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

**PRODUCT ASSESSMENT REPORT OF A BIOCIDAL PRODUCT FOR NATIONAL AUTHORISATION APPLICATIONS**

(submitted by the evaluating Competent Authority)



PATAPPAT

Product type 14

Difenacoum

Case Number in R4BP: BC-VF001195-47

Case Number NA-MAC: BC-GU067230-28

Evaluating Competent Authority: FR

Date: February 2018

Updated: May 2022

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**Note to the reader**

This PAR has been updated with the data provided by the applicant and is based on the PAR of the first authorisation and the subsequent successive assessments (administrative change, major change, …).

In this consolidated PAR, the assessments related to the new data are at the end of the concerned section and are highlighted in grey.

The SPC (in the section 1 of the PAR) corresponds to the currently authorised uses in France.

**Disclaimer regarding user category**

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

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

Consequently, in the SPC in Part 1, uses for “professionals” are mentioned according to the agreed standard SPC, but they not relevant in France. It is proposed that each cMS adapts the conditions of authorization of the product according to its own legislation.

1. **History of the dossier**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Application type** | **refMS** | **Case number in the refMS** | **Decision date** | **Assessment carried out (i.e. first authorisation / amendment /renewal)** |
| NA-APP | *FR* | *NA* | 23.02.2012 | Initial assessment : NYNA D+ PATE |
| NA-BBS | *FR* | *NA* | 11.10.2012 | Same product – PATAPPAT |
| NA-RNL | *FR* | BC-VF001195-47 | 06/03/2018 | Renewal of the authorisation |
| NA-ADC | *FR* | BC-FQ045975-15 | 11.02.2019 | Administrative change |
| NA-MAC | *FR* | BC-GU067230-28 | 24.05.2022 | Addition of outdoor uses: “Rat and Mouse – Trained professionals and professionals– Outdoor around the buildings” and ” Rat and mouse – Trained professionnals - Outdoor open areas, external landfills and waste” |

# Summary of product characteristics for a biocidal product

## Administrative information

### Trade name(s) of the product

| **Trade name(s)** | PATAPPAT |
| --- | --- |
|  |  |

### Authorisation holder

|  |  |  |
| --- | --- | --- |
| **Name and address of the authorisation holder** | **Name** | SBM développement SAS |
| **Address** | 60 chemin des mouilles 69130 Ecully  France |
| **Authorisation number** | FR-2012-0497 | |
| **R4BP asset reference number** | FR-0005659-0000 (2014/FR/3737/1) | |
| **Date of the authorisation** | 11/10/2012 | |
| **Expiry date of the authorisation** | 01/07/2024 | |

### Manufacturer(s) of the product

|  |  |
| --- | --- |
| **Name of manufacturer** | IRIS |
| **Address of manufacturer** | 1126A Avenue Du Moulinas - Route De Saint Privat  30340 SALINDRES  France |
| **Location of manufacturing sites** | 1126A Avenue Du Moulinas - Route De Saint Privat  30340 SALINDRES  France |

|  |  |
| --- | --- |
| **Name of manufacturer** | INDUSTRIAL CHIMICA SRL |
| **Address of manufacturer** | Via Sorgaglia 40  I-35020 ARRE (PD)  Italy |
| **Location of manufacturing sites** | Via Sorgaglia 40  I-35020 ARRE (PD)  Italy |

|  |  |
| --- | --- |
| **Name of manufacturer** | KOLLANT S.r.l |
| **Address of manufacturer** | Via C. Colombo 7-7/A  30030 Vigonovo (VE)  Italy |
| **Location of manufacturing sites** | Via C. Colombo 7-7/A  30030 Vigonovo (VE)  Italy |

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

|  |  |
| --- | --- |
| **Active substance** | Difenacoum |
| **Name of manufacturer** | ACTIVA |
| **Address of manufacturer** | Via Feltre, 32  20132 MILAN  Italy |
| **Location of manufacturing sites** | Via Tre Ponti, 22  37050 MS. MARIA DI ZEVIO (VR)  Italy |

## Product composition and formulation

### Qualitative and quantitative information on the composition of the product

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

### Type of formulation

|  |
| --- |
| Ready-to-use bait: paste |

## Hazard and precautionary statements according to Regulation (EC) 1272/2008

|  |  |
| --- | --- |
| **Classification** | |
| Hazard category | Repr. 1B  STOT RE 2 |
| Hazard statement | H360D: May damage the unborn child  H373: May cause damage to organs through prolonged or repeated exposure |
|  | |
| **Labelling** | |
| Signal words | Danger |
| Hazard statements | H360D: May damage the unborn child  H373: May cause damage to organs through prolonged or repeated exposure |
| Precautionary statements | P201: Obtain special instructions before use.  P202: Do not handle until all safety precautions have been read and understood.  P260: Do not breathe dust/fumes/gas/mist/vapours/spray.  P280: Wear protective gloves/protective clothing/eye protection/face protection.  P308 + P313: If exposed or concerned: Get medical advice/attention.  P314: Get medical advice/attention if you feel unwell.  P405: Store locked up.  P501: Dispose of unused product, its packaging (….) and all other waste, in accordance with local regulations. |
|  | |
| Note | **-** |

## Authorised use(s)

### Use description

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

|  |  |
| --- | --- |
| **Product Type** | 14 |
| **Where relevant, an exact description of the authorised use** | Not relevant for rodenticides |
| **Target organism(s) (including development stage)** | Mus musculus (house mice)  *Rattus norvegicus* (brown rat)  *Rattus rattus* (black or roof rat) |
| **Field(s) of use** | Indoor |
| **Application method(s)** | Bait formulations:  - Ready-to-use bait to be used in tamper-resistant bait stations[[1]](#footnote-2)  - *[Covered and protected baiting points]* |
| **Application rate(s) and frequency** | Bait products:  Rats: 180 g of bait per baiting point distance 5 to 10 m.  Mice: 30 g of bait per baiting point distance 1 to 2 m. |
| **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)*  **Primary packaging**  The product is wrapped individually in heat-sealed paper sachet of 10 g.  **Secondary packaging**  The 10 g wrapped pieces of paste are put in plastic heat-sealed bags (5, 10, 15, 18 and 20 kg). |

