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 RENEWAL OF NATIONAL AUTHORISATION APPLICATIONS**

(submitted by the evaluating Competent Authority)



[PARATOX]

Product type [14]

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

Case Number in R4BP: [BC-NW001106-28]

Evaluating Competent Authority: [FR]

Date: [19/01/2018]

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**Note to the reader:**

This consolidated PAR for the renewal of the product authorisation is based on the PAR of the first authorisation, 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...) 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 the renewal of the product 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 the renewal.

**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 for renewal 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 (updated PAR – 2017)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Application type** | **refMS** | **Case number in the refMS** | **Decision date** | **Assessment carried out (i.e. first authorisation / amendment /renewal)** |
| NA-APP | *FR* | n.a. | 21/10/2011 | Initial assessment: SORKIL AVOINE SPECIALE |
| n.a | *FR* | n.a. | 28/12/2012 | *Frame formulation establishment* |
| n.a | *FR* | n.a. | 08/02/2013 | *Product within a frame formulation: PARATOX* |
| NA-MAC | *FR* | n.a. | 12/12/2013 | *Addition of a user category (non-professionals) and a packaging type (bulk for professional users only).* |
| NA-ADC | *FR* | BC-WH002783-34 | 31/10/2014 | *Addition of the name CEREOX D* |
| n.a | *FR* | n.a. | 21/11/2014 | *Post-authorisation data* |
| NA-RNL | *FR* | BC-NW001106-28 | 02/02/2018 | *Renewal of the authorisation*  |

n.a.: not applicable

**Authorised uses**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **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 | Individual sachetsBulk |
| 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 | Individual sachets |
| Mice (*Mus musculus*) | 25 g to 30 g of product / bait station at distances of 3 meters apart |

**Intended uses for renewal**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **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 | Individual sachetsBulkPre-filled bait stations |
| Mice (*Mus musculus*) | 25 g to 30 g of product / bait station at distances of 3 meters apart |

# General information about the product Application (initial PAR - 2011)

## Applicant

|  |  |
| --- | --- |
| **Company Name:** | EDIALUX France |
| **Address:** | ZA Macon Est |
| **City:** | Replonges |
| **Postal Code:** | F-01750 |
| **Country:** | France |
| **Telephone:** | +33.385.318.910 |
| **Fax:** |  |
| **E-mail address:** |  |

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

|  |  |
| --- | --- |
| **Name:** | Mr Rudi Vermeulen |
| **Function:** | Regulatory Affairs |
| **Address:** | Rijksweg 28 |
| **City:** | Bornem |
| **Postal Code:** | B-2880 |
| **Country:** | Belgium |
| **Telephone:** | +32.(0).499.981.756 |
| **Fax:** |  |
| **E-mail address:** | rve@edialux.be |

## Current authorisation holder

|  |  |
| --- | --- |
| **Company Name:** | EDIALUX France |
| **Address:** | ZA Macon Est |
| **City:** | Replonges |
| **Postal Code:** | F-01750 |
| **Country:** | France |
| **Telephone:** | +33.385.318.910 |
| **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:** | +33.385.318.910 |
| **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:** | 01/04/2010 |

|  |  |
| --- | --- |
| **Application reported complete:** | 30/08/2010 |
| **Authorisation granted** | 01/10/2010 |
| **Type of application:** | Product authorisation |
| **Further information:** | - |

## Information about the biocidal product

### General information

|  |  |
| --- | --- |
| **Trade name:** | SORKIL AVOINE SPECIALE |
| **Manufacturer’s development code number(s), if appropriate:** | EDI-200 |
| **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/wNo substance of concern |
| **Formulation type:** | Cereal grains |
| **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):** | NoNo |

### Information on the intended use(s)

|  |  |
| --- | --- |
| **Overall use pattern (manner and area of use):** | TP14 - Rodenticide VIII.3.1 Granular bait |
|  | The grain bait is limited to indoor use indomestic, industrial and commercialbuildings including in farm buildings. |
| **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 publicV.2 ProfessionalV.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:** | VI.2 Covered applicationVI.2.1 Covered application in bait stations.The product is a ready to use grain bait and contains 50 ppm of difenacoum.Rat: 80 g up to 200 g of product / bait station at distances of 15 meters apart. Mouse: 25 g up to 30 g of product / bait station at distances of 3 meters apart.These distances, so as the number and timings of application, are in function of infestation rate and can be modified upon experience of bait uptake during the campaign.Bait must be securely deposited in a way to minimize the risk for non-target animals and for children. Where possible, baits are secured so that they cannot be dragged away by the rodents. Bait stations will be used.The common strategy is to explore the site, locate runs, burrows, droppings or signs of damage and place the bait boxesat entry points into buildings in areaswhere rats are known to feed. For the mice control, as mice are sporadic feeders, many bait points are placed throughout the areas where mice are known to feed.Bait points are inspected frequently and replenished when bait take is observed. Depending on infestation rate, an advised frequency of inspection is 3 to 5 days. Although a professional will eventually for practical reasons synchronise hisinspection frequency with a work week so keeping inspections twice or once a week, so have 3.5 to 7 days inspection interval. 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 must be removed from the site, cleaned up and the bait and bait remainders must be disposed of in accordance with local requirements. |

|  |  |
| --- | --- |
|  | As long as there is visual bait consumption, fresh bait will be placed.When during 5 consecutive inspections no uptake at all has been recorded and supplementary no other sign suggests the eventual presence of rodents, the campaign can be ended. Anyhow, during the first 6 months after the end, vigilance is required in order to be responsive on any re-infestation of the area. So with a minimal effort new uproar can be stopped.Rodent control can be initiated at any moment of the year upon the presence of the target animal through direct traces/signals/markers.Autumn and winter are more favorable times for indoor applications. |
| **Potential for release into the environment (yes/no):** | Yes |
| **Potential for contamination of food/feedingstuff (yes/no)** | No |
| **Proposed Label:** | Control of rats and mice in domestic,industrial and commercial buildingsincluding in farm buildings.Rat: 80 g up to 200 g of product atintervals of 15 meters apart.Mouse: 25 g up to 30 g of product atintervals of 3 meters apart. |
| **Use Restrictions:** | Use only inside buildings in secured baitstations out of reach of children anddomestic 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. |

**Intended uses for 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 | Individual sachetsBulkPre-filled bait stations |
| Mice (*Mus musculus*) | 25 g to 30 g of product / bait station at distances of 3 meters apart |

### 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):** | 960 g/kg |
| **Inclusion directive:** | 2008/81/EC |
| **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 2017**

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 assessement 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 AVOINE SPECIALE does not contain any substance of concern according to the Technical Notes for Guidance on data requirements.

**Renewal 2017**

PARATOX does not contain any substance of concern according to the Guidance on the BPR Volume III Human Health – Part B Risk Assessment[[1]](#footnote-1).

## Documentation

### Data submitted in relation to product application

**Identity, physicochemical and analytical method data**

Physico-chemical studies on SORKIL AVOINE SPECIALE were provided by Edialux: appearance, explosive properties, oxidising properties, autoflammability, flammability properties, density, storage stability, dustiness, attrition resistance, flowability and particle size distribution.

An analytical method to determine the active substance in the formulation SORKIL AVOINE SPECIALE 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**

* Report No Mo3826. 2013. Determination of physico-chemical properties and storage stability test for EDI-200 [cut oat - grain bait (AB)] 2 weeks at 54°C and up to 24 months
* Report No 23460. 2014. pH of a 1% dispersion and particle size distribution (by dry sieving) of EDI 200 AB-ROD (difenacoum 0.005% w/w) AB.
* Videau. 2014 SORKIL AVOINE SPECIALE vis-à-vis de la lumière
* Renewal of authorisation: No additional data was provided.

**Efficacy data**

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.).

Some of the studies were performed on a whole wheat formulation (SORKIL G - old formulation, see detailed composition in Confidential document). This formulation is different from SORKIL AVOINE SPECIALE because of the type of grain and the dyestuff and because it contains fewer appetent agents. But it is a grain formulation containing 50 ppm of difenacoum and the same rate of bittering agent so the results can be taken into account in order to support the product authorization of SORKIL AVOINE SPECIALE.

* Renewal of authorisation: field test on *R.rattus* with another formulation EDI-250\_24 (0.00024 %w/w difenacoum) has been submitted.

**Toxicology data**

The applicant did not submit new toxicological data on active substance. An acute dermal study, irritation and sensitisation studies on biocidal product were provided.

* Renewal of authorisation: No additional data was provided.

**Ecotoxicology data**

The applicant has not provided ecotoxicological study with the biocidal product. The environmental risk assessment for SORKIL AVOINE SPECIALE 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.

* Renewal of authorisation

No additional data was provided.

### Access to documentation

In the frame of the authorisation of SORKIL AVOINE SPECIALE 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 2011

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 AVOINE SPECIALE is technically equivalent to the source of Pelgar assessed for annex I inclusion.

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.

## Classification, labelling and packaging – PAR 2011, updated 2017

### **Harmonised classification of the biocidal product**

No classification is required for SORKIL AVOINE SPECIALE.

**Renewal - 2017**

Classification of PARATOX

| **Classification** |
| --- |
| Hazard category | Repr. 1BSTOT RE 2 |
| Hazard statement | H360D: May damage the unborn childH373: May cause damage to organs (blood) through prolonged or repeated exposure |

### **Labelling of the biocidal product**

No labelling is required for SORKIL AVOINE SPECIALE.

**Renewal – 2017**

Labelling of PARATOX

|  |
| --- |
| **Labelling** |
| Signal words | DangerGHS 08 |
| Hazard statements | H360D: May damage the unborn childH373: May cause damage to organs (blood) through prolonged or repeated exposure |
| Precautionary statements | P201: Obtain special instructions before use.P202: Do not handle until all safety precautions have been read and understood.P260: Do not breathe dust/fumes/gas/mist/vapours/spray.P280: Wear protective gloves/protective clothing/eye protection/face protection.P308 + P313: IF exposed or concerned: Get medical advice/attention.P314: Get medical advice/attention if you feel unwell.P405: Store locked up.P501: Dispose of contents/container to … [*… in accordance with local/regional/national/international regulation]* |

### **Packaging of the biocidal product**

Primary packaging:

SORKIL AVOINE SPECIALE is supplied in small individual bait bags of polypropylene foil from 20 to 200g.

SORKIL AVOINE SPECIALE is supplied in bulk too without being packed in smaller individual bait bags:

- in bucket of polypropylene (PP) from 800g to 10kg

- in one big bag of PP foil, this bag functions as a liner inside a cardboard box from 800g to 10kg and inside a multilayered paper bag from 5 to 25kg.

Secondary packaging:

- Bucket of polypropylene (200 g – 10 kg)

- Cardboard box of corrugated cardboard (200 g – 10 kg)

- Multilayered paper bag of Kraft paper (5 kg – 25 kg)

- Prefilled bait station of polypropylene (20 g – 200 g)

Packaging size and category of users :

|  |  |
| --- | --- |
| Category of users | Packaging size |
| Professional | >3 kg |
| Non professional | < 3 kg |

Packaging size and target organisms:

Excluding the prefilled bait stations, the different kind of packaging are destined for both type of target organisms, rats and mice.

Prefilled mouse bait stations have a size range from 20 grams to 50 grams (i.e. 1 or 2 individual bait bags of 20, 25, 30, 35, 40 or 50 grams).

Prefilled rat bait stations have a size range from 20 grams to 200 grams (i.e. 1 or 2 individual bait bags of 20, 25, 30, 35, 40, 50, 75, 100, 150 or 200 grams).

**Renewal – 2017**

The non-professionals user category is removed.

PARATOX is supplied in individual PP sachets containing 25, 30, 40, 50, 75,100, 150 or 200 g of grains

The PP sachets are packed in 3 kg - 5 kg -10 kg - 12.5 kg in

- Bucket of PP

- Cardboard box of corrugated cardboard

- Multilayered paper bag of Kraft paper

PARATOX is supplied in tamper-resistant pre-filled bait stations with PP sachets:

* for mice, 1\*25 g or 1\*30 g ;
* for rats, 4\*25g, 3\*30 g, 2\*40 g, 2\*50 g, 2\*75 g, 1\*100 g, 1\*150 g or 1\*200g.

PARATOX is supplied in bulk grains packed in PP buckets, multi-layered paper bags with PP coating or woven laminated PP bags: 3 kg, 5 kg, 10 kg or 20 kg.

## Physico/chemical properties and analytical methods - PAR 2011

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:

- Appearance of the active substance

Results of the assessment: For appearance, the data provided are acceptable. The results are reported in paragraph 2.3.1.

### **Physico-chemical properties (evaluated in the PAR 2011)**

**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 GeneralPhysico­chemical PropertiesSafePharm Laboratories Report No. 2109/0005 |
| Colour | Off-white at20.0 ± 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.

**Table 2: Physico-chemical properties of the biocidal product:**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Method** | **Purity/Specification** | **Results** | **Reference** |
| Physical state and nature | Visual inspection | EDI-200 0.0047% Difenacoum | Cut grains | Garcia, M.T. 2010 |
| Colour | Visual inspection | EDI-200 0.0047% Difenacoum | Blue turquoise | Garcia, M.T. 2010 |
| Odour | Comparison to other characteristic odours | EDI-200 0.0047% Difenacoum | Grain odour | Garcia, M.T. 2010 |
| Explosive properties | OCDE 113 | EDI-200 0.0047% Difenacoum | The heat of decomposition was below 500J/g. Therefore test on explosive properties was not necessaryNot explosive | Krach, M., 2010 |
| Oxidizing properties | EC A.17 | EDI-200 0.0047% Difenacoum | No oxidizing properties | Krach, M., 2010 |
| Flash point | Not applicable |  |  |  |
| Autoflammability | EC A.16 | EDI-200 0.0047% Difenacoum | No self ignition up to 387°C | Krach, M., 2010 |
| Other indications of flammability | EC A.10 | EDI-200 0.0047% Difenacoum | Not highly flammable | Krach, M., 2010 |
| Acidity / Alkalinity |  |  | See commentand conclusionbelow the table |  |
| Relative density / bulk density | CIPAC MT 159 | EDI-200 0.0047% Difenacoum | Pour density : 0.714 g/mL Tap density : 0.727 g/mL | Garcia, M.T. 2010 |
| Storage stability – stability and shelf life | 4-years storage stability |  | Study on going until 03/12/2013See conclusion below the table |  |
| Effects of temperature | 2 weeks at 54°C | EDI-200 0.0047% Difenacoum | The weight loss of the test item after storage for 2 weeks at 54°C was 3.4%. No other significant changes in the appearance and the packaging material were observed after storage for 2 weeks at 54°C.Difference of content of the active substance: -8.7 % deviation from T=0 value after the accelerated storage procedure for 14 days at 54°CSee comment and conclusion below the table | Garcia, M.T. 2010 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Effects of light | Not submitted |  | See conclusion below the table |  |
| Reactivity towards container material | Visual description (integrity, sealing, leakage, dimensional stability) | Container material: Polypropylene (PP) bag (35g) | The appearance of the packaging was unchanged throughout the study. The sample stays in sound condition, sealed and without leakage after 2 weeks at 54°CSee comment below the table |  |
| Technical characteristics in dependence of the formulation type | DustinessCIPAC MT 171 | EDI-200 0.0047% Difenacoum | Nearly dust free | Krach, M., 2010 |
| Attrition resistanceCIPAC MT178.2 | EDI-200 0.0047% Difenacoum | 91.91% | Garcia, M.T. 2010 |
| FlowabilityCIPAC MT172 and MT170 | EDI-200 0.0047% Difenacoum | After 5 liftings, no sample remained on the 5 mm sieve. | Garcia, M.T. 2010 |
| Compatibility with other products |  |  | The product is a ready-to-use product and is not intended to be added to any other product. |  |
| Surface tension | Not applicable |  |  |  |
| Viscosity | Not applicable |  |  |  |
| Particle size distribution | CIPAC MT 59.2 and 58.2 | EDI-200 0.0047% Difenacoum | 99.37% of particles are upper than 850 µm.See comment and conclusion below the table | Garcia, M.T. 2010 |

Acidity/Alkalinity:

The fact that the product is solid and is not intended to be dispersed in water is not an acceptable justification for non submission of the pH and acidity/alkalinity.

pH value (1% in water) should have been provided and acidity/alkalinity too if relevant (depending of the pH).

Storage stability:

The difenacoum content is lower by 8.7% after storage 14 days at 54°C. The accepted difference is 5% (Manual FAO). A justification has been provided by the applicant:

The decrease of the active substance content does not necessarily happen through shelf life. Grains are a natural material with intrinsic heterogeneous characteristics. Particularly the size and the porosity of the surface will have an impact on the overall volumetric adsorption upon the grain of the premix containing the active substance. The size of individual sampled grain kernels can have a minor variation of measured active substance concentration as experienced on different analyses of the same batch.

The appearance, pour and tap density, dustiness, attrition resistance and particle size distribution were measured after 2 weeks at 54°C and no significant changes were observed.

Efficacity studies performed after 2 weeks at 54°C show that the product is palatable and effective.

Difenacoum is thermically stable (temperature of decomposition is upper 250°C).

Indeed the difference may be due to the heterogeneity of batches (grains within a batch may have different contents of active substance). Therefore the sampling should be adapted to overcome the heterogeneity of batches.

So the accelerated storage stability study is accepted despite the difference in difenacoum content is upper than 5%.

Reactivity towards container material:

The compatibility of SORKIL AVOINE SPECIALE in bucket of polypropylene (PP) and in one big bag of PP foil has not been tested but is not necessary as the compatibility of grains in polypropylene (PP) bag (35g) has been tested and accepted.

Particle size distribution:

The CIPAC MT 59.2 and 58.2 methods are not well adapted.

**Conclusion (PAR 2011):**

A 4-years storage stability study is on-going and has to be provided. The study should be performed with test items in quantity sufficient to overcome the heterogeneity problem. Intermediate results at 2 years have to be provided. pH (acidity and alkalinity if relevant) and effect of light have to be provided also.

The particle size distribution (CIPAC MT 59.4 (ii)) is required in post registration too.

* **Assessment of the frame formulation establishment: Addendum to the PAR 2012: SORKIL AVOINE SPECIALE**

Data submitted: variations of compositions within the frame formulation.

The biocidal product SORKIL AVOINE SPECIALE is a rodenticide product (TP14) containing 0.005% w/w of Difenacoum. This product is proposed as reference product for the establishment of the frame formulation.

Evaluation of the reference SORKIL AVOINE SPECIALE product authorization dossier was performed using studies performed on the reference product.

No study was submitted for this frame formulation establishment dossier.

Considering that the change consists only on a physical change of the carrier and the non Phys-Chem classification of this carrier, dangerous physicochemical properties can be considered as similar between the reference product and the product within the frame formulation.

For the technical characteristics some differences could appear because of the physical change:

* Attrition and dustiness: these properties depend on the coating. As the coating is strictly the same between the reference product and the product within the frame formulation, these properties can be considered as similar between the reference product and the product within the frame formulation.
* Pour and tap density, flowability and granulometry: these properties depend on the size of the carrier. As these properties could change, there are required for characterization of the product within the frame formulation.

The other properties can be considered as similar between the reference product and the product within the frame formulation.

No data were submitted on the packaging of products covered by the frame formulation. The allowed packaging will be those allowed for the reference product.

**Conclusion (Addendum to the PAR 2012):**

Considering that the change consists only on a physical change of the carrier, the non Phys-Chem classification of this carrier and that the global composition does not change, dangerous physicochemical properties can be considered as similar between the reference product and the product within the frame formulation. For the technical characteristics some differences could appear because of the physical change. Pour and tap density, flowability and granulometry could change so there are required for characterization of the product within the frame formulation. The other properties can be considered as similar between the reference product and the product within the frame formulation.

The allowed packaging will be those allowed for the reference product.

* **Assessment of the submitted post-authorisation data (addendum PAR 2014):**

Light effect :

The notifier has provided an explanation for non submission of light effect datas Indeed, SORKIL AVOINE SPECIALE is conditionned in white opaque film. The packagings are opaque and the product is placed in boxes away from the light. Then, light is not expected to have any impacts on this biocidal product.

Anses considers this argument as acceptable.

Long term storage stability study:

**Table 3:** Determination of physico-chemical properties and storage stability test for EDI-200 (cut oat- grain bait (AB)); 2 weeks at 54°C and up to 24 months at ambient conditions, S. Manka, 2013. Batch n°: L0909

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **T0** | **After 2 weeks at 54°C** | **After 12 months at 25°C** | **After 24 months at 25°C** |
| **Appearance** | cut grains, blue-turquoise, grain odor | No change | No change | No change |
| **Appearance of packaging** | sample in sound conditions sealed and without leakage | No change | No change | No change |
| **Content of AS (% w/w)** | 0.00470 | 0.00429 | 0.00486 | 0.00416 |
| **Variation of AS (%)** | / | -8.7% | +3.4% | -11.5% |
| **Particle Size Distribution** | Dust fraction <250µm :0.07%<150µm : 0.06% | Dust fraction <250µm :0.035%<150µm : 0.03% | / | / |
| **Flowability** | 100% | 100% | / | / |
| **Pour density** | 0.714 | 0.695 | / | / |
| **Tap density** | 0.727 | 0.722 | / | / |
| **Attrition resistance** | 99.91% | 99.94% | / | / |

Quantification of AS has been done by HPLC UV detection (chromatograms of standard and sample have been provided) with the method evaluated in the PAR.

Conclusion: Storage stability study results are acceptable. The biocidal product is stable 2 weeks at 54°C and 2 years at ambient temperature.

pH and particle size distribution:

**Table 4:** pH of 1% dispersion and particle size distribution (by dry sieving) of EDI 200 AB-ROD (difenacoum 0.005% w/w) AB, B. De Ryckel, 2014, Study n° 23460.

|  |  |  |
| --- | --- | --- |
| **Tests** | **Methods** | **Results** |
| pH of a 1% dispersion in water | CIPAC Method MT 75.3 | 5.51 |
| Particle size distribution (by dry sieving) | CIPAC Method MT 170 | % of particles |
| > 500 µm | 99.61 |
| 100-500 µm | 0.22 |
| 75-100 µm | 0.04 |
| 40-75 µm | 0.03 |
| <40 µm(including loss of dust) | 0.12 |
| >75 µm | 99.86 |
| < 75 µm | 0.14 |

Though the method provided for the determination of particle size distribution (method CIPAC MT 170) is not the one required in post-registration (method CIPAC MT 59.4 (ii)), particle size distribution and pH are considered as acceptable.

All data evaluated in this addendum to the PAR are summarized in Table 5.

**Table 5: Physico-chemical properties of the biocidal product (evaluated in the addendum to the PAR 2014):**

|  | **Method** | **Purity/Specification** | **Results** | **Reference** |
| --- | --- | --- | --- | --- |
| Acidity / Alkalinity | CIPAC MT 75.3 | EDI-200 AB-ROD (difenacoum 0.005% w/w)Batch L0909 | pH=5.51Conclusion: pH study is acceptable at room temperature. | B. De Ryckel, (2014), Study n° 23460 |
| Storage stability – stability and shelf life | 2-years storage stability | EDI-250 AB-ROD (difenacoum 0.005% w/w)Batch L1209 | **Determination of physico-chemical properties and storage stability test for EDI-200 (cut oat- grain bait (AB)); 2 weeks at 54°C and up to 24 months at ambient conditions, S. Manka, 2013. Batch n°: L0909**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | T0 | After 2 weeks at 54°C | After 12 months at 25°C | After 24 months at 25°C |
| Appearance | blue-turquoise cereal grains with weak grain odour | No change | No change | No change |
| Appearance of packaging  | sample in sound conditions sealed and without leakage | No change | No change | No change |
| Content of AS **(% w/w)** | 0.00470 | 0.00429 | 0.00486 | 0.00416 |
| Variation of AS (%) | / | -8.7% | +3.4% | -11.5% |
| Particle Size Distribution | Dust fraction <250µm :0.07%<150µm : 0.06% | Dust fraction <250µm :0.035%<150µm : 0.03% | / | / |
| Flowability | 100% | 100% | / | / |
| Pour density | 0.714 | 0.695 | / | / |
| Tap density | 0.727 | 0.722 | / | / |
| Attrition resistance | 99.91% | 99.94% | / | / |

Quantification of AS has been done by HPLC UV detection (chromatograms of standard and sample have been provided) with the method evaluated in the PAR.Results after 2 years show a decrease of 11.5% in AS content. This is higher than the acceptable limit of 10%. However, the difference with 10% is lower than the variability of the method (due to low AS content and highly heterogeneous formulation), it cannot be excluded that the limit of 10% is really reached. FR considers the shelf life of biocide product is demonstrated.Conclusion: Storage stability study results are acceptable. The biocidal product is stable 2 weeks at 54°C and 2 years at ambient temperature in PP bag packaging. The product being a solid, if it is compatible with a type of packaging, it is considered compatible with every types of packaging. | S. Manka (2013), Study n° Mo3906 |
| Effects of light | Non submission data submitted |  | The notifier has provided an explanation for non submission of light effect data. Indeed, PARATOX is conditionned in white opaque film. The packagings are opaque and the product is placed in boxes away from the light. Then, light is not expected to have any impacts on this biocidal product.Anses considers this argument as acceptable and recommends to store away from light. |  |
| Particle size distribution | CIPAC MT 170 | EDI-200 AB-ROD (difenacoum 0.005% w/w)Batch L0909 | **Particle size distribution (by dry sieving) of EDI 200 AB-ROD (difenacoum 0.005% w/w) AB, B. De Ryckel, 2014, Study n° 23460.**

|  |  |
| --- | --- |
|  | % of particles |
| > 500 µm | 99.61 |
| 100-500 µm | 0.22 |
| 75-100 µm | 0.04 |
| 40-75 µm | 0.03 |
| < 40 µm(including loss of dust) | 0.12 |
| > 75 µm | 99.86 |
| < 75 µm | 0.14 |

Conclusion: 99.61% of particles are upper than 500 µm. The dust content of the test item represents less than 0.14%. When the product is supplied in bulk, Anses recommends wearing protecting gloves and a respiratory protection equipment during decanting. Thus no friability test will be needed. | B. De Ryckel (2014), Study n° 23460 |

|  |
| --- |
| **General conclusion on the physical, chemical and technical properties of the product for renewal of national authorisation applications - 2017** |
| The product PARATOX is an RB ready to use bait formulation. All studies have been performed in accordance with the current requirements and the results are deemed to be acceptable. It is not explosive and has no oxidising properties. The product is not flammable.The appearance of the product is a blue-turquoise cut grains with a characteristic grain odour.Storage stability study results are acceptable. The biocidal product is stable 2 weeks at 54°C and 2 years at ambient temperature with a PP film bag packaging. The product being a solid, if it is compatible with a type of packaging, it is considered compatible with every types of packaging.FR CA recommends to store away from light due to the sensitivity of the active substance to light.The technical characteristics are acceptable for an RB ready to use formulation. |

### **Risk assessment for Physico-chemical properties**

PARATOX is not highly flammable, not auto-flammable (up to 387°C), not explosive and does not have oxidizing properties according to GHS guideline. FR considers these conclusions are still valid for CLP classification as no formulant is expected to be classified for PC CLP properties.

### **Analytical methods – PAR 2011**

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

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

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

- Validation data for the determination of difenacoum in sediment.

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

- A validated method for the analysis of difenacoum in animal and human tissues Results of the assessment: The method is validated and is acceptable.

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

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

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

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

|  |  |
| --- | --- |
|  | 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. |
| active substance in the formulation: | HPLC-UV |

**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.

**Active substance in the formulation:**

After extraction in methanol, the active substance content is determined by high performance liquid chromatography (HPLC) with UV detection at 254 nm according to the internal standard method. The analytical method provided is validated.

## Effectiveness against target organisms

### **Function**

Main group 03: Pest Control Product Type 14: Rodenticide

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

SORKIL AVOINE SPECIALE is used to control rodents. The target organisms to be controlled are brown rat (*Rattus norvegicus*), roof rat or house rat (*Rattus rattus*) and house mouse (*Mus musculus*).

The products, organisms or objects to be protected are stored products or food, public health, historical buildings or technical objects.

### **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: studies has been performed with the product SORKIL AVOINE SPECIALE – PAR 2011**

Choice feeding tests on SORKIL AVOINE SPECIALE on rats and mice on 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 AVOINE SPECIALE on rats and 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 100% in 10 days and 100% in 11 days.

Field and semi-field tests performed on a whole wheat formulation SORKIL G are also presented in the dossier. This formulation is different from SORKIL AVOINE SPECIALE because of the type of grain and the dyestuff and because it contents fewer appetent agents. But it is a grain formulation containing 50 ppm of difenacoum and the same rate of bittering agent so the results can be taken into account in order to support the product authorization of SORKIL AVOINE SPECIALE. The efficacy on rats and mice was respectively 95% in 20 days and 100% in 29 days.

Choice feeding tests on rats with fresh baits, 1-year and 2-year aged test baits have also been performed with SORKIL G.

All efficacy studies results are presented in annex 3.

The application rates recommended by the applicant are the following:

Rats: (*Rattus norvegicus* and *Rattus rattus)*

80 g up to 200 g product/secured bait point at intervals of 15 m apart.

Mice: (*Mus musculus*)

25 g up to 30 g products/secured bait point at intervals of 3 m apart.

The product is applied in bait stations by professional and non-professional users in discrete locations within the infested area. Distances between each bait station, so as the number and timings of application and the amount of product depends of several factors: the treatment site, the size and severity of the infestation.

* **Renewal of authorisation - 2017**

For the renewal of the product PARATOX (0.005 % w/w difenacoum), no change in the composition has been declared.

As the new version of the TNsG PT14 was not in force at the time of the renewal of this authorization, conclusion on efficacy remains the same as for the first authorization for *Rattus norvegicus* and for *Mus musculus*.

Indeed, 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).

No efficacy data had been submitted to demonstrate the efficacy of the product against black rat (*Rattus rattus*) for the first authorisation. Although such data were not required by FR CA for the initial authorization, it has been decided in coordination group (CG-5, 2014) that read across between both rat species was not acceptable and efficacy data with black rat should be provided to support the claim.

An additional field test on *R.rattus* with another formulation at 0.0024 % w/w difenacoum where only the content of the active substance differs, has been provided by the applicant in the context of the renewal and read-across is therefore acceptable. This study, which is presented in Annex 3, demonstrates the efficacy of the product against black rats. The comparison between the formulation EDI-250\_24 and the EDI-200 (PARATOX) is presented in the confidential part of the PAR.

Consequently, the product PARATOX (0.005 % 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*) indoor at doses claimed.

Uses and doses validated for PARATOX are the following:

|  |  |  |  |
| --- | --- | --- | --- |
| **Product** | **Target organisms** | **Application rate and intervals** | **Use area** |
| PARATOXBait containing 0.005% w/w of difenacoum. | Rats (*Rattus norvegicus* and *Rattus rattus)* | 80 - 200 g / bait point separated by 15 meters  | Indoor  |
| Mice (*Mus musculus*) | 25 - 30 g / bait point separated by 3 meters  | Indoor  |

### Occurrence of resistance

* **Renewal of authorisation - 2017**

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**

French authority in charge of the risk assessment assessed that SORKIL AVOINE SPECIALE has shown a sufficient efficacy for the control of mice and rats for an indoor use in domestic, industrial and commercial buildings including in farm buildings.

The application rates validated are the following:

Rats: (*Rattus norvegicus and Rattus rattus)*

80 g to 200 g product/secured bait point at intervals of 15 m apart.

Mice: (*Mus musculus*)

25 g up to 30 g products/secured bait point at intervals of 3 m apart.

* **Assessment of the frame formulation establishment: Addendum to the PAR 2012: SORKIL AVOINE SPECIALE**

Within the framework of the establishment of the frame formulation requested by the applicant, the differences between compositions of the reference product SORKIL AVOINE SPECIALE and the frame formulation are slight.

The proposed variation of the composition of the frame formulation can be considered as minor and the efficacy of all the products in this frame formulation will be similar to the reference product SORKIL AVOINE SPECIALE.

**Conclusion**

The efficacy studies submitted by the applicant in the first demand for the first product authorization dossier allow also proving the efficacy of the frame formulation SORKIL AVOINE SPECIALE for the uses in the building by professional.

Therefore, effective uses and doses for all the products within the frame formulation are the same than those validated for the first authorization of the reference product SORKIL AVOINE SPECIALE.

* **Assessment of the major change: Addendum to the PAR 2013: PARATOX**

In addition to the bulk packaging, SORKIL AVOINE SPECIALE is also supplied in sachets and pre-filled bait stations of different amounts. The applicant has to adapt the amount per sachet and bait boxes to the efficient doses. The amount of bait per bait station must not exceed the recommended application rates.

* **Assessment of the submitted post-registration data (addendum PAR 2014):**

No resistance phenomenon has been reported by the applicant since the first authorization.

* **Renewal of authorisation – 2017**

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

## Exposure assessment

### Description of the intended use(s) – PAR 2011

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

**Table 2.6.1 Summary of intended uses**

|  |  |  |
| --- | --- | --- |
| **MG/PT** | **Field of uses envisaged** | **Likely concentrations at which a.s. will be used** |
| Main group 03; PT 14 | Professional uses |
| Rodenticide used indoors inindustrial and commercialbuildings including in farmbuildings | 0.005% w/w |
| Non-professional uses |
| Rodenticide used indoors indomestic areas | 0.005% w/w |

SORKIL AVOINE SPECIALE is intended to be used for control of mice *(Mus musculus)*, brown rats *(Rattus norvegicus)* and black rats *(Rattus rattus)* in domestic, industrial and commercial buildings including in farm buildings. The control of mice and rats is based on the principle of applying baits on infested areas with obvious tracking of faeces, and smears next to holes and harbourages.

The product is ready-to-use grain bait with no dilution and or other substances added for application. It is manually applied by trained professional users and by non-professional users in secured bait boxes or bait stations

For rat control, the recommended dose is 80 g up to 200 g of product at intervals of 15 meters apart.

For mouse control, the recommended dose is 25 g up to 30 g of product at intervals of 3 meters apart.

* **Renewal of authorisation**

The intended uses are only for professionals.

###  **Assessment of exposure to humans and the environment – PAR 2011**

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, the FR CA decided to use the exposure estimations issued from the CEFIC study for the assessment of SORKIL AVOINE SPECIALE.

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 – PAR 2011, updated 2017**

**2.6.1.1 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.”*

 **2.6.1.2 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 AVOINE SPECIALE does not contain any substance of concern.

**Renewal 2017**

Considering the following definition of a substance of concern set in the Guidance on the BPR Volume III Human Health – Part B Risk Assessment, PARATOX does not contain any substance of concern.

 **2.6.1.3 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 4 of this report ”Toxicology – biocidal product”.

Acute dermal toxicity, skin and eye irritation and skin sensitisation studies have been provided on the product containing 0.005% of difenacoum, according to the OECD guidelines.

Justifications for non-submission of data have been submitted for acute oral and inhalation toxicity studies and dermal absorption study.

- Acute dermal toxicity

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 dryness to 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 for SORKIL AVOINE SPECIALE.

- Irritation and corrosivity

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

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 for SORKIL AVOINE SPECIALE.

- 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 by the RMS.

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

Justification for non submission:

- Dermal absorption

The 3% value for dermal absorption cannot be used without a letter of access to the Sorex company dossier. Indeed, this value is the property of Sorex Company, even if it is presented in the Assessment Report of Difenacoum, List of endpoints, September 2009. Finally, the justification for non-submission of data cannot be considered as acceptable. That is the reason why a default factor of 100% for dermal absorption should be used as a first tier for risks characterization. Nevertheless, based on the physico-chemical properties of difenacoum, on the low dermal absorption values observed with different formulations containing 0.005% of difenacoum and on the dermal absorption of other similar second generation anticoagulants, a default value of 10% was considered for the risk assessment of SORKIL AVOINE SPECIALE (see table below).

|  |  |  |  |
| --- | --- | --- | --- |
| Compound | Molecular mass | Log Pow | Dermal absorption (from the assessment reports of active substances) |
| Difethialone | 539 g/mol | 6.29 | 4% (*in vitro* and *in vivo* data) |
| Bromadiolone | 527 g/mol | > 3 | 10% (default value) and 1.6 % (*in vitro* studies on products) |
| Brodifacoum | 523 g/mol | 6.12 | 5% (*in vitro* study, worst case) |
| Flocoumafene | 542 g/mol | 6.12 | 10% (default value) and 4 % (based on the dermal absorption of other second generation anticoagulants) |
| Difenacoum | 444.5 g/mol | 7.6 | 0.047% (*in vitro* study on wax block and paste) and 3 % (*in vitro* study on grain) |

- Acute oral and inhalation toxicity

According to the CLP exemptions rules based on calculations, the product is not classified for its acute oral toxicity.

Concerning the inhalation route, as the preparation is neither a gas nor a volatile liquid, nor a powder and the application method does not generate aerosol, particles or droplets in an inhalable size range (MMAD < 50 µm), it can be considered that inhalatory exposure is not a relevant route of human exposure.

In conclusion, the justifications for non-submission of data are considered acceptable.

The harmonised classification of the active substance is the following:

|  |
| --- |
| Classification under regulation(EC) 1272/2008 |
| Acute Tox. 2 H300STOT Rep. 1 H372Aquatic. Acute 1 H400Aquatic Chronic 1 H410No specific concentration limit |

Based on the results of the studies, the concentration of the active substance and of the compounds contained in the product and according to the above classification, SORKIL AVOINE SPECIALE is not classified.

**Renewal 2017 -** The harmonised classification of the active substance is the following: 2017

|  |
| --- |
| Classification under regulation (EC) 1272/2008 |
| Acute Tox 1 – H300 ; H310 ; H330STOT RE 1 – H372 (blood)Repr. 1B – H360DRepr. 1B; H360D: C ≥ 0,003 %STOT RE 2; H373: 0,002 % ≤ C < 0,02 %STOT RE 1; H372: C ≥ 0,02 % |

Based on the results of the studies, the concentration of the active substance and of the compounds contained in the product and according to the above classification, PARATOX should be classified:

- Repr. 1B - H360D: May damage the unborn child

- STOT RE 2 - H373: May cause damage to organs (blood) through prolonged or repeated exposure

- Other studies

The product is not intended to be used with other biocidal products. Therefore, no additional study was conducted.

In addition, the product is not intended to be used in feeding stuff and no industrial processing or domestic preparation is intended. Therefore, no data on residue was submitted.

* **Assessment of the major change: Addendum to the PAR 2013: PARATOX**

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 4 of this report ”Toxicology – biocidal product”.

Acute dermal toxicity, skin and eye irritation and skin sensitisation studies have been provided on the product containing 0.005% of difenacoum, according to the OECD guidelines. A dermal absorption study was submitted with a difenacoum based pellet bait.

Justifications for non-submission of data have been submitted for acute oral and inhalation toxicity studies.

* Dermal absorption

The dermal absorption of difenacoum formulated as pellet bait (containing 0.05 g/kg difenacoum) was investigated *in vitro* using human skin. The percentage of absorbed difenacoum was 0.027%. The total recovery of difenacoum was 94.2% when skin discs were exposed to 394 mg/cm2 of the product (equivalent to 20.4 µg a.s./cm2) for 8 hours.

* Acute dermal toxicity

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 dryness to 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 for PARATOX.

* Irritation and corrosivity

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

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 for PARATOX.

* 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*.[[13]](#footnote-13), the “*proposed non-RI LLNA[[14]](#footnote-14) 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 by the RMS.

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

Justification for non submission:

* Acute oral and inhalation toxicity

According to the CLP exemptions rules based on calculations, the product is not classified for its acute oral toxicity.

Concerning the inhalation route, as the preparation is neither a gas nor a volatile liquid, nor a powder and the application method does not generate aerosol, particles or droplets in an inhalable size range (MMAD < 50 µm), it can be considered that inhalatory exposure is not a relevant route of human exposure.

In conclusion, the justifications for non-submission of data are considered acceptable.

The harmonised classification of the active substance is the following:

|  |  |
| --- | --- |
| Classification under directive 67/548/EEC | Classification under regulation (EC) 1272/2008 |
| T+ R28T R48/25N, R50/53No specific concentration limit  | Acute Tox. 2 H300STOT Rep. 1 H372Aquatic. Acute 1 H400Aquatic Chronic 1 H410No specific concentration limit |

Based on the results of the studies, the concentration of the active substance and of the compounds contained in the product and according to the above classification, PARATOX is not classified.

* Other studies

The product is not intended to be used with other biocidal products. Therefore, no additional study was conducted.

In addition, the product is not intended to be used in feeding stuff and no industrial processing or domestic preparation is intended. Therefore, no data on residue was submitted.

* **Renewal of authorisation: 2017**
* 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 (SD) is higher than 25% of the mean. Therefore, the SD value 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 (corresponding to the receptor fluid + the skin) is 0.04% (instead of 0.027% as previously proposed). This value has been taken into account in the risk assessment for the renewal of the product.

### **Exposure**

SORKIL AVOINE SPECIALE (PT14) is a ready-to-use rodenticide containing 0.005% (w/w) of difenacoum (purity: 960 g/kg). Baits are packaged in sachets for professional and non‑professional users or in bulk for professional users. The baits are placed in bait stations (bait boxes or secured bait stations) out of reach of children and domestic animals. The wear of gloves is advised by the applicant.

SORKIL AVOINE SPECIALE is also provided in prefilled bait boxes. Concerning this packaging, the exposure is considered as negligible during the first application. However, if they are refilled with recharge baits (bulk or sachet), the exposure will be similar to the application in non-prefilled bait boxes presented in the followings sections for professional or non-professional users.

**2.6.2.1 Exposure of professional users**

**Primary exposure** *Dermal exposure*

Based on all the measured exposure data (75th percentile) from the CEFIC study, the amount of product on fingers/hands **during the decanting** was 96.45 mg for 3 kg decanted grain bait (value adopted by FI RMS in the CAR of difenacoum). 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 loading of bait boxes16) and 1.6 kg for mouse (25 g of grains per bait boxes; 63 loading of bait boxes)

- Frequency: one manipulation per day,

- Dermal absorption: 10%,

- Body weight: 60 kg.

The quantities of 200 g, which corresponds to the maximal efficient dose for rat and 25 g, which corresponds to the minimal efficient dose for mouse, are used for the exposure scenarios and cover the applied doses range.

Therefore, the systemic dose of difenacoum on fingers/hands during decanting is:

- For rat: 3.38x10-5 mg/kg bw/day

- For mouse: 4.22 x10-6 mg/kg bw/day.

Based on all the measured exposure data (75th percentile) from the CEFIC study, the amount of product on fingers/hands **during the loading** was 3.71 mg/manipulation (value adopted by FI RMS in the CAR of difenacoum). Although Edialux considers that maximum 30 bait points are treated per day, FR CA has used the harmonized number of manipulations for rodenticides anticoagulant set in the HEEG opinion agreed at TMIII 2010. Therefore, considering 63 loadings per day, the systemic dose of difenacoum on fingers/hands during loading is 1.95x10-5 mg/kg bw/day (for rat and mouse because the amount of disposed bait is not taken into account, as mentioned by HEEG opinion draft).

Based on all the measured exposure data (75th percentile) from the CEFIC study, the amount of product on fingers/hands **during the cleaning** was 4.52 mg/manipulation (value adopted by FI RMS in the CAR of difenacoum). The cleaning consists to throw the residual product in the garbage and to clean the bait box with a brush but without water.

Although Edialux considers that maximum 30 bait points are collected per day, FR CA have used the harmonized number of manipulations for rodenticides anticoagulant[[15]](#footnote-15) set in the HEEG opinion agreed at TMIII 2010. Therefore, considering 16 cleanings per day, the systemic dose of difenacoum on fingers/hands during loading is 6.03x10-6 mg/kg bw/day (for rat and mouse because the amount of disposed bait is not taken into account, as mentioned by HEEG opinion draft).

In conclusion, the total systemic dermal exposure is set at 5.93x10-5 / 2.97x10-5 mg/kg bw/day without PPE for rat and mouse, respectively. The exposure is reduced by a factor of 10 down to 5.93x10-6 / 2.97x10-6 mg/kg bw/day for rat and mouse, respectively when gloves are worn (10% gloves penetration factor). According to the HEEG opinion agreed at TMI10 (default protection factors for protective clothing and gloves), a further refinement is possible considering a glove penetration factor of 5% for solids. In this case, the total systemic dermal exposure is 2.96x10-6 / 1.49x10-6 mg/kg bw/day for rat and mouse, respectively.

*Inhalation exposure*

Exposure by inhalation route is relevant **during decanting** of the product. The overall 75th percentile of air monitoring product residue per replicate was found at 1.92 mg product/m3 (value adopted by FI RMS in the CAR of difenacoum).

The following parameters were considered:

- Duration of manipulation: 15 minutes per day for rat and 3 minutes per day for mouse.

- 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 5.00x10-7 mg/kg bw/day and 1.00x10-7 mg/kg bw/day for rat and mouse, respectively.

*Total exposure*

The total systemic exposure resulting from inhalation and dermal contacts with the product is 5.98x10-5 / 2.98x10-5 mg a.s/kg bw/day without gloves for rat and mouse, respectively. The systemic exposure is reduced to 6.43x10-6 / 3.07x10-6 mg a.s/kg bw/day for rat and mouse, respectively, with gloves, considering a 10% penetration factor or 3.46x10-6 / 1.59x10-6 mg a.s/kg bw/day for rat and mouse, respectively, with gloves, considering a 5% penetration factor.

The estimations above are representative for exposure to SORKIL AVOINE SPECIALE in bulk but they represent a very worst case when the product is supplied and applied 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 as the sachet prevents dermal contacts. Therefore, only exposure during cleaning can be considered: 6.03x10-6 mg a.s/kg bw/day without gloves and 6.03x10-7 mg a.s/kg bw/day with gloves (10 % penetration factor) (for rat and mouse because the amount of disposed bait is not taken into account, as mentioned by HEEG opinion draft).

**Secondary exposure**

Secondary exposure of users could result in the handling of dead rodents. However, this scenario is excluded due to unrealistic assumptions (very low amount of difenacoum is expected on the fur because SORKIL AVOINE SPECIALE is an oral bait and toxicokinetics data showed that urine is a minor route of excretion for difenacoum).

In Annex 5 “Safety for professional operators”, results of the exposure calculations for the active substance for the professional user are laid out.

* **Assessment of the major change: Addendum to the PAR 2013: PARATOX**

PARATOX is a ready-to-use rodenticide containing 0.005% (w/w) of difenacoum (purity: 960 g/kg). Baits are packaged in plastic sachets for professional and non-professional users or in bulk for professional users. In the case of plastic sachet, it can be assumed that there is no decanting phase and no exposure is expected during loading in bait points.

PARATOX is also provided in prefilled bait boxes. Concerning this packaging, the exposure is considered as negligible during the first application. However, if they are refilled with recharge baits (bulk for professionals or sachet for professionals and non-professionals), the exposure will be similar to the application in non-prefilled bait boxes presented in the followings sections for professional or non-professional users.

**Primary exposure**

As a worst case, exposure has been assessed considering PARATOX supplied as loose grains at the maximum recommended dose of 200 g for the control of rats. This approach covers the packaging in sachets and in prefilled bait stations. This also covers human exposure during the control of mice, where the recommended doses are lower.

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 equipment 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 loading of bait boxes[[16]](#footnote-16))
* 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 without individual protective equipment.

*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 PARATOX is supplied in plastic 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.

**Secondary exposure**

Secondary exposure of users could result in the handling of dead rodents. However, this scenario is excluded due to unrealistic assumptions (very low amount of difenacoum is expected on the fur because PARATOX is an oral bait and toxicokinetics data showed that urine is a minor route of excretion for difenacoum).

* **Renewal of authorisation - 2017**

**Primary exposure**

Considering the revision of dermal absorption value according to 2012 EFSA guidance. (0.04% instead of 0.027) exposure calculation has been revised as follows:

|  |  |  |  |
| --- | --- | --- | --- |
| **Tier** | **Inhalation exposure** | **Dermal exposure** | **Total exposure** |
|  | **mg / kg bw /day** | **mg / kg bw /day** | **mg / kg bw /day** |
|  |  |
| Professional exposure : Bulk formulation (exposure during decanting, loading and cleaning phases) |
| Tier I: Without PPE | 2.51 x 10-6 | 1.36 x 10 -7 | 2.64 x 10-6 |
| Tier IIa : PPE – mask  | 2.51 x 10-7 | 1.36 x 10 -7 | 3.87 x 10-7 |
| Professional exposure\* : Bulk formulation (loading and cleaning phases) packaging < 10kg without decanting  |
| Tier I: Without PPE | - | 6.31 x 10 -8 | 6.31 x 10 -8 |
| Professional exposure : Sachet formulation (exposure during cleaning phase) |
| Tier I: Without PPE | - | 2.02 x 10 -8  | 2.02 x 10 -8  |

\* For packaging below 10 kg, a decanting phase could be not necessary as its weight allows the worker to handle it from a bait point to another.

**Secondary exposure**

Secondary exposure of users could result in the handling of dead rodents. However, this scenario is excluded due to unrealistic assumptions (very low amount of difenacoum is expected on the fur because PARATOX is an oral bait and toxicokinetics data showed that urine is a minor route of excretion for difenacoum).

**2.6.2.2 Exposure of non-professional users and the general public**

**Primary exposure**

As a worst case, the same assumptions as for professional exposure was considered except for the number of manipulations set at 5 loadings and 5 cleaning per day for non­professional according to the HEEG opinion document and in the absence of PPE.

*Dermal exposure*

Based on all the measured exposure data (75th percentile) from the CEFIC study, the amount of product on fingers/hands **during the decanting** was 96.45 mg for 3 kg decanted grain bait (value adopted by FI RMS in the CAR of difenacoum). The following parameters were taken into account:

- Active substance in product: 0.005%,

- Quantity of decanted product: 1 kg for rat (200 g of grains per bait boxes;

5 loading of bait boxes) and 0.1 kg for mouse (25 g of grains per bait

boxes; 5 loading of bait boxes),

- Frequency: one manipulation per day,

- Dermal absorption: 10%,

- Body weight: 60 kg.

Therefore, the systemic dose of difenacoum on fingers/hands during decanting is:

- For rat: 2.68x10-6 mg/kg bw/day

- For mouse: 3.35x10-7 mg/kg bw/day.

Based on all the measured exposure data (75th percentile) from the CEFIC study, the amount of product on fingers/hands **during the loading** was 3.71 mg/manipulation for 200 g which was the value adopted by FI RMS in the CAR of difenacoum. Considering 5 loadings per day, the systemic dose of difenacoum on fingers/hands during loading is 1.55x10-6 mg/kg bw/day (for rat and mouse because the amount of disposed bait is not taken into account, as mentioned by HEEG opinion draft).

Based on all the measured exposure data (75th percentile) from the CEFIC study, the amount of product on fingers/hands **during the cleaning** was 4.52 mg/manipulation (value adopted by FI RMS in the CAR of difenacoum). Considering 5 cleanings per day, the systemic dose of difenacoum on fingers/hands during loading is 1.88x10-6 mg/kg bw/day (for rat and mouse because the amount of disposed bait is not taken into account, as mentioned by HEEG opinion draft).

In conclusion, the total systemic dermal exposure is set at 6.11x10-6 mg/kg bw/day for rat and 3.76x10-6 mg/kg bw/day for mouse.

*Inhalation exposure*

Exposure by inhalation route is relevant **during decanting** of the product. The overall 75th percentile of air monitoring product residue per replicate was found at 1.92 mg product/m3 (value adopted by FI RMS in the CAR of difenacoum).

The following parameters were considered:

- Duration of manipulation: 15 minutes 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 5.00x10-7 mg/kg bw/day.

*Total exposure*

The total systemic exposure resulting from inhalation and dermal contacts with the product is 6.61x10-6 mg a.s/kg bw/day for rat and 3.86x10-6 mg/kg bw/day for mouse.

The estimations above are representative for exposure to SORKIL AVOINE SPECIALE in bulk but they represent a very worst case when the product is supplied and applied in sachets.

As a reasonable case, since SORKIL AVOINE SPECIALE is only supplied and applied in sachets for non-professional users, it can be assumed that there is no decanting phase and no exposure is expected during loading in bait points as the sachets prevent inhalation and dermal contacts. Therefore, only exposure during cleaning can be considered: 1.88x10-6 mg a.s/kg bw/day for rat and mouse.

**Secondary exposure**

Exposure of non users could result from the handling of dead rodents or ingesting poison baits. The “*handling of dead rodents*” scenario is excluded due to unrealistic assumptions (very low amount of difenacoum is expected on the fur because SORKIL AVOINE SPECIALE is an oral bait and toxicokinetics data showed that urine is a minor route of excretion for difenacoum).

For the scenario “*oral exposure by ingesting bait*”, a reverse scenario was calculated. Based on the AEL of 1.1x10-6 mg a.s/kg bw/day, a body weight of 10 kg and an oral absorption of 68% (as stated in the assessment report of difenacoum [Activa/Pelgar Study]), ingestion of more than 0.3 mg of product per day (corresponding to 1.6x10-5 mg a.s) by an infant is needed to exceed the AEL.

In Annex 6 “Safety for non-professional operators and the general public”, the results of the exposure calculations for the active substance for the non-professional user and the general public are laid out.

* **Assessment of the major change: Addendum to the PAR 2013: PARATOX**

**Primary exposure**

For non-professional users, considering the available packaging (only in plastic sachet or in prefilled bait station with recharge baits in plastic sachets), 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 difenacoum 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.

* **Renewal of authorisation - 2017**

Non professional uses are no longer claimed for the renewal of authorisation.

**Secondary exposure**

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.

**2.6.2.3 Exposure to residues in food**

Based on the intended uses, no residue assessment was performed (Annex 7 “Residue behaviour”).

### **Risk characterisation**

#### Risk for 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/kg bw/day for short, medium and long-term exposures).

**Primary exposure**

Based on the risk assessment of the active substance, the risk for professional users resulting from the intended use is unacceptable when SORKIL AVOINE SPECIALE is supplied in bulk, even if gloves are worn (%AEL at 315% with a gloves penetration factor of 5% for rat and 144% with a gloves penetration factor of 5% for mouse).

For SORKIL AVOINE SPECIALE supplied and applied in sachet, the risk resulting from the intended use is considered as acceptable when professionals are wearing gloves with a penetration factor of 10% (%AEL at 55% for rat and mouse). Gloves are anyway recommended to help prevent rodent-borne disease.

Moreover, the mention “do not open the sachet” has to be added in the label of the product.

The conclusion is the same for the pre-filled boxes. Consequently, the refilling of the boxes must be done with sachets and professionals have to wear gloves.

**Secondary exposure**

As no secondary exposure is expected for professional users, no risk has been identified.

* **Assessment of the major change: Addendum to the PAR 2013: PARATOX**

The estimated exposures for the professional users are compared to the systemic AEL of difenacoum set in the assessment report (1.1x10-6 mg/kg bw/day for short, medium and long-term exposures).

**Primary exposure**

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 PARATOX as loose grains (%AEL is set at 31%) and without any protection equipment for PARATOX in sachet (%AEL is set at 1.2%). 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 | 1.2 | Acceptable |

**Secondary exposure**

As no secondary exposure is expected for professional users, no risk has been identified.

* **Renewal of authorisation - 2017**

**Primary exposure**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Scenario** | **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 | 2.64 x 10-6 | 240 | Unacceptable |
| Professional (with respiratory protection APF 10 during decanting) | 1.1x10-6 | 3.87 x 10-7 | 35.2 | Acceptable |
| **Professional exposure : Bulk formulation (loading and cleaning phases) packaging < 10kg without decanting**  |
| Professional (without PPE) | 1.1x10-6 | 6.31 x 10 -8 | 6 | Acceptable |
| **Sachet formulation (exposure during cleaning phase)** |
| Professional (without PPE) | 1.1x10-6 | 2.02 x 10-8 | 1.84 | Acceptable |

Based on the risk assessment of the active substance, the risk for professional users is acceptable when respiratory protection is worn during the decanting of PARATOX product as loose grains (%AEL is set at 35.2%) and without any protection equipment for use of PARATOX product in sachet (%AEL is set at 1.84%). 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 without 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 mitigation measure is necessary: Decanting is to be avoided. In case decanting cannot be avoided, an RPE of APF 10 has to be used.

**Secondary exposure**

As no secondary exposure is expected for professional users, no risk has been identified.

**No change of PPE and RMMs in the framework of the renewal of the authorisation.**

**2.6.3.2 Risk for non-professional users and the general public**

The estimated exposure for the non-professional users is compared to the systemic AEL of difenacoum set in the assessment report, such as for professional users (1.1x10-6 mg/kg bw/day for short, medium and long-term exposures).

**Primary exposure**

Based on the risk assessment of the active substance, the risk for non-professional users resulting from the intended use is considered as unacceptable, even when considering the presence of a sachet (%AEL at 171% for rat and mouse) or thus, considering the pre-filled boxes.

**Secondary exposure**

Based on a reverse scenario, more than 0.3 mg of product per day should be ingested by an infant to exceed the AEL. This indicates that infants are at significant risk of poisoning as 0.3 mg corresponds to only 1.5x10-4% of the product of 200 g (rat) and to 1.2x10-3% of the product of 25 g (mouse). Therefore, even if SORKIL AVOINE SPECIALE contains a bittering agent which reduces the likelihood of ingestion, the baits should be placed in areas which do not allow access to children and in secured bait boxes. Product label (“do not open the sachet”) and good practice must advise users preventing access to bait by children and infants.

* **Assessment of the major change: Addendum to the PAR 2013: PARATOX**

The estimated exposure for the non-professional users is compared to the systemic AEL of difenacoum set in the assessment report, such as for professional users (1.1x10-6 mg/kg bw/day for short, medium and long-term exposures).

**Primary exposure**

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 PARATOX in sachet (%AEL is set at 0.5%). The exposure from the use of prefilled stations (with sachet) is covered by this scenario.

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

* **Renewal of authorisation - 2017**

Non professional uses are no longer claimed for the renewal of authorisation

**Secondary 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 PARATOX 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.

* **Renewal of authorisation - 2017**

**Secondary exposure**

**No change of RMMs in the framework of the renewal of the authorisation.**

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 **2.6.3.3 Risk for consumers via residues**

Since no contamination is expected for feeding stuffs, the risk for consumers via residues was not assessed.

 **2.6.3.4 Summary of risks characterisation for SORKIL AVOINE SPECIALE**

**Treatment against rats:**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Scenario** | **AEL****(mg/kg bw/d)** | **Exposure (mg/kg bw/d)** | **% AEL** | **Conclusion** |
| **bulk formulation (exposure during decanting, loading and cleaning phases)** |
| Professional (without gloves) | 1.1 x 10-6 | 5.98 x 10-5 | 5433 | Unacceptable |
| Professional (with gloves ; penetration factor of 10 %) | 1.1 x 10-6 | 6.43 x 10-6 | 584 | Unacceptable |
| Professional (with gloves ; penetration factor of 5 %) | 1.1 x 10-6 | 3.46 x 10-6 | 315 | Unacceptable |
| **sachet formulation (exposure during cleaning phase)** |
| Professional (without gloves) | 1.1 x 10-6 | 6.03 x 10-6 | 548 | Unacceptable |
| Professional (with gloves ; penetration factor of 10 %) | 1.1 x 10-6 | 6.03 x 10-7 | 55 | **Acceptable** |
| Non professional (without gloves) | 1.1 x 10-6 | 1.88 x 10-6 | 171 | Unacceptable |

**Treatment against mice:**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Scenario** | **AEL****(mg/kg bw/d)** | **Exposure (mg/kg bw/d)** | **% AEL** | **Conclusion** |
| **bulk formulation (exposure during decanting, loading and cleaning phases)** |
| Professional (without gloves) | 1.1 x 10-6 | 2.98 x 10-5 | 2711 | Unacceptable |
| Professional (with gloves ; penetration factor of 10 %) | 1.1 x 10-6 | 3.07 x 10-6 | 279 | Unacceptable |
| Professional (with gloves ; penetration factor of 5 %) | 1.1 x 10-6 | 1.59 x 10-6 | 144 | Unacceptable |
| **sachet formulation (exposure during cleaning phase)** |
| Professional (without gloves) | 1.1 x 10-6 | 6.03 x 10-6 | 548 | Unacceptable |
| Professional (with gloves ; penetration factor of 10 %) | 1.1 x 10-6 | 6.03 x 10-7 | 55 | **Acceptable** |
| Non professional (without gloves) | 1.1 x 10-6 | 1.88 x 10-6 | 171 | Unacceptable |

* **Assessment of the frame formulation establishment: Addendum to the PAR 2012: SORKIL AVOINE SPECIALE**

Based on available data on active substance and information submitted on the frame formulation, the toxicological classification for the frame formulation is unchanged.

Based on the concentration and classification of the active substance and of formulants, the toxicological properties of SORKIL AVOINE SPECIALE can be considered as similar between reference product and products from frame formulation.

No new exposure assessment was done since the modification of composition has been considered as minor.

* **Assessment of the major change: Addendum to the PAR 2013: PARATOX**

**Summary of risks characterisation for PARATOX**

**Treatment against rats (covers treatment against mice) :**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Scenario** | **AEL (mg/kg bw/d)** | **Exposure(mg/kg bw/d)** | **% AEL** | **Conclusion** |
| **bulk formulation (exposure during decanting, loading and cleaning phases)** |
| Professional (without gloves) | 1.1 x 10-6 | 2.6 x 10-6 | 236 | Unacceptable |
| Professional (with mask during decanting ; penetration factor of 10 %) | 1.1 x 10-6 | 3.4 x 10-7 | 31 | Acceptable |
| **sachet formulation (exposure during cleaning phase)** |
| Professional (without gloves) | 1.1 x 10-6 | 1.4 x 10-8 | 1.2 | Acceptable |
| Non-professional (without PPE) | 1.1x10-6 | 5.1 x 10-9 | 0.5 | Acceptable |

**Specific use restriction and issues accounted for product labelling:**

* Wear respiratory protection equipment during decanting of grains in bulk.
* Gloves have to be worn to help prevention against rodent-borne disease.
* Do not open the sachets.
* Apply strict hygiene measures: do not eat, drink or smoke during handling of the product and wash hands after use of the product.
* Tamper-resistant bait boxes should be clearly marked to show that they contain rodenticides and that they should not contain other products than rodenticides.
* Baits must be unattainable to children, pets or other non-target animals in order to minimize the risk of poisoning.
* Do not place tamper-resistant bait boxes on surfaces in contact with food, feed or drinks and beverages.
* Collect uneaten bait, bait fragments dragged away from the tamper-resistant bait boxes and dead rodents, during and after treatment.
* Remove all bait points after the end of treatment.
* **Renewal of authorisation - 2017**

**Registration renewal: Summary of risks characterisation for PARATOX**

Considering the revision of dermal absorption value according to 2012 EFSA guidance. (0.04% instead of 0.027) risk caracterisation has been revised as follows:

**Treatment against rats (covers treatment against mice) :**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Scenario** | **AEL (mg/kg bw/d)** | **Exposure(mg/kg bw/d)** | **% AEL** | **Conclusion** |
| **bulk formulation (exposure during decanting, loading and cleaning phases)** |
| Professional (without PPE) | 1.1 x 10-6 | 2.64 x 10-6 | 240 | Unacceptable |
| Professional (with mask during decanting ; penetration factor of 10 %) | 1.1 x 10-6 | 3.87 x 10-7 | 35.2 | Acceptable |
| **sachet formulation (exposure during cleaning phase)** |
| Professional (without PPE) | 1.1 x 10-6 | 2.02 x 10-8 | 1.84 | Acceptable |

The conclusions of the risk assessment remain unchanged.

**No change of PPE and RMMs in the framework of the renewal of the authorisation.**

## Risk assessment for the environment – PAR 2011

### **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.

**2.7.1.2 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.

**2.7.1.3 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.

**2.7.1.4 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.

**2.7.1.5 Distribution**

***2.7.1.5.1 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 (TGD18) 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.

***2.7.1.5.2 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**

**2.7.2.1 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.

18 Technical Guidance Document on Risk Assessment, Part II, 2003

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.

 **2.7.2.2 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.

 **2.7.2.3 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.

 **2.7.2.4 PBT Assessment**

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

 **2.7.2.5 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).

 **2.7.2.6 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 difenacoum­based 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.

 **2.7.2.7 Summary of PNEC**

***2.7.2.7.1 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 pg/L**

 ***2.7.2.7.2 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.**

 ***2.7.2.7.3 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**

 ***2.7.2.7.4 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)**

 ***2.7.2.7.5 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** p**g/kg food** equivalent to
**PNECoral for birds = 0.1** p**g/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** p**g/kg food** equivalent to
**PNECoral for mammals = 0.3** p**g/kg bw/d**

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

**Table 2.7.2.7: 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 **p**g/kg food eq. to 0.1 **p**g/kg bw/d |
| PNECoral for mammals | NOEC= 0.6 mg/kg food NOAEL=0.03 mg/kg bw/d | 90 | 7 **p**g/kg food eq. to 0.3 **p**g/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 AVOINE SPECIAL. There is no substance of concern in the formulated product. Therefore the whole environment risk assessment of SORKIL AVOINE SPECIAL is based on data obtained from the Competent Authority report of the active substance difenacoum as agreed at the Annex I inclusion stage.

**2.7.3.1 Aquatic compartment (including water, sediment and STP)**

Product SORKIL AVOINE SPECIAL 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.

**2.7.3.2 Terrestrial compartment**

According to the TNsG on data requirements (Ch. 2.5, Part B) additional data are required from rodenticidal products if they are used outside buildings in the form of baits, granulates and powder. As the intended uses proposed by the applicant are only indoor application,, no further study is needed for the terrestrial compartment.

**2.7.3.3 Non compartment specific effects relevant to the food chain (secondary**

**poisoning)**

In the SORKIL AVOINE SPECIAL impregnated grains, no substance of concern has been identified, and hence the secondary poisoning is caused entirely by the active substance difenacoum.

**2.7.3.4 Summary of PNECs**

In the product SORKIL AVOINE SPECIAL 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**

The product SORKIL AVOINE SPECIAL 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 inside industrial, commercial and residential buildings.

The applicant considers the following application rates for treatments inside buildings only:

* Rat: from 80 g to 200 g of product (i.e. 3 to 6 blocks of 30 g or 1 to 2 blocks of 80g) / bait station at distances of up to 15 meters apart.
* Mouse: from 25 g to 30 g of product (i.e. 1 block) / bait station at distances of 3 meters apart.

Bait points are inspected frequently and replenished when bait take is observed. Depending on infestation rate, an advised frequency of inspection is 3 to 5 days. Although a professional will eventually for practical reasons synchronise the inspection frequency with a work week so keeping inspections twice or once a week, so have 3.5 to 7 days inspection interval.

**2.7.4.1 Inside buildings – Impregnated grain applied in bait stations**

The product SORKIL AVOINE SPECIAL is a ready-to-use impregnated grains based product with 0.005% of difenacoum. These impregnated grains are placed in secured bait stations and used indoor only.

According to the product instructions:

* As SORKIL AVOINE SPECIAL is a ready-to-use impregnated grains based product, packed in bags or provided in bulk, but always placed in secured bait stations, the application type “bait-box” of the EUBEES ESD PT14[[17]](#footnote-17) (2003) is applied for the following exposure calculations.
* The SORKIL AVOINE SPECIAL baits are placed only in bait stations.
* The product is used inside buildings only.
* Number of bait stations: 20 inside, 5 meters apart for rats, 3 meters apart for mice.
* Day 1: Treatment with 200 g product per box for rat, 30 g product per box for mouse.
* Day 7, 14 and 21: bait refilling.

As the product is applied indoor only, no environmental compartment is exposed to SORKIL AVOINE SPECIAL. Nevertheless primary and secondary poisoning cannot be excluded. Indeed, pets living in treated buildings could be exposed directly to the product. Moreover even if the product is applied inside buildings, rats can live 3 to 11 days before dying. Therefore, they have the time to escape outside buildings and to be eaten by predators.

Primary and secondary poisoning calculations are carried out considering the ‘in and around buildings’ scenario from the EUBEES ESD PT14 (2003) as a worst case scenario in view of the fact that the product is applied inside buildings only.

 ***2.7.4.1.1 PEC in surface water and sediment***

As SORKIL AVOINE SPECIALE is intended to be used indoor only, no exposure to surface water and sediment is expected.

 ***2.7.4.1.2 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 AVOINE SPECIALE product.

 ***2.7.4.1.3 PEC in soil and groundwater***

As SORKIL AVOINE SPECIALE is intended to be used indoor only, no exposure to soil and groundwater is expected.

***2.7.4.1.4 Non-compartment specific effects relevant to the food chain (primary***

***and secondary poisoning)***

**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 AVOINE SPECIALE and in the representative product presented in the Annex I inclusion dossier for the active substance.

According to EUBEES ESD PT14 (2003), 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 (Larsen, 2003). Some defaults parameters 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 AVOINE SPECIAL) and is used in quantitative risk assessment for the long-term situation.

According to ESD (Larsen, 2003), 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 these ESD

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

FIR: food intake rate of the indicator species,

BW: indicator species body weight,

C: concentration of the active substance in fresh diet,

AV: avoidance factor,

PT: fraction of diet obtained in treated area and

PD: the fraction of the food type in the diet.

In Tier 2 Step 1 (worst case) AV, PT and PD are all set at 1; in Step 2 (realistic worst case) these AV and PT are refined to 0.9 and 0.8, respectively.

When 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 (section 2.8.2.6), 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 for 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[[18]](#footnote-18) meeting these values are used for qualitative risk assessment of primary poisoning in acute situation.

**Table 2.7.4.1 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 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 2.7.4.1 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.

**Secondary poisoning**

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

As no exposure of the aquatic compartment is foreseen with the use of SORKIL AVOINE SPECIALE inside buildings, no risk assessment for secondary poisoning through the aquatic food chain is required.

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

As no exposure of the terrestrial compartment is foreseen with the use of SORKIL AVOINE SPECIALE inside buildings, no risk assessment for secondary poisoning through the terrestrial food chain is needed.

***Secondary poisoning for 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 **-** rodent­eating mammal or rodent-eating bird is assessed in EUBEES ESD PT14 (2003).

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 AVOINE SPECIALE and in the representative product presented in the Annex I inclusion dossier for the active substance. .

According to the ESD (Larsen, 2003) 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:

- 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:

**ETE = (FIR/BW) \* C \* AV \* PT \* PD (mg/kg bw/day),
ECn =** E**n-1 n=1 ETE \* (1 – EL)n**

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.

* Tier 1 PECoral for short term situation is calculated according to the equation 22 in ESD (Larsen, 2003):



**Table 2.7.4 3: Estimated concentration (EC) of difenacoum in target rodents (rats) in mg a.sikg bw at different times during a control operation**

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

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 Table 2.8.4.4 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 the table 2.8.4.-4 below, are used for Tier 1 quantitative risk assessment of secondary poisoning in the long­term situation.
* 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 2.7.4 4: Predicted environmental concentrations of difenacoum in food of predator (PEC oral) for acute and long-term situations.**

**Table 2.7.4 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**

***2.7.5.1 Primary poisoning***

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

**Table 2.7.5.-1: Tier 1 risk characterisation of primary poisonin**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **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 2.7.5-2: 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 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.

Nevertheless, as the product SORKIL AVOINE SPECIALE is intended to be used indoor and in bait stations only, primary poisoning can therefore be considered negligible as domestic animals can be kept away from the product, and wild animals other than rats and mice are not expected to be found inside buildings.

***2.7.5.2 Secondary poisoning***

The only relevant scenario of secondary poisoning in the case of an indoor application only is for 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 2.7.5-3: 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 2.8.4.1.4. 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 2.8.2.7.5.

**Table 2.7.5-4: 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 (Table 2.8.5-4).

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 2.8.4.2.1.

**Table 2.7.5-5: 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 2.8.5- 5). 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) to difenacoum. Only one day exposure of predators is assumed in the ESD, 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 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.

However, considering the fact that SORKIL AVOINE SPECIALE is intended to be used indoor only, it can be assumed that, applying use restrictions (such as collecting dead rodents), the risk for secondary poisoning will be lower.

Nevertheless, in order to reduce the risk of secondary poisoning, it is very important to follow the use instructions and the risk reduction measures of the rodenticidal baits (see Section 3).

* **Assessment of the frame formulation establishment: Addendum to the PAR 2012: SORKIL AVOINE SPECIALE**

The environmental risk assessment initially carried out for the first authorization of product SORKIL AVOINE SPECIALE and for the frame formulation establishment can be considered as valid for this application.

Based on the detailed compositions and the classification of each formulant, the difference between the reference product SORKIL AVOINE SPECIALE and the frame formulation are considered as minor and without impact on the ecotoxicity. The initial risk assessment carried out for the reference product SORKIL AVOINE SPECIALE can be considered applicable for the frame formulation.

* **Assessment of the major change: Addendum to the PAR 2013: PARATOX**

The environmental risk assessment initially carried out for the first authorization of product PARATOX and for the frame formulation establishment can be considered as valid for this application.

* **Renewal of authorisation – 2017**

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 0.0625 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 PARATOX.

Regarding this new information, the conclusion of the environmental risk assessment remains unchanged.

## Measures to protect man, animals and the environment

*See Summary of Product Characteristics (SPC).*

# Proposal for the decision - renewal 2017

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

1. **Administrative information**

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

| **Trade name(s)** |  |
| --- | --- |
| PARATOXCEREOX D |  |

**1.2. Authorisation holder**

|  |  |  |
| --- | --- | --- |
| **Name and address of the authorisation holder** | **Name** | LARC |
| **Address** | ZA de Kerampaou29140 MELGVENFrance |
| **Authorisation number** |  |
| **R4BP asset reference number** |  |
| **Date of the authorisation** |  |
| **Expiry date of the authorisation** |  |

**1.3. Manufacturer of the product**

|  |  |
| --- | --- |
| **Name of manufacturer** | LARC |
| **Address of manufacturer** | ZA de Kerampaou29140 MELGVENFrance |
| **Location of manufacturing sites** | ZA de Kerampaou29140 MELGVENFrance |

**1.4. Manufacturer of the active substance**

|  |  |
| --- | --- |
| **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 | 0.005 |

**2.2. Type of formulation**

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

**3. Hazard and precautionary statements according to Regulation (EC) 1272/2008**

| **Classification** |
| --- |
| Hazard category | Repr. 1BSTOT RE 2 |
| Hazard statement | H360D: May damage the unborn childH373: May cause damage to organs (blood) through prolonged or repeated exposure |
|  |
| **Labelling** |
| Signal words | DangerGHS 08 |
| Hazard statements | H360D: May damage the unborn childH373: May cause damage to organs (blood) through prolonged or repeated exposure |
| Precautionary statements | P201: Obtain special instructions before use.P202: Do not handle until all safety precautions have been read and understood.P260: Do not breathe dust/fumes/gas/mist/vapours/spray.P280: Wear protective gloves/protective clothing/eye protection/face protection.P308 + P313: IF exposed or concerned: Get medical advice/attention.P314: Get medical advice/attention if you feel unwell.P405: Store locked up.P501: Dispose of contents/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[[19]](#footnote-19) - *[Covered and protected baiting points]*  |
| **Application rate(s) and frequency** | Bait products:- rat: 80 to 200 g of bait per baiting point. - mice: 25 to 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)*- Bait formulations:PP sachets containing 25, 30, 40, 50, 75,100, 150 or 200 g of grains.The PP sachets are packed in 3 kg, 5 kg, 10 kg or, 12.5 kg buckets or cardboard.Pre-filled bait stations with PP sachets are also available: * for mice, 1\*25 g or 1\*30 g ;
* for rats, 4\*25 g, 3\*30 g, 2\*40 g, 2\*50 g, 2\*75 g, 1\*100 g, 1\*150 g or 1\*200 g.

Bulk grains packed in PP buckets, multi-layered paper bags with PP coating or woven laminated PP bags: 3 kg, 5 kg, 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***

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| --- |
| - 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***

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

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| - |

**4.2. Use description**

**Table 2. Use # 2 – *(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[[20]](#footnote-20) |
| **Application rate(s) and frequency** | - 25 to 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:PP sachets containing 25, 30 g of grains.The PP sachets are packed in 3 kg, 5 kg, 10 kg or, 12.5 kg buckets or cardboard.Pre-filled bait stations with PP sachets are also available : - for mice, 1\*25 g or 1\*30 g. |

***4.2.1.* *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. |

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

|  |
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| - |

***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***

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| --- |
| - When placing bait stations close to 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***

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

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**4.3. Use description**

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

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| --- | --- |
| **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** | - 80 to 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:PP sachets containing 25, 30, 40, 50, 75,100, 150 or 200 g of grains.The PP sachets are packed in 3 kg, 5 kg, 10 kg or, 12.5 kg buckets or cardboard.Pre-filled bait stations with PP sachets are also available : - for rats, 4\*25 g, 3\*30 g, 2\*40 g, 2\*50 g, 2\*75 g, 1\*100 g, 1\*150 g or 1\*200 g. |

***4.3.1.* *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. |

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

|  |
| --- |
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***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***

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

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**5. General directions for use**

**5.1. Instructions for use6**

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| --- |
| - 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.- Wear protective chemical resistant gloves during product handling phase (glove material to be specified by the authorisation holder within the product information).- Decanting is to be avoided. In case decanting cannot be avoided, an RPE of APF 10 has to be used.- 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.- 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). |

**5.2. Risk mitigation measures**

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| --- |
| - 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. |

**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**

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| - 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.- Store in places prevented from the access of children, birds, pets and farm animals.- Shelf life: 24 months.**- In France only**: Do not store at a temperature above 25°C. |

**6. Other information**

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| --- |
| - **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.)- 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 data1 submitted in support of the evaluation of the active substance – PAR 2011***

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Section No** | **Reference No** | **Author** | **Year** | **Title** | **Owner of data** | **Letter** **Yes** | **Access****of****No** | **Data****protectionclaimed****Yes No** |
|  |  |
| A3.3 | Report No.2109/0005 | Walker JA and Mullee, DM | 2007 | Difenacoum: Determination of General Physico-chemical PropertiesSafePharm 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 |  |  |  |  |

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

***List of new data submitted in support of the evaluation of the biocidal product -– PAR 2011 updated 2017***

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Section No** | **Reference No** | **Author** | **Year** | **Title** | **Owner of data** | **Letter****Yes** | **Access****of****No** | **Data****protectionclaimed****Yes No** |
|  |  |
| Doc IIIB3.1, 3.6,3.7, 3.12 | Report No Mo3826 | M.T. Garcia | 2010 | Determination of physico- chemical properties and storage stability test for EDI-200 [cut oat – grain bait (AB)] | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 3.2 | Report No20091137.02 | M. Krack | 2010 | EDI-200 [Cut Oat (grain bait, AB)]Explosive properties A.14 | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 3.3 | Report No20091137.04 | M. Krack | 2010 | EDI-200 [Cut Oat (grain bait, AB)]Oxidising Properties A.17 | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 3.4 | Report No20091137.01 | M. Krack | 2010 | EDI-200 [Cut Oat (grain bait, AB)]Flammability (solids) A.10 | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 3.4 | Report No20091137.03 | 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 | Report No20091137.05 | M. Krack | 2010 | EDI-200 [Cut Oat (grain bait, AB)]Dustiness of granules (CIPAC MT 171) | Edialux Formulex NV |  |  |  |  |

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Section No** | **Reference No** | **Author** | **Year** | **Title** | **Owner of data** | **Letter****Yes** | **Access****of****No** | **Data****protectionclaimed****Yes No** |
|  |  |
| Doc IIIB 3 | Report No20091138.01 | M. Krack | 2010 | EDI-200 [Cut Oat (grain bait, AB)], sample stored at 54°C for 14 daysDustiness of granules (CIPAC MT 171) | Edialux Formulex NV |  |  |  |  |
|  | Report NoMo3826 | S. Manka | 2013 | Determination of physico-chemical properties and storage stability test for EDI-200 [cut oat - grain bait (AB)] 2 weeks at 54°C and up to 24 months at ambient conditions | Edialux Formulex NV |  |  | X |  |
|  | Report No23460 | B. de Ryckel | 2014 | pH of a 1% dispersion and particle size distribution (by dry sieving) of EDI 200 AB-ROD (difenacoum 0.005% w/w) AB | Edialux Formulex NV |  |  | X |  |
|  | - | V. Videau | 2014 | SORKIL AVOINE SPECIALE vis-à-vis de la lumière | Edialux |  |  |  | X |
| Doc IIIB 4 | Report No MV031 | M.T. Garcia | 2010 | Determination of Difenacoum in Grain Baits | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 4 | Report No Mo3825 | M.T. Garcia | 2010 | Validation of method MV031: Determination of Difenacoum in Grain Baits | Edialux Formulex NV |  |  |  |  |
| Doc IIIB5.10.1 | XXX | XXX | 1998 | Efficacité du Sorkil-G,Rodenticide à base de 0.005% de difénacoum, contre le rat surmulot (Rattus norvegicus Berkenhout),XXX | Edialux Formulex NV |  |  |  |  |
| Doc IIIB5.10.2 | XXX | XXX | 1999 | Efficacité du Sorkil-G,Rodenticide à base de 0.005% de difénacoum, contre la souris grise (Mus musculus L.) XXX | Edialux Formulex NV |  |  |  |  |

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Doc IIIB5.10.3 | XXX | XXX | 2000 | 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 IIIB5.10.4 | XXX | XXX | 2010 | Bait choice- EDI 200 AB-ROD fresh bait with difenacoum, Rats (*Rattus norvegicus*) | Edialux Formulex NV |  |  |  |  |
| Doc IIIB5.10.5 | XXX | XXX | 2010 | Bait choice- EDI 200 AB-ROD aged bait with difenacoum, Rats (*Rattus norvegicus*)XXX | Edialux Formulex NV |  |  |  |  |
| Doc IIIB5.10.6 | XXX | XXX | 2010 | Bait choice- EDI 200 AB-ROD fresh bait with difenacoum, Mice (*Mus musculus*)XXX | Edialux Formulex NV |  |  |  |  |
| Doc IIIB5.10.7 | XXX | XXX | 2010 | Bait choice- EDI 200 AB-ROD aged bait with difenacoum, Mice (*Mus musculus*)XXX | Edialux Formulex NV |  |  |  |  |
| Doc IIIB5.10.8 | XXX | XXX | 2011 | Palatability and efficiency of EDI 200 AB-ROD for rats and mice in the field, XXX | Edialux Formulex NV |  |  |  |  |
|  | XXX | XXX | 2016 | Evaluation of the efficacy of EDI-250\_24 (blue oat rodenticide containing 0.0024% w/w difenacoum) for the control of black rat infestations in and around agricultural buildings. | LARC |  |  | X |  |

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Doc IIIB6.1.2 | XXX | XXX | 2010 | Sorkil rodenticide cut oat grain bait (AB), Acute dermal toxicity in the ratXXX | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 6.2 | XXX | XXX | 2010 | Sorkil rodenticide cut oat grain bait (AB), Skin irritation test in the rabbitXXX | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 6.2 | XXX | XXX | 2010 | Sorkil rodenticide cut oat grainbait (AB), Eye irritation test inthe rabbitXXX | Edialux Formulex NV |  |  |  |  |
| Doc IIIB 6.3 | XXX | XXX | 2010 | Sorkil rodenticide cut oat grainbait (AB), Local lymph nodeassay in the mouseXXX | Edialux Formulex NV |  |  |  |  |
| Doc IIC B6.6 (1) | - | Chambers JG and Snowdon PJ | 2004 | Study to Determine Potential Exposure to Operators During Simulated Use of Anticoagulant Rodenticide BaitsSynergy Laboratories Ltd., Report No. SYN/1302. Unpublished. | CEFIC |  |  |  |  |

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Section No** | **Reference No** | **Author** | **Year** | **Title** | **Owner of data** | **Letter****Yes** | **Access****of****No** | **Data****protectionclaimed****Yes No** |
|  |  |
| Doc IIC B6.6 (2) | - | Vetter D and Sendor T | 2006 | Estimation of the frequency of dermal exposure during the occupational use of rodenticides. Report of EBRC Consulting under contact to CEFIC Rodenticide Working Group. Unpublished. | CEFIC |  |  |  |  |

**Annex 2: Analytical methods residues – active substance (PAR – 2011)**

**Difenacoum**

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

matrix limit relevant residue reference or comment

plant products LOQ= Difenacoum

0.01mg/kg

food of animal LOQ= Difenacoum

origin 0.01mg/kg

|  |  |
| --- | --- |
| soil LOQ=0.0214 **p**g/gdrinking water LOQ = 0.05**p**g/Lsurface water LOQ = 0.05**p**g/L | Difenacoum Difenacoum Difenacoum |

air Unnecessary due to the low vapour pressure of difenacoum

body fluids / LOQ= Difenacoum

tissues 0.01mg/kg

**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 Brodifaco um and Difenaco um 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 **p**g/g | *HPLC – UV-VIS* Activa /PelGar Brodifaco um and Difenaco um 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 Brodifaco um and Difenaco um Task Force |

**Methods for drinking water and surface water**

reference matrix LOQ principle comment owner

(µg/l)

reference matrix LOQ principle comment owner

(µg/l)

|  |  |  |
| --- | --- | --- |
| 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 **p**g/l | *HPLC – MS/MS* Activa /PelGar Brodifaco um and Difenaco um 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 Brodifaco um and Difenaco um Task Force |

**Annex 3: Efficacy of the active substance from its use in the product – PAR 2011 updated 2017**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **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 | B5.10.1-Rat indoor |
| 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). | B5.10.2-mice-field |
| SORKIL-G (old formulation) | Albino rat22 ratsControl: 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. | B5.10.3-rat-aged |
| SORKIL AVOINE SPECIALE | 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 female100% 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. | B5.10.4-rat-fresh |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Test substance** | **Test organisms** | **Test system / Concentrations applied / exposure time** | **Test results: effects, mode of action, resistance** | **Reference** |
| SORKIL AVOINE SPECIALE | 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 needs4-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 female100% 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. | B5.10.5-rat-aged |
| SORKIL AVOINE SPECIALE | CD1 mice (*Mus musculus*) 10 mice (5 males, 5 females) | Choice feeding test: fresh bait.Quantity sufficient to meet each animal’s daily needs4-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 female100% 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. | B5.10.6-mice-fresh |
| SORKIL AVOINE SPECIALE | 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 female100% 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. | B5.10.7-mice-aged |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Test substance** | **Test organisms** | **Test system / Concentrations applied / exposure time** | **Test results: effects, mode of action, resistance** | **Reference** |
|  | Rat and miceBased on daily consumption: 11mice and 10 rats | Field testPrivate house in urban environment and chocolate factory in industrial site.5 bait stations for mice filled with 20 g ofproduct 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 of3 days, Post treatment census: duration of 6 day |  |  |
| SORKIL AVOINESPECIALE | 100 % control of the mouse population was achieved 11 days after the first bait take and100 % control of the rat population wasachieved 10 days after the first bait take. | B5.10-8\_field |
| EDI-250\_24(24 ppm difenacoum) | Black rats*Rattus rattus* | Field testCensus baiting technique, which involved the following phases: Pre-treatment censusPre-treatment lag phase (2 days)Treatment censusPost-treatment lag phase (3 days)Post-treatment censusDuring 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 rats around the sites.Acclimatization: 25 days (100 g of oat per station per day)Treatment : 100 g of bait per day in each lockable bait station, every 3 to 15 meters (total 11 bait stations) during11 daysPost-baiting: 5 days(150-200 g of oat per station per day)Mortality was observed from the first day of intoxication and noted about every 2 days until the end of the trial. | Estimated efficacy = 100 %.Pre-baiting plateau = 632 g/dayPost-baiting = no consumption observed.2 dead ratsR.I = 2 | XXX |

**Annex 4: Toxicology and metabolism –active substance – PAR 2011 updated 2017**

**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)

**Renewal 2017**

**Classification**

|  |  |
| --- | --- |
| with regard to toxicological data (according to the criteria in Reg. 1272/2008) | Acute Tox 1 – H300 ; H310 ; H330STOT RE 1 – H372 (blood)Repr. 1B – H360DRepr. 1B; H360D: C ≥ 0,003 %STOT RE 2; H373: 0,002 % ≤ C < 0,02 %STOT RE 1; H372: C ≥ 0,02 % |

**Annex 5: Toxicology – biocidal product – PAR 2011 updated 2017**

**SORKIL AVOINE SPECIALE**

**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** | **Species** | **dose levels** | **Value** | **Remarks** | **Reference** |
|  | **Guideline** | **Strain Sex no/group** | **duration of exposure** | **LD50/LC50** |  |  |
| Dermal | OECD 402 | Sprague | 2000mg/kg bw | > 2000mg/kg bw | No mortality | XXX |
|  |  | Dawley |  |  | No systemic effects | 2010 |
|  |  | 5/sex |  |  | Some reversible cutaneous reactions |  |

Dermal irritation test:

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Species** | **Method** | **Average score 24, 48 and 72 h** | **Reversibility yes/no** | **Result** | **Remarks** | **Reference** |
| Erythema | Oedema |
| Albinos NZ rabbit3 males | OECD 404 Semi-occlusive, 4h | 0 | 0 | na | Not irritant |  | XXX 2010 |

Ocular irritation test:

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Species** | **Method** | **Average Score (24h, 48h, 72h)** | **Result** | **Reversibilit****y****yes/no** | **Remarks** | **Reference** |
| Cornea | Iris | Conjunctiva |
| Redness | Chemosis |
| Albinos NZ rabbit3 males | OECD405 | 0 | 0 | 1.22 | 0.33 | Not irritant | Redness reversible between day 4 and 6. Chemosis reversible on day 3. |  | XXX 2010 |

Sensitisation test:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Species** | **Method** | **Result** | **Remark** | **Reference** |
| CBA/J mice | Non radioactive cell counting | SI < 1.4: not | Not acceptable | XXX |
| 4 | LLNA: 5, 10, 25% in ethanol/water | sensitiser | (method not currently | 2010 |
| females/group | (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 |  | validated) |  |

Dermal absorption:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Species** | **Method** | **Result** | **Remark** | **Reference** |
| Human skin *in vitro* | Skin contact with a pellet bait formulation containing 0.005% (w/w) difenacoum during 8 hours.Sampling during 24h | 0.04% | Assessed according to the EFSA guidance  | XXX 2011 |

**Additional toxicological information**

Short-term toxicity studies None

|  |  |
| --- | --- |
| Toxicological data on active substance(s) (not tested with the preparation)Toxicological data on non-active substance(s)(not tested with the preparation) | NoneNone |

Further toxicological information None

|  |
| --- |
| **Renewal 2017****Classification and labelling proposed for the preparation with regard to toxicological properties**  |
| Regulation 1272/2008/EC | Repr.1B – H360D STOT RE2-H373 |

**Annex 6: Safety for professional operators – PAR 2011, updated 2017**

**SORKIL AVOINE SPECIALE**

**Exposure assessment**

**Exposure scenarios for intended uses**

Primary exposure of professionals – Sorkil avoine speciale in bulk (exposure during decanting, loading and cleaning considered (rat)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Component** | **CAS** | **ActualDermalTotal[mg/day]** | **ActualDermalTotal[mg/kg/d]** | **InhalationExposure[mg/m3]** | **Model** |
| Tier 1 (without PPE) | Difenacoum | 56073-07-5 | 3.56 x10-3 | 5.93x10-5 | 5.0x10-7 | Cefic study |
| Tier 2 a(gloves penetration factor: 10%) | Difenacoum | 56073-07-5 | 3.56 x10-4 | 5.93x10-6 | 5.0x10-7 | Cefic study |
| Tier 2 b(gloves penetration factor: 5%) | Difenacoum | 56073-07-5 | 1.78x10-4 | 2.96x10-6 | 5.0x10-7 | Cefic study |

Primary exposure of professionals – Sorkil avoine speciale in bulk (exposure during decanting, loading and cleaning considered (mouse)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Component** | **CAS** | **ActualDermalTotal[mg/day]** | **ActualDermalTotal[mg/kg/d]** | **InhalationExposure[mg/m3]** | **Model** |
| Tier 1 (without PPE) | Difenacoum | 56073-07-5 | 1.78 x10-3 | 2.97x10-5 | 1.0x10-7 | Cefic study |
| Tier 2 a(gloves penetration factor: 10%) | Difenacoum | 56073-07-5 | 1.78x10-4 | 2.97x10-6 | 1.0x10-7 | Cefic study |
| Tier 2 b(gloves penetration factor: 5%) | Difenacoum | 56073-07-5 | 8.94x10-5 | 1.49x10-6 | 1.0x10-7 | Cefic study |

Primary exposure of professionals – Sorkil avoine speciale in sachet (exposure only during cleaning) (rat)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Component** | **CAS** | **Actual** | **Actual** | **Inhalation** | **Model** |
|  |  |  | **Dermal** | **Dermal** | **Exposure** |  |
|  |  |  | **Total** | **Total** | **[mg/m3]** |  |
|  |  |  | **[mg/day]** | **[mg/kg/d]** |  |  |
| Tier 1 (without PPE) | Difenacoum | 56073-07-5 | 3.6 2x10-4 | 6.03x10-6 | Notapplicable | Cefic study |
| Tier 2 (gloves penetration factor: 10%) | Difenacoum | 56073-07-5 | 3.62 x10-5 | 6.03x10-7 | Notapplicable | Cefic study |

Primary exposure of professionals – Sorkil avoine speciale in sachet (exposure only during cleaning) (mouse)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Component** | **CAS** | **Actual** | **Actual** | **Inhalation** | **Model** |
|  |  |  | **Dermal** | **Dermal** | **Exposure** |  |
|  |  |  | **Total** | **Total** | **[mg/m3]** |  |
|  |  |  | **[mg/day]** | **[mg/kg/d]** |  |  |
| Tier 1 (without PPE) | Difenacoum | 56073-07-5 | 3.6 2x10-4 | 6.03x10-6 | Notapplicable | Cefic study |
| Tier 2 (gloves penetration factor: 10%) | Difenacoum | 56073-07-5 | 3.62 x10-5 | 6.03x10-7 | Notapplicable | Cefic study |

Risk assessment (rat)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Scenario** | **Component** | **CAS** | **AEL [mg/kg/d]** | **Absorption [%]** | **Total syst exposure** [**mg/kg bw/d]** | %AEL | **Risk** |
|  |  |  |  | inhalation | dermal |  |
| SORKIL AVOINE SPECIALE in bulk |
| Professional (without gloves) | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 10 | 5.98x10-5 | 5433 | Unaccepta ble |
| Professional (gloves penetration factor: 10%) | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 10 | 6.43x10-6 | 584 | Unaccepta ble |
| Professional (gloves penetration factor: 5%) | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 10 | 3.46x10-6 | 315 | Unaccepta ble |
| SORKIL AVOINE SPECIALE in sachet |
| Professional (without gloves) | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 10 | 6.03x10-6 | 548 | Unaccepta ble |
| Professional (gloves penetration factor: 10%) | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 10 | 6.03x10-7 | 55 | Acceptable |

Risk assessment (mouse)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Scenario** | **Component** | **CAS** | **AEL [mg/kg/d]** | **Absorption [%]** | **Total syst exposure** [**mg/kg bw/d]** | %AEL | **Risk** |
|  |  |  |  | inhalation | dermal |  |
| SORKIL AVOINE SPECIALE in bulk |
| Professional (without gloves) | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 10 | 2.98x10-5 | 2711 | Unaccept able |
| Professional (gloves penetration factor: 10%) | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 10 | 3.07x10-6 | 279 | Unaccept able |
| Professional (gloves penetration factor: 5%) | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 10 | 1.59x10-6 | 144 | Unaccept able |
| SORKIL AVOINE SPECIALE in sachet |
| Professional (without gloves) | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 10 | 6.03x10-6 | 548 | Unaccept able |
| Professional (gloves penetration factor: 10%) | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 10 | 6.03x10-7 | 55 | Acceptab le |

Renewal 2017 : Risk assessment (rat)

(Risk assessment of mouse is covered by risk assessment of rat)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Scenario** | **Component** | **CAS** | **AEL [mg/kg/d]** | **Absorption [%]** | **Total syst exposure** [**mg/kg bw/d]** | %AEL | **Risk** |
|  |  |  |  | inhalation | dermal |  |
| PARATOX in bulk |
| Professional (without PPE) | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 0.04 | 2.64x10-6 | 240 | Unacceptable |
| Professional (with mask : inh. penetration factor: 10%) | Difenacoum | 56073-07-5 | 1.1x10-6 | 10 | 0.04 | 3.87x10-7 | 35.2 | Acceptable |
| PARATOX in sachet |
| Professional (without PPE) | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 0.04 | 2.02x10-8 | 1.84 | Acceptable |

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

**SORKIL AVOINE SPECIALE**

**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 (Annex IIIB, point 6.6 )**

Primary exposure: non-professional use

Secondary exposure, acute: child ingesting bait Secondary exposure, chronic: none

Conclusion:

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

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 (rat):

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Scenario** | **Component** | **CAS** | **Potential Dermal Total [mg/kg/d]** | **Inhalation Exposure [mg/m3]** | **Model** |
| Sachet not considered: exposure during decanting, loading and cleaning (worst case) |
| Non | Difenacoum | 56073-07- | 6.11x10-6 | 5.0x10-7 | Cefic study |
| professional |  | 5 |  |  |  |
| Sachet considered: exposure only during cleaning considered (reasonable case) |
| Non | Difenacoum | 56073-07- | 1.88x10-6 | na | Cefic study |
| professional |  | 5 |  |  |  |

Details for the exposure estimates (mouse):

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Scenario** | **Component** | **CAS** | **Potential Dermal Total [mg/kg/d]** | **Inhalation Exposure [mg/m3]** | **Model** |
| Sachet not considered: exposure during decanting, loading and cleaning (worst case) |
| Non | Difenacoum | 56073-07- | 3.76x10-6 | 1.0x10-7 | Cefic study |
| professional |  | 5 |  |  |  |
| Sachet considered: exposure only during cleaning considered (reasonable case) |
| Non | Difenacoum | 56073-07- | 1.88x10-6 | na | Cefic study |
| professional |  | 5 |  |  |  |

Risk assessment (rat)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Scenario** | **Component** | **CAS** | **AEL [mg/kg/d ]** | **Absorption [%]** | **Total syst exposure****[mg/kg bw/d] [mg/m3]** | **%AEL** | **Risk** |
|  |  |  |  | inha latio n | derm al |  |
| Sachet not considered: exposure during decanting, loading and cleaning (worst case) |
| Non-professional | Difenacoum | 56073-07- 5 | 1.1x10-6 | 100 | 10 | 6.61x10-6 | 601 | Unaccept able |
| Sachet considered: exposure only during cleaning considered (reasonable case) |
| Non-professional | Difenacoum | 56073-07- 5 | 1.1x10-6 | 100 | 10 | 1.88x10-6 | 171 | Unaccept able |

Risk assessment (mouse)

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Scenario** | **Component** | **CAS** | **AEL [mg/kg/d]** | **Absorption [%]** | **Total syst exposure****[mg/kg bw/d] [mg/m3]** | **%AEL** | **Risk** |
|  |  |  |  | inhala tion | derm al |  |
| Sachet not considered: exposure during decanting, loading and cleaning (worst case) |
| Non-professional | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 10 | 3.86x10-6 | 351 | Unaccept able |
| Sachet considered: exposure only during cleaning considered (reasonable case) |
| Non-professional | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 10 | 1.88x10-6 | 171 | Unaccept able |

**Annex 8: Residue behaviour**

**SORKIL AVOINE SPECIALE**

The intended use descriptions of the SORKIL AVOINE SPECIALE 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.

1. Guidance on the Biocidal Products Regulation Volume III Human Health – Part B Risk Assessment, October 2015. [↑](#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. TNsG chapter 4 Data requirements for substances of concern version 4.3.1; April 2000 [↑](#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. "An evaluation of performance standards and non-radioactive endpoints for the LLNA – The report and recommendations of ECVAM Workshop 65" (2008) [↑](#footnote-ref-13)
14. Non-radioactive LLNA [↑](#footnote-ref-14)
15. HEEG opinion on harmonising the number of manipulations in the assessment of rodenticides (anticoagulant), agreed at TMII2010 [↑](#footnote-ref-15)
16. HEEG opinion on harmonising the number of manipulations in the assessment of rodenticides (anticoagulant), agreed at TMII2010 [↑](#footnote-ref-16)
17. J. Larsen, danish EPA, Emission scenario document for biocides used as rodenticides, May 2003 [↑](#footnote-ref-17)
18. Addendum relevant to biocides to the TGD on Risk Assessment, PNECoral derivation for the primary and secondary poisoning asessment of anti-coagulant rodenticides [↑](#footnote-ref-18)
19. See document CA-Nov16-Doc.4.x-Final on the concept of tamper-resistant bait stations. [↑](#footnote-ref-19)
20. See document CA-Nov16-Doc.4.x-Final on the concept of tamper-resistant bait stations. [↑](#footnote-ref-20)