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 MAJOR CHANGE AND RENEWAL OF NATIONAL AUTHORISATION APPLICATIONS**

(submitted by the evaluating Competent Authority)



TITANIUM B

Product type 14

[Difenacoum as included in the Union list of approved active substances]

Case Number in R4BP: [BC-HL033256-41 and BC-PJ034272-42]

Evaluating Competent Authority: [FR]

Date: [28/12/2018]

Contents

[0 History of the dossier (updated PAR – 2017) 4](#_Toc532482121)

[1 General information about the product application (initial PAR – 2013) 6](#_Toc532482122)

[1.1 Applicant 6](#_Toc532482123)

[1.2 Current authorisation holder 7](#_Toc532482124)

[1.3 Proposed authorisation holder 7](#_Toc532482125)

[1.4 Information about the product application 8](#_Toc532482126)

[1.5 Information about the biocidal product 8](#_Toc532482127)

[1.5.1 General information 8](#_Toc532482128)

[1.5.2 Information on the intended use(s) - initial PAR – 2013 9](#_Toc532482129)

[1.5.3 Information on active substance(s) 11](#_Toc532482130)

[1.5.4 Information on the substance(s) of concern 12](#_Toc532482131)

[1.6 Documentation 12](#_Toc532482132)

[1.6.1 Data submitted in relation to product application 12](#_Toc532482133)

[1.6.2 Access to documentation 14](#_Toc532482134)

[2 Summary of the product assessment 15](#_Toc532482135)

[2.1 Identity related issues – PAR 2013 15](#_Toc532482136)

[2.2 Classification, labelling and packaging 15](#_Toc532482137)

[2.2.1 Harmonised classification of the biocidal product 15](#_Toc532482138)

[2.2.2 Labelling of the biocidal product 15](#_Toc532482139)

[2.2.3 Packaging of the biocidal product 16](#_Toc532482140)

[2.3 Physico/chemical properties and analytical methods 17](#_Toc532482141)

[2.3.1 Active ingredient 17](#_Toc532482142)

[2.3.2 Biocidal product 19](#_Toc532482143)

[2.4 Effectiveness against target organisms 30](#_Toc532482144)

[2.4.1 Function 30](#_Toc532482145)

[2.4.2 Organism(s) to be controlled and products, organisms or objects to be protected. 30](#_Toc532482146)

[2.4.3 Effects on Target organisms 31](#_Toc532482147)

[2.4.4 Mode of action including time delay 33](#_Toc532482148)

[2.4.5 Occurrence of resistance 33](#_Toc532482149)

[2.4.6 Evaluation of the Label Claims 34](#_Toc532482150)

[2.4.7 Summary of efficacy assessment 35](#_Toc532482151)

[2.5 Exposure assessment 36](#_Toc532482152)

[2.5.1 Description of the intended use(s) – PAR 2013 36](#_Toc532482153)

[2.5.2 Assessment of exposure to humans and the environment 36](#_Toc532482154)

[2.6 Risk assessment for human health 37](#_Toc532482155)

[2.6.1 Hazard potential 37](#_Toc532482156)

[Risk assessment for human health 39](#_Toc532482157)

[2.6.2 Human exposure assessment 40](#_Toc532482158)

[2.6.3 Risk characterisation 48](#_Toc532482159)

[2.7 Risk assessment for the environment (PAR 2013) 51](#_Toc532482160)

[2.7.1 Distribution of the active substance, difenacoum, in the environment 51](#_Toc532482161)

[2.7.2 Effects of the active substance on environmental organisms 53](#_Toc532482162)

[2.7.3 Effects on environmental organisms for biocidal product 57](#_Toc532482163)

[2.7.4 Environmental exposure assessment 57](#_Toc532482164)

[2.7.5 Risk characterisation for the environment 66](#_Toc532482165)

[2.8 Measures to protect man, animals and the environment 71](#_Toc532482166)

[3 Proposal for the decision – major change and renewal 2018 72](#_Toc532482167)

[Annex 1: List of studies reviewed 87](#_Toc532482225)

[Annex 2: Analytical methods residues – active substance – 2013 96](#_Toc532482226)

[Annex 3: Efficacy of the active substance from its use in the product – 2013 updated 2017 99](#_Toc532482227)

[Annex 4: Toxicology and metabolism –active substance - 2013 107](#_Toc532482228)

[Annex 5: Toxicology – biocidal product, 2013 108](#_Toc532482229)

[Annex 6: Safety for professional operators, 2013, updated 2017 110](#_Toc532482230)

[Annex 7: Safety for non-professional operators and the general public, 2013 111](#_Toc532482231)

[Annex 8: Residue behaviour 112](#_Toc532482232)

[Annex 9: Technical equivalence of the Pelgar source of Difenacoum 113](#_Toc532482233)

**Note to the reader:**

This consolidated PAR for the evaluation of the submitted post-autorization data for TITANIUM B is based on the PAR of the reference product, in which all necessary addenda have been included.

In part 1 and 2 of this consolidated PAR:

* each section contains the initial assessment and the subsequent successive assessments (minor change, major change, post authorisation data, same...) in a chronological order. These assessments are pointed out with specific titles corresponding to the type of application and the year at which it was delivered.
* the assessments related to post-authorization data assessment are at the end of each section and are highlighted in grey.

In part 3 of the consolidated PAR “proposal for decision”: the summary of product characteristics is pointed out and corresponds to the decision for post-autorization data assessment.

**Disclaimer regarding user category**

For the risk assessment of PT14, two user categories have been addressed depending on the quantity of manipulated product and the possibility of using PPE: non-professional users and professional users.

In France, any professional user needs a dedicated national certificate, hence it is expected that he/she has the required competence to access to biocidal products that are authorized for professional users they are thus considered as « trained professional users ».

Consequently, in the SPC in Part 3, uses for “professionals” are mentioned according to the agreed standard SPC, but they not relevant in France. It is proposed that each cMS adapts the conditions of authorization of the product according to its own legislation.

# History of the dossier

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Application type** | **refMS** | **Case number in the refMS** | **Decision date** | **Assessment carried out (i.e. first authorisation / amendment / renewal)** |
| NA-APP | *FR* | n.a. | 10/10/2013 | Initial assessment: SORKIL G GRAINS |
| NA-BBS | *FR* | BC-ES025333-36 | 05/07/2017 | Same product: TITANIUM B |
| NA-MAC | *FR* | BC-HL033256-41 | 28/12/2018 | *Reduction of the concentration of difenacoum (from 0.005 % to 0.0025 %)*  *Modification of the product composition*  *Addition of a user category (non-professionals)* |
| NA-RNL | *FR* | BC-PJ034272-42 | 28/12/2018 | *Renewal of the authorisation and Post-authorisation data* |
| Post-autorisation data | *FR* | - | - | *Post-Autorisation data assessment :* |

n.a.: not applicable

**Authorised uses - 2017**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Users** | **Target organisms** | **Application rate** | **Field of use** | **Packagings** |
| Professionals | Rats (*Rattus rattus* and *Rattus norvegicus*) | 80 g to 200 g of product / bait station at distances of 15 meters apart | Indoor and outdoor around buildings | Individual sachets Unwrapped |
| Mice (*Mus musculus*) | 25 g to 30 g of product / bait station at distances of 3 meters apart |

**Intended uses for major change and renewal - 2017**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Users** | **Target organisms** | **Application rate** | **Field of use** | **Packagings** |
| Professionals | Rats (*Rattus rattus* and *Rattus norvegicus*) | 80 g to 200 g of product / bait station at distances of 15 meters apart | Indoor  and outdoor around buildings | Individual sachets  Unwrapped Pre-filled bait stations |
| Mice (*Mus musculus*) | 25 g to 30 g of product / bait station at distances of 3 meters apart |
| Non professionnals | Rats (*Rattus rattus* and *Rattus norvegicus*) | 80 g to 200 g of product / bait station at distances of 15 meters apart | Indoor  and outdoor around buildings | Individual sachets  Pre-filled bait stations |
| Mice (*Mus musculus*) | 25 g to 30 g of product / bait station at distances of 3 meters apart | Indoor |

# General information about the product application (initial PAR – 2013)

## Applicant

|  |  |
| --- | --- |
| **Company Name:** | EDIALUX France |
| **Address:** | ZA Macon Est |
| **City:** | Replonges |
| **Postal Code:** | F-01750 |
| **Country:** | France |
| **Telephone:** | 00.33.385.356.714 |
| **Fax:** | - |
| **E-mail address:** | - |

**Person authorised for communication on behalf of the applicant:**

|  |  |
| --- | --- |
| **Name:** | Dominique AMBROSI |
| **Function:** | Director of Ambrosi Scientific Consulting |
| **Address:** | Les chevrières |
| **City:** | Chaintré |
| **Postal Code:** | F-71570 |
| **Country:** | France |
| **Telephone:** | 00.33.385.356.714 |
| **Fax:** | - |
| **E-mail address:** | dambrosi@ambrosiconsulting.com |

* **Major change and renewal applications - 2018**

|  |  |
| --- | --- |
| **Name:** | Virginie VIDEAU |
| **Function:** |  |
| **Address:** | ZA Macon Est |
| **City:** | Replonges |
| **Postal Code:** | F-01750 |
| **Country:** | France |
| **Telephone:** | 00 33 385 31 89 10 |
| **Fax:** | - |
| **E-mail address:** | virginie.videau@edialux.com |

## Current authorisation holder

|  |  |
| --- | --- |
| **Company Name:** | EDIALUX France |
| **Address:** | ZA Macon Est |
| **City:** | Replonges |
| **Postal Code:** | F-01750 |
| **Country:** | France |
| **Telephone:** | 00.33.385.356.714 |
| **Fax:** | - |
| **E-mail address:** | - |
| **Letter of appointment for the applicant to represent the authorisation holder provided (yes/no):** | No |

## Proposed authorisation holder

|  |  |
| --- | --- |
| **Company Name:** | EDIALUX France |
| **Address:** | ZA Macon Est |
| **City:** | Replonges |
| **Postal Code:** | F-01750 |
| **Country:** | France |
| **Telephone:** | 00.33.385.356.714 |
| **Fax:** | - |
| **E-mail address:** | - |
| **Letter of appointment for the applicant to represent the authorisation holder provided (yes/no):** | No |

## Information about the product application

|  |  |
| --- | --- |
| **Application received:** | 2012-03-17 |
| **Application reported complete:** | 2010-06-22 |
| **Type of application:** | Product authorisation |
| **Further information:** | - |

## Information about the biocidal product

### General information

|  |  |
| --- | --- |
| **Trade name:** | SORKIL G GRAINS |
| **Manufacturer’s development code number(s), if appropriate:** | EDI-300 |
| **Product type:** | PT14 - Rodenticide |
| **Composition of the product (identity and content of active substance(s) and substances of concern; full composition see confidential annex):** | Active substance’s identity and content: Difenacoum 0.005% w/w  No substance of concern |
| **Formulation type:** | Grain bait |
| **Ready to use product (yes/no):** | Yes |
| **Is the product the very same (identity and content) to another product already authorised under the regime of directive 98/8/EC (yes/no);**  **If yes: authorisation/registration no. and product name:**  **or**  **Has the product the same identity and composition like the product evaluated in connection with the approval for listing of active substance(s) on to Annex I to directive 98/8/EC (yes/no):** | No  No |

* **Assessment of major change and renewal (2018)**

|  |  |
| --- | --- |
| **Trade name:** | TITANIUM B |
| **Manufacturer’s development code number(s), if appropriate:** | EDI-300\_25 |
| **Product type:** | PT14 - Rodenticide |
| **Composition of the product (identity and content of active substance(s) and substances of concern; full composition see confidential annex):** | Active substance’s identity and content: Difenacoum 0.0025% w/w  No substance of concern |
| **Formulation type:** | Grain bait |
| **Ready to use product (yes/no):** | Yes |
| **Is the product the very same (identity and content) to another product already authorised under the regime of directive 98/8/EC (yes/no);**  **If yes: authorisation/registration no. and product name:**  **or**  **Has the product the same identity and composition like the product evaluated in connection with the approval for listing of active substance(s) on to Annex I to directive 98/8/EC (yes/no):** | No  No |

### Information on the intended use(s) - initial PAR – 2013

|  |  |
| --- | --- |
| **Overall use pattern (manner and area of use):** | **Professional Uses**  Rodenticide used indoors and around industrial and commercial buildings including farm buildings  **Non-professional uses**  Rodenticide used in and around buildings  Field of use  IV.1 indoor use  IV.2 outdoor use |
| **Target organisms:** | I.1.1.1 Brown rat: *Rattus norvegicus*  I.1.1.2 Roof rat, House rat: *Rattus rattus*  I.1.1.3 House mouse: *Mus musculus* |
| **Category of users:** | V1 Non professional / general public  V.2 Professional  V.3 Specialised professional |
| **Directions for use including minimum and maximum application rates, application rates per time unit (e.g. number of treatments per day), typical size of application area:** | Method of application  VI.2: covered application  VI.2.1: covered application in bait stations or under cover.  The product is a ready to use grain bait and contains 50 ppm of difenacoum.  The product is applied manually, at measured amounts in secured bait boxes. The applicator uses gloves.  The product is placed in commercially available bait stations. Only professionals may use an alternative of commercial bait stations as bait trays inside pieces of drainage pipe or under sections of slate, board or corrugated iron which are firmly popped against a wall and suitable weighted.  For rat control, the recommended dose is 80 - 200 g of product at distances depending on infestation rate of up to 15 meters between 2 stations depending on infection rate. For mouse control, the recommended dose is 25 - 30 g of product at distances of up to 3 meters between 2 stations depending on infestation rate.  The common strategy is to explore the site, locate runs, burrows, droppings or signs of damage and place the bait boxes at entry points into buildings and around area where rats are known to feed. For the mice control, as mice are sporadic feeders, many bait points are placed throughout the area where mice are known to feed.  Bait points are inspected frequently and replenished when bait take is observed. At starting of treatment: interval for inspection is twice a week, afterwards weekly. During the bait inspections, also a search in the zone will be done for dead rodents. These rodents will be eliminated following local requirements in order to avoid secondary poisoning of predators.  When no further bait take is observed, bait stations should not been left in place, All bait stations should be removed from the site, cleaned up and the bait and bait remainders should be disposed of in accordance with local requirements. |
| **Potential for release into the environment (yes/no):** | No |
| **Potential for contamination of food/feedingstuff (yes/no)** | No |
| **Proposed Label:** | For rat control, the recommended dose is 80 g up to 200 g of product at distances of up to 15 meters apart.  For mouse control, the recommended dose is 25 g up to 30 g of product at distances of 3 meters apart. |
| **Use Restrictions:** | Use only in secured bait stations out of reach of children and domestic animals.  Good field practice of rodent control involves several measures as cleaning-up of bait and bait containers after treatment period, removing any potential harbourages, etc. |

### Information on active substance(s)

|  |  |
| --- | --- |
| **Active substance chemical name:** | Difenacoum |
| **CAS No:** | 56073-07-5 |
| **EC No:** | 259-978-4 |
| **Purity (minimum, g/kg or g/l):** | > 99.5% w/w |
| **Inclusion directive:** | [2008/81/EC](http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32008L0081:EN:NOT) |
| **Date of inclusion:** | 1st April 2010 |
| **Is the active substance equivalent to the active substance listed in Annex I to 98/8/EC (yes/no):** | Yes |
| **Manufacturer of active substance(s) used in the biocidal product:** |  |
| **Company Name:** | Pelgar International Ltd |
| **Address:** | Unit 13, Newman Lane |
| **City:** | Alton, Hampshire |
| **Postal Code:** | GU34 2QR |
| **Country:** | Great Britain |
| **Telephone:** | + 44(0) 1420 80744 |
| **Fax:** | + 44(0) 1420 80733 |
| **E-mail address:** | info@pelgar.co.uk |

* **Renewal application (2018)**

**COMPARATIVE ASSESSMENT**

The claimed product formulation and more specifically the active substance concentration for the renewal application (0.0025% w/w) are identical to what was assessed in the frame of the major change application.

Difenacoum does meet the exclusion criteria laid down in Article 5(1)(c) of Regulation (EU) No 528/2012. Difenacoum does meet the conditions laid down in Article 10(1)(a) and (e) of Regulation (EU) No 528/2012 if approved, and is therefore considered as a candidate for substitution.

A comparative assessment has been carried out at the European level. According to Article 1 of Commission Implementing Decision (EU) 2017/1532 of 7 September 2017 addressing questions regarding the comparative assessment of anticoagulant rodenticides in accordance with Article 23(5) of Regulation (EU) No 528/2012 of the European Parliament and of the Council. 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.

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.

### Information on the substance(s) of concern

SORKIL G GRAINS does not contain any substance of concern according to the Technical Notes for Guidance on data requirements.

## Documentation

### Data submitted in relation to product application

**Identity, physicochemical and analytical method data**

Physico-chemical studies on SORKIL G GRAINS were provided by Edialux: appearance, density, storage stability, dustiness, attrition resistance, flowability and particle size distribution.

Other physico-chemical studies on another product were provided by Edialux too: flammability, autoflammability, explosive and oxidising properties.

An analytical method to determine the content of the active substance in the formulation SORKIL G GRAINS has been provided by Edialux.

Data on the active substance required at the product authorization stage as stated in the AR about the active substance have been provided by Pelgar:

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

**Post-authorisation data:**

* 2 year storage stability test under room temperature of Sorkil G = EDI-300 in polypropylene (PP) bags
* **Assessment of major change and renewal (2018)**

The following studies were submitted:

* Report n° 17-904017-005. 2017. Chemical stability during and after an accelerated storage procedure for 8 weeks at 40 ± 2°C on EDI-300\_25.
* Report n° 17-904017-006. 2017. Storage procedure for 6 months at 20±2 °C.
* Report n° 17-904017-008. 2017. Validation of analytical method for the determination of difenacoum in the EDI-300\_25.
* **Assessment of post-authorisation data (2021):**

The following study was submitted:

Final Report n° 17-904017-010. 2019. Chemical stability after a storage procedure for 24 months at 20 ± 2°C on EDI-300\_25.

**Efficacy data**

* **First authorization SORKIL G GRAINS 2013**

The following efficacy studies were submitted:

* Bait choice - **EDI 200 BB-ROD** fresh bait with 0.005% difenacoum, Mice (***Mus musculus***)
* Bait choice - **EDI 200 BB-ROD** fresh bait with 0.005% difenacoum, Rats (***Rattus norvegicus***)
* Bait choice - **EDI 200 BB-ROD** aged bait with 0.005% difenacoum, Mice (***Mus musculus***)
* Bait choice - **EDI 200 BB-ROD** aged bait with 0.005% difenacoum, Rats (***Rattus norvegicus***)
* Palatability and efficiency of **EDI 200 AB-ROD** for rats and mice in the field
* Effectiveness of **SORKIL-G**, rodenticide based on 0.005% difenacoum, against the grey mouse (***Mus musculus* L.**). (Test performed in a pig stock)
* Effectiveness of **SORKIL-G**, rodenticide based on 0.005% difenacoum, against the brown rat (***Rattus norvegicus* berkenhout**). (Test performed indoors)
* Evaluation of the loss of effectiveness through ageing of the rodenticide **SORKIL-G**, based on 0.005% difenacoum, for the elimination of the brown rat (***Rattus norvegicus* berkenhout**) and the grey mouse (***Mus musculus* L.**).

The studies were performed on whole wheat formulations: **SORKIL G** and **SORKIL G GRAINS** (see detailed composition in confidential document). These formulations are different from SORKIL G GRAINS because of the type of grain, the dyestuff and the content of appetent agents. But as these products are grain formulations containing 50 ppm of difenacoum and the same rate of bittering agent, the results can be taken into account in order to support the product authorization of SORKIL G GRAINS.

* **Assessment of major change and renewal (2018)**

The following efficacy studies were submitted:

* A free-choice laboratory test was carried out with house mice (*Mus musculus*), with the product EDI-300\_24 (0.0024 % w/w difenacoum).
* A free-choice laboratory test was carried out with brown rats (*Rattus norvegicus*), with the product EDI-300\_24 (0.0024 % w/w difenacoum).
* A free-choice laboratory test was carried out with black rats (*Rattus rattus*), with the product EDI-300\_24 (0.0024 % w/w difenacoum).
* A free-choice laboratory test was carried out with house mice (*Mus musculus*), with the product EDI-600\_24 (0.0024 % w/w bromadiolone).
* A free-choice laboratory test was carried out with brown rats (*Rattus norvegicus*), with the product EDI-600\_24 (0.0024 % w/w bromadiolone).
* A free-choice laboratory test was carried out with black rats (*Rattus rattus*), with the product EDI-600\_24 (0.0024 % w/w bromadiolone).
* A field test was carried out with house mice (*Mus musculus*), with the product EDI 600\_24 (0.0024 % w/w bromadiolone).
* A field test was carried out with brown rats (*Rattus norvegicus*), with the product EDI-600\_24 (0.0024 % w/w bromadiolone).
* A field test was carried out with black rats (*Rattus rattus*), with the product EDI-600\_24 (0.0024 % w/w bromadiolone).
* A free-choice laboratory test was carried out with black rats (*Rattus rattus*), with exposure to a 26 months aged formulation of the product EDI-300\_24 (0.0024 % w/w difenacoum).

**Toxicology data**

The applicant did not submit new toxicological data on active substance. Acute dermal toxicity, skin and eye irritation and skin sensitisation studies have been provided on another grain formulation containing 0.005% difenacoum. A dermal penetration study was submitted with a difenacoum pellet bait. Extrapolation to SORKIL G GRAINS was accepted since it is expected that the differences do not impact the toxicity.

**Ecotoxicology data**

The applicant has not provided ecotoxicological study with the biocidal product. The environmental risk assessment for SORKIL G GRAINS has been done by the Reference Member State using the Competent Authority Report on the active substance difenacoum supported by the Task Force Activa/Pelgar.

### Access to documentation

In the frame of the authorisation of SORKIL G GRAINS supported by Edialux France, the applicant Edialux France has submitted a letter of access to all data on difenacoum submitted by Pelgar International Ltd under directive 98/8/EC for the purpose of Annex I listing.

# Summary of the product assessment

## Identity related issues – PAR 2013

A new 5-batch analysis has been submitted by Pelgar at the EU level. The assessment of the technical equivalence of the new 5-batch analysis versus the reference source of Pelgar used for annex I inclusion has been performed. The conclusion is that the source of Pelgar with the new specifications used in SORKIL G GRAINS is technically equivalent to the source of Pelgar assessed for annex I inclusion.

The confidential document presenting this assessment is attached to this PAR. See the confidential appendix “Technical equivalence Difenacoum Pelgar (new specifications)” for detailed information.

The composition of the product is confidential and is presented in a confidential annex. There is no substance of concern.

## Classification, labelling and packaging

### Harmonised classification of the biocidal product

No classification is required for SORKIL G GRAINS.

### Labelling of the biocidal product

No labelling is required for SORKIL G GRAINS.