#### Use-specific instructions for use

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

#### Use-specific risk mitigation measures

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| --- |
| * 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. |

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

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

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

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

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### Use description

Table 2. Use # 2 *(not relevant in France)* – House mice – professionals – indoor

|  |  |
| --- | --- |
| **Product Type** | 14 |
| **Where relevant, an exact description of the authorised use** | Not relevant for rodenticides |
| **Target organism(s) (including development stage)** | *Mus musculus* (house mice) |
| **Field(s) of use** | Indoor |
| **Application method(s)** | Ready-to-use bait to be used in tamper-resistant bait stations[[2]](#footnote-3) |
| **Application rate(s) and frequency** | - 30 g of bait per bait station. If more than one bait station is needed, the minimum distance between bait stations should be of 1 meter. |
| **Category(ies) of users** | Professionals |
| **Pack sizes and packaging material** | Minimum pack size of 3 kg*.*  **Primary packaging**  The product is wrapped individually in heat-sealed paper sachet of 10 g.  **Secondary packaging**  The 10 g wrapped pieces of paste are put in plastic heat-sealed bags (5, 10, 15, 18 and 20kg). |

#### Use-specific instructions for use

|  |
| --- |
| * The bait stations should be visited at least every 2 to 3 days at the beginning of the treatment and at least weekly afterwards, in order to check whether the bait is accepted, the bait stations are intact and to remove rodent bodies. Re-fill bait when necessary. * *[When available]* Follow any additional instructions provided by the relevant code of best practice. |

#### Use-specific risk mitigation measures

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

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

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

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

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### Use description

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

|  |  |
| --- | --- |
| **Product Type** | 14 |
| **Where relevant, an exact description of the authorised use** | Not relevant for rodenticides |
| **Target organism(s) (including development stage)** | *Rattus norvegicus* (brown rat)  *Rattus rattus* (black or roof rat) |
| **Field(s) of use** | Indoor |
| **Application method(s)** | Ready-to-use bait to be used in tamper-resistant bait stations |
| **Application rate(s) and frequency** | - 180 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*.*  **Primary packaging**  The product is wrapped individually in heat-sealed paper sachet of 10 g.  **Secondary packaging**  The 10 g wrapped pieces of paste are put in plastic heat-sealed bags (5, 10, 15, 18 and 20kg). |

#### Use-specific instructions for use

|  |
| --- |
| * The bait stations should be visited only 5 to 7 days after the beginning of the treatment and at least weekly afterwards, in order to check whether the bait is accepted, the bait stations are intact and to remove rodent bodies. Re-fill bait when necessary. * *[When available]* Follow any additional instructions provided by the relevant code of best practice. |

#### Use-specific risk mitigation measures

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

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

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

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

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### Use description

Table 4. Use # 4 – House mice and/or rats – Trained professionals – Outdoor around the 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)  *Rattus rattus* (black or roof rat) |
| **Field(s) of use** | Outdoor  Outdoor around the buildings |
| **Application method(s)** | Bait formulations:  - Ready-to-use bait to be used in tamper-resistant bait stations[[3]](#footnote-4)  - *[Covered and protected baiting points]* |
| **Application rate(s) and frequency** | Bait products:  Rats: 180 g of bait per baiting point distance 5 to 10 m.  Mice: 30 g of bait per baiting point distance 1 to 2 m. |
| **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)*  **Primary packaging**  The product is wrapped individually in heat-sealed paper sachet of 10 g.  **Secondary packaging**  The 10 g wrapped pieces of paste are put in polyethylene heat-sealed bags (5, 10, 15, 18 and 20 kg). |

#### 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. * [When available] Follow any additional instructions provided by the relevant code of best practice. * Baiting points must be covered and placed in strategic sites to minimise the exposure to non-target species. |

#### 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 use the product close to surface waters (e.g. rivers, ponds, water channels, dykes, irrigation ditches). |

#### 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. |

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

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

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### Use description

Table 5. Use # 5 – *(not relevant in France)*– House mice and/or rats – professionals – Outdoor around the 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)  *Rattus rattus* (black or roof rat) |
| **Field(s) of use** | Outdoor  Outdoor around the buildings |
| **Application method(s)** | Bait formulations:  - Ready-to-use bait to be used in tamper-resistant bait stations[[4]](#footnote-5)  - *[Covered and protected baiting points]* |
| **Application rate(s) and frequency** | Bait products:  Rats: 180 g of bait per baiting point distance 5 to 10 m.  Mice: 30 g of bait per baiting point distance 1 to 2 m. |
| **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)*  **Primary packaging**  The product is wrapped individually in heat-sealed paper sachet of 10 g.  **Secondary packaging**  The 10 g wrapped pieces of paste are put in polyethylene heat-sealed bags (5, 10, 15, 18 and 20 kg). |

#### Use-specific instructions for use

|  |
| --- |
| * Protect bait from the atmospheric conditions. Place the bait stations in areas not liable to flooding. * The bait stations should be visited at least every 2 to 3 days for mice and 5 to 7 days for rats 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. * 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. |

#### Use-specific risk mitigation measures

|  |
| --- |
| * Do not apply this product directly in the burrows. * Do not use the product close to surface waters (e.g. rivers, ponds, water channels, dykes, irrigation ditches). |

#### 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. |

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

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

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### Use description

Table 6. Use # 6 – House mice and/or rats – Trained professionals – Outdoor open areas, external landfills and waste disposals

|  |  |
| --- | --- |
| **Product Type** | 14 |
| **Where relevant, an exact description of the authorised use** | Not relevant for rodenticides |
| **Target organism(s) (including development stage)** | *Mus musculus* (house mice)  *Rattus norvegicus* (brown rat)  *Rattus rattus* (black or roof rat) |
| **Field(s) of use** | Outdoor open areas, external landfills and waste disposals |
| **Application method(s)** | Bait formulations:  - Ready-to-use bait to be used in tamper-resistant bait stations[[5]](#footnote-6)  - *[Covered and protected baiting points]* |
| **Application rate(s) and frequency** | Bait products:  Rats: 180 g of bait per baiting point distance 5 to 10 m.  Mice: 30 g of bait per baiting point distance 1 to 2 m. |
| **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)*  **Primary packaging**  The product is wrapped individually in heat-sealed paper sachet of 10 g.  **Secondary packaging**  The 10 g wrapped pieces of paste are put in polyethylene heat-sealed bags (5, 10, 15, 18 and 20 kg). |

