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

**PRODUCT ASSESSMENT REPORT OF A BIOCIDAL PRODUCT FOR MAJOR CHANGE AND RENEWAL OF NATIONAL AUTHORISATION APPLICATIONS**



CONTROL 25

Product type 14

Bromadiolone included in the Union list of approved active substances

Case Number in R4BP:

Evaluating Competent Authority: France

Date: March 2018

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Note to the reader:

**Disclaimer regarding general information**

This consolidated PAR for the renewal of the product authorisation CONTROL 25 is based on the PAR of the first authorisation CONTROL granted by IE on 2012, in which all addenda have been included.

In part 1, 2 and 3 of this consolidated PAR:

⁻ each section contains the initial assessment and the subsequent successive assessments (major change and 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 they were delivered.

⁻ the assessments related to the renewal and last major change (assessed concomitantly with the renewal) of the product are indicated at the end of each section and are highlighted in grey.

In part 4 of the consolidated PAR “proposal for decision”: the summary of product characteristics is pointed out and corresponds to the decision for the renewal, including the major change.

**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 4, uses for “professionals” are mentioned according to the agreed standard SPC, but they not relevant in France. In case of mutual recognitions, it is proposed that each cMS adapts the conditions of authorization of the product according to its own legislation.

**0-History of the dossier**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Application type** | **refMS** | **Case number in the refMS** | **Decision date** | **Assessment carried out (i.e. first authorisation / amendment /renewal)** |
| NA-APP | *IE* | na | 09/10/2012 | CONTROL, initial assessment |
| NA-MRS | *FR* | na | 20/08/2014 | CONTROL |
| NA-ADC | *FR* | BC-JK017153-49 | 06/10/2015 | Addition of trade names |
| NA-BBS | *FR* | BC-EX022969-02 | 11/07/2016 | Same product CONTROL 25 |
| NA-MAC | *FR* | BC-YX000784-00 | 09.03.2018 | *Reduction of the concentration of bromadiolone (from 0.005 % to 0.0025 %)*  *Addition of trade names* |
| NA-RNL | *FR* | BC-BC030684-61 | 09.03.2018 | *Renewal of the authorisation* |

na: not applicable

**Authorised uses (0.005 % of bromadiolone) - 2016**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Users** | **Target organisms** | **Application rate** | **Field of use** | **Packagings** |
| Professionnals | Rats (*Rattus rattus* and *Rattus norvegicus*) | High infestation :50-100 g of product / bait station separated by 5 meters  Low infestation:50-100 g of product / bait station separated by 10 meters | In and around buildings  Open areas and waste dumps | Individual sachets in paper tea  and cartridge in PP  Minimum pack size :5 kg |
| Mice (*Mus musculus*) | High infestation : 25 g of product / bait station separated by 2 meters  Low infestation: 25 g of product / bait station separated by 5 meters |
| Field mice  Apodemus sylvaticus | High infestation : 25 g of product / bait station separated by 2 meters  Low infestation: 25 g of product / bait station separated by 5 meters |
| Non professionnal | Rats (*Rattus rattus* and *Rattus norvegicus*) | High infestation :50-100 g of product / bait station separated by 5 meters  Low infestation:50-100 g of product / bait station separated by 10 meters | In and around buildings | Individual sachets in paper tea  and cartridge in PP  Maximum pack size :1,5 kg |
| Mice (*Mus musculus*) | High infestation : 25 g of product / bait station separated by 2 meters  Low infestation: 25 g of product / bait station separated by 5 meters |
| Field mice  Apodemus sylvaticus | High infestation : 25 g of product / bait station separated by 2 meters  Low infestation: 25 g of product / bait station separated by 5 meters |

**Intended uses for major change and renewal (0.0025 % of bromadiolone) - 2017**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Users** | **Target organisms** | **Application rate** | **Field of use** | **Packagings** |
| Professionals | Rats (*Rattus norvegicus*) | High infestation : 50 g to 100 g of product / bait station separated by 5 meters  Low infestation: 50 g to 100 g of product / bait station separated by 10 meters | In and around buildings  Open areas and waste disposal sites | Individual sachets  In secured bait boxes or others covered bait stations |
| Mice (*Mus musculus*) | High infestation : 20 g to 30 g of product / bait station separated by 2 meters  Low infestation: 20 g to 30 g of product / bait station separated by 5 meters | In and around buildings | Individual sachets  In secured bait boxes or others covered bait stations |
| Field mice (*Apodemus sylvaticus*) | High infestation : 50 g of product / bait station separated by 2 meters  Low infestation: 50 g of product / bait station separated by 5 meters | Around buildings | Individual sachets  In secured bait boxes or others covered bait stations |
| Voles (*Microtus arvalis and Arvicola terrestris*) | High infestation : 20 g to 30 g of product / bait station separated by 3 meters  Low infestation: 20 g to 30 g of product / bait station separated by 5 meters | Around buildings | Individual sachets  In secured bait boxes or others covered bait stations |
| Non professionnals | Rats (*Rattus norvegicus*) | High infestation : 50 g to 100 g of product / bait station separated by 5 meters  Low infestation: 50 g to 100 g of product / bait station separated by 10 meters | In and around buildings | Individual sachets  In secured bait boxes |
| Mice (*Mus musculus*) | High infestation : 20 g to 30 g of product / bait station separated by 2 meters  Low infestation: 20 g to 30 g of product / bait station separated by 5 meters | In buildings | Individual sachets  In secured bait boxes |
| Field mice (*Apodemus sylvaticus*) | High infestation : 50 g of product / bait station separated by 2 meters  Low infestation: 50 g of product / bait station separated by 5 meters | Around buildings | Individual sachets  In secured bait boxes or others covered bait stations |
| Voles (*Microtus arvalis and Arvicola terrestris*) | High infestation : 20 g to 30 g of product / bait station separated by 3 meters  Low infestation: 20 g to 30 g of product / bait station separated by 5 meters | Around buildings | Individual sachets  In secured bait boxes or others covered bait stations |

# **General information about the product application – initial PAR 2012**

An application for authorisation was made to the Pesticide Registration and Control Division of the Department of Agriculture Fisheries and Food by Belgagri S.A. for the biocidal product Control on 30th June 2011 in accordance with the provisions set out by Commission Directive 2008/81/EC.

This Product Assessment Report is for:

|  |  |
| --- | --- |
| **Trade name:** | Control |
| **Authorisation No.:** | IE/BPA 70173 (Professional and Trained Professional) IE/BPA 70174 (Non-professional) |

## **Applicant/Authorization Holder**

|  |  |
| --- | --- |
| **Company Name:** | Belgagri |
| **Address:** | Rue des Tuiliers 1  B 4480 ENGIS BELGIUM |
| **Tel:** | +32 85 519 519 |
| **E-mail:** | [belgagri@belgagri.com](mailto:belgagri@belgagri.com) |

## Representative of the Applicant/Authorisation Holder (where applicable)

|  |  |
| --- | --- |
| **Company Name:** | Ambrosi Scientific Consulting |
| **Address:** | Les Chevrieres  208 Chemin du Casson F-71570 Chaintre FRANCE |
| **Tel:** | +33 (0)3 85 35 67 14 |

## Marketing/Distributing Company (where applicable)

|  |  |
| --- | --- |
| **Company Name:** | Belgagri |
| **Address:** | Rue des Tuiliers 1  B 4480 ENGIS BELGIUM |
| **Tel:** | +32 81 83 04 83 |
| **E-mail:** | [belgagri@belgagri.com](mailto:belgagri@belgagri.com) |

## General Information on the Biocidal Product

|  |  |
| --- | --- |
| **Trade name:** | Control |
| **Manufacturer’s development code number(s):** | N/A |
| **Active substance content (% w/w):** | 0.005% w/w bromadiolone |
| **Main group:** | MG3 – Pest control |

|  |  |
| --- | --- |
| **Product type:** | PT14 - Rodenticides |
| **Product Specification:** | See Confidential Annex |
| **Site of product formulation:** | See Confidential Annex |
| **Formulation type:** | Ready-to-use (RB) Grain bait (AB) |
| **Ready to use product (yes/no):** | Yes (Only RTU products to be authorised) |
| **Chemical/micro-organism:** | Chemical substance |
| **Contain or consist of GMOs[[1]](#footnote-1) (yes/no):** | N/A |
| **Is the product already notified /authorised (yes/no);**  **If yes:**  **product name:** | No |
| **Is the biocidal product equivalent to the product assessed for the purpose of Annex I inclusion to 98/8/EC (yes/no):** | No. |

|  |  |
| --- | --- |
| **Manufacturer of Formulated Product:** | Belgagri |
| **Address:** | Rue des Tuiliers 1 B 4480 ENGIS BELGIUM |
| **Tel:** | +32 81 83 04 83 |
| **E-mail:** | [belgagri@belgagri.com](mailto:belgagri@belgagri.com) |
| **Contact:** | Antoine Trigaux |

## Information on active substance(s)[[2]](#footnote-2)

|  |  |
| --- | --- |
| **Active substance chemical name:** | Bromadiolone |
| **IUPAC name:** | 3-[3-(4’-bromobiphenyl-4-yl)-3-hydroxy-1-phenylpropyl]-4- hydroxycoumarin |
| **CAS No:** | 28772-56-7 |
| **EC No:** | 249-205-9 |
| **Purity (minimum, g/kg or g/l):** | >980g/kg |
| **Molecular formula:** | C30H23BrO4 |
| **Structural formula:** | O  O  H  O  Br  O  H |
| **Manufacturing site:** | See Confidential Annex |
| **Specification of pure active substance:** | See Confidential Annex |
| **Is a new active substance data package (source) supplied (yes/no):** | No |

5

|  |  |
| --- | --- |
| **If yes, Is the active substance equivalent to the active substance listed in Annex I to 98/8/EC (yes/no):** | N/A |
| **If no, does the applicant have a LoA to the active substance data packaged used to support Annex I inclusion (yes/no):** | Yes  (Pelgar International Ltd.) |

|  |  |
| --- | --- |
| **Manufacturer of active substance(s):** | Pelgar International Ltd. |
| **Address:** | Unit 13  Newman Lane  Alton  Hants. GU34  2QR UK |
| **Tel:** | +44 1420 80744 |
| **E-mail:** | [info@pelgar.co.uk](mailto:info@pelgar.co.uk) |

**Renewal 2017**

**COMPARATIVE ASSESSMENT**

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

A comparative assessment has been carried out at the European level. According to Article 1 of Commission Implementing Decision (EU) 2017/1532 of 7 September 2017 addressing questions regarding the comparative assessment of anticoagulant rodenticides in accordance with Article 23(5) of Regulation (EU) No 528/2012 of the European Parliament and of the Council. In the absence of anticoagulant rodenticides, the use of rodenticides containing other active substances would lead to an inadequate chemical diversity to minimize the occurrence of resistance in the target harmful organisms.

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

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

|  |  |
| --- | --- |
| **Main Group:** | MG02 (Pest control) |
| **Product-type:** | PT14 (Rodenticide) |
| **Intended use:** | Bromadiolone grain bait to control rodents indoors and outdoors for the protection of public health. |
| **Target organisms:** | (I.1) Rodents  (I.1.1) Murids  (I.1.1.1) Brown rats (*Rattus Norvegicus*)  (I.1.1.3) House mouse (*Mus musculus*)  (I.1.1.4) Field mouse (Other *Muride*) |
| **Development stage:** | (II.1) Juveniles  (II.2) Adults |
| **Function:** | Rodenticide |
| **Mode of action:** | Anticoagulant  III.2 long-term action  III.2.1 anticoagulant  III.2.1.1 ingestion toxin  III.2.1.1.1 ingestion by eating |
| **Application aim:** | Organisms or objects to be protected:  VII.1 Stored products  VII.2 Health protection  VII.3 Materials protection (historical buildings, technical objects) |
| **Category of users:** | V.1Non-professional (general public/amateur)  V.2 Professionals  V.3Trained professionals |
| **Area of use (indoors/outdoors):** | IV.1 Indoors (warehouses, houses, outbuildings)  IV.2 Outdoors (in and around buildings, waste dumps, open areas). Waste dumps and open area use is restricted to Professionals only. |
| **Directions for use including minimum and maximum application rates, typical size of application area:** | IE/BPA 70173, IE/BPA 70174  Indoors and outdoors (in and around buildings and open areas) Rats (Adult and Juvenile):  Secure 50-100g of bait in covered, tamper resistant baiting stations spaced 10m apart (5m apart in areas of high infestation) in areas where rats are active. Regularly check bait consumption and replace consumed or spoilt bait until consumption has stopped.  Repeat treatment in situations where there is evidence of new infestation (e.g. fresh tracks or droppings).  Mice (Adult and Juvenile):  Secure 25g of bait, in covered, tamper resistant baiting stations spaced 5m apart (2m apart in high infestation areas) in areas where mice are active. Regularly check bait consumption and replace consumed or spoilt bait until consumption has stopped. Repeat treatment in situations where there is evidence of new infestation (e.g. fresh tracks or droppings). |
| **Application method:** | A grain bait contained and covered in secured bait stations. |
| **Interval between applications:** | Inspect baits frequently (particularly during the first 10 to 15 days) and regularly check bait consumption and, when required, replace consumed or spoilt bait until consumption has stopped.  Repeat treatment in case of new infestation, new tracks or fresh droppings. |
| **Typical treatment time:** | 6 weeks for rats and mice |
| **Potential for release into the environment (yes/no):** | Yes. The bodies of the dead rodents must be quickly removed, buried or incinerated to avoid a secondary intoxication for predators of the rodents. |
| **Potential for contamination of food/feedingstuff (yes/no):** | No |

## Documentation

### Data submitted in relation to product application

A full new product dossier was submitted by Belgagri S.A. in support of the product Control containing bromadiolone.

Please see the attached reference list in Annex IV.

* **Major change and renewal applications 2017**

New data have been provided to support the major change.

### Access to documentation

Lodi S.A., Belgagri S.A. and BIO 6 S.A. have letters of access to data held by PelGar International Ltd which was used to support the Annex I listing of the active substance bromadiolone in Directive 98/8/EC. Lodi S.A., Belgagri S.A. and BIO 6 S.A. do not have access to the Annex III product data package held by PelGar International Ltd.

Lodi S.A. has a letter of access to product data held by Belgagri S.A. relating to bromadiolone formulated as grain baits.

Lodi S.A. has a letter of access to product data held by BIO 6 S.A. relating to bromadiolone formulated as grain baits.

Please Note: BIO 6 S.A. is a joint venture between Lodi S.A. and Belgagri S.A.

* **Major change and renewal application 2017**

Additional LOA has been submitted.

# Classification, labelling and packaging

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

## Harmonised classification of the active substance

Bromadiolone is not currently classified in Annex I of Council Directive 67/548/EEC or according to Annex VI of Regulation (EC) no 1907/2006 (REACH). The following classification and labelling is proposed on the basis of available data resulting from the review programme for bromadiolone and is provided in the table below according to Directive 67/548/EEC/Regulation (EC) 1272/2008. Additionally, the extrapolation of these proposals using the BG RCI converter tool (<http://www.gischem.de/ghs/konverter)> is also provided in the table below in accordance with Regulation (EC) 1272/2008.

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

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Symbol(s):** |  |  | **Pictogram(s):** |  |
| **Indication(s) of danger:** | T+ Very Toxic N Dangerous for | the Environment | **Signal word(s):** | Danger |
| **Risk phrases:** | R26/27/28: Very toxic by inhalation, in contact with skin and if swallowed.  R48/23/24/25: Toxic: Danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed.  R61: May cause harm to the unborn child.  R50/53: Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment. | | **Hazard statements:** | H300: Fatal if swallowed.  H310: Fatal in contact with skin. H330: Fatal if inhaled.  H360D: Suspected of damaging the unborn child.  H372: Causes damage to organs through prolonged or repeated exposure through inhalation. H400: Very toxic to aquatic life H410: Very toxic to aquatic life with long lasting effects. |
| **Safety phrases:** | S45: In case of accident or if you feel unwell, seek medical advice immediately. Show label where possible.  S53: Avoid exposure – obtain special instructions before use.   1. This material and its container must be disposed of as hazardous waste. 2. Avoid release to the environment. Refer to special instructions/safety data sheet. | | **Precautionary statements:** | P201: Obtain special instructions before use. P273: Avoid release to the environment. P308 + P313: IF exposed or concerned: Get medical advice/attention.  P314: Get medical advice/attention if you feel unwell.  P501: Dispose of contents/container to hazardous waste facilities in accordance with national regulations. |

Specific concentration limits for bromadiolone are proved below in accordance with Directive 67/548/EEC:

|  |  |  |
| --- | --- | --- |
| **Specific** | C≥0.5% | T+;R61-26/27/28 - T; R48/23/24/25 |
| **concentration** | 0.25%≤C<0.5% | T+; R26/27/28 – T; R48/23/24/25 |
| **limits:** | 0.025%≤C<0.25% | T; R23/24/25 – T; R48/23/24/25 |
|  | 0.0025%≤C<0.025% | Xn; R20/21/22 – R48/20/21/22 |

Additionally, bromadiolone is thermally stable below 200°C, its melting point. It is not classified as highly flammable and does not undergo self ignition below its melting point. It is not considered to be explosive or to have oxidising properties. There is no record that it has reacted with any storage container during many years of industrial production. It is concluded therefore, that there are no hazards associated with its physico-chemical properties under normal conditions of use.

* **Major change and renewal applications - 2017**

The harmonised classification of the active substance according to the ATP 9 of the CLP regulation is as follows:

|  |  |
| --- | --- |
| **Classification - Regulation (EC) 1272/2008** |  |
| Hazard category | Acute Tox. 1  STOT RE 1  Repr. 1B  Aquatic Acute 1  Aquatic Chronic 1 |
| Hazard statement | H300  H310  H330  H372 (blood)  H360D  H400  H410 |
| Specific concentration limits and M-factor | STOT RE 2; H373: 0,0005 % ≤ C < 0,005 %  STOT RE 1; H372: C ≥ 0,005 % Repr. 1B; H360D: C ≥ 0,003 %  M-factor 1 |

## Harmonised classification and labelling of the biocidal product

The current classification and labelling, based on the biocidal product evaluation for Control Block, is provided in the tables below according to Directive 99/45/EC and Regulation (EC) 1272/2008, Annex VI, Part 3.

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

|  |  |  |
| --- | --- | --- |
| **Symbol(s):** | N/A | N/A |
| **Indication(s) of danger:** | N/A | N/A |
| **Risk phrases:** | N/A | |
| **Safety phrases:** | S1+S2: Keep locked up and out of reach of children  S13: Keep away from food, drink and animal feeding stuffs.  S20 + S21: When using do not eat, drink or smoke.  S35: This material and its container must be disposed of in a safe way.  S46: If swallowed, seek medical advice immediately and show this container or label.  S49: Keep only in the original container.  S61: Avoid release to the environment. Refer to special instructions/safety data sheet. | |

* **Major change and renewal applications - 2017**

Classification and Labelling of the biocidal product CONTROL 25 according to the CLP Regulation (EC) 1272/2008:

|  |  |
| --- | --- |
| **Pictogram(s):** |  |
| **Signal word(s):** | Warning |
| **Hazard category** | STOT RE 2 |
| **Hazard statements:** | H373 (blood) |
| **Precautionary statements** | P260 Do not breathe dust  P314 Get Medical advice/attention if you feel unwell.  P501: Dispose of contents/container in accordance with national regulations. |

**Physical-chemical properties:**

Not explosive, oxidising or highly flammable and therefore does not classify from a physical­chemical point of view.

**Toxicology:**

There is no toxicology classification for the product under the Directive 99/45.

There is no toxicology classification for the product under the CLP Regulation 1272/2008.

* **Major change and renewal applications - 2017**

Under the CLP regulation, a classification STOT RE 2 – H373 (blood) is required.

**Environment:**

There is no environmental classification for the product under the Directive 99/45.

There is no environmental classification for the product under the CLP Regulation 1272/2008.

**Other:**

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

**Additional Labelling Requirements:**

|  |  |
| --- | --- |
| Addition safety Information: | To avoid risks to human health and the environment, comply with the instructions for use. |
|  | Harmful to wildlife. |
|  | Use bait containers clearly marked “poison” at all surface baiting points. |
|  | Remove all remains of bait, dead rodents during and after treatment and dispose of safely. |
|  | Apply only in positions inaccessible to children and pets. |
| Special labelling provisions for | Use Biocides Safely and Sustainably. |
| Ireland: | (IE/BPA 70173) Not For Amateur Sale. |
|  | It is illegal to use this product for uses or in a manner other than that prescribed on this label. |
| If a separate leaflet is attached to or supplied with the product, add the following information to the front label: | Read attached instructions before use. |

**2.3. Packaging**

**Packaging described in the PAR of IE for the first authorisation of the product CONTROL**

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

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

**Amateur product packaging:**

On the basis of the packaging details presented, it is considered appropriate to limit aspects of the packaging for amateur users as a risk mitigation measure. Packaging restrictions are to be limited to pre-baited bait stations and refill packs with a maximum pack-size of 500g.

Additionally, the block bait should be supplied to the amateur market in sachets/wrapped in order to reduce exposure risks to amateur operators during application to bait stations

**Amateur product packaging: Cardboard box**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Container description:** | Cardboard box | | | |
| **Pack size(s):** | 250g | 400g | 300g | 500g (can) |
| **Baits per pack:** | 10 x 25g 5 x 50g | 8 x 50g 16 x 25g 4 x 100g | 6 x 50g and 2 bait stations in soft PVC. | Loose bait or 5 x 100g |
| **Pack**  **dimensions (LxWxH):** | 85 x 135x 90 | 85x135x180 | 85 x 135 x 180 | 102 x 115 |
| **Packaging materials:** | Cardboard box or can (500g only). 24 units contained in an outer cardboard box. | | | |
| **Ready-to-use (yes/no)** | Yes | | | |
| **Shelf-life:** | 2 years. | | | |
| **Conditions of storage:** | Store in dry, cool area. Store in tightly closed packaging. Keep in original containers. Store away from damp or wet conditions. Keep away from children. | | | |

**Professional product packaging: Cardboard box**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Container description:** | Cardboard box | | | |
| **Pack size(s):** | 1kg | 600g | 1kg (can) | 1.2kg (can) |
| **Baits per pack:** | 10 x 100g 20 x 50g 40 x 25g | 12 x 50g 24 x 25g 6 x 100g | Loose bait. | Loose bait |
| **Pack**  **dimensions (LxWxH):** | 85 x 135x 180 | 85x135x180 | 240 x 55 | 240 x 55 |
| **Packaging materials:** | Cardboard box or can. 24 boxes contained in an outer cardboard box. | | | |
| **Ready-to-use (yes/no)** | Yes | | | |
| **Shelf-life:** | 2 years. | | | |
| **Conditions of storage:** | Store in dry, cool area. Store in tightly closed packaging. Keep in original containers. Store away from damp or wet conditions. Keep away from children. | | | |

**Professional product packaging: Bucket**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Container description:** | Plastic Bucket | | | | | | | |
| **Pack size(s):** | 800g (pot) | 2kg | 2.5kg | 3kg | 4kg | 5kg | 6kg | 10kg |
| **Baits per pack:** | Loose bait | Loose bait or 20 x 100g | 50x50g or loose bait | 30x100g or loose bait | 40x100g or loose bait | 50x100g or loose bait | 60x100g or loose bait | Loose bait |
| **Pack**  **Dimensions**  **(LxWxH):** | 116x116 x206 | 244 x 173 | 244 x  173 | 244 x  173 | 207 x 300x 213 | 300x275 | 288 x  230 | 288 x 330 |
| **Packaging materials:** | PP. Outer cardboard box containing 4 buckets or 24 x 800g pots. | | | | | | | |
| **Ready-to-use (yes/no)** | Yes | | | | | | | |
| **Shelf-life:** | 2 years | | | | | | | |
| **Conditions of storage:** | Store in dry, cool area. Store in tightly closed packaging. Keep in original containers. Store away from damp or wet conditions. Keep away from children. | | | | | | | |

**Professional product packaging: Double layer Kraft paper bag**

|  |  |  |
| --- | --- | --- |
| **Container description:** | Paper Bag | |
| **Pack size(s):** | 25kg | 20kg |
| **Baits per pack:** | Lose bait | Lose bait |
| **Pack dimensions (LxWxH):** | 445 x 750 | 445 x 750 |
| **Packaging materials:** | Double layer Kraft paper bag and an internal plastic layer (PE). | |
| **Ready-to-use (yes/no)** | Yes | |
| **Shelf-life:** | 2 years. | |
| **Conditions of storage:** | Store in dry, cool area. Store in tightly closed packaging. Keep in original containers. Store away from damp or wet conditions. Keep away from children. | |

**Packaging details:**

Pack size: IE/BPA 70174 – **Maximum Amateur refill pack size of**

**500g**

Pre-baited stations (PP/PE): 1 x 25g (mice) and 100g: 1 x100g, 2 x 50g or 4 x 25g (rats). (Prebaited or refillable).

Cardboard box case: 300g, 400g and 500g (can), (the bait must be supplied in PP wrapped inner packs or units, each containing enough bait for one point)

Bait sizes: 25g , 50g and 100g.

IE/BPA 70173: Professional packs.

Pre-baited stations (PP/PE): 1 x 25g (mice) and 100g: 1 x100g, 2 x 50g or 4 x 25g (rats). (Prebaited or refillable).