* **Assessment of major change and renewal (2018)**

**Classification and labelling of the products according to the Regulation (EC) 1272/2008**

Classification of the product TITANIUM B according to the CLP Regulation (EC) 1272/2008 (ATP9) is as follows:

| **Classification** | |
| --- | --- |
| Hazard category | STOT RE 2 |
| Hazard statement | H373 (blood): May cause damage to organs through prolonged or repeated exposure |
|  | |
| **Labelling** | |
| Signal words | Warning |
| Hazard statements | H373 (blood): May cause damage to organs through prolonged or repeated exposure |
| Precautionary statements | P101 If medical advice is needed, have product container or label at hand.  P102 - Keep out of reach of children.  P103 - Read label before use.  P260: Do not breathe dust/fumes/gas/mist/vapours/spray.  P314: Get medical advice/attention if you feel unwell.  P501: Dispose of contents/container in accordance with local/regional/national/international regulation |
|  | |
| Note | **-** |

### Packaging of the biocidal product

The packaging of the biocidal product as deposited by the notifier is:

**For professional users:**

SORKIL G GRAINS is supplied in sachet or loose.

PP sachets (20-200 g for rats and 25-30 g for mice) are packed in:

- PP, PE or HDPE bucket (800 g-10 kg)

- Cardboard box (800 g-10 kg)

- Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) (800 g-25 kg)

- Tamper resistant prefilled bait station in cardboard box (200 g-10 kg)

Loose baits are packed in:

- PP bucket (800g-10kg)

- Cardboard box with one PP bag inside (800g-10kg)

- Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) with one PP bag inside (800g-25kg)

**For non-professional users:**

SORKIL G GRAINS is supplied only in sachet.

PP sachets (20-200g for rats and 25-30g for mice) are packed in:

- PP or HDPE bucket (150g-1.5kg)

- Cardboard box (150g-1.5kg)

- Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) (150g-1.5kg)

- Tamper resistant prefilled bait station in cardboard box (25g-1.5kg)

* **Assessment of major change and renewal (2018)**

**Packagings accepted by FR CA for the major technical modification of the product TITANIUM B:**

**For professional users:**

Minimum pack size of 3 kg (in France: 5 kg)

TITANIUM B is supplied in sachet or loose.

PP sachets (20-200 g for rats and 25-30 g for mice) are packed in:

- PP, PE or HDPE bucket (3-10 kg);

- Cardboard box (3-10 kg);

- Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) (3-25 kg);

- Prefilled bait station in cardboard box (3-10 kg).

Loose baits are packed in:

- PP bucket (3-10 kg);

- Cardboard box with one PP bag inside (3-10 kg);

- Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) with one PP bag inside (3-10 kg).

In accordance with HEEG Opinion 12 packaging for loose bait is limited to 10 kg in order to avoid inhalation exposure during decanting.

**For non professional users:**

TITANIUM B is supplied only in sachet.

PP sachets (20-150 g for rats and 25-30 g for mice) are packed in:

- PP or HDPE bucket (up to 150 g)

- Cardboard box (up to 150 g)

- Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) (up to 150 g)

- Prefilled bait station in cardboard box (up to 150 g)

## Physico/chemical properties and analytical methods

### Active ingredient

#### Identity, origin of active ingredient

The source of the active substance used in the product SORKIL G GRAINS is equivalent to one of the sources used for annex I inclusion.

#### Physico-chemical properties and analytical methods for determination of active ingredient and impurities in the technical active ingredient – PAR 2013

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

**Physico-chemical properties**

1- Appearance of the active substance

Results of the assessment: the data provided are acceptable. The results are reported below:

Table 1: Physico-chemical properties of the active substance:

|  | Method/ Guideline | Purity/Specification | Result | Reference |
| --- | --- | --- | --- | --- |
| Physical state | Visual assessment in accordance with Council Directive 98/8/EC, Annex IIA, III, 3.3 | Purity: 99.5% w/w difenacoum,  Batch number 04253 | Slightly clumping powder at 20.0 ± 0.5°C | Walker JA and Mullee, DM (2007)  Difenacoum: Determination of General Physico-chemical Properties  SafePharm Laboratories Report No. 2109/0005 |
| Colour | Off-white at 20.0 ± 0.5°C |
| Odour | No determination was performed as the test material was considered to be harmful by inhalation |

Other physico-chemical properties are presented in the CAR of Difenacoum of the Activa / Pelgar Brodifacoum and Difenacoum Task Force. Edialux has a letter of access for these data.

**Analytical methods**

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

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

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

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

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

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

|  |  |
| --- | --- |
|  | Principle of method |
| Technical active substance as manufactured: | Difenacoum quantified in technical grade material by HPLC with UV detection at 254 nm using an internal standard. |
| Impurities in technical active substance: | Impurities in technical grade material quantified by HPLC with UV detection using either an internal or external standard. |

**Technical active substance as manufactured:**

The determination of the active substance was performed by HPLC with method of the internal standard, using the UV detector. It is based on the comparison between the ratio of the difenacoum analytical standard peak area versus 1.3.5-triphenylbenzene internal standard peak area and the same ratio determined in the sample under examination where a known amount of internal standard (I.S) was added. The analytical method is considered to be acceptable.

**Impurities in technical active substance:**

The analytical method and the related validation data for the determination of impurities in the difenacoum technical substance described in the CAR (endpoint A4.1(2)) is also considered to be acceptable but is confidential and can be found in Annex for Confidential Data and Information in the CAR of Difenacoum of Activa/Pelgar Brodifacoum and Difenacoum Task Force.

### Biocidal product

#### Identity, composition of the biocidal product

The biocidal product is not the same as the one assessed for the inclusion of the active substance in annex I of directive 98/8/EC.

Code number: EDI-300

The composition of the product is confidential and is presented in a confidential annex. There is no substance of concern.

#### Physico-chemical properties

Some studies have been performed on an other grain product: SORKIL G GRAINS (formulation EDI-200), results from these studies could be extrapolated to the product SORKIL G GRAINS on a case by case basis. When the read-across is accepted, it is indicated in the table.

**Table : Physico-chemical properties of the biocidal product (evaluated in the PAR 2013)**

| **(Sub)Section (Annex point)** | | **Method** | **Purity/specifications** | **Results** | **Reference** |
| --- | --- | --- | --- | --- | --- |
| **B3.1** | **Appearance (IIB, III 3.1)** | | | | |
|  | Physical state and nature | Visual | Formulation EDI-300  Batch L1209  0.005% Difenacoum | Cereal grains at 21°C | Manka, S. (2012) |
|  | Colour | Visual | Formulation EDI-300  Batch L1209  0.005% Difenacoum | Blue turquoise at 21°C | Manka, S. (2012) |
|  | Odour | Olfactory  Comparison to other characteristic odors | Formulation EDI-300  Batch L1209  0.005% Difenacoum | Weak grain odor at 21°C | Manka, S. (2012) |
| **B3.2** | **Explosive properties (IIB, III 3.2)** | OCDE 113 | Formulation EDI-200  0.0047% Difenacoum | The heat of decomposition was below 500J/g. Therefore test on explosive properties was not necessary.  Not explosive.  Read across acceptable for the product SORKIL G GRAINS (EDI-300).  See comment below the table. | Krach, M. (2010) |
| **B3.3** | **Oxidising properties (IIB, III 3.3)** | EC A.17 | Formulation EDI-200  0.0047% Difenacoum | No oxidising properties  Read across acceptable for the product SORKIL G GRAINS (EDI-300).  See comment below the table. | Krach, M. (2010) |
| **B3.4** | **Flash-point and other indications of flammability or spontaneous ignition (IIB, III 3.4)** | | | | |
|  | Flash point | Not required as the product is a solid | | |  |
|  | Auto-flammability | EC A.16 | Formulation EDI-200  0.0047% Difenacoum | No self ignition up to 387°C.  Read across acceptable for the product SORKIL G GRAINS (EDI-300).  See comment below the table. | Krach, M. (2010) |
|  | Other indications of flammability: | EC A.10 | Formulation EDI-200  0.0047% Difenacoum | Not highly flammable.  Read across acceptable for the product SORKIL G GRAINS (EDI-300).  See comment below the table. | Krach, M. (2010) |
| **B3.5** | **Acidity / alkalinity (IIB, III 3.5)** | | | | |
|  | pH value | Analogus CIPAC MT75.3 | Formulation EDI-300  Batch L1209  0.005% Difenacoum | Not provided.  See comment below. | Manka, S. (2012) |
| **B3.6** | **Relative density (IIB, III 3.6)** | | | | |
|  | Relative density | CIPAC MT159 | Formulation EDI-300  Batch L1209  0.005% Difenacoum | Pour density: 0.789 g/mL  Tap density: 0.819 g/mL | Manka, S. (2012) |
| **B3.7** | **Storage stability-stability and shelf life (IIB, III 3.7)** | | | | |
|  | Stability after accelerated storage for 14 days at 54 °C | 14 days, 54°C | Formulation EDI-300  Batch L1209  0.005% Difenacoum | Appearance of the test item, physico-chemical properties and technical characteristics have not changed.  Difference of content of the active substance: -8.6% deviation from T=0 after the storage for 14 days at 54°C.  See comment below the table | Manka, S. (2012) |
|  | Shelf life following storage at ambient temperature | 24 months at 25°C storage stability study | Formulation EDI-300  Batch L1209  0.005% Difenacoum | Appearance of the test item, physico-chemical properties and technical characteristics have not changed.  Difference of content of the active substance: -2.8% deviation from T=0 after the storage for 24 months at 25°C.  See comment below the table. | Manka, S. (2012) |
|  | Reactivity towards container material | 24 months at 25°C storage stability study  Visual inspections for integrity, sealing and leakage | Formulation EDI-300  Batch L1209  0.005% Difenacoum 10 PP bags (35g) in cardboard box | No alteration observed during the 24 months.  Cardboard box with 10 sachets of 35g has been weighted after 12 months and 24 months. The weight loss after 12 months ranges between -0.03 and 6.10% and after 24 months at 25°C between -0.23 and 5.63%.  See comment below | Manka, S. (2012) |
|  | 14 days, 54°C  Visual inspections for integrity, sealing and leakage | Formulation EDI-300  Batch L1209  0.005% Difenacoum 10 PP bags (35g) in cardboard box | After 14 days at 54 °C, no alteration observed.  Cardboard box with 10 sachets of 35g has been weighted after 14 days at 54°C. The weight loss after 2 weeks at 54°C ranges between 4.75 and 5.22%.  See comment below | Manka, S. (2012) |
| **B3.8** | **Technical characteristics (IIB, III 3.8)** | | | | |
|  | ***Wettability*** | Not required as the product is a ready to use grain bait | | |  |
|  | ***Persistent foaming*** | Not required as the product is a ready to use grain bait | | |  |
|  | ***Suspensibility*** | Not required as the product is a ready to use grain bait | | |  |
|  | ***Spontaneity of dispersion*** | Not required as the product is a ready to use grain bait | | |  |
|  | ***Dilution stability*** | Not required as the product is a ready to use grain bait | | |  |
|  | ***Dry sieve test*** | See particle size distribution | | |  |
|  | ***Wet sieve test*** | Not required as the product is a ready to use grain bait | | |  |
|  | ***Dust content*** | CIPAC MT171 | Formulation EDI-300  Batch L1209  After 24 months at 25°C  0.00486% Difenacoum  Gravimetric method | Nearly dust free  (Collected dust: 0.3mg) | Ferron, N.  (2012) |
|  | ***Attrition resistance of granules*** | CIPAC MT178 | Formulation EDI-300  Batch L1209  0.005% Difenacoum | 99.97% | Manka, S. (2012) |
|  | ***Emulsifiability / Emulsion stability / Re-emulsifiability*** | Not required as the product is a ready to use grain bait | | | |
|  | ***Stability of dilute emulsions*** | Not required as the product is a ready to use grain bait | | |  |
|  | ***Flowability*** | CIPAC MT172 | Formulation EDI-300  Batch L1209  0.005% Difenacoum | After 20 liftings, no sample remained on the 5 mm sieve. | Manka, S. (2012) |
|  | ***Pourability (including rinsed residue)*** | Not required as the product is a ready to use grain bait | | |  |
| **B3.9** | **Compatibility with other products (IIB, III 3.9)** | This ready to use grain bait is not intended to be used or mixed with other products. | | |  |
| **B3.10** | **Surface tension and viscosity (-)** | | | | |
|  | Surface tension | Not required as the product is a ready to use grain bait | | |  |
|  | Viscosity | Not required as the product is a ready to use grain bait | | |  |
| **B 3.11** | **Particle size distribution (-)** | CIPAC MT59.2 and MT 58.2  CIPAC MT 170 | Formulation EDI-300  Batch L1209  0.005% Difenacoum  Formultion EDI-300 after 24 months  Batch L1209  0.00486% Difenacoum | 99.91% of particles are upper than 850 µm.  92.67% of particles are upper than 3.35mm and 7.23% of particles are between 2 and 3.35mm  See comment and conclusion below the table | Manka, S. (2012) |

Explosive and oxidising properties, flammability and auto-flammability:

The read across is acceptable for these properties. The difference in composition between the product SORKIL G GRAINS and the product SORKIL G GRAINS tested is 0.8% without the carrier and the carrier has been changed. The common and new formulants have no oxidising and no explosive properties and are not flammable.

The product SORKIL G GRAINS is considered to have no oxidising and no explosive properties and to be neither highly flammable nor auto-flammable at ambient temperature.

pH:

The pH has been measured only after 24 months storage. The value on a fresh sample is missing and is required in post registration.

Storage stability:

- 24 months at 25°C storage stability study:

After two years the active substance content decreases of 2.8% with a variation of +8.8% after one year. The accepted variation is 10% according to the Monography 17. Appearance of the test item, physico-chemical properties and technical characteristics (pour and tap density, attrition resistance and particle size distribution) have not changed. So FR considers that the product is stable during 2 years.

- 14 days at 54°C study:

The active substance content after 14 days at 54°C is -8.6%. The difference in active substance content is higher than 5% which is the accepted variation according to the FAO manual[[1]](#footnote-1) (§4.6.2). Appearance of the test item, physico-chemical properties and technical characteristics (pour and tap density, attrition resistance and particle size distribution) have not changed. Difenacoum is thermically stable (temperature of decomposition is upper 250°C). Possibility of adsorption of the active substance on the matrix has not been investigated. The variation of active substance content may be due to the heterogeneity of grains within batches (grains from a batch may have different contents of active substance). Besides variations of active substance content have been observed during the long term stability storage study. Therefore the sampling should be adapted to overcome this heterogeneity. The effect of temperature should be demonstrated by the submission of a new accelerated storage stability study (14 days at 54°C or at a lower temperature) with acceptable results.

So FR considers that the shelf life of the product SORKIL G GRAINS is 2 years.

The appearance (integrity, sealing and leakage) of the PP sachet during the storage stability studies has not changed. The compatibility of the product SORKIL G GRAINS with the PP sachet of 35g has been demonstrated which covers all the claimed packagings.

The effect of light has not been provided and FR recommends to store away from light due to the sensitivity of the active substance to light.

Particle size distribution:

The CIPAC MT 59.2 and 58.2 methods are not well adapted for grain baits. The particle size distribution with the method CIPAC MT 170 already performed on the product SORKIL G GRAINS after 24 months is more suitable. This property is required on the fresh product.

**Data requirements – PAR 2013**

An accelerated storage stability study (14 days at 54°C or at a lower temperature) is required with CIPAC MT46.

The pH (and acidity/alkalinity if necessary) with CIPAC MT 75.3 and particle size distribution with CIPAC MT 170 are required on the product SORKIL G GRAINS in post registration.

* **Assessment of major change and renewal (2018)**

Based on the differences and co-formulants, the new composition TITANIUM B can be considered as similar as the old composition SORKIL G GRAIN (see confidential annex). A read across with SORKIL G GRAINS for physico-chemical properties of TITANIUM B can be considered as acceptable.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **Reference** |
| Storage stability test – 8 weeks at 40 °C | CIPAC 46.3 | TITANIUM B  (0.0025% w/w of difenacoum)  Batch n°SG4517 | Determination of physico-chemical properties and storage stability test packed in commercial packaging:   |  |  |  |  | | --- | --- | --- | --- | |  | Initial | After 4 weeks at 40°C | After 8 weeks at 40°C | | Appearance | Heterogeneous blue wheat grain, odourless | Heterogeneous blue wheat grain, odourless | Heterogeneous blue wheat grain, odourless | | Appearance of packaging | Cardboard box with PP bags inside | Cardboard box with PP bags inside | Cardboard box with PP bags inside | | Variation of weight (%) |  | -1.2% | -1.6% | | Content of AS | 0.00262% w/w | 0.00256% w/w | 0.00251% w/w | | Variation of AS (%) |  | -2.3% | -4.2% |   Quantification of AS will be done by HPLC UV detection with the method evaluated in the part 2.2.4.  Conclusion: Accelerated storage stability study (8 weeks at 40°C) allows to consider that the product is stable in Cardboard box with PP bags inside.  The product being a solid, if it is compatible with a type of packaging, it is considered compatible with every types of packaging. | DEMANGEL, B. (2017), Study n°17-904017-005 |
| Storage stability test – long term storage at ambient temperature | CIPAC 46.3  3 years storage stability  GIFAP n°17  CIPAC 178  CIPAC 171.1 | TITANIUM B  (0.0025% w/w of difenacoum)  Batch n° SG4517 | Determination of physico-chemical properties and storage stability test packed in commercial packaging:   |  |  |  |  | | --- | --- | --- | --- | |  | Initial | After 6 months at 20±2 °C | After 3 years at rt | | Appearance | Heterogeneous blue wheat grain, odourless | Heterogeneous blue wheat grain, odourless | The study is currently ongoing. | | Appearance of packaging | Cardboard box with PP bags inside | Cardboard box with PP bags inside | | Variation of weight (%) |  | +0.2% | | Content of AS | 0.00262% w/w | 0.00255% w/w | | Variation of AS (%) |  | -2.7% | | Attrition resistance | - | 99.8% | | Dust content | - | 5.2 mg  Nearly dust free |   Quantification of AS will be done by HPLC UV detection with the method evaluated in the part 2.2.4. | DEMANGEL, B. (2017), Study n°17-904017-006 |

|  |
| --- |
| **Conclusion on the physical, chemical and technical properties of the product** |
| The product TITANIUM B is an RB ready-to-use bait formulation. All studies will be performed in accordance with the current requirements. It is not explosive and has no oxidising properties. The product is not flammable.  The product is stable 8 weeks at 40°C and according to the read across with the product SORKIL G GRAINS, a shelf life of 2 years at ambient temperature can be grant for the biocidal product. However, the results of both storage stability tests are currently on progress and both results are needed to prove the stability of the product in post-authorization.  eCA recommends to store at a temperature below 40°C and away from light due to the sensitivity of the active substance to light.  Its technical characteristics are acceptable an RB ready-to-use formulation. |

* **Assessment of Post-autorisation data (2021)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **Reference** |
| Storage stability test – **long term storage at ambient temperature** | CIPAC 46.3  2 years storage stability  GIFAP n°17 | TITANIUM B  (0.0025% w/w of difenacoum)  Batch n° SG4517 | Determination of physico-chemical properties and storage stability test packed in commercial packaging:   |  |  |  |  | | --- | --- | --- | --- | |  | Initial | After 12 months at 20±2 °C | After 24 months at 20±2 °C | | Appearance | Heterogeneous blue wheat grain,  odourless | Heterogeneous blue oat grain, odourless | Heterogeneous blue oat grain, odourless | | Appearance of packaging | Cardboard box with PP bags inside | Cardboard box with PP bags inside | Cardboard box with PP bags inside | | Variation of weight (%) | - | +0.4% | 0.0% | | Content of AS | 0.00262 | 0.00253 | 0.00238 | | Variation of AS (%) | - | -3.4% | -9.2% |   Quantification of AS is done by HPLC UV detection with the method evaluated in the part 2.2.4. | DEMANGEL, B. (2019), Final Study n° 17-904017-006 |

**Conclusion:**

The product is stable 8 weeks at 40°C. A shelf life of 2 years at ambient temperature has been granted for the biocidal product during the initial assessment of the product.

Final results of the long-term storage stability study with the new composition has been provided. Based on these results, a shelf life of 24 months at ambient temperature can be granted for the biocidal product.

#### Risk assessment for Physico-chemical properties

* **Assessment of major change and renewal (2018)**

Based on the differences, the physico-chemical hazards of the product TITANIUM B are similar between the old and new composition.

Therefore refer to the product assessment report related to SORKIL G GRAINS product authorisation under Regulation UE n° 528/2012 for the physico-chemical hazards of the product.

#### Analytical method for determining the active substance and relevant component in the biocidal product

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Sample** | **Test substance** | **Analytical method** | **Linearity \*** | **Fortification range/ number of measurements** | **Specificity** | **Recovery rate (%)** | | | **Repeatability \*** | **Reference** |
| **range** | **Mean** | **St dev.** |  |
| EDI-300-blank | Difenacoum | HPLC-UV (DAD) 254 nm | 0.0015-0.0040 mg/mL, 6 concentrations in triplicate  r2=0.9998 | Fortification levels : 0.0052%, 3 replicates in duplicate | No interference at the retention time of difenacoum | At 0.0052%: 98.1-100.2% | At 0.0052%: 99.4% | At 0.0052%: 1.1% | 5 measures,  RSD= 3.78% | Garcia, MT. (2009)  Manka, S. (2012)  Final report not provided |

\* The provided analytical method is validated on a different grain bait formulation: SORKIL G GRAINS (EDI-200). The method is validated at 0.005 mg/kg of difenacoum. Linearity and repeatability are acceptable for the product SORKIL G GRAINS.

Data have been performed on the product SORKIL G GRAINS (EDI-300) presented in the table:

- Specificity of the method: by analysing a placebo, EDI-300-blank without active substance.

- Recovery rate: using three spiked placebo samples

It is concluded that the provided method is validated and acceptable for the product SORKIL G GRAINS.

* **Assessment of major change and renewal (2018)**

Report: Validation of analytical method for the determination of difenacoum in the EDI-300\_25, RICAU, H. 2017

Study GLP n° 17-904017-008

Test facility: DEFITRACES  
Z.A. des Andrés  
150, rue Pré-Magne  
69126 BRINDAS  
FRANCE

Principle of the method:

A method to determine difenacoum in the biocidal product EDI-300\_25 (TITANIUM B) by HPLC – UV was submitted. The test item is quantified by HPLC method (Column: reversed phase) using UV detection (320 nm) after extraction.

The validation of this method was considered in compliance with SANCO 3030/99 rev 4.