#### 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. * [When available] Follow any additional instructions provided by the relevant code of best practice. * Baiting points must be covered and placed in strategic sites to minimise the exposure to non-target species. |

#### Use-specific risk mitigation measures

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

#### 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. |

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

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

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## General directions for use

### Instructions for use6

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| * Read and follow the product information as well as any information accompanying the product or provided at the point of sale before using it. * Carry out a pre-baiting survey of the infested area and an on-site assessment in order to identify the rodent species, their places of activity and determine the likely cause and the extent of the infestation. * Remove food which is readily attainable for rodents (e.g. spilled grain or food waste). Apart from this, do not clean up the infested area just before the treatment, as this only disturbs the rodent population and makes bait acceptance more difficult to achieve. * The product should only be used as part of an integrated pest management (IPM) system, including, amongst others, hygiene measures and, where possible, physical methods of control. * The product should be placed in the immediate vicinity of places where rodent activity has been previously explored (e.g. travel paths, nesting sites, feedlots, holes, burrows etc.). * Where possible, bait stations must be fixed to the ground or other structures. * Bait stations must be clearly labelled to show they contain rodenticides and that they must not be moved or opened *(see section 5.3 for the information to be shown on the label)*. * *[If national policy or legislation requires it]* When the product is being used in public areas, the areas treated should be marked during the treatment period and a notice explaining the risk of primary or secondary poisoning by the anticoagulant as well as indicating the first measures to be taken in case of poisoning must be made available alongside the baits. * Bait should be secured so that it cannot be dragged away from the bait station. * Place the product out of the reach of children, birds, pets and farm animals and other non-target animals. * Place the product away from food, drink and animal feeding stuffs, as well as from utensils or surfaces that have contact with these. * 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. * For non-emptiable sachets - Do not open the sachets containing the bait. |

### Risk mitigation measures

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

### 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. |

### 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]*. * Do not discharge unused product on the ground, into water courses, into pipes (sink, toilets…) nor down the drains. |

### 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 |

## Other information

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| --- |
| * 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. |

* **Renewal 2017**

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

***Comparative assessment***

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

In summary it can be concluded that the criteria according Article 23(3) a), b) BPR are not fulfilled.

Therefore, the authorisation of this product will be renewed for 5 years.

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

NYNA D+ PATE does not contain any substance of concern according to the Technical Notes for Guidance on data requirements[[6]](#footnote-7).

* **Renewal application (2017)**

PATAPPAT does not contain any substance of concern according to the Guidance on the BPR Volume III Humana Health – Part B Risk Assessment[[7]](#footnote-8).

## Documentation

### Data submitted in relation to product application

**Identity, physicochemical and analytical method data**

Physico-chemical properties studies were provided by Triplan. Some data have been provided using product with old composition and some others with the new composition:

* Explosive properties, oxidising properties performed on NYNA D+ old formulation. The results were extrapolated for the current formulation NYNA D+ PATE.
* The other required physico-chemical properties performed on NYNA D+ PATE, current formulation.

An analytical method to determine the active substance in the formulation NYNA D+ PATE (current formulation) was provided by Triplan.

Data on the active substance required at the product authorization stage as stated in the Assessment Report of the active substance and provided by Activa:

- Analytical data to prove the isomeric composition and impurity profile of the active substance,

- Appearance of the active substance,

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

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

- Validation data for the determination of difenacoum in sediment.

* **Renewal application (2017)**

In the frame of the initial active substance approbation (2009), post approbation data as listed above were required.

Those data were provided in the frame of the renewal assessment report.

* **NA MAC application (2022)**

No additional data was provided in the frame of the major change request.

**Efficacy data**

The following efficacy studies were submitted:

* Efficacy laboratory study of NYNA D+ paste rodenticide containing 0.005% difenacoum with albino house mice (*Mus musculus*).
* Efficacy field study for NYNA D+, paste rodenticide, containing 0.005% difenacoum with black rats (*Rattus rattus*).

Studies were performed with the old formulation NYNA D+ (see detailed composition in confidential document). This formulation is different from the NYNA D+ PATE because of the type of two preservatives not listed in PT6, the pigment and it also contains fewer appetent agents. But it is a paste formulation containing 0.005% p/p of difenacoum and it is the same rate of bittering agent then results can be taken into account in order to support the product authorization of NYNA D+ PATE. Moreover, in order to support the resistance information, new data carried out with literature references were submitted during the evaluation.

* **Renewal application (2017)**

No additional data was provided in the frame of the product authorisation renewal.

* **NA MAC application (2022)**

No additional data was provided in the frame of the major change request.

**Toxicology data**

The applicant did not submit new toxicological data on active substance. The following toxicological studies performed with NYNA D+ BLOC SP were submitted:

* Acute dermal and oral studies,
* Skin and eye irritation studies,
* Sensibilisation study.

The extrapolation of the results to NYNA D+ PATE has been accepted because it is not expected that the difference between the two formulations impacts the toxicity.

* **Renewal application (2017)**

No additional data was provided in the frame of the product authorisation renewal.

* **NA MAC application (2022)**

No additional data was provided in the frame of the major change request.

**Ecotoxicology data**

The applicant has not provided ecotoxicological study with the biocidal product. The environmental risk assessment for NYNA D+ PATE has been done by the authority in charge of the risk assessment, using the Competent Authority Report on the active substance supported by the Task Force Activa/Pelgar.

* **Renewal application (2017)**

No additional data was provided in the frame of the product authorisation renewal.

* **NA MAC application (2022)**

No additional data was provided in the frame of the major change request.

### Access to documentation

The authorisation holder has a letter of access for the data package on the basis of which the active substance difenacoum (CAS 56073-07-5; EC 259-978-4) was approved under the regulation 528/2012, through Commission Implementing Regulation 2017/1379.

# Summary of the product assessment

## Identity related issues

Data were required at the product authorization stage as stated in the AR about the active substance and were provided by Activa:

- Analytical data to prove the isomeric composition and impurity profile of the active substance.

