weeks at 54°C are lower than 5% for HDPE bottle, PP bag with cardboard box, PP bucket and Doypack. No significant changes of characteristics of test item or packaging were observed. For the PE bag with cardboard box, the mean deviation on the three studies is lower than 5% and no significant changes of characteristics of test item or packaging were observed. For the PP woven bag, the weight deviation between the initial time and after	"Packaging stability used for Difenacoum grain bait after accelerated storage". Richerioux, S. Report no.: LODI.56/2011. 2011-11-10.

Section	Study	Method	Results	Comment	Reference
			Test item: 243.98g, 215.98g and 205.10g Total: 270.83g, 242.98g and 232.03g. <u>Analysis at T14:</u> Physical properties: Red whole wheat. PE bag with cardboard box: Transparent bag with presence of wheat dust – cardboard box with grey and dry internal wall. PE bag: 3.483g (1.84%), 3.554g (1.48%) and 3.593g (1.81%). Cardboard box: 23.092g (-1.44%), 22.579g (-3.99%), 23.571g (-3.60%). Test item: 230.92g (-5.35%), 206.73g (-4.28%), 195.51g (-4.68%) Total: 257.48g (-4.93%), 232.86g (-4.16%), 221.68g (-4.46%). **PP bag with cardboard box:** <u>Analysis at T0:</u> Physical properties: Red whole wheat. PP bag with cardboard box: Transparent bag - cardboard box with grey and dry internal wall. PP bag: 6.836g. Cardboard box: 23.530g. Test item: 210.15g. Total: 240.45g. <u>Analysis at T14:</u>	two weeks accelerated storage was over 5%. The study is acceptable.	

Section	Study	Method	Results	Comment	Reference
			Physical properties: Red whole wheat. PP bag with cardboard box: Transparent bag with presence of wheat dust - cardboard box with grey and dry internal wall. PP bag: 7.019g (2.68%). Cardboard box: 23.114g (-1.77%). Test item: 204.68g (-2.60%). Total: 234.80g (-2.35%). **PP bucket:** <u>Analysis at T0:</u> Physical properties: Red whole wheat. PP bucket: White and non-porous internal wall. PP bucket: 44.136g. Test item: 346.54g. Total: 390.68g. <u>Analysis at T14:</u> Physical properties: Red whole wheat. PP bucket: White and non-porous internal wall with presence of wheat dust. PP bucket: 44.587g (1.02%). Test item: 340.06g (-1.87%). Total: 384.64g (-1.55%).		

Section	Study	Method	Results	Comment	Reference
			Doypack: Analysis at T0: Physical properties: Red whole wheat. Doypack: Deformable bag with internal wall in aluminium, non-porous. Doypack: 11.709g Test item: 223.07g Total weight: 234.77g Analysis at T14: Physical properties: Red whole wheat. Doypack: Deformable bag with internal wall in aluminium, non-porous – presence of wheat dust. Doypack: 12.015g (2.61%) Test item: 222.99g (-0.04%) Total weight: 235.00g (0.098%) **PP bag:** Analysis at T0: Physical properties: Red whole wheat. PP bag: White woven bag. PP bag: 4.967g. Test item: 186.27g.		

<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>Total: 191.24g.

<u>Analysis at T14:</u>
Physical properties: Red whole wheat.
PP bag: White woven bag – presence of wheat dust.
PP bag: 5.664g (14.03%).
Test item: 173.79g (-6.70%).
Total: 179.47g (-6.15%).</td><td></td><td></td></tr>
<tr><td>1.7.2</td><td>Shelf life (storage ambient temperatures for two years)</td><td>In compliance with GIFAP Monograph No. 17.

pH (CIPAC Handbook J – MT 75.3 Method (2000))</td><td>Physical & Chemical properties:
<table>
<tr><th>Time</th><th>0</th><th>6 months</th><th>12 months</th><th>2 yrs</th></tr>
<tr><td>Appearance</td><td>Dark red seeds</td><td>Dark red seeds</td><td>Dark red seeds</td><td>Dark red seeds</td></tr>
<tr><td>Packaging</td><td>Transparent plastic bag</td><td>Transparent plastic bag</td><td>Transparent plastic bag</td><td>Transparent plastic bag</td></tr>
<tr><td rowspan="3">Packaging weight</td><td>Bag 12: 53.2g</td><td>52.4g (-1.5%)</td><td></td><td></td></tr>
<tr><td>Bag 13: 54.1</td><td></td><td>51.1 (-3.7%)</td><td></td></tr>
<tr><td>Bags 14 & 15:</td><td></td><td></td><td>51.8g
51.3g</td></tr>
</table></td><td>Carried out to GLP. The test item is considered stable for 2 years at ambient temperatures.

The pH at T0 was not given.

The study is acceptable.</td><td>“Chemical stability and physico-chemical tests after a storage procedure for 2 years at 20 ± 2^{o}C on Difenacoum grain bait”.
Demangel, Benjamin. Report no.: 09-902018-002. 11th August 2011.</td></tr>
</table>

Section	Study	Method	Results	Comment	Reference

	54.2g 53.7g			(-4.4% mean)

The appearance of the test item is considered to be stable after the storage procedure for 2 years at 20 ± 2°C, no significant change of weight was observed.

The packaging material is considered to be stable after the storage procedure for 2 years at 20 ± 2°C.

Time	**0**	**6 months**	**12 months**	**2 yrs**
Difenacoum content (% w/w)	0.0052	0.0043	0.0046	0.0044
Deviation from the declared value (%) * deviation from T0 value (%)	+4.0	-17.3*	-11.5*	-15.4*

The test item is considered to be stable after a storage procedure for 2 years at 20 ± 2°C.

Note that the declared content was 0.005% w/w.

Time	**2 yrs**
pH at 1% w/v in standard water D	6.19 after 1 min

Section	Study	Method	Results	Comment	Reference
			(at 21.4°C and 21.5°C respectively) 6.24 after 10 min The pH at T0 was not given.		

Conclusion:

The packaging material is stable after accelerated storage (14 days at 54°C) with all deviations in packaging and sample weights being below 5%. For the PP woven bag, the weight deviation between the initial time and after two weeks accelerated storage was over 5% (deviation of 14.03% for the PP woven bag and -6.70% for the test item). The Difenacoum grain bait is considered compatible with all the packaging tested with the exception of the PP woven bag. There were no significant changes of characteristics of the test item or packaging observed. The appearance, the weight of the test item and the packaging material are considered to be stable after 2 years storage at ambient temperatures. The deviation in the active substance content was lower in this study at -15.4% (0.0008 mg/kg decrease) than the one submitted in the PAR {22% decrease (0.0106 mg/kg decrease)}.

Based on the result above, the PP woven bag packaging in contact with unwrapped grain bait is considered incompatible as a packaging medium in direct contact with the difenacoum block bait. As such product should not be placed on the market under these conditions. However, it is acceptable to continue with the pack size using a PP woven bag where the grain bait or PP woven bag is contained in an inner or outer PP bag, respectively, since the above data indicates that a PP airproof lining bag is acceptable and meets the criteria for packing stability with the difenacoum grain bait.

Table 3.1.3.3: Summary of the Physical and Chemical Properties of the Biocidal Product Paste/Pasta bait

Section	Study	Method	Results	Comment	Reference
1.7.1a	Storage stability (Accelerated storage – 14 days at 54°C)	GIFAP Monograph No. 17 CIPAC MT 46	**PP Bucket:** <u>Analysis at T0:</u> Physical properties: Red and greasy paste in individual sachet Bucket: White and non-porous internal wall. Bucket: 44.034g. Test item: 208.47g Total weight: 252.13g <u>Analysis at T14:</u> Physical properties: Red and greasy paste in individual sachet Bucket: White and non-porous internal wall with presence of grease. Bucket: 44.440g (0.92%) Test item: 207.69g (-0.37%) Total weight: 252.13g (-0.15%) **Doypack:** <u>Analysis at T0:</u> Physical properties: Red and greasy paste in individual sachet Doypack: Bag with internal wall in aluminium, non-porous. Doypack: 11.809g Test item: 148.48g	Carried out to GLP. Differences of packaging and sample weights after accelerated storage during 2 weeks are lower than 5%. No significant changes of characteristics of test item or packaging were observed. The Difenacoum paste bait is considered compatible with all the packaging tested. The study is acceptable.	"Packaging stability used for Difenacoum paste bait after accelerated storage". Richerioux, S. Report no.: LODI.55-2011. 2011-11-10.

Section	Study	Method	Results	Comment	Reference
			Total weight: 160.29g Analysis at T14: Physical properties: Red and greasy paste in individual sachet Doypack: Bag with internal wall in aluminium, non-porous with presence of grease. Doypack: 12.119g (2.63%) Test item: 148.37g (-0.07%) Total weight: 160.49g (0.12%) **PP prebaited baitbox:** Analysis at T0: Physical properties: Red and greasy paste in individual sachet. Prebaited baitbox: Black box with non-porous internal wall. Prebaited baitbox: 50.156g. Test item: 18.011g Total: 68.167g. Analysis at T14: Physical properties: Red and greasy paste in individual sachet. Prebaited baitbox: Black box with non-porous internal wall, presence of grease at the site of the paste. Prebaited baitbox: 50.395g (0.48%).		

Section	Study	Method	Results	Comment	Reference
			Test item: 17.766g (-1.36%) Total: 68.162g (-0.01%). **PS prebaited baitbox:** <u>Analysis at T0:</u> Physical properties: Red and greasy paste in individual sachet. Prebaited baitbox: Black box with non-porous internal wall. Prebaited baitbox: 12.205g. Test item: 19.330g Total: 31.534g. <u>Analysis at T14:</u> Physical properties: Red and greasy paste in individual sachet. Prebaited baitbox: Black box with non-porous internal wall – presence of grease at the site of the paste. Prebaited baitbox: 12.471g (2.18%). Test item: 18.561g (-3.98%). Total: 31.032g (-1.59%). **PE bag with cardboard box:** <u>Analysis at T0:</u> Physical properties: Red and greasy paste in individual sachet. PE bag with cardboard box: Transparent bag - cardboard box with grey		

Section	Study	Method	Results	Comment	Reference
			and dry internal wall. PE bag: 3.420g. Cardboard box: 23.568g Test item: 136.64g. Total: 163.63 g. <u>Analysis at T14:</u> Physical properties: Red and greasy paste in individual sachet. PE bag with cardboard box: Transparent bag with presence of grease-cardboard box with grey and dry internal wall. PE bag: 3.547g (3.71%). Cardboard box: 22.924g (-2.73%) Test item: 130.14g (-4.76%). Total: 156.61 (-4.29%) **PP bag with cardboard box:** <u>Analysis at T0:</u> Physical properties: Red and greasy paste in individual sachet. PP bag with cardboard box: Transparent bag - cardboard box with grey and dry internal wall. PE bag: 6.923g. Cardboard box: 23.509g. Test item: 140.78g.		