Validation data:

|  |  |  |  |
| --- | --- | --- | --- |
| Specificity | To demonstrate the specificity of the method, four solutions are analysed and chromatograms have been provided for:   * Solvent blank * Formulation blank * Reference item * Test item   No interference was found: no peak appears in the formulation blank and solvent blank at the retention time of difenacoum.  The method is specific to difenacoum in EDI-300\_25. | | |
| Linearity | Linearity was studied by carrying out five concentrations between 50% and 150% of the concentration in the test item. (= between 1.21 mg/L and 3.71 mg/L). | | |
| Compound | Linearity % | |
| Difenacoum | 1.21 mg/L to 3.71 mg/L  Y = 0.412 X + 0.012  R = 0.9972  n = 5 | |
| Precision | Repeatability was evaluated by analysing twice five test item solutions. | | |
| Compound | Mean (% w/w) | Repeatability (RSD) |
| Difenacoum | 0.00263% | 1.06% |
| Accuracy | Accuracy was determined by comparison of the reference items and 2 reconstituted test items solutions at 100% and 102% of the theoretical concentrations of 2.47 mg/L. Two injections of each preparation are made. The accuracy results are expressed as the recovery rate.   |  |  |  |  | | --- | --- | --- | --- | | Fortification level | Recovery rate (%) | Mean recovery rate (%) | n | | 100%  (2.47 mg/L) | 100.4-101.2 | 100.8 | 2 | | 102%  (2.51 mg/L) | 101.3-101.2 | 101.2 | 2 | | | |

|  |
| --- |
| **Conclusion on the methods for detection and identification of the product** |
| Provided analytical methods are fully validated for the determination of the active substance difenacoum at 25 ppm in the product EDI-300\_25 (TITANIUM B).  For the analytical methods for determining relevant components and/or residues in different matrices, please refer to the product assessment report related to SORKIL G GRAINS product authorisation under Regulation UE n° 528/2012. |

#### Analytical methods for determining relevant components and/or residues in different matrices

The analytical methods for determination of residues of active substance in different matrices (soil, air, drinking and surface water, body fluids and tissues, in food and feedstuff) provided in the CAR of the active substance or required at the product authorization stage as stated in the AR of Difenacoum are presented in annex I of this document.

## Effectiveness against target organisms

### Function

MG 03: Pest Control

Product Type 14: Rodenticide

### Organism(s) to be controlled and products, organisms or objects to be protected.

* **First authorisation SORKIL G GRAINS 2013**

According to the uses claimed by the applicant, SORKIL G GRAINS is intended to be used to control rodents. The target organisms to be controlled are brown rats (*Rattus norvegicus*), black rats (*Rattus rattus*) and house mice (*Mus musculus*).

The product is intended to be applied in and around buildings. The products, organisms or objects to be protected are stored products or food, public health, historical buildings or technical objects.

The application rates recommended and uses claimed by the applicant are the following: PAR 2013

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Target organisms | Dosage claimed | Distance between 2 bait points, for high and low infestation | Time delay of the action of the product | Frequency and method of controls | Area of use |
| **Professional users** | | | | | |
| Rats  *Rattus norvegicus*  *Rattus rattus* | 80 to 200 g / bait point | 15 meters | 3 to 11 days | Visual control every 3 to 7 days | In and around buildings |
| House mouse  *Mus musculus* | 25 to 30 g / bait point | 3 meters |
| **Non professionnal users** | | | | | |
| Rats  *Rattus norvegicus*  *Rattus rattus* | 80 to 200 g / bait point | 15 meters | 3 to 11 days | Visual control every 3 to 7 days | In and around buildings |
| House mouse  *Mus musculus* | 25 to 30 g / bait point | 3 meters |

* **Assessment of major change and renewal (2018)**

The product TITANIUM B was initially authorised for use against *Mus musculus*, *Rattus norvegicus* and *Rattus rattus*, in and around buildings by professional and non-professional users with a shelf-life of 2 years.

The initial application rates were the following:

Rats (brown rats, black rats): 80-200 g bait/secured bait point separated by 5-10 m.

Mice (house mice): 25-30 g bait/secured bait point separated by 2-5 m.

Now the applicant requires an authorisation for the same product but containing 0.0025 % w/w difenacoum instead of 0.005 % w/w, for a longer shelf-life up to 36 months and additional uses:

- For professional users: in and around buildings against mice (*Mus musculus)* and rats (*Rattus norvegicus* and *Rattus rattus*)

- For non-professional users: indoor against mice (*Mus musculus*) and in and around buildings against rats (*Rattus norvegicus* and *Rattus rattus*).

The application rates recommended by the applicant are the following:

* Rats: 80-200 g grains/secured bait point separated by 15 m.
* Mice: 25-30 g grains/secured bait point separated by 3 m.

### Effects on Target organisms

Anticoagulants Rodenticides disrupt the blood-cutting mechanisms. Signs of poisoning in rodents are those associated with an increased tendency to bleed, leading ultimately to profuse haemorrhage. After feeding on bait containing the active substance 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. As the active substance has a long acting action, death will usually occur within 3-11 days of ingesting a lethal dose and animals often die out of sight in their nest or burrow.

* **First authorisation: PAR 2013**

Choice feeding tests on SORKIL G GRAINS on brown rats and house mice with fresh and aged baits were conducted and the results are presented in the dossier. The studies show that the product is palatable (treated bait intake at least 20% of the total food consumption in choice feeding tests) and effective (100% mortality in less than 14 days in the choice feeding tests).

Field tests on SORKIL G GRAINS on brown rats and house mice were conducted and the results are also presented in the dossier. Both studies on rats and mice were performed in sites with a low level of infestation (10 rats and 11 mice) and in both sites the operator has made an early stop of pre-baiting after 7 days despite the bait consumption has not levelled off. Despite this practice, the efficacy on rats and mice was respectively estimated to 100% in 10 days and 100% in 11 days.

Field and semi-field tests performed on a whole wheat formulation SORKIL G show that efficacy on rats and mice was respectively estimated to 95% in 20 days and 100% in 29 days.

Choice feeding tests on rats with fresh baits, 1-year and 2-year aged baits have also been performed with SORKIL G and show that efficacy was in all cases > 85%.

All efficacy studies results are presented in annex 3.

* **Assessment of major change and renewal (2018)**

To support the efficacy of the new formulation of the product TITANIUM B (EDI-300\_25) when the concentration of active substance in the formulation is decreased to 0.0025 % w/w difenacoum), the applicant has submitted new efficacy data with the product EDI-300\_24 and EDI-600\_24.

The products EDI-300\_25 and EDI-300\_24 have close compositions with the following differences: the active substance is reduced to 24 ppm in the product EDI-600\_24 instead of 25 ppm in the product EDI-300\_25 replaced by 1 ppm more carrier.

Therefore efficacy studies conducted with EDI-300\_24 are acceptable to demonstrate the efficacy of TITANIUM B (EDI-300\_25).

The products EDI-300\_25 and EDI-600\_24 are similar block baits with the following differences: the active substance is difenacoum (25 ppm) in the product EDI-300\_25 instead of bromadiolone (24 ppm) in the product EDI-600\_24.

The applicant has performed choice feeding tests on both products in order to compare the palatability and mortality and results allowed the read across since mortality and palatability are similar.

Hence results from the field tests carried out with the product EDI-600\_25 and showing an estimated efficacy of 100% can be extrapolated to the current formulation TITANIUM B (EDI-300\_25).

Therefore efficacy studies conducted with EDI-600\_24 are acceptable to demonstrate the efficacy of TITANIUM B (EDI-300\_25).

All efficacy studies results are presented in annex 3 and the compositions of all tested products are presented in the confidential part of the PAR.

Regarding the claimed uses, submitted efficacy data are compliant with the requirements of the TNsG PT14 (2009), and the results of these tests are respecting the criteria of the TNsG PT14 (2009).

As for rats, the field test has been performed at the dose level of 100 g instead of the minimal claimed of 80g, then, the range 80-200 g cannot be accepted but the range rate of 100-200 g is validated.

As for mice, no field test has been performed at the dose level of 30 g of the minimal claimed of 25 g then, the range 25-30 g cannot be accepted cannot be accepted but the application rate of 30 g is validated.

French competent authorities (FR CA) assessed that the product TITANIUM B has shown sufficient efficacy and can be used for the control of rats (*Rattus norvegicus* and *Rattus rattus*) at the claimed application rate of 100-200g / bait station and, house mice (*Mus musculus*), at the claimed application rate of 30 g /bait station.

Nevertheless, according to the TNsG for product evaluation PT14 (2009), to support a shelf life of 36 months (of the new formulation), test with a 36 months aged product should be submitted.

A free-choice laboratory test was carried out with black rat (*Rattus rattus*), exposed to a 26 months aged EDI\_300\_24 formulation. The results are compliant with the criteria of the TNsG PT14 (2009).

The palatability test was performed with aged formulation on blackrat, as the lowest palatability was obtained with this species when exposed to the fresh formulation of EDI 300\_24

Then only a efficacy on a 26 months aged bait is demonstrated.

|  |
| --- |
| **Conclusion on the efficacy of the product** |
| The product TITANIUM B (0.0025 % w/w difenacoum has shown a sufficient efficacy and can be used for the control of rats (*Rattus norvegicus* and *Rattus rattus*) and house mice (*Mus musculus*) at the dose claimed:   * for professional users: in and around buildings for each target organism (*Mus musculus*, *Rattus norvegicus* and *Rattus rattus*) * for non-professional users: indoor against mice (*Mus musculus*) and in and around buildings against rats (*Rattus norvegicus* and *Rattus rattus)*   Nevertheless to support a shelf life of 36 months, test with a 36 months aged product should be submitted. According to the palatability test performed with 26 months aged product support a maximal shelf life of 26 months. |

### Mode of action including time delay

Difenacoum acts as a vitamin K1 antagonist. It interferes with the regeneration of prothrombin disturbing the normal blood clotting mechanisms and increasing tendency to bleed. The main site of its action is the liver, where several of the blood coagulation precursors under vitamin K dependent post translation processing take place before they are converted into the respective procoagulant zymogens. Difenacoum acts as an inhibitor of K1 epoxide reductase, preventing the regeneration of vitamin K and preventing activation of clotting factors.

### Occurrence of resistance

* **Assessment of major change and renewal (2018)**

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[[2]](#footnote-2); Lund, 1984[[3]](#footnote-3); Pelz et al. 1995[[4]](#footnote-4)). 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[[5]](#footnote-5)). 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[[6]](#footnote-6)).

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

House mice carrying the homozygous Y139C sequence variant were found to be highly resistant to warfarin and bromadiolone.

So, resistance to second generation anticoagulant rodenticides should not be minimized.

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.

### Evaluation of the Label Claims

* **First authorisation SORKIL G GRAINS 2013**

FR CA assessed that the product SORKIL G GRAINS has shown a sufficient efficacy for the control of house mice (*Mus musculus*) and rats (*Rattus norvegicus, Rattus rattus*) in and around buildings.

* **Assessment of major change and renewal (2018)**

Uses and doses validated for the renewal and major change of TITANIUM B are the following:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Users** | **Target organisms** | **Application rate** | **Field of use** | **Packagings** |
| Professionals | Rats (*Rattus rattus* and *Rattus norvegicus*) | 100 g to 200 g of product / bait station at distances of 15 meters apart | Indoor  and around buildings | Individual sachets  Unwrapped Pre-filled bait stations |
| Mice (*Mus musculus*) | 30 g of product / bait station at distances of 3 meters apart |
| Non professionnals | Rats (*Rattus rattus* and *Rattus norvegicus*) | 100 g to 200 g of product / bait station at distances of 15 meters apart | Indoor  and around buildings | Individual sachets  Pre-filled bait stations |
| Mice (*Mus musculus*) | 30 g of product / bait station at distances of 3 meters apart | Indoor |

To ensure a satisfactory level of efficacy and avoid the development of resistance, the recommendations proposed in the SPC have to be implemented.

***Required information linked to efficacy assessment***

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.

### Summary of efficacy assessment

* **First authorization SORKIL G GRAINS 2013**

The product SORKIL G GRAINS has shown a sufficient efficacy and can be used for the control of mice *(Mus musculus)* and rats (*Rattus norvegicus* and *Rattus rattus*) in and around buildings. Nevertheless, in the absence of supporting data on *Rattus rattus*, suitable information (as a field test) demonstrating the efficacy against black rat of SORKIL G GRAINS will need to be provided in support of the authorisation. Furthermore, a monitoring of the resistance phenomenon of rodent populations toward the active substance difenacoum and resistant strategies management must be put in place. The collected information must be sent every 2 years to the Anses within the framework of a post-authorization monitoring.

* **Assessment of major change and renewal (2018)**

French competent authorities (FR CA) consider that the elements presented in the dossier confirm, when the concentration of active substance in the formulation is decreased to 0.0025 % w/w difenacoum, the efficacy of the product TITANIUM B:

- For professional users against house mice (*Mus musculus*) and rats (*Rattus norvegicus* and *Rattus rattus*) for use in and around buildings;

- For non-professional users against house mice (*Mus musculus*) for use indoor and against rats (*Rattus norvegicus and Rattus rattus*) for use in and around buildings;

## Exposure assessment

### Description of the intended use(s) – PAR 2013

Difenacoum is used as rodenticide (product type PT14 according to EU Biocidal Product Directive).

The validated application rates and intended uses are the following:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Target organisms | Dosage claimed | Distance between 2 bait points | Time delay of the action of the product | Frequency and method of controls | Area of use |
| **Professional users** | | | | | |
| Rats  *Rattus norvegicus*  *Rattus rattus* | 80 to 200 g / bait point | 15 meters | 3 to 11 days | Inspect and resupply the bait stations, 3 days after application then once a week as long as the bait is consumed. | In and around buildings |
| House mouse  *Mus musculus* | 25 to 30 g / bait point | 3 meters |
| **Non professionnal users** | | | | | |
| Rats  *Rattus norvegicus*  *Rattus rattus* | 80 to 200 g / bait point | 15 meters | 3 to 11 days | Inspect and resupply the bait stations, 3 days after application then once a week as long as the bait is consumed. | In and around buildings |
| House mouse  *Mus musculus* | 25 to 30 g / bait point | 3 meters |

The product SORKIL G GRAINS is intended to be used for control of mice (*Mus musculus*), brown rats (*Rattus norvegicus*) and black rats (*Rattus rattus*) in and around buildings. The control of mice and rats is based on the principle of applying baits in infested areas with obvious tracking of faeces, and smears next to holes and harbourages*.*

### Assessment of exposure to humans and the environment

**Assessment of human exposure**

No new human exposure studies have been submitted. In the dossier, Edialux assessed the human exposure based on the default values of the TNsG on human exposure, 2007[[7]](#footnote-7). Therefore, since Edialux provided a letter of access for the CEFIC unpublished study “*Study to determine potential exposure to operators during simulated use of anticoagulant rodenticide baits*” of Chambers J.G. and Snowdon P.J. (2004)[[8]](#footnote-8); the FR CA decided to base the human exposure assessment for professionals on this study as done by the RMS (Finland) of the active substance in the Assessment report of difenacoum. This study examined the inhalation and dermal exposures associated with all activities involved in using a grain bait (decanting material from a large container to a pail, filling and placing bait points, and clean-up and disposal of bait points). The used grain bait containing coumatetralyl was selected as a worst case representative product of all cereal-based rodenticide baits. In this study, 10 replicates were performed at 1, 5 and 10 manipulations. Therefore, Anses decided to use the exposure estimations issued from the CEFIC study for the assessment of SORKIL G GRAINS.

For non professional users, the same CEFIC study and assumptions were used for the estimation of human exposure since the values available in the TNsG and User Guidance (Human exposure to biocidal products – TNsG June 2002 – version 1) are considered as unrealistic (see argumentation in the Assessment report on difenacoum).

Additionally, the Human Exposure Expert Group (HEEG) opinion on harmonising the number of manipulations in the assessment of rodenticides (anticoagulant)[[9]](#footnote-9), agreed at the European Technical meeting TMII2010 was taken into account for the estimation of the number of manipulations for professionals and non professionals.

## Risk assessment for human health

### Hazard potential

#### Toxicology of the active substance

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

The following corresponds to the summary of the derivation of the AELs from the Doc I of the final CAR of difenacoum:

*“The lowest LOAEL in a repeated dose study, i.e. the teratogenicity study in rabbits, is chosen as the basis to establish the AOEL (there was no NOAEL). In this study, the maternal LOAEL was 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 according to the agreement during peer-review discussion. A further supportive argument for an additional assessment factor comes from the higher potency of the second generation anticoagulants compared to warfarin, and from the much higher vulnerability of human foetuses to vitamin K deficiency compared to rodents. To extrapolate from LOAEL to NOAEL an assessment factor of 2 is considered justified due to the deep slope of the dose response curve. After correction for bioavailability of 68%, a NOAEL for MOE (0.00034 mg/kg bw/day) and an AOEL of 0.0000011 mg/kg bw/day are used for risk characterisation. These values are applied both to acute and repeated exposure scenarios.”*

#### Toxicology of the substance(s) of concern

Considering the following definition of a substance of concern set in the TNsG on data requirement chapter 4[[10]](#footnote-10), “*the substance is regarded as a substance of concern if [...] it is classified as dangerous* ***and*** *its concentration in the product exceeds the classification limit set in the Council Directive 88/379/EEC, as amended by Directive 1999/45/EC, for a particular dangerous property* ***or*** *the other classification limit indicated for the substance in a preparation set in Annex I of Council Directive 67/548/EEC* ***or*** *causes that the overall sum of the concentrations of dangerous substances in the product exceeds the limit for classification of the preparation set in Council Directive 88/379/EEC, as amended by Directive 1999/45/EC, for a particular dangerous property*”, SORKIL G GRAINS does not contain any substance of concern.

#### Toxicology of the biocidal product

The toxicology of the biocidal product was examined according to standard requirements of Directive 98/8/EC. The product was not a dummy product in the EU- review program for inclusion of the active substance in Annex I of Directive 98/8/EC.

The basis for the health assessment of the biocidal product is laid out in Annex 5 of this report ”Toxicology – biocidal product”.

Acute dermal toxicity, skin and eye irritation and skin sensitisation studies have been provided on another grain bait product (EDI-200) containing 0.005% of difenacoum. All the ingredients remain the same with the same or less concentrations except for the cereal which is replaced with a slight increase by whole wheat. Therefore, since it is not expected that the differences of composition between these two formulations impact the results, the extrapolation to SORKIL G GRAINS was accepted.

* + - * 1. ***Percutaneous absorption***

The dermal absorption of difenacoum formulated as pellet bait (containing 0.005% w/w difenacoum) was investigated using human skin *in vitro*. The average percentage of absorbed difenacoum was 0.027%. The total recovery of difenacoum was 94.2% when skin discs were exposed to 20.4 µg a.s./cm2 for 8 hours.

* + - * 1. ***Acute toxicity***

ORAL ROUTE:

No study was submitted. Based on the composition of SORKIL G GRAINS, no classification is required for this endpoint.

DERMAL ROUTE:

Neither mortality, systemic clinical signs nor macroscopic anomalies were observed in the acute dermal toxicity study (LD50 > 2000 mg/kg). Concerning local effects, a slight erythema was noted in one female animal (1/5) at 24, 48 and 72 hours post-dose. A slight to moderate dryness was noted in four female animals since day 2 or day 3. The cutaneous reactions were totally reversible on day 5.

Based on the results, no classification is required this endpoint.

INHALATION ROUTE:

No acute toxicity study by inhalation route was submitted. Based on the low vapour pressure of difenacoum and considering the composition of SORKIL G GRAINS, the product is not classified for this endpoint.

* + - * 1. ***Irritation and corrosivity***

SKIN IRRITATION:

No cutaneous reaction (erythema and oedema) was observed on the treated area, whatever the examination time.

EYE IRRITATION:

Slight to moderate conjunctival redness was noted in all the animals, totally reversible between day 4 and day 6, associated with a slight to moderate chemosis totally reversible between day 1 and day 3.

Based on these results of the irritation guideline assays on rabbit’s skin and eye, no classification is required.

* + - * 1. ***Sensitisation***

A non-radioactive LLNA using cell counting was submitted. This method is not currently validated. Furthermore, according to the publication of Basketter *et al*.[[11]](#footnote-11), the “*proposed non-RI LLNA[[12]](#footnote-12) uses cell number as a correlate of cell proliferation, but, as other modifications to the standard LLNA were also made, the method constitutes a major change*.” Therefore this test was considered non acceptable.

Based on the composition of SORKIL G GRAINS, no ingredients were listed as a skin sensitizer. Therefore, it is not expected that this product is a skin sensitizer.

* + - * 1. ***Other studies***

The product does not contain any substance of concern. Therefore, no additional study was conducted.

* **Assessment of major change and renewal (2018)**

### Risk assessment for human health

The product TITANIUM B is a cereal grain bait, ready-to-use rodenticide containing 0.0025% of difenacoum.

Baits are packaged in PP sachets or in bulk for professional users.

For non-professional users, bait is supplied only in PP sachet

The major change request is for a decrease in the active substance content (from 50 ppm to 25 ppm) and for the addition of a non-professional use (formulation provided in sachet PP for the use against rats and mice).

For the major change request, no new data has been submitted.

Taking into account the decrease in active substance content, the assessment of effects on human health is considered covered by the assessment realised in the initial PAR.

**Information on dermal absorption**

The dermal absorption of difenacoum formulated as pellet bait (containing 0.05 g/kg difenacoum) was investigated *in vitro* using human skin. This study is interpreted according to the Guidance on Dermal Absorption (EFSA Journal 2012; 10(4): 2665:)

* At t = 12h, more than 75% of the dose is absorbed; therefore, tape strips values have to be removed from the dermal absorption calculation
* Standard deviation is higher than 25% of the mean. Therefore, the SD has to be added to the mean value.
* Recovery is less than 95%, therefore, a normalization has to be done.

In this context, the percentage of absorbed difenacoum is 0.04% (instead of 0.027% as previously proposed).

For the risk assessment, a dermal absorption value of 0.04% has been used.

### Human exposure assessment

The biocidal product is a ready-to-use grain rodenticide containing 0.005 % of the active substance intended to be applied indoors and around industrial and commercial buildings including farm building, by professionals and non professionals for the control of rats and mice.

* + - 1. **Identification of main paths of human exposure towards active substance from its use in biocidal product**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Exposure path** | **Industrial use** | **Professional use** | **General public** | ***via* the environment** |
| Inhalation | Not relevant | Yes | Yes | Negligible |
| Dermal | Not relevant | Yes | Yes | Negligible |
| Oral | Not relevant | No | Yes | Negligible |

* + - 1. **Direct exposure as a result of use of the active substance in biocidal product**

SORKIL G GRAINS is available as loose grains for professional use only or packaged in plastic sachet and prefilled bait stations for professional and non-professional uses. The exposure from the use of prefilled bait stations is covered by the loose grain and sachet scenarios.

* + - * 1. ***Exposure of professional users***

As a worst case, exposure has been assessed considering SORKIL G GRAINS supplied as loose grains at the maximum recommended dose of 200 g (rat’s dose). This approach covers the packaging in sachet and in prefilled bait stations. In these cases, it can be assumed that there is no decanting phase and no exposure is expected during loading in bait points. This approach also covers human exposure during the control of mice, where the recommended doses are 25-30g/bait point.

Exposure by inhalation route is relevant **during the decanting of loose grains**. Based on the CEFIC study and taking into account the HEEG opinion on an harmonised approach for the assessment of rodenticides (anticoagulants) agreed at TMII 2011, the indicative air concentration is 9.62 mg product/m3.

The following parameters were considered:

* duration of manipulation: 15 minutes per day (3 minutes per 3 kg decanting; 12.6 kg decanted per day)
* Inhalation rate: 1.25 m3/hour
* Inhalation absorption: 100 %
* Active substance in product: 0.005 %
* Body weight: 60 kg

Based on these assumptions, the systemic concentration of difenacoum is 2.5 x 10-6 mg/kg bw/day without respiratory protection and 2.5 x 10-7 mg/kg bw/day when professional wear a respiratory equipement during decanting (protection factor 90%).