The assessment of the technical equivalence of the source of difenacoum from Activa versus the reference source of Pelgar used for annex I inclusion has been performed. The conclusion is that the source of Activa used in NYNA D+ PATE is technically equivalent to the source of Pelgar assessed for annex I inclusion. The confidential document is attached to this PAR as the addendum to the CAR of difenacoum is not available yet. See the confidential appendix “Technical equivalence Difenacoum Activa” for detailed information.

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

## Classification, labelling and packaging – PAR 2012, updated 2017

### Harmonised classification of the biocidal product

No classification is required for NYNA D+ PATE.

* **Renewal application (2017)**

| **Classification** | |
| --- | --- |
| Hazard category | Repr. 1B  STOT RE 2 |
| Hazard statement | H360D: May damage the unborn child  H373: May cause damage to organs through prolonged or repeated exposure |

### Labelling of the biocidal product

No labelling is required for NYNA D+ PATE.

* **Renewal application (2017)**

|  |  |
| --- | --- |
| **Labelling** | |
| Signal words | Danger    GHS 08 |
| Hazard statements | H360D: May damage the unborn child  H373: May cause damage to organs through prolonged or repeated exposure |
| Precautionary statements | P201: Obtain special instructions before use.  P202: Do not handle until all safety precautions have been read and understood.  P260: Do not breathe dust/fumes/gas/mist/vapours/spray.  P280: Wear protective gloves/protective clothing/eye protection/face protection.  P308 + P313: If exposed or concerned: Get medical advice/attention.  P314: Get medical advice/attention if you feel unwell.  P405: Store locked up.  P501: Dispose of contents/container to … [*… in accordance with local/regional/national/international regulation]* |

### Packaging of the biocidal product

Primary packaging:

For professionals and non-professionals, the product is wrapped individually in heat-sealed paper sachet of 10 g.

Secondary packaging:

The 10 g wrapped pieces of paste are put in plastic heat-sealed bags (100 g, 200 g, 500 g, and 1000 g).

Tertiary packaging:

The bags are put in cardboard boxes (quality: chromoduplex GD2) (100 g, 200, 500, 1000 g) or in varnished iron circular boxes with a plastic cap (200, 500, 600 g) or in waterproof plastic buckets (polyethylene) (from 2 to 18 kg) with a waterproof cape.

* **Renewal application (2017)**

Only packaging for professional users are maintained.

Primary packaging:

The product is wrapped individually in heat-sealed paper sachet of 10 g.

Secondary packaging:

The 10 g wrapped pieces of paste are put in plastic heat-sealed bags (100 g, 200 g, 500 g, and 1000 g). Bag sizes can also be from 5-10-15-18-20 kg.

## Physico/chemical properties and analytical methods – PAR 2012, updated 2017

Data on the active substance difenacoum required at the product authorization stage as stated in the Assessment Report (AR) of the active substance and provided by Activa:

- Appearance of the active substance.

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

### Physico-chemical properties

Table 1: Physico-chemical properties of the active substance

|  | Method/ Guideline | Purity/Specification | Result | Reference |
| --- | --- | --- | --- | --- |
| Physical state | Visual examination | 99.5% w/w difenacoum  Batch number 03090205 | Solid powder at ca. 22°C | CH-082/2010 |
| Colour | Visual examination | 99.5% w/w difenacoum  Batch number 03090205 | Faint beige (Sigma-aldrich Color Chart) |
| Odour | Olfactory test | 99.5% w/w difenacoum  Batch number 03090205 | Characteristic |

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

Table 2: Physico-chemical properties of the biocidal product

For the studies performed on NYNA D+ old formulation, results from these studies could be extrapolated to the current formulation of NYNA D+ PATE. The differences in composition between the two formulations were evaluated and considered as acceptable for each property under consideration.

|  | Method | Purity/Specification | Results | Reference |
| --- | --- | --- | --- | --- |
| Physical state and nature | Visual inspection at room temperature | 0.048 g/kg difenacoum | Homogenous paste  Bait ready for use (RB) | 10-920010-009 |
| Colour | Turquoise blue |
| Odour |  |  | Not determined |  |
| Explosive properties | Differential Scanning Calorimetric method (DSC) | 0.045 g/kg difenacoum  tested on NYNA D+ (old formulation) | Not explosive | 09-920010-001 |
| Oxidizing properties | Literature survey | 0.045 g/kg difenacoum  tested on NYNA D+ (old formulation) | No oxidizing properties | 09-920010-001 |
| Flash point | Not applicable |  |  |  |
| Autoflammability | EC A16 | 0.048 g/kg difenacoum | No self ignition up to 400°C | 10-920010-009 |
| Other indications of flammability | EC A10 | 0.048 g/kg difenacoum | Not highly flammable | 10-920010-009 |
| Acidity / Alkalinity | CIPAC MT 75.3 | 0.048 g/kg difenacoum | 1% m/v in standard water D  6.64 at 20.3°C after 1 min.  6.32 at 20.6°C after 10 min.  The measured pH value is higher than 4 and lower than 10, therefore no further testing is required | 10-920010-010 |
| Relative density / bulk density | EC A3 | 0.048 g/kg difenacoum | D (19.7°C/4.0°C) = 1.335 ± 0.003 g/cm3 | 10-920010-009 |
| Storage stability – stability and shelf life | 2-years storage stability |  | See conclusion below the table |  |
| Effects of temperature | CIPAC MT 46.3 | 0.048 g/kg difenacoum | The aspect of the test item was considered to be stable after an accelerated storage procedure for 14 days at 54°C.  Difference of content of the active substance:  - 4.2% deviation from T=0 value after the accelerated storage procedure for 14 days at 54°C  See comment and conclusion below the table | 10-920010-010 |
| Effects of light |  |  | Not required since the product will be stored protected from light. |  |
| Reactivity towards container material | Not submitted |  | See conclusion below the table |  |
| Technical characteristics in dependence of the formulation type | Not applicable |  |  |  |
| Compatibility with other products |  |  | The product is never used with other products including biocidal products |  |
| Surface tension | Not applicable |  |  |  |
| Viscosity | Not applicable |  |  |  |
| Particle size distribution | Not applicable |  |  |  |

Storage stability:

The pH was measured after 14 days at 54°C and no significant changes were observed.