Section	Study	Method	Results	Comment	Reference
			Total: 171.21g. <u>Analysis at T14:</u> Physical properties: Red and greasy paste in individual sachet. PP bag with cardboard box: Transparent bag - cardboard box with grey and dry internal wall. PE bag: 7.074g (2.18%). Cardboard box: 22.954g (-2.36%). Test item: 135.36g (-3.85%). Total: 165.38g (-3.41%). **PE bag:** <u>Analysis at T0:</u> Physical properties: Red and greasy paste in individual sachet. PE bag: Transparent bag. PE bag: 3.410g. Test item: 137.42g. Total: 140.84g. <u>Analysis at T14:</u> Physical properties: Red and greasy paste in individual sachet. PE bag: Transparent bag with presence of grease. PE bag: 3.556g (4.28%).		

Section	Study	Method	Results	Comment	Reference
			Test item: 131.03g (-4.65%). Total: 134.59g (-4.44%). **PP bag:** <u>Analysis at T0:</u> Physical properties: Red and greasy paste in individual sachet. PP bag: Transparent bag. PP bag: 6.916g. Test item: 134.70g. Total: 141.62g. <u>Analysis at T14:</u> Physical properties: Red and greasy paste in individual sachet. PP bag: Transparent bag with presence of grease. PP bag: 7.239g (4.67%). Test item: 129.59g (-3.79%). Total: 136.83g (-3.38%). **Coextruded bag:** <u>Analysis at T0:</u> Physical properties: Red and greasy paste in individual sachet. Coextruded bag: Transparent bag (with print on external wall). Coextruded bag: 5.556g.		

Section	Study	Method	Results	Comment	Reference
			Test item: 97.464g. Total: 103.03g. <u>Analysis at T14:</u> Physical properties: Red and greasy paste in individual sachet. Coextruded bag: Transparent bag with presence of grease. Coextruded bag: 5.799g (4.37%). Test item: 96.343g (-1.15%). Total: 102.14g (-0.86%). **PE bag with cardboard box:** <u>Analysis at T0:</u> Physical properties: Red and greasy paste. PE bag with cardboard box: Transparent bag – cardboard box with grey and dry internal wall. PE bag + test item: 233.202g. Cardboard box: 23.393g. Total: 256.59g. <u>Analysis at T14:</u> Physical properties: Red and greasy paste. PE bag with cardboard box: Transparent bag with presence of paste – cardboard box with grey and dry internal wall.		

Section	Study	Method	Results	Comment	Reference
			PE bag + test item: 226.59g (-2.83%). Cardboard box: 23.021g (-1.59%). Total: 249.61g (-2.72%). **PP bucket as cartridge:** <u>Analysis at T0:</u> Physical properties: Red and greasy paste. PP bucket: White and non-porous internal wall. PP bucket: 44.086g. Test item: 376.08g. Total: 420.17g. <u>Analysis at T14:</u> Physical properties: Red and greasy paste. PP bucket: White and non-porous internal wall with presence of paste and grease. PP bucket: 44.533g (1.01%). Test item: 373.74g (-0.62%). Total: 418.33g (-0.44%).		
1.7.2	Shelf life (storage ambient temperatures	In compliance with GIFAP Monograph	**Physical & Chemical properties:**	Carried out to GLP. The test item is considered stable	"Chemical stability and physico-chemical tests

<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>for two years)</td>
<td>No. 17.

pH (CIPAC Handbook J – MT 75.3 Method (2000))</td>
<td>
<table>
<tr><th>Time</th><th>0</th><th>6 months</th><th>12 months</th><th>2 yrs</th></tr>
<tr><td>Appearance</td><td>Pink paste</td><td>Pink paste</td><td>Pink paste</td><td>Pink paste</td></tr>
<tr><td>Packaging</td><td>White opaque plastic box with transparent paper bag containing the paste</td><td>White opaque plastic box with transparent paper bag containing the paste</td><td>White opaque plastic box with transparent paper bag containing the paste</td><td>White opaque plastic box with transparent paper bag containing the paste</td></tr>
<tr><td>Packaging weight</td><td>371.5g</td><td>370.9g (-0.16%)
309.9g after sampling</td><td>308.8g (-0.35%)
252.1g after sampling</td><td>251.1g (-0.40%)</td></tr>
<tr><td colspan="5">The appearance of the test item is considered to be stable after the storage procedure for 2 years at 20 ± 2°C, no significant change of weight was observed.
The packaging material is considered to be stable after the storage procedure for 2 years at 20 ± 2°C.</td></tr>
</table>
<table>
<tr><th>Time</th><th>0</th><th>6 months</th><th>12 months</th><th>2 yrs</th></tr>
</table>
</td>
<td>for 2 years at ambient temperatures.

The pH at T0 was not given.

The study is acceptable.</td>
<td>after a storage procedure for 2 years at 20 ± 2°C on Difenacoum Pasta Bait”. Demangel, Benjamin. Report no.: 09-902018-006. 11th August 2011.</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>
<table>
<tr><td>Difenacoum content (% w/w).</td><td>0.0052</td><td>0.0048</td><td>0.0052</td><td>0.0047</td></tr>
<tr><td>Deviation from the declared value (%)
* deviation from T0 value</td><td>+4.0</td><td>-7.7*</td><td>0*</td><td>-9.6*</td></tr>
<tr><td colspan="5">No significant change was observed in the content after the storage procedure for 2 years at 20 ± 2°C.
Note that the declared content was 0.005% w/w.</td></tr>
</table>
<table>
<tr><th>Time</th><th>2 yrs</th></tr>
<tr><td>pH at 1% w/v in standard water D (at 22°C)</td><td>5.82 after 1 min
5.91 after 10 min</td></tr>
<tr><td colspan="2">The pH at T0 was not given.</td></tr>
</table>
</td><td></td><td></td></tr>
</table>

Conclusion:

The packaging material is stable after accelerated storage (14 days at 54°C) with all deviations in packaging and sample weights being below 5%. There were no significant changes of characteristics of the test item or packaging observed. The Difenacoum paste bait is considered compatible with all the packaging tested. The appearance, the weight of the test item and the packaging material are considered to be stable after 2 years storage at ambient temperatures. The deviation in the active substance content in this study was higher at -9.6% (0.0005 mg/kg decrease) than the one submitted in the PAR {0.19% decrease (0.0001 mg/kg decrease)}.

Expert opinions:

Author	Date	Problem	Expert opinion	Conclusion
Dr. Suren Husinec, University of Belgrade, Institute of Chemistry, Technology and Metallurgy, Department of Chemistry. E-mail: depchem@chem.bg.ac.yu Scientific Councillor of the Institute, expert in the field of synthesis, analysis and formulations of biocides. Signed off by: Dr. Vlatka Vajs (Director)	15th December 2011.	Significant decrease in active substance content of between 17.5 and 21% in the block and grain baits in the study report of the stability of Difenacoum baits after storage at ambient temperatures.	The grain formulation of Difenacoum bait presents a heterogeneous mixture of grain, flavouring, attractant, dye and a solution of the active ingredient. Due to the anatomy of the wheat grain the fruit coat and the grain are united and cannot be separated while grain is not too old. The outer coat of the grain is made up of several layers and they protect the main, nutritious part of the grain. Over the time protective layers tend to crack thus enabling molecules from the formulation to penetrate deep into the grain itself. The analytical method used for the determination of Difenacoum active ingredient consists in the first stage to extract Difenacoum from the formulation. Difenacoum on itself has a very poor solubility in organic solvents and the usually present an obstacle in quantitative determination. On the other side incorporation of molecules of Difenacoum into cracks of the protective layer of the grain makes molecules almost being binded to the matrix thus making their extraction almost impossible. With block formulation the situation is slightly different. A large proportion in mass of the block is paraffin which acts almost as a solvent of molecules of Difenacoum. Over the time intermolecular bonds between the molecule of Difenacoum which in large proportion is made up of aromatic hydrocarbon blocks and components of paraffin, hydrocarbons become stronger. As a result, as in previous case,	RMS accepts the expert opinion.

<table>
<tr><th>Author</th><th>Date</th><th>Problem</th><th>Expert opinion</th><th>Conclusion</th></tr>
<tr><td></td><td></td><td></td><td>extracting Difenacoum from paraffin formulation over the time is becoming more and more difficult.

In both cases, grain formulation and block formulation over the time give lower results in concentration of Difencoaum but field studies do not show the decrease in efficacy – this is a clear indication that the concentration of the active ingredient does not change although looking only at analytical results it does not seem so.

In both cases analytical results after two years are within the tolerance limit, almost at the edge in case of grain but still within the limit.</td><td></td></tr>
<tr><td>Dr.ir O. Pigeon,
FAO/WHO JMPS Member.</td><td>December 14th 2011.</td><td>Tolerances of content of active substance.</td><td>The tolerances for formulated products refer to the average result obtained and take into account of manufacturing, sampling and analytical variations; lower is the content of active substance and higher are these variations.