*Dermal exposure*

Based on the CEFIC study and taking into account the *HEEG opinion on an harmonised approach for the assessment of rodenticides (anticoagulants)* agreed at TMII 2011, the indicative amount of product on fingers/hands **during the decanting** was 93 mg per 3 kg of decanted product, when considering 1 to 4 decanting times per day and 52.3 mg per 3 kg of decanted product when considering more than 4 decanting times per day. Since the quantity of decanted product is 12.6kg (200 g per bait point; 63 loadings), 52.3 mg of product was considered.

The following parameters were taken into account:

* Active substance in product: 0.005%,
* Quantity of decanted product: 12.6 kg for rat (200 g of grains per bait boxes; 63 loadings of bait boxes[[13]](#footnote-13)),
* Frequency: one manipulation per day,
* Dermal absorption: 0.027 %,
* Body weight: 60 kg.

Therefore, the systemic dose of difenacoum on fingers/hands during decanting is 4.9 x 10-8 mg/kg bw/day.

Based on the CEFIC study and taking into account the *HEEG opinion on an harmonised approach for the assessment of rodenticides (anticoagulants)* agreed at TMII 2011, the amount of product on fingers/hands **during the loading** was 2.04 mg for the assessment of more than 4 manipulations per day (the agreed number is 63 manipulations for professional use based on the HEEG opinion on harmonising the number of manipulations in the assessment of rodenticides (anticoagulant) agreed at TMIII 2010). Therefore, considering 63 manipulations per day, the systemic dose of difenacoum on fingers/hands during loading is 2.9 x 10-8 mg/kg bw/day.

Based on the CEFIC study and taking into account the *HEEG opinion on an harmonised approach for the assessment of rodenticides (anticoagulants)* agreed at TMII 2011, the amount of product on fingers/hands **during the cleaning** was 3.79 mg/manipulation for the assessment of more than 4 manipulations per day (the agreed number is 16 cleanings for professional use based on the HEEG opinion on harmonising the number of manipulations in the assessment of rodenticides (anticoagulant) agreed at TMIII 2010). Therefore, considering 16 cleanings per day, the systemic dose of difenacoum on fingers/hands during cleaning is 1.4 x10-8 mg/kg bw/day.

In conclusion, the total systemic dermal exposure is set at 9.2 x 10-8 mg/kg bw/day.

*Total exposure*

The total systemic exposure resulting from inhalation and dermal contacts with the product is 2.6 x 10-6 mg/kg bw/day without any individual protective equipment. Considering the protection of respiratory equipment during decanting, the total systemic exposure is 3.4 x 10-7 mg/kg bw/day.

The estimations above represent a very worst case when SORKIL G GRAINS is supplied in sachets. In this case, it can be assumed that there is no decanting phase and no exposure is expected during loading in bait points. Therefore, only exposure during cleaning can be considered: 1.4 x 10-8 mg a.s/kg bw/day without gloves.

*In Annex 6 „Safety for professional operators“, the results of the exposure calculations for the active substance and the substance of concern for the professional user are laid out.*

* + - * 1. ***Exposure of non-professional users***

For non-professional users, considering the available packaging (only in plastic sachet or in prefilled bait station), it can be assumed that there is no decanting phase and no exposure is expected during loading in bait points.

Based on the CEFIC study and taking into account the *HEEG opinion on an harmonised approach for the assessment of rodenticides (anticoagulants)* agreed at TMII 2011, the amount of product on fingers/hands **during the cleaning** was 3.79 mg for the assessment of more than 4 manipulations per day and 4.52 mg for the assessment of up to 4 manipulations per day (the agreed number is 5 cleanings for non-professional use based on the HEEG opinion on harmonising the number of manipulations in the assessment of rodenticides (anticoagulant) agreed at TMIII 2010). As a worst-case, considering 5 manipulations per day, the amount of product of 4.52 mg is used and therefore, the systemic dose of alphachloralose on fingers/hands during cleaning is 5.1 x 10-9 mg/kg bw/day.

In conclusion, the total systemic dermal exposure is set at 5.1 x 10-9 mg/kg bw/day.

*In Annex 7 “Safety for non-professional operators and the general public”, the results of the exposure calculations for the active substance and the substance of concern for the non-professional user and the general public are laid out.*

| **Tier** | **Inhalation exposure** | **Dermal exposure** | **Total exposure** |
| --- | --- | --- | --- |
| PPE | Systemic dose | Systemic dose | Systemic dose |
|  | mg a.i. / kg bw /day | mg a.i. / kg bw /day | mg a.i. / kg bw /day |
| **Task – time frame:** | **Scenario ( population) – frequency** | | |
| Sachet and prefilled stations | | | |
| Without PPE | na | 5.1 x 10-9 | 5.1 x 10-9 |

* + - 1. **Indirect exposure as a result of use of the active substance in biocidal product**

Exposure of non users, especially infants, could result from the handling of dead rodents or ingesting poison baits.

***Handling of dead rodents (adult, child, infant) – acute scenario***

Secondary exposure of users and non users could result in the handling of dead rodents. However, this scenario is excluded because it is considered of low relevance due to unrealistic assumptions (TNsG on human exposure (2007)). Exposure due to this senario is considered negligible.

***Oral exposure by ingesting bait (infant) – acute scenario***

A reverse scenario was calculated. Based on the short-term AEL of 1.1x10-6 mg a.s/kg bw/day, a body weight of 10 kg and an oral absorption of 68%, ingestion of more than 0.3 mg of product per day is needed to exceed the AEL.

* + - 1. **Combined exposure**

Not relevant

* **Assessment of major change and renewal (2018)**

**Identification of main paths of human exposure towards active substance and substances of concern from its use in biocidal product**

| **Summary table: relevant paths of human exposure** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Exposure path** | **Primary (direct) exposure** | | | **Secondary (indirect) exposure** | | | |
| **Industrial use** | **Professional use** | **Non-professional use** | **Industrial use** | **Professional use** | **General public** | **Via food** |
| Inhalation | n.a | Yes | No | n.a | n.a | No | n.a |
| Dermal | n.a | Yes | Yes | n.a | n.a | No | n.a |
| Oral | n.a | No | No | n.a | n.a | Yes | n.a |

***List of scenarios***

| **Summary table: scenarios** | | | |
| --- | --- | --- | --- |
| **Scenario number** | **Scenario**  (e.g. mixing/ loading) | **Primary or secondary exposure**  **Description of scenario** | **Exposed group**  (e.g. professionals, non-professionals, bystanders) |
| 1. | Primary dermal and inhalation exposure during decanting, loading and cleaning phases | **Primary dermal and inhalation exposure**  The product is a ready to use product supplied in PP sachets or in bulk; therefore exposure during decanting, loading and cleaning is considered.  For bulk bait packaging below 10 kg a decanting phase is not expected as its weight allows the worker to handle it from a bait point to another. So, only exposure during loading and cleaning is considered. | Professional user |
| 2. | Primary dermal exposure during cleaning phase | **Primary dermal exposure**  The product is a ready to use product in PP sachet therefore only exposure during cleaning is considered. | Non-professional user |
| 3. | Ingestion of product by an infant | **Secondary exposure**  Oral exposure of toddler by ingestion of grain bait. | General public - toddler |

***Industrial exposure***

Not applicable.

***Professional exposure***

*Scenario [1]: Primary dermal and inhalation exposure during loading, decanting and cleaning phases for professional users*

| **Description of Scenario [1]** | | | | |
| --- | --- | --- | --- | --- |
| TITANIUM B is a ready-to-use product supplied in PP sachets or in bulk.  According to the HEEG opinion 10 , an exposure phase of 1 decanting, 63 loading and 16 cleanings is considered. Dermal exposure is based on the HEEG opinion 12: Harmonised approach for the assessment of rodenticides.  As a worst-case, the application dose of 200g for the use against rat is taken into account; the dose for the use against mice being lower, the exposure assessement is considered covered.  The exposure assessment during the use of a bulk formulation is a worst-case compared to a formulation supplied in sachet.  For bulk bait packaging below 10 kg for which a decanting phase is not expected, only exposure during loading and cleaning is considered. | | | | |
|  | Parameters1 | Unit | Value | Source |
| Tier 1 | Amount of exposure to product (75th percentile) during decanting | mg | 52.3 | HEEG opinion 12 |
| Manipulation per day | - | 1 | HEEG opinion 10 |
| Amount of exposure to product (75th percentile) during loading | mg | 2.04 | HEEG opinion 12 |
| Manipulation per day | - | 63 | HEEG opinion 10 |
| Amount of exposure to product (75th percentile) during clean-up | mg | 3.79 | HEEG opinion 12 |
| Manipulation per day | - | 16 | HEEG opinion 10 |
| Inhalation absorption value | % | 100 | - |
| Dermal absorption value | % | 0.04 | - |
| Concentration of a.s in the product | % | 0.0025 | - |
| Body weight | kg | 60 | HEAD hoc recommendation 14 |
| Tier 22 | Gloves protection factor | % | 95 | HEEG opinion 9 |
| Respiratory protection factor APF | - | 4 | HEEG opinion 9 |
| Tier 2b (bulk bait package sizes ≤ 10kg, without decanting) | No PPE | - | - | - |

1 Include generic parameters (e.g. respiration rates, exposed skin areas, exposure times) and protection/penetration rates for PPE. Use footnotes for references and justifications.

2 Only include the parameters changed with respect to the previous Tier.

**Calculations for Scenario [1]**

| **Summary table: estimated exposure from professional uses** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake** | **Estimated dermal uptake** | **Estimated oral uptake** | **Estimated total uptake** |
| **Bulk Formulation** | | | | | |
| **Exposure during decanting, loading and cleaning phases** | | | | | |
| Scenario [1] | Tier 1/ No PPE | 1.25 x 10-6 | 6.81 x 10-8 | - | 1.32 x 10-6 |
| Scenario [1] | Tier 2a/ PPE (Gloves | 1.25 x 10-6 | 3.41 x 10-9 | - | 1.26 x 10-6 |
| Scenario [1] | Tier 2a/ PPE (gloves + RPE (APF 4 during decanting)) | 3.13 x 10-7 | 3.41 x 10-9 | - | 3.17 x 10-7 |
| **Exposure during loading and cleaning phases, without decanting phase** | | | | | |
| Scenario [1] | Tier 2b/ No PPE, package sizes ≤ 10kg | - | 3.15 x 10-8 |  | 3.15 x 10-8 |
| **Sachet Formulation** | | | | | |
| Scenario [1] | No PPE | - | 1.01 x 10-8 | - | 1.01 x 10-8 |

***Non-professional exposure***

*Scenario [2]:* Primary dermal exposure during cleaning phase

| **Description of Scenario [2]** | | | | |
| --- | --- | --- | --- | --- |
| TITANIUM B is a ready-to-use product supplied in PP sachets.  According to the HEEG opinion 10 , an exposure phase of 5 cleanings is considered. Dermal exposure is based on the HEEG opinion 12: Harmonised approach for the assessment of rodenticides.  As a worst-case, the application dose of 200g for the use against rat is taken into account; the dose for the use against mice being lower, the exposure assessment is considered covered. | | | | |
|  | Parameters1 | Unit | Value | Source |
| Tier 1 | Amount of exposure to product (75th percentile) during clean-up | mg | 4.52 | HEEG opinion 12 |
| Manipulation per day | - | 5 cleaning | HEEG opinion 10 |
| Dermal absorption value | % | 0.04 | - |
| Concentration of a.s in the product | % | 0.0025 | - |
| Body weight | kg | 60 | HEAD hoc recommendation 14 |

1 Include e.g. generic parameters and protection/penetration rates for PPE if relevant. Use footnotes for references and justifications.

2 Only include the parameters changed with respect to the previous Tier.

**Calculations for Scenario [2]**

| **Summary table: systemic exposure from non-professional uses** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Exposure scenario** | **Tier/PPE** | **Estimated inhalation uptake** | **Estimated dermal uptake** | **Estimated oral uptake** | **Estimated total uptake** |
| Scenario [2] | Tier 1/ No PPE | - | 3.77 x 10-9 | - | 3.77 x 10-9 |

***Exposure of the general public***

The estimation of general public exposure is considered covered by the initial assessment.

Therefore, please refer to the product assessment report related to SORKIL G GRAIN product authorisation under Regulation UE n° 528/2012*.*

***Monitoring data***

None

***Summary of exposure assessment***

| **Scenarios and values to be used in risk assessment** | | | | |
| --- | --- | --- | --- | --- |
| Scenario number | | Exposed group  (e.g. professionals, non-professionals, bystanders) | Tier/PPE | Estimated total uptake |
| Bulk formulation | | | | |
| 1. | | Professionals (Bulk) | Tier 1/No PPE | 1.32 x 10-6 |
| 1. | | Professionals (Bulk) | Tier 2a/PPE (gloves) | 1.26 x 10-6 |
| 1. | | Professionals (Bulk) | Tier 2a/PPE (gloves + RPE (APF 4) during decanting) | 3.17 x 10-7 |
| 1. | | Professionals (Bulk, package sizes ≤ 10kg ) | Tier 2b/No PPE, without decanting | 3.15 x 10-8 |
| Sachet formulation | | | | |
| 1. | Professionals (PP Sachet) | | Tier 1/No PPE | 1.01 x 10-8 |
| 2. | Non-professionals (PP sachet ) | | Tier 1/No PPE | 3.77 x 10-9 |

### Risk characterisation

* + - 1. **Risk for direct exposure**
         1. ***Professional users***

The estimated exposures for the professional users are compared to the systemic AEL of difenacoum set in the Assessment Report (1.1x10-6 mg a.s/kg bw/day).

Based on the risk assessment of the active substance, the risk for professional users resulting from the intended use is acceptable only with respiratory protection during decanting for SORKIL G GRAINS as loose grains (%AEL is set at 31%) and without any protection equipment for SORKIL G GRAINS in sachet (%AEL is set at 1.2%) (see Annex 6 for detailed calculations). The exposure from the use of prefilled stations is covered by the scenarios above.

However, gloves are recommended to help prevent rodent-borne disease.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Scénario** | **AEL (mg/kg bw/d)** | **Exposure (mg/kg bw/d)** | **%AEL** | **Risk** |
| **Bulk formulation (exposure during decanting, loading and cleaning phases)** | | | | |
| Professional  (without PPE) | 1.1x10-6 | 2.6 x 10-6 | 236 | Unacceptable |
| Professional  (with respiratory protection during decanting) | 1.1x10-6 | 3.4 x 10-7 | 31 | Acceptable |
| **Sachet formulation (exposure during cleaning phase)** | | | | |
| Professional  (without PPE) | 1.1x10-6 | 1.4 x 10-8 | 1.3 | Acceptable |

* + - * 1. ***Non-professional users***

The estimated exposures for the non professional users are compared to the systemic AEL of difenacoum set in the Assessment Report (1.1x10-6 mg a.s/kg bw/day).

Based on the risk assessment of the active substance, the risk for non-professional users resulting from the intended use is acceptable without gloves for SORKIL G GRAINS in sachet or in prefilled stations (%AEL is set at 0.5%) (see Annex 6 for detailed calculations).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Scénario** | **AEL (mg/kg bw/d)** | **Exposure (mg/kg bw/d)** | **%AEL** | **Risk** |
| **Sachet formulation and prefilled station (exposure during cleaning phase)** | | | | |
| Non-professional  (without PPE) | 1.1x10-6 | 5.1 x 10-9 | 0.5 | Acceptable |

* + - 1. **Risk for indirect exposure**

Based on a reverse scenario, more than 0.3 mg of product per day should be ingested by infant to exceed the AEL. This indicates that infants are at significant risk of poisoning. Therefore, even if SORKIL G GRAINS contains a bittering agent which reduces the likelihood of ingestion, the baits must be unattainable which do not allow access to children.

Product label (“do not open the sachet”) and good practice advise users to prevent access to bait by children and infants.

* + - 1. **Risk for combined exposure**

Not relevant.

* + - 1. **Summary of risks characterisation of the product for human health**

No unacceptable risk has been observed for professionals using SORKIL G GRAINS as loose grains, only with respiratory protection during decanting and considering the maximum recommended dose of 200 g/bait point.

No unacceptable risk has been observed for professionals and non-professionals using SORKIL G GRAINS in sachet, without gloves and considering the maximum recommended dose of 200 g/bait point.

The exposure from the use of prefilled stations is covered by the scenarios above.

For the indirect scenario “Infant ingesting bait”, an unacceptable risk was observed. Therefore, even if SORKIL G GRAINS contains a bittering agent which reduces the likelihood of ingestion, the baits must be unattainable which do not allow access to children. Product label (“do not open the sachet”) and good practice advise users to prevent access to bait by children and infants.

* **Assessment of major change and renewal (2018)**

**Reference values to be used in Risk Characterisation**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Reference** | **Study** | **NOAEL (LOAEL)** | **AF1** | **Correction for oral absorption** | **Value** |
| AEL short-term | Teratogenicity in rabbit | LOAEL = 0.001 mg/kg bw/day | 600  (safety factor of 300 and a safety factor of 2 due to extrapolation from LOAEL to NOAEL) | Yes, 68% | 0.0000011 mg/kg bw/day |
| AEL medium-term | Teratogenicity in rabbit | LOAEL = 0.001 mg/kg bw/day | 600  (safety factor of 300 and a safety factor of 2 due to extrapolation from LOAEL to NOAEL) | Yes, 68% | 0.0000011 mg/kg bw/day |
| AEL long-term | Teratogenicity in rabbit | LOAEL = 0.001 mg/kg bw/day | 600  (safety factor of 300 and a safety factor of 2 due to extrapolation from LOAEL to NOAEL) | Yes, 68% | 0.0000011 mg/kg bw/day |
| ARfD | Not applicable |  |  |  |  |
| ADI | Not applicable |  |  |  |  |

1 Please explain background and reason for assessment factor.

***Risk for industrial users***

Not applicable.

***Risk for professional users***

**Systemic effects**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Task/**  **Scenario** | **Tier** | **AEL**  **mg/kg bw/d** | **Estimated uptake**  **mg/kg bw/d** | **Estimated uptake/ AEL (%)** | **Acceptable**  **(yes/no)** |
| **Bulk formulation** | | | | | |
| 1/ Professionals (Bulk) | Tier 1/No PPE | 1.1 x 10-6 | 1.32 x 10-6 | 120 | No |
| 1/ Professionals (Bulk) | Tier 2/PPE (gloves) | 1.1 x 10-6 | 1.26 x 10-6 | 114 | No |
| 1/ Professionals (Bulk) | Tier 2/PPE (gloves + RPE (APF 4) during decanting) | 1.1 x 10-6 | 3.17 x 10-7 | 29 | Yes |
| 1/ Professionals (package sizes ≤ 10kg) | Tier 2b/No PPE, without decanting | 1.1 x 10-6 | 3.15 x 10-8 | 3 | Yes |
| **Sachet formulation** | | | | | |
| 1/ Professionals (PP Sachet) | Tier 1/No PPE | 1.1 x 10-6 | 1.01 x 10-8 | 0.9 | Yes |

**Local effects**

Not applicable*-*

**Conclusion**

The risk for professional users is considered acceptable with PPE (gloves and RPE with at least an Assigned Protection Factors of 4 during the decanting phase) for baits in bulk and with no PPE for baits in PP sachets. The exposure from the use of prefilled stations is covered by the scenarios cited above.

For packaging below 10 kg for which a decanting phase is not expected, the risk is acceptable with no PPE.

Therefore, a restriction of packaging to 10kg is proposed to prevent the inhalation exposure and to reduce the use of PPE. Moreover, the following risk mitigation measure is necessary: Decanting is to be avoided. In case decanting cannot be avoided, an RPE of APF 4 has to be used.

***Risk for non-professional users***

**Systemic effects**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Task/**  **Scenario** | **Tier** | **AEL**  **mg/kg bw/d** | **Estimated uptake**  **mg/kg bw/d** | **Estimated uptake/ AEL**  **(%)** | **Acceptable**  **(yes/no)** |
| 2./ Non-professionals (PP sachet ) | Tier 1/No PPE | 1.1 x 10-6 | 3.77 x 10-9 | 0 | Yes |

**Local effects**

Not applicable*-*

**Conclusion**

The risk for non-professional users is considered acceptable with no PPE.

Gloves are anyway recommended to prevent rodent-borne disease. Moreover, the mention “do not open the sachet” has to be added in the label of the product.

***Risk for the general public***

The risk for the general public is considered covered by the initial assessment.

Therefore, please refer to the product assessment report related to SORKIL G GRAIN product authorisation under Regulation UE n° 528/2012*.*

**Conclusion**

Please refer to the product assessment report related to SORKIL G GRAIN product authorisation under Regulation UE n° 528/2012*.*

***Risk characterisation from combined exposure to several active substances or substances of concern within a biocidal product***

Not applicable

## 

## Risk assessment for the environment (PAR 2013)

### Distribution of the active substance, difenacoum, in the environment

The summary of information about the active substance is carried out with the data from the CAR of difenacoum owned by the Activa/Pelgar difenacoum & Brodifacoum Task Force. No new ecotoxicological information on the active substance Difenacoum has been submitted in the product dossier.

#### Biodegradation of difenacoum

According to the OECD tests 301B and 302D, difenacoum is not readily or inherently biodegradable. No studies on degradation in soil is available, but using the calculated value of Kp of 1.34 and considering the absence of biodegradation of difenacoum, it can be assumed that half-life in soil is over 300 days. It was assumed during technical meeting (TMII-04) that no further degradation studies are needed for intended uses in sewers and in and around building.

So the risk assessment is based on the assumption that difenacoum is not readily biodegradable and that the half-life in soil is over 300 days.

#### Hydrolysis as a function of pH

According to the test OECD 111, the half-life (DT50) of difenacoum is over 1 year at pH 4, 7 and 9 at 25°C. The active substance is hydrolytically stable.

#### Photolysis in water

The active substance undergoes rapid photodegradation. Half-life varied from 0.6 hours to 3.8 hours. Greater than 80% photolysis was noted to have occurred by around five hours. Two breakdown products above 10% of the initial difenacoum concentration were detected and the proposal for the identification of structures was made. The photodegradation is regarded as a minor removal process for difenacoum and the exposure to water is low, therefore it was stated that no further characterisation of metabolites was requested.

#### Photodegradation in air

Photodegradation characteristics of the active substance have been estimated using the EPIWIN v. 3.12 models in the CAR of the Task Force Difenacoum dossier. Difenacoum has an estimated half-life of approximately 2 hours; therefore it is predicted to have a negligible effect on stratospheric ozone. It is predicted not to be a potential greenhouse gas. Finally, difenacoum has a low volatility (Henry’s law constant< 0.046 Pa.m3.mol-1) and emissions to the air compartment are expected to be low.

#### Distribution

##### Adsorption/desorption

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 ionise at environmental relevant pH. Difenacoum has also a low water solubility and a high log Kow.

According to the Technical Guidance Document (TGD[[14]](#footnote-14)) Part 3, Table 4, the QSAR equation used to calculate the log Koc from the log Kow (7.62, QSAR estimation) is:

**log Koc = 0.81 log Kow + 0.1**  (chemical class: Predominantly hydrophobics)

The properties of difenacoum may hamper the estimation of log Kow that is why it should be considered with some caution. The calculated log Koc is 6.27 and Koc = 1 871 544.

In the difenacoum dossier it has been stated that, according to its behaviour, the active substance would not be mobile and would be expected to absorb irreversibly to soil particles. Significant leaching could be expected to occur only in recently contaminated soil under alkaline conditions. Under other conditions, binding to the inorganic component of soil would be largely irreversible. The rate of binding is likely to be limited by steric hindrance of reaction in forming the cation bridge from the organic material.

##### Accumulation

The aquatic BCF has been estimated with calculation method because the fish bioconcentration test was invalid. In the absence of valid measured log Kow, the estimated value of log Kow used is 7.6. This value allows to calculate an estimated BCF for fish: 9010 (according to EPIWIN v 3.12) and 35 645 (Equation 75, TGD).

In order to remain coherent with the Annex I inclusion dossier, BCF for fish value of 9010 is used to perform secondary poisoning evaluation via aquatic trophic chain.

This log Kow is also entered the equation 82d of the TGD to get a BCFearthworm equal to 477 729.

The calculations show that difenacoum has a considerable bioaccumulation potential in aquatic and terrestrial organisms.

### Effects of the active substance on environmental organisms

#### Aquatic compartment (including water, sediment and STP)

Difenacoum is very toxic to aquatic organisms. Difenacoum was equally toxic to fish (LC50= 0.33 mg a.s/L, OECD 203), daphnia (EC50= 0.91 mg a.s/L, OECD 202) and algae (EbC50 =0.14 mg a.s/L, OECD 201). Nevertheless, a lower fish test result (LC50=0.064 mg/L) is available in the difenacoum dossier of Sorex Limited. Therefore, it is used for the derivation of PNECwater in the difenacoum Task force Annex I inclusion dossier as recommended in the CAR.

In the absence of any ecotoxicological data for sediment-dwelling organisms, the PNECsediment was calculated using the equilibrium partitioning method.

Difenacoum has shown to degrade photolytically in water in laboratory conditions and it may form degradation products exceeding 10% of the parent compound. The metabolites are not considered to have ecotoxicological significance, because photolysis is considered to be a minor transformation path for difenacoum and the exposure to water via the STP is expected to be low.

Difenacoum did not cause any effects on the activated sludge respiration inhibition up to the nominal concentration of 999.7 mg/L (OECD 209). Because all test concentrations exceeded the water solubility of difenacoum, the water solubility of 0.48 mg/L will be used as PNECSTP.

#### Atmosphere

No data are available on the biotic effects in the atmosphere. Difenacoum is not expected to contribute to global warming, ozone depletion in the stratosphere, or acidification on the basis of its physical or chemical properties.

#### Terrestrial compartment

Difenacoum caused no toxic effects on earthworms up to the nominal concentration of 994 mg/kg dry weight (OECD 207). Difenacoum may not be bioavailable to earthworms in soil which would explain the low toxicity. No studies on soil microorganisms or plants were submitted.

The photolysis degradation products are not considered ecotoxicologically relevant because the direct exposure of difenacoum to soil is expected to be low.

Toxicity of difenacoum in birds increased with exposure time. Difenacoum was considered as moderately toxic in acute oral exposure (LD50= 153 mg/Kg bw), toxic in 5-day dietary test (LC50=1.4 mg/Kg feed) and very toxic in the reproduction test (NOEC= 0.31 mg/Kg water, exposure via drinking water). Several dose related effects were detected in the reproduction test: increased adult mortality, increased mortality of 14-day old hatchlings, increased liver and spleen weights in adult females, a declining trend in number of eggs laid/hen/day, declining trend in viability of eggs. Due to methodological deficiencies the reproduction test is not considered to represent the worst case, and therefore the PNECoral of birds was derived from the dietary test. Difenacoum is very toxic to mammals, and rats seem to be particularly susceptible. The PNECoral for birds and mammals has been used for the risk characterization of primary and secondary poisoning.

#### PBT Assessment

Due to the properties of persistence, accumulation and toxicity of difenacoum, this substance fulfills the PBT criteria.

#### Non compartment specific effects relevant to the food chain

As already stated in the previous sections, difenacoum is concern for bioaccumulation with a calculated log Kow of 7.62, a high predicted aquatic BCF of 9 010 (US EPA EPIWIN) or 35 645 (TGD) and a high predicted terrestrial BCF of 477 729 (TGD). The active substance is not readily biodegradable and is of low solubility (0.5 mg/L pH7). Therefore, difenacoum has a considerable bioaccumulation potential in aquatic and terrestrial organisms.

The primary concern is from predators eating the rodent carcasses and earthworms which have ingested the active substance absorbed to soil. In guidance document for TP14, the active substance is considered to be placed in protected bait point. Therefore, a risk should be taken into account for primary poisoning mainly for birds and mammals of equal or smaller size than the target rodents. Also when target animals carry bait away from e.g. bait stations, non-target animals may be exposed. For the risk characterization of primary poisoning, the PNECoral described in section 2.8.2.6 will be used.

Also requiring consideration are predators eating fish or earthworms which have accumulated difenacoum from water and soil. The secondary exposure should be taken in consideration. The applicant has submitted, in the Annexe I inclusion dossier, one acceptable study where effects of difenacoum are studied and reported in Barn Owls which have been exposed to poisoned mice. However, the PNECoral for birds and mammals are derivated from a bird 5-day dietary test and a 90-day subchronic test in rat provided in the Activa/Pelgar difenacoum Task Force Annex I inclusion dossier as described below (part 2.8.2.6).

#### Effects assessment of metabolites formed in target organisms

A metabolism study presented in the Activa/Pelgar difenacoum Task Force Annex I inclusion dossier (doc IIIA-6.4 of the CAR) shows that total excreted radioactivity in rat faeces and urine (7 days after single dosing, low and high dose) was 41-71% of the dose administered. Two major faecal metabolites F7 and F8 (max 11.3% and 7.3%, respectively) were identified as isomers of hydroxylated difenacoum. Two other major metabolites, F5 and F6 (max 12.2% and 8.0 %, respectively) were characterised as isomers of difenacoum-based structure which formed glucuronide conjugates. Unchanged difenacoum was present at maximum at 2.9 %. The excretion and retention of radioactivity was also investigated after the final dose following administration of seven consecutive daily oral doses, no substantial differences in excretion patterns between single and repeated level oral doses was observed.

No information on toxicity of these four major metabolites is available. Considering that the metabolites could be potent as anticoagulants, the sum of these four metabolites and unchanged difenacoum in faeces will be taken into account in PEC calculation with assumption that the toxicity of metabolites is comparable to parent (data from the validated CAR of the Activa/Pelgar difenacoum Task Force Annex I inclusion dossier). Therefore in the environmental exposure calculations, it is assumed that 40% of excreted amount in urine and faeces is metabolised and that 40 % of administered total amount is unchanged difenacoum in faeces (data from the CAR of the Activa/Pelgar difenacoum Task Force Annex I inclusion dossier). These assumptions represent a worse case for release.

#### Summary of PNEC

##### PNEC for aquatic organisms:

The PNECwater is derived from the lowest available LC50 value 0.064 mg/L (fish test) with an assessment factor of 1000 as only data on acute toxicity is available. Therefore,

**PNECwater = 0.06 μg/L**

##### PNEC for sediment-dwelling organisms:

In the absence of data on sediment-dwelling organisms, the PNECsediment is derived from the equilibrium partitioning method.

**PNECsediment = 2.51 mg/kg wet weight.**

##### PNEC for STP micro-organisms:

As described in section 2.8.2.1, the water solubility of 0.48 mg/L is used as the PNECSTP.

**PNECSTP = 0.48 mg/L**

##### PNEC for terrestrial organisms:

The PNECsoil is derived from the experimental data. An assessment factor of 1000 was applied to the LC50 > 994 mg/kg issued from an earthworms study to derive the PNECsoil.

PNECsoil = 0.994 mg/kg dry weight (0.877 mg/kg wet weight)

Nevertheless, as only one experimental test result is available, the PNECsoil derived with the equilibrium partitioning method (EPM) from the aquatic PNEC has also been taken into account:

PNECsoil = 2.04 mg/kg wet weight

Because the PNECsoil derived from the earthworms test is lower, it will be used for the risk characterization. So,

**PNECsoil = 0.994 mg/kg dry weight (0.877 mg/kg wet weight)**

##### PNEC for birds and mammals

PNECoral for birds is derived from the LC50 of 1.4 mg/kg food origin from the 5-day dietary test. The appropriate assessment factor according to the TGD is 3000. In order to transform the LC50 to LD50, LC50 is multiplied with average food consumption (13.5 g) and divided by average body weight 71.3 g. The food consumption and body weight are averaged for all treatment groups and over the 5-day exposure period. The resulting LD50 is 0.3 mg/kg bw/d. The PNECoral value kept for the risk assessment is:

**PNECoral for birds = 0.5 μg/kg food** equivalent to

**PNECoral for birds = 0.1 μg/kg bw/d**

PNECoral for mammals is derived from the NOAEL of 0.03 mg/kg bw/d origin from the 90-day subchronic test in rat (A6.4.1). The NOAEL is transformed to NOEC (concentration in food) by multiplying with the conversion factor of 20 (TGD, Table 22). The appropriate assessment factor according to the TGD is 90. The PNECoral value kept for the risk assessment is:

**PNECoral for mammals = 7 μg/kg food** equivalent to

**PNECoral for mammals = 0.3 μg/kg bw/d**

The PNECoral for birds and mammals have been used for the risk characterization of primary and secondary poisoning.

Table 2.8.2.7: summary of the difenacoum PNECs

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Compartment** | | **Test Value** | **AF** | | **PNEC** |
| Aquatic | PNECwater | LC50 =0.064 mg/l | 1000 | | 0.064 µg/L |
| PNECsediment | PNECwater in eq. 70 (TGD) | | | 2.51 mg/kg wet weight |
| PNECSTP | Water solubility= 0.48 mg/l | | | 0.48 mg/L |
| Terrestre | PNECsoil | LC50 >994 mg/kg | | 1000 | 0.994 mg/kg dry weight  0.877 mg/kg wet weight |
| PNECoral for birds | LC50 =1.4 mg/kg food  LD50= 0.3 mg/kg bw/d | | 3000 | 0.5 μg/kg food eq. to  0.1 μg/kg bw/d |
| PNECoral for mammals | NOEC= 0.6 mg/kg food  NOAEL=0.03 mg/kg bw/d | | 90 | 7 μg/kg food eq. to  0.3 μg/kg bw/d |

### Effects on environmental organisms for biocidal product

It is important to notice that the applicant did not provide ecotoxicological data about the biocidal product SORKIL G GRAINS. There is no substance of concern in the formulated product. Therefore the whole environment risk assessment of SORKIL G GRAINS is based on data obtained from the Competent Authority report of the active substance difenacoum as agreed at the Annex I inclusion stage.

#### Aquatic compartment (including water, sediment and STP)

Product SORKIL G GRAINS is an impregnated grains based product that contains difenacoum as active substance and denatonium benzoate as an aversive compound. Since difenacoum is the only substance of concern, the ecotoxicological effects can be derived from the effect studies conducted with the active substance.

#### Terrestrial compartment

In the SORKIL G GRAINS, no substance of concern has been identified, and hence the ecotoxicological effects for the terrestrial compartment can be derived from the effect studies conducted with the active substance.

#### Non compartment specific effects relevant to the food chain (secondary poisoning)

In the SORKIL G GRAINS, no substance of concern has been identified, and hence the secondary poisoning assessment can be carried out on the active substance difenacoum only.

#### Summary of PNECs

In the product SORKIL G GRAINS no substance of concern has been identified. Therefore the whole environment risk assessment is based on data obtained from the active substance difenacoum.

### Environmental exposure assessment

|  |
| --- |
| * **Assessment of major change and renewal (2018)**   New information was submitted at the renewal stage of the approval of difenacoum :  - A bioaccumulation tests in fish lead to a new BCF of 1100 L/kg which was lower than the predicted BCF of 9010 L/kg and 35645 L/kg. It was assumed in the original risk assessment that secondary poisoning via the aquatic food chain would not be significant due to low water solubility and high adsorption tendency of difenacoum.  Even though risk is identified in the terrestrial food chain for birds, the risk via poisoned rodents is considered significantly higher compared to risk via earthworms or other invertebrates. Thus, conclusion from the original assessment is not changed.  - An earthworm reproduction test: this test permits to revise the PNECsoil of 0.625 mg/kg dw which could have an impact only for open area uses (not intended for this dossier). Therefore, this new PNECsoil has no impact on the previous conclusion for TITANIUM B.  Furthermore, in the first authorization of the product TITANIUM B based on the risk assessment of the product SORKIL G GRAINS, the active substance content assessed was 0.005% w/w of difenacoum. For the renewal, the applicant claimed an active substance content of 0.0025% w/w of difenacoum. Regarding this new information, the renewal assessment is cover by the first authorization presented below. Therefore, the conclusion of the environmental risk assessment remains unchanged. |

The product SORKIL G GRAINS is a ready-to-use impregnated grains based product, packed in bags or provided in bulk, with 0.005% of difenacoum. These impregnated grains are placed in secured bait stations, which have to be replenished regularly during the infestation period. According to the applicant, the product is intended to be used in bait boxes in and around buildings.

Emission calculations are carried out considering the default parameters of the ESD PT14 as well as specific information on the product provided by the applicant (realistic case):

* The application type ‘bait-box’ of the ESD PT14 is applied for the following calculations in the exposure scenarios.
* Number of bait stations: 30 (20 inside and 10 outside, 15 meters apart for rats, 3 meters apart for mouse).
* Day 1: Treatment with 200 g product per bait point for rat, 30 g product per bait point for mouse.
* Day 7, 14 and 21: bait refilling. During a typical campaign baiting, 1.5 replenishments over 28 days are considered.
* The only primary compartment to be exposed during ‘in and around use’ is the soil.
* 40% of ingested active substance is indirectly released via urine and faeces as unchanged difenacoum and difenacoum-based metabolites according to metabolism and toxicokinetics study (section 2.8.2.6).
* The scenario in the ESD PT14 is primarily based on grains provided in bulk, as a worst case. Therefore the estimated direct release (*Frelease-D-soil*)during application is set to 0.01.
* According to the product instructions, bait stations are placed 15 m apart, which gives a soil area indirectly exposed of 1650 m² for rats (330 m² for mice with baits at 3 meters from each other). Direct release is concentrated in a 10 cm strip in front of and to both sides of each bait point (0.09 m2).
  + - 1. **PEC in surface water and sediment**

Exposure of surface water and sediment after the treatment with rodenticides in and around buildings is only relevant for indoor application of liquid poisons, residues from mixing and cleaning (ESD PT14) when a release is foreseen via the STP. Therefore the exposure of surface water and sediment is considered negligible for the application of SORKIL G GRAINS.

* + - 1. **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 a potential for rapid photo-oxidative degradation in the air (half-life about two hours). The exposure of air is therefore considered negligible for the application of SORKIL G GRAINS product.

* + - 1. **PEC in soil and groundwater**

The only primary compartment to be exposed during ‘in and around use’ is the soil. The PEC in soil and ground water) are presented in the table below. No degradation was considered.

**Table 2.8.4.3‑1: In and around buildings - Rat and mouse control campaign – Scenarios considering the typical campaign according to the product instructions and the ESD TP14.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **IN AND AROUND BUILDING (Bait boxes)** | | | **Typical campaign**  **Rat** | **Typical campaign**  **Mouse** | **Unit** |
| INPUTS | Q*prod:* | Amount of product used in control operation for each bait box | 200 | 30 | g |
| Fc*product*: | Fraction of active substance in product | 0.005 | 0.005 | % |
| Nsites: | Number of outsite application sites | 10 | 10 | - |
| N*refil*: | Number of refilling times | 1.5 | 1.5 | - |
| F*release-D, soil*: | Fraction of product released directly to soil | 0.01 | 0.01 | - |
| F*release-ID, soil*: | Fraction released indirectly to soil | 0.4 | 0.4 | - |
| F*metabolised:* | Fraction of active ingredient metabolised | 0.6 | 0.6 | - |
| AREA*exposed*: | Area directly exposed to rodenticide originating from bait box | 0.09 | 0.09 | m2 |
| AREA*exposed-ID* | Area indirectly exposed to rodenticide | 1650 | 330 | m2 |
| Koc | Organic carbon adsorption coefficient | 1.87E+06 | 1.87E+06 | L.Kgwwt-1 |
| DEPTH*soil*: | Depth of exposed soil | 0.1 | 0.1 | m |
| RHO*soil*: | Density of exposed soil | 1700 | 1700 | kg/m3 |
| OUTPUTS | Elocal*soil-campaign, direct*: | Direct emission to soil from a campaign | 1.50E-03 | 2.25E-04 | g/camp |
| Elocal*soil-campaign, indirect*: | Indirect emission to soil from a campaign | 5.94E-02 | 8.91E-03 | g/camp |
| Elocal*soil-campaign*: | Total emission to soil from a campaign | 6.09E-02 | 9.14E-03 | g/camp |
| Clocal*soil-D* | Local concentration in soil due to direct release (AREAexposed-D) after a campaign: | 9.80E-03 | 1.47E-03 | mg/kgwwt |
| Clocal*soil-ID* | Concentration in soil due to indirect (disperse= AREAexposed-ID ) release after a campaign: | 2.12E-04 | 1.59E-04 | mg/kgwwt |
| Clocal*soil* | Worst case total concentration in soil = PECsoil | 1.00E-02 | 1.63E-03 | mg/kgwwt |
| Clocal*soil mean concentration* | Mean concentration in soil. The total amount of product release (=Elocalsoil-campaign) is divided by the whole area exposed (=AREAexposed-ID) | 2.17E-04 | 1.63E-04 | mg/kgwwt |
| **PEC are calculated according to the TGD, part II (2003)** | | | | | |
| PEC local soil | | PEC in soil | 1.00E-02 | 1.63E-03 | mg/kgwwt |
| Kpsoil | | Partition coefficient solid-water in soil | 3.74E+04 | 3.74E+04 | [L.kg-1] |
| Ksoil water | | Soil-water partitioning coefficient | 5.61E+04 | 5.61E+04 | [m3.m-3] |
| PEC local soil porewater = Cporewater | | Mean concentration in groundwater (based on mean concentration in soil considering the area for indirect release) | 6.57E-09 | 4.93E-09 | mg/L |

* + - 1. **Non-compartment specific effects relevant to the food chain (primary and secondary poisoning)**
         1. ***Primary poisoning***

The risk assessment for the primary poisoning presented below was extracted from the Annex I inclusion dossier for the active substance considering that difenacoum concentration is identical in the product SORKIL G GRAINS and in the representative product presented in the Annex I inclusion dossier for the active substance.

According to the ESD PT14, primary poisoning hazard to mammals and birds (both wild and domestic) can be considered small in the scenario “In and around buildings”. In scenarios where difenacoum is placed in protected bait point, there is the risk for primary poisoning mainly for birds and mammals of equal size or smaller as the target rodents, which may be able to enter the bait stations. Also when target animals carry bait away from e.g. bait stations, non-target animals may be exposed.

Worst case exposure estimations are based on the equations and default values proposed by the ESD PT14. Some defaults may be replaced by product-specific properties. 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. **The worst case Tier 1 PECoral is 50 mg/kg** (difenacoum present at 0.005% w/w in SORKIL G GRAINS) and is used in quantitative risk assessment for the long-term situation.

According to ESD PT14, a Tier 2 evaluation assessment can be done estimating the daily uptake of a compound (ETE) by non-target animals according to the equation 19 of the ESD PT14

(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 the elimination of the active substance is taken into account the expected concentration of active substance (EC) in animal is calculated with the following equation:

**EC = ETE x (1-El)**

where El is the fraction of daily uptake eliminated (number between 0 and 1, default 0.3).

According to the toxico-kinetic study (section2.8.2.6), 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 is no other data available. Calculations of ETE and EC values for worst case and realistic worst case situations are presented in the Table below. According to the guidance agreed at 23rd Competent Authority meeting these values are used for qualitative risk assessment of primary poisoning in acute situation.

**Table 2.8.4.4‑1:** 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

|  |
| --- |
|  |

Calculations of the expected concentrations (EC) for 5 days exposure considering elimination are calculated according to the ESD PT14 equation 21 as a worst case i.e. AV, PT and PD are set to 1.

According to the guidance agreed at 23rd CA meeting EC5 values are used for quantitative risk assessment of primary poisoning in the long-term situation.

**Table 2.8.4.4‑2: Expected concentrations of difenacoum (EC5) in non-target animals for the long-term situations (worst case).**

|  |
| --- |
|  |
| Among the anticoagulant poisoning incidents, dogs are common victims. The intoxication of dogs is easily detected as they live together with man. Intoxication incidents of wild animals may often remain unobserved. Small non-target rodents, such as voles, and small, granivorous birds can feed on rodenticidal baits because they can pass through the entrance hole of a bait station. Exposure may also arise if target animals carry bait away from the bait station. The domestic animals at risk are dog, pig and hen. Birds eating cereal and weed seeds like sparrows, pigeons and pheasants are possible wild species that may be at risk of primary poisoning. |

* + - * 1. ***Secondary poisoning***

Secondary poisoning via the aquatic food chain

As no exposure of the aquatic compartment is foreseen with the use of SORKIL G GRAINS in and around buildings, no risk assessment for secondary poisoning through the aquatic food chain is required.

Secondary poisoning via the terrestrial food chain

***The earthworm-eating mammal or bird***

According to the TGD secondary poisoning through the terrestrial route is soil → terrestrial organisms (earthworm) → earthworm-eating mammal or bird. Since birds and mammals consume worms with their gut contents and the gut of earthworms can contain substantial amounts of soil, the exposure of the predators may be affected by the amount of substance present in the soil.

PECoralpredator is calculated for rat application, considering the mean concentration in soil, for the refined scenario as:

**PEC oral,predator = Cearthworm** (eq 80, TGD, 2003)

**Cearthworm = (BCFearthworm\*Cporewater+ Clocalsoil\*Fgut\*CONVsoil)/ (1+Fgut kgdwt/kgwwt\*CONVsoil kgwwt/kgdwt)** (eq 82c, TGD 2003).

No measured BCF for earthworm is available and the calculated **BCF** **of 477 729** **L/kgwet earthworm** (section **2.8.1.5.2**) is used in the calculations.

**Cearthworm** = (477 729 L/kgwet earthworm x 6.57E-09 mg/L + 2.17E-04 mg/kgwwt x 0.1 kgdwt/kgwwt x 1.13 kgwwt/kgdwt)/(1+0.1 \*1.13) = **2.84E-03 mg/kgwet earthworm.** for rat treatment

According to the TGD, 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 0.00284 mg/kgwet earthwom x 0.5 = **1.42E-03 mg/kgwet earthworm.** This value is conservative for the mice treatment so it is the only one taken into account for the following risk assessment.

For mice treatment this value is **PECoral,predator=1.07E-03 mg/kgwet earthworm**

***The rodent-eating mammal or the rodent-eating bird***

As secondary poisoning assessment according to the TGD considers the oral intake of a chemical only via fish or worms, another food chain rodenticide (bait) →rodent → rodent-eating mammal or rodent-eating bird is assessed in the ESD PT14.

The risk assessment for the secondary poisoning presented below was extracted from the Annex I dossier for the active substance inclusion considering that difenacoum concentration is identical in the product SORKIL G GRAINS and in the representative product presented in the Annex I inclusion dossier for the active substance.

According to the ESD PT14 for secondary poisoning hazard, in uses in and around buildings, it is assumed that predators among mammals and birds may occur inside buildings or they may hunt rats in the immediate vicinity of buildings (parks and gardens or further away); also scavengers may search for food close to buildings and thus secondary poisoning through poisoned rats exists.

For estimation of secondary poisoning risk through poisoned rats, tiered approach is presented in the ESD PT14:

* The Tier 1 assessment of secondary poisoning is based on the concentration in the predator's or scavenger's food i.e. poisoned rodents (concentration in food); the predator is assumed to catch the rodent after last meal on day 5 or day 14.
* The Tier 2 assessment of long-term secondary poisoning is based on the expected concentration in predators compared to PNECoral expressed as a daily dose; the predators accumulate difenacoum by feeding on poisoned target rodents during one day (rodents ate baits every day during 5 and 14 days).

Therefore, the amount of difenacoum in rats is estimated according to equations 19 and 21 in ESD PT14:

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

In calculations AV and PT for rodent are set to 1 and PD values to 1, 0.5 and 0.2. The daily elimination is assumed to be 40%, see details in section 2.8.2.6**.** Results are presented in the following Table.

|  |
| --- |
| **Table 2.8.4.4‑3: Estimated concentration (EC) of difenacoum in target rodents (rats) in mg a.s./kg bw at different times during a control operation** |

* Tier 1 PECoral for short term situation is calculated according to the equation 22 in the ESD PT14;

**PEC oral, predator = (ECn +ETE) x F rodent)**

using value 1 for Frodent (non-target animal consume 100% of their daily intake on poisoned rodents).

where

Frodent : fraction of poisoned rodents in predator's diet

ECn: 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.

These values, presented in the table 2.8.4.2-6 below, are used for qualitative risk assessment of secondary poisoning in acute situation.

* Tier 1 PECoral for long term situation is calculated in a similar way, but the Frodent is set to 0.5, which means that it is assumed that non-target animal consume 50 % of their daily intake on poisoned rodents. These values, presented in below, are used for Tier 1 quantitative risk assessment of secondary poisoning in the long-term situation.

**Table 2.8.4.4‑4: Predicted environmental concentrations of difenacoum in food of predator (PEC oral) for acute and long-term situations.**

|  |
| --- |
|  |

* Tier 2 for long-term exposure: According to guidance agreed by the CA the PECoral is the concentration of active substance in non-target animals after a single day of exposure (mg/kg bw) using values PD of 1 (100% bait consumption by rodent) and Frodent of 0.5. PECoral values presented in the table below are used for Tier 2 quantitative risk assessment of secondary poisoning in the long-term situation.

**Table 2.8.4.4‑5: 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, Frodent 0.5.**

|  |
| --- |
|  |

### Risk characterisation for the environment

* + - 1. **Aquatic compartment**

Exposure scenario is not considered relevant in the EUBEES 2 ESD for rodenticides. Difenacoum is not expected to occur to any significant extent following the use of SORKIL G GRAINS in and around buildings. Therefore, PEC values for difenacoum in surface water and sediment are assumed to be negligible and have not been further considered.

* + - 1. **Atmosphere**

For difenacoum, the estimated half-life for the hydroxyl reaction in air is 2.08 hours, the vapour pressure as determined by OECD 104 is <5 x 10-5 Pa and the Henry's law constant is <4.6 x 10-2 Pa.m3.mol-1. Therefore difenacoum is not expected to volatilize to air in significant quantities.

* + - 1. **Terrestrial compartment (including groundwater)**

PNEC values for the terrestrial compartment were calculated in the section 2.8.2.7. While PEC values for the in and around buildings scenario were presented in section 2.8.4.3.

The Table 2.8.5.3‑1 below presents PEC/PNEC ratios for terrestrial compartment including groundwater.

**Table 2.8.5.3‑1: PEC/PNEC ratios for the terrestrial compartment (incl. groundwater)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **IN AND AROUND BUILDING** | **PEC** | | **PNEC** | **PEC/PNEC** | |
| **Typical campaign** | |  | **Typical campaign** | |
| **rat** | **mouse** | **rat** | **mouse** |
| **Typical scenario considering 1.5 replenishments of the bait points per campaign and the metabolisation of the substance in rodents – Worst case concentration in soil in the area just around the bait point.** | | | | | |
| Terrestrial (mg/kg wwt) | 1.00E-02 | 1.63E-03 | 0.877 | 1.14E-02 | 1.86E-03 |
| **Typical scenario considering 1.5 replenishments of the bait points per campaign and the metabolisation of the substance in rodents – Calculations based on mean concentrations in soil considering the area for indirect release** | | | | | |
| Groundwater (µg/L) | 6.57E-06 | 4.93E-03 | 0.01\* | Acceptable | Acceptable |

\*0.01µg/L corresponds on the threshold value for the toxicity in drinking water issued from the human health section.

No unacceptable risk is identified in the terrestrial compartment (including groundwater) when the product SORKIL G GRAINS is used in and around building against rats and mice.

* + - 1. **Primary poisoning**

Concentration of the bait is compared to the PNECoral expressed as the concentration in food.

**Table 2.8.5.4‑1: Tier 1 risk characterisation of primary poisoning.**

|  |
| --- |
|  |
| |  |  |  |  | | --- | --- | --- | --- | |  | PEC mg/kg food | PNEC µg/kg food | PEC/PNEC | | Birds | 50 | 0.5 | 100000 | | Mammals | 50 | 7 | 7143 | |

With a Tier 1 Approach, the risk for primary poisoning in birds and mammals is not acceptable.

The expected concentrations (EC) in the non-target animals after five days exposure have been calculated with the tier 2 assumptions, i.e, PT=0.8 and AV=0.9. The PNECoral is expressed as the daily dose.

**Table 2.8.5.4‑2: Tier 2 risk characterisation of primary poisoning.**

|  |
| --- |
|  |
|  |

With a Tier 2 Approach, the risk for primary poisoning is not acceptable in the non-target animals.

The risk characterisation indicates a very high risk to non-target mammals and birds from direct eating of bait. Primary poisoning incidents can be minimised by preventing the access of non-target animals to the baits. It is assumed in the ESD PT14 that if the rodenticide baits are used according to the label instructions, the risk for primary poisoning is negligible. However, it is stated at the EU level that 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.

* + - 1. **Secondary poisoning**
         1. ***Secondary poisoning via aquatic food chains***

As no exposure of the aquatic environment is foreseen with the use of SORKIL G GRAINS in and around buildings, no risk assessment for secondary poisoning through the aquatic food chain is needed.

* + - * 1. ***Secondary poisoning via the terrestrial food chain***

***The earthworm-eating mammal or bird***

In the terrestrial environment birds and mammals may be at risk for secondary poisoning if they feed on contaminated soil organisms. The risk characterization is done separately for birds and mammals to be consequent with the calculations done according to the ESD PT14.

**Table 2.8.5.5‑1: Secondary poisoning for earthworm-eating mammals and birds ”in and around buildings”.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **PECoral,predator (µg/kgwet earthworm)** | **PNEC oral**  **µg/kg food** | **PEC/PNEC**  **(mammals)** | **PEC/PNEC**  **(birds)** |
| **In and around building – Mean concentration** | | | | |
| ***Rat treatment:*** | **1.42** | **PNEC oral mammal:7**  **PNEC oral bird:0.5** | **0.2** | **2.84** |
| ***Mice treatment:*** | **1.07** | **0.15** | **2.1** |

The PEC/PNEC ratio exceeds 1 for earthworm-eating birds.

PECoralpredator is calculated for rat and mice applications, considering the mean concentration in soil. The risk is due to feeding on contaminated soil invertebrates in the whole area indirectly exposed to rodenticide. Despite of the calculated risk, the RMS considers the secondary poisoning via earthworms less important than secondary poisoning via the food chain bait → rodent → rodent-eating birds or mammals as calculated below.

***The rodent-eating mammal or bird***

A qualitative assessment of the acute secondary poisoning is made by comparing the concentration in the rodents to LD50 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 qualitative assessment indicates 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.

**Table 2.8.5.5‑2: Qualitative assessment of acute secondary poisoning.**

|  |
| --- |
|  |

* **Tier 1 assessment of long term secondary poisoning**

The Tier 1 assessment of secondary poisoning is based on the concentration in the predator's or scavenger's food, i.e. poisoned rodents. The rodents are assumed to consume entirely the bait (PD = 1), while half of the predator's or scavenger's daily food intake is poisoned rodents (Frodent = 0.5). The rodents are assumed to eat the baits in 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 catch the rodent after last meal on day 5 or day 14. Only resistant rodents are assumed to eat bait 14 day. The calculation of concentrations in rodents is explained in detail in Section 2.8.4.4.2.2. The PNECoral is based on the highest concentration causing no effects in the test with long-term exposure. The derivations of PNECs are explained in Section 2.8.2.7.

**Table 2.8.5.5‑3: Tier 1 risk characterisation of secondary poisoning. Expected concentration in target rodents is compared to the PNECoral expressed as concentration in food. Rodents are assumed to consume entirely bait (PD=1). Half of the predator's diet is poisoned rodents (Frodent=0.5).**

|  |
| --- |
|  |

The Tier 1 risk characterisation shows that there is an unacceptable risk for secondary poisoning of mammals and birds.

Resistant rodents can feed on the poisoned baits longer and accumulate higher difenacoum residues than non-resistant rodents. Resistant rodents can continue to feed difenacoum up to two weeks, while the non-resistant rodents stop feeding after 5 days. Based on the calculations, the resistant rodents cause about 1.5 times higher risk for secondary poisoning of birds and mammals than non-resistant rodents.

* **Tier 2 assessment of long term secondary poisoning**

In the Tier 2 assessment of long-term secondary poisoning the expected concentration in predators is compared to PNECoral expressed as a daily dose. The predators accumulate difenacoum by feeding on poisoned target rodents during one day. The rodents are assumed to eat entirely the bait (PD = 1), whereas half of the predator's or scavenger's daily food intake is poisoned rodents (Frodent = 0.5). The rodents are assumed to eat the baits in five or fourteen successive days. The susceptible rodents are assumed to stop feeding after 5 days, but resistant rodents are assumed to continue feeding until day 14. The calculation of expected concentrations is explained in detail in Section 2.8.4.4.2.2.

**Table 2.8.5.5‑4: Tier 2 risk characterisation of long term secondary poisoning. The expected concentrations in predatory birds and mammals are compared to the PNECoral expressed as daily dose.**

|  |
| --- |
|  |

Also the Tier 2 risk characterisation shows a high risk for secondary poisoning (Table 2.8.4.3‑1). The PNECoral expressed as a dose is approximately equal for birds and mammals, and the sensitivity of the species used in calculations is determined predominantly by the ratio of daily food consumption to body weight so that the higher ratio results in the higher risk. No data are available on the sensitivity of the example species (the species listed in Table 12 of the ESD PT14) to difenacoum. Only one day exposure of predators is assumed in the ESD PT14, but it is mentioned that predators could be exposed over several days. This would mean higher accumulation in predators, because daily elimination of difenacoum from the predators is assumed to be less than the ingested amount. On the other hand, it is unlikely that all worst case assumptions would materialize simultaneously in nature. It is likely that in the long-term exposure, the prey rodents do not eat only the bait and also the fraction of poisoned rodents in the predator's diet can be lower than 50%. The resistant rodents cause somewhat higher risk for predators than non-resistant rodents, but the difference is smaller than in the Tier 1 assessment.

The applicant has submitted two experimental studies on the secondary poisoning in Barn Owls. Tier 1 and Tier 2 risk characterisation are recalculated for the Barn Owl on the basis of the measured concentrations in rats and mice with the experimental data provided in the difenacoum Task Force Annex I inclusion dossier. The risks are significantly lower than with the ESD PT14 calculations however they are still considerably higher than 1 indicating risk for secondary poisoning of the Barn Owls.

A review of the available monitoring data was provided in the difenacoum Task Force Annex I inclusion dossier to characterize the risk of secondary poisoning. Most of the incidents were due to misuse, abuse or unspecified use. Only few incidents resulted from approved use of difenacoum. However, like theoretical calculations and experimental results, the monitoring data clearly show that difenacoum poses an inacceptable risk for secondary poisoning. While all available information indicates risk, it does not tell the frequency of secondary poisoning incidents among wildlife.

In order to reduce the risk of primary and secondary poisoning, it is mandatory to follow the use instructions of rodenticidal baits. It is considered that these instructions will be respected by trained professional users.

Regarding the non-professional users, the risk of primary and secondary poisoning is considered as limited for indoor application. The outdoor application for non-professional users should be authorised only if the specific use restrictions can be applied to reduce the risk for primary and secondary poisoning.

* + - 1. **Overall conclusion**

No studies were conducted with the product SORKIL G GRAINS for the environment; therefore the environmental risk assessment has been carried out with data on the active substance from the CAR of difenacoum owned by the Activa/Pelgar difenacoum & Brodifacoum Task Force. The environmental risk is considered as limited for the use in and around building by professional and indoor for non professional, in strict compliance with the specific use instructions of rodenticidal baits and the use restrictions to reduce the risk for primary and secondary poisoning presented below.

## Measures to protect man, animals and the environment

*See Summary of Product Characteristics (SPC).*

# Proposal for the decision – major change and renewal 2018

**Summary of product characteristics for a biocidal product**

**1. Administrative information**

**1.1. Trade name(s) of the product**

| **Trade name(s)** | TITANIUM B |
| --- | --- |
|  |  |

**1.2. Authorisation holder**

|  |  |  |
| --- | --- | --- |
| **Name and address of the authorisation holder** | **Name** | EDIALUX |
| **Address** | ZA MACON EST  01750 REPLONGES  France |
| **Authorisation number** |  | |
| *Suffixes to the authorisation number linked to trade names* |  | |
| *R4BP asset reference number* |  | |
| **Date of the authorisation** |  | |
| **Expiry date of the authorisation** |  | |

**1.3. Manufacturer(s) of the product**

|  |  |
| --- | --- |
| **Name of manufacturer** | EDIALUX |
| **Address of manufacturer** | ZA MACON EST  01750 REPLONGES  France |
| **Location of manufacturing sites** | ZA MACON EST  01750 REPLONGES  France |

**1.4. Manufacturer(s) of the active substance(s)**

|  |  |
| --- | --- |
| **Active substance** | Difenacoum |
| **Name of manufacturer** | PELGAR INTERNATIONAL LTD |
| **Address of manufacturer** | UNIT 13 Newman Lane  GU34 2QR ALTON  United-Kingdom |
| **Location of manufacturing sites** | UNIT 13 Newman Lane  GU34 2QR ALTON  United-Kingdom |

**2. Product composition and formulation**

**2.1. Qualitative and quantitative information on the composition of the product**

| **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 | 0.0026 (technical) |

**2.2. Type of formulation**

|  |
| --- |
| Ready-to-use bait: grain |

**3. Hazard and precautionary statements**

| **Classification** | |
| --- | --- |
| Hazard category | STOT RE 2 |
| Hazard statement | H373: May cause damage to organs (blood) through prolonged or repeated exposure |
|  | |
| **Labelling** | |
| Signal words | Warning |
| Hazard statements | H373: May cause damage to organs (blood) through prolonged or repeated exposure |
| Precautionary statements | P101: If medical advice is needed, have product container or label at hand.  P102: Keep out of reach of children.  P103: Read label before use.  P260: Do not breathe dust/fumes/gas/mist/vapours/spray.  P314: Get medical advice/attention if you feel unwell.  P501: Dispose of contents/container to … [*… in accordance with local/regional/national/international regulation]* |
|  | |
| Note |  |

**4. Authorised use(s)**

**4.1. Use description**

**Table 1. Use # 1 – House mice and/or rats – trained professionals – indoor**

|  |  |
| --- | --- |
| **Product Type** | 14 |
| **Where relevant, an exact description of the authorised use** | Not relevant for rodenticides |
| **Target organism(s) (including development stage)** | Mus musculus (house mice)  *Rattus norvegicus* (brown rat)  *Rattus rattus* (black or roof rat) |
| **Field(s) of use** | Indoor |
| **Application method(s)** | Bait formulations:  - Ready-to-use bait to be used in tamper-resistant bait stations[[15]](#footnote-15)  - *[Covered and protected baiting points]* |
| **Application rate(s) and frequency** | Bait products:  - Rats: 100-200 g of bait per baiting point.  - Mice: 30 g of bait per baiting point. |
| **Category(ies) of users** | Trained professionals |
| **Pack sizes and packaging material** | Minimum pack size of 3 kg*.*  *(****In France only*** *: minimum pack size of 5 kg)*  Package is restricted to separately packed bags with a maximum of 10 kg per packed bag.  TITANIUM B is supplied in sachet or loose.  PP sachets (20-200 g for rats and 25-30 g for mice) are packed in:  - PP, PE or HDPE bucket (3-10 kg),  - Cardboard box (3-10 kg),  - Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) (3-25 kg),  - Prefilled bait station in cardboard box (3-10 kg).  Loose baits are packed in:  - PP bucket (3-10 kg),  - Cardboard box with one PP bag inside (3-10 kg),  - Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) with one PP bag inside (3-10 kg). |

***4.1.1.* *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. |

***4.1.2 Use-specific risk mitigation measures***

|  |
| --- |
| - Where possible, prior to the treatment inform any possible bystanders (e.g. users of the treated area and their surroundings) about the rodent control campaign *[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.  *-* Do not use the product as permanent baits for the prevention of rodent infestation or monitoring of rodent activities.  - Do not use the product in pulsed baiting treatments. |

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

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

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

|  |
| --- |
|  |

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

|  |
| --- |
|  |

**4.2. Use description**

**Table 2. Use # 2 Rats – trained professionals – outdoor around buildings**

|  |  |
| --- | --- |
| **Product Type** | 14 |
| **Where relevant, an exact description of the authorised use** | Not relevant for rodenticides |
| **Target organism(s) (including development stage)** | *Rattus norvegicus* (brown rat)  *Rattus rattus* (black or roof rat) |
| **Field(s) of use** | Outdoor around buildings |
| **Application method(s)** | Bait formulations:  - Ready-to-use bait to be used in tamper-resistant bait stations.  - *[Covered and protected baiting points]* |
| **Application rate(s) and frequency** | Bait products:  - Rats: 100-200 g of bait per baiting point. |
| **Category(ies) of users** | Trained professionals |
| **Pack sizes and packaging material** | Minimum pack size of 3 kg*.*  *(****In France only*** *: minimum pack size of 5 kg)*  - Bait formulations:  Package is restricted to separately packed bags with a maximum of 10 kg per packed bag.  TITANIUM B is supplied in sachet or loose.  PP sachets (20-200 g for rats) are packed in:  - PP, PE or HDPE bucket (3-10 kg),  - Cardboard box (3-10 kg),  - Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) (3-25 kg),  - Prefilled bait station in cardboard box (3-10 kg).  Loose baits are packed in:  - PP bucket (3-10 kg),  - Cardboard box with one PP bag inside (3-10 kg),  - Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) with one PP bag inside (3-10 kg). |

***4.2.1.* *Use-specific instructions for use***

|  |
| --- |
| - Protect bait from the atmospheric conditions. Place the baiting points in areas not liable to flooding.  - Replace any bait in baiting points in which bait has been damaged by water or contaminated by dirt.  - Remove the remaining product at the end of treatment period.  - *[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].* |

***4.2.2 Use-specific risk mitigation measures***

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

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

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

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

|  |
| --- |
|  |

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

|  |
| --- |
|  |

**4.3. Use description**

**Table 3. Use # 3 *(not relevant in France)*– House mice – professionals – indoor**

|  |  |
| --- | --- |
| **Product Type** | 14 |
| **Where relevant, an exact description of the authorised use** | Not relevant for rodenticides |
| **Target organism(s) (including development stage)** | *Mus musculus* (house mice) |
| **Field(s) of use** | Indoor |
| **Application method(s)** | Ready-to-use bait to be used in tamper-resistant bait stations[[16]](#footnote-16) |
| **Application rate(s) and frequency** | Bait products:  - Mice: 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. |
| **Category(ies) of users** | Professionals |
| **Pack sizes and packaging material** | Minimum pack size of 3 kg*.*  - Bait formulations:  Package is restricted to separately packed bags with a maximum of 10 kg per packed bag.  TITANIUM B is supplied in sachet or loose.  PP sachets (25-30 g for mice) are packed in:  - PP, PE or HDPE bucket (3-10 kg),  - Cardboard box (3-10 kg),  - Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) (3-25 kg),  - Prefilled bait station in cardboard box (3-10 kg).  Loose baits are packed in:  - PP bucket (3-10 kg),  - Cardboard box with one PP bag inside (3-10 kg),  - Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) with one PP bag inside (3-10 kg). |

***4.3.1.* *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. |

***4.3.2 Use-specific risk mitigation measures***

|  |
| --- |
|  |

***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. |

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

|  |
| --- |
|  |

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

|  |
| --- |
|  |

**4.4. Use description**

**Table 4. Use # 4 *(not relevant in France)*– Rats – professionals – indoor**

|  |  |
| --- | --- |
| **Product Type** | 14 |
| **Where relevant, an exact description of the authorised use** | Not relevant for rodenticides |
| **Target organism(s) (including development stage)** | *Rattus norvegicus* (brown rat)  *Rattus rattus* (black or roof rat) |
| **Field(s) of use** | Indoor |
| **Application method(s)** | Ready-to-use bait to be used in tamper-resistant bait stations |
| **Application rate(s) and frequency** | Bait products:  - Rats: 100-200 g of bait per bait station. If more than one bait station is needed, the minimum distance between bait stations should be of 15 meters. |
| **Category(ies) of users** | Professionals |
| **Pack sizes and packaging material** | Minimum pack size of 3 kg*.*  - Bait formulations:  Package is restricted to separately packed bags with a maximum of 10 kg per packed bag.  TITANIUM B is supplied in sachet or loose.  PP sachets (20-200 g for rats) are packed in:  - PP, PE or HDPE bucket (3-10 kg),  - Cardboard box (3-10 kg),  - Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) (3-25 kg),  - Prefilled bait station in cardboard box (3-10 kg).  Loose baits are packed in:  - PP bucket (3-10 kg),  - Cardboard box with one PP bag inside (3-10 kg),  - Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) with one PP bag inside (3-10 kg). |

***4.4.1.* *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. |

***4.4.2 Use-specific risk mitigation measures***

|  |
| --- |
|  |

***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. |

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

|  |
| --- |
|  |

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

|  |
| --- |
|  |

**4.5. Use description**

**Table 5. Use # 5 *(not relevant in France)*– Rats – professionals – outdoor around buildings**

|  |  |
| --- | --- |
| **Product Type** | 14 |
| **Where relevant, an exact description of the authorised use** | Not relevant for rodenticides |
| **Target organism(s) (including development stage)** | *Rattus norvegicus* (brown rat)  *Rattus rattus* (black or roof rat) |
| **Field(s) of use** | Outdoor around buildings |
| **Application method(s)** | Ready-to-use bait to be used in tamper-resistant bait stations |
| **Application rate(s) and frequency** | Bait products:  - Rats: 100-200 g of bait per bait station. If more than one bait station is needed, the minimum distance between bait stations should be of 15 meters. |
| **Category(ies) of users** | Professionals |
| **Pack sizes and packaging material** | Minimum pack size of 3 kg*.*  - Bait formulations:  Package is restricted to separately packed bags with a maximum of 10 kg per packed bag.  TITANIUM B is supplied in sachet or loose.  PP sachets (20-200 g for rats) are packed in:  - PP, PE or HDPE bucket (3-10 kg),  - Cardboard box (3-10 kg),  - Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) (3-25 kg),  - Prefilled bait station in cardboard box (3-10 kg).  Loose baits are packed in:  - PP bucket (3-10 kg),  - Cardboard box with one PP bag inside (3-10 kg),  - Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) with one PP bag inside (3-10 kg). |

***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.  - 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. |

***4.5.2 Use-specific risk mitigation measures***

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

***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 stations 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. |

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

|  |
| --- |
|  |

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

|  |
| --- |
|  |

**4.6. Use description**

**Table 6. Use # 6 – House mice – general public – indoor**

|  |  |
| --- | --- |
| **Product Type** | 14 |
| **Where relevant, an exact description of the authorised use** | Not relevant for rodenticides |
| **Target organism(s) (including development stage)** | *Mus musculus* (house mice) |
| **Field(s) of use** | Indoor |
| **Application method(s)** | Ready-to-use bait *[in sachets for loose bait]* to be used in tamper-resistant bait stations[[17]](#footnote-17). |
| **Application rate(s) and frequency** | Bait products:  - 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. |
| **Category(ies) of users** | General public |
| **Pack sizes and packaging material** | Maximum pack size of 150 g  TITANIUM B is supplied only in sachet.  PP sachets (20-150 g for rats and 25-30 g for mice) are packed in:  - PP or HDPE bucket (Rats and mice: up to 150 g; Mice: up to 50 g)  - Cardboard box (Rats and mice: up to 150 g; Mice: up to 50 g)  - Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) (Rats and mice: up to 150 g; Mice: up to 50 g)  - Prefilled bait station in cardboard box (Rats and mice: up to 150 g; Mice: up to 50 g) |

***4.6.1.* *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. |

***4.6.2 Use-specific risk mitigation measures***

|  |
| --- |
|  |

***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***

|  |
| --- |
|  |

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

|  |
| --- |
|  |

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

|  |
| --- |
|  |

**4.7. Use description**

**Table 7. Use # 7 – Rats – general public – indoor**

|  |  |
| --- | --- |
| **Product Type** | 14 |
| **Where relevant, an exact description of the authorised use** | Not relevant for rodenticides |
| **Target organism(s) (including development stage)** | *Rattus norvegicus* (brown rat)  *Rattus rattus* (black or roof rat) |
| **Field(s) of use** | Indoor. |
| **Application method(s)** | Ready-to-use bait *[in sachets for loose bait]* to be used in tamper-resistant bait stations2. |
| **Application rate(s) and frequency** | Bait products:  - 100-200 g of bait per bait station. If more than one bait station is needed, the minimum distance between bait stations should be of 15 meters. |
| **Category(ies) of users** | General public |
| **Pack sizes and packaging material** | Maximum pack size of 150 g.  TITANIUM B is supplied only in sachet.  PP sachets (20-150 g for rat) are packed in:  - PP or HDPE bucket (up to 150 g),  - Cardboard box (up to 150 g),  - Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) (up to 150 g),  - Prefilled bait station in cardboard box (up to 150 g). |

***4.7.1.* *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. |

***4.7.2 Use-specific risk mitigation measures***

|  |
| --- |
|  |

***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***

|  |
| --- |
|  |

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

|  |
| --- |
|  |

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

|  |
| --- |
|  |

**4.8. Use description**

**Table 8. Use # 8 – Rats – general public – outdoor around buildings**

|  |  |
| --- | --- |
| **Product Type** | 14 |
| **Where relevant, an exact description of the authorised use** | Not relevant for rodenticides |
| **Target organism(s) (including development stage)** | *Rattus norvegicus* (brown rat)  *Rattus rattus* (black or roof rat) |
| **Field(s) of use** | Outdoor around buildings |
| **Application method(s)** | Ready-to-use bait *[in sachets for loose bait]* to be used in tamper-resistant bait stations2. |
| **Application rate(s) and frequency** | Bait products:  - 100-200 g of bait per bait station. If more than one bait station is needed, the minimum distance between bait stations should be of 15 meters. |
| **Category(ies) of users** | General public |
| **Pack sizes and packaging material** | Maximum pack size of 150 g.  TITANIUM B is supplied only in sachet.  PP sachets (20-150 g for rat) are packed in:  - PP or HDPE bucket (up to 150 g),  - Cardboard box (up to 150 g),  - Multilayered kraft paper bag (alternative OPET/LDPE alternative PE) (up to 150 g),  - Prefilled bait station in cardboard box (up to 150 g). |

***4.8.1.* *Use-specific instructions for use***

|  |
| --- |
| - Place the bait stations in areas not liable to flooding.  - Replace any bait in a bait station in which bait has been damaged by water or contaminated by dirt.  - The 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. |

***4.8.2 Use-specific risk mitigation measures***

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

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

|  |
| --- |
|  |

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

|  |
| --- |
|  |

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

|  |
| --- |
|  |

**5. General directions for use**

**5.1. Instructions for use**

|  |
| --- |
| **FOR PROFESSIONAL AND TRAINED PROFESSIONAL USERS**  - 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 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.  - *[Where required by the risk assessment:*  *-* 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.  ***FOR TRAINED PROFESSIONAL ONLY****- 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.  ***FOR PROFESSIONNALS ONLY*** 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.  ***FOR PROFESSIONNALS ONLY*** 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. * Place the bait in the baiting point by using a dosage devise. Specify the methods to minimise dust (e.g. wet wiping). * Decanting is to be avoided. In case decanting cannot be avoided, an RPE of APF 10 has to be used.   **FOR NON PROFESSIONAL USERS**  - Read and follow the product information as well as any information accompanying the product or provided at the point of sale before using it.  - Prior to the use of rodenticide products, non-chemical control methods (e.g. traps) should be considered.  - 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.  - Bait stations should be placed in the immediate vicinity where rodent activity has been observed (e.g. travel paths, nesting sites, feedlots, holes, burrows etc.).  - Where possible, bait stations must be fixed to the ground or other structures.  - *[*Do not open the sachets containing the bait *- where relevant for the bait formulation in the product].*  - Place bait stations out of the reach of children, birds, pets, farm animals and other non-target animals.  - Place bait stations away from food, drink and animal feeding stuffs, as well as from utensils or surfaces that have contact with these.  - Do not place bait stations near water drainage systems where they can come into contact with water.  - When using the product do not eat, drink or smoke. Wash hands and directly exposed skin after using the product.  - Remove the remaining bait or the bait stations at the end of the treatment period. |

**5.2. Risk mitigation measures**

|  |
| --- |
| **FOR PROFESSIONAL AND TRAINED PROFESSIONAL USERS**  - 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".  - ***FOR TRAINED PROFESSIONAL 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.  - ***FOR TRAINED PROFESSIONAL ONLY*** 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 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]*.  - ***FOR PROFESSIONAL ONLY*** 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].*  - ***FOR PROFESSIONAL ONLY*** Do not use baits containing anticoagulant active substances as permanent baits for the prevention of rodent infestation or monitoring of rodent activities.  - ***FOR PROFESSIONAL ONLY.*** 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").   - ***FOR PROFESSIONAL ONLY*** 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.  **FOR NON PROFESSIONAL USERS**  - Consider preventive control measures (plug holes, remove potential food and drinking as far as possible) to improve product intake and reduce the likelihood of reinvasion.  - Do not use anticoagulant rodenticides as permanent baits (e.g. for prevention of rodent infestation or to detect rodent activity).  - The product information (i.e. label and/or leaflet) shall clearly show that:   * 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.  - Search for and remove dead rodents during treatment, at least as often as bait stations are inspected.  - 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]*. |

**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. |

**5.4. Instructions for safe disposal of the product and its packaging**

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

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

|  |
| --- |
| - Store in a dry, cool and well ventilated place. Keep the container closed and away from direct sunlight.  - Do not store at temperatures above 40°C.  - Store in places prevented from the access of children, birds, pets and farm animals.  - Shelf life: 24 month |

**6. Other information**

|  |
| --- |
| - (In France only: The authorisation holder has to monitor the resistance phenomenon of rodent populations toward the active substance difenacoum. Results of the resistance monitoring must be submitted at the renewal of the product.)  - The authorisation holder must provide the results of the long-term (2 years) storage study with the new formulation within 24 months in post-authorization.  - Because of their delayed mode of action, anticoagulant rodenticides may take from 4 to 10 days to be effective after effective 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. |

Annex 1: List of studies reviewed

##### List of new data[[18]](#footnote-18) submitted in support of the evaluation of the active substance - PAR 2013

| **Section No** | **Reference No** | **Author** | **Year** | **Title** | **Owner of data** | **Letter of Access** | | **Data protection claimed** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  | **Yes** | **No** | **Yes** | **No** |
| A3.3 | Report No. 2109/0005 | Walker JA and Mullee, DM | 2007 | Difenacoum: Determination of General Physico-chemical Properties  SafePharm Laboratories | Pelgar |  |  |  |  |
| A4.2 (c) | CEMR-4470 | Marshall L. | 2009 | Validation of a method for the determination of Difenacoum residues in sediment | Activa / PelGar Brodifacoum and Difenacoum Task Force |  |  |  |  |
| A4.2 (c) | CEMR-4469 | Marshall L. | 2009 | Validation of a method for the determination of Difenacoum residues in animal Matrices (Liver and Muscle) and Crop matrix | Activa / PelGar Brodifacoum and Difenacoum Task Force |  |  |  |  |
| A4.2 (e) | CEMR-4469 | Marshall L. | 2009 | Validation of a method for the determination of Difenacoum residues in animal Matrices (Liver and Muscle) and Crop matrix | Activa / PelGar Brodifacoum and Difenacoum Task Force |  |  |  |  |

##### List of new data submitted in support of the evaluation of the biocidal product – PAR 2013 updated 2018

| **Section No** | **Reference No** | **Author** | **Year** | **Title** | **Owner of data** | **Letter of Access** | | **Data protection claimed** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  | **Yes** | **No** | **Yes** | **No** |
| Doc IIIB 3.2 | Report No 20091137.02 | M. Krack | 2010 | EDI-200 [Cut Oat (grain bait, AB)]  Explosive properties A.14 | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 3.3 | Report No 20091137.04 | M. Krack | 2010 | EDI-200 [Cut Oat (grain bait, AB)]  Oxidising Properties A.17 | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 3.4.2 | Report No 20091137.01 | M. Krack | 2010 | EDI-200 [Cut Oat (grain bait, AB)]  Flammability (solids) A.10 | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 3.4.1 | Report No 20091137.03 | M. Krack | 2010 | EDI-200 [Cut Oat (grain bait, AB)]  Auto-flammability (solids – determination of relative self-ignition temperature) A.16 | Edialux Formulex NV |  |  |  |  |
| Doc IIIB  3.5 / 3.12 | Mo3907  Amendment No.2 | Manka S. | 2012 | Determination of physic-chemical properties and storage stability test for EDI-300 [Whole wheat (grain bait, AB)], 2 weeks at 54° C and up to 24 months at ambient conditions.  Biogenius | Edialux Formulex NV |  |  |  |  |
| Doc IIIB  3.6 / 3.7 /3.8 | Mo3907  Study plan | Bublitz M. | 2010 | Determination of physic-chemical properties and storage stability test for EDI-300 [Whole wheat (grain bait, AB)], 2 weeks at 54° C and up to 24 months at ambient conditions  Biogenius | Edialux Formulex NV |  |  |  |  |
| Doc IIIB  3.6 / 3.7 /3.8 | Mo3907  Amendment No.1 | Manka S. | 2011 | Determination of physic-chemical properties and storage stability test for EDI-300 [Whole wheat (grain bait, AB)], 2 weeks at 54° C and up to 24 months at ambient conditions  Biogenius | Edialux Formulex NV |  |  |  |  |
| Doc IIIB  3.6 / 3.7 /3.8 | Mo3907  2 weeks interim report | Bublitz M. | 2010 | Determination of physic-chemical properties and storage stability test for EDI-300 [Whole wheat (grain bait, AB)], 2 weeks at 54° C and up to 24 months at ambient conditions  Biogenius | Edialux Formulex NV |  |  |  |  |
| Doc IIIB  3.7 | 12-905021-001  Study Plan | Demangel B. | 2012 | Dustiness of granular products  on EDI-300 (Whole wheat grain bait, AB)  Défitraces | Edialux Formulex NV |  |  |  |  |
| Doc IIIB  4.1 | MV031 | Bublitz M. | 2010 | Determination of Difenacoum in Grain Baits Content - HPLC – Internal Standards Standard method  Biogenius | Edialux Formulex NV |  |  |  |  |
| Doc IIIB  4.1 | Mo3825 | Bublitz M. | 2010 | Validation of method MV031 : Determnation of Difenacoum in grain bait | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 5.10.1 | XXX | XXX | XXX | Efficacité du Sorkil-G, Rodenticide à base de 0.005% de difénacoum, contre le rat surmulot (Rattus norvegicus Berkenhout),  XXX | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 5.10.2 | XXX | XXX | XXX | Efficacité du Sorkil-G, Rodenticide à base de 0.005% de difénacoum, contre la souris grise (Mus musculus L.)  XXX | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 5.10.3 | XXX | XXX | XXX | Évaluation de la perte d'efficacité au cours du vieillissement du rodenticide Sorkil-G à base de 0.005% de difénacoum pour lutter contre le surmulot (Rattus norvegicus Berkenhout) et la souris grise (Mus musculus L.), XXX | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 5.10.4 | XXX | XXX | XXX | Bait choice- EDI 200 AB-ROD fresh bait with difenacoum, Rats  (*Rattus norvegicus*) | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 5.10.5 | XXX | XXX | XXX | Bait choice- EDI 200 AB-ROD aged bait with difenacoum, Rats  (*Rattus norvegicus*)  XXX | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 5.10.6 | XXX | XXX | XXX | Bait choice- EDI 200 AB-ROD fresh bait with difenacoum, Mice  (*Mus musculus*)  XXX | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 5.10.7 | XXX | XXX | XXX | Bait choice- EDI 200 AB-ROD aged bait with difenacoum, Mice  (*Mus musculus*)  XXX | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 5.10.8 | XXX | XXX | XXX | Palatability and efficiency of EDI 200 AB-ROD for rats and mice in the field, XXX | Edialux Formulex NV |  |  |  |  |
|  | XXX | XXX | XXX | Evaluation of the efficacy of EDI-600\_24 (grain rodenticide containing 0.0024% w/w bromadiolone) for the control of black rat infestations in and around agricultural buildings. | EDIALUX |  |  | X |  |
|  |  | XXX | XXX | Expert opinion similarity Sorkil G Grains vs Rakil, black rat |  |  |  |  |  |
| Doc IIIB 6.1.2 | XXX | XXX | XXX | Sorkil rodenticide cut oat grain bait (AB), Acute dermal toxicity in the rat  XXX | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 6.2.1 | XXX | XXX | XXX | Sorkil rodenticide cut oat grain bait (AB), Skin irritation test in the rabbit  XXX | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 6.2.2 | XXX | XXX | XXX | Sorkil rodenticide cut oat grain bait (AB), Eye irritation test in the rabbit  XXX | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 6.3 | XXX | XXX | XXX | Sorkil rodenticide cut oat grain bait (AB), Local lymph node assay in the mouse  XXX | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 6.4 | XXX | XXX | XXX | Difenacoum - In vitro absorption from Pelleted Bait through Dermatomed Human Skin Using [14C]-Difenacoum | PelGar International Ltd / Edialux Formulex NV |  |  |  |  |
| Doc IIC B6.6 (1) | XXX | XXX | XXX | Study to Determine Potential Exposure to Operators During Simulated Use of Anticoagulant Rodenticide Baits  XXX | CEFIC |  |  |  |  |
| Doc IIC B6.6 (2) | - | XXX | XXX | Estimation of the frequency of dermal exposure during the occupational use of rodenticides. XXX | CEFIC |  |  |  |  |

* **Major change application and renewal 2018**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| * **Author(s)** | **Year** | **Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published** | **Data Protection Claimed (Yes/No)** | **Owner (PUB / ORG)** | **Date of first submission** |
| XXX | XXX | Study on the palatability and efficacy of a 0.0024% w/w Difenacoum red wheat bait in house mouse (*Mus musculus*), XXX | Y | Edialux |  |
| XXX | XXX | Study on the palatability and efficacy of a 0.0024% w/w difenacoum wheat bait in brown rat (*Rattus norvegicus*), XXX | Y | Edialux |  |
| XXX | XXX | Study on the palatability and efficacy of a 0.0024% w/w difenacoum wheat bait in black rat (*Rattus rattus*), XXX | Y | Edialux |  |
| XXX | XXX | Evaluation of the efficacy of EDI 600\_24 (grain rodenticide containing 0.0024% w/w bromadiolone) for the control of house mouse infestations in and around agricultural buildings, XXX | Y | Edialux |  |
| XXX | XXX | Evaluation of the efficacy of EDI 600\_24 (grain rodenticide containing 0.0024% w/w bromadiolone) for the control of brown rat infestations in and around agricultural buildings, XXX | Y | Edialux |  |
| XXX | XXX | Evaluation of the efficacy of EDI 600\_24 (grain rodenticide containing 0.0024% w/w bromadiolone) for the control of black rat infestations in and around agricultural buildings, XXX | Y | Edialux |  |
| XXX | XXX | Study on the palatability and efficacy of a 0.0024% w/w bromadiolone wheat bait in house mouse (*Mus musculus*), XXX | Y | Edialux |  |
| XXX | XXX | Study on the palatability and efficacy of a 0.0024% w/w bromadiolone wheat bait in brown rat (*Rattus norvegicus*), XXX | Y | Edialux |  |
| XXX | XXX | Study on the palatability and efficacy of a 0.0024% w/w bromadiolone wheat bait in black rat (*Rattus rattus*), XXX | Y | Edialux |  |
| XXX | XXX | Study on the palatability and efficacy of a 26-months-old Difenacoum red wheat bait in Black Rat (*Rattus rattus*), XXX | Y | Edialux |  |

* **Major change and renewal of the biocidal product TITANIUM B:**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Author(s)** | **Year** | **Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published** | **Data Protection Claimed (Yes/No)** | **Owner (PUB / ORG)** | **Date of first submission** |
| DEMANGEL, B. | 2017 | Chemical stability during and after an accelerated storage procedure for 8 weeks at 40 ± 2°C on EDI-300\_25  Study n°17-904017-005  DEFITRACES  GLP Study | Y | EDIALUX | 2017 |
| DEMANGEL, B. | 2017 | Storage procedure for 6 months at 20±2 °C  Study n°17-904017-006  DEFITRACES  GLP Study | Y | EDIALUX | 2017 |
| RICAU, H. | 2017 | Validation of analytical method for the determination of difenacoum in the EDI-300\_25.  Study n°17-904017-008  DEFITRACES  GLP Study | Y | EDIALUX | 2017 |
| DEMANGEL, B. | 2019 | Chemical stability after a storage procedure for 24 months at 20 ± 2°C on EDI-300\_25  Final study n°17-904017-006  DEFITRACES  GLP Study | Y | EDIALUX | 2021 |

Annex 2: Analytical methods residues – active substance – 2013

**Difenacoum**

**Matrix, action levels, relevant residue and reference**

|  |  |  |  |
| --- | --- | --- | --- |
| matrix | limit | relevant residue | reference or comment |
| plant products | LOQ= 0.01mg/kg | Difenacoum |  |
| food of animal origin | LOQ= 0.01mg/kg | Difenacoum |  |
| soil | LOQ= 0.0214 μg/g | Difenacoum |  |
| drinking water | LOQ = 0.05 μg/L | Difenacoum |  |
| surface water | LOQ = 0.05 μg/L | Difenacoum |  |
| air | Unnecessary due to the low vapour pressure of difenacoum | | |
| body fluids / tissues | LOQ= 0.01mg/kg | Difenacoum |  |

**Methods suitable for the determination of residues (monitoring methods)**

**Methods for products of plant origin**

| reference | matrix | LOQ (mg/kg) | principle | comment | | owner |
| --- | --- | --- | --- | --- | --- | --- |
| Marshall, L., 2009, Method Validation for the Determination of Difenacoum in Animal Matrices (Liver and Muscle) and Crop Matrix (Oilseed Rape), CEM Analytical Services Limited, Study CEMR-4469 | Oil-seed rape | LOQ= 0.01mg/kg | *LC-MS/MS* |  | Activa / PelGar Brodifacoum and Difenacoum Task Force | | |

**Methods for foodstuffs of animal origin**

| reference | matrix | LOQ (mg/kg) | principle | comment | owner |
| --- | --- | --- | --- | --- | --- |
| Marshall, L., 2009, Method Validation for the Determination of Difenacoum in Animal Matrices (Liver and Muscle) and Crop Matrix (Oilseed Rape), CEM Analytical Services Limited, Study CEMR-4469 | Meat | LOQ= 0.01mg/kg | *LC-MS/MS* |  | Activa / PelGar Brodifacoum and Difenacoum Task Force |

**Methods for soil**

| reference | LOQ (mg/kg) | principle | comment | owner |
| --- | --- | --- | --- | --- |
| Morlacchini, M., 2006, Residues determination of Brodifacoum, Difenacoum and Bromadiolone in soil, CERZOO (Italy), Study CZ/05/002/Activa/Soil | LOQ= 0.0214 μg/g | *HPLC – UV-VIS* |  | Activa / PelGar Brodifacoum and Difenacoum Task Force |

**Methods for sediment**

| reference | LOQ (mg/kg) | principle | comment | owner |
| --- | --- | --- | --- | --- |
| Marshall, L., 2009, Validation of a Method for the Determination of Difenacoum Residues in Sediment, CEM Analytical Services Limited, Study CEMR-4470 | LOQ= 0.01mg/kg | LC-MS/MS |  | Activa / PelGar Brodifacoum and Difenacoum Task Force |

**Methods for drinking water and surface water**

| reference | matrix | LOQ (µg/l) | principle | comment | owner |
| --- | --- | --- | --- | --- | --- |
| Martinez M.P. 2005. Difenacoum Technical: Validation of the Analytical Method for the Determination of the Residues in Drinking, Ground and Surface waters, Test Laboratory of ChemService S.r.l. ChemService Study No. CH-288/2005 | Water | LOQ = 0.05 μg/l | *HPLC – MS/MS* |  | Activa / PelGar Brodifacoum and Difenacoum Task Force |

**Methods for air**

| reference | LOQ (µg/m3) | principle | comment | owner |
| --- | --- | --- | --- | --- |
| Unnecessary due to the low vapour pressure of difenacoum | | | | |

**Methods for body fluids/tissue**

| reference | matrix | LOQ (mg/kg) | principle | comment | owner |
| --- | --- | --- | --- | --- | --- |
| Marshall, L., 2009, Method Validation for the Determination of Difenacoum in Animal Matrices (Liver and Muscle) and Crop Matrix (Oilseed Rape), CEM Analytical Services Limited, Study CEMR-4469 | Liver | LOQ= 0.01mg/kg | *LC-MS/MS* |  | Activa / PelGar Brodifacoum and Difenacoum Task Force |

Annex 3: Efficacy of the active substance from its use in the product – 2013 updated 2017

* **First authorization SORKIL G GRAINS 2013**

| **Test substance** | **Test organisms** | **Test system / Concentrations applied / exposure time** | **Test results: effects, mode of action, resistance** | **Reference** |
| --- | --- | --- | --- | --- |
| SORKIL-G (old formulation) | Norway rat (*Rattus norvegicus*)  22 wild strain rats, males and females. | Semi-field trial (warehouse).  Choice feeding test: 150 g/day of test bait and control bait in one of 2 of 18 feeding dishes.  4-day preconditioning, 16-day choice. | 21 dead: 13 females and 8 males, 1 female survived. (95% mortality)  Appetence index is 1.63 | XXX |
| SORKIL-G (old formulation) | House mouse (*Mus musculus*)  About 50 mice based on control bait consumption. | Field trial (piggery).  Choice feeding test: 20 g of control diet and/or test bait per day and per feeding dish.  44-day test with 5-day preconditioning, 17-day choice feeding period, 17-day bait feeding period and 5-day post baiting period. | Whole mice population eradicated in 29 days.  Good efficacy (100% mortality). | XXX |
| SORKIL-G (old formulation) | Albino rat  22 rats  Control: 2 rats, 1 male and 1 female | Laboratory test.  Choice feeding test: fresh baits, 1-year and 2-year aged test baits.  Dose: 10 g of control diet and/or test bait per day during acclimatisation period, 50 g during treatment period.  5-day preconditioning, 2-day bait feeding period and 21-day control bait period. | Mortality rates > 85% whatever the ageing of the test product.  The efficacy is good: 85-90% in 21 days. | XXX |
| SORKIL G GRAINS | CD rat (*Rattus norvegicus*)  10 rats (5 males, 5 females) | Choice feeding test: fresh bait.  Quantity sufficient for daily needs.  4-day preconditioning, 8-day pre-test control diet intake, 4-day choice feeding period and at least 14-day post treatment observations. | Amount of intake of the treated baits:  - 33.78% for male  - 47.12% for female  100% mortality was observed in 14 days in both male and female. The times to death were 3 to 8 days after the first intake of treated baits. | XXX |
| SORKIL G GRAINS | CD rat (*Rattus norvegicus*)  10 rats (5 males, 5 females) | Choice feeding test: 2 weeks, 54°C aged bait.  Quantity sufficient to meet each animal’s daily needs  4-day preconditioning, 8-day pre-test control diet intake, 4-day choice feeding period and at least 14-day post treatment observations. | Amount of intake of the treated baits:  - 30.93% for male  - 60.47% for female  100% mortality was observed in 14 days in both male and female. The times to death were 3 to 10 days after the first intake of treated baits. | XXX |
| SORKIL G GRAINS | CD1 mice (*Mus musculus*)  10 mice (5 males, 5 females) | Choice feeding test: fresh bait.  Quantity sufficient to meet each animal’s daily needs  4-day preconditioning, 8-day pre-test control diet intake, 4-day choice feeding period and at least 14-day post treatment observations. | Amount of intake of the treated baits:  - 74.45% for male  - 51.72% for female  100% mortality was observed in 14 days in both male and female. The times to death were 4 to 11 days after the first intake of treated baits. | XXX |
| SORKIL G GRAINS | CD1 mice (*Mus musculus*)  10 mice (5 males, 5 females) | Choice feeding test: 2 weeks, 54°C aged bait.  4-day preconditioning, 8-day pre-test control diet intake, 4-day choice feeding period and at least 14-day post treatment observations. | Amount of intake of the treated baits:  - 94.43% for male  - 80.78% for female  100% mortality was observed in 14 days in both male and female. The times to death were 3 to 11 days after the first intake of treated baits. | XXX |
| SORKIL G GRAINS | Rat and mice  Based on daily consumption: 11 mice and 10 rats | Field test  Private house in urban environment and chocolate factory in industrial site.  5 bait stations for mice filled with 20 g of product and 6 bait stations filled with 150 g of bait for rats.  Pre-trial survey, Pre-treatment census: duration of 7 days, Lag phase 1: duration of 2 days, Bait treatment, Lag phase 2: duration of 3 days, Post treatment census: duration of 6 day | 100 % control of the mouse population was achieved 11 days after the first bait take and 100 % control of the rat population was achieved 10 days after the first bait take. | XXX |

* **Major change application and renewal 2018**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Experimental data on the efficacy of the biocidal product against target organism(s)** | | | | | | | |
| **Function** | **Field of use envisaged** | **Test substance** | **Test organism(s)** | **Test method** | **Test system / concentrations applied / exposure time** | **Test results: effects** | **Reference** |
| Rodenticide | Indoor and around buildings | EDI-300\_24 0.0024% w/w difenacoum | House mice  *Mus musculus*  10 males  10 females | Laboratory study  Method based on: Technical Notes for Guidance on Product Evaluation – Product type 14  House mice: 20 animals (10 males and 10 females  Intoxication duration:  4 days with daily measurement of mortality and food consumption | Acclimatization: 4 days  Males and females in 2 different cages at room temperature  Day 0: reference food and bait biocidal product have been given:  - 60 g per cage of reference food for the assessment of palatability,  - 60 g per cage of biocidal product during 4 consecutive days with daily consumption measurements.  Mortality was observed during 21 days every 24 hours or until the death of all animals. | Palatability = 78 %  Mortality = 100 %  in a period from day 4 to day 9  R.I. = 1 | XXX |
| Rodenticide | Indoor and around buildings | EDI-600\_24 0.0024% w/w bromadiolone | House mice *Mus musculus*  29 mice | Field study  EPPO PP 1/114(2)  Census baiting technique, which involved the following phases:  Pre-treatment census  Pre-treatment lag phase  Treatment census  Post-treatment lag phase  Post-treatment census  During each assessment the food/bait at each station was weighed and replenished, and the consumption in grams was calculated.  During the treatment census, searches were conducted for dead and dying mice around the sites. | Acclimatization: 11 days (20 g of semonela per station per day)  Treatment: 30 g of bait per day in each lockable bait station – total 10 bait stations) during 19 days  Post-baiting: 6 days  (20 g of semonela per station per day) | Estimated efficacy = 100 %  Pre-baiting plateau = 143g/day  Post-baiting = 0 g  R.I. = 1 | XXX |
| Rodenticide | Indoor and around buildings | EDI-300\_24 0.0024% w/w difenacoum | Brown rats  *Rattus norvegicus*  5 males  5 females | Laboratory study  Method based on:  Technical Notes for Guidance on Product Evaluation – Product type 14  Brown rat: 10 animals (5 males and 5 females)  Intoxication duration:  4 days with daily measurement of mortality and food consumption | Acclimatization: 4 days  in individual cage at room temperature.  Day 0: reference food and bait biocidal product have been given:  - 50 g per animal of reference food for the assessment of palatability,  - 50 g per animal of biocidal product during 4 consecutive days with daily consumption measurements.  Mortality was observed during 21 days every 24 hours or until the death of all animals. | Palatability = 78 %  Mortality = 90 %  in a period from day 3 to day 8  R.I. = 1 | XXX |
| Rodenticide | Indoor and around buildings | EDI-600\_24 0.0024% w/w bromadiolone | Brown rats  *Rattus norvegicus*  33 rats | Field study  EPPO PP 1/114(2)  Census baiting technique, which involved the following phases:  Pre-treatment census  Pre-treatment lag phase  Treatment census  Post-treatment lag phase  Post-treatment census  During each assessment the food/bait at each station was weighed and replenished, and the consumption in grams was calculated. During the treatment census, searches were conducted for dead and dying mice around the sites. | Acclimatization: 13 days (100 g of wheat per station per day)  Treatment: 100 g of bait per day in each lockable bait station –total 12 bait stations) during 17 days  Post-baiting: 7 days  (100 g of wheat per station per day) | Estimated efficacy = 100 %  Pre-baiting plateau = 652 g/day  Post-baiting = 0 g  R.I. =1 | XXX |
| Rodenticide | Indoor and around buildings | EDI-300\_24 0.0024% w/w difenacoum | Black rats  *Rattus rattus*  5 males  5 females | Laboratory study  Method based on:  Technical Notes for Guidance on Product Evaluation – Product type 14  Brown rat: 10 animals (5 males and 5 females)  Intoxication duration:  4 days with daily measurement of mortality and food consumption | Acclimatization: 4 days  in individual cage at room temperature.  Day 0: reference food and bait biocidal product have been given:  - 40 g per animal of reference food for the assessment of palatability,  - 40 g per animal of biocidal product during 4 consecutive days with daily consumption measurements.  Mortality was observed during 21 days every 24 hours or until the death of all animals. | Palatability = 63 %  Mortality = 100 %  in a period from day 4 to day 8  R.I. = 1 | XXX |
| Rodenticide | Indoor and around buildings | EDI-600\_24 0.0024% w/w bromadiolone | Black rats  *Rattus rattus*  34 rats | Field study  EPPO PP 1/114(2)  Census baiting technique, which involved the following phases:  Pre-treatment census  Pre-treatment lag phase  Treatment census  Post-treatment lag phase  Post-treatment census  During each assessment the food/bait at each station was weighed and replenished, and the consumption in grams was calculated. During the treatment census, searches were conducted for dead and dying mice around the sites. | Acclimatization: 13 days (100 g of oat per station per day)  Treatment: 100 g of bait per day in each lockable bait station –total 12 bait stations) during 17 days  Post-baiting: 7 days  (100 g of oat per station per day) | Estimated efficacy = 100 %  Pre-baiting plateau = 673.3g/day  Post-baiting = 0 g  R.I. =1 | XXX |
| Rodenticide | Indoor and around buildings | EDI-300\_24  (red wheat bait containing 0.0024% w/w difenacoum)  Aged 26 months | Black rat  *Rattus rattus*  5 males  5 females  (individually caged)  Wild rodents | Laboratory study  Method based on:  Technical Notes for Guidance on Product Evaluation – Product type 14  Black rat: 10 animals (5 males and 5 females)  Intoxication duration:  4 days with daily measurement of mortality and food consumption | Acclimatization: 4 days  in individual cage at room temperature.  Day 0: reference food and bait biocidal product have been given:  - 40 g per animal of reference food for the assessment of palatability,  - 40 g per animal of biocidal product during 4 consecutive days with daily consumption measurements.  Mortality was observed during 21 days every 24 hours or until the death of all animals. | Palatability = 56 %  Mortality = 100 %  in a period from day 5 to day 8  R.I. = 1 | XXX |
| Rodenticide | Indoor and around buildings | EDI-600\_24 0.0024% w/w bromadiolone | House mice  *Mus musculus*  10 males  10 females | Laboratory study  Method based on:  Technical Notes for Guidance on Product Evaluation – Product type 14  House mice: 20 animals (10 males and 10 females)  Intoxication duration:  4 days with daily measurement of mortality and food consumption | Acclimatization: 4 days  Males and females in 2 different cages at room temperature  Day 0: reference food and bait biocidal product have been given:  - 60 g per cage of reference food for the assessment of palatability,  - 60 g per cage of biocidal product during 4 consecutive days with daily consumption measurements.  Mortality was observed during 21 days every 24 hours or until the death of all animals. | Palatability = 68 %  Mortality = 100 %  in a period from day 4 to day 11  R.I. = 1 | XXX |
| Rodenticide | Indoor and around buildings | EDI-600\_24 0.0024% w/w bromadiolone | Brown rats  *Rattus norvegicus*  5 males  5 females | Laboratory study  Method based on:  Technical Notes for Guidance on Product Evaluation – Product type 14  Brown rat: 10 animals (5 males and 5 females)  Intoxication duration:  4 days with daily measurement of mortality and food consumption | Acclimatization: 4 days  in individual cage at room temperature.  Day 0: reference food and bait biocidal product have been given:  - 50 g per animal of reference food for the assessment of palatability,  - 50 g per animal of biocidal product during 4 consecutive days with daily consumption measurements.  Mortality was observed during 21 days every 24 hours or until the death of all animals. | Palatability = 61 %  Mortality = 90 %  in a period from day 4 to day 8  R.I. = 1 | XXX |
| Rodenticide | Indoor and around buildings | EDI-600\_24 0.0024% w/w bromadiolone | Black rats  *Rattus rattus*  5 males  5 females | Laboratory study  Method based on:  Technical Notes for Guidance on Product Evaluation – Product type 14  Black rat: 10 animals (5 males and 5 females)  Intoxication duration:  4 days with daily measurement of mortality and food consumption | Acclimatization: 4 days  in individual cage at room temperature.  Day 0: reference food and bait biocidal product have been given:  - 40 g per animal of reference food for the assessment of palatability,  - 40 g per animal of biocidal product during 4 consecutive days with daily consumption measurements.  Mortality was observed during 21 days every 24 hours or until the death of all animals. | Palatability = 65 %  Mortality = 100 %  in a period from day 6 to day 9  R.I. = 1 | XXX |

Annex 4: Toxicology and metabolism –active substance - 2013

**Difenacoum**

Threshold Limits and other Values for Human Health Risk Assessment

| **Summary** | | | |
| --- | --- | --- | --- |
|  | Value | Study | SF |
| AEL long-term | 0.0000011 mg/kg bw/day | Teratogenicity in rabbit | 600 |
| AEL medium-term | 0.0000011 mg/kg bw/day | Teratogenicity in rabbit | 600 |
| AEL acute | 0.0000011 mg/kg bw/day | Teratogenicity in rabbit | 600 |
|  | | | |

|  |  |
| --- | --- |
| Inhalative absorption: not reported |  |
| Oral absorption: 68 % |  |
| Dermal absorption: 0.047 % for wax block bait and paste (Activa Pelgar study) – 3 % for pellet and grain baits (Sorex study) |  |

Annex 5: Toxicology – biocidal product, 2013

**SORKIL G GRAINS**

|  |  |  |
| --- | --- | --- |
| **General information** | | |
| Formulation Type: cereal grains |  | |
| Active substance(s) (incl. content): 0.005% difenacoum | |  |
| Category |  | |

| **Acute toxicity, irritancy and skin sensitisation of the preparation** | |
| --- | --- |
| LD50 oral : not classified for acute oral toxicity based on CLP exemptions based on calculations |  |
| Rat LD50 dermal (OECD 402) > 2000 mg/kg bw |  |
| Rat LC50 inhalation : justification for non-submission of data |  |
| Skin irritation (OECD 404) : not irritant |  |
| Eye irritation (OECD 405): not irritant |  |
| Skin sensitisation (OECD 429; modified LLNA): Study not acceptable – not sensitising based on CLP exemptions based on calculations |  |

Acute toxicity tests:

| Route | Method Guideline | Species Strain Sex no/group | dose levels  duration of exposure | Value LD50/LC50 | Remarks | Reference |
| --- | --- | --- | --- | --- | --- | --- |
| Dermal | OECD 402 | Sprague Dawley  5/sex | 2000mg/kg bw | > 2000mg/kg bw | No mortality  No systemic effects  Some reversible cutaneous reactions | XXX |

Dermal irritation test:

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Species | Method | Average score 24, 48 and 72 h | | Reversibility yes/no | Result | Remarks | Reference |
| Erythema | Oedema |
| Albinos NZ rabbit  3 males | OECD 404  Semi-occlusive, 4h | 0 | 0 | na | Not irritant |  | XXX |

Ocular irritation test:

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Species | Method | Average Score (24h, 48h, 72h) | | | | Result | Reversibility yes/no | Remarks | Reference |
| Cornea | Iris | Conjunctiva | |
| Redness | Chemosis |
| Albinos NZ rabbit  3 males | OECD 405 | 0 | 0 | 1.22 | 0.33 | Not irritant | Redness reversible between day 4 and 6.  Chemosis reversible on day 3. |  | XXX |

Sensitisation test:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Species** | **Method** | **Result** | **Remark** | **Reference** |
| CBA/J mice  4 females/group | Non radioactive cell counting LLNA: 5, 10, 25% in ethanol/water (7:3) (v/v) on day 1, 2, 3. Sacrifice on Day 6 and determination of the proliferation of lymphocytes in the draining auricular lymph nodes by cell counting | SI < 1.4: not sensitiser | Not acceptable (method not currently validated) | XXX |

| **Additional toxicological information** | | | | |
| --- | --- | --- | --- | --- |
| Short-term toxicity studies | None |  |  |  |
| Toxicological data on active substance(s) (not tested with the preparation) | None |  |  |  |
|  |  |  |  |  |
| Toxicological data on non-active substance(s) (not tested with the preparation) | None |  |  |  |
|  |  |  |  |  |
| Further toxicological information | None | | | |

Annex 6: Safety for professional operators, 2013, updated 2017

**SORKIL G GRAINS**

**Exposure assessment**

| **Exposure scenarios for intended uses** |
| --- |

**Primary exposure of professionals**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Component | CAS | Actual Dermal Total  [mg/kg/d] | Inhalation Exposure  [mg/kg/d] | Model |
| Bulk | | | | | |
| Tier 1:  Without PPE | Difenacoum | 56073-07-5 | 9.2 x 10-8 | 2.5 x 10-6 | CEFIC study |
| Tier 2:  With respiratory protection | Difenacoum | 56073-07-5 | 9.2 x 10-8 | 2.5 x 10-7 | CEFIC study |
| Sachet | | | | | |
| Tier 1:  Without PPE | Difenacoum | 56073-07-5 | 1.4 x 10-8 | na | CEFIC study |

Risk assessment

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Component | CAS | AEL [mg/kg/d] | Absorption [%] | | Inhal  [mg/kg/d] | Derm  [mg/kg/d] | Total syst exposure  [mg/kg bw/d] | % AEL | Risk |
|  |  |  |  | inhalation | dermal |  |  |  |  |  |
| Bulk | | | | | | | | | | |
| Tier 1:  Without PPE | Difenacoum | 56073-07-5 | 1.1 x 10-6 | 100 | 0.027 | 2.5 x 10-6 | 9.2 x 10-8 | 2.6 x 10-6 | 236 | Non acceptable |
| Tier 2:  With respiratory protection | Difenacoum | 56073-07-5 | 1.1 x 10-6 | 100 | 0.027 | 2.5 x 10-7 | 9.2 x 10-8 | 3.4 x 10-7 | 31 | Acceptable |
| Sachet | | | | | | | | | | |
| Tier 1:  Without PPE | Difenacoum | 56073-07-5 | 1.1 x 10-6 | 100 | 0.027 | na | 1.4 x 10-8 | 1.4 x 10-8 | 1.3 | Acceptable |

Annex 7: Safety for non-professional operators and the general public, 2013

**SORKIL G GRAINS**

| **General information** | | |
| --- | --- | --- |
| Formulation Type: cereal grain |  | |
| Active substance(s) (incl. content): difenacoum 0.005% | |  | |
| Category |  | |
| Authorisation number |  | |

| **Difenacoum** |
| --- |

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

| **Exposure scenarios for intended uses** | |
| --- | --- |
| Primary exposure: non-professional use |  |
| Secondary exposure, acute: child ingesting bait |  |
| Secondary exposure, chronic: none |  |

Conclusion:

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

The accidental ingestion of baits poses a risk to infants since the AEL is exceeded when infant ingests more than 0.3 mg of product per day.

Details for the exposure estimates:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Component** | **CAS** | **Actual Dermal Total**  **[mg/kg/d]** | **Inhalation Exposure**  **[mg/m³]** | **Model** |
| **Without PPE** | **Difenacoum** | **56073-07-5** | **5.1 x 10-9** | **na** | **CEFIC study** |

Risk assessment

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Component** | **CAS** | **AEL [mg/kg/d]** | **Absorption [%]** | | **Total syst exposure**  **[mg/kg bw/d]** | **% AEL** | **Risk** |
|  |  |  | **inhalation** | **dermal** |  |  |  |
| **Difenacoum** | **56073-07-5** | **1.1 x 10-6** | **100** | **0.027** | **5.1 x 10-9** | **0.5** | **Acceptable** |

Annex 8: Residue behaviour

**SORKIL G GRAINS**

The intended use descriptions of the SORKIL G GRAINS for which authorisation is sought indicate that these uses are not relevant in terms of residues in food and feed. No further data are required concerning the residue behaviour.

Annex 9: Technical equivalence of the Pelgar source of Difenacoum

**(new specifications)**

Information on the full composition of the product and assessment of the technical equivalence of the active substance are detailed in additional confidential annex of this document.

1. Manual on development and use of FAO and WHO specifications for pesticides ; November 2010 - second revision of the First Edition [↑](#footnote-ref-1)
2. 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. [↑](#footnote-ref-2)
3. 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. [↑](#footnote-ref-3)
4. 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 [↑](#footnote-ref-4)
5. 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. [↑](#footnote-ref-5)
6. 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 [↑](#footnote-ref-6)
7. Human exposure to biocidal products – TNsG June 2007 [↑](#footnote-ref-7)
8. Chambers JG and Snowdon PJ - Study to Determine Potential Exposure to Operators During Simulated Use of Anticoagulant Rodenticide Baits - Synergy Laboratories Ltd., Report No. SYN/1302. Unpublished. [↑](#footnote-ref-8)
9. HEEG (Human Exposure Expert Group) opinion on Harmonising the number of manipulations in the assessment of rodenticides (anticoagulants); June 2010 [↑](#footnote-ref-9)
10. [↑](#footnote-ref-10)
11. "An evaluation of performance standards and non-radioactive endpoints for the LLNA – The report and recommendations of ECVAM Workshop 65" (2008) [↑](#footnote-ref-11)
12. Non-radioactive LLNA [↑](#footnote-ref-12)
13. HEEG opinion on harmonising the number of manipulations in the assessment of rodenticides (anticoagulant), agreed at TMII2010 [↑](#footnote-ref-13)
14. Technical Guidance Document on Risk Assessment, Part II, 2003 [↑](#footnote-ref-14)
15. See document CA-Nov16-Doc.4.x-Final on the concept of tamper-resistant bait stations. [↑](#footnote-ref-15)
16. See document CA-Nov16-Doc.4.x-Final on the concept of tamper-resistant bait stations. [↑](#footnote-ref-16)
17. See document CA-Nov16-Doc.4.x-Final on the concept of tamper-resistant bait stations. [↑](#footnote-ref-17)
18. Data which have not been already submitted for the purpose of the Annex I inclusion. [↑](#footnote-ref-18)