**Conclusion – PAR 2012**

The shelf life study (2 years at room temperature) is missing and is required in post registration. The study shouldbe performed with test items in quantity sufficient to overcome the heterogeneity problem. Intermediate results at one year should be provided.

The reactivity toward heat-sealed paper sachet of 10g is missing and is required in post registration. The tested material should be clearly identified in the study.

* **Renewal application (2017)**

**Assessment of the submitted post-registration data (2017) – NYNA D+ PATE**

Post-authorisation data required in the frame of the initial product authorisation (2012) were assessed for the renewal application.

**Table 3: Physico-chemical properties of the biocidal product**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Property** | **Guideline and Method** | **Purity of the test substance (% (w/w)** | **Results** | **Reference** |
| Storage stability test – **long term storage at ambient temperature** | CIPAC 46.3  2-years storage stability | NYNA D + PATE  (0.005% w/w of difenacoum)  Batch No. 221/10 | Determination of physico-chemical properties and storage stability test at rt packed in PE film bag:   |  |  |  |  | | --- | --- | --- | --- | |  | Initial | After 12 months at rt | After 24 months at rt | | Appearance | Homogeneous blue-turquoise paste | Homogeneous blue-turquoise paste | Homogeneous blue-turquoise paste | | Appearance of packaging | Cardboard box containing a transparent plastic bag | Cardboard box containing a transparent plastic bag | Cardboard box containing a transparent plastic bag | | Content of AS | 0.0048% | 0.0046% | 0.0045% | | Variation of AS (%) | - | -4.2% | -6.3% | | Weight (g) | 1355.8 | 1276.8 | 1276.7 | | Difference of weight (%) | - | -6.0% | -6.0% | | pH value (CIPAC 75.3) | 6.32 |  | 5.15 |   Quantification of AS has been done by HPLC UV detection with the method evaluated in the PAR.  Conclusion: The storage during 24 months at rt allow to consider that the product is stable in the claimed packaging (PE film bag) under tested conditions.  The product being a solid, if it is compatible with one type of packaging, it is considered compatible with every types of packaging. The product is thus compatible with paper thermofuse bags (10g). | DEMANGEL, B. (2013), Study No. 10-920010-011 |

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| **General conclusion on the physical, chemical and technical properties of the product for renewal of national authorisation applications – PAR 2017** |
| The product NYNA D + PATE (same product as PATAPPAT) is a ready to use paste 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 product is a blue paste and with no specific odor. Storage stability study results are acceptable. The biocidal product is stable 2 weeks at 54°C and 2 years at ambient temperature with a PE film bag packaging.  Considering the product is a solid and it is compatible with PE film bag, compatibility with every other claimed packagings is considered acceptable.  eCA recommends to store away from light due to the sensitivity of the active substance to light.  Its technical characteristics are acceptable for a paste ready to use formulation. |

* **NA-MAC application (2022)**

No modifications in the physico-chemical evaluation.

### Analytical methods – PAR 2012

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

- Analytical data to prove the isomeric composition and impurity profile of the active substance,

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

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

- Validation data for the determination of difenacoum in sediment.

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

- Analytical data to prove the isomeric composition and impurity profile of the active substance

Results of the assessment:

→ The method provided doesn’t allow to identify and quantify separately the two diastereoisomers. Nevertheless FR CA considers that the provided data allow the determination of the isomeric composition.

→ The submitted data allow to determine the impurity profile.

See table below and the confidential appendix “Technical equivalence Difenacoum Activa” for detailed information.

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

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

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

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

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

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

|  |  |
| --- | --- |
|  | Principle of method |
| Technical active substance as manufactured: | HPLC-UV |
| Impurities in technical active substance: | - |
| Active substance in the formulation: | HPLC-UV |

**Technical active substance as manufactured:**

The determination of the active substance was performed by HPLC using an internal standard and UV detector at 275nm. The quantification of difenacoum is achieved by comparing the ratio of the analytical standard peak area versus 1,3,5-triphenylbenzene internal standard (IS) peak area and the same ratio determined for a sample containing a known amount of internal standard (I.S). The analytical method is considered to be acceptable.

**Impurities in technical active substance:**

No methods required since there are no impurities higher than 0.1% w/w.

**Active substance in the formulation:**

**Report:** Validation of an analytical method for the determination of difenacoum in NYNA D + PATE, RICAU, H. 2010

**Study GLP N°:** 09-920010-004

**Test facility:** DEFITRACES

Z.A. des Andrés

150, rue Pré-Magne

69126 BRINDAS

FRANCE

Test item: NYNA D+ PATE, batch 112/09

Principle of the method:

Samples are extracted with methanol, blended and filtered. Determination is performed with HPLC-UV (320nm) using a Zorbax SB-phenyl column.

The validation of this method was considered in compliance with SANCO 3029/99.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Sample** | **Test substance** | **Analytical method** | **Test item preparation** | **Linearity** | **Specificity** | **Recovery rate (%)** | **Precision**  **repeatability** | **Reference** |
| **Range** |
| NYNA D+ PATE | Difenacoum | HPLC with UV detection | Preparation of the test item solution:  A quantity of about 2.5 g (to the nearest 0.1 mg) of the test item was weighed into a 250-mL round-bottomed flask. A volume of 50 mL of methanol and few glass balls were added. The round-bottomed flask was heated under reflux for about 90 minutes at 80°C. The hot solution was filtered over a filter No. 1 (or equivalent) and the extract was transferred into a 50-mL volumetric flask by filtering on a new filter No. 1. The flask was made to volume with methanol. The solution was diluted 2.5 times with methanol. A vial was prepared for analysis. | Calibration solutions of the reference items at five concentrations between 50% and 150% of the expected concentration were analysed.  The response of the detector during the analysis of difenacoum was linear within the range of 0.64 mg/L to 2.04 mg/L (y = 34757151 X - 572; R = 0.9996). | No interference was observed in the solvent blank, the formulation blank, the reference item and the test item at the retention time of difenacoum | Accuracy was checked by analysis of two reconstituted samples with known amounts of difenacoum reference items. The accuracy results of difenacoum were in conformity with SANCO/3030/99 rev. 4 requirements.  Indeed, the recovery results should be in the range 80%-120% (formulations containing less than 0.01%) and they were experimentally equal to 91.5% and 88.0%. | Precision was checked by replicate analyses of the test item (n = 5).  The mean concentration of difenacoum in the test item was equal to 0.00256% w/w.  In the case of difenacoum, the precision was acceptable as the R.S.D. was lower than the result of the modified Horwitz equation: 5.16 < 6.07 (C = 0.00004). | 09-920010-004 |

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| **Conclusion on the methods for detection and identification of the product** |
| Provided analytical method is fully validated for the determination of the active substance difenacoum at 50 ppm in the product NYNA D+ PATE. |

## Risk assessment for Physico-chemical properties

NYNA D+ PATE is a ready-to-use rodenticide. It is a homogenous paste, not highly flammable, not auto-flammable (up to 400°C), not explosive and does not have oxidizing properties

The accelerated storage (14 days at 54°C) shows that NYNA D+ PATE is stable. Other data are missing (shelf life and reactivity toward container material) and are required in post registration.

* **Renewal application (2017)**

PATAPPAT is not highly flammable, not auto-flammable (up to 400°C), not explosive and does not have oxidizing properties according to GHS guideline. eCA considers these conclusions are still valid and do not impact the CLP classification. No formulant is expected to be classified for physico-chemical CLP properties.

* **NA-MAC application (2022)**

No modifications in the physico-chemical evaluation.

## Effectiveness against target organisms

### Function

MG 03: Pest Control

Product Type 14: Rodenticide

* + 1. **Organism(s) to be controlled and products, organisms or objects to be protected**

According to the uses claimed by Triplan, NYNA D+ PATE is intended to be used to control rodents inside buildings (private, public including farm buildings).. The target organisms to be controlled are brown rat *(Rattus norvegicus),* roof rat or house rat (*Rattus rattus)* and wild and house mouse *(Mus musculus).*

The products, organisms or objects to be protected are public health, domestic animal heath, and material protection (historical building, technical objects).

* + 1. **Effects on Target organisms**

Anticoagulants rodenticides disrupt the blood-cutting mechanisms. Signs of poisoning in rodents are those associated with an increased tendency to bleed, leading ultimately to profuse haemorrhage. After feeding on bait containing the active substance for 2-3 days the animal becomes lethargic and slow moving. Signs of bleeding are often noticeable and blood may be seen around the nose and anus. As symptoms develop, the animal will lose its appetite and will remain in its burrow or nest for increasingly long periods of time. As the active substance has a long acting action, death will usually occur within 4 -10 days of ingesting a lethal dose and animals often die out of sight in their nest or burrow.

The application rates recommended by the applicant are the following:

Rats: (*Rattus norvegicus and Rattus rattus)*

180 g paste/secured bait point separated by 5-10 m.

Mice: (*Mus musculus*)

30 g paste/secured bait point separated by 1-2 m

The product is intended to apply in secured bait stations by professional and non-professional users on infested areas with obvious tracking of feces, and smears next to holes and harbourages. Distances between each bait station, so as the number and timings of application and the amount of product, depend on several factors: the treatment site, the size and severity of the infestation.

The applicant submitted following studies:

Laboratory study with albino house mice *(Mus musculus)*:

In this study, the test system was well conduced with the old formulation NYNA D+ (free and no choice food, and control lot). Within 3 days baiting, the results pointed out that, the consumption of the bait is lower than the control animals’ usual food (average of 55%), but sufficient to obtain a total efficacy (100% of mortality) at day 10. Average mortality time has been 6.7 days for the free choice lot and 7.4 days for the efficacy.

Despite a low acceptance of bait, this laboratory trial has proved a high level of efficacy (100% of mortality).

Field trial on Black rat wild strain (*Rattus rattus*):

A field study with black rats was conducted using the old formulation NYNA D+, with a pig farm (black rats). The application rate applied in secured bait was 100 g of bait. Within 8 days baiting, the field trial showed a large range of acceptability. However, the pre-baiting stage was very long (67 days) due to the high competition of food in pig farm and the unusual food behavior of rats.

**In spite of these factors, the consumption of bait was sufficient to obtain 94 % of mortality. This mortality rate is in adequacy with the results assessed in the laboratory with albino house mice and** **confirms the efficacy of the product NYNA D+ PATE.**

**All efficacy studies results are presented in annex 3a.**

* **Renewal application (2017)**

For the renewal of the authorisation of the product PATAPPAT (0.005 % w/w difenacoum), no change in the composition has been declared and no further data have been submitted to the dossier.

Uses and doses validated for PATAPPAT are the following:

|  |  |  |  |
| --- | --- | --- | --- |
| **Product** | **Target organisms** | **Application rate and intervals** | **Use area** |
| PATAPPAT  Bait paste containing 0.005% w/w of difenacoum. | Rats (*Rattus norvegicus* and *Rattus rattus)* | 180 g / bait point separated by 5 to 10 meters | In buildings |
| Mice (*Mus musculus*) | 30 g / bait point separated by 1 to 2 meters |

* **NA-MAC application (2022)**

The efficacy assessment performed for the use of the product against rats and mice in buildings is considered to cover the efficacy assessment for outdoor uses at the same claimed application rates against rats and mice.

* + 1. **Occurrence of resistance**

The use of massive anticoagulants in the management of rodents since the 1970's has been at the origin of the first batches of resistance (genetic and not behavioral) to the first generation of anticoagulants (coumafene in particular).

Recent 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 (*Rattus norvegicus*) populations to coumafene.

Only an exhaustive study carried out at the French and European levels could enable pointed-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*”).

Indeed, we cannot sustain that resistance to difenacoum in all geographical areas where it could be used cannot occur and the occurrence of resistance has an impact on the dosages and efficacy of rodenticides used in a more consequent way. Thus, it compels users to take into account the following precautions to reduce the possibility of rodents developing a resistance to difenacoum:

* Products have always to be used in accordance with the label.
* Efficacy level has to be monitored (periodic check) and the case of reduced efficacy has to be investigated for possible evidence of resistance.
* Treatment has to be alternated with active substances having different mode of action.
* Integrated pest management (combination of chemical control, physical and hygienic measures) has to be taken into account.
* Difenacoum must not be used in an area where resistance to this active substance is suspected or established.
* If signs of resistance begin to appear, then, every effort has to be made to eradicate the population. The measures necessary for eradication will vary in different situations; they may involve a number of procedures using both chemical and non-chemical ways.