The tolerances proposed in the general FAO/WHO specifications are the following:
<table><tr><th>Declared content in g/kg or g/l at 20°C ± 2°C</th><th>Tolerance</th></tr><tr><td>Up to 25</td><td>± 15% of the declared content for “homogeneous” formulations (EC, SL etc)</td></tr></table></td><td>RMS accepts the expert opinion.</td></tr>
</table>

<table>
<tr><th>Author</th><th>Date</th><th>Problem</th><th>Expert opinion</th><th>Conclusion</th></tr>
<tr><td></td><td></td><td></td><td>
<table>
<tr><td></td><td>or
± 25% of the declared content for “heterogeneous” formulations (GR, WG etc)</td></tr>
<tr><td>Above 25 up to 100</td><td>± 10% of the declared content</td></tr>
<tr><td>Above 100 up to 250</td><td>± 6% of the declared content</td></tr>
<tr><td>Above 250 up to 500</td><td>± 5% of the declared content</td></tr>
<tr><td>Above 500</td><td>± 25 g/kg or g/l</td></tr>
<tr><td colspan="2">Note: In each range the upper limit is included</td></tr>
</table>

We can consider that the formulated products as block bait (BB), granular bait (GB), ...are heterogeneous formulations and that the tolerance of ± 25% can be applied for this kind of product containing <25 g/kg active substance.</td><td></td></tr>
<tr><td>Dr. Romain Lasseur,
Fundamental and Applied Toxicology (PhD),
Habilitation in Research Project Management (HDR),
Toxinnov.
8 Rue d’Aquitaine 69210 BULLY.</td><td>4th January 2012</td><td>Statement regarding the difficulties to extract Difenacoum from wheat used as rodenticides bait.</td><td>Wheat is an important food source for commercial rodent as rats (Rattus sp) and mice (Mus sp). It enters as a major component in their daily intake. This is the main reason explain rodent living around farms, cereals storage or around cereal processing industry. As a consequence, wheat based bait is palatable for rodent as it contain wheat in the formulation. Wheat bait mixed with anticoagulant used as rodenticides is excellent bait as it contains only the added anticoagulant to the</td><td>RMS accepts the expert opinion.</td></tr>
</table>

Author	Date	Problem	Expert opinion	Conclusion
Email: lasseur@free fr Anticoagulant toxicity, Anticoagulant resistance, Rodent field management Expert.			formulation, know not to affect palatability of wheat in rodent. Difenacoum is a high effective anticoagulant widely used in rodent control in the field as in house. Efficacy was proved in different rodent as rats (*Rattus* sp) and mice (*Mus* sp). Difenacoum active ingredient is formulated in different type of bait (blocks, soft bait, grain...). This active ingredient is known, regarding bibliography, to have a slow degradation rate in different matrix, as the soil, in formulation bait or in live organisms. Focused on bait based products, Difenacoum is known to degrade slowly and this degradation is not as function as bait type containing Difenacoum (blocks, soft bait or grain). Moreover, it is well known that, regarding analytical methods, extraction efficacy of anticoagulant from bait is different from a formulation to another. Extraction efficacy of anticoagulant from block bait is better than extraction efficacy from grain bait and in particular from wheat bait based. Due to possible irreversible migration (and not degradation) of active ingredient (Difenacoum) inside the wheat grain, extraction process not allows to recover the entire Difenacoum dose injected in the initial formulation. This problem is observed with a minor importance in other bait than grain bait (wheat bait) due to usuage of wheat flour instead of	

Author	Date	Problem	Expert opinion	Conclusion
			wheat. Moreover, it is ask to wheat based bait containing Difenacoum to respect 5% variation index after 2 years storage. 5% corresponds to variability index of the analytical method cited as the reference (HPLC/UV detector). To conclude, it seems, to answer this technical problem of difficulty and variation of extraction index of Difenacoum from wheat based bait, WHO guidelines have to be considered as the reference where it indicates that a tolerance of a maximum of 25% of variability in active ingredient can be acceptable. In parallel, what is important for the end-user of the wheat based bait containing Difenacoum, is that bait work effectively as rodenticides after 2 years storage (maximum delay between industrial production and usage of the bait by end-user). In case of difficulty of active ingredient extraction from wheat bait, such studies (bait fresh produced and bait after 2 years storage) have to be conducted to show similarity in term of efficacy in targeted rodent.	

A further study on the stability of difenacoum was submitted by the Applicant (27.3.2012) and is evaluated below:

Report No:	Biolytics Study no. 11-TOX014.
Title:	"Analysis of difenacoum with the evidence of no degradation products in 2 years old bait"
Author(s):	Isabelle Fourel.
Date:	9th February 2012
GLP: Yes/No	No.
Background:	The aim of the study was to compare the concentrations of the active ingredient in "fresh" bait and in bait that was kept at ambient temperatures for 2 years. The "fresh" bait was then artificially deteriorated to demonstrate that there is no evidence of degradation products in the 2 year old matrix.
Principle of the Method:	The difenacoum broken and whole baits were aged for 2 years at ambient temperatures (20°C with no light). The 2-year old baits and the "fresh" baits (broken and whole) were then analysed by LC-MS. The difenacoum broken and whole "fresh" baits were degraded through forced degradation by: 1. Heating – heating the baits in a drying oven at 60°C ± 5°C away from light, for 5 days. 2. Acid degradation – the baits were mixed with 5 ml chlorhydric acid 0.1N in methanol and kept in a drying oven for 2 hours at 60°C away from light. 5ml of NaOH 0.1N in methanol was added to neutralise prior to analysis. Pure difenacoum was put through the heat and acid degradation procedure as well.
Chromatograms	Chromatograms for the fresh baits (broken and whole), two year old bait (broken and whole), the acid stressed baits, the heat stressed baits and the pure difenacoum were provided. The chromatograms of the non-deteriorated baits were compared with the chromatograms of the deteriorated baits.
Results:	The concentration of difenacoum was higher in the fresh baits than in the 2-year old baits. Acid and heat stress led to the production of degradation products which differed depending on the kind of stress they were submitted to. There was no difference in the degradation products for the broken and whole baits that underwent the

	same test. Four degradation products appeared after the acid or heat stress of the broken or whole baits. These were m/z 476, 354.9, 447, 409 (with RT 18.09, 19.17, 20.21 and 17.70 min respectively). The degradation products observed at retention times 19.17, 20.21 and 17.7 min appeared when baits were acid or heat stressed but were missing from fresh or two year old baits. The quantity of degradation product at retention time 18.09 min increased in acid stressed bait but was already present in fresh and two year old baits in equivalent proportions. There is no increase in the quantity of this degradation product after 2-years storage.
Conclusion:	Three of the four degradation products were not found in either the "fresh" bait or the two year old bait. One degradation product, which was found in both the "fresh" and aged baits, was found at higher levels in the acid stressed bait. Therefore, it can be concluded that difenacoum does not break down during storage for two years at ambient temperature. The difference in the difenacoum concentration between "fresh" bait and 2 year old bait is mostly like to be due to extraction problems and not a result of Difenacoum degradation. The extraction problems most likely arise due to interactions between difenacoum and the bait matrix.

Conclusion:

Difenacoum does not degrade during storage for two years at ambient temperatures.

Overall conclusion:

The Irish CA considers that the storage stability information provided in the PAR and in this Addendum, supports a shelf life for the block bait, grain bait and paste bait of two years (24 months), based on the efficacy of the products being maintained over a two year period and the nominal content of active substance (0.05 g/kg) remaining within the FAO requirement of ± 25% specified limits. The product was 90-100% efficacious when stored for 24 months. In the interests of animal welfare the Irish CA does not believe further efficacy testing is necessary on these products.

The packaging material is stable after accelerated storage (14 days at 54^{o}C) with all deviations in packaging and sample weights being below 5% with the exceptions of the cardboard box for the block bait and the PP woven bag for the grain bait which had deviations above 5%. There were no significant changes of characteristics of the test

item or packaging observed. The Difenacoum block, grain and paste baits are considered compatible with all the packaging tested (with the exceptions noted above).

The appearance, the weight of the test item and the packaging material are considered to be stable after 2 years storage at ambient temperatures. The deviation in the active substance content for the block bait was much lower in the new studies provided, at 6.4% (0.0003 mg/kg increase) and -3.9% (0.0016 mg/kg decrease) than the one submitted in the PAR {17.5% decrease (0.0092 mg/kg decrease)}. The deviation in the active substance content for the grain bait was lower in the new study at -15.4% (0.0008 mg/kg decrease) than the one submitted in the PAR {22% decrease (0.0106 mg/kg decrease)}. The deviation in the active substance content for the paste bait in the new study was higher at -9.6% (0.0005 mg/kg decrease) than the one submitted in the PAR {0.19% decrease (0.0001 mg/kg decrease)}.

The expert opinions provided support the theory that Difenacoum does not degrade over time but becomes bound to the grain 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.

Shelf life:

2-year shelf life proposed for Difenacoum block bait, grain bait and paste/pasta bait.

Annex 2 - Revised PAR – September 2016

Product Assessment Report

Ruby Block

Active substance:	**Difenacoum**
Product-type:	**PT 14: Rodenticides**
Type of application:	**Authorisation**
Authorisation No:	**IE/BPA 70002 (non-professional product)** **IE/BPA 70025 (professional product)**
Date:	**07 September 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

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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 Block 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 Block
Authorisation No.:	IE/BPA 70002 (non-professional) IE/BPA 70025 (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 Block	IE/BPA 70026	Hygeia Chemicals Ltd.	Supplemental Authorisation (Back-2-Back Authorisation)

66.1 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]

66.3 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]

66.4 General Information on the Biocidal Product

Trade name:	Ruby Block
Manufacturer's development code no:	N/A
Active substance content (% w/w):	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) Block Bait (BB)
Ready-to-use (RTU) product (yes/no):	Yes (Only RTU products to be authorised)
Chemical/micro-organism:	Chemical substance
Contain or consist of GMOs[30] (yes/no):	N/A
Is the product already notified /authorised (yes/no); If yes: product name:	Yes (Notified under transitional arrangements with the PRCD) Ruby Block, PCS 94704
Is the biocidal product equivalent to the product assessed for the purpose of Annex I inclusion to 98/8/EC (yes/no):	No.

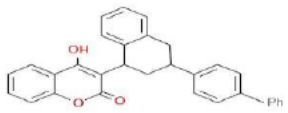
Manufacturer of Formulated Product:	LODI S.A.
Address:	Parc d'activities des quatre routes Grand Fougeray 35390 France
Tel:	[redacted]
E-mail:	[redacted]

66.5 Information on active substance(s)[31]

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
EC No:	259-978-4
Purity (minimum, g/kg or g/l):	>960 g/kg (96.0% w/w)

30 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.

31 Please insert additional columns as necessary

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]

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

Main Group:	MG02 (Pest control)
Product-type:	PT14 (Rodenticide)
Intended use:	Difenacoum block bait to control rodents indoors, outdoors and in sewers 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, open areas) Sewers (IE/BPA 70025 only)
Directions for use including minimum and maximum application rates, typical size of application area:	Rats: 90-100g of blocks spaced 10m apart (5m apart in high infestation areas). Typical treatment time 6 weeks. Mice: 20-30g of blocks spaced 5m apart (3m apart in high infestation areas). Typical treatment time 6 weeks.
Application method:	Wax bait blocks contained in secured bait stations
Interval between applications:	When required. Regularly check bait consumption and 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

66.7 Documentation

66.7.1 Data submitted in relation to product application

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

According to the Assessment Report (17-09-2009) *'No classification of products containing 50 mg/kg or 75 mg/kg difenacoum would be necessary according to Directive 1999/45/EC. However, specific*

concentration limits of difenacoum have been agreed by the Technical Committee on Classification and Labelling.'