Cardboard box: 600g and 1kg

Bucket (PP) and cardboard box: 1kg, 2kg, 2.5kg, 5kg, 10kg, 12kg, 15kg, 20kg

Double Layer Kraft Bag: with internal PE plastic layer Bait sizes: 25, 50g, 100g

Container materials[[3]](#footnote-3): Cardboard box container – cardboard

Bucket container – PP

Pre-baited bait station –PP/PE Bait sachet/wrapping: PP

Safety features: Covered bait stations (tamper resistant)

Wrapped bait (sachets)

**Packaging accepted for the first authorisation of the product CONTROL 25 in France**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Type of packaging** | **Size/volume of the packaging** | **Material of the packaging** | **Type and material of closure(s)** | **Intended user (e.g. professional, non-professional)** | **Compatibility of the product with the proposed packaging materials (Yes/No)** |
| Bag | Min 5kg | Polyethylene | / | Professional | Y |
| Box (loose) | Min 5kg | Cardboard box with inner liner | / | Professional | Y |
| Paper | Min 5kg | Paper bag with inner layer in Polyethylene | / | Professional | Y |
| Bucket | Min 5kg | Polypropylene | / | Professional | Y |
| Sachets | 1.5kg | Polpypropylene | / | Non professional | Y |

* **Major change and renewal applications - 2017**

**Packaging claimed for the major change and accepted for the renewal of the product CONTROL 25**

For professionnals and non professionals, the baits can be packed in PE/PP sachets of 10-25-50-100g, or in loose. Nevertheless, for non professionnles, baits cannot be supplied in loose.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Type of packaging** | **Size/volume of the packaging** | **Material of the packaging** | **Type and material of closure(s)** | **Intended user (e.g. professional, non-professional)** | **Compatibility of the product with the proposed packaging materials (Yes/No)** |
| Sachets | 10-25-50-100g | PE or PP sachets then packed in PE or PP bucket (1-25kg), cardboard box (1-25kg), paper bag with PE lining (1-25kg) | / | Professional | Y |
| Bucket (loose) | 1-25kg | PP or PE | / | Professional | Y |
| Bag (loose) | 1-25kg | Paper bag with PE lining | / | Professional | Y |
| Box (loose) | 1-25kg | Carboard box | / | Professional | Y |
| Sachets | 10-25-50-100g | PE or PP sachets then packed in PP or PE bucket (up to 500g), cardboard box (up to 500g), paper bag with PE lining (up to 500g) | / | Non-professional | Y |
| Bucket (loose) | Up to 500g | PP or PE | / | Non-professional | Y |
| Bag (loose) | Up to 500g | Paper bag with PE lining | / | Non-professional | Y |
| Box (loose) | Up to 500g | Carboard box | / | Non-professional | Y |

# Summary of the product assessment

## Physico/chemical properties and analytical methods

Active substance (taken from the CAR):

Bromadiolone does not exhibit hazardous physical-chemical properties. Bromadiolone is a white odourless powder. It has low vapour pressure; Henry’s law constant (8.99 x 10-7 Pa.m3.mol-1 or 4.25 x 10-4 Pa.m3.mol-1) was calculated based on an experimentally derived (extrapolated) value of 2.13 x 10- 8 Pa at 25 °C or on a published vapour pressure of 2 x 10-6 Pa at 20 °C. The solubility of bromadiolone in water is pH dependant with the highest solubility of 0.18-1.2 g/l at pH 9-10 and 20°C (~0.1 mg/l at pH 4-5 and 2.48-18.4 mg/l at pH 7 and 20°C). Correspondingly, the log Pow ranges between 2.5-3.2 at pH 9-10 to >5 at pH 4-5 (3.8-4.1 at pH 7). The pH dependency is thought to be due to the dissociation of the hydroxyl-group in the coumarin moiety of bromadiolone with predicted relevant pKa’s of 4.5 and 9.0 for the enolic and ketalic forms respectively (i.e. technically not feasible to experimentally determine the pKa). The solubility in organic solvents tested ranged from 3 mg/l in n-heptane to 15 g/l in methanol at 20°C. The melting point was determined as a broad range of 172.4-201.7°C (98.8%) or as 198.3-199.8°C (~100%). Given that bromadiolone is a mixture of two diasteromers, which can have different physical and chemical properties, the broad range is not considered atypical. Bromadiolone decomposes before boiling. Bromadiolone is not highly flammable, explosive or oxidizing.

Biocidal product:

The biocidal product Control is not explosive, oxidising or highly flammable and does not classify from a physical chemical point of view. The test item is stable after accelerated storage for two weeks at 54oC. The test item is stable for two years at ambient temperatures. The test item is a ready-to-use grain bait and is not intended to be added or mixed with any other product.

* **Major change and renewal applications - 2017**

A provisional shelf life of 2 years can be granted based on the results of the accelerated storage study with the formulation at 25ppm. However, a shelf life study for CONTROL 25 is required in post authorisation with a time limit of 2 years.

### Identity related issues

The source of active substance used in the biocidal product Control is not the same source of active substance that is listed in Annex I of 98/8/EC. However, the two sources have been deemed equivalent.

**Composition of the biocidal product Control**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Component** | **% w/w** | **g/kg** | **Chemical name** | **CAS no** | **Function** |
| Concentrate containing:  - Bromadiolone 2.5%  + other components which are identified in the confidential section. | 0.2 (0.005% technical active substance) | 2.0  (0.05 g/kg technical active substance) | 3-[3-(4’-bromobiphenyl- 4-yl)-3-hydroxy-1- phenylpropyl]-4- hydroxycoumarin | 28772-56-7 | Active ingredient |
| Co-formulants | See Confidential Data and Information (Annex I) | | | | |

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

* **Major change and renewal applications - 2017**

Please see details of the change of composition in the confidential annex.

The modifications are discussed in confidential annex of the PAR with a comparison between the old (50ppm) and the new composition (25 ppm).

### Physico-chemical properties

The source of active substance used in the biocidal product Control is not the same source of active substance that is listed in Annex I of 98/8/EC. Poland did an equivalence check on the PelGar International Ltd. source of Bromadiolone compared with the Activa source of Bromadiolone. Poland found the two sources to be equivalent. The RefMS accepts Poland’s assessment. Pelgar International Ltd. provided a letter of access to Belgagri S.A for their source of active substance.

### Physical, Chemical and Technical Properties of the Biocidal Product Summary of the Physical and Chemical Properties of the Biocidal Product Control - 2012

**Assessement performed for the first authorisation**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Section** | **Study** | **Method** | **Results** | **Comment** | **Reference** |
| 1.1 | Appearance | OPPTS 830.6304 OPPTS 830.6303 OPPTS 830.6302 | Aspect: green oats grain Odour: cereal  Colour: green (10GY 5/6) | Carried out to GLP. Carried out at 20oC. The study is acceptable. | “Determination of physical properties of Bromadiolone grain bait”. Study no. LODI.01/2011. 2011-02- 23. C. Magnier. |
| 1.2.1 | Explosive properties | Examination of the components. | “The test substance is a mixture of components. It’s composed of hulled grain of oat, green colouring agent, Bromadiolone 2,5% with bitter agent, sorbic acid, colza oil and propylene glycol. Examination of the components in the test substance establishes beyond reasonable doubt that they do not contain any chemically instable of highly energetic groups that might lead to an explosion. Hulled grain of oat, green colouring agent, sorbic acid, colza oil are food products without explosive properties. Bromadiolone contains alcohol, ester and halocarbon groups. These groups are no plosophores (bond grouping known to give explosive properties). The bitter agent contains carboxylic acid, amid and quaternary ammonium groups. These groups are not considered as plosophores. It is furthermore not to be expected that an interaction between the different components occurs”  Not explosive. | The RefMS accepts the Notifiers justification. The grain bait is not explosive. | “Explosive properties of Bromadiolone grain bait”. Study no. LODI.37/2011. 2011-06-23. S. Richerioux. |
| 1.2.2 | Oxidising properties | Examination of the components. | “The test substance is a mixture of components. Examination of components establishes beyond reasonable doubt that the test item is incapable of showing a positive result in the test described in the EC. A17 guideline. The components do not contain any group that might act as an oxidising agent. The oxygen atoms that are present in Bromadiolone, acid sorbic, colza oil and propylene glycol are bonded to carbon as an alcohol or an acid group. Hence, these components do not have oxidising properties. Green colouring have an unknown structure | The RefMS accepts the Notifiers justification. The grain bait is not oxidising. | “Oxidising properties of Bromadiolone grain bait”. Study no. LODI.02/2011. 2011-05-05. C. Magnier. |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Section** | **Study** | **Method** | **Results** | **Comment** | **Reference** |
|  |  |  | but it is expected that these component do not contain oxidising properties. It is furthermore not to be expected that an interaction between the different components occurs resulting in an oxidising chemical.”  Not oxidising. |  |  |
| 1.3.1 | Flash point |  | No flash point data is required for solids. See 1.3.2, Flammability below. |  |  |
| 1.3.2 | Flammability | EEC method A 10. | “The flame of the gas burner did ignite the test substance pile. The test substance burned with a yellow flame and turned into a charred residue. A light gray smoke was observed. After removal of the ignition source, the flame goes out, no propagation of combustion was observed.”  Not highly flammable. | Carried out to GLP. The preliminary test was performed. There was no propagation of combustion along 200 mm length of the pile within 4 minutes. Therefore performance of the main test was not required. The grain bait is considered “not highly flammable”. The study is acceptable. | “Flammability of Bromadiolone grain bait”. Study no. LODI.03/2011. 2011-03-30. C. Magnier. |
| 1.3.3 | Auto-  flammability |  |  | See section 1.3.2 above. |  |
| 1.4.1 | Free acidity/ Alkalinity | CIPAC MT 191 & 75.3 | Not required as the pH(1%) is 6.91 after 10 minutes at 20oC.  [If the pH is between 4 and 10 then the determination of acidity or alkalinity is not required.] | Carried out to GLP. The acidity or alkalinity test was not required and thus was not performed. The RefMS agrees that the acidity/alkalinity test is not required. The study is acceptable. | “Acidity-Alkalinity of Bromadiolone grain bait”. Study no. LODI.05/2011. 2011-03-01. C. Magnier. |
| 1.4.2 | pH (1 %) | CIPAC MT 75.3 | pH(1%) = 6.91 after 10 minutes at 20oC. | See 1.4.1 above. | See 1.4.1 above. |
| 1.5.1 | Viscosity |  |  | Not applicable as the product is a solid (grain). |  |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Section** | **Study** | **Method** | **Results** | | | | | **Comment** | **Reference** |
| 1.5.2 | Surface tension |  |  | | | | | Not applicable as the product is a solid (grain). |  |
| 1.6 | Relative density | OECD 109 NF T20-053 | 1.377 | | | | | Carried out to GLP. Carried out with a pycnometer at 20oC ± 2oC. The study is acceptable. | “Relative density of Bromadiolone grain bait”. Study no. LODI.01/2011. 2011-03-18. C. Magnier. |
| 1.7.1 | Storage stability  (accelerated storage – 14 days at 54oC) | CIPAC MT 46  GIFAP monograph no17. | **Aspect:**  T0 = Green oats T14 = Green oats  **Odour =** T0 = None T14 = None  **Content of active substance:** | | | | Carried out to GLP. The test item is stable for 14 days at 54oC, which indicates that the test item will be stable when stored for 2 years at ambient temperatures. The study is acceptable. | | “Chemical stability after accelerated storage of Bromadiolone grain baits 0.005%”. Study no. LODI.02/2010. 2010-03- 04. C. Magnier. |
|  | **Conc. (mg/kg)** | **Deviation from declared content** | **Deviation from T0** |
| T0 | 50.38 | + 0.76% |  |
| T14 | 51.10 | + 2.2% | +1.43% |
| **Note:** The declared value of the active substance was 50 mg/kg. | | | |
| 1.7.2 | Shelf life (storage ambient temperatures, 6 months, one year and two years)  years) | GIFAP monograph no17. | **Aspect:**  T0 = Green oat  T6 months = Green oat  T1 yr = Green oat  T2 yr = Green oat  **Odour:**  T0 = without odour  T6 months = without odour  T1 yr = without odour  T2 yr = without odour  **Content of active substance:**   |  |  |  |  | | --- | --- | --- | --- | |  | **Conc. (mg/kg)** | **Deviation from declared content** | **Deviation from**  **T0** | | T0 | 50.4 | +0.8% |  | | T6 m | 39.0 | -22.6% | -22.62% | | T1 yr | 41.9 | -16.2% | -16.87% | | T2 yr | 48.6 | -2.8% | -3.57% |   **Note:** The declared value of the active substance was 50 mg/kg.  **Variation in active substance content:**  The company has stated that “The difference between the results after 6 months,1 year and 2 years of storage at ambient temperature can be due to variations of analysis (HPLC analysis, extraction, manual injection,..). Moreover, the sample is not completely homogeneous (because it’s a solid sample), and the quantity of active substance can differ between two different analysis. Also the study made by Biolytics company shows that there are no degradation products in Bromadiolone grain bait (Control) after two years of storage at 20oC.” See section 3.1.4 below. | | | | Carried out to GLP.  The decrease in active substance content is quite high at the 6 month and 1 year time points but remains within the ± 25% criteria (FAO). At the 2-year time point the decrease in active substance content is <5%. The RefMS accepts the Applicant’s justification for the apparent decrease in active substance content at the 6 month and 1 year time-points.  Bromadiolone has been shown not to degrade after storage for 2 years at ambient temperature. Degradation products were only found when the test item was subjected to acid degradation (see section 3.1.4).  No significant change was observed concerning the aspect of the test item after 6 months, 1 year and 2 years storage.  The grain bait is considered stable after storage for 2 years at ambient temperatures.  The aged bait (2 weeks at 54oC) which simulates bait that has been stored for two years at ambient temperature was found to be 100% efficacious for both mice and rats. Its palatability was also deemed acceptable. Please see section 3.2 Efficacy of the Biocidal Product for full evaluation. | | “Chemical stability after storage at 20oC ± 2oC after 6 months, one year and two years of Bromadiolone grain baits 0.005%”. Study no. LODI.05/2010.A.  2012-03-22. Sandra Richerioux. |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Section** | **Study** | **Method** | **Results** | | | | | **Comment** | **Reference** |
| 1.7.3 | Packaging stability |  | **Physical properties observed for the grain bait in all packaging types:**  T0 = Green grain. T6months = Green grain T1year = Green grain  **PE bag with cardboard box:** | | | | | Carried out to GLP. Carried out at ambient temperatures (20 ± 2oC).  Deviation in the weights of the packaging and test item are all lower than 5% for all the packaging after 6 months and 1year at ambient temperature. No significant changes were observed in the aspect of the packaging and test item after 6 months and 1 year storage.  The packaging tested is acceptable. | “Packaging stability used for Bromadiolone Grain bait”. Study no.LODI.46/2011. Sandra Richerioux. |
|  | **Weight** | | | |
| **PE bag (g)** | **Cardboard box (g)** | **Test item (g)** | **Total (g)** |
| T0 | 3.555 | 23.504 | 230.85 | 257.91 |
| T6 | 3.579 | 23.464 | 227.70 | 254.76 |
| Deviation | +0.68% | -0.17 | -1.36% | -1.22% |
| T1year | 3.576 | 24.101 | 225.12 | 252.82 |
| Deviation | +0.59% | +2.54% | -2.48% | -1.97% |
| T0 = Transparent bag – cardboard box with grey and dry internal wall. T6months = Presence of dust grain on internal wall of the bag  T1year = Presence of dust grain on internal wall of the bag – dry cardboard box.  **PP bag with cardboard box:** | | | | |
|  | **Weight** | | | |
|  | **PP bag (g)** | **Cardboard box (g)** | **Test item (g)** | **Total (g)** |
| T0 | 7.691 | 23.098 | 226.58 | 257.37 |
| T6months | 7.725 | 23.024 | 222.61 | 253.39 |
| Deviation | +0.44% | -0.32% | -1.75% | -1.55% |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Section** | **Study** | **Method** | **Results** | | | | | | | | **Comment** | **Reference** |
|  |  |  | T1year | 7.723 | | 23.591 | | 221.18 | | 252.49 |  |  |
| Deviation | +0.42% | | +2.13% | | -2.38% | | -1.90% |
| T0 = Transparent bag – cardboard box with grey and dry internal wall. T6months = Presence of dust grain on internal wall of the bag  T1year = Presence of dust grain on internal wall of the bag – dry cardboard box.  **HDPE Bottle:** | | | | | | | |
|  | | **Weight** | | | | | |
|  | | **Bottle (g)** | | **Test item (g)** | | **Total (g)** | |
| T0 | | 58.182 | | 348.10 | | 406.28 | |
| T6months | | 58.439 | | 347.77 | | 406.24 | |
| Deviation | | +0.44% | | -0.09% | | -0.01% | |
| T1year | | 58.485 | | 347.54 | | 406.05 | |
| Deviation | | +0.52% | | -0.16% | | -0.06% | |
| T0 = Non-porous internal wall.  T6months = Presence of dust grain on internal wall of the bottle T1year = Presence of dust grain on internal wall of the bottle  **PP Bucket:** | | | | | | | |
|  | | **Weight** | | | | | |
|  | | **Bucket (g)** | | **Test item (g)** | | **Total (g)** | |
| T0 | | 44.087 | | 379.12 | | 423.207 | |
| T6months | | 44.351 | | 378.15 | | 422.50 | |
| Deviation | | +0.60% | | -0.26% | | -0.17% | |

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Section** | **Study** | **Method** | **Results** | | | | **Comment** | **Reference** |
|  |  |  | T1year | 44.368 | 377.17 | 421.54 |  |  |
| Deviation | +0.64% | -0.51% | -0.39% |
| T0 = Non-porous internal wall.  T6months = Presence of dust grain on internal wall of the bucket T1year = Presence of dust grain on internal wall of the bucket  **Woven PP bag with PE inner liner:** | | | |
|  | **Weight** | | |
|  | **Bag (g)** | **Test item (g)** | **Total (g)** |
| T0 | 5.601 | 128.70 | 134.30 |
| T6months | 5.821 | 124.55 | 130.37 |
| Deviation | +3.93% | -3.22% | -2.93% |
| T1year | 5.703 | 125.97 | 131.68 |
| Deviation | +1.82% | -2.12% | -1.95% |
| T0 = White woven bag  T6months = Presence of dust grain on internal wall of the bag T1year= Presence of dust grain on internal wall of the bag | | | |
| 1.8.1 | Wettability |  |  | | | | Not required. The product is a ready to use grain bait. |  |
| 1.8.2 | Persistent foaming |  |  | | | | Not required. The product is a ready to use grain bait. |  |
| 1.8.3.1 | Suspensibility |  |  | | | | Not required. The product is a ready to use grain bait. |  |
| 1.8.3.2 | Dispersibility |  |  | | | | Not required. The product is a ready to use grain bait. |  |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Section** | **Study** | **Method** | **Results** | **Comment** | **Reference** |
| 1.8.4 | Wet/dry sieving test |  |  | Not required. The product is a ready to use grain bait. This is only required for WPs, SCs, granules and tablets. |  |
| 1.8.5 | Particle size distribution |  |  | Not applicable. The product is a ready to use grain bait. This is only required for powders and granules. |  |
| 1.8.6 | Water content |  |  | Not required. The product is a ready to use grain bait. |  |
| 1.8.7 | Emulsion stability |  |  | Not required. The product is a ready to use grain bait. |  |
| 1.8.8 | Flowability, Pourability, Dustability |  |  | Not required. The product is a ready to use grain bait. |  |
| 1.9 | Physical compatibility |  |  | Not applicable. The product is a ready to use grain bait and is not intended to be mixed with any other product. |  |

**Conclusions:**

The biocidal product Control is not explosive, oxidising or highly flammable and does not classify from a physical/chemical point of view. The test item is stable after storage for two weeks at 54oC. The test item is stable for 2 years at ambient temperatures. The packaging material is stable after storage at ambient temperatures (20oC ± 2oC) for 1year with all deviations in packaging and sample weights being below 5%. There were no significant changes of characteristics of the test item or packaging observed after 1year of storage. The Bromadiolone grain bait is considered compatible with all the packaging tested. The test item is a ready-to-use grain bait and is not intended to be added or mixed with any other product.

**Data requirements:**

Information on the reactivity of the grain bait towards the container material for the 2 year time points has been requested and will be provided when complete *(the approximate date of submission is week 29, 2013).*

**The grain bait is compatible with the following packaging:**

PE bag with cardboard box, PP bag with cardboard box, HDPE Bottle, PP Bucket and Woven PP bag with PE inner liner.

**Proposed shelf life for the grain bait:**

The grain bait is stable after storage for 2 weeks at 54oC (+1.43%). There was an apparent decrease in active substance content at the 6 month (-22.62%) and 1 year (-16.87%) time points during the ambient storage stability test. However, at the 2-year time point the decrease in active substance content is -3.57%. The Applicant submitted a justification for the apparent decrease in active substance content at the two time-points which was accepted by the RefMS. A separate study showed that Bromadiolone did not degrade after storage for 2 years at ambient temperature. Degradation products were only found when the test item was subjected to acid degradation (see section 3.1.4). No significant change was observed concerning the aspect of the test item after 6 months, 1 year and 2 years storage at ambient temperatures. The aged bait (2 weeks at 54oC) which simulates bait that has been stored for two years at ambient temperature was found to be 100% efficacious for both mice and rats. Its palatability was also deemed acceptable.

Overall, since the grain bait remains 100% efficacious, palatable, and does not generate breakdown products of toxicological concern after storage and since the decrease in active substance content after 2-years storage at ambient temperatures is <5%, a two year shelf life is proposed.

**Shelf life:** 2-years.

* **Major change and renewal applications - 2017**

**eCA comment for the renewal:** physico chemical properties and safety properties are acceptable for the new formulation CONTROL 25. However, a new stability study was required for the renewal and is described below.

**New data have been provided to support the new formulation CONTROL 25:**

| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **FR evaluation** | **Reference** |
| --- | --- | --- | --- | --- | --- |
| Storage stability test – **accelerated storage** | CIPAC MT 46  GIFAP Monograph No. 17  Analytical method (see validation data below)  14 days at 54°C | Bromadiolone grain bait  Batch AB20160502 | Active substance content:   |  |  | | --- | --- | | T0 | T14d | | 27.2ppm | 26.7ppm |   Decrease of 1.8% | Only the active substance content has been measured. Taking into account the other differences of composition, technical properties are not necessary.  Moreover the packaging material has not been provided  Moreover the T0 value is not the sample before accelerated storage but a sample stored 14 days at 20°C.  The product is considered stable after storage 14 days at 54°C. | Picardat T. 2016  LODI.02/2016 |

|  |
| --- |
| **General conclusion on the physical, chemical and technical properties of the product CONTROL 25 for renewal of national authorisation applications** |

|  |
| --- |
| The product CONTROL 25 is a ready to use grain 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 green oat grains and with no specific odour. Storage stability study results are acceptable. The biocidal product (previous formulation) is stable 2 weeks at 54°C and 2 years at ambient temperature with a PE 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.  The new formulation is considered stable after 14 days at 54°C. **However a two year shelf life study with the new composition should be provided to confirm the stability of the product.**  eCA recommends to store away from light due to the sensitivity of the active substance to light.  It’s technical characteristics are acceptable for a ready to use grain bait formulation. |

### Analytical methods

**Assessment for the first authorisation**

Control was not assessed as part of the Annex I inclusion process therefore the Notifer has submitted the following method of analysis to cover the outstanding data gap.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Report:** | No information given. | | | |
| **Title:** | “Analytical validation for determination of Bromadiolone in grain bait” | | | |
| **Author(s):** | Sandra Richerioux | | | |
| **Date:** | 2011-06-24 | | | |
| **GLP: Yes/No** | No. Conducted according to LodiGroup SOPs. | | | |
| **Principle of the Method:** | The test item is quantified by liquid chromatograpy using a reverse phase column and a UV detector (310nm).  Extraction method:  Extraction solution: n-butyl acetate/methanol/acetic acid (90/8/2 %v/v). Preparation of the test item solutions:  The grain bait is ground with a mixer. A quantity of about 10g of the test item is weighed into a 250mL flask. A volume of 100mL of extraction solution is added. The solution is put on ultrasonic bath for 15 minutes and is shaken on magnetic stirrer for 30 minutes. The solution is decanted for minimum 4 hours and filtered on Buchner. 25mL of the extracted solution is transferred into 50mL volumetric flask. 10mL of internal standard solution (400mg/L) is added and the flask is made to volume with methanol. The diluted solution is filtered on 0.20µm PTFE filter. | | | |
| **Linearity:** | The calibration curve was provided and was linear. The operator prepared 5 solutions containing 80%, 90%, 100%, 110% and 120% of the concentration of test item in solution. Three injections were carried out at each concentration (2.0mg/L; 2.25mg/L; 2.50mg/L; 2.75mg/L; 3.0mg/L).  The correlation coefficient, r2 was 0.9996. | | | |
| **Precision/repeatability:** | Three solutions were prepared of a concentration C (~ 2.4825 mg/l) of the product. Three injections of each solution were carried out and the RSD was calculated.  Intermediary fidelity (mg/l): | | | |
|  | **1st Injection** | **2nd Injection** | **3rd Injection** |
| **Solution a** | 2.49 | 2.51 | 2.49 |
| **Solution b** | 2.56 | 2.55 | 2.57 |
| **Solution c** | 2.50 | 2.52 | 2.55 |
| % RSD = 1.165  Intralaboratory fidelity (mg/l): | | | |
|  | **1st Injection** | **2nd Injection** | **3rd Injection** |
| **Solution a** | 2.56 | 2.52 | 2.51 |
| **Solution b** | 2.56 | 2.55 | 2.57 |
| **Solution c** | 2.50 | 2.52 | 2.55 |
| % RSD = 0.943 | | | |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Accuracy:** | The operator spiked a placebo with 50, 100 and 150% of the theoretical concentration of test item. Three injections were carried out per solution. The mean recovery (MR) was calculated for each solution, see table below. | | | | |
|  | **50% doped placebo** | **100% doped placebo** | **150% doped placebo** | **Average of MR** |
| Recoveries | 98.19, 99.68,  99.52 | 99.59, 99.08,  99.24 | 99.32, 100.05,  98.96 | 99.29% |
| Mean recovery (MR) | 99.12% | 99.30% | 99.45% |
| The recoveries are in the range 90-110%. The accuracy is acceptable. | | | | |
| **Specificity** | The specificity was investigated by analysing a placebo in solution and the test item in solution stressed with acetic acid. The sample was stressed by adding 5ml of acetic acid. If a peak appears the resolution must be greater than 2.  The placebo grain in solution contained no peaks that could interfere with the Bromadiolone peak.  The stressed grain bait had Rs > 2 (the resolution was greater than 2). | | | | |
| **Interferences** | No interfering peak was observed in the chromatogram for the placebo grain in solution. | | | | |
| **Limit of quantification:** | The operator injected a solution containing 50 ppm of test item and calculated the S/N ratio. The operator divided by 10 then by 2 the concentration of the test item until obtaining a S/N ratio lower than 10.  LOQ = 0.1 mg/kg | | | | |
| **Limit of detection** | The operator injected a solution containing 10 ppm of test item and calculated the S/N ratio. The operator divided by 10 then by 2 the concentration of the test item until obtaining a S/N ratio lower than 3.  LOD = 0.005 mg/kg | | | | |

**Conclusion:**

The method of analysis is acceptable for the determination of Bromadiolone in the grain bait.

**Data requirements:** None.

A report investigating the possible breakdown products of Bromadiolone after 2 years of storage at ambient temperatures was submitted by the Applicant. The results are outlined below.

|  |  |
| --- | --- |
| **Report:** | Biolytics study no 12-TOX007 |
| **Title:** | “Analysis of Bromadiolone with the evidence of no degradation products in 2 years old bait” |
| **Author(s):** | Isabelle Fourel. |
| **Date:** | April 2012 |
| **GLP: Yes/No** | No. |
| **Background:** | The aim of the study was to show the evidence or non-evidence of degradation products of Bromadiolone in “fresh” bait and in 2 year old bait kept in controlled temperature conditions.  The “fresh” bait was then artificially deteriorated to demonstrate that there is no evidence of degradation products in the 2 year old matrix. |
| **Principle of the Method:** | The Bromadiolone grain bait was aged for 2 years at ambient temperatures (20oC with no light). The 2-year old bait and the “fresh” grain bait were then analysed by LC/MS Triple Quadripole.  The Bromadiolone bait were degraded through forced degradation by:   1. Heat degradation – two samples of each specimen (weighed dry baits) plus a sample of pure Bromadiolone powder are kept in a drying oven at 60oC ± 5oC away from light, for 5 days. 2. Acid degradation – two samples of the specimen (weighed dry baits) were mixed with 5ml chlorhydric acid 0.1N in methanol and kept in a drying oven for 2 hours at 60oC away from light. 5ml of NaOH 0.1N in methanol was added to neutralise prior to analysis.   Pure Bromadiolone was put through the heat and acid degradation procedure as well. |
| **Chromatograms:** | Chromatograms for the fresh bait (grain), two year old bait (grain), the acid stressed baits, the heat stressed baits, the heat stressed Bromadiolone, the non­stressed pure Bromadiolone and blanks were provided. |
| **Mass spectra:** | Analyses showed that no fragment ion was common between the Bromadiolone mass spectrum and the degradation products mass spectra. |
| **Results:** | The chromatograms of the non-deteriorated baits and the deteriorated baits were compared. Acid stress led to the production of degradation products.  Acid stress: |
| The degradation products which appeared after the acid stress of the grain bait were found at m/z 425.4 (RT 18.9/19.2/19.5/20.68/20.8 min), 447 (RT 20.2 min), 495 (RT 20.4 min), 427.5 (RT 22.4/22.8 min), 351.4 (RT 23.9 min), 395.3 (RT 24.5/24.7 min), 407.4 (RT 25 to 26 min) and 377.4 (RT 28.4 min).  Heat stress: |
| No degradation products were present in the baits after being left at 60oC during 5 days.  Pure Bromadiolone: |
| No degradation product was present in the Bromadiolone after being left at 60oC |

|  |  |
| --- | --- |
|  | for 5 days.  The degradation products observed appeared when baits where acid stressed but  were missing from fresh and two year old baits. No degradation product was present in the bait after being heat stressed. No degradation product was present in heat stressed Bromadiolone. |
| **Conclusion** | The aim of the study was to look for degradation products of Bromadiolone in two kinds of baits: fresh bait and bait that has been kept in controlled temperature conditions for two years. |
|  | In order to prove that Bromadiolone did not lead to degradation products during storage of baits, fresh bait was submitted to acid and heat forced degradation tests. |
|  | After LC-MS analysis, the mass spectra were compared and no fragment ions were common between Bromadiolone mass spectrum and the ones of the observed degradation products (acid stressed bait). |
|  | There is no similarity between Bromadiolone and the observed degradation products from the acidified baits. Bromadiolone is very stable in the bait during the storage. |

**Conclusion:**

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

**Data requirements:** None.

* **Major change and renewal applications - 2017**

**eCA comment:** a new method has been required since the active substance content has been decreased. The applicant has provided a new study which is described below:

**Report:** Picardat T. 2016, Validation of the analytical method for the determination of bromadiolone in bromadiolone grain bait 25ppm Report no LODI.01/2016.

Principle of the method:

The test item is quantified by LC method using UV detection (265nm) after solid-liquid extraction.

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

Validation data:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Specificity | To demonstrate the specificity of the method, two solutions are analysed and chromatograms have been provided for:   * Formulation blank * Stressed test item (with acetic acid)   No interference was found: no peak appears in the formulation blank.  There are two different peaks for bromadiolone. | | | |
| Linearity | Linearity was studied by carrying out five concentrations between 50% and 150% of the concentration in the test item. (= between 2.39mg/L and 7.16mg/L. Twice determinations have been made at each concentration.  Linearity has been determined for each peak of difenacoum  Calibration curves have been provided with a R2 higher than 0.99. | | | |
| Compound | Linearity % | | |
| Bromadiolone peak 1 | 2.39mg/L to 7.16mg/L  Y = 55.18785 X + 22.46961 R = 0.99769  n=5 | | |
| Bromadiolone peak 2 | 2.39mg/L to 7.16mg/L  Y = 13.17202 X + 5.24318 R = 0.99774  n=5 | | |
| Extraction efficiency | Due to the solid/liquid extraction, extraction yield has been determined:  Five samples of known concentration are prepared and analyzed twice. The extraction yield is determined for each sample and the mean extraction yield is calculated from these five solutions.  Result: Mean extraction yield 77.78% | | | |
| Precision | Repeatability was evaluated by analysing ten sample solutions. | | | |
| Compound | | Mean | Repeatability (RSD) |
| Difenacoum | | 0.00269% | RSD = 0.81% |
| Accuracy | Accuracy was determined by analysis 3 sample solutions containing 80%, 100% and 120% of the theoretical concentrations of 25ppm. Two injections of each preparation are made. The accuracy results are expressed as the recovery rate.   |  |  |  |  |  | | --- | --- | --- | --- | --- | | Fortification level | Recovery rate | Mean recovery rate | RSD (%) | n | | 80%: 0.00224% | No data provided | 95.09 | - | 2 | | 100%: 0.00261% | No data provided | 103.83 | - | 2 | | 120%: 0.00299 | No data provided | 100.33 |  | 2 | | | | |

|  |
| --- |
| **Conclusion on the methods for detection and identification of the product CONTROL 25** |
| The provided analytical method is fully validated for the determination of the active substance bromadiolone at 25ppm in the product.  For the analytical methods for determining relevant components and/or residues in different matrices, please refer to the product assessment report related to CONTROL 25 product authorisation under Regulation UE n° 528/2012. The applicant has a letter of access to Annex II data on the active substance bromadiolone. |

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

Not applicable.

## Efficacy of the Biocidal Product

Bromadiolone is intended to be used to control rodent pests, both indoors and outdoors, in and around buildings, open areas and waste sites (grain based products are not used in sewers). The target species are brown rat (*Rattus norvegicus*), house mouse (*Mus musculus*/*domesticus*) and other murids (other *Muridae*). Comprehensive laboratory and field data submitted for annex I inclusion and evaluated in the CAR confirmed that bromadiolone is an effective rodenticide for the control of mice and rats. In addition, new data using the grain formulation was provided in the form of laboratory and field studies to verify the proposed label claims.

CONTROL is a ready-to-use rodenticide grain bait containing 0.005% (w/w) bromadiolone. The efficacy of the product was assessed against the proposed label claims. The ready-to-use baits are available in sachets of 25g, 50g and 100g and in a variety of pack sizes. For professional users 100g sachets or loose grain provided in numerous pack sizes are proposed.

The applicant submitted additional effectiveness data in the form of six trial reports from trials conducted under a wide range of conditions (laboratory & field). These trials were conducted according to a variety of standards and protocols. Four trials were conducted under laboratory conditions (2 mice; 2 rats) whilst two field based trials assessed efficacy against mice & rats. The laboratory trials were all choice tests conducted to suitable standards. The studies demonstrated that CONTROL (fresh and aged bait) is palatable to and effective in controlling populations of house mice and brown rats according to the criteria given in the TNsG on product evaluation.

In the laboratory studies evaluated for annex I inclusion the mean acceptance levels observed for rats was 36.3% with a mean time to death of 4.1 and 4.6 days using fresh and aged baits respectively. For mice, the acceptance level was 55.8% with a mean time to death of 4.5 days and 5.2 days for the two trials respectively (100% mortality) using both fresh and aged baits. The data confirmed that even bait that had been stored under ambient conditions for two years remained attractive and effective against rats and mice. In the trials efficacy was total in less than 14 days.

The first laboratory trial assessing the palatability and control of mice used freshly manufactured bait which observed 58.8% acceptance of the grain bait. A mean time of 4.5 days until mortality was observed with 100% mortality achieved. The next study evaluated the palatability and effectiveness of artificially aged bait (54°C for 2 weeks). 52.7% acceptance was observed and the mean time to death was 5.2 days. The third study assessed the effectiveness of fresh bait on Norway rats, with a 37.5% acceptance level recorded and a mean time to death of 4.1 days (100% mortality achieved). Again, Norway rats were used in the fourth study, this time with aged bait. An acceptance level of 35.1% was observed and 100% mortality was achieved in a mean of just 4.6 days. Across the four laboratory studies provided the average bait intake was ≥46% (range ~35.1%-58.8%) of the total food consumption in all of the studies and effectiveness exceeded 100% mortality in less than 14 days in the choice feeding tests.

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

Field tests were conducted on mice and rats and the experimental data on the effectiveness of the product against target organisms are summarized in the table below.

**Table 3.2.1a: Effectiveness data - CONTROL**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Test product** | **Test organisms** | **Test system / Concentrations applied / exposure time** | **Test conditions** | **Test results: effects, mode of action, resistance** | **Reference** |
| CONTROL, freshly | CD-1 mice (*Mus musculus*) | Laboratory test.  Choice feeding test: fresh baits. | The animals were individually caged. | The mean acceptance of the test item was 58.8% (S.D. 13.4%). | XXX |
| manufactured | 10 animals (5 males, 5 females) | 4-day pre-test control diet intake assessment, 4-day bait feeding period and 14-day control bait period. Unrestricted access to the test bait and to palatable and familiar alternative food (challenge diet) during the 4-day test period. The quantity of food placed in each pot was sufficient to meet each animal’s daily needs. | Normal laboratory requirements: 18 - 24°C, a relative humidity range of 30% to 80%, with between 10 and 25 air changes per hour, and with a 12-hour light-dark cycle | Total mortality was observed in both male and female mice. The mean time to death was 4.5 days (3 to 7 days) after the first intake of treated baits.  The efficacy was total: 100% in 14 days. |  |
| CONTROL, stored | CD-1 mice (*Mus* | Laboratory test. | The animals were | The mean acceptance of the test | XXX |
| at 54°C for a | *musculus*) | Choice feeding test: aged baits. | individually caged. | item was 52.7% (S.D. 13.2%). |  |
| period of 2 weeks. | 10 animals (5 males, 5 females) | 4-day pre-test control diet intake assessment, 4-day bait feeding period and 14-day control bait period. Unrestricted access to the test bait and to palatable and familiar alternative food (challenge diet) during the 4-day test period. The quantity of food placed in each pot was sufficient to meet each animal’s daily needs. | Normal laboratory requirements: 18 - 24°C, a relative humidity range of 30% to 80%, with between 10 and 25 air changes per hour, and with a 12-hour light-dark cycle | Total mortality was observed in both male and female mice. The mean time to death was 5.2 days (3 to 11 days) after the first intake of treated baits.  The efficacy was total: 100% in 14 days. |  |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| CONTROL, freshly  manufactured | CD Norway rat (*Rattus norvegicus*).  10 animals (5 males, 5  females) | Laboratory test.  Choice feeding test: fresh baits.  4-day pre-test control diet intake  assessment, 4-day bait feeding period and 14-day control bait period. Unrestricted access to the test bait and to palatable and familiar alternative food (challenge diet) during the 4-day test period. The quantity of food placed in each pot was sufficient to meet each animal’s daily needs. | The animals were individually caged.  Normal laboratory  requirements: 18 - 24°C, a relative humidity range of 30% to 80%, with between 10 and 25 air changes per hour, and with a 12-hour light-dark cycle | The mean acceptance of the test item was 37.5% (S.D. 16.1%).  Total mortality was observed in  both male and female mice. The mean time to death was 4.1 days (3 to 5 days) after the first intake of treated baits.  The efficacy was total: 100% in 14 days. | XXX |
| CONTROL, stored at 54°C for a period of 2 weeks | CD Norway rat (*Rattus*  *norvegicus*).  10 animals (5 males, 5  females) | Laboratory test.  Choice feeding test: aged baits.  4-day pre-test control diet intake  assessment, 4-day bait feeding period and 14-day control bait period. Unrestricted access to the test bait and to palatable and familiar alternative food (challenge diet) during the 4-day test period. The quantity of food placed in each pot was sufficient to meet each animal’s daily needs. | The animals were  individually caged.  Normal laboratory  requirements: 18 - 24°C, a relative humidity range of 30% to 80%, with between 10 and 25 air changes per hour, and with a 12-hour light-dark cycle | The mean acceptance of the test  item was 35.1% (S.D. 11.5%).  Total mortality was observed in  both male and female mice. The mean time to death was 4.6 days (3 to 5 days) after the first intake of treated baits.  The efficacy was total: 100% in 14 days | XXX |
| CONTROL | Wild house mouse (*Mus musculus*). | Field test carried out on a breeding, pig farm. | Natural conditions.  The quantity of food placed | The efficacy measured was 95% | XXX |
|  | At least 14, estimated by pre-treatment bait census | After a pre-bait until the mice were feeding readily on the bait (28 days), baiting was carried out. The non- poisoned baits were replaced by the product to be tested for 13 days. On each day's treatment, the bait stations were emptied then refilled. Post­baiting (6 days) was done to assess the level of the survival rodent population. | in each bait station was sufficient to meet each animal’s daily needs. |  |  |
| CONTROL | Wild Norway rat (*Rattus norvegicus*). | Field test carried out on a breeding, pig farm. | Natural conditions.  The quantity of food placed | The efficacy measured was 91.2% | XXX |
|  | At least 14, estimated by pre-treatment bait census | After a pre-bait until the mice were feeding readily on the bait (28 days), baiting was carried out. The non- poisoned baits were replaced by the product to be tested for 13 days. On each day's treatment, the bait stations were emptied then refilled. Post­baiting (8 days) was done to assess the level of the survival rodent population. | in each bait station was sufficient to meet each animal’s daily needs. |  |  |

On the basis of the efficacy data submitted, the level of efficacy of the product CONTROL for the intended uses presented in the table below is acceptable.

|  |  |  |  |
| --- | --- | --- | --- |
| **Product** | **Target organisms** | **Application rate and intervals** | **Use area** |
| CONTROL  Bait containing 0.005% w/w of bromadiolone. | Rats\* (*Rattus norvegicus* and *Rattus rattus*) | 100 g / bait point separated by 5-10 meters | in and around buildings |
| Mice (*Mus musculus*) | 25 g / bait point separated by 2-5 meters | in and around buildings |
| Field mice (*Apodemus sylvaticus*) | 50 g / bait point separated by 2-5 meters | in and around buildings |

\*Field test against *Rattus rattus* is requested at the renewal of the authorization

### Function/Field of use

**Main Group (MG): 3 – Pest control**

Product Type (PT): 14 Function: Rodenticide VIII.3.1: Granular bait

Field of use

IV.1 Indoor use

IV.2 Outdoor use

User category

V.1 non professional / general public

V.2 professional

V.3 specialised professional

Function / Mode of action III.2 long term action III.2.1 anticoagulant III.2.1.1 ingestion toxin III.2.1.1.1 ingestion by eating

Target organisms to be controlled I.1.1.1 Brown rat: *Rattus norvegicus* I.1.1.3 House mouse: *Mus musculus* I.1.1.4 Other *Muridae* (Field mouse)

Developmental stages of target organisms to be controlled

II.1 Juveniles

II.2 Adults

Organisms or objects to be protected

VII.1 Stored product protection/food protection

VII.2 Health protection

VII.3 Material protection (historical buildings, technical objects)

Method of application VI.2: covered application

VI.2.1: covered application in bait stations.

VI.2.21: other covering

### Dose/Mode of action

Bait should be placed in discrete locations within the infested area and placed in secure, (preferably dry) tamper-proof baiting stations, bait boxes of pipe sections. Rodenticide baits containing 50 ppm bromadiolone as the active substance are intended for use in and around buildings, in open areas and waste dumps. It is used as a response to an infestation. The number of baits depends on the site type and the infestation level.

The bait is easy to place where the rodents are active, near rodent burrows, against walls, along travel routes (runways) and should preferably be positioned between the rodents’ place of shelter and their food supply.

Adapt the number of baits and the distances according to the infestation level.

### **Effects on the target organisms (efficacy)**

Bromadiolone is a second generation anticoagulant which acts by antagonism to vitamin K. Anticoagulant rodenticides, including bromadiolone, are vitamin K antagonists. The main site of action is the liver, where several of the blood coagulation precursors undergo vitamin K dependent post translation processing before they are converted into the respective procoagulant zymogens. The specific point of action is thought to be the inhibition of K1 epoxide reductase. The anticoagulants accumulate and are stored in the liver until broken down. The plasma prothrombin (procoagulant factor II) concentration provides a suitable guide to the severity of acute intoxication and to the effectiveness and required duration of the antidote therapy (vitamin K1).

Signs of poisoning in rodents and other mammals are those associated with an increased tendency to bleed, leading ultimately to profuse haemorrhage. After feeding on bait containing bromadiolone for 2-3 days the animal becomes lethargic and slow moving. Signs of bleeding are often noticeable and blood may be seen around the nose and anus. As symptoms develop the animal will lose its appetite and will remain in its burrow or nest for increasingly long periods of time. Death will occur within 4- 7 days of ingesting a lethal dose and animals often die out of sight in their nest or burrow.

Bromadiolone is a second-generation anticoagulant which blocks recycling of vitamin K in the liver causing the reserves of active vitamin K in the blood to be gradually depleted. Second-generation anticoagulants are long acting and so a single dose is effective. Vitamin K contributes to the formation of blood clotting factors and in doing so is converted from an “active” form to an inactive form. The inactive form is returned to the lover where it is regenerated by an enzyme to be re-used. Once this recycling enzyme is blocked by bromadiolone, the reserves of active vitamin K in the blood are gradually depleted. The rodent dies due to the failure of its blood clotting system.

### Known limitations (e.g. resistance)

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[[4]](#footnote-4); Lund, 1984[[5]](#footnote-5); Pelz et al. 1995[[6]](#footnote-6)). 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[[7]](#footnote-7)). 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[[8]](#footnote-8)).

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.

### Humaneness

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

**Table 3.2.1: Effectiveness data - CONTROL**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Test product** | **Test organisms** | **Test system / Concentrations applied / exposure time** | **Test conditions** | **Test results: effects, mode of action, resistance** | **Reference** |
| CONTROL, freshly | CD-1 mice (*Mus musculus*) | Laboratory test.  Choice feeding test: fresh baits. | The animals were individually caged. | The mean acceptance of the test item was 58.8% (S.D. 13.4%). | XXX |
| manufactured | 10 animals (5 males, 5 females) | 4-day pre-test control diet intake assessment, 4-day bait feeding period and 14-day control bait period. Unrestricted access to the test bait and to palatable and familiar alternative food (challenge diet) during the 4-day test period. The quantity of food placed in each pot was sufficient to meet each animal’s daily needs. | Normal laboratory requirements: 18 - 24°C, a relative humidity range of 30% to 80%, with between 10 and 25 air changes per hour, and with a 12-hour light-dark cycle | Total mortality was observed in both male and female mice. The mean time to death was 4.5 days (3 to 7 days) after the first intake of treated baits.  The efficacy was total: 100% in 14 days. |  |
| CONTROL, stored | CD-1 mice (*Mus* | Laboratory test. | The animals were | The mean acceptance of the test | XXX |
| at 54°C for a | *musculus*) | Choice feeding test: aged baits. | individually caged. | item was 52.7% (S.D. 13.2%). |  |
| period of 2 weeks. | 10 animals (5 males, 5 females) | 4-day pre-test control diet intake assessment, 4-day bait feeding period and 14-day control bait period. Unrestricted access to the test bait and to palatable and familiar alternative food (challenge diet) during the 4-day test period. The quantity of food placed in each pot was sufficient to meet each animal’s daily needs. | Normal laboratory requirements: 18 - 24°C, a relative humidity range of 30% to 80%, with between 10 and 25 air changes per hour, and with a 12-hour light-dark cycle | Total mortality was observed in both male and female mice. The mean time to death was 5.2 days (3 to 11 days) after the first intake of treated baits.  The efficacy was total: 100% in 14 days. |  |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Test product** | **Test organisms** | **Test system / Concentrations applied / exposure time** | **Test conditions** | **Test results: effects, mode of action, resistance** | **Reference** |
| CONTROL, freshly | CD Norway rat (*Rattus norvegicus*). | Laboratory test.  Choice feeding test: fresh baits. | The animals were individually caged. | The mean acceptance of the test item was 37.5% (S.D. 16.1%). | XXX |
| manufactured | 10 animals (5 males, 5 | 4-day pre-test control diet intake | Normal laboratory | Total mortality was observed in |  |
|  | females) | assessment, 4-day bait feeding period and 14-day control bait period. Unrestricted access to the test bait and to palatable and familiar alternative food (challenge diet) during the 4-day test period. The quantity of food placed in each pot was sufficient to meet each animal’s daily needs. | requirements: 18 - 24°C, a relative humidity range of 30% to 80%, with between 10 and 25 air changes per hour, and with a 12-hour light-dark cycle | both male and female mice. The mean time to death was 4.1 days (3 to 5 days) after the first intake of treated baits.  The efficacy was total: 100% in 14 days. |  |
| CONTROL, stored | CD Norway rat (*Rattus* | Laboratory test. | The animals were | The mean acceptance of the test | XXX |
| at 54°C for a | *norvegicus*). | Choice feeding test: aged baits. | individually caged. | item was 35.1% (S.D. 11.5%). |  |
| period of 2 weeks. | 10 animals (5 males, 5 | 4-day pre-test control diet intake | Normal laboratory | Total mortality was observed in |  |
|  | females) | assessment, 4-day bait feeding period and 14-day control bait period. Unrestricted access to the test bait and to palatable and familiar alternative food (challenge diet) during the 4-day test period. The quantity of food placed in each pot was sufficient to meet each animal’s daily needs. | requirements: 18 - 24°C, a relative humidity range of 30% to 80%, with between 10 and 25 air changes per hour, and with a 12-hour light-dark cycle | both male and female mice. The mean time to death was 4.6 days (3 to 5 days) after the first intake of treated baits.  The efficacy was total: 100% in 14 days. |  |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Test product** | **Test organisms** | **Test system / Concentrations applied / exposure time** | **Test conditions** | **Test results: effects, mode of action, resistance** | **Reference** |
| CONTROL | Wild house mouse (*Mus musculus*). | Field test carried out on a breeding, pig farm. | Natural conditions.  The quantity of food placed | The efficacy measured was 95% | XXX |
|  | At least 14, estimated by pre-treatment bait census | After a pre-bait until the mice were feeding readily on the bait (28 days), baiting was carried out. The non- poisoned baits were replaced by the product to be tested for 13 days. On each day's treatment, the bait stations were emptied then refilled. Post­baiting (6 days) was done to assess the level of the survival rodent population. | in each bait station was sufficient to meet each animal’s daily needs. |  |  |
| CONTROL | Wild Norway rat (*Rattus norvegicus*). | Field test carried out on a breeding, pig farm. | Natural conditions.  The quantity of food placed | The efficacy measured was 91.2% | XXX |
|  | At least 14, estimated by pre-treatment bait census | After a pre-bait until the mice were feeding readily on the bait (28 days), baiting was carried out. The non- poisoned baits were replaced by the product to be tested for 13 days. On each day's treatment, the bait stations were emptied then refilled. Post­baiting (8 days) was done to assess the level of the survival rodent population. | in each bait station was sufficient to meet each animal’s daily needs. |  |  |

* **Major change application - 2017**

The product CONTROL (0.005 % w/w bromadiolone) was initially authorized for use against *Mus musculus*, *Rattus norvegicus*, *Rattus rattus* and *Apodemus sylvaticus*, in and around buildings, by non-professional and professional users, and open areas, landfills and waste dumps by professional users.

The major change consists in reduction of active substance concentration (0.005 to 0.0025 % w/w bromadiolone), and addition of target organisms voles (*Arvicola terrestris* and *Microtus arvalis*).

The name of this product is now CONTROL 25.

The application rates recommended by the applicant are the following:

Rats: 50-100 g grains/secured bait point separated by 5-10 m.

Field mice: 50 g grains/secured bait point separated by 2-5 m.

Mice and voles: 20-30 g grains/secured bait point separated by 2-5 m.

The products, organisms or objects to be protected are private buildings and farms.

French competent authorities (FR CA) assessed that:

* The product CONTROL 25 (0.0025 % bromadiolone) has shown a sufficient efficacy and can be used for the control of house mice (*Mus musculus)* at the application rate of 25-30 g (instead of 20 g claimed as a minimum)*,* for the control of field mice *(Apodemus sylvaticus)* at the application rate of 50 g, and for the control of brown rats (*Rattus norvegicus)* at the application rate of 100 g (instead of 50 g claimed as a minimum), in and around buildings, and open areas for professional and non-professional users and, in in waste dumps and landfills by professional users only.

No efficacy data have been submitted to demonstrate the efficacy of the product against black rat (*Rattus rattus*).

For information, in France, the claim “use against *R. norvegicus* “ is not acceptable, only the general claim “use against rats” is considered as valid. For the claim ”use against rats”, efficacy must be also shown on *R. rattus*. Consequently, suitable information (such as a field test) demonstrating the efficacy against black rats of the product CONTROL 25, at the claimed application rate, need to be provided in the post- authorisation, within one year.

* The efficacy of the product CONTROL 25 against voles (*Microtus arvalis* and *Arvicola terrestris*) is demonstrated in laboratory tests (palatability and mortality).

Nevertheless no field test was performed on water voles (*Arvicola terrestris)* but the applicant submitted some arguments stating that an extrapolation can be made from the efficacy demonstrated in the field test for common voles (*Microtus arvalis*) to water voles (*Arvicola terrestris*) since laboratory tests conducted with the product CONTROL 25 showed equivalent palatability and efficacy for both species. FR CA considers that the extrapolation of results from common voles to water voles is not acceptable as these two species are different in their size and behaviour as habitat, food diet...

Moreover, the submitted field test against common voles *Microtus arvalis* was conducted in the field (meadow) and above all the product was applied directly inside the holes of treated zone. The method of application in the field trial is not representative for this claim.

Furthermore, the new transitional Guidance on Efficacy assessment for PT 14 Rodenticides (2016), even if not applied for this dossier, confirm that behaviours between these both species are different and then requires for use against voles at least two vole species which differ in size and behaviour, for example water voles (*Arvicola amphibious*), bank vole (*Myodes glareolus*) and common voles *Microtus arvalis*.

|  |
| --- |
| **Conclusion on the efficacy of the product** |
| French competent authorities (FR CA) consider that :   * the elements presented in the dossier to support the efficacy of the product CONTROL 25 (0.0025 % w/w bromadiolone) for the control of house mice (*Mus musculus*) and field mice (*Apodemus sylvaticus*) are sufficient for the uses claimed. * The product CONTROL 25 (0.0025 % w/w bromadiolone) has shown a sufficient efficacy against brown rats (*Rattus norvegicus*). However in France, efficacy must be shown on both species *R. norvegicus* and *R. rattus*. Suitable information (such as a field test) demonstrating the efficacy against black rats of the product CONTROL 25, at the claimed application rate, will need to be provided in support of the authorisation, within one year after authorisation. * The elements presented in the dossier to support the efficacy of the product CONTROL 25 against voles (*Microtus arvalis* and *Arvicola terrestris*) were insufficient: indeed, the field study submitted for the common vole *Microtus arvalis* was conducted in an area (field) and with an application method (bait directly inside holes) non representative of the use claimed. Moreover, for the water vole *Arvicola terrestris*, no field test was conducted and the arguments presented for the extrapolation of field test from common vole to water vole are not acceptable as both species are different in their size and their behaviour (habitat, food diet,...). |

Experimental data on the effectiveness of the product against target organisms are summarized in the table below.

**Table 3.2.1c: Effectiveness data – CONTROL 25**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Experimental data on the efficacy of the biocidal product against target organism(s)** | | | | | | | |
| **Function** | **Field of use envisaged** | **Test substance** | **Test organism(s)** | **Test method** | **Test system / concentrations applied / exposure time** | **Test results: effects** | **Reference** |
| Rodenticide | Indoor and outdoor | GRAIN BROMADIOLONE 25 ppm  Fresh bait | Brown rats  *Rattus norvegicus*  5 males  5 females. | Laboratory test | Acclimatization: 4 days in individual cage at room temperature.  Day 0: reference food and bait biocidal product have been given:  - 50 g per animal of reference food for the assessment of palatability,  - 50 g per animal of biocidal product during 4 consecutive days with daily consumption measurements.  Mortality was observed until the death of all animals. | Palatability = 46 %  Mortality = 90 %  in a period from day 4 to day 8  R.I=1 | XXX |
| Rodenticide | Indoor and outdoor | Aged Bromadiolone grain 25 ppm  2 years aged | Brown rats  *Rattus norvegicus*  5 males  5 females. | Laboratory test | Acclimatization: 4 days in individual cage at room temperature.  Day 0: reference food and bait biocidal product have been given:  - 40 g per animal of reference food for the assessment of palatability,  - 20-30 g per animal of biocidal product during 8 consecutive days with daily consumption measurements.  Mortality was observed until the death of all animals. | Palatability = 52 %  Mortality = 100 %  in a period from day 4 to day 8  R.I=2  choice feeding test extended until D8 | XXX |
| Rodenticide | Indoor and outdoor | GRAIN BROMADIOLONE 25 ppm  Fresh bait | Brown rats  *Rattus norvegicus* | Field test  Census baiting technique, which involved the following phases:  Pre-treatment census  Pre-treatment lag phase  Treatment census  Post-treatment lag phase  Post-treatment census  During each assessment the food/bait at each station was weighed and replenished, and the consumption in grams was calculated. During the treatment census, searches were conducted for dead and dying rats around the sites. | Acclimatization: 11 days (100 g of wheat per station per day)  Treatment : 100 g of bait per day in each lockable bait station –total 12 bait stations) during 14 days  Post-baiting: 4 days  (100 g of wheat per station per day)  Mortality was observed from the first day of intoxication and noted daily or every 2 days until the end of the trial. | Estimated efficacy = 96.9 %.  Pre-baiting plateau = 606.7 g/day  Post-baiting = 18.8 g/day  R.I=2 | XXX |
| Rodenticide | Indoor and outdoor | GRAIN BROMADIOLONE 25 ppm  Fresh bait | House mice  *(Mus musculus)*  10 males  10 females. | Laboratory test | Acclimatization: 4 days in individual cage at room temperature.  Day 0: reference food and bait biocidal product have been given:  - 25 g per animal of reference food for the assessment of palatability,  - 25 g per animal of biocidal product during 4 consecutive days with daily consumption measurements.  Mortality was observed until the death of all animals. | Palatability = 61 %  Mortality = 90 %  in a period from day 7 to day 9  RI= 1 | XXX |
| Rodenticide | Indoor and outdoor | Aged Bromadiolone grain 25 ppm  2 years aged | House mice  *(Mus musculus)*  10 males  10 females. | Laboratory test | Acclimatization: 4 days in individual cage at room temperature.  Day 0: reference food and bait biocidal product have been given:  - 10 g per animal of reference food for the assessment of palatability,  - 20 g per animal of biocidal product during 4 consecutive days with daily consumption measurements.  Mortality was observed until the death of all animals. | Palatability = 47 %  Mortality = 90 %  in a period from day 7 to day 18  RI= 3  Dose testing bait higher than challenge diet and choice feeding test extended until D18 | XXX |
| Rodenticide | Indoor and outdoor | GRAIN BROMADIOLONE 25 ppm  Fresh bait | House mice  *Mus musculus* | Field test  Census baiting technique, which involved the following phases:  Pre-treatment census  Pre-treatment lag phase  Treatment census  Post-treatment lag phase  Post-treatment census  During each assessment the food/bait at each station was weighed and replenished, and the consumption in grams was calculated. During the treatment census, searches were conducted for dead and dying mice around the sites. | Acclimatization: 11 days (25 g of semolina per station per day)  Treatment : 25 g of bait in each lockable bait station (total 11 bait stations) during 14 days  Post-baiting: 4 days  (25 g of semolina 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 = 95.03 %  Pre-baiting plateau = 181 g/day  Post-baiting = 9.1 g /day  R.I=1 | XXX |
| Rodenticide | Indoor and outdoor | GRAIN BROMADIOLONE 25 ppm  Fresh bait | Common voles  *(Microtus arvalis)*  10 wild rodents trapped in field | Laboratory test | Acclimatization: 4 days in separate cages at room temperature.  Day 0: reference food and bait biocidal product have been given during 4 consecutive days with daily consumption measurements.  Mortality was observed until the death of all animals. | Palatability = 73 %  Mortality = 100 %  in a period from day 7 to day 11  RI=1 | XXX |
| Rodenticide | Indoor and outdoor | OAT Bromadiolone 25 ppm  Fresh bait | Water voles  *(Arvicola terrestris)*  10 wild rodents trapped in field | Laboratory test | Acclimatization: 4 days in separate cages at room temperature.  Day 0: reference food and bait biocidal product have been given during 4 consecutive days with daily consumption measurements.  Mortality until the death of all animals. | Palatability = 86 %  Mortality = 100 %  in a period from day 7 to day 11  RI= 1 | XXX |
| Rodenticide | Indoor and outdoor | OAT Bromadiolone 25 ppm  Fresh bait | Field mice  *Apodemus sylvaticus* | Field test  census baiting technique (which involved pre-treatment census/  pre-treatment lag phase/  Treatment census/  post-treatment lag phase/  post-treatment census) and a count of the different holes used by field mouse in a defined perimeter. For this test, the perimeter was defined as a rectangle of 10 meters by 10 meters (100m2) where holes were precisely identified and counted  During each assessment the food/bait at each station was weighed and replenished, and the consumption in grams was calculated. During the treatment census, searches were conducted for dead and dying mice around the sites. | Acclimatization: 21 days (40 g of semolina per station per day)  Treatment : 50 g of bait in each lockable bait station next to each holes (total 10 bait stations) during 16 days  Post-baiting: 7 days  (40 g of semolina 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 = 160 g/day  Post-baiting = 0 g / day  R.I=2 | XXX |
| Rodenticide | Indoor and outdoor | GRAIN BROMADIOLONE 25 ppm  Fresh bait | Common voles  *(Microtus arvalis)* | Field test  Technique of hole activity measurement in a control zone vs in the treated zone. The different holes (zones control and treated) used by common vole in the defined perimeter were marked and monitored. | For the control zone, 26 holes were marketed in the defined perimeter and 32 in the treated zone. Each zone was separated from other zone with minimum 100 m distance to avoid impact of voles of 1 zone to other zones.  For the treated zone, 10 g of the product were placed inside the hole and a leaf was placed over the hole entrance to monitor rodent activity. The monitoring was done all each day for 15 days.  The efficacy of the treatment is calculated taking into account the difference of hole activity between control zone and treated zone. In each zone, a mean of hole activity the last 5 days of monitoring was calculated.  = ((mean hole activity control zone last 5 days – mean hole activity treated zone last 5 days)/ mean hole activity control zone last 5 days) \* 100 | Estimated efficacy = 100 %  R.I= 3  Application method (bait directly inside holes) non representative of the use claimed | XXX |

* **Renewal application - 2017**

For the renewal of the authorization of the product CONTROL 25 (0.0025 % w/w bromadiolone) no change in the composition has been declared and no further data have been submitted to complete the dossier. Therefore the conclusions on efficacy will remain the same as for the major change dossier.

|  |  |  |  |
| --- | --- | --- | --- |
| **Product** | **Target organisms** | **Application rate and intervals** | **Use area** |
| CONTROL 25  Bait containing 0.0025% w/w of bromadiolone. | Rats\* (*Rattus norvegicus* and *Rattus rattus*) | 100 g / bait point separated by 5-10 meters | in and around buildings  open areas, waste dumps and landfills |
| Mice (*Mus musculus*) | 25-30 g / bait point separated by 2-5 meters |
| Field mice (*Apodemus sylvaticus*) | 50 g / bait point separated by 2-5 meters |

\*under the condition of the submission of a field test on *R. rattus* within 1 year post authorisation.

## Biocidal Product Risk Assessment (Human Health and the Environment)

### Description of the intended use(s)

The product Control is a rodenticide. It is a ready-to-use grain bait which contains 50 ppm (0.005% w/w) Bromadiolone (CAS No.28772-56-7) used by professional and amateur users. Bromadiolone baits are used indoors and outdoors to kill mice and rats, in non-agricultural open areas and in waste dumps: they are placed at the appropriate places in bait stations or covered under a curved tile, a wooden board or in a piece of tube; the animals eat some of the product and die.

* **Major change and renewal applications - 2017**

Major change:

The applicant requires an authorization for the same product but containing 0.0025 % w/w bromadiolone instead 0.005 % w/w in and around buildings, open areas and in landfills / waste dumps for each target organism (*Mus musculus*, *Apodemus sylvaticus*, *Rattus norvegicus and Rattus rattus)*

The name of this product is now CONTROL 25.

The application rates recommended by the applicant are the following:

Rats: 100 g /secured bait point separated by 5-10 m.

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

Field mice: 50 g /secured bait point separated by 2-5 m.

### Hazard Assessment for Human Health

No new exposure studies have been submitted for evaluation. Signs of poisoning in rodents and other mammals are those associated with an increased tendency to bleed, leading ultimately to profuse haemorrhage. Non-target organisms are most at risk from secondary poisoning, i.e. consumption of rodent carcasses by predators such as raptors.

**3.3.2.1. Toxicology of the active substance**

Bromadiolone is a second-generation single-dose anticoagulant rodenticide. It disrupts the normal blood clotting mechanisms resulting in increased bleeding tendency and, eventually, profuse haemorrhage and death. Like all anticoagulant rodenticides, bromadiolone is structurally similar to vitamin K. Blood forms a clot at the site of injury by virtue of a complicated ‘clotting cascade’, involving numerous clotting factors. The clotting factors are made in the liver as inactive precursors, converted to active form and allowed to circulate in the bloodstream. Vitamin K is employed in the liver in the activation process, and is used in a continuous cyclic process involving several enzymes. The anticoagulant rodenticides block these enzymes, preventing regeneration of the vitamin K and preventing activation of the clotting factors.

Bromadiolone requires labelling with the symbol T+ and the risk phrases R 28 ‘Very toxic if swallowed’; R27 ‘Very toxic in contact with the skin’ and R26 ‘Very toxic by inhalation’. Bromadiolone is not classified as a skin irritant, eye irritant or a skin sensitiser.

Repeated dosing studies show effects on blood coagulation and death at low doses (µg/kg bw/day), and therefore labelling with R48/23/24/25 is warranted.

The Commission Working Group of Specialised Experts on Reproductive Toxicity has unanimously recommended that all AVK rodenticides should collectively be regarded as human teratogens due to the structural similarity to and the same mode of action as the known developmental toxicant warfarin (meeting in Ispra, 19-20 September 2006). Therefore based on read across data from warfarin, bromadiolone is considered to be a possible developmental toxicant and requires the classification as Reprotoxic with the labelling R61, may cause harm to the unborn child.

No oral absorption value could be set on the LiphaTech study, but the absorption was > 70 % of the administered dose, based on (carcass, bile- and urinary excretion, Task Force study). The major route of excretion was via the faeces accounting for ca 50-60 % of the dose, whilst approximately 1-5 % was excreted via urine. Bile investigations showed that biliary elimination plays a major role in the excretion. No parent bromadiolone was excreted in bile or urine. The main retention site was the liver. A non-guideline study in three cows was completed (LiphaTech). According to this study bromadiolone does not seem to accumulate into milk. The information from the ADME studies was not enough to propose a full metabolism pathway for any of the applicants but the study provided by LiphaTech identified one major metabolite in faeces as a hydroxylated analogue of bromadiolone; hydroxylation was proposed on the benzylic carbon atom. No dermal absorption study were performed on the active substance alone (it was only provided for the formulated product or mixed with bait), but a default value of 10% could be used if considered necessary.

Dermal penetration in humans was estimated as < 1.6% for a powdered product. Based on data from in vitro human skin studies with two representative products containing bromadiolone, the dermal absorption was less than 0.3% for the wax block formulations.

In acute oral toxicity studies, bromadiolone was very toxic to rats with a LD50 to the rat of between 0.56 and 1.31 mg/kg bw. Bromadiolone is slightly less toxic to dogs with a LD50 value of 8.1 mg/kg bw. The symptoms were observed 1-2 days prior to death and included signs of internal haemorrhage, which were confirmed at necropsy. Bromadiolone was also acutely toxic by dermal administration, with an LD50 of 1.71 mg/kg bw in rabbits (LiphaTech) and with a combined sexes dermal LD50 value of 23.3 mg/kg in rats (Task Force). The LC50 by inhalation, in rats was 0.43 µg/L (LiphaTech). Waiving of inhalation studies has been accepted for Task Force, since operator exposure through inhalation is unlikely to occur based in the information presented concerning production procedures and based on the physical-chemistry data showing low vapour pressure. However, a classification as R26 ‘Very toxic by inhalation’ is warranted based on the other applicant’s data (LiphaTech).

Bromadiolone is not considered to be a skin or eye irritant or a skin sensitiser.

**Summary of bromadiolone subchronic, chronic, mutagenic and reproductive toxicity.**

Repeated dose oral studies showed that at doses as low as 20 μg/kg/day in the dog, lethal effects developed after 64 to 85 days administration. The clinical signs, haematological and post mortem data were consistent with the known pharmacological action of the active substance; impairment of the clotting cascade and increased prevalence of haemorrhage leading to death. There were no indications of other secondary toxicities: histopathology revealed no hypertrophy or hyperplasia of the target organ, the liver. In the 90-day oral exposure study in rabbits (data provided by Task Force), a significant increase in prothrombin time was seen in the 1 µg/kg dose group. The overall NOAEL for repeat dose effects for both applicants is 0.5 µg/kg/day based on the absence of adverse effects in this dose group. The dermal exposure is expected to be low as the use of gloves when handling the baits is expected, and route-to-route extrapolation based on data from the acute oral and dermal studies does not indicate that dermal exposure constitutes a greater risk than oral exposure. Therefore, waiving of a repeat dose dermal toxicity study has been accepted. Also, due to that bromadiolone has a low vapour pressure and exposure via inhalation is expected to be negligible both during production and during the use of bait blocks, waiving of the repeat dose inhalation study has been accepted. The subchronic dermal toxicity study is also waived. A subchronic oral study has been performed for bromadiolone using the rabbit as test species, which may be used in route-to-route extrapolation. The highly cumulative nature of the material means that lower doses, administered over several days, can also be predicted to cause death. In all cases death was caused by the specific pharmacological action of the molecule, inducing fatal haemorrhage. The mechanism of clotting inhibition caused by hydroxy coumarin type anticoagulant rodenticides is dependent on inhibition of vitamin K epoxide or vitamin K reductases and is unaffected by route of application. Therefore specific repeat dose dermal or inhalation studies would not provide any additional useful information to that obtained in various species in repeat dose and subchronic studies by the oral route.

A non-guideline study in the dog submitted by LiphaTech demonstrated that after ingestion of a single lethal dose or repeated administration of sublethal doses of bromadiolone on five occasions at 48 hour intervals, antidotal therapy consisting of slow intravenous injection of vitamin K followed by 7 days of oral administration of vitamin K resulted in rapid and complete recovery.

A study in rat with bromadiolone pellets (50 ppm end use product) submitted by LiphaTech also showed that vitamin K can reverse the effects. However, the effectiveness varied with the duration of exposure to bromadiolone.

Bromadiolone was not mutagenic in a standard range of in vitro and in vivo tests. The carcinogenicity study and the chronic toxicity study were waived. Performing long-term exposure studies is technically difficult when studying highly toxic substances such as bromadiolone, since dose levels, at which toxicity is identifiable but without rendering high levels of lethality, are hard to predict. The waiving is accepted, also considering the lack of genotoxicity.

The molecules both have significant structural similarity to vitamin K. This structural similarity is responsible for the ability to interfere with i.e. block the enzymes used to regenerate vitamin K. The major differences in the active substances lie in their ‘tails’, which have varying degree of lipophilicity. There is long term experience with warfarin, widely used in anti-clotting therapy in humans for over forty years, with no association with increased incidence of cancer. The absence of adverse effects in millions of humans following four decades of long term warfarin therapy is considered sufficient evidence that warfarin is not carcinogenic. The structural similarity of bromadiolone to warfarin (see below), together with the negative results in the guideline mutagenicity tests, indicates that bromadiolone is not carcinogenic.



Warfarin Bromadiolone

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In addition, evidence is presented to show that it would not be possible to perform a meaningful long­term study in any species because of the accumulative nature and high toxicity of the active substance. Reproductive effects of bromadiolone can not be excluded by the submitted two-generation reproduction toxicity study (Task Force), but since long term exposure studies are technically hard to perform for such highly toxic substances as bromadiolone, no new study will be required. As with carcinogenicity, the primary reason for not requiring such a study is the long-term use of the structurally similar molecule warfarin in humans without association with adverse effects on fertility. The 2-generation study is therefore accepted as waived for both applicants.

A teratogenicity study on rabbit showed severe fetal malformations following exposure to maternally toxic levels of bromadiolone (Task Force). However, the possibility that the effects seen may have been due to non-specific influences such as generalised toxicity cannot be excluded. Bromadiolone was not embryotoxic or teratogenic in guideline studies in rat and rabbit (LiphaTech). However, based on the structural similarity to and the same mode of action as warfarin, bromadiolone is considered as a possible developmental toxicant. The Commission Working Group of Specialised Experts on Reproductive Toxicity has unanimously recommended that all AVK rodenticides should collectively be regarded as human teratogens due to the structural similarity to and the same mode of action as the known developmental toxicant warfarin (meeting in Ispra, 19-20 September 2006). Therefore based on read across data from warfarin, bromadiolone is considered to be a possible developmental toxicant and requires the classification as Reprotoxic with the labelling R61, may cause harm to the unborn child.

The toxicological studies do not indicate any neurotoxic effects. A neurotoxicity study would be scientifically unjustified and would not provide any new data. Based on this and animal welfare grounds it is deemed unnecessary to conduct a neurotoxicity study and applicant’s justification is accepted. Also, the mechanism for bromadiolone as an anticoagulant is well known and no mechanistic studies were considered necessary.

There are no case reports from the manufacturer concerning adverse effects in users applying the products. The Task Force submitted data on poisoning cases with bromadiolone. During the time period 1996–1999 a total of 115 calls concerning bromadiolone were received by the Milan Poisons Center, 98 of which involved clinical cases among humans or animals. The most common route of exposure was through ingestion and in 55% of the cases children under the age of four years were exposed. The symptoms were reported in eleven human cases and included vomiting, gastric pyrosis and itching. Only one case was reported with haematological problems. Vitamin K1 is the antidote, and it is important to monitor the clotting ability of the blood (prothrombin time) to continue the treatment long enough. If diagnosis is made quickly and appropriate therapy is instituted the prognosis is good.

The derivation of an acceptable level of exposure value for single use (AELacute) is based on the teratogenicity study in rabbits submitted by Task Force. It is based on the LOAEL of 2 µg/kg bw, using a safety factor of 600 (10 for interspecies and 10 for intraspecies variability, 2 for using LOAEL instead of NOAEL and an extra factor of 3 for severity of effects) and with correction of 70% oral absorption, resulting in an AELacute of 0.0023 µg/kg bw. To derive an AELmedium, for repeated exposure, the subchronic study in rabbit submitted by Task Force is used. The NOAEL in this study is 0.5 µg/kg bw based on the prolonged prothrombin time seen at 1 µg/kg bw. With a safety factor of 300 and with correction of of 70% oral absorption, this would lead to an AELmedium/chronic of 0.0012 µg/kg bw.

**Data requirements:** (List if applicable) None.

**3.3.2.2. Toxicology of the biocidal product**

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

**Summary of acute toxicity data for the biocidal product Control**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Parameter** | **Test material** | **Species** | **Result** | **Classification** | **Ref.** |
| Acute Oral Toxicity | Bromadiolone grain bait. Batch: AB201101 broma | Rat, female, Sprague- Dawley, SPF Caw, 6 in total. | LD50 > 2000 mg/kg bw | none. | XXX |
| **Acceptable (Y/N): Yes** | | **Method:** OECD 423 (2002) | | **GLP (Y/N):**  **Yes** |
| **Comments:** No mortality occurred during the study at 2000mg/kg. There were no clinical signs observed. 2g of paste bait was powdered and mixed with water and filtered before use. Considering the water solubility of the active substance is extremely low, the use of a water vehicle for gavage is questionable. A less polar vehicle may have been more appropriate. | | | | |
| Acute Dermal Toxicity | Bromadiolone grain bait. Batch: AB201101 broma | Rat, male & female, Sprague- Dawley, SPF Caw, 10 in total. | LD50 > 2000 mg/kg bw | none. | XXX |
| **Acceptable (Y/N): Yes** | | **Method:** OECD 402 (1987) | | **GLP (Y/N):**  **Yes** |
| **Comments:** No mortality occurred during the study at 2000mg/kg. No cutaneous reactions or systemic clinical signs related to the administration of the test item were observed. Some green colouration for the paste dye was noted. Considering the water solubility of the active substance is extremely low, the use of a water vehicle for dermal application is questionable. | | | | |
| Acute Inhalation Toxicity | none none | | none none | | none |
| **Acceptable (Y/N):** | | **Method:** | | **GLP (Y/N):** |
| **Comments:** Inhalation exposure is not appropriate for this formulation. Active substance has very low volatility and is only present at 0.005% (w/w) in the grain. Company justification accepted. | | | | |
| Information | none none none none none | | | | |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Parameter** | **Test material Species** | | | | | | **Result Classification** | | | | | | | | **Ref.** | | |
| on mixture of biocidal products | **Acceptable (Y/N): Yes** | | | | | | **Method:** | | | | | | | | **GLP (Y/N):** | | |
| Not applicable since following the proposed uses of grain bait and the label claims, the rodenticide bait is not intended to be used in a mix with other biocidal products. Company justification accepted. | | | | | | | | | | | | | | | | |
| Acute Skin Irritation | Bromadiolone grain bait. Batch: AB201101 broma | | | Rabbit, male, NZW, 3 in total | | | No irritation | | | | none | | | | XXX | | |
| **Acceptable (Y/N): Yes** | | | | | | **Method:** OECD 404 (2002) | | | | | | | | **GLP (Y/N):**  **Yes** | | |
| **Comments:** The test item was applied as supplied at a dose of 0.5 g, on an undamaged skin area of one flank of each animal for 4 hours. No cutaneous reactions (erythema and oedema) were observed on the treated areas. | | | | | | | | | | | | | | | | |
| Acute Eye Irritation | Bromadiolone grain bait. Batch: AB201101 broma | | | Rabbit, male, NZW, 3 in total | | | Slight irritation | | | | none | | | | XXX | | |
| **Acceptable (Y/N): Yes** | | | | | | **Method:** OECD 405 (2002) | | | | | | | | **GLP (Y/N):**  **Yes** | | |
| **Comments:** The test item was reduced to a fine powder. The test item was applied at a dose of 0.1 g instilled into the conjunctival sac of one eye in each animal. | | | | | | | | | | | | | | | | |
|  | **Cornea** | | | | **Iris** | | | | **Conjunctivae** | | | | | | | |
| **Redness** | | | | **Chemosis** | | | |
| **Time/Anima**  **l** | **1** | **2** | | **3** | **1** | | **2** | **3** | **1** | | **2** | **3** | **1** | | **2** | **3** |
| 24 hours | 0 | 1 | | 1 | 0 | | 0 | 0 | 1 | | 1 | 1 | 1 | | 0 | 0 |
| 48 hours | 0 | 0 | | 0 | 0 | | 0 | 0 | 1 | | 0 | 1 | 1 | | 0 | 0 |
| 72 hours | 0 | 0 | | 0 | 0 | | 0 | 0 | 1 | | 0 | 1 | 1 | | 0 | 0 |
| **Mean individual scores 24, 48 and 72 h** | **0.0** | **0.3** | | **0.3** | **0.0** | | **0.0** | **0.0** | **1.0** | | **0.3** | **1.0** | **1.0** | | **0.0** | **0.0** |
| No Classification required. | | | | | | | | | | | | | | | | |
| Skin  Sensitisatio n (M&K) | Bromadiolone grain bait. Batch: BB201101 broma | | | Guinea Pig, female, Dunkin-Hartley strain, 5 in negative control, 11 in treated groups. | | | negative | | | | none | | | | XXX | | |
| **Acceptable (Y/N): No** | | | | | | **Method:** OECD 406 (1992) | | | | | | | | **GLP (Y/N):**  **Yes** | | |
| It is not clear from the results what “diffuse redness, not corresponding to erythema” is. In the results section of the report at 30% (1/2 MNIC) after 24 h and 48 h 4 animals and 2 animals show erythema if the aforementioned “diffuse redness” is classified as erythema this signifies a positive result. | | | | | | | | | | | | | | | | |

**Conclusion:**

According to the results of the toxicological studies, Control does not classify with respect to Directive 1999/45/EC or Regulation (EC) No 1272/2008. However, safety phrases and precautionary statements are proposed by the Rapporteur. One issue that does not seem to be addressed by the acute studies above is the solubility of bromadiolone in aqueous media. This insolubility could affect the amount of active substance in doses applied.

**Data requirements:** (List if applicable) None.

* **Major change application - 2017**

The resulst of the toxicological studies performed with CONTROL are extrapolable to CONTROL 25.

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

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

**Summary of toxicological properties of the co-formulants in Control**

|  |  |  |
| --- | --- | --- |
| **Identity** | | **Function** |
| **Common name** | **CAS No.** |
| Bromadiolone 2.5%, No Dye, 0.5% DB containing Bromadiolone at 2.5%  containing Denatonium benzoate at 0.5% | Mixture  28772-56-7  3734-33-6 | Active substance  Repulsive, bittering agent |
| Monopropylene glycol | 57-55-6 | Solvent |
| Green colour  containing yellow dye (E102), Tri sodium salt of 5-hydroxy (1- p-sulphophenyl) 4- ( p-sulphophenylazo) pyrazol -3- carboxylicacid, at 2% maximum  containing blue dye (patent V E131),  m-Hydroxytetraethyldiaminotriphenylcarbinol anhydride disulfonic acid sodium salt,  at 2% maximum | Mixture  1934-21-0  20262-76-4 | Dying agent Dying agent  Dying agent |
| Rapeseed oil | 8002-13-9 | Appetent |
| Sorbic acid | 110-44-1 | In can preservative |
| Oats | Not relevant | Carrier |

### Exposure Assessment for Human Health

The most relevant route of exposure to the active substance is the dermal route. For exposure assessment only active substance from paste has been modelled. The paste product typically takes the form of a solid waxy block with a strong sweet smell containing 0.005% w/w bromadiolone.

In the final CAR for bromadiolone, LiphaTech a worst case dermal absorption of 1.6% was used for the products Super Caid Bloc and Super Caid AS Appat. However, the dermal absorption is lower for wax bloc products, which has also been shown for Task Force. Therefore the exposure to wax block products are recalculated for a dermal absorption of 0.32% which is similar to what was used for Task Force (i.e. 0.36% even though data for this applicant suggest that the dermal absorption of Protect-B as a wax block is even lower). 10% was applied when no data is available on the formulation.

The products Control Bloc, Control Pasta and Cluster grain were regarded as similar to wax blocks in nature and thus best represented with a dermal absorption of 0.36% as agreed for wax blocks in the Bromadiolone CAR. Grain bait was deemed to be best represented by a dermal absorption rate of 1.6% (derived as a worst case for powder products in the bromadiolone CAR).

* **Major change and renewal applications - 2017**

Major change:

During the first assessment, the dermal absorption value of 1.6% has been refused regarding the letter of access submitted by the applicant.

As a worst-case approach, a dermal absorption value of 4% (agreed at WG V 2016) has been used for the risk assessment of grain formulation containing bromadiolone. This value can be used for the product containing 25 ppm since no effect of the concentration on the dermal absorption is expected at this low concentration.

Renewal:

No new data submitted.

The active substance has a low vapour pressure, therefore the potential for evaporation is low, and hence the potential for inhalation exposure is low. Inhalation exposure is only of concern during the formulation process where the active substance has a potential for becoming airborne when mixed with dry bait ingredients. In the case of wax blocks, inhalation exposure is irrelevant. Inhalation exposure from handling grain bait during loading/application and cleaning is also proposed as negligible. The only relevant inhalation exposure is assumed to be that from the decanting of loose grain, pellets and granules due to the potential release of airborne dusts.

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

***Key Endpoints for Exposure Assessment***

The derivation of an acceptable level of exposure value for single use (AELacute) is based on the teratogenicity study in rabbits submitted by Task Force. It is based on the LOAEL of 2 µg/kg bw, using a safety factor of 600 (10 for interspecies and 10 for intraspecies variability, 2 for using LOAEL instead of NOAEL and an extra factor of 3 for severity of effects) and with correction of 70% oral absorption, resulting in an AELacute of 0.0023 µg/kg bw. To derive an AELmedium, for repeated exposure, the subchronic study in rabbit submitted by Task Force is used. The NOAEL in this study is 0.5 µg/kg bw based on the prolonged prothrombin time seen at 1 µg/kg bw. With a safety factor of 300 and with correction of 70% oral absorption, this would lead to an AELmedium, chronic of 0.0012 µg/kg bw.

**3.3.3.1. Exposure to professional users**

|  |  |  |
| --- | --- | --- |
| **MG/PT** | **Field of uses envisaged** | **Likely concentrations at which a.s. will be**  **used** |
| Main group 03; PT 14 | **Professional uses** | |
| Rodenticide used in and around buildings Use in sewerage (only against rats) | 0.005% w/w |
| **Non-professional uses** | |
| Rodenticide used in and around buildings | 0.005% w/w |

There are two groups of humans which may be potentially exposed to the rodenticide baits : those who handle, apply and dispose of the product or other residues such as carcasses or faeces (direct exposure) and those who may be incidentally exposed while the product is in use (incidental exposure).

**Method of application**

Control bait is made of grain to which the active substance has been added. These Bromadiolone baits are used indoors and outdoors to kill mice and rats, in non-agricultural open areas and in waste dumps: they are placed at the appropriate places in bait stations or covered under a curved tile, a wooden board or in a piece of tube; the animals eat some of the product and die.

Baits must be 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. Preferably bait stations will be used where the bait can't be hidden, fixed or locked up.

The common strategy is to explore the site, locate runs, burrows, droppings or signs of damage and place the bait boxes at entry points into buildings and around areas where 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.

For house and field mice control, the recommended dose is 10 to 30 g per bait point every 2 to 5 meters.

For rat control, the recommended dose is 30 to 60 g of bait every 5 to 10 meters.

There are three phases for the human exposure: - Application phase:

Application of rodenticides by professionals and non-professionals.

In and around buildings, in open areas and in waste dumps the product is applied manually, at measured amounts, in bait boxes or covered. Professional users are assumed to wear protective gloves when handling the product unlike amateur users.

Bait points are controlled regularly. Any bait eaten or damaged has to be replaced. Depending on infestation rate, an advised frequency of inspection is 3 to 5 days. During the bait inspections, also a search in the zone will be done for dead rodents.

- Use phase:

Post-application, *i.e.* from the use of rodenticide products and from contact with the product (*e.g*. residential exposure including indoor air contamination, contact with the product during use). The use phase is the period when the biocidal product is waiting to be consumed by the target organism. This means that no primary exposure of humans is intended and should not take place (please refer to point 3.2.4 Secondary exposure).

- Disposal phase:

Disposal (including handling of surplus formulated product, burning/incineration, dumping, empty containers, dead rodents (carcasses) disposal).

When no further bait take is observed, bait stations must 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.

**Human exposure assessment**

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

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Exposure path** | **Industrial use1)** | **Professional use2)** | **General public3)** | ***via* the environment4)** |
| Inhalation5) | Not appropriate | Yes | Yes | No |
| Dermal6) | Not appropriate | Yes | Yes | No |
| Oral | Not appropriate | No | Yes | No |

1. Industrial use (manufacture of active substance and formulation of products) is not covered by BPD. Workers in formulation manufacture are not exposed to levels of a.s. that would affect blood clotting.
2. Includes non-trained professionals.
3. Indirect exposure due to transient mouthing by infants is included in the scenarios for the general public.
4. According to the TNsG, indirect exposure *via* the environment is considered to be of minor importance as the release of rodenticides to the environment is limited.
5. The skin is the main exposure route with a small proportion of inhalation exposure to dust when grain-based baits are mechanically handled by professionals. The active substance is of low volatility and it is incorporated at very low concentrations into a solid, non-volatile matrix. Therefore inhalation exposure is considered as negligible.

Except for the grain block bait which is always packed in individual sachets for both professionals and general public and for grain bait only for the amateurs, dermal contact with the product is a realistic scenario.The magnitude of human exposure to paste bait can be assessed by applying standard exposure models of TNsG[[9]](#footnote-9) for human exposure (2007) or the Harmonised approach for the assessment of rodenticides (anticoagulants) endorsed at TM II 2011 for professionals and amateurs users. Moreover, CONSEXPO 4.1 model can be used to assess the exposure to the biocidal product used by non­professionals.

The following basic primary exposure pathways have to be considered for a risk assessment in order to sum up the exposure of humans to Bromadiolone. The main exposure path is direct skin contact during the use of the biocidal product.

Ingestion is a secondary pathway or an accidental primary exposure during the use of the biocidal product.

Inhalation is considered as negligible.

According to the various pathways, the following absorptions will be applied in the assessment:

- Inhalatory uptake fraction: 1 (default value of 100%);

Inhalation rate: 1.25 m3/h (default value)

- Dermal uptake: 0.36% for a wax block, paste and grain block. grain bait was deemed  
to be best represented by a dermal absorption rate of 1.6% ( derived as a worst case for powder products in the bromadiolone CAR). 10% when no data is available on the formulation.

- Oral uptake fraction 1 (default value of 100% as a worst-case scenario), and 0.7  
(refinement as oral absorption is 71-77% in ADME study).

**Professional exposure**

For professional use, the operator is trained in the correct use of the bait, *i.e.* placement, number of bait points/boxes required based on the infestation rate area, the amount of bait or number of bait place packs per bait point/box and safe handling procedures.

The use of PPE - disposable gloves and a dust mask may be employed when decanting bait and disposable gloves may be employed when loading bait boxes and disposing of remaining bait and carcasses. However, when the bait is contained within a bait box there will be no exposure of the operator to the product.

PPE (coverall, boots and gloves) is required as standard when the bait is used in sewage systems.

***Exposure calculations – professionals***

The CEFIC/EBPF Rodenticides Data Development Group conducted an operator exposure study using flocoumafen (which may be considered a suitable surrogate for all other second generation anti­coagulants) to determine exposure during simulated use of rodenticide baits (*XXX*, unpublished, confidential). This study examined exposure to wax blocks (20g wax block baits, 5 blocks/bait box) and grain bait. Guidance is also taken from a confidential paper entitled “Harmonised Approach for Rodenticides” by the German Competent Authority, Bundesanstalt für Arbeitsschutz und Arbeitsmedizin (BAuA).

The daily exposure frequency and its division between different tasks are based on a survey organised by CEFIC (and based on a questionnaire answered by selected pest control companies in several EU countries), and on an agreement between Member States on the common approach for exposure assessment and ECB guidelines. Based on an in vitro study of formulated active (bait:saline incorporated bromadiolone 0.00255 w/w) and a representative wax block formulation (0.005 % w/w) a worst case value of 0.36% was obtained that was used for this risk assessment (Bromadiolone LOEP). Grain bait was deemed to be best represented by a dermal absorption rate of 1.6% ( derived as a worst case for powder products in the bromadiolone CAR).

The application of Control Bloc bait is regarded as a suitable worst case scenario for Control Paste and Control Bar products. In the Chambers study operators secured 5 compressed wax blocks (each of 20g, in total 100g bait per box) into a bait station by pushing bait mounting pegs in the stations through holes in wax blocks. The paste is individually packed in a filter paper bag thus minimising dermal contact. The cluster bait is also packed in individual sachets for both professionals and general public use. Considering the packaging of the paste and cluster grain products block bait values are considered appropriate as worst case.

The Chambers study determined exposure from the decanting phase from the following scenario: 3kg grain bait is decanted from 25kg drums into a 10L plastic bucket (termed 1 manipulation). Decanting of 3kg portions are performed 1, 5, and 10 times. The results show an increase in exposure with increasing manipulations. The determined value is lower than that used by Finland in their exposure estimates in the CAR. The proposed value of **52.34mg (of grain bait) per decanting of 3kg grain bait** is determined to represent the dermal exposure for this manipulation. The following assessment considers both the total used amount of grain in the decanting process and the number of bait station manipulations per day.

For professional operators the potential total daily dermal exposure (assuming the previously agreed number of 63bait station loadings from TM III/10 is applied and a total of 200g bait is applied per bait station, thus requiring 12.6kg grain bait in total) from the decanting-phase is **220mg** grain product per day (i.e. 52.3mg X 12.6kg / 3kg).

***Dermal Exposure during the loading and placement of bait stations:***

The Chambers study determined exposure from the application phase from the following scenario: 5 operators transferred 200g of loose grain bait from a 10L bucket using a plastic scoop into a bait station, this was repeated to give a total of 1, 5 and 10 manipulations. The proposed value of **2.04mg (of grain bait) per bait station application** is determined to represent the dermal exposure for this manipulation. If we consider the total daily number of applications to 63 bait stations then this represents a total calculated daily dermal exposure of **128mg** grain product per day (i.e. 2.04mg X 63). No linear relationship was found between exposure and the handled amount of grain per bait station, therefore the value of 2.04mg per bait station application is assumed regardless of the total amount of grain bait loaded into each bait station.

***Dermal Exposure during the cleaning of bait stations:***

The Chambers study determined exposure from the cleaning phase from the following scenario: 5 operators emptied a loaded bait station containing 200g of grain bait, into a 10L bucket. This was repeated to give a total of 1, 5 and 10 such manipulations. The proposed value of **3.79mg (of grain bait) per bait station manipulation** is determined to represent the potential dermal exposure for this activity. If we consider the total daily number of cleaning manipulations to be done on 16 bait stations then this represents a total calculated daily dermal exposure of **60.6mg** grain product per day (i.e. 3.79mg X 16). No linear relationship was found between exposure and the handled amount of grain per bait station, therefore the value of 3.79mg per bait station cleanup is assumed regardless of the total amount of grain bait emptied from each bait station.

***Inhalation Exposure:***

A pilot study (*XXX*, unpublished, confidential) done previously determined the only relevant inhalation exposure occurred during the decanting of loose treated grain. Inhalation exposure measurements from the handling of grain bait during loading and cleaning phases was negligible (similar results obtained for wax blocks). Inhalation exposure is only assessed for the decanting phase.

***Inhalation Exposure during the decanting of grain bait:***

The Chambers study determined exposure from the decanting phase from the following scenario: 3kg grain bait is decanted from 25kg drums into a 10L plastic bucket (termed 1 manipulation). Decanting of 3kg portions are performed 1, 5, and 10 times. A statistical comparison of the inhalation data for 5 and 10 manipulations of these 3kg grain portions indicates no difference between the datasets. This implies that the inhalation exposure is similar whether 3kg, 15kg or 30kg of grain is decanted in total. The proposed 75th percentile air concentration value of **9.62mg/m3 (of grain bait) per decanting event of grain bait** is determined to represent the inhalation exposure for this manipulation. If we consider the total daily number of 63 bait stations for loading with 200g in each, then a total of 12.6kg of treated grain is required. The results of the Chambers Study indicate that the total inhalation exposure to grain dusts will be **9.62mg/m3** air and that the time required for 5 and 10 X 3kg manipulations varied from 1 – 4 minutes. For the purposes of exposure assessment the following values are taken as defaults: total time for decanting = 5 minutes; inhalation rate = 1.25m3/hr; inhalation absorption = 100%; operator body weight = 60kg.

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

|  |  |
| --- | --- |
| **Pest Control Operator, No PPE:** | |
| **Inhalation Exposure:** | |
| Air concentration of dusts from the decanting phase | **9.62mg/m3** |
| Exposure to dusts inhaled while decanting: (respiration 1.25m3/hr, 5min decanting time)  Systemic dose from inhaled dusts: (inhalation absorption 100%, bw 60kg) | 9.62 mg/m3 X (1.25m3/hr X 5/60) = 1.002 mg  (1.002 mg / 60kg) X (0.005 / 100) =  **8.35×10-7 mg/kg** |
| **Dermal Exposure:** | |
| Amount of exposure to product (75th percentile) following decanting of 12.6kg treated grain. | **220 mg** |
| Amount of bromadiolone on fingers/hands (0.005% in grain) | 220 mg X (0.005 / 100) = 1.1X10-2 mg |
| Amount of exposure to product (75th percentile) during loading and placement of 63 bait stations in one day.  Amount of bromadiolone on fingers/hands (0.005% in grain) | (2.04 mg per bait station) **128mg**  128 mg X (0.005 / 100) = 6.4X10-3 mg |

|  |  |
| --- | --- |
| Amount of exposure to product (75th percentile) during clean-up and disposal of 16 bait stations  Amount of bromadiolone on fingers/hands (0.005% in grain) | (3.79 mg per bait station) **60.6mg**  60.6 mg x (0.005 / 100) = 3.0x10-3 mg |
| Total Dermal dose of product dusts per day: | (1.1x10-2 mg + 6.4x10-3 mg + 3.0x10-3 mg)  =  2.04x10-2 mg |
| Total Dermal Systemic dose per day (bromadiolone concentration 0.005%, dermal absorption 1.6%, bw 60 kg). | (2.04x10-2 mg x (1.6/ 100)) / 60kg = 5.5x10-6 mg/kg |
| Total Systemic Dose per day: (Inhaled dose + dermal dose) | (5.5x10-6+ 8.35x10-7) mg/kg =  **6.3×10-6 mg/kg bw/day**  **0.0062 tg/kg bw/day** |
| Expressed as a % of the AEL: |  |
| AEL = 0.0012 μg/kg bw/day | **516%** |
|  |  |
| **Pest Control Operator,With PPE (gloves and Mask[90% reduction in exposure])** | |
| Default 10-fold reduction of exposure. | **0.00062 tg/kg bw/day** |
| Expressed as a % of the AEL: |  |
| AEL = 0.0012 μg/kg bw/day | **52%** |
|  |  |
|  |  |
|  |  |
| **Non-Trained Professional (e.g. farmer), No PPE:** | |
| Amount of exposure to product (75th percentile) during loading and placement a single bait station.  Amount of bromadiolone on fingers/hands (0.005% in grain)  Systemic dose after a single manipulation: (assuming 1.6% dermal absorption, bw 60kg)  Amount of exposure to product (75th percentile) during clean-up of a single bait station.  Amount of bromadiolone on fingers/hands after 1 manipulation (0.005% in grain)  Systemic dose after a single manipulation: (assuming 1.6% dermal absorption, bw 60kg)  Systemic dose resulting from application of grain product to 10 bait sites plus 10 bait sites cleaned per day, no PPE (bromadiolone  concentration 0.005%, dermal absorption 10%, bw 60 kg). For non-trained professionals and amateurs, 10 manipulations per day  are assumed in this risk assessment because non-trained‑ | 2.04 mg  2.04 mg x(0.005 / 100) = 1.02x 10-4 mg  (1.02 x 10-4 mg x (1.6 / 100)) / 60kg = 2.7x 10-8 mg/kg  3.79mg  3.79 mg x(0.005 / 100) = 1.875x 10-4 mg  (1.875 x 10-4 mg x (1.6 / 100)) / 60kg = 5.00x 10-8 mg/kg  ((2.7 x 10-8 mg/kg x 10)  + (5.00 x 10-8 mg/kg x 10)) =  **7.7 x 10-8 mg/kg/day**  **0.0001 tg/kg bw/day** |

|  |  |
| --- | --- |
| professionals (e.g. farmers) and amateurs are expected to handle much smaller amounts of baits daily, baits are pre packed in polyethylene sachets, thus, the exposure is at a lower level than for  the pest control operators. In addition decanting is not taken into account for these users. |  |
| Expressed as a % of the AOEL: |  |
| AEL = 0.0012 μg/kg bw/day | **8%** |
| **Non-Trained Professional (e.g. farmer), With PPE (gloves):** | |
| Default 10-fold reduction of exposure. | **7.7 x 10-9 mg/kg/day**  **0.00001 μg/kg bw/day** |
|  |  |
| Expressed as a % of the AOEL: |  |
| AEL = 0.0012 μg/kg bw/day | **0.8%** |
|  |  |

* **Major change and renewal applications – 2017**

No new data submitted.

The conclusion remains unchanged.

**3.3.3.2. Exposure to non-professional users**

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

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

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Product type** | **Exposure scenario** | **PPE** | **Inhalation uptake** | **Dermal uptake** |
| 14 | Non-professional (amateur) | None | Not relevant | 5.00× 10-8 mg/kg 0.00005 μg/kg bw/day |
| 14 | Non- professional (amateur) | None | Not relevant | 7.7 x 10-8 mg/kg/day 0.0001 μg/kg bw/day |

1) scenario 1, 2) scenario 2.

Scenario 1: No dermal contact during placing of baits due to sealed bait boxes. Potential exposure is only during clean-up. Default exposure value for cleanup is 3.79mg product per bait site, bromadiolone present at a concentration of 0.005% (w/w), 60kg body mass, 1.6% dermal absorption value. The value is calculated from the cleanup exposure per bait station of ((5.00×10-8 mg/kg) × 10).

Scenario 2: Assuming that conventional bait boxes are loaded then the exposure is equal to that of the non-trained professional (e.g. farmer) with no PPE.

* **Major change and renewal applications – 2017**

Major change:

Only non-propfessional uses are concerned by the major change.

Taking into account the decrease of active substance in CONTROL 25, the risk assessment is covered and no change in the conclusion is expected.

Renewal:

No new data submitted.

The conclsuion remains unchanged.

**3.3.3.3. Exposure to children/workers/general public**

Bait points should be covered or protected in such a way to prevent access to the bait. However, the ingestion of bait by infants has been assessed as a potential secondary exposure route associated with the use of Bromadiolone in rodenticide products. Secondary exposure is anticipated to be acute in nature. Two different scenarios of secondary exposure are available, the ‘handling of dead rodents’ scenario and the ‘transient mouthing of poison bait’ scenario. The former is excluded from the risk assessment due to unrealistic assumptions. The estimated exposure for the ‘transient mouthing of poison bait’ scenario is either 2.5×10-2 mg/kg or 5.0×10-5 mg/kg, depending on the default assumptions. This results in Margin of Exposure MOE values of 0.004 or 10 (NOAEL modified for severity of effect and use of LOAEL), respectively. It shows that infants are at significant risk for secondary exposure, i.e. there is no safe use for children.

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

**Oral exposure infant.** TNsG Assumptions: Transient mouthing of poison bait (10mg) treated with repellent: (10mg X 0.00005) / 10kg bw

**Transient mouthing infant.** User Guidance Assumptions: Transient mouthing of poison bait (5000mg) without repellent; (5000mg X 0.00005) / 10kg bw

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Total dose (mg/kg b.w./day)** | | **% AELacute (0.0023 µg/kg b.w.)** |
| Oral exposure infant | 0.075 |  | 3.2 \* 106% |
| Transient mouthing infant | 0.000 | 035 | 1521 |

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

**3.3.3.4. Exposure to consumers from residues in food**

Not applicable.

**3.3.3.5. Overall Summary**

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

### Risk Characterisation for Human Health

**3.3.4.1. Professional users**

The exposure assessment for professional pest control operators (PCOs) under reasonable worst case assumptions (63 loadings and 16 clean-ups/day), as presented in section 3.3.3.1, yielded a potential dermal exposure leading to a systemic dose 0.0062μg/kg/day day for an unprotected operator during bait handling operations. Comparison to calculated NOAEL for MOE shows that the use of rodenticide baits containing 0.005% bromadiolone results in a margin of exposure of 18

Since pest control operators wear protective gloves by default during pest control operations, a refined assessment is conducted. The resulting margin of exposure (MOE = 188) indicates that the use of rodenticide baits containing 0.005% bromadiolone does not cause a risk for PCOs if gloves are worn. The exposure assessment for non-trained professionals (e. g., farmers) under reasonable worst case assumptions (ten loadings and ten clean-ups/day), yielded a potential dermal exposure leading to a systemic dose of 0.0001μg/kg/day day for an unprotected person. Without PPE, the resulting margin of exposure (MOE = 1167) indicates that use of rodenticide baits containing 0.005 % bromadiolone is not a risk at the stated exposure frequency. A refined assessment was, conducted since wearing of protective gloves is recommended in the instructions for use. The resulting margin of exposure (MOE =11667) indicates a high level of protection for non-trained professional users when gloves are worn.

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

* **Major change and renewal applications - 2017:**

No new data submitted.

The conclsuion remains unchanged.

**3.3.4.2. Non-professional users**

Grains are supplied either in pre-sealed bags or for professionals as loose, treated grain for use in covered/protected bait points or refillable bait boxes. An exposure assessment has been performed taking into account potential exposure both from application and post-application tasks as a worst­case scenario. In the calculations, amateurs were assumed to load 10 bait points and clean 10 bait points per day in the absence of PPE. The estimated daily systemic dose, 0.0001tg/kg bw/day, results in an MOE value of 1167 showing that there is no risk to amateurs.

* **Major change and renewal applications - 2017:**

Major change:

Only non-propfessional uses are concerned by the major change.

Taking into account the decrease of active substance in CONTROL 25, the risk assessment is covered and no change in the conclusion is expected.

Renewal:

No new data submitted.

The conclsuion remains unchanged.

**3.3.4.3. Children/Workers/general public**

As a potential secondary exposure route, associated with the use of bromadiolone in rodenticide products, ingestion of wax block bait by infants has been assessed. Secondary exposure is anticipated to be acute in nature. The estimated exposure for the scenario, 2.5×10-2 mg/kg/day or 5.0×10-5 mg/kg/day, depending on the default assumptions, results in MOE values of 0.004 or 10 (NOAEL modified for severity of effect and use of LOAEL), respectively indicating that infants are at risk of poisoning. This should be addressed by ensuring all bromadiolone products targeted for amateur use are provided in sealed packs and tamper resistant bait boxes with a bittering agent. The potential exposure due to dermal contact with poisoned rodents is not included in the risk assessment because the available scenarios are unrealistic.

**3.3.4.4. Consumers from residues in food**

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

**3.3.4.5. Overall Summary**

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

Using both the MOE and AEL approaches for risk assessment indicates that there is a satisfactory margin between the predicted exposure and the NOAEL (LOAEL) for intended uses by trained professionals with PPE, untrained professionals and amateurs (with and without PPE). The product is deemed suitable for authorisation and appropriate personal protective equipment is advised.

Secondary exposure from transient mouthing of the product exceeds the AEL reference value (0.0023tg/kg/day), both with the assumption of 0.01 g and 5 g of product ingested by infants. This is of concern. There is no margin of safety using the existing data and models. There is no safe scenario for indirect exposure if estimated according to TNsG and User Guidance. Mitigation and protection measures such as the inclusion of bittering agents and the enclosure of product in sealed packs and tamper resistant bait boxes are essential to reducing the risk of secondary exposure. Baits should not be placed where food, feeding stuffs or drinking water could be contaminated.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Workplace operation** | **PPE** | **Exposure path** | **Dose**  **(μg/kg/day)** | **MOE** | **%AEL** |
| Trained Professional: Decanting placing of baits and clean-up. | None | Dermal, hands | 0.0062 | 18 | 516 |
| Trained Professional: Decanting placing of baits and clean-up. | Protective gloves mask | Dermal, hands | 0.00062 | 188 | 52 |
| Non-Trained Professional: Placing of pre-packed baits and clean-up | None | Dermal, hands | 0.0001 | 1167 | 8% |
| Non-Trained Professional: Placing of pre-packed baits and clean-up | Protective gloves | Dermal, hands | 0.00001 | 11667 | 0.8% |
| Amateur:  Placing of pre-packed baits and clean-up | None | Dermal, hands | 0.0001 | 1167 | 8% |
| Secondary Exposure Transient Mouthing of bait by infants | -- | Oral | 5.0×10-5 (TNsG)  2.5×10-2  (User Guidance) | 10  0.004 |  |

### Hazard assessment for the environment

The Swedish Competent Authority completed an assessment report of the active substance Bromadiolone in 2008 (updated 2010). The environmental fate and behaviour and ecotoxicology of the active substance were examined extensively according to the standard biocide legislative information requirements.

The results of this environmental assessment can be found in the CAR. No further fate and behaviour or ecotoxicology studies were identified as necessary to support the authorisation of the active substance. The endpoints and labelling regarding the environmental risks for the active substance must be taken into consideration for the product.

An overview of the EU review of environmental fate and behaviour and ecotoxicology for Bromadiolone are now presented.

**3.3.5.1. Environmental fate and behaviour of the active substance**

Bromadiolone is not readily biodegradable under environmentally relevant conditions or during sewage treatment processes. It is also not inherently biodegradable. No hydrolysis was found at the investigated pH 7, and 9, so hydrolysis of Bromadiolone is not expected to be a significant process in the environment. Photolysis of Bromadiolone in aqueous solution is rapid with a half-life of 12 hours or less. Degradation studies in soil have not been performed by the Bromadiolone Task Force and their justification for not conducting the studies state that the release of Bromadiolone is only local. This justification has been accepted.

Bromadiolone is strongly adsorbed to soil and the KOC values range between 1563 and 41600 ml/g, which corresponds to ‘slightly mobile’ to “non-mobile” according to the SSLRC classification index. It can be estimated that Bromadiolone, even if released indirectly to soil in small quantities, is unlikely to reach groundwater in significant quantities.

The rapid photolysis rate in air (t1/2 ca 2 hours), the low vapour pressure of Bromadiolone and the low Henry’s law constant together show that the active substance is not expected to volatilise to or persist in air in significant quantities.

A strong tendency to adsorb to sediment combined with a high degree of photo-instability means that Bromadiolone is unlikely to remain in the water column of surface waters.

BCF was derived by calculation from log Kow, resulting in BCF values of 339 to 575. It can be concluded that Bromadiolone has a slight potential to bioaccumulate.

**3.3.5.2. Environmental hazard of the active substance (ecotoxicology)**

No further ecotoxicological studies were identified as necessary to support the authorisation of the active substance and no studies were submitted to support the authorisation of the biocidal product.

**Table 3.3.5.2-1 Summary of the environmental and eco-toxicological data for the active substance Bromadiolone**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Parameter** | **Test material** | **Species** | **Result** | **Classification** | **Ref.** |
| Lethality/ LC50  Acute toxicity (Fish) – aquatic compartment | Bromadiolone | Rainbow trout | Bromadiolone is acutely toxic to fish with an LC50 of 2.86  mg/l (nominal concentration), | 99/45 Toxic to aquatic  organisms  1272/2008 No  classification | XXX |
| **Acceptability (Y/N):** Y | | **Method:** OECD TG 203 | | **GLP (Y/N):**  Y |
| **Comments:** No further studies on toxicity to fish have been submitted with the argument that there is only limited and local exposure to fish. These arguments are considered acceptable. | | | | |
| Lethality/ LC50  Acute toxicity (Invertebrates)  – aquatic compartment | Bromadiolone | Daphnia Magna | Bromadiolone is acutely toxic to invertebrates with an LC50  of 5.79 mg/l (nominal concentration), | 99/45 Toxic to aquatic  organisms  1272/2008 No  classification | A 7.4.1.2 |
| **Acceptability (Y/N):** Y | | **Method:** OECD 202 | | **GLP (Y/N):**  Y |
| **Comments:** No further studies on toxicity to invertebrates have been submitted with the argument that there is only limited and local exposure to the water compartment. These arguments are considered acceptable. | | | | |
| Growth  inhibition on  Algae 72h  EC50 – aquatic compartment | Bromadiolone | *Pseudokirchneriella subcapitata* | Bromadiolone is acutely toxic to alga with an  EC50 of 1.14  mg/l (nominal  concentration), | 99/45 Toxic to aquatic  organisms  1272/2008 No  classification | A 7.4.1.3 |
| **Acceptability (Y/N):** Y | | **Method:** OECD TG 201 | | **GLP (Y/N):**  Y |
| **Comments:** The alga was found to be the most sensitive of the three aquatic organisms tested, with an ErC50 of 1.14 mg/L. | | | | |
| Growth  inhibition of aquatic plants | Bromadiolone | *Lemna minor* | No toxicity was detected at any  stages of the study. | No  classification | A 7.5.3.5.2 |
| **Acceptability (Y/N):** Y | | **Method:** OECD Guideline Lemna Growth Inhibition Test (March 2006) | | **GLP (Y/N):**  Y |
| **Comments:** The two most significant points are first that the solubility of the test substance was very low compared to what was found both in water solubility tests and in other aquatic studies and second that only one test concentration was used. The study gives no information that is useful for the risk assessment and will not be used further. | | | | |
| Microorganisms Aerobic microbial processes in aquatic | Bromadiolone | Activated sludge – 3 hours | EC50 = 132.8 mg/L (nominal) | No  classification |  |
| **Acceptability (Y/N):** Y | | **Method:** OECD TG 209 | | **GLP (Y/N):** Y |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| compartment | **Comments:** The test with micro-organisms in activated sludge showed that concentrations that cause inhibition of these micro-organisms are high indicating that it is not likely that Bromadiolone will have a negative impact on the microbial processes in a sewage treatment plant. | | | | |
| Effects on sediment dwelling organisms | N/A | N/A | N/A | N/A | N/A |
| **Acceptability (Y/N):** N/A | | **Method:** N/A | | **GLP (Y/N):** N/A |
| **Comments:** The applicant for active substance approval justifies the absence of studies on sediment dwelling organisms with the argument that there only will be limited exposure for organisms in the aquatic compartment. The RMS for active substance approval (Sweden) considers the applicant’s justification acceptable. When no tests on sediment toxicity have been performed the PNEC for sediment dwelling organisms can be calculated with the equilibrium partitioning method according to TGD II, section 3.5.2.3., equation 70. | | | | |
| Toxicity to earthworms | Bromadiolone | *Eisenia fetida* | No effects of Bromadiolone were found on earthworms in any of the concentrations. | No  classification | A7.5.1.2 |
| **Acceptability (Y/N):** Y | | **Method:** OECD TG 207 | | **GLP (Y/N):** Y |
| **Comments:** Tests with micro-organisms and plants are not considered necessary bearing in mind the absence of toxicity observed in this study. | | | | |
| Toxicity to mammals | Bromadiolone | Rat | LD50  1.31 mg/kg bw | Bromadiolone should be classified as Very Toxic (T+) and labelled with the risk phrases R 28 “Very toxic if swallowed” and R27 “Very toxic in contact with skin” | XXX |
| **Acceptability (Y/N):** Y | | **Method:** OECD TG 401 | | **GLP (Y/N):** Y |
| **Comments:** The corresponding acute rat LD50 from the other applicant LiphaTech S.A.S was slightly lower, 0.56-0.84 mg/kg bw/d. | | | | |
| Acute toxicity to birds | Bromadiolone | Bobwhite quail | LD50 =  134 mg/kg bw | n/a | XXX |
| **Acceptability (Y/N):** Y | | **Method:** OPPTS 850.2100 | | **GLP (Y/N):** Y |
| **Comments:** | | | | |
| Long-term toxicity to birds | Bromadiolone | Bobwhite quail | 5-day LC50 = 62 mg/kg food | n/a | XXX |
| **Acceptability (Y/N):** Y | | **Method:** OPPTS 850.2100 | | **GLP (Y/N):** Y |
| **Comments:** | | | | |
| Reproductive toxicity to birds | Bromadiolone | Japanese quail | NOEC = 0.039 mg/kg | n/a | XXX |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  | bw/day 0.26 mg/L drinking water |  |  |
| **Acceptability (Y/N):** Y | | **Method:** OECD TG 206 | | **GLP (Y/N):** Y |
| **Comments:** | | | | |

**3.3.5.3. Conclusion**

**Aquatic:**

Bromadiolone is toxic to fish, aquatic invertebrates and algae under the Classification criteria as set out Directive 99/45 (DPD). Another active substance applicant’s data indicated Bromadiolone was very toxic to aquatic organisms based on the results of an acute algae study. Bromadiolone is classified Aquatic Acute 1; H400 and Aquatic Chronic 1; H410 using the Classification criteria of the CLP regulation 1272/2008.

The most sensitive organism in the aquatic tests was green alga with a nominal ErC50 of 1.14 mg/L. This gives a **PNECwater** of 1.14/1000 (acute studies available only)/3 (uncertainties due to photolytic degradation) **= 3.8 x 10-4 mg/L**.

The test with micro-organisms in activated sludge showed that concentrations that cause inhibition of these micro-organisms are high indicating that it is not likely that Bromadiolone will have a negative impact on the microbial processes in a sewage treatment plant. This gives a **PNECSTP** of 132.8/100 (No NOEC or EC10 was available) **= 1.33 mg/L.** There was a study conducted on aquatic plants and it indicated no toxicity however the study was not considered useful for the risk assessment/characterisation process.

There justifiably were no studies on sediment dwelling organisms. The PNEC for sediment dwelling organisms was calculated using the equilibrium partitioning method. In order to obtain a value that could be used in the equation, an average value of 14770 ml/g was calculated from four of the five soils available. The **PNECsediment = 0.83 mg/kg w/w**

**Terrestrial:**

Exposure of soil organisms to Bromadiolone by direct contamination of soil may occur following use in and around buildings and waste dumps. It is also possible that soil may become exposed following the spreading of sewage sludge from a sewage treatment plant that has been exposed to Bromadiolone used in sewers.

No effects of Bromadiolone were found on earthworms in any of the concentrations. The PNECsoil of 918 mg/kg ww (1331 mg/kg/day adjusted for soil humidity)/1000 = 0.918 mg/kg ww. Tests with soil micro-organisms and terrestrial plants were not considered necessary bearing in mind the absence of toxicity observed in the earthworm study. Additionally, Bromadiolone is not expected to be toxic to soil micro-organisms or terrestrial plants on the basis of the mode of action.

When one terrestrial study is only available the PNEC should also be calculated from the aquatic toxicity data using equilibrium partitioning calculations giving a result of **PNECsoil =** (443/1700) x 3.8 x10-4 x 1000 **= 9.9 x 10-2 mg/kg.** Due to the uncertainties associated with using the **PNECsoil** determined by the two active substance applicants the value determined using the equilibrium partitioning calculations was used.

Bromadiolone is very toxic to birds. Effects were found in birds in acute, short-term and long term tests. Consumption of bait on a single occasion led to a body concentration of Bromadiolone of 96-188 mg/kg bw and a lethal effect. A single dose of 62.5 mg/kg bw caused sublethal effects, since cowering was observed at this dose. If 79μg Bromadiolone per kg bw and day is consumed during a 42 day exposure period effects can be observed that might lead to effects on the population level. The long-term PNEC for birds was determined by using the NOEC values calculated from the bird reproduction study. The **PNECoral** in birds is 0.039 mg/kg bw/day/30 **= 0.0013mg/kg bw/day.** Bromadiolone is also very toxic to mammals. According to the mammalian toxicity data, Bromadiolone should be classified as Very Toxic (T+) and labelled with the risk phrases R 28 “Very toxic if swallowed” and R27 “Very toxic in contact with skin”. Due to lack of inhalation data presented in this dossier a classification proposal for acute inhalation toxicity cannot be made. However, the RMS is aware of other data indicating that classification with T+; R26 is appropriate. The **PNECoral** in mammals **= 0.0000056 mg/kg bw/day.** These PNECoral values were used in risk characterisation of primary and secondary poisoning.

**Bioaccumulation:**

The quality of the bioaccumulation study (A 7.4.3.3.1) was not acceptable; however the results indicated long term toxicity at a concentration as low as 0.14μg/L. These effect concentrations are several orders of magnitude lower than the concentrations found to cause acute toxicity. Two bioconcentration studies have been conducted in the tissues of fish under artificial conditions in the laboratory. In a study with bluegill sunfish the maximum bioconcentration factor for Bromadiolone was 460 for whole fish. In non-edible tissues the maximum BCF was 1,658 and in edible tissues 161. In a second study with channel catfish, the bioconcentration factors in whole fish ranged from 24 (day 1) to 74 (day 14). In edible and non-edible tissues the maximum bioconcentration factors were 59 and 641, respectively. Two fish bioconcentration studies were performed by the Task Force, but both failed. Taking all the results together, the fish studies are of low reliability, and therefore BCF was derived by calculation from log Kow, resulting in BCF values of 339 to 575. It is concluded that Bromadiolone has the potential to bioaccumulate.

**Data requirements not addressed:** None

**3.3.5.4. Environmental hazard of the biocidal product**

The products in the EU- review program for inclusion of the active substance in Annex I of Directive 98/8/EC were bait blocks (solid wax block bait formulation) and coral grain containing Bromadiolone. There were no aquatic or terrestrial (earthworm, other invertebrate, avian toxicity or mammals) data generated on bait blocks or cereal grain containing Bromadiolone. The aquatic, terrestrial, avian and mammalian toxicity data used for the assessment of the biocidal product was based on data determined in the Bromadiolone active substance studies.

No new ecotoxicology studies were performed for the biocidal product being assessed.

**Summary of environmental and eco-toxicological data for the biocidal product containing Bromadiolone:**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Parameter** | **Test material** | **Species** | **Result** | **Classification** | **Ref.** |
| No tests  conducted using biocidal product | n/a | n/a | n/a | n/a | n/a |
| **Acceptability (Y/N):** n/a | | **Method:** n/a | | **GLP (Y/N):** n/a |
| **Comments:** n/a | | | | |

**Conclusion:**

The most sensitive organism in the aquatic tests was green alga with a nominal ErC50 of 1.14 mg/L.

The test with micro-organisms in activated sludge showed that concentrations that cause inhibition of these micro-organisms are high indicating that it is not likely that Bromadiolone will have a negative impact on the microbial processes in a sewage treatment plant.

There justifiably were no studies on sediment dwelling organisms.

No effects of Bromadiolone were found on earthworms in any of the concentrations.

Effects were found in birds in acute, short-term and long term tests. Consumption of bait on a single occasion led to a body concentration of Bromadiolone of 96-188 mg/kg bw and a lethal effect. A single dose of 62.5 mg/kg bw caused sublethal effects, since cowering was observed at this dose. If 79μg Bromadiolone per kg bw and day is consumed during 42 days effects can be observed that might lead to effects on the population level.

According to the mammalian toxicity data, Bromadiolone should be classified as Very Toxic (T+) and labelled with the risk phrases R 28 “Very toxic if swallowed” and R27 “Very toxic in contact with skin”. Due to lack of inhalation data presented in this dossier a classification proposal for acute inhalation toxicity cannot be made. However, the CA is aware of other data indicating that classification with T+; R26 is appropriate.

No further studies were identified as necessary.

**Data requirements not addressed:** None

**3.3.5.5. Environmental hazard of the co-formulants (substances of concern)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Identity** | | **Function** | **Content**  **(% w/w)** | **Classification** |
| **Common name** | **CAS No.** |
| Bromadiolone 2.5%, No Dye, 0.5% DB *containing Bromadiolone at 2.5%*  *XXX* | Mixture  *28772-56-7*  *XXX* | *Active substance*  *XXX* | 0.20  *0.005*  *XXX* | R50/53  XXX |
| XXX | XXX | XXX | XXX | No  classification |
| XXX  *XXX*  *XXX* | XXX  *XXX*  *XXX* | XXX  *XXX*  *XXX* | XXX  *XXX*  *XXX* | No  classification |
| XXX | XXX | XXX | XXX | No  classification |
| XXX | XXX | XXX | XXX | No  classification |
| XXX | Not relevant | XXX | XXX | No  classification |
| **TOTAL:** | |  | **100.00** |  |

None of the co-formulants are substances of concern for the environment. The Bromadiolone stock contains 2.5% active substance and 0.5% of a bittering agent which classifies R52/53. This stock is used to prepare the product. As the preparation contains less than 0.25% content of the product w/w it does not exceed the threshold value of 0.25% w/w of substances meaning it does not classify as Aquatic Chronic 1-4 H410-413 (R50/53).

### Exposure Assessment for the Environment

* **Major change and renewal applications - 2017:**

|  |
| --- |
| In the first authorization of the product CONTROL 25, the claimed used “waste dump” and “open areas” were assessed. Nevertheless, these uses were not proposed by the applicant at the renewal authorization. Therefore, the original assessment proposed below should not be taken into account for these two scenarios. |

An overview of the environmental exposure assessment for the biocidal product is presented in this section. The environmental exposure assessed during the review process and the current intended use is similar. Detailed calculations are provided in Annex VI which accompanies this Product Authorisation Report (PAR).

The rodenticide product is used by professional and amateur users. The product is intended for indoors use, in and around buildings and for outdoors uses in non-agricultural open areas and waste dumps. It is not supported for use in sewers; however the applicant has included this scenario in their application as a worst case scenario.

It is always used in the same manner for all these purposes. Bait points are placed throughout the infested areas with 10 to 30 g per bait point for mice and 25 to 100 g per bait point for rats. Application sites are located 2-5 m apart for mice and 5-10 m apart for rats. Shorter distance is used in severe infestations. The number of baits and the distances should be adapted to the infestation level. Bait points are inspected frequently and replenished when bait has been eaten.

Bait points are protected to help prevent access to non-target animals. In situations where bait boxes cannot be used, the bait is covered / protected such that non-target organisms cannot reach it. Dead rodents are removed for disposal in order to prevent them being eaten by non-target animals and birds. When no more bait is eaten and rodent activity stops, the remains of all baits are removed for disposal.

Based on the environmental fate and behaviour of Bromadiolone, as outlined in Annex VI of this Product Authorisation Report, the environmental exposure assessment was conducted.

**3.3.6.1. Aquatic compartment**

As mentioned previously the product is not supported for use in sewers but the scenario has been included as part of the risk assessment for the other scenarios. Therefore exposure to the aquatic compartment has been assessed through the STP route also. Based on worst case ESD assumptions the maximum predicted environmental concentration (PEC) of the active substance for microorganisms in the STP is 4.44 x 10-5 mg/L. The corresponding amount in surface water is 4.37 x 10-6 mg/L. The maximum permissible concentration by directive 80/778/EEC (amended by 98/83/EC) of 0.1 μg/L is not exceeded in surface waters. 9.90 x 10-4 mg/kg wet weight is predicted to occur in sediment during an emission episode. Full details of the calculations are contained in Annex VI.

**3.3.6.2. Atmospheric compartment**

Bromadiolone has a low vapour pressure (< 5x10-5 Pa) and Henry’s Law constant (4.25 x 10-4 Pa.m3mol-1). Release to air via water is expected to be negligible.

This is also supported by calculations using the TGD on risk assessment for percent release to air from a sewage treatment plant where no release to air is predicted. Releases to air from use of bait within covered/protected bait points or bait boxes are considered to be negligible.

Therefore, it can be considered that there are no releases to air of Bromadiolone from use or disposal phases.

**3.3.6.3. Terrestrial compartment**

Exposures of soil to the active substance occurs via direct (spillages) and disperse release (deposition by urine and faeces) after the use of the product in and around buildings, open areas and waste dumps. As mentioned previously the product is not supported for use in sewers however exposure to agricultural soil via spreading of sludge from an STP has been included as part of the worst case risk assessment.

Using ESD worst-case assumptions of the typical usage patterns and release mechanisms, the maximum concentration in agricultural soil (averaged over 30 d) after 10 years of sludge application from STP is 1.62 x 10-4 mg/kg wwt.

The highest concentration of Bromadiolone in soil following use in and around buildings is 0.0468 mg/kg wwt under ESD realistic worst case conditions (see table below). This scenario assumes the bait stations are filled 5 times during the campaign. The ESD estimates that given more realistic usage patterns only 2.6 fills of the bait are required. This, in conjunction with the 100 g per bait point recommended by the applicant, lowers the estimated soil concentration to 0.0097 mg/kg wwt.

For the open areas scenario ESD realistic worst-case conditions assume one application site is treated twice with the product. The fraction released during use and application is 0.25. The exposed soil area is assumed to be the lower half of the burrow wall surrounding an 8 cm diameter tunnel, with a soil mixing depth of 10 cm and up to 30 cm from the entrance hole. The amount of product used at each refilling in the control operation is not specified by the ESD. However, the Reviewer notes the ESD states *“* A typical initial dose for a rat hole in the Nordic countries is 100-200 g grain.hole-1. However, in e.g. France a typical dose for a rat hole is about 50-100 g product.*”* The applicant supports a dosage of 100 g bait per refill and this has been used in the exposure assessment. The local concentration arising in soil after a campaign is predicted to be 0.173 mg/kg wwt.

The default area for a waste dump defined in the ESD is 1 ha. If bait points are placed at distances of 5 m apart in a grid covering the entire dump this would yield a total of 441 points (21 x 21). 100 g in each bait point corresponds to a total loading of 44.1 kg of bait. This is higher than the default value considered in the ESD under realistic worst-case conditions (40 kg). Consequently the applicant’s exposure calculation is not sufficient to support this use. The Reviewer generated new exposure calculations for this use. The local concentration arising in soil after such a campaign is predicted to be 0.00817 mg/kg wwt. A more realistic campaign would use a total of 11 kg of bait resulting in a local concentration of 0.00204 mg/kg wwt.

|  |  |  |
| --- | --- | --- |
| **In and around buildings** | **Open areas** | **Waste dumps** |
| Amount of product used in control | Amount of product used at each | Area of waste dump: 1 ha |
| operation for each bait box: | refilling in the control operation: | Amount of product per station: |
| 0.25 kg (ESD), 0.1 kg (applicant). | 100 g | 100 g |
| Realistic worst-case: 21 day | Realistic worst-case: 6 day | Spacing between blocks: |
| campaign | campaign | 5 m (worst case), 10 m (realistic) |
| Bait stations: 10 | Bait stations: 1 | Total mass of product used: |
| No. of replenishments: 5 (2.6 | No. of replenishments: 2 | 21 x 21 x 100 g = 44.1 kg (worst |
| realistic) | Fraction of product released to soil | case) |
| Bait stations are 5 m apart. | during application: 0.05 | 11 x 10 x 100 g = 11 kg (realistic) |
| Fraction released due to spillage: | Fraction of product released to soil | No. of replenishments: 7 |
| 0.01 | during use: 0.2 | Fraction of active ingredient |
| Fraction ingested: 0.99 Spillage area: 0.09 m2 (0.1 m around station) |  | released to soil through urine, faeces and dead animals: 0.9. |
| Frequented area: 550 m2 (10 m around building) |  |  |

**3.3.6.4. Groundwater**

Exposure of groundwater may occur as a result of soil exposure which occurs via residues present in sewage sludge after using the product in sewers and via direct (spillages) and disperse release (urine and faeces) after the use of the product in the scenarios in and around buildings, open areas and waste dumps. As an indication for potential groundwater levels, the concentration in soil porewater in the various scenarios was examined. It should be noted that this is a worst-case assumption, neglecting transformation and dilution in deeper soil layers. A summary of the PECs obtained are presented in the table below. The calculated value for the open areas scenario exceeds the EU trigger value of 0.1 µg/L. However this figure is derived from a soil concentration value in a small localised area in the immediate vicinity of the baiting point. When taken in the context of a larger area (field, park, etc.) this figure would be several orders of magnitude lower. The same argument applies to the figure calculated for the in and around buildings scenario which is driven principally by direct release in the vicinity of the baiting point. In addition it must be noted that these two scenarios give a value for groundwater under industrial soil – not agricultural soil as specified by the ESD.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Scenario** | **In and around buildings** | | **Open area** | **Waste dumps** | | **Sewer system** |
|  | **Worst case** | **Realistic** |  | **Worst case** | **Realistic** |  |
| **PEC groundwater (mg/l)** | 2.55E-04 | 5.30E-05 | 9.43E-04 | 4.45E-05 | 1.11E-05 | 4.09E-07 |

**3.3.6.5. Primary & Secondary poisoning**

Detailed explanations and calculations for primary and secondary poisoning are found in Annex VI of this PAR.

The PNEC values are determined from the results presented in the Bromadiolone CAR and are also represented in the hazard assessment section in this section of the PAR.

**PNECoral values for birds and mammals exposed to Bromadiolone**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Organism group** | **Species / test** | **Results1** | **Assessment factor** | **PNEC**  **(concentration in food, mg/kg)3** | **PNEC**  **(dose, mg/kg b.w./d)3** |
| **Acute** | | | | | |
| Birds | Partridge, short-LC50= term toxicity study  (10 days) | 28.9 mg/kg  food | 3 000 | 0.00963 | 0.00120 |
| Mammals | Rats, 28 days repeated dose test | NOAEL2 =  2.5 \*10-3 mg/kg b.w./d | 300 | 1.67\*10-4 | 8.33\*10-6 |
| **Long-term** | | | | | |
| Birds | Japanese quail Reproduction test 42 days | NOEC = 0.039 mg/kg b.w./day | 30 | 0.0104 | 0.0013 |
| Mammals | Rabbit 90 days | NOAEL = 5\*10-4 mg/kg b.w./day | 90 | 0.000186 | 0.0000056 |

The empirical risk assumes direct or indirect consumption of the deployed baits. A summary of the main exposure calculation results are presented next:

**Primary poisoning:**

For primary poisoning the initial PECoral values assume that there is no bait avoidance by the non­target animals and that they obtain 100% of their diet in the treated area and have access to the product.

For the acute tier 1 assessment the PECoral is 50 mg/kg (Bromadiolone present at 0.005% w/w in the product) and is used in quantitative risk assessment for the acute and long-term situation.

For the acute tier 2 assessment the body weights, daily food intakes and estimates of Bromadiolone ingestion, based on sufficient bait being accessible to satisfy a day’s food intake requirement, are presented below for representative non-target mammals.

**Tier 2 Calculations of ETE for non-target animals consuming baits treated with 0.005% Bromadiolone**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Non-target animals** | **Typical body weight (g)a** | **Daily mean food intake (g dry weight/day)** | **Concentration of Bromadiolone in bait (mg/kg)** | **ETE, concentration of Bromadiolone after one meal (one day) (mg/ kg b.w.)** | |
| **Step 1** | **Step 2** |
| Tree sparrow | 22 | 7.6a | 50 | 17.3 | 12.4 |
| Chaffinch | 21.4 | 6.42a | 50 | 15.0 | 10.8 |
| Wood pigeon | 490 | 53.1a | 50 | 5.42 | 3.90 |
| Pheasant | 953 | 102.7a | 50 | 5.39 | 3.88 |
| Dog | 10 000 | 456b | 50 | 2.28 | 1.64 |
| Pig | 80 000 | 600c | 50 | 0.375 | 0.270 |
| Pig, young | 25 000 | 600c | 50 | 1.20 | 0.864 |

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

In the second tier assessment long-term exposure, also has to be taken into account in the evaluation of primary poisoning of rodenticides. The EC (expected concentration of active substance in the animal) after metabolism and other elimination is calculated.

**Expected concentration of Bromadiolone in the animal after one meal followed by a 24-hour elimination period**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Species** | **Estimated daily uptake of a compound (ETE) (mg/kg b.w./d)** | | **Fraction of daily uptake eliminated (number between 0 and 1) (EI)** | **Expected concentration of active substance in the animal (EC) (mg/kg b.w./d)** | |
| **Step 1** | **Step 2** | **Step 1** | **Step 2** |
| Tree sparrow | 17.3 | 12.4 | 0.3 | 12.1 | 8.68 |
| Chaffinch | 15.0 | 10.8 | 0.3 | 10.5 | 7.56 |
| Wood pigeon | 5.42 | 3.90 | 0.3 | 3.79 | 2.73 |
| Pheasant | 5.39 | 3.88 | 0.3 | 3.77 | 2.72 |
| Dog | 2.28 | 1.64 | 0.3 | 1.60 | 1.15 |
| Pig | 0.375 | 0.270 | 0.3 | 0.263 | 0.189 |
| Pig, young | 1.20 | 0.864 | 0.3 | 0.840 | 0.605 |

According to the guidance agreed at the 23rd Biocides CA meeting, EC5 values are used for quantitative risk assessment of primary poisoning in the long-term situation. Calculations of the expected concentrations (EC) for 5-days exposure considering elimination are calculated.

**ECoral for different relevant species**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Days** | **ECoral (mg/kg b.w./d)** | | | | | | |
| **Species** | **Tree sparrow** | **Chaffinch** | **Wood pigeon** | **Pheasant** | **Dog** | **Pig** | **Young pig** |
| Day 1 after first meal | 17.3 | 15.0 | 5.42 | 5.39 | 2.28 | 0.375 | 1.20 |
| Day 2 before new meal | 12.1 | 10.5 | 3.79 | 3.77 | 1.60 | 0.266 | 0.840 |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Day 3 before new meal | 20.6 | 17.9 | 6.45 | 6.41 | 2.72 | 0.449 | 1.43 |
| Day 4 before new meal | 26.5 | 23.0 | 8.31 | 8.26 | 3.50 | 0.577 | 1.84 |
| Day 5 before new meal | 30.7 | 26.6 | 9.61 | 9.56 | 4.05 | 0.666 | 2.13 |

The previously presented PNEC values for each representative animal are compared with the ETE values to provide an indication of the risk to non-target animals ingesting a daily dose of bait containing Bromadiolone.

**Secondary poisoning:**

A summary of the calculations for the exposure assessment for the active substance for secondary poisoning are presented next.

In the terrestrial food chain, secondary poisoning is possible via contaminated soil invertebrates and rodents, and the latter animals are the most likely source of Bromadiolone residues in raptorial birds and predatory mammals. Here the food chain is as follows: rodenticide (bait) → rodent → rodent­eating mammal or rodent-eating bird.

For the first tier assessment of secondary poisoning, the maximum residue levels in target rodents that arise on day-5 after the last meal (ETEoral predator) are compared to the PNEC values for concentration in food.

Accordingly, the residues of Bromadiolone in a target rodent in mg a.s./kg b.w. at different times during a control operation (concentration of active substance in rodenticide bait 0.005%) are calculated firstly:

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Residues of rodenticide in target animal,**  **mg a.s./kg b.w. with bait consumption expressed as PD**  **0.2 0.5 1** | | |
| **A normal non-resistant target rodent stops eating on day 5** | |  |  |
| Day 1 after the first meal\* | 1.00 | 2.50 | 5.00 |
| Day 2 before new meal\*\* | 0.70 | 1.75 | 3.50 |
| Day 5 before new meal | 1.77 | 4.43 | 8.87 |
| Day 5 after the last meal | 2.77 | 6.93 | 13.9 |
| Day 6\*\* | 1.94 | 4.85 | 9.71 |
| Day 7 (mean time to death)\*\* | 1.36 | 3.40 | 6.79 |
| **A target rodent continues eating due to resistance** | |  |  |
| Day 14 after the meal | 3.31 | 8.28 | 16.6 |

\* Equation for ETE is used for calculation of rodenticide in target animal on Day 1 immediately after first meal. \*\*Equation for EC (primary poisoning) is used for calculating the value for Day 2 before new meal.

A refined tier 2 risk assessment was also required and considered exposure of relevant species of predators, based on their bodyweights and food intakes. Food intake of non-target animals can vary significantly, depending on the metabolic rates of species, the nature of their food, weather conditions, time of year, etc. Several bird and mammal species are chosen to refine the risk assessment including **for birds**: barn owl, kestrel, little owl and tawny owl, and **for Mammals**: fox, polecat, stoat and weasel.

The expected concentrations of active substance in non-target animals (predators / carnivores) due to secondary poisoning after a single day of exposure (concentration of active substance in rodenticide bait 0.005%) with the following conditions: Rodents feed 100% on rodenticide, and predators / carnivores feed 50% on poisoned rodents, is as follows:

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | | | **Normal susceptible rodents caught on day 5, before their last meal.** | | **Normal susceptible rodents caught on day 5 just after their last meal** | | **Resistant rodents caught on day 14 just after their last meal** | |
| **Species** | | **Body weight \*)** | **Daily mean food intake\*)** | **Amount a.s. consumed by the non- target animal\*\*** | **Concentration in non-target animal** | **Amount a.s. consumed by the non- target animal\*\*\*** | **Concentration in non-target animal** | **Amount a.s. consumed by the non- target animals\*\*\*\*** | **Concentration in non-target animal** |
| **(g)** | **(g)** | **(mg)** | **(mg a.s./kg b.w.)** | **(mg)** | **(mg a.s./kg b.w.)** | **(mg)** | **(mg a.s./kg b.w.)** |
| Barn Owl | *Tyto alba* | 294 | 72.9 | 0.32 | 1.10 | 0.51 | 1.72 | 0.61 | 2.06 |
| Kestrel | *Falco tinnuncul.* | 209 | 78.7 | 0.35 | 1.68 | 0.55 | 2.62 | 0.65 | 3.13 |
| Little owl | *Athene noctua* | 164 | 46.4 | 0.21 | 1.26 | 0.32 | 1.97 | 0.39 | 2.35 |
| Tawny Owl | *Strix aluco* | 426 | 97.1 | 0.43 | 1.01 | 0.67 | 1.58 | 0.81 | 1.89 |
| Fox | *Vulpes vulpes* | 5 700 | 520.2 | 2.31 | 0.41 | 3.62 | 0.63 | 4.32 | 0.76 |
| Polecat | *Mustela putorius* | 689 | 130.9 | 0.58 | 0.85 | 0.91 | 1.32 | 1.09 | 1.58 |
| Stoat | *Mustela erminea* | 205 | 55.7 | 0.25 | 1.21 | 0.39 | 1.89 | 0.46 | 2.26 |
| Weasel | *Mustela nivalis* | 63 | 24.7 | 0.11 | 1.74 | 0.17 | 2.72 | 0.21 | 3.25 |

**3.3.6.6. Overall Summary of exposure assessment**

The biocidal product is a ready-to-use bait containing 0.005% Bromadiolone as the active substance. Bromadiolone is a second-generation single-dose anticoagulant rodenticide. It is used against rat at the maximal rate of 100g of product equivalent to 5 mg a.s. per baiting post and against mouse at 30g product equivalent to 1.5 mg a.s. by baiting post. This formulation is intended for indoor and outdoor uses.

PECs were calculated in accordance with the ESD for PT14. These calculations are outlined in the previous section. Based on environmental fate and behaviour of Bromadiolone the following PEC values were determined:

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Scenario** | **In and around buildings** | | **Open area** | **Waste dumps** | | **Sewer system** |
|  | **Worst case** | **Realistic** |  | **Worst case** | **Realistic** |  |
| **PEC soil (mg/kg wwt)** | 4.68E-02 | 9.36E-03 | 1.73E-01 | 7.41E-03 | 2.04E-03 |  |
| **PEC groundwater (mg/l)** | 2.55E-04 | 5.10E-05 | 9.43E-04 | 4.04E-05 | 1.11E-05 |  |
| **PEC microorganisms (mg/l)** |  |  |  |  |  | 4.44E-05 |
| **PEC surface water (mg/l)** |  |  |  |  |  | 4.37E-06 |
| **PEC agricultural soil (mg/kg wwt)** |  |  |  |  |  | 1.62E-04 |
| **PEC sediment (mg/kg wwt)** |  |  |  |  |  | 9.90E-04 |
| **PEC groundwater (ag) (mg/l)** |  |  |  |  |  | 4.09E-07 |

No new data related to the environment fate and behaviour or the ecotoxicology of the active substance or the biocidal product has been submitted by the applicant.

PNECs were calculated based on the studies submitted for the EU approval of the active substance. PECS for assessment of primary and secondary poisoning were determined based on the ESD for PT14 and the TGD (2003).

### Risk Characterisation for the Environment

* **Major change and renewal applications - 2017:**

|  |
| --- |
| In the first authorization of the product CONTROL 25, the claimed used “waste dump” and “open areas” were assessed. Nevertheless, these uses were not proposed by the applicant at the renewal authorization. Therefore, the original assessment proposed below should not be taken into account for these two scenarios. |

Bromadiolone products are non-selective and can pose a risk of primary and secondary poisoning to non-target animals.

Product containing Bromadiolone are placed at secured bait points. To maximise exposure of the target rodents and minimise unintended exposure of other non-target vertebrates, the products are placed where they are most likely to be encountered by the target organisms (e.g. on habitual rat­runs).

The type of secured bait point suitable for a given situation is determined on a case-by-case basis, taking into account such factors as shielding from sunlight and moisture necessary to maintain bait integrity and the level of security required to prevent access to and/or interference by non-target animals etc.

The risks posed by products containing 50 mg Bromadiolone/kg are characterised for the following scenarios:

1. Sewers, where only bait blocks are applicable;
2. In and around buildings (houses, animal houses, commercial and industrial sites), both blocks and grains;
3. Open areas, both blocks and grains;
4. Waste dumps, both blocks and grains.

**3.3.7.1. Aquatic compartment**

A contamination of surface water with Bromadiolone from the placing of product in and around buildings, in open areas and on waste dumps is highly unlikely. A lack of exposure to surface water is also stated in the EUBEES 2 emission scenario document. Contamination of surface waters is however expected to arise following use of bait blocks in sewers.

The most sensitive organism in the aquatic tests was green alga with a nominal ErC50 of 1.14 mg/L. This **PNECwater** of 1.14/1000 (acute studies available only)/3 (uncertainties due to photolytic degradation) **= 3.8 x 10-4 mg/L**.

The test with micro-organisms in activated sludge showed that concentrations that cause inhibition of these micro-organisms are high indicating that it is not likely that Bromadiolone will have a negative impact on the microbial processes in a sewage treatment plant. This gives a **PNECSTP** of 132.8/100 (No NOEC or EC10 was available) **= 1.33 mg/L.**

The PNEC for sediment dwelling organisms was calculated using the equilibrium partitioning method. In order to obtain a value that could be used in the equation, an average value of 14770 ml/g was calculated from four of the five soils available. The **PNECsediment = 0.83 mg/kg w/w**

The risk characterisation for the aquatic compartment is presented in the following table applying the relevant PEC values as indicated in the table in the overall summary of the exposure assessment **section 3.3.6.6** above.

**Aquatic PEC/PNEC ratios using the realistic worst case scenario**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Exposed compartment** | **Endpoint** | **PNEC** | **PEC** | **Risk quotient PEC/PNEC** |
| Surface water | Green algae  ErC50 of 1.14 mg/L | **3.8 x 10-4 mg/L**. | 4.37E-06 mg/l | ≤ 1 |
| Sediment | Equilibrium partitioning method  14770 ml/g | **0.83 mg/kg w/w** | 9.90E-04 (mg/kg w/w) | ≤ 1 |
| STP | Micro-organisms in activated sludge EC50 = 132.8 mg/L (nominal) | **1.33 mg/L** | 4.44E-05 mg/l | ≤ 1 |

The PEC/PNEC risk quotient in all compartments are below the trigger value of 1 indicating Bromadiolone following the recommended use of the product does not cause an unacceptable risk to aquatic organisms, sediment dwelling organisms or biological processes at the sewage treatment plant.

Bromadiolone is not readily biodegradable under environmentally relevant conditions or during sewage treatment processes. Accordingly, the degradation of Bromadiolone in sediment is also anticipated to be low. However, it has limited exposure to the aquatic compartment and this is confirmed by the PEC calculations. The PEC/PNEC ratio is below the level that leads to an unacceptable risk, thus the risk for unacceptable accumulation in sediment can be regarded as low.

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

* **Major change and renewal applications - 2017:**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| For the risk characterization in groundwater, PECgroundwater is equal to 2.55E-04 mg/L for the worst case. According to the human health, 0.01µg/L corresponds on the threshold value for the toxicity in drinking water. Consequently, the risk in groundwater for the “in and around” scenario is unacceptable.  A FOCUS modelling was carried out to refine the PEC groundwater. Considering the ESD “in and around buildings” the area around the farm is 55m long and 10m wide. Extrapolate to a hectare; it is a very conservative and worst-case way. As well, we consider twelve applications per year.  Application rate is calculated from Bromadiolone concentration in soil of 0.615g/application as a realistic worst-case leading to a dose rate of 3.38E-02 g.camp-1 (with Qprod = 100g ; Fcproduct = 0.0025% ; Nrefil = 1.5 ; Frelease-D,soil = 0.001 because of the use of sachet ; Frelease-ID,soil = 0.9)   |  |  | | --- | --- | | Model used | FOCUS PEARL 4.4.4. | | Years of simulation | 1 | | Application rate | 0.000615 kg.ha-1 | | Standard crop for arable land | Alfalfa | | Application depth | Incorporation 0 cm | | Date of application | Twelve applications per year | | Molar mass | 527.4 g.mol-1 | | Vapour pressure | 2.13E-08 Pa at 20°C | | Water solubility | 18.4 mg.L-1 at 20°C | | Kom | 8567.28 L.kg-1 at 20°C | | Freundlich exponent | 1 | | DT50soil | 1E+06 d at 12°C | | Coefficient for uptake for plant | 0 | | Molar activation energy | 54 kJ.mol-1 |   Results :   |  |  |  |  | | --- | --- | --- | --- | | RESULT\_TEXT | CONCENTRATION | LOCATION | IRRIGATION\_SCHEME | | Concentration closest to the 80th percentile (ug/L) | 0.000000 | CHATEAUDUN | FOCUS | | Concentration closest to the 80th percentile (ug/L) | 0.000000 | HAMBURG | No | | Concentration closest to the 80th percentile (ug/L) | 0.000000 | JOKIOINEN | No | | Concentration closest to the 80th percentile (ug/L) | 0.000000 | KREMSMUENSTER | No | | Concentration closest to the 80th percentile (ug/L) | 0.000000 | OKEHAMPTON | No | | Concentration closest to the 80th percentile (ug/L) | 0.000000 | PIACENZA | FOCUS | | Concentration closest to the 80th percentile (ug/L) | 0.000000 | PORTO | FOCUS | | Concentration closest to the 80th percentile (ug/L) | 0.000000 | SEVILLA | FOCUS | | Concentration closest to the 80th percentile (ug/L) | 0.000000 | THIVA | FOCUS |   According to the FOCUS modelling and with a very worst-case approach, the risk is acceptable in groundwater for the use of CONTROL 25 in and around buildings. |

**3.3.7.2. Atmospheric compartment**

There are no releases to air of Bromadiolone from use or disposal phases. No risk is identified.

**3.3.7.3. Terrestrial compartment**

Contamination of soil following the use of product in sewers is highly unlikely during application and use. However, soil may contain low concentrations of Bromadiolone from the spreading of sludge on land derived from waste water treatment works receiving water after the baiting of sewer systems.

Exposure of the terrestrial compartment (soil) will also occur when product is deployed outdoors. Exposure is assumed to arise through a combination of transfer (direct release) and deposition via urine and faeces (disperse release) onto soil.

Bromadiolone products are applied in open areas by inserting them inside the openings of the tunnels of the target rodents and soil exposure is assumed to occur to the burrow floor.

One terrestrial study is only available, accordingly the PNEC should also be calculated from the aquatic toxicity data using equilibrium partitioning calculations giving a result of **PNECsoil** = (443/1700) x 3.8 x10-4 x 1000 = **9.9 x 10-2 mg/kg**. Due to the uncertainties associated with using the PNECsoil determined by the two active substance applicants the value determined using the equilibrium partitioning calculations was used.

**Aquatic PEC/PNEC ratios using the realistic worst case scenario**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Exposed compartment** | **Endpoint** | **PNEC** | **PEC** | **Risk quotient PEC/PNEC** |
| In and around  buildings | Equilibrium partitioning calculations | 9.9 x 10-2 mg/kg | 4.68E-02 mg/kg w/w | ≤ 1 |
| Open areas | Equilibrium partitioning calculations | 9.9 x 10-2 mg/kg | 1.73E-01 mg/kg w/w | 1.74 |
| Waste dump | Equilibrium partitioning calculations | 9.9 x 10-2 mg/kg | 7.41E-03 mg/kg w/w | ≤ 1 |
| Sewer application | Equilibrium | 9.9 x 10-2 mg/kg | 1.62E-04 mg/kg | ≤ 1 |
| of sewage sludge | partitioning calculations |  | w/w |  |

The PEC/PNEC ratios were less than 1 when used in and around buildings, waste dumps and for sewer applications indicating that Bromadiolone, following recommended use of the product, does not cause unacceptable risk to organisms in any of these terrestrial compartments assessed.

The PEC/PNEC ratio was greater than 1 when used in open areas indicating that Bromadiolone, following recommended use of the product, causes an unacceptable risk to organisms in this terrestrial compartment. However, the PEC/PNEC ratio based on the open area PEC **represents only a localised hotspot** of contamination near the entrance of each baited tunnel.

**3.3.7.4. Primary poisoning**

The risk for primary and secondary poisoning via the aquatic food chain, e.g. of predatory fish, is not considered further, since the exposure to the aquatic environment is limited and since available data on fish suggests that Bromadiolone does not have a high potential for bioaccumulation in fish tissues.

**Acute exposure:**

Non-target mammals and birds are unlikely to enter sewers and feed on product in sewage systems. Therefore, there will be no significant exposure following the use of product in sewers. Rats that live underground in sewers are also unlikely to take bait and deposit significant quantities in accessible places above ground, thus preventing exposure to non-target animals living above sewers. In conclusion, the risks to non-target mammals and birds following the use of bait blocks containing Bromadiolone in sewers are considered to be very low.

The empirical risk assumes direct or indirect consumption of the deployed baits in and around buildings, in open areas and waste dumps. For primary poisoning the initial PECoral values assume that there is no bait avoidance by the non-target animals and that they obtain 100% of their diet in the treated area and have access to the product.

**Tier I risk assessment: PECoral/PNECoral ratio for birds and mammals exposed to Bromadiolone**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **PECoral**  **(concentration in food, mg/kg)** | **PNECoral**  **(concentration in food, mg/kg)** | **Risk quotient PEC / PNEC** |
| **Acute** | | | |
| Bird | 50 | 0.00963 | 5192 |
| Mammal | 50 | 1.67\*10-4 | 299401 |
| **Long-term** | | | |
| Bird | 50 | 0.0104 | 4808 |
| Mammal | 50 | 0.000186 | 268817 |

The ratios PEC/PNEC are above 1 indicating a potential risk. Therefore, a refined tier 2 assessment is set out below, based on representative species.

The refined tier 2 risk assessment considers exposure of relevant species of predators, based on their bodyweights and food intakes. Food intake of non-target animals can vary significantly, depending on the metabolic rates of species, the nature of their food, weather conditions, time of year, etc.

**Tier 2 acute risk assessment: PECoral/PNECoral for non-target animals accidentally exposed to bait containing Bromadiolone after one meal**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Non-target animals** | **ETE, concentration of Bromadiolone after one meal (one day) (mg/kg b.w.)** | | **PNECoral (dose, mg/kg b.w./d)** | **PEC/PNEC** | |
| **Step 1** | **Step 2** | **Step 1** | **Step 2** |
| Tree sparrow | 17.3 | 12.4 | 0.00120 | 14 417 | 10 333 |
| Chaffinch | 15.0 | 10.8 | 0.00120 | 12 500 | 9 000 |
| Wood pigeon | 5.42 | 3.90 | 0.00120 | 4 517 | 3 250 |
| Pheasant | 5.39 | 3.88 | 0.00120 | 4 492 | 3 233 |
| Dog | 2.28 | 1.64 | 8.33\*10-6 | 273 709 | 196 879 |
| Pig | 0.375 | 0.270 | 8.33\*10-6 | 45 018 | 32 413 |
| Pig, young | 1.20 | 0.864 | 8.33\*10-6 | 144 058 | 103 721 |

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

The ratios PEC/PNEC are above 1 indicating a potential risk even after refinement. **Long -term exposure:**

**Tier 2 long-term risk assessment: ECoral/PNECoral ratio after 5-day elimination of Bromadiolone**

|  |  |  |  |
| --- | --- | --- | --- |
| **Species** | **ECoral after 5 days (mg/kg b.w./d)** | **PNECoral**  **(mg/kg b.w./d)** | **Risk quotient ECoral/PNECoral** |
| Tree sparrow | 30.7 | 0.0013 | 2.36\*104 |
| Chaffinch | 26.6 | 0.0013 | 2.05\*104 |
| Wood pigeon | 9.61 | 0.0013 | 0.739\*104 |
| Pheasant | 9.56 | 0.0013 | 0.735\*104 |
| Dog | 4.05 | 0.0000056 | 7.23\*105 |
| Pig | 0.666 | 0.0000056 | 1.19\*105 |
| Pig, young | 2.13 | 0.0000056 | 3.80\*105 |

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

**3.3.7.5. Secondary poisoning**

It is unlikely that target rodents that have ingested bait blocks containing Bromadiolone will leave the sewer system and be exposed, in significant numbers, to predators or scavengers. Therefore, the secondary poisoning risks from the use of bait blocks in sewers are considered to be very low.

For the first tier assessment of secondary poisoning in and around buildings, in open areas and waste dumps, the maximum residue levels in target rodents that arise on day-5 after the last meal (ETEoral predator) are compared to the PNEC values for concentration in food. The first tier assessment also assumes the following three levels of Bromadiolone bait consumption: 20%, 50% and 100% of the daily food intake of the target rodents. For long-term exposure, it is assumed that the rodents have fed entirely on rodenticide and that the non-target animals consume 50% of their daily intake on poisoned rodents.

**Tier 1 risk assessment of secondary poisoning at day 5 (non-resistant rodents**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Organism group** | **PNECoral (mg a.s./kg b.w.)** | **ETEoral, predator (mg a.s./kg b.w.)** | | | **PECoral/PNECoral – day 5** | | |
| PD values | - | 0.2 | 0.5 | 1.0 | 0.2 | 0.5 | 1.0 |
| **Acute** | | | | | | | |
| Birds | 0.00120 | 2.77 | 6.93 | 13.9 | 2 308 | 5 775 | 11 583 |
| Mammals | 8.33\*10-6 | 3.33\*105 | 8.32\*105 | 1.67\*106 |
| **Long-term** | | | | | | | |
| Birds | 0.0013 | 1.39 | 3.47 | 6.95 | 1 069 | 2 669 | 5 346 |
| Mammals | 0.0000056 | 2.48\*105 | 6.20\*105 | 1.24\*106 |

**Table VI.1.8-3: Tier 1 risk assessment of secondary poisoning at day 14 (resistant rodents)**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Organism group** | **PNECoral (mg a.s./kg b.w.)** | **ETEoral, predator (mg a.s./kg b.w.)** | | | **PECoral/PNECoral – day 14** | | |
| PD values | - | 0.2 | 0.5 | 1.0 | 0.2 | 0.5 | 1.0 |
| **Acute** | | | | | | | |
| Birds | 0.00120 | 3.31 | 8.28 | 16.6 | 2 758 | 6 900 | 13 833 |
| Mammals | 8.33\*10-6 | 3.97\*105 | 9.94\*105 | 1.99\*106 |
| **Long-term** | | | | | | | |
| Birds | 0.0013 | 1.66 | 4.14 | 8.30 | 1 277 | 3 185 | 6 385 |
| Mammals | 0.000 0056 | 2.96\*105 | 7.39\*105 | 1.48\*106 |

According to the tier 1 assessment the risk for secondary poisoning of non-target predator birds and mammals during acute and long-term exposure via rodents poisoned with Bromadiolone is very high. Therefore, a refined tier 2 assessment is set out below, based on representative species.

The refined tier 2 risk assessment considers exposure of relevant species of predators, based on their bodyweights and food intakes. Food intake of non-target animals can vary significantly, depending on the metabolic rates of species, the nature of their food, weather conditions, time of year, etc.

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

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Species** | **Exposure** | **ETE oral predators (mg a.s./kg/d)** | **PNECoral (mg a.s./kg/d)** | **Ratio ETE oral predators / PNECoral** |
| Barn owl | Day 5 before the last meal | 1.10 | 0.0013 | 846 |
| Day 5 after the last meal | 1.72 | 1 323 |
| Day 14 after the last meal | 2.06 | 1 585 |
| Kestrel | Day 5 before the last meal | 1.68 | 0.0013 | 1 292 |
| Day 5 after the last meal | 2.62 | 2 015 |
| Day 14 after the last meal | 3.13 | 2 408 |
| Little owl | Day 5 before the last meal | 1.26 | 0.0013 | 969 |
| Day 5 after the last meal | 1.97 | 1 515 |
| Day 14 after the last meal | 2.35 | 1 808 |
| Tawny owl | Day 5 before the last meal | 1.01 | 0.0013 | 777 |
| Day 5 after the last meal | 1.58 | 1 215 |
| Day 14 after the last meal | 1.89 | 1 454 |
| Fox | Day 5 before the last meal | 0.41 | 0.0000056 | 7.32\*104 |
| Day 5 after the last meal | 0.63 | 1.13\*105 |
| Day 14 after the last meal | 0.76 | 1.36\*105 |
| Polecat | Day 5 before the last meal | 0.85 | 0.0000056 | 1.52\*105 |
| Day 5 after the last meal | 1.32 | 2.36\*105 |
| Day 14 after the last meal | 1.58 | 2.82\*105 |
| Stoat | Day 5 before the last meal | 1.21 | 0.0000056 | 2.16\*105 |
| Day 5 after the last meal | 1.89 | 3.38\*105 |
| Day 14 after the last meal | 2.26 | 4.04\*105 |
| Weasel | Day 5 before the last meal | 1.74 | 0.0000056 | 3.11\*105 |
| Day 5 after the last meal | 2.72 | 4.86\*105 |
| Day 14 after the last meal | 3.25 | 5.80\*105 |

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

**3.3.7.6. Overall Summary**

Based on toxicity data Bromadiolone presents a hazard to birds and non-target mammals. Non-target vertebrate animals may be exposed to product containing Bromadiolone, either directly by ingestion of exposed product (primary poisoning) or indirectly by ingestion of the carcasses of target rodents that contain Bromadiolone residues (secondary poisoning). Bromadiolone products are non-selective and can pose a risk of primary and secondary poisoning to non-target animals. There are many uncertainties associated with quantification of the risk associated with the use of Bromadiolone products. Overall, because of the toxic nature of rodenticides and the over-riding public health requirement it is more appropriate to develop and validate risk management measures than to refine the risk assessment procedures further. It is noted that the product contains a bittering agent and this may deter some non-target animals. It is also noted that the attractiveness of the product may be impacted by the use of dye.

**Primary poisoning:**

Overall, all acute and long-term PECoral/PNECoral ratios are above the trigger value of 1 indicating acute and long-term unacceptable risks. Even when avoidance and elimination are taken into account the empirical exposure levels result in unacceptable risks to birds and mammals.

**Secondary poisoning:**

All ratios ETEoral predators / PNECoral are above the trigger value of 1 indicating an unacceptable risk of secondary poisoning. Even when avoidance and elimination are taken into account the empirical exposure levels result in unacceptable risks to birds and mammals.

**Conclusion for primary and secondary poisoning:**

Due to the risk assessment results for primary and secondary poisoning and the uncertainty associated with quantification of this risk, risk mitigation measures must be taken into account to lead to an acceptable use of the rodenticide product.

* **Major change and renewal applications - 2017:**

|  |
| --- |
| No studies were conducted with the product CONTROL 25 for the environment part; therefore the environmental risk assessment has been carried out with data from the CAR of bromadiolone.  The environmental risk is considered as acceptable for the intended uses except for the primary and secondary poisoning. The specific use restriction must be applied to reduce the risk for primary and secondary poisoning. |

**The following risk mitigation measures are proposed to mitigate the primary and secondary poisoning risk to non-target mammals and lead to an acceptable use of this rodenticide:**

* Use of an integrated management strategy and precautionary systems
* Unless under the supervision of a pest control operator use or other competent person do not use anticoagulants as permanent baits
* There should be proper and secure placing of baits so as to minimise the risk of consumption by other animals or children. Where possible secure baits so they cannot be dragged away.
* Users should select tamper-resistant bait boxes, secured bait boxes, covered applications or burrow baiting (placing of bait in appropriate containers or under a curved tile or in a piece of tube) to minimize exposure of non-target animals
* Monitor and replenish bait stations as appropriate
* Frequent visits to bait stations to ensure that any bait that is split or dragged out of bait stations is removed
* Unconsumed baits must be collected after termination of the control campaign and dispose of them in accordance with local requirements
* Remove dead and moribund rodents at frequent intervals, at least as often as baits are checked or replenished during a baiting campaign
* Baits should be deployed in accordance with the product labelling
* Baits should be deployed in accordance with other approved guidance on good practice.
* Restrict the use of the product to treatment campaigns of limited duration
* To minimise the likelihood of target rodents developing resistance to second-generation anticoagulant rodenticides, long-term deployment of baits as a preventative control measure is not recommended
* The resistance status of the population should be taken into account when considering the choice of rodenticide to be used.
* When the product is being used in public areas, the areas treated must be marked during the treatment period and a notice explaining the risk of primary and secondary poisoning by the anticoagulant as well as indicating the first measure to be taken in case of poisoning must be made available alongside the baits
* **Major change and renewal applications - 2017:**

No new ecotoxicological information has been submitted at the renewal of the approval of the active substance bromadiolone and in the product dossier.

Furthermore, in the first authorization of the product CONTROL 25 performed by IE, the active substance content assessed was 0.005% w/w of bromadiolone. For the renewal, the applicant claimed an active substance content of 0.0025% w/w of bromadiolone. Regarding this new information, the renewal assessment is cover by the assessment performed by IE and presented here below.

Therefore, the conclusion of the environmental risk assessment remains unchanged.

# Proposal for Decision

1. Administrative information

1.1. Trade name(s) of the product

| **Trade name(s)** | CONTROL 25 |
| --- | --- |
|  | Très Puissant  Bromacereal  Souris - Céréale décortiquée  Rat - Céréale décortiquée  Mulo 25  Cereox B25  Roddex Avoine Bromadiolone  Grain Bromadiolone  Rat & Souris Grain Bromadiolone |

1.2. Authorisation holder

|  |  |  |
| --- | --- | --- |
| **Name and address of the authorisation holder** | **Name** | BELGAGRI SA |
| **Address** | Rue des Tuiliers, 1  4480 Engis  BELGIUM |
| **Authorisation number** |  | |
| *Suffixes to the authorisation number linked to trade names* |  | |
| *R4BP asset reference number* |  | |
| **Date of the authorisation** |  | |
| **Expiry date of the authorisation** |  | |

1.3. Manufacturer(s) of the product

|  |  |
| --- | --- |
| **Name of manufacturer** | BELGAGRI SA |
| **Address of manufacturer** | Rue des Tuiliers 1  4480 Engis  Belgium |
| **Location of manufacturing sites** | Rue des Tuiliers 1  4480 Engis  Belgium |

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

|  |  |
| --- | --- |
| **Active substance** | Bromadiolone |
| **Name of manufacturer** | PELGAR |
| **Address of manufacturer** | Unit 13, Newmann Lane Industrial Estate Alton  GU34 2 QR Ampshire  United Kingdom |
| **Location of manufacturing sites** | Prazska  280 02 Kolin  Czech Republic |

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 (%)** |
| --- | --- | --- | --- | --- | --- |
| Bromadiolone | 3-[3-(4'-Bromo[1,1'-biphenyl]-4-yl)-3-hydroxy-1-phenylpropyl]-4-hydroxy-2H-1-benzopyran-2-one | Active substance | 28772-56-7 | 249-205-9 | 0.0025 |

2.2. Type of formulation

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

3. Hazard and precautionary statements

| Hazard statements | H373 (blood) |
| --- | --- |
| Precautionary statements | P260 Do not breathe dust  P314 Get Medical advice/attention if you feel unwell.  P501: Dispose of contents/container in accordance with national regulations. |

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)  (**in France only** : *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[[10]](#footnote-10)  - *[Covered and protected baiting points]* |
| **Application rate(s) and frequency** | Bait products:  - rats: 100 g of bait per baiting point.  - mice: 25-30 g of bait per baiting point. |
| **Category(ies) of users** | Trained professionals |
| **Pack sizes and packaging material** | Minimum pack size of 3 kg*.*  *(****In France only*** *: minimum pack size of 5 kg)*  Package is restricted to separately packed bags with a maximum of 10 kg per packed bag.  Grain bait wrapped in PE/PP sachets (10-25-50-100 g) or unwrapped, and packed in:   * PP or PE bucket   (Baits in sachets: 3-25 kg or unwrapped baits: 3-10 kg)   * Cardboard box   (Baits in sachets: 3-25 kg or unwrapped baits: 3-10 kg)   * Paper craft bag with inner liner in PE   (Baits in sachets: 3-25 kg or unwrapped baits: 3-10 kg) |

4.1.1. Use-specific instructions for use

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

4.1.2 Use-specific risk mitigation measures

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

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

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

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

|  |
| --- |
|  |

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

|  |
| --- |
|  |

4.2. Use description

**Table 2. Use # 2 Mice and/or rats and/or fiel mice – trained professionals – outdoor around buildings**

|  |  |
| --- | --- |
| **Product Type** | 14 |
| **Where relevant, an exact description of the authorised use** | Not relevant for rodenticides |
| **Target organism(s) (including development stage)** | *Mus musculus* (house mice)  *Rattus norvegicus* (brown rat)  *Apodemus sylvaticus* (field mice)  (**in France only** : *Rattus rattus* (black or roof rat)) |
| **Field(s) of use** | Outdoor around buildings |
| **Application method(s)** | Bait formulations:  - Ready-to-use bait to be used in tamper-resistant bait stations.  - *[Covered and protected baiting points]* |
| **Application rate(s) and frequency** | Bait products:  - rats: 100 g of bait per baiting point.  - mice: 25-30 g of bait per baiting point.  - field mice: 50 g of bait per baiting point. |
| **Category(ies) of users** | Trained professionals |
| **Pack sizes and packaging material** | Minimum pack size of 3 kg*.*  *(****in France only*** *:* Minimum pack size of 5 kg)  Package is restricted to separately packed bags with a maximum of 10 kg per packed bag.  Grain bait wrapped in PE/PP sachets (10-25-50-100 g) or unwrapped, and packed in:   * PP or PE bucket   (Baits in sachets: 3-25 kg or unwrapped baits: 3-10 kg)   * Cardboard box   (Baits in sachets: 3-25 kg or unwrapped baits: 3-10 kg)   * Paper craft bag with inner liner in PE   (Baits in sachets: 3-25 kg or unwrapped baits: 3-10 kg) |

4.2.1. Use-specific instructions for use

|  |
| --- |
| - Protect bait from the atmospheric conditions. Place the baiting points in areas not liable to flooding.  - Replace any bait in baiting points in which bait has been damaged by water or contaminated by dirt.  - Remove the remaining product at the end of treatment period.  - *[When available]* Follow any additional instructions provided by the relevant code of best practice.  *- [For outdoor use, baiting points must be covered and placed in strategic sites to minimise the exposure to non-target species].* |

4.2.2 Use-specific risk mitigation measures

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

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

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

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

|  |
| --- |
|  |

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

|  |
| --- |
|  |

4.3. Use description

**Table 3. Use # 3 – Rats– trained professionals – Outdoor open areas & waste dumps**

|  |  |
| --- | --- |
| **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)  (**in France only**, *Rattus rattus* (black or roof rat)) |
| **Field(s) of use** | Outdoor open areas  Outdoor waste dumps |
| **Application method(s)** | - Ready-to-use bait to be used in tamper-resistant bait stations.  *- [Covered and protected baiting points]* |
| **Application rate(s) and frequency** | Bait products:  100 g of bait per baiting point. |
| **Category(ies) of users** | Trained professionals only |
| **Pack sizes and packaging material** | Minimum pack size of 3 kg*.*  *(***in France only** *:* Minimum pack size of 5 kg)  Package is restricted to separately packed bags with a maximum of 10 kg per packed bag.  Grain bait wrapped in PE/PP sachets (10-25-50-100 g) or unwrapped, and packed in:   * PP or PE bucket   (Baits in sachets: 3-25 kg or unwrapped baits: 3-10 kg)   * Cardboard box   (Baits in sachets: 3-25 kg or unwrapped baits: 3-10 kg)   * Paper craft bag with inner liner in PE   (Baits in sachets: 3-25 kg or unwrapped baits: 3-10 kg) |

4.3.1. Use-specific instructions for use

|  |
| --- |
| - Protect bait from the atmospheric conditions. Place the bait stations in areas not liable to flooding.  - Replace any bait in baiting points in which bait has been damaged by water or contaminated by dirt.  - Remove the remaining product at the end of treatment period *[Not applicable where explicitly authorised according to addenda 4]*.  - *[When available]* Follow any additional instructions provided by the relevant code of best practice.  *- [For outdoor use, baiting points must be covered and placed in strategic sites to minimise the exposure to non-target species].* |

4.3.2 Use-specific risk mitigation measures

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

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

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

|  |
| --- |
|  |

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

|  |
| --- |
|  |

4.4. Use description

**Table 4. Use # 4 *(not relevant in France)*– 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[[11]](#footnote-11) |
| **Application rate(s) and frequency** | 25-30 g of bait per bait station. If more than one bait station is needed, the minimum distance between bait stations should be of 2 meters. |
| **Category(ies) of users** | Professionals |
| **Pack sizes and packaging material** | Minimum pack size of 3 kg*.*  (**In France only** : minimum pack size of 5 kg)  Package is restricted to separately packed bags with a maximum bag size of 10 kg.  Grain bait wrapped in PE/PP sachets (10-25-50-100g) or unwrapped, and packed in:   * PP or PE bucket   (Baits in sachets: 3-25 kg or unwrapped baits: 3-10 kg)   * Cardboard box   (Baits in sachets: 3-25 kg or unwrapped baits: 3-10 kg)   * Paper craft bag with inner liner in PE   (Baits in sachets: 3-25 kg or unwrapped baits: 3-10 kg) |

4.4.1. Use-specific instructions for use

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| - 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. |

4.4.2 Use-specific risk mitigation measures

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

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

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

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

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4.5. Use description

**Table 5. Use # 5 *(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) |
| **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** | - 100 g of bait per bait station. If more than one bait station is needed, the minimum distance between bait stations should be of 5 meters. |
| **Category(ies) of users** | Professionals |
| **Pack sizes and packaging material** | Minimum pack size of 3 kg*.*  Package is restricted to separately packed bags with a maximum bag size of 10 kg.  Grain bait wrapped in PE/PP sachets (10-25-50-100 g) or unwrapped, and packed in:   * PP or PE bucket   (Baits in sachets: 3-25 kg or unwrapped baits: 3-10 kg)   * Cardboard box   (Baits in sachets: 3-25 kg or unwrapped baits: 3-10 kg)   * Paper craft bag with inner liner in PE   (Baits in sachets: 3-25 kg or unwrapped baits: 3-10 kg) |

4.5.1. Use-specific instructions for use

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| - 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. |

4.5.2 Use-specific risk mitigation measures

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

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

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

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

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4.6. Use description

**Table 6. Use # 6 *(not relevant in France)*– House mice and/or rats and/or field mice – professionals – outdoor around buildings**

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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)** | Mus musculus (house mice)  *Rattus norvegicus* (brown rat)  *Apodemus sylvaticus* (field mice) |
| **Field(s) of use** | Outdoor around buildings |
| **Application method(s)** | Ready-to-use bait to be used in tamper-resistant bait stations |
| **Application rate(s) and frequency** | Bait products:  - rats: 100 g of bait per baiting point.  - mice: 25-30 g of bait per baiting point.  - field mice: 50 g of bait per baiting point. |
| **Category(ies) of users** | Professionals |
| **Pack sizes and packaging material** | Minimum pack size of 3 kg*.*  Package is restricted to separately packed bags with a maximum bag size of 10 kg  Grain bait wrapped in PE/PP sachets (10-25-50-100 g) or unwrapped, and packed in:   * PP or PE bucket   (Baits in sachets: 3-25 kg or unwrapped baits: 3-10 kg)   * Cardboard box   (Baits in sachets: 3-25 kg or unwrapped baits: 3-10 kg)   * Paper craft bag with inner liner in PE   (Baits in sachets: 3-25 kg or unwrapped baits: 3-10 kg) |

4.6.1. Use-specific instructions for use

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| - Protect bait from the atmospheric conditions (e.g. rain, snow, etc.). Place the bait stations in areas not liable to flooding.  - The bait stations should be visited *[for mice -* at least every 2 to 3 days at*]* *[for rats -* only 5 to 7 days after*]* the beginning of the treatment and at least weekly afterwards, in order to check whether the bait is accepted, the bait stations are intact and to remove rodent bodies. Re-fill bait when necessary.  - Replace any bait in a bait station in which bait has been damaged by water or contaminated by dirt.  - *[When available]* Follow any additional instructions provided by the relevant code of best practice. |

4.6.2 Use-specific risk mitigation measures

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

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

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

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

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

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4.7. Use description

**Table 7. Use # 7 – House mice – general public – 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)** | *Mus musculus* (house mice) |
| **Field(s) of use** | Indoor |
| **Application method(s)** | Ready-to-use bait *[in sachets for loose bait]* to be used in tamper-resistant bait stations[[12]](#footnote-12). |
| **Application rate(s) and frequency** | Bait products:  - 25-30 g of bait per bait station. If more than one bait station is needed, the minimum distance between bait stations should be of 2 meters. |
| **Category(ies) of users** | General public |
| **Pack sizes and packaging material** | Grain bait wrapped in PE/PP sachets (10-25-50-100 g) and packed in:   * PP or PE bucket   (Baits in sachets: up to 150 g)   * Cardboard box   (Baits in sachets: up to 150 g)   * Paper craft bag with inner liner in PE   (Baits in sachets: up to 150 g) |

4.7.1. Use-specific instructions for use

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| - The bait stations should be visited at least every 2 to 3 days at the beginning of the treatment and at least weekly afterwards, in order to check whether the bait is accepted, the bait stations are intact and to remove rodent bodies. Re-fill bait when necessary. |

4.7.2 Use-specific risk mitigation measures

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

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

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

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4.8. Use description

**Table 8. Use # 8 – Rats – general public – indoor**

|  |  |
| --- | --- |
| **Product Type** | 14 |
| **Where relevant, an exact description of the authorised use** | Not relevant for rodenticides |
| **Target organism(s) (including development stage)** | *Rattus norvegicus* (brown rat)  ***In france only:*** *Rattus rattus* (black or roof rat) |
| **Field(s) of use** | Indoor. |
| **Application method(s)** | Ready-to-use bait *[in sachets for loose bait]* to be used in tamper-resistant bait stations[[13]](#footnote-13). |
| **Application rate(s) and frequency** | Bait products:  100 g of bait per bait station. If more than one bait station is needed, the minimum distance between bait stations should be of 5 meters. |
| **Category(ies) of users** | General public |
| **Pack sizes and packaging material** | Grain bait wrapped in PE/PP sachets (10-25-50-100 g) and packed in:   * PP or PE bucket   (Baits in sachets: up to 150 g)   * Cardboard box   (Baits in sachets: up to 150 g)   * Paper craft bag with inner liner in PE   (Baits in sachets: up to 150 g) |

4.8.1. Use-specific instructions for use

|  |
| --- |
| - The bait stations should be visited only 5 to 7 days after the beginning of the treatment and at least weekly afterwards, in order to check whether the bait is accepted, the bait stations are intact and to remove rodent bodies. Re-fill bait when necessary. |

4.8.2 Use-specific risk mitigation measures

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

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

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

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4.9. Use description

**Table 9. Use # 9 – Rats – general public – outdoor around buildings**

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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)  ***In france only:*** *Rattus rattus* (black or roof rat) |
| **Field(s) of use** | Outdoor around buildings |
| **Application method(s)** | Ready-to-use bait *[in sachets for loose bait]* to be used in tamper-resistant bait stations[[14]](#footnote-14). |
| **Application rate(s) and frequency** | Bait products:  Rats: 100 g of bait per bait station. If more than one bait station is needed, the minimum distance between bait stations should be of 5 meters. |
| **Category(ies) of users** | General public |
| **Pack sizes and packaging material** | Grain bait wrapped in PE/PP sachets (10-25-50-100 g) and packed in:   * PP or PE bucket   (Baits in sachets: up to 150 g)   * Cardboard box   (Baits in sachets: up to 150 g)   * Paper craft bag with inner liner in PE   (Baits in sachets: up to 150 g) |

4.9.1. Use-specific instructions for use

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| --- |
| - Place the bait stations in areas not liable to flooding.  - Replace any bait in a bait station in which bait has been damaged by water or contaminated by dirt.  - The bait stations should be visited only 5 to 7 days after the beginning of the treatment and at least weekly afterwards, in order to check whether the bait is accepted, the bait stations are intact and to remove rodent bodies. Re-fill bait when necessary. |

4.9.2 Use-specific risk mitigation measures

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

4.9.3 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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4.9.4 Where specific to the use, the instructions for safe disposal of the product and its packaging

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

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4.10. Use description

**Table 10. Use # 10 – field mice – general public – outdoor around buildings**

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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)** | *Apodemus sylvaticus* (field mice) |
| **Field(s) of use** | Outdoor around buildings |
| **Application method(s)** | Ready-to-use bait *[in sachets for loose bait]* to be used in tamper-resistant bait stations[[15]](#footnote-15) |
| **Application rate(s) and frequency** | Bait products:  Field mice: 50 g of bait per bait station. If more than one bait station is needed, the minimum distance between bait stations should be of 2 meters. |
| **Category(ies) of users** | General public |
| **Pack sizes and packaging material** | Grain bait wrapped in PE/PP sachets (10-25-50g) and packed in:   * PP or PE bucket   (Baits in sachets: up to 150 g)   * Cardboard box   (Baits in sachets: up to 150 g)   * Paper craft bag with inner liner in PE   (Baits in sachets: up to 150 g) |

4.10.1. Use-specific instructions for use

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| --- |
| - Place the bait stations in areas not liable to flooding.  - Replace any bait in a bait station in which bait has been damaged by water or contaminated by dirt.  - The bait stations should be visited only 5 to 7 days after the beginning of the treatment and at least weekly afterwards, in order to check whether the bait is accepted, the bait stations are intact and to remove rodent bodies. Re-fill bait when necessary. |

4.10.2 Use-specific risk mitigation measures

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

4.10.3 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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4.10.4 Where specific to the use, the instructions for safe disposal of the product and its packaging

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4.10.5. 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 use

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| **FOR PROFESSIONAL AND TRAINED PROFESSIONAL USERS**  - Read and follow the product information as well as any information accompanying the product or provided at the point of sale before using it.  - Carry out a pre-baiting survey of the infested area and an on-site assessment in order to identify the rodent species, their places of activity and determine the likely cause and the extent of the infestation.  - Remove food which is readily attainable for rodents (e.g. spilled grain or food waste). Apart from this, do not clean up the infested area just before the treatment, as this only disturbs the rodent population and makes bait acceptance more difficult to achieve.  - The product should only be used as part of an integrated pest management (IPM) system, including, amongst others, hygiene measures and, where possible, physical methods of control.  - The product should be placed in the immediate vicinity of places where rodent activity has been previously explored (e.g. travel paths, nesting sites, feedlots, holes, burrows etc.).  - Where possible, bait stations must be fixed to the ground or other structures.  - Bait stations must be clearly labelled to show they contain rodenticides and that they must not be moved or opened *(see section 5.3 for the information to be shown on the label)*.  - *[If national policy or legislation requires it]* When the product is being used in public areas, the areas treated should be marked during the treatment period and a notice explaining the risk of primary or secondary poisoning by the anticoagulant as well as indicating the first measures to be taken in case of poisoning must be made available alongside the baits.  - Bait should be secured so that it cannot be dragged away from the bait station.  - Place the product out of the reach of children, birds, pets and farm animals and other non-target animals.  - Place the product away from food, drink and animal feeding stuffs, as well as from utensils or surfaces that have contact with these.  - *[Where required by the risk assessment:*  Wear protective chemical resistant gloves during product handling phase (glove material to be specified by the authorisation holder within the product information).  *Where relevant, specify any other PPE[[16]](#footnote-16) (e.g. goggles or mask) required when handling the product]*  - When using the product do not eat, drink or smoke. Wash hands and directly exposed skin after using the product.  ***FOR TRAINED PROFESSIONAL ONLY*** *The* frequency of visits to the treated area should be at the discretion of the operator, in the light of the survey conducted at the outset of the treatment. That frequency should be consistent with the recommendations provided by the relevant code of best practice.  - If bait uptake is low relative to the apparent size of the infestation, consider the replacement of bait points to further places and the possibility to change to another bait formulation.  - If after a treatment period of 35 days baits are continued to be consumed and no decline in rodent activity can be observed, the likely cause has to be determined. Where other elements have been excluded, it is likely that there are resistant rodent so consider the use of a non-anticoagulant rodenticide, where available, or a more potent anticoagulant rodenticide. Also consider the use of traps as an alternative control measure.  ***FOR PROFESSIONNALS ONLY*** Consider preventive control measures (e.g. plug holes, remove potential food and drinking as far as possible) to improve product intake and reduce the likelihood of reinvasion.  ***FOR PROFESSIONNALS ONLY*** Remove the remaining bait or the bait stations at the end of the treatment period.  Bait in sachets: Do not open the sachets containing the bait.  Loose grains: Place the bait in the baiting point by using a dosage devise. Specify the methods to minimise dust (e.g. wet wiping).  Loose grains: Decanting is to be avoided. In case decanting cannot be avoided, an RPE of APF 10 has to be used.  **FOR NON PROFESSIONAL USERS**  - Read and follow the product information as well as any information accompanying the product or provided at the point of sale before using it.  - Prior to the use of rodenticide products, non-chemical control methods (e.g. traps) should be considered.  - Remove food which is readily attainable for rodents (e.g. spilled grain or food waste). Apart from this, do not clean up the infested area just before the treatment, as this only disturbs the rodent population and makes bait acceptance more difficult to achieve.  - Bait stations should be placed in the immediate vicinity where rodent activity has been observed (e.g. travel paths, nesting sites, feedlots, holes, burrows etc.).  - Where possible, bait stations must be fixed to the ground or other structures.  - Do not open the sachets containing the bait*.*  - Place bait stations out of the reach of children, birds, pets, farm animals and other non-target animals.  - Place bait stations away from food, drink and animal feeding stuffs, as well as from utensils or surfaces that have contact with these.  - Do not place bait stations near water drainage systems where they can come into contact with water.  - When using the product do not eat, drink or smoke. Wash hands and directly exposed skin after using the product.  - Remove the remaining bait or the bait stations at the end of the treatment period. |

5.2. Risk mitigation measures

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| **FOR PROFESSIONAL AND TRAINED PROFESSIONAL USERS**  - Where possible, prior to the treatment inform any possible bystanders about the rodent control campaign *[in accordance with the applicable code of good practice, if any]*".  - The product information (i.e. label and/or leaflet) shall clearly show that the product shall only be supplied to trained professional users holding certification demonstrating compliance with the applicable training requirements (e.g. "for trained professionals only".  - ***FOR TRAINED PROFESSIONAL ONLY*** Do not use in areas where resistance to the active substance can be suspected.  - Products shall not be used beyond 35 days without an evaluation of the state of the infestation and of the efficacy of the treatment.  - ***FOR TRAINED PROFESSIONAL ONLY*** Do not rotate the use of different anticoagulants with comparable or weaker potency for resistance management purposes. For rotational use, consider using a non-anticoagulant rodenticide, if available, or a more potent anticoagulant.  - Do not wash the bait stations or utensils used in covered and protected bait points with water between applications.  - Dispose dead rodents in accordance with local requirements *[The method of disposal shall be described specifically in the national SPC and be reflected on the product label]*.  - ***FOR PROFESSIONAL ONLY*** To reduce risk of secondary poisoning, search for and remove dead rodents at frequent intervals during treatment (e.g. at least twice a week). *[Where relevant, specify if more frequent or daily inspection is required].*  - ***FOR PROFESSIONAL ONLY*** Do not use baits containing anticoagulant active substances as permanent baits for the prevention of rodent infestation or monitoring of rodent activities.  - ***FOR PROFESSIONAL ONLY.*** The product information (i.e. label and/or leaflet) shall clearly show that:   * the product shall not be supplied to the general public (e.g. "for professionals only"). * the product shall be used in adequate tamper resistant bait stations (e.g. "use in tamper resistant bait stations only"). * users shall properly label bait stations with the information referred to in section 5.3 of the SPC (e.g. label bait stations according to the product recommendations").   - ***FOR PROFESSIONAL ONLY*** Using this product should eliminate rodents within 35 days. The product information (i.e. label and/or leaflet) shall clearly recommend that in case of suspected lack of efficacy by the end of the treatment (i.e. rodent activity is still observed), the user should seek advice from the product supplier or call a pest control service.  **FOR NON PROFESSIONAL USERS**  - Consider preventive control measures (plug holes, remove potential food and drinking as far as possible) to improve product intake and reduce the likelihood of reinvasion.  - Do not use anticoagulant rodenticides as permanent baits (e.g. for prevention of rodent infestation or to detect rodent activity).  - The product information (i.e. label and/or leaflet) shall clearly show that:  the product shall be used in adequate tamper resistant bait stations (e.g. "use in tamper resistant bait stations only").  users shall properly label bait stations with the information referred to in section 5.3 of the SPC (e.g. "label bait stations according to the product recommendations").  - Using this product should eliminate rodents within 35 days. The product information (i.e. label and/or leaflet) shall clearly recommend that in case of suspected lack of efficacy by the end of the treatment (i.e. rodent activity is still observed), the user should seek advice from the product supplier or call a pest control service.  - Search for and remove dead rodents during treatment, at least as often as bait stations are inspected.  - Dispose dead rodents in accordance with local requirements *[The method of disposal shall be described specifically in the national SPC and be reflected on the product label]*. |

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

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| - 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

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| - 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: 2 years. |

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 brodifacoum. Results of the resistance monitoring must be submitted at the renewal of the product.)  - (**in France only** : The authorisation holder must provide a field test on R. rattus within 1 year in post authorisation)  - A two year shelf life study with the new composition should be provided to confirm the stability of the product within 2 years.  - 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**

*See initial PAR*

List of studies for the biocidal product submitted for the major change and renewal

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| --- | --- | --- | --- | --- | --- |
| **Sections** | **Author(s)** | **Year** | **Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published** | **Data Protection Claimed (Yes/No)** | **Owner (PUB / ORG)** |
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1. A copy of any written consent(s) of the competent authorities to the deliberate release into the environment of the GMOs for research and development purposes where provided for by Part B of the above-mentioned Directive was provided. [↑](#footnote-ref-1)
2. Please insert additional columns as necessary [↑](#footnote-ref-2)
3. PP = polypropylene, PS = polystyrene, PE = polyethylene, HDPE = high-density polyethylene, PVC = polyvinylchloride [↑](#footnote-ref-3)
4. 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-4)
5. 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-5)
6. 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-6)
7. 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-7)
8. 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-8)
9. Human exposure to Biocidal products-Technical Notes for Guidance, June 2007 [↑](#footnote-ref-9)
10. See document CA-Nov16-Doc.4.x-Final on the concept of tamper-resistant bait stations. [↑](#footnote-ref-10)
11. See document CA-Nov16-Doc.4.x-Final on the concept of tamper-resistant bait stations. [↑](#footnote-ref-11)
12. See document CA-Nov16-Doc.4.x-Final on the concept of tamper-resistant bait stations. [↑](#footnote-ref-12)
13. See document CA-Nov16-Doc.4.x-Final on the concept of tamper-resistant bait stations. [↑](#footnote-ref-13)
14. See document CA-Nov16-Doc.4.x-Final on the concept of tamper-resistant bait stations. [↑](#footnote-ref-14)
15. See document CA-Nov16-Doc.4.x-Final on the concept of tamper-resistant bait stations. [↑](#footnote-ref-15)
16. The evaluating body should keep in mind that where a technical/organisational measure is feasible, it has priority over personal protective equipment (according to Directive 98/24/EC) and should be considered to prevent exposure. [↑](#footnote-ref-16)