The authorization holder should report any observed resistance incidents to the Competent Authorities (CA) or other appointed bodies involved in resistance management every two years.

* **Renewal application (2017)**

Resistance to the first generation anticoagulants has been widely reported in both *Rattus norvegicus* and *Mus domesticus* since the late 1950's. The incidence of resistance to first generation anticoagulants in areas in which it is established is commonly 25-85%.

The enzyme vitamin K 2, 3 epoxide reductase (VKOR) is the target for anticoagulants. Modifications in the protein structure due to polymorphisms on the gene coding the VKOR may induce anticoagulant resistance. Most resistant strains are characterised by one single nucleotide polymorphism (SNP). These SNPs cause the exchange of one amino acid in the VKOR enzyme. The biochemical mechanism of anticoagulant resistance has been studied in several geographic strains/VKORC1-variants of the Norway rat. Amino acid substitutions in the VKOR seem to alter its structure and function, resulting in decreased sensitivity to anticoagulant inhibition, depending on strain characteristics.

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

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

Some degree of resistance to difenacoum has been reported in the UK, Denmark, France and Germany but this is usually found in certain populations of rodents highly resistant to first generation anti-coagulants (Greaves et al., 1982[[8]](#footnote-9); Lund, 1984[[9]](#footnote-10); Pelz et al. 1995[[10]](#footnote-11)). 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[[11]](#footnote-12)). 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[[12]](#footnote-13)).

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.

* + 1. **Evaluation of the Label Claims**

The authority in charge of the risk assessment assessed that the product NYNA D+ PATE has shown a sufficient efficacy for the control of mice and rats for an indoor use in domestic, public and private including farm buildings.

The application rates validated are the following:

Rats: (*Rattus norvegicus and Rattus rattus)*

- 180g paste/secured bait point separated by 5-10 m (instead of 5-6 m presented in the label). These intervals between bait points have to be corrected in the product label in accordance with those validated.

Mice: (*Mus musculus*)

- 30 g paste/secured bait point separated by 1-2 m.

According to Triplan, users have to apply 18 sachets/bait point for rats and 3 sachets/bait point for mice. The applicant has to adapt the amount per sachet and bait boxes to the efficient doses. The amount of bait per bait station must not exceed the validated application rates.

The label claim reflects the efficacy data of the product. Nevertheless because of cross-resistances occurrence to second-generation anticoagulants, the product label has to contain information on resistance management for rodenticides:

* Products have always to be used in accordance with the label.
* Efficacy level has to be monitored (periodic check) and the case of reduced efficacy has to be investigated for possible evidence of resistance.
* Treatment has to be alternated with active substances having different mode of action.
* Integrated pest management (combination of chemical control, physical and hygienic measures) has to be taken into account.
* Difenacoum must not be used in an area where resistance to this substance is suspected or established.
* Users should report straightforward to the registration holder any alarming signals which could be assumed to be resistance development.
* **Renewal application (2017)**

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

Uses and doses validated for PATAPPAT are the following:

|  |  |  |  |
| --- | --- | --- | --- |
| **Product** | **Target organisms** | **Application rate and intervals** | **Use area** |
| PATAPPAT  Bait paste containing 0.005% w/w of difenacoum | Rats (*Rattus norvegicus* and *Rattus rattus)* | 180 g / bait point separated by 5 to 10 meters | In buildings |
| Mice (*Mus musculus*) | 30 g / bait point separated by 1 to 2 meters |

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

* **NA-MAC application (2022)**

The efficacy assessment performed for the use of the product against rats and mice in buildings is considered to cover the efficacy assessment for outdoor uses at the same claimed application rates against rats and mice.

## Exposure assessment

### Description of the intended use(s) – PAR 2012

The doses and uses validated are the following:

|  |  |  |  |
| --- | --- | --- | --- |
| Product | Field of use envisaged | User | Likely concentration at which active substance will be used |
| Main group 03;  PT 14  NYNA D+ PATE  Paste containing 0.005% p/p of difenacoum | In buildings for control of rats (brown and black rats) | Professionals | 180 g paste/secured bait point separated by 5-10 m. |
| In buildings for control of mice. | Professionals | 30 g paste/secured bait point separated by 1-2 m. |
| In buildings for control of rats (brown and black rats). | Non  professionals | 180 g paste/secured bait point separated by 5-10 m. |
| In buildings for control of mice. | Non  professionals | 30 g paste/secured bait point separated by 1-2 m. |

According to Triplan, NYNA D+ PATE is intended to be used inside buildings (public, private and farms buildings) for control of house mice (*Mus musculus*), brown rats (*Rattus norvegicus*) and black rats (*Rattus rattus*).

The control of mice and rats is based on the principle of applying baits on infested areas with obvious tracking of feces, and smears next to holes and harbourages.

The product is ready-to-use (paste) and it is manually applied by trained professional users and by non-professional users in secured bait boxes or bait stations.

Over a period of 28 days for application, cleaning, refilling (4 times over 28 days period) and collect of dead rodents.

Professionals:

According to Triplan, a professional applies 180 g baits per secured point for the control of rats (18 sachets of 10 g pieces of paste) and 30 g baits per secured points for the control of mice (3 sachets of 10 g pieces of paste).

According to Triplan, the worst case is 30 bait points treated per day plus remains of 30 bait points collected. However, in the *HEEG opinion on harmonizing the number of manipulations in the assessment of rodenticides (anticoagulants)* agreed at the European Technical Meeting TM III 2010, 60 loadings and 15 cleanings bait stations per day are considered for professional using wax block/paste bait in sachets.

Non-professionals:

According to Triplan, a non-professional applies 180 g baits per secured point for the control of rats (18 sachets of 10 g pieces of paste) and 30 g baits per secured points for the control of mice (3 sachets of 10 g pieces of paste).

According to Triplan, the worst case is 4 bait points treated per day plus remains of 4 bait points collected. However, in the *HEEG opinion on harmonizing the number of manipulations in the assessment of rodenticides (anticoagulants)* agreed at TM III 2010, 5 loadings and 5 cleanings bait stations per day are considered for non-professional using wax block/paste bait in sachets.

The professional or non-professional users are exposed to ready-to-use paste containing 0.005% (w/w) difenacoum.

* **Renewal application (2017)**

The intended uses are only for professionals.

* **NA-MAC application (2022)**

The doses and uses validated are the following:

|  |  |  |  |
| --- | --- | --- | --- |
| **Product** | **Field of use envisaged** | **User** | **Likely concentration at which active substance will be used** |
| Main group 03;  PT 14  NYNA D+ PATE  Paste containing 0.005% p/p of difenacoum | In and around buildings  and  Outdoor open areas, external landfills and waste disposals  for control of rats (brown and black rats) | Professionals | 180 g paste/secured bait point separated by 5-10 m. |
| In and around buildings  and  Outdoor open areas, external landfills and waste disposals  for control of mice. | Professionals | 30 g paste/secured bait point separated by 1-2 m. |

### Assessment of exposure to humans and the environment – PAR 2012

**Assessment of human exposure**

No new human exposure studies have been submitted. In the dossier, Triplan assessed the human exposure based on the TNsG on human exposure, section 7.2 of part 3 – June 2002. This document only contains a series of examples for human exposure assessment and should not be considered as reference data. Therefore, since Triplan provided a letter of access for the unpublished CEFIC study “*Snowdon P.J. Study to determine potential exposure to operators during simulated use of anticoagulant rodenticide baits*”, the FR CA decided to base the human exposure assessment for professionals on this study as done by the RMS (Finland) of the active substance in the Assessment report on difenacoum. This study examined exposure to 20 g wax block baits containing 0.004 % flocoumafen (five blocks/bait box) using 10 replicates for each measurement. This study is considered as representative of the human exposure of wax block rodenticide baits. Considering that similar dermal absorptions were obtained for wax blocks and pastes in the Assessment report on difenacoum and that a similar application/manipulation is expected with these products, the FR CA decides to use the exposure estimations issued from the CEFIC study for the assessment of NYNA D+ PATE. Furthermore, this study could be considered as very worst case concerning the application since NYNA D+ PATE is wrapped individually in heat-sealed paper sachet.

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

Additionally, the Human Exposure Expert Group (HEEG) opinion on harmonising the number of manipulations in the assessment of rodenticides (anticoagulant), agreed at TMII2010 and the HEEG opinion on an harmonised approach for the assessment of rodenticides (anticoagulants) agreed at TMII2011 were taken into account for the estimation of exposure for professionals and non-professionals.

* **Renewal application (2017)**

The intended uses claimed for PATAPPAT authorisation’s renewal are only for professional users.

* **NA-MAC application (2022)**

The exposure assessment performed for the use of the product in buildings (against rats and mice) is considered to cover the exposure assessment for outdoor uses since the claimed application doses are the same (180 g for rats and 30 g for mice) and no change in the size of the packaging is requested.

**Assessment of environmental exposure**

It is important to notice that the applicant did not provide ecotoxicological data about the biocidal product NYNA D+ PATE. So all the environment risk assessment is based on data extrapolated from the active substance, difenacoum.

Bronopol is used in the biocidal product as preservative. This substance is classified as ”Very toxic for aquatic organisms” according to the Directive 67/548/CEE. Moreover, the substance is also notified in the frame of biocidal directive as product type 6 : in-can preservatives and evaluated by Spanish Competent Authority to be included in the Annex I of the Directive 98/8/CE. Therefore, as no data with the biocidal product is available, the FR CA considered that the environmental risk assessment should take into account bronopol. The environmental risk assessment is summarized in section 2.8 of this document.

## Risk assessment for human health

### Hazard potential

#### Toxicology of the active substance

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

The following corresponds to the summary of the derivation of the AELs from the final Assessment report of difenacoum:

*“The lowest LOAEL in a repeated dose study, i.e. the teratogenicity study in rabbits, is chosen as the basis to establish the AOEL (there was no NOAEL). In this study, the maternal LOAEL was 0.001 mg/kg bw/day. Default assessment factors of 10 for inter-species variability and 10 for inter-individual variability are applied. Furthermore, due to the toxicological significance and uncertainty in the database, an additional safety factor of 3 for teratogenicity is used for all anticoagulant rodenticides according to the agreement during peer-review discussion. A further supportive argument for an additional assessment factor comes from the higher potency of the second generation anticoagulants compared to warfarin, and from the much higher vulnerability of human foetuses to vitamin K deficiency compared to rodents. To extrapolate from LOAEL to NOAEL an assessment factor of 2 is considered justified due to the deep slope of the dose response curve. After correction for bioavailability of 68%, a NOAEL for MOE (0.00034 mg/kg bw/day) and an AOEL of 0.0000011 mg/kg bw/day are used for risk characterisation. These values are applied both to acute and repeated exposure scenarios.”*

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

Considering the following definition of a substance of concern set in the TNsG on data requirement chapter 4 (2000), “*the substance is regarded as a substance of concern if [...] it is classified as dangerous* ***and*** *its concentration in the product exceeds the classification limit set in the Council Directive 88/379/EEC, as amended by Directive 1999/45/EC, for a particular dangerous property* ***or*** *the other classification limit indicated for the substance in a preparation set in Annex I of Council Directive 67/548/EEC* ***or*** *causes that the overall sum of the concentrations of dangerous substances in the product exceeds the limit for classification of the preparation set in Council Directive 88/379/EEC, as amended by Directive 1999/45/EC, for a particular dangerous property*”, NYNA D+ PATE does not contain any substance of concern.

* **Renewal application (2017)**

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

#### Toxicology of the biocidal product

The toxicology of the biocidal product was examined according to standard requirements of Directive 98/8/EC. The product was not a dummy product in the EU- review program for inclusion of the active substance in Annex I of Directive 98/8/EC. The basis for the health assessment of the biocidal product is laid out in Annex 5 