Classification and Labelling of the biocidal product, Ruby Block, 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 Block, 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 70025) 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 Block, as presented by the applicant, 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:	Box container					
Pack size(s):	150g	240g	260g	300g	450g	~~600g~~
Baits per pack:	5x30g 10x15g	8x30g 12x20g 16x15g	13x20g	10x30g 15x20g 20x15g	15x30g 30x15g	~~20x30g~~ ~~30x20g~~ ~~40x15g~~
Pack dimensions (LxWxH):	100x47x155 140x90x100	140x55x180	140x55x180	140x55x180 140x80x210	140x70x210	~~140x80x190~~
Packaging materials:	Cardboard					
Ready-to-use	Yes					

(yes/no)	
Shelf-life:	2 years
Conditions of storage:	Store in dry, cool area. Store in tightly closed packaging. Keep in original containers. Store away from damp or wet conditions. Keep away from children.

Container description:	Bucket container	
Pack size(s):	300g	~~3kg~~
Baits per pack:	10x30g, 15x20g, 20x15g	~~100x30g, 150x20g, 200x15g~~
Pack dimensions (LxWxH):	130x130x130	~~290x200x210~~
Packaging materials:	PP or PE	
Ready-to-use (yes/no)	Yes	
Shelf-life:	2 years	
Conditions of storage:	Store in dry, cool area. Store in tightly closed packaging. Keep in original containers. Store away from damp or wet conditions. Keep away from children.	

Container description:	Pre-baited bait station			
Pack size(s):	20g	30g	50g	100g
Baits per pack:	1x20g	1x30g	1x50g	2x50g
Pack dimensions (LxWxH):	135x42x80	135x42x80	300x130x70 140x80x40	230x190x90 200x150x80
Packaging materials:	PVC, PP, PS or cardboard bait box			
Ready-to-use (yes/no)	Yes			
Shelf-life:	2 years			
Conditions of storage:	Store in dry, cool area. Store in tightly closed packaging. Keep in original containers. Store away from damp or wet conditions. Keep away from children.			

Professional product packaging:

Container description:	Box container
Pack size(s):	10kg
Baits per pack:	125x80g, 334x30g, 500x20g, 667x15g

Pack dimensions (LxWxH):	390x290x240
Packaging materials:	Cardboard
Ready-to-use (yes/no)	Yes
Shelf-life:	2 years
Conditions of storage:	Store in dry, cool area. Store in tightly closed packaging. Keep in original containers. Store away from damp or wet conditions. Keep away from children.

Container description:	Bucket container			
Pack size(s):	3kg	5kg	10kg	10kg (crochet)
Baits per pack:	100x30g, 150x20g, 200x15g	63x80g, 167x30g, 250x20g, 334x15g	125x80g, 334x30g, 500x20g, 667x15g	100x100g, 125x80g
Pack dimensions (LxWxH):	290x200x210	290x200x270	380x290x220	380x290x350
Packaging materials:	PP or PE			
Ready-to-use (yes/no)	Yes			
Shelf-life:	2 years			
Conditions of storage:	Store in dry, cool area. Store in tightly closed packaging. Keep in original containers. Store away from damp or wet conditions. Keep away from children.			

Container description:	Pre-baited bait station			
Pack size(s):	20g	30g	50g	100g
Baits per pack:	1x20g	1x30g	1x50g	2x50g
Pack dimensions (LxWxH):	135x42x80	135x42x80	300x130x70 140x80x40	230x190x90 200x150x80
Packaging materials:	PVC, PP, PS or cardboard bait box			
Ready-to-use (yes/no)	Yes			
Shelf-life:	2 years			
Conditions of storage:	Store in dry, cool area. Store in tightly closed packaging. 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 block bait should be supplied to the amateur market in sachets/wrapped in order to reduce exposure risks to amateur operators during application to bait stations.

Pack size:	IE/BPA 70002 – Maximum pack size of 500g
	Pre-baited stations: 30g (mice) and 100g (rats)
	Refill packs: 150g, 160g, 240g, 260g, 300g, 450g (the bait must be supplied in inner packs or units, each containing enough bait for one point)
	IE/BPA 70025
	Pre-baited stations: 30g (mice) and 100g (rats)
	Refill packs: 3kg, 5kg and 10kg (the bait should be supplied in inner packs or units, each containing enough bait for one point)
Container materials[32]:	Box container – cardboard
	Bucket container – PP or PE
	Pre-baited bait station – PVC, PP, PS or cardboard
Safety features:	Covered bait stations (tamper resistant)
	Wrapped bait (sachets)

[32] PP = polypropylene, PS = polystyrene, PE = polyethylene, HDPE = high-density polyethylene, PVC = polyvinylchloride

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 Block is not explosive, oxidising or flammable and therefore does not classify from a physical/chemical point of view. The test item is stable after storage for two years at ambient temperature. The test item is a ready-to-use block 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 Block 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 Block

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 Block 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 Block 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

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

Section	Study	Method	Results	Comment	Reference
1.1.1	Appearance	Observation.	Appearance: Red solid block. Odour: Slightly waxed.	See 1.7.1b below.	
1.1.1	Appearance	OPPTS 830.6302 OPPTS 830.6303 OPPTS 830.6304	Colour (Munsell code): Red-rose (10 RP4/12) Physical state: blocks Odour: characteristic	Carried out to GLP. Study is acceptable.	NOTOX Project 490521. "Determination of physic-chemical properties of difenacoum block baits". Brekelmans, Ir. M.J.C. 17th September 2010.
1.1.2	Melting point	EEC A1 OECD 102	Melting point: 52.8 - 54.5°C (326 – 328K) Reaction and/or decomposition of the test substance was observed starting at 75°C (348K).	Carried out to GLP. The melting temperature of difenacoum block baits was determined using DSC. Study is acceptable.	NOTOX Project 490521. "Determination of physic-chemical properties of difenacoum block 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,*	The IE-CA accepts that difenacoum was determined not to be	

Section	Study	Method	Results	Comment	Reference
			Butterworths, London 1979}, and its 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.	explosive as part of the Annex I inclusion process (expert statement). IE-CA accepts the justification provided by the notifier that Ruby Block is not explosive.	
1.2.1	Explosive properties		A reasoned statement was provided by the Notifier. Difenacoum block bait is not explosive.	The IE-CA accepts the Notifiers justification. Difenacoum block bait is not explosive.	NOTOX Project 490521. "Determination of physic-chemical properties of difenacoum block baits". Brekelmans, Ir. M.J.C. 17th September 2010.
1.2.2	Oxidising properties		Neither the active substance nor the solvent present oxidising properties. Examination of the structure establishes 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)*.	The IE-CA accepts that difenacoum was determined not to be oxidising as part of the Annex I inclusion process. IE-CA accepts the justification provided by the notifier that Ruby Block is not oxidising.	
1.2.2	Oxidising		A reasoned statement was provided by the Notifier.	The IE-CA accepts the	NOTOX Project

Section	Study	Method	Results	Comment	Reference
	properties		Difenacoum block bait is not oxidising.	Notifiers justification. Difenacoum block bait is not oxidising.	490521. "Determination of physic-chemical properties of difenacoum block 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.		
1.3.2	Flammability		There are no components present in the formulation that present flammability properties.	The IE-CA accepts that difenacoum was determined to be not highly flammable as part of the Annex I inclusion process. A justification is not acceptable in this case, however further information was supplied, see 1.3.2 below to show that the block bait is not highly flammable.	
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	Carried out to GLP. The test substance is considered "not highly flammable". The study is	NOTOX Project 490521. "Determination of physic-chemical

Section	Study	Method	Results	Comment	Reference
			flame and turned into a charred residue. White smoke was observed. After removal of the ignition source, the flame extinguished after 2 seconds and no propagation of combustion was observed. Performance of the main test was not required.	acceptable.	properties of difenacoum block baits". Brekelmans, Ir. M.J.C. 17th September 2010.
1.3.3	Auto-flammability	EEC A.16 (relative self-ignition temperature for solids)	A strong exothermic effect of the test substance was observed. The temperature of the test substance reached 400°C at an oven temperature of 256°C. The self-ignition temperature of the test item is 256°C.	Carried out to GLP. The self-ignition temperature of the test item is 256°C. The study is acceptable.	NOTOX Project 490521. "Determination of physic-chemical properties of difenacoum block baits". Brekelmans, Ir. M.J.C. 17th September 2010.
1.4.1	Free acidity/ Alkalinity		Not applicable, the product is a ready to use block bait, which is a solid block at ambient temperatures.	Accept justification.	
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 during NOTOX project 490522 to be 6.1. Therefore since this pH was within the pH range 4-10 the acidity/alkalinity test was not required and thus not performed.	IE-CA agrees that the acidity/alkalinity test is not required.	NOTOX Project 490521. "Determination of physic-chemical properties of difenacoum block 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>1.4.2</td><td>pH (1 %)</td><td></td><td>Not applicable, the product is a ready to use block bait, which is a solid block at ambient temperatures.
See comment in 1.4.1.</td><td>No data required.</td><td></td></tr>
<tr><td>1.5.1</td><td>Viscosity</td><td></td><td>Not applicable, the product is a ready to use block bait.</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 ready to use block bait.</td><td>Accept justification.</td><td></td></tr>
<tr><td>1.6</td><td>Relative density</td><td></td><td>Not applicable, the product is a ready to use block bait, which is a solid block at ambient temperatures.</td><td>Accept justification.</td><td></td></tr>
<tr><td>1.6</td><td>Density</td><td>CIPAC MT 109 (density of liquids and solids)
EC. A.3.</td><td>Density: 1.28 g/cm^3
Relative density: 1.28</td><td>Carried out to GLP. A gas comparison pycnometer was used for the determination of the density and relative density of the test item. The study is acceptable.</td><td>NOTOX Project 490521. “Determination of physic-chemical properties of difenacoum block 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^{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 block (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></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^{o}C. Results indicate that the block bait will be stable for</td><td>Study report: Stability of Difenacoum baits after accelerated storage procedure. Biannic, Marie-Laure. 7th January 2008.</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>
<table>
<tr><td>Agent conc. in ppm</td><td>52.7</td><td>49.6</td><td>44.9</td><td>39.2</td><td>43.0</td></tr>
<tr><td>Deviation from the declared value</td><td>+ 5.4%</td><td>- 0.8%</td><td>- 10.2%</td><td>- 21.6%</td><td>- 14%</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, which would indicate that the block bait will be stable for a minimum of 2 years at ambient temperature.</td><td>a minimum of two years at ambient temperature. The study is acceptable.</td><td></td></tr>
<tr><td>1.7.1b</td><td>Storage stability
(Accelerated storage – 14 days at 54^{o}C)</td><td>GIFAP Monograph No. 17
CIPAC MT 46</td><td><u>Analysis at T0:</u>
Aspect: Red block
Odour: Slightly waxed
Contents: 0.0045% of difenacoum

<u>Analysis at T14:</u>
Aspect: Red block
Odour: Slightly waxed
Contents: 0.0042% of difenacoum (-6.66% after accelerated storage)</td><td>Carried out to GLP. The results of the study indicate that the test item is stable for 2 weeks at 54^{o}C and 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.</td><td>Study No: LODI.15/2009.
Study report: Chemical stability after accelerated storage of difenacoum block baits 0.005%. Magnier, Claire. 23rd November 2009.</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>1.7.1c</td><td>Storage stability
(Accelerated storage – 18 weeks at 30^{o}C)</td><td>FAO, SANCO/3030/99 (a.i. content)
OPPTS 830.6302 (colour, Munsell code)
OPPTS 830.6303 (physical state)
OPPTS 830.6304 (odour)
CIPAC MT 75.3 (pH (1%))</td><td>Difenacoum content (g/kg):
Before: 0.0462
After: 0.0430

Appearance:
Before: Red (10 RP4/12), block, characteristic odour.
After: Red (10 RP4/12), block, no characteristic odour.

pH (1% in water):
Before: 6.1
After: 6.9</td><td>Carried out to GLP. The test item is stable after 18 weeks storage at 30^{o}C, which indicates that the test item will be stable for 2 years at ambient temperatures. The results are acceptable.</td><td>NOTOX Project 490522.
“Determination of the accelerated storage stability of difenacoum block baits by heating”.
Brekelmans, Ir. M.J.C. 17th September 2010.</td></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 block (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>52.7</td><td>57.1</td><td>43.5</td></tr>
<tr><td>Deviation from the declared value</td><td>5.40%</td><td>8.35%</td><td>-17.46%</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</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>
</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>temperatures.</td><td></td><td></td></tr>
<tr><td>1.7.3</td><td>Packaging stability (20°C)</td><td></td><td>Packaging in prebaited baitbox (PP):
<table>
<tr><th></th><th colspan="4">Weight</th></tr>
<tr><th></th><th>Prebaited box (g)</th><th>Cardboard box (g)</th><th>Test item (g)</th><th>Total (g)</th></tr>
<tr><td>T_0</td><td>234.92</td><td>29.932</td><td>101.07</td><td>365.93</td></tr>
<tr><td>$T_{6months}$</td><td>234.98</td><td>30.347</td><td>100.95</td><td>366.33</td></tr>
<tr><td>Deviation</td><td>+0.03%</td><td>+1.39%</td><td>-0.12%</td><td>+0.11%</td></tr>
<tr><td>T_{1year}</td><td>234.30</td><td>29.941</td><td>100.19</td><td>364.97</td></tr>
<tr><td>Deviation</td><td>-0.26%</td><td>0.03%</td><td>-0.87%</td><td>-0.26%</td></tr>
<tr><td>$T_{18\ months}$</td><td>234.96</td><td>30.224</td><td>100.39</td><td>365.60</td></tr>
<tr><td>Deviation</td><td>0.02%</td><td>0.98%</td><td>-0.67%</td><td>-0.09%</td></tr>
<tr><td>T_{2years}</td><td>234.55</td><td>29.806</td><td>99.902</td><td>364.64</td></tr>
<tr><td>Deviation</td><td>-0.16%</td><td>-0.42%</td><td>-1.16%</td><td>-0.35%</td></tr>
</table>
T_0 = Dry and clean prebaited baitbox. Regtangular cardboard box with clean and dry internal wall. The test item is rectangular red block with grains and slightly friable corner.
$T_{6months}$ = Dry and clean prebaited baitbox. Regtangular cardboard box with clean and dry internal wall. The test item is rectangular red block with grains and slightly friable corner.
T_{1year} = Dry and clean prebaited baitbox. Regtangular cardboard box with clean and dry internal wall. The test item is rectangular red block with grains and slightly friable corner.</td><td>Carried out to GLP.
The weight deviations are lower than 5% for all the packagings after 24 months of storage at 20°C ± 2°C. No significant change was observed on the packaging and samples aspect.
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 submitted as the study is still on-going.</td><td>Study report “Compatibility between difenacoum block bait and packagings after 3 years of storage at 20°C”. Study No. LODI.03/2014. Tallon, Anaïs. 2016-04-19.</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>
$T_{18\ months}$ = Dry and clean prebaited baitbox. Regtangular cardboard box with clean and dry internal wall. The test item is rectangular red block with grains and slightly friable corner.
$T_{2\ years}$ = Dry and clean prebaited baitbox. Regtangular cardboard box with clean and dry internal wall. The test item is rectangular red block with grains and slightly friable corner.

Packaging in bucket (PP) with unwrapped blocks:
<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>52.974</td><td>176.05</td><td>229.03</td></tr>
<tr><td>$T_{6months}$</td><td>53.011</td><td>175.96</td><td>228.96</td></tr>
<tr><td>Deviation</td><td>+0.07%</td><td>-0.05%</td><td>-0.03%</td></tr>
<tr><td>T_{1year}</td><td>53.021</td><td>175.72</td><td>228.78</td></tr>
<tr><td>Deviation</td><td>0.09%</td><td>-0.19%</td><td>-0.11%</td></tr>
<tr><td>$T_{18\ months}$</td><td>53.047</td><td>175.61</td><td>228.66</td></tr>
<tr><td>Deviation</td><td>0.14%</td><td>-0.25%</td><td>-0.16%</td></tr>
<tr><td>T_{2years}</td><td>53.063</td><td>175.43</td><td>228.50</td></tr>
<tr><td>Deviation</td><td>0.17%</td><td>-0.35%</td><td>0.23%</td></tr>
</table>

T_0 = Dry and clean bucket. Test item rectangular red block with grains and slightly friable corner.
$T_{6months}$ = Dry bucket. Presence of block dust in the bottom of the bucket. Test item rectangular red block with grains and slightly friable corner.
T_{1year} = Dry bucket. Presence of block dust in the bottom of the bucket. Test item rectangular red block with grains and slightly friable corner.
$T_{18\ months}$ = Dry bucket. Presence of block dust in the
</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>bottom of the bucket. Test item rectangular red block with grains and slightly friable corner.
$T_{2\ years}$ = Dry bucket. Presence of block dust in the bottom of the bucket. Test item rectangular red block with grains and slightly friable corner.

Packaging in bucket (PP) with blocks wrapped in inner sachet (PP):
<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>53.398</td><td>127.51</td><td>180.90</td></tr>
<tr><td>$T_{6months}$</td><td>53.415</td><td>127.26</td><td>180.67</td></tr>
<tr><td>Deviation</td><td>+0.03%</td><td>-0.20%</td><td>-0.13%</td></tr>
<tr><td>T_{1year}</td><td>53.420</td><td>126.27</td><td>179.69</td></tr>
<tr><td>Deviation</td><td>0.04%</td><td>-0.97%</td><td>-0.67%</td></tr>
<tr><td>$T_{18\ months}$</td><td>53.419</td><td>126.18</td><td>179.60</td></tr>
<tr><td>Deviation</td><td>0.04%</td><td>-1.04%</td><td>-0.72%</td></tr>
<tr><td>T_{2years}</td><td>53.425</td><td>126.00</td><td>179.44</td></tr>
<tr><td>Deviation</td><td>0.05%</td><td>-1.18%</td><td>-0.81%</td></tr>
</table>
T_0 = Dry and clean bucket. Test item rectangular red block in inner sachet dry and clean.
$T_{6months}$ = Dry and clean bucket. Test item rectangular red block in inner sachet dry and clean..
T_{1year} = Dry and clean bucket. Test item rectangular red block in inner sachet dry and clean..</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>
$T_{18\ months}$ = Dry and clean bucket. Test item rectangular red block in inner sachet dry and clean.
$T_{2\ years}$ = Dry and clean bucket. Test item rectangular red block in inner sachet dry and clean.

Packaging in cardboard box with block wrapped in inner sachet (PP):
<table>
<tr><th></th><th colspan="3">Weight</th></tr>
<tr><th></th><th>Cardboard box (g)</th><th>Test item (g)</th><th>Total (g)</th></tr>
<tr><td>T_0</td><td>46.098</td><td>346.30</td><td>392.40</td></tr>
<tr><td>$T_{6months}$</td><td>46.941</td><td>344.52</td><td>391.42</td></tr>
<tr><td>Deviation</td><td>+1.83%</td><td>-0.51%</td><td>-0.25%</td></tr>
<tr><td>T_{1year}</td><td>46.129</td><td>341.88</td><td>388.01</td></tr>
<tr><td>Deviation</td><td>0.07%</td><td>-1.28%</td><td>-1.12%</td></tr>
<tr><td>$T_{18\ months}$</td><td>46.625</td><td>341.95</td><td>388.59</td></tr>
<tr><td>Deviation</td><td>1.14%</td><td>-1.26%</td><td>-0.97%</td></tr>
<tr><td>T_{2years}</td><td>46.056</td><td>342.00</td><td>386.58</td></tr>
<tr><td>Deviation</td><td>-0.09%</td><td>-1.24%</td><td>-1.48%</td></tr>
</table>

T_0 = Rectangular cardboard box with clean and dry internal wall. Test item rectangular red block in inner sachet dry and clean.
$T_{6months}$ = Rectangular cardboard box with clean and dry internal wall. Test item rectangular red block in inner sachet dry and clean.
</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>
T_{1year} = Rectangular cardboard box with clean and dry internal wall. Test item rectangular red block in inner sachet dry and clean.
$T_{18\ months}$ = Rectangular cardboard box with clean and dry internal wall. Test item rectangular red block in inner sachet dry and clean.
$T_{2\ years}$ = Rectangular cardboard box with clean and dry internal wall. Test item rectangular red block in inner sachet dry and clean.

Packaging in cardboard box with unwrapped block in bag:
<table>
<tr><th rowspan="2"></th><th colspan="4">Weight</th></tr>
<tr><th>Cardboard box (g)</th><th>Test item (g)</th><th>Bag (g)</th><th>Total (g)</th></tr>
<tr><td>T_0</td><td>45.323</td><td>320.00</td><td>4.924</td><td>370.25</td></tr>
<tr><td>$T_{6months}$</td><td>46.251</td><td>318.52</td><td>5.045</td><td>370.03</td></tr>
<tr><td>Deviation</td><td>+2.05%</td><td>-0.46%</td><td>+2.46%</td><td>-0.06%</td></tr>
<tr><td>T_{1year}</td><td>45.423</td><td>316.4</td><td>4.97</td><td>366.79</td></tr>
<tr><td>Deviation</td><td>0.22%</td><td>-1.13%</td><td>0.93%</td><td>-0.93%</td></tr>
<tr><td>$T_{18\ months}$</td><td>45.862</td><td>316.35</td><td>4.966</td><td>367.72</td></tr>
<tr><td>Deviation</td><td>1.19%</td><td>-1.14%</td><td>0.85%</td><td>-0.68%</td></tr>
<tr><td>T_{2years}</td><td>45.310</td><td>315.17</td><td>4.973</td><td>365.53</td></tr>
<tr><td>Deviation</td><td>-0.03%</td><td>-1.51%</td><td>1.00%</td><td>-1.27%</td></tr>
</table>
T_0 = Rectangular cardboard box with clean and dry internal wall. Dry and clean bag. Test item rectangular red block with slightly friable corner.
$T_{6months}$ = Rectangular cardboard box with clean and dry internal wall. Presence of block dust in the bottom of the
</td><td></td><td></td></tr>
</table>

Section	Study	Method	Results	Comment	Reference
			bag. Test item rectangular red block with slightly friable corner. T_{1year} = Rectangular cardboard box with clean and dry internal wall. Presence of block dust in the bottom of the bag. Test item rectangular red block with slightly friable corner. $T_{18\ months}$ = Rectangular cardboard box with clean and dry internal wall. Presence of block dust in the bottom of the bag. Test item rectangular red block with slightly friable corner. $T_{2\ years}$ = Rectangular cardboard box with clean and dry internal wall. Presence of block dust in the bottom of the bag. Test item rectangular red block with slightly friable corner.		
1.8.1	Wettability		Not applicable, the product is a ready to use block bait.	Accept justification.	
1.8.2	Persistent foaming		Not applicable, the product is a ready to use block bait.	Accept justification.	
1.8.3.1	Suspensibility		Not applicable, the product is a ready to use block bait.	Accept justification.	
1.8.3.2	Dispersibility		Not applicable, the product is a ready to use block bait.	No data required.	
1.8.4	Wet/dry sieving test		Not applicable, the product is a ready to use block bait.	Accept justification.	
1.8.5	Particle size distribution in suspension	Only for powders and granules	Not applicable, the product is a ready to use block bait.	Accept justification.	
1.8.6	Water content		Not applicable, the product is a ready to use block bait.	No data required.	
1.8.7	Emulsion stability	Only for ECs and ready for use emulsions	Not applicable, the product is a ready to use block bait.	Accept justification.	
1.8.8	Flowability,	Flowability only for	Not applicable, the product is a block.	Accept justification.	

Section	Study	Method	Results	Comment	Reference
	pourability and dustability	granular preparations, pourability only for suspensions and dustability only for dustable powders.			
1.9	Physical compatibility		Not applicable, the product is a ready-to-use block bait and is not intended to be added or mixed with any other product.	Accept justification.	

Conclusions:

The biocidal product Ruby Block 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 block 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 Baitbox

PP bucket

PP bucket with blocks wrapped in inner PP sachet

Cardboard box with blocks wrapped in inner PP sachet

Cardboard box with unwrapped block in bag

Data requirements/clarifications:

None.

3.1.4. Analytical methods

Ruby Block 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>09-902018-005</td></tr>
<tr><td>Title:</td><td>“Analytical method validation for the determination of difenacoum in difenacoum block 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>After a methanol dilution and heating under reflux for 90 minutes the extract was filtered and diluted again in methanol and acetonitrile. Difenacoum was then quantified by liquid chromatography using a reverse phase column and UV detector at 310 nm. The purity of the reference standard difenacoum used was 970 g/kg.</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>0.88</td><td rowspan="2">95</td></tr>
<tr><td>Extract 1 100%</td><td>0.92</td><td>0.87</td></tr>
<tr><td>Extract 2 100%</td><td>0.92</td><td>0.92</td><td rowspan="2">98</td></tr>
<tr><td>Extract 2 100%</td><td>0.92</td><td>0.89</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>0.46</td><td rowspan="2">100</td></tr>
<tr><td>Extract 1 50%</td><td>0.46</td><td>0.46</td></tr>
<tr><td>Extract 2 50%</td><td>0.46</td><td>0.45</td><td rowspan="2">99</td></tr>
<tr><td>Extract 2 50%</td><td>0.46</td><td>0.46</td></tr>
</table>
The recovery results are between 95 - 100%, 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 3.34 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.
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 analytical method described above has been successfully validated for linearity, precision, accuracy and specificity.

Data requirements:

None.

Table 3.1.4.3

Report:	Study No. LODI.17/2009
Title:	"Analytical method validation for determination of difenacoum in difenacoum bait (pasta grain and block)."
Author(s):	Magnier, Claire.
Date:	4th November 2009.
GLP: Yes/No	Yes.
Guideline:	CITAC/EURACHEM
Principle of the Method:	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 09-902018-005 and 05-912011-001.
Linearity:	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 $r^2 > 0.99$.
Precision/repeatability:	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.

<table>
<tr><td></td><td>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>Block bait</td><td>100.43 %</td><td>97.22%</td><td>98.99%</td><td>99.88%</td></tr>
</table></td></tr>
<tr><td>Specificity:</td><td>There was no peak observed in either the block placebo or extraction solution chromatograms. An adjacent peak appeared in the stressed block but the resolution being higher than 2 (R = 2.16), 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.

3.3. Efficacy of the Biocidal Product

Ruby block is a ready-to-use rodenticide block bait containing 0.005% (w/w) difenacoum or 50 ppm difenacoum. The efficacy of the products was assessed against the proposed label claims. Both amateur and professional uses are proposed in and around buildings. Professional users can also use the product in sewers.

The applicant submitted new data in the form of 10 trial reports where both fresh and aged blocks under a wide range of conditions (laboratory and field) were tested and evaluated for their effectiveness. Studies were conducted according to a variety of standards and protocols. Five of the studies were conducted under laboratory conditions with wild strains of mice (2 studies) and rats (3 studies). In two of the studies wild rodents were captured in the field and acclimatized prior to commencing baiting trials. The laboratory studies were all choice tests conducted according to recognised standards. The studies have shown that Ruby Wax block 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 study a mouse infested restaurant (estimated population ~157 mice) was used to establish the effectiveness of fresh block bait. Efficacy following census pre and post-baiting demonstrated a reduction in the mouse population of over 97% after just 7 days of baiting. In the second study the site chosen was also a restaurant with a significant mouse problem estimated at 220 individuals. After a 9-day treatment phase with a 2-year aged bait an efficacy specification approaching 90% was achieved. The third study was a laboratory choice test using 10 house mice and fresh bait. 100% control was achieved within 5 days of using the wax block bait. The next study investigated the palatability and control levels after an accelerated storage study (14 days at 54^{o}C). The bait proved palatable and effective with 100% mortality achieved in just 4 days (10 mice). 10 brown rats were used for the next study with poisoned bait provided for just 2 days. 90% control was achieved in the following days, with the remaining individual having consumed very low levels of block. 22 brown rats were used in the next study again with a short poisoning period using fresh and aged (6 month old) baits. 95% control was achieved with the fresh bait and 100% with the aged with the sole surviving female having consumed very low levels of the block bait. In the next test 22 rats were used in a study on fresh and 12-month aged blocks. 90% control was achieved with the fresh bait and total control achieved with the aged bait. Neophobia was considered by the experiment coordinator as being a factor in the results. A poultry and deer breeding farm was chosen for another study on brown rats. Based on census baiting ~150 rats were estimated as existing on site with free access to significant quantities of alternative animal feed. After a 7-day baiting period the population reduction was calculated at 95%. A rat infested restaurant (~81 rats) was chosen for the next study. Aged bait (2 year old) was used resulting in 89.1% control after a short 5-day baiting period. The final study considered the sewer treatment of a rat infestation in Belgium. Wax blocks in polystyrene containers were hung above the high water point in a sewer. 23 days after the initial baits were hung there was a marked reduction in their consumption indicating a reduction in the test population.

The block bait formulation proved to be highly palatable and effective against both rats and mice in the tests. Both fresh and aged baits (6, 12 and 24 months after manufacture) provided 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 block formulation is particularly suitable for baiting in damp or wet conditions (i.e. sewers), whereby it can be moulded into polystyrene jars and hung above the high water level to attract and bait rats. Results from the study carried out in a sewer demonstrated the products effectiveness and inherent resistance to mould growth.

6.2.1. 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 block formulation was provided in the form of laboratory and field studies to verify the proposed label claims.

Product	Codes*	Terms*	GIFAP codes
Block	VIII.3.3	Block-bait	BB

6.2.2. Dose/Mode of action

Blocks 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 block of 30g every 3 to 5 metres
For rats: place 3 blocks of 30g 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 representative product is 50 mg/kg.

6.2.3. 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).

6.2.4. 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.

6.2.5. 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 have been submitted to the Rapporteur Member State about the distribution and incidence of resistance in the house mouse or black rat in Europe. Resistance was discussed comprehensively 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.

6.2.6. 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 Block against the intended target organisms

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
DIFEBLOC, containing 0.005ppm difenacoum	Wild grey mice (*Mus musculus*)	Field study: experiment conducted in restaurant. 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.	*Block bait/ Field efficacy/ Mice /Product at T0* Very good palatability and acceptance for the paraffin block bait DIFEBLOC. Excellent efficacy (97.1%) achieved.	***IIIB5-10_01*** -, LODI, Efficacy trial: Rodenticide block containing 0.005% Difenacoum, against house mice (*Mus musculus*), Trial date: 10th April to 6th May, 2007. Unpublished
DIFEBLOC, containing 0.005ppm difenacoum	Wild grey mice (*Mus musculus*)	Field study: experiment conducted in restaurant. Test was performed on product stored for 2 years.	The method used has been inspired by the French method called "method no. 002 from Biological Trials Commission (C.E.B) ",	*Block bait/ Field efficacy/ Mice / Product at T2 years* Good acceptance for the two year old paraffin block bait, despite the change of food type. The efficacy almost reached the 90 % required by the	***IIIB5-10_02*** -, LODI, Efficacy trial: Rodenticide block containing 0.005% Difenacoum, after 2 years ageing, against

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
			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.	guidelines (89.1%).	house mice (*Mus musculus*), Trial date= 2nd to 29th March, 2009. Unpublished
DIFEBLOC, containing 0.005ppm difenacoum	*Mus domesticus*	Laboratory conditions. Test was performed on product stored for 14 days at 54°C.	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	*10_03_A_Block bait/ Lab efficacy/ Mice / Product at T0.* The study showed that, when freshly manufactured, DIFEBLOC wax block is palatable to Swiss House mice, with a mean palatability against a ground laboratory diet of 66.4%. The formulation also resulted in 100% mortality after a four-day choice between this formulation and challenge diet. It is apparent from this test that the test item, DIFEBLOC wax blocks, when freshly manufactured, should be acceptable for product authorisation.	***IIIB5-10_03a*** Prescoot C.V, Efficacy assessment, using the bait choice feeding test, of Difebloc wax blocks (T0) containing 50 mg.kg-1 difenacoum, using CD-1 albino house mouse, Study reference VPU Study Plan Number VPU/10/004, VPU trial

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
			1980.		No. GB01-10-R009, Project number 153SRI10P, trial code SRIT10-1001-153P. Unpublished
DIFEBLOC, containing 0.005ppm difenacoum	*Mus domesticus*	Laboratory conditions. Test was performed on product stored for 14 days at 54°C.	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.	*10_03_B_Block bait/ Lab efficacy/ Mice / Product at T14days and 54°C* The study showed that, after a storage period of 2 weeks at 54°C, DIFEBLOC wax block is palatable to Swiss House mice, with a mean palatability against the ground laboratory diet of 53.1%. The formulation also resulted in 100% mortality after a four-day choice between this formulation and challenge diet. It is apparent from this test that the test item, DIFEBLOC wax blocks, following storage of 2 weeks at 54°C, should be acceptable for product authorisation.	***IIIB5-10_03b*** Prescott C.V., Efficacy assessment, using the bait choice feeding test, of Difebloc wax blocks (T2weeks accelerated) containing 50 mg.kg-1 difenacoum, using CD-1 albino house mouse, Study reference VPU Study Plan Number VPU/10/005, VPU trial No. GB01-10-R010, Project number 153SRI10P, trial code SRIT10-1002-153P. Unpublished
Belgabloc, containing 0.005ppm difenacoum	Wild brown rats *(Rattus*	Laboratory housing with rats captured in fields from an external enclosure.	The method used has been inspired by the French method called	*Block bait/ Semi field efficacy/ Rats /Fresh product (T0)*	***IIIB5-10_04*** Latteur G., CRA Gembloux, Efficacy

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
	norvegicus)	Test was performed on product stored for 2 years.	"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.	The palatability of BELGABLOC was rated very highly in comparison to safe crushed wheat. In the study BELGABLOC achieved an efficacy specification of 90%.	test performed on BELGABLOC, paraffinic bait block containing 0.005% of Difenacoum, against brown rats (*Rattus norvegicus* Berkenhout), at different storages stages (Appetizing test included), rapport 965, May 1997. Unpublished
Belgabloc, containing 0.005ppm difenacoum	Albinos brown rats *(Rattus norvegicus)*	Laboratory: external enclosure process with species captured in field. Test was performed on fresh product and product stored for 6 months.	The method used has been inspired by the French method called "method no. 002 from Biological Trials Commission (C.E.B) ", Method for practical	*Block bait/ Laboratory efficacy/ Rats /Product at T0 and T6* The palatability of BELGABLOC did not decreased after 6 months of storage at ambient temperature (20°C), it's rate of	***IIIB5-10_05*** Latteur G., CRA Gembloux, Efficacy test through different period of time, performed on BELGABLOC,

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
			efficacy trials of raticides: • Adopted on 1960, derived from the work of Chitty and Dotty in the 1940. • Revised by OEPP in 1980.	active substance also remained intact. The block bait has an efficacy of 95 % at T0 and 100% at T6.	containing 0.005% of Difenacoum, against brown rats (*Rattus norvegicus*), rapport complement 980, April 1998. Unpublished
Probloc, containing 0.005ppm difenacoum	Albinos brown rats *(Rattus norvegicus)*	Laboratory: household process Test was performed on fresh product and product with a storage of 12 months	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.	*Block bait/ Laboratory efficacy/ Rats /Product at T0 and T12* Palatability of PROBLOC did not decreased during 12 months of storage at ambient temperature (20°C). The block bait has an efficacy of 90 % at T0 and 100% at T12.	***IIIB5-10_06*** De Proft M., CRA Gembloux, Efficacy test through different period of time, performed on PROBLOC, bait ready to use, containing 0.005% of Difenacoum, against brown rats (*Rattus norvegicus*), rapport complement 9547,

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
					1999. Unpublished
Racobloc, containing 0.005ppm difenacoum	Wild brown rats *(Rattus norvegicus)*	Laboratory conditions. 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.	*Block bait/ Field efficacy/ Rats / Fresh product (T0)* Very good acceptance of the bait RACO BLOCS despite the changing of food type. Excellent efficacy observed, markedly higher to the 90 % (95%) required by the guidelines.	***IIIB5-10_07*** Grolleau G., Panciroli J., Pest Control Assistance (PCA), Experimentation, in nature, of block bait against rats (*Rattus Norvegicus*) 2005. Unpublished
DIFEBLOC, containing 0.005ppm difenacoum	Wild brown rats *(Rattus norvegicus)*	Field study: experiment conducted in restaurant. Test was performed on product with a storage of	The method used has been inspired by the French method called "method no. 002 from Biological Trials	*Block bait/ Field efficacy/ Rats / Product at T2 years* Good acceptance for the two years old paraffin blocks bait of DIFEBLOC,	***IIIB5-10_08*** -, LODI, Efficacy trial: Rodenticide block containing 0.005%

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
		12 months	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.	despite the changing of food type. Efficacy reaches almost the 90 % required by the guidelines.	Difenacoum, after 2 years ageing, against rats (*Rattus norvegicus*), Trial date= 6th April to 13th May, 2009. Unpublished
Probloc, containing 0.005ppm difenacoum	Sewer rats (*Rattus norvegicus*)	Field: study conducted in sewer The Probloc wax blocks were 150g blocks packed in polystyrene foam jars. Probloc remained stable despite being in a damp environment prone to flooding.	Aim of study was to test the resistance of Probloc to the very damp conditions in a sewer system, to monitor the uptake of the blocks by rats in "field" conditions and to monitor the uptake over time.	*Block bait/ Field efficacy/ Black rat /* Good acceptance of the bait was observed. Blocks were assessed 10 and 23 days after placing the bait. There was a markedly lower consumption at the 2nd assessment timing indicating that the population had diminished dramatically (56% blocks eaten vs 12%). No dead rats were found but this is not unusual in an open sewer system. After 23 days	***IIIB5-10_09*** Field trial with Probloc wax baits against sewer rats, March 1st-23rd 2010. Unpublished.

Test substance	Test organism (s)	Test system	Test conditions	Test results, mode of action, resistance	References
				most of the blocks remaining were still relatively intact considering the difficult environmental conditions.	

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

6.3.1. Description of the intended use(s)

Ruby Block is a rodenticide wax block 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. Use of this product in fields will be covered under the Plant Protection Product Directive. Ruby Block takes the form of a solid waxy block with a strong sweet smell. It contains 0.005 % (w/w) or 50 ppm difenacoum, a second generation 4-hydroxy coumarin, a superwafarin anticoagulant, which causes death due to 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. These are held together with an edible wax such that the block retains its integrity under humid conditions. The blocks are made in a range of shapes and sizes, being typically rectangular, and are available in weights of 20g, 30g and 100g. The blocks are dyed red to make them unattractive to wildlife, birds in particular.

6.3.2. 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.

6.3.2.1. 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**

Parameter	Test material	Species	Result	Classification	Ref.
	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 Toxicity	Difenacoum technical, 97.7 % w/w purity	Rat CRL:(WI)BR (Wistar), female / male	Males: LC_{50} = 20.74µg/L/4h Females: LC_{50} = 16.27µg/L/4h	T+; R26 / Acute Tox. 2; H330	[redacted] (1995) 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-coagulent 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):**

Parameter	Test material	Species	Result	Classification	Ref.
					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 % 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.

6.3.2.2. 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 Block

Parameter	Test material	Species	Result	Classification	Ref.
Acute Oral Toxicity	Difenacoum wax block bait.	Rat, female, Sprague-	LD_{50} > 2000 mg/kg bw	none.	[redacted] (2009). study

Parameter	Test material	Species	Result	Classification	Ref.
	Batch: PB090209	Dawley, SPF Caw, 6 in total.			number: TAO423 PH-09/0085
	Acceptable (Y/N): Yes		**Method:** OECD 423 (2002)		**GLP (Y/N): Yes**
	Comments: No mortality occurred during the study at 2000mg/kg. There were no clinical signs observed. 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). Considering the water solubility of the active substance is extremely low, the use of a water vehicle for gavage is questionable because we do not know the content of difenacoum prior to gavage. 2g of wax block was powdered and mixed with 10 ml water and then filtered before use.				
Acute Dermal Toxicity	Difenacoum wax block bait. Batch: PB090209	Rat, male & female, Sprague-Dawley, SPF Caw, 10 in total.	LD_{50} > 2000 mg/kg bw	none.	[redacted] (2009). study number: TAD PH-09/0085
	Acceptable (Y/N): Yes		**Method:** OECD 402 (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 extremely 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 wax block formulation. Active substance has very low volatility and is only present at 0.005% (w/w) in the solid, wax 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 BLOCK BAIT and the label claims, the rodenticide BLOCK BAIT is not intended to be used in a mix with other biocidal products. Company justification accepted.				
Acute Skin Irritation	Difenacoum wax block bait. Batch: PB090209	Rabbit, male, NZW, 3 in total	No irritation	none	[redacted] (2009). study number: IC-OCDE PH-09/0085
	Acceptable (Y/N): Yes		**Method:** OECD 404 (2002)		**GLP (Y/N): Yes**
	Comments: The test item was reduced to a fine powder with a coffee mill. 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.				
Acute Eye Irritation	Difenacoum wax block bait. Batch: PB090209	Rabbit, male, NZW, 3 in total	Slight irritation	none	[redacted] (2009). study number: IO-OCDE PH-09/0085
	Acceptable (Y/N): Yes		**Method:** OECD 405 (2002)		**GLP (Y/N): Yes**
	Comments: The test item was reduced to a fine powder with a coffee mill. The test item was applied at a dose of 0.1 g instilled into the conjunctival sac of one eye in each animal. After 1 hr the treated eyes of animals A9664 and A9665 were rinsed to				

<table>
<tr><th>Parameter</th><th>Test material</th><th>Species</th><th>Result</th><th>Classification</th><th>Ref.</th></tr>
<tr><td></td><td colspan="5">wash out remaining residual material. Ocular conjunctivae reactions observed during the study were slight to moderate and totally reversible by 48 hr in the three animals. Company report accepted. Results (expressed as mean of the 24, 48 and 72 hr time points per animal) do not warrant classification.
<table>
<tr><th>Animal number</th><th>A9650</th><th>A9664</th><th>A9665</th></tr>
<tr><td>Corneal Opacity</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>Iritis</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>Redness</td><td>1.7</td><td>0.7</td><td>0.7</td></tr>
<tr><td>Chemosis</td><td>1.0</td><td>0.3</td><td>0.3</td></tr>
<tr><td>Result</td><td>negative</td><td>negative</td><td>negative</td></tr>
</table></td></tr>
<tr><td>Skin Sensitisation (M&K)</td><td>Difenacoum wax block bait. Batch: PB090209</td><td>Guinea Pig, female, Dunkin-Hartley strain, 5 in negative control, 11 in treated groups.</td><td>negative</td><td>none</td><td>[redacted] (2009). study number: SMK PH-09/0085</td></tr>
<tr><td></td><td colspan="2">Acceptable (Y/N): No</td><td colspan="2">Method: OECD 406 (1992)</td><td>GLP (Y/N): Yes</td></tr>
<tr><td></td><td colspan="5">Comments: The test item was reduced to a fine powder with a coffee mill but then assessed as unsuitable for intradermal injection. Changes made to the protocol of the GPMT included induction by topical application only. This test should have being revised and concluded as a Buehler test instead of an M&K test in order to carefully ascertain the results. In its present form it is similar to a Buehler but with too few animals in the study. Potentiation by injection of test material with Freund's Complete Adjuvant has not been performed; taking all these things into consideration the company report is rejected. Suitable positive controls were reported. In the original CAR, the applicant submitted two sensitisation studies with a 2.5% liquid concentrate of difenacoum, one Magnusson & Kligman test and one Buehler test (see Doc IIIA, CAR). The RMS concluded that the available studies (both negative) provided sufficient evidence for no sensitisation potential by the active substance. It is therefore unlikely that the product ruby wax is a skin sensitiser on the basis of its difenacoum content.</td></tr>
</table>

Conclusion:
According to the results of the toxicological studies, Ruby Block (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 does not seem to be 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 x 10^{-4} g/l at pH 6.5 or < 0.5mg per litre, 3.72 x 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.

6.3.2.3. 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 Block

Co-formulant	Function	% w/w	CAS/EU no.	EU Current Classification
Denatonium Benzoate (+other components of the difenacoum concentrate)	Bittering agent	0.001 (+0.194)	3734-33-6	Xn; R20/22 Xi; R37, R38, R41 N; R52/53 (MSDS PelGar)
				Acute Tox4; H332/H302 STOT SE 3 ; H335 Skin irritation2 ; H315 Eye damage 1 ; H318 Aquatic Chronic 3; H412r)
Cochineal Red 4R E124	Food dye	0.68	2611-82-7	Not classified
Propylene glycol	Co-solvent	2.38	57-55-6	Not classified
Potassium Sorbate	Bitter agent	0.04	24634-61-5	Xi; R36 (MSDS Brenntag)
				Eye Irritation 2; H319
Natural Vanilla Aroma	Aromatic agent	0.02		Not classified
Paraffin waxes	Bait base	26.80		Not classified
Flour	Bait base	60.88		Not classified
Splinter of Maize		2.40		Not classified
Splinter of wheat		3.60		Not classified
Sugar		3.00		Not classified

6.3.3. Exposure Assessment for Human Health

The most relevant route of exposure to the active substance is the dermal route. For exposure assessment only active substance from wax blocks has been modelled. The block product typically takes the form of a solid waxy block with a strong sweet smell containing 0.005% w/w difenacoum. The 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, inhalation exposure is irrelevant. Inhalation exposure from handling grain bait during loading/application and cleaning is also proposed as negligible. The

only relevant inhalation exposure is assumed to be that from the decanting of loose grain, pellets and granules due to the potential release of airborne dusts.

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, (teratogenicity 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 Block 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**

6.3.3.1. Exposure to professional users

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 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 of 10 blocks. 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 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 – 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 (20g wax block baits, 5 blocks/bait box) 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 x 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 × (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 product to five bait sites 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%**

6.3.3.2. 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.

6.3.3.3. 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. 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:

$3.4\times10^{-4} / 2.5\times10^{-2}$ = **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.

6.3.3.4. Exposure to consumers from residues in food

Not applicable.

6.3.3.5. 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 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.

6.3.4. Risk Characterisation for Human Health

6.3.4.1. 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.

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) without 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.

6.3.4.2. Non-professional users

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.

6.3.4.3. 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.

6.3.4.4. Consumers from residues in food

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

6.3.4.5. 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 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 ecotoxicology 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".*[33]

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 IE-CA 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 IE-CA 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}*

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mg/l, with PNECwater of 0.06 µg/l the risk ratio will be 0.00016[34]. 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 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."[19]

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 IE-CA 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.[35] The IE-CA 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 PNECwater 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 is 480µg/l (the limit of solubility). In the absence of any ecotoxicological data for sediment-dwelling organisms, the PNECsediment was calculated using the equilibrium partitioning method resulting in a value of 2.51 mg/kg (wet weight).

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

35 "*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)

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 PNECsoil of 0.877 mg/kg wet weight was determined.

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

Difenacoum is very toxic to birds, with the $PNEC_{oral}$ of birds determined to be 0.5 µg/kg food or 0.1 µg/kg bw/d. Difenacoum is also very toxic to mammals The PNECoral 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 Blocks 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 Block 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 Block, 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, in sewers, and open areas. The product is applied as a wax block in secured bait stations. The directions for use including minimum and maximum application rates are:

Rats: 90-100 g of blocks spaced 10 m apart (5 m apart in high infestation areas). Typical treatment time 6 weeks.

Mice: 20-30 g of blocks spaced 5 m apart (3 m apart in high infestation areas). Typical treatment time 6 weeks.

3.3.6-1. Aquatic compartment

Ruby Block is used in sewer systems to control rats and mice. Consequently, exposure to the aquatic compartment occurs through the STP route. Based on worst case assumptions [36] 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 to 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 wax blocks 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.

[36] Realistic worst-case: 21 days campaign

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

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 2.41x 10^{-3} mg/kg wwt. The highest concentration of difenacoum in soil from in and around buildings[37] is 0.0348 mg/kg wwt under realistic worst case conditions (200 g of product/bait point, each bait point is 5 m apart).

The notifier also proposes to use the product in open areas. The IE-CA notes no scenario is prescribed in the ESD for the use of wax blocks in open areas. The notifier used the scenario for the outdoor use of impregnated grain in open areas to support the authorisation of the wax block. This approach has been used in the past for other rodenticides and is deemed acceptable by the IE-CA. 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. However, the IE-CA notes the ESD states "Wax blocks are only allowed for use in feeding stations in the Nordic countries; however, in many other countries in the EU wax blocks (100-200 g) may be placed directly inside holes. 20-30 g wax block baits are also commonly used in several countries e.g. in UK." Consequently, the use of 200 g by the notifier in the exposure assessment seems reasonable and is deemed acceptable by the IE-CA. 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[38], the maximum concentration in soil from applications in waste dumps is predicted to be 0.0082 mg/kg wwt.

37 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 double the proposed amount.

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 wax blocks)

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

38 Waste dumps

Amount of product used in control operation per application: For high infestations of rats the blocks are spaced 5 m apart. This could potentially result in a maximum of ~441 blocks (21, 100 m lines of 21 blocks, 5 m apart) in a 1 ha area during high infestations. This would correspond to ~44.1 kg of product

No. of replenishments: 7

Fraction of active ingredient released to soil through excreta and dead bodies 0.9.

Area of waste dump: 1 ha

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.

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 wax blocks 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 □g/L.

Table 3.3.6.4-1. Predicted Environmental Concentration (□g/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 blocks are spaced 5 m apart. According to calculations provided by the IE-CA this could potentially result in a maximum of 441 blocks (21 100 m lines of 21 blocks, 5 m apart) in a 1 ha area during high infestations. This would correspond to ~44.1 kg of product. This is higher than the default value considered in the ESD under realistic worst-case conditions. Consequently the notifiers exposure calculation is not sufficient to support this use. The IE-CA generated new exposure calculations for this use

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 baits. 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 Blocks. 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 Blocks result in unacceptable risks to birds and mammals (see ANNEX VI).

3.3.7. Risk Characterisation for the Environment

Ruby Block is used in sewer systems, in and around buildings, open areas and waste dumps to control rats and mice. Exposure to the aquatic compartment occurs through the STP route. Exposure of soil to the active substance occurs via residues present in sewage sludge after using wax blocks in sewers 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 Blocks 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 Block 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 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 wax blocks 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 Block 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: sewers, in and around buildings, open areas and waste dumps. Therefore, normal use of Ruby Blocks 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 Block bait. One day's consumption of difenacoum 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's 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 Block 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% of the total ingested. 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 Blocks. Due to high food intake in relation to the body weight, 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 Block 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 when 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 Blocks. The derivation of $PNEC_{oral}$ for birds and mammals is outlined in Annex VI. The derivation of PEC values for mammals and birds that consume fish and earthworms is outlined in ANNEX VI. These values assume direct ingestion of Ruby Block by the prey, and rely 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 Block 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 Blocks, 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 Block, 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 with lower residues in other tissues including the fat tissue. 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 carries s 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 should 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.
- For use in sewers where there is no risk to children, companion animals and non-target species blocks should be secured to available structures by wire to ensure the block is not washed away.
- 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:

This product contains paraffin wax, which is combustible and vapours from molten wax are flammable.

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 required, 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

This product contains paraffin wax.

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 Block, 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 Block 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.

From the results of acute toxicology studies presented for the product, Ruby Block (containing 0.0055 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. 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.

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 secured in sealed packs and 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. Additionally, baits should be placed in areas inaccessible to children.

An environmental exposure and effects assessment for the product indicated that difenacoum in Ruby Block 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 Block does not adversely impact non-target organisms in the aquatic or terrestrial compartments when used according to label instructions. However, there is a high potential 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 appropriate and available risk mitigation measures, as outlined in section 3.4.

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 Block 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 Block is for a period of 5-years with an annual renewal.

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

Only ready-to-use Ruby Block 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 rats and mice (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 only 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. The product can also be utilised in sewers. 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 be used for rodent control in tamper resistant, secured bait stations or other secure coverings. However, for use in sewers where there is no risk to children, companion animals and non-target species blocks should be secured to available structures by wire to ensure the block is not washed away.

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

Wax blocks shall be secured to the bait station(s) so that rodents cannot 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.

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 Block, the authorisation holder shall provide statistics to PRCD on the import and export from Ireland and also manufacture statistics where appropriate for Ruby Block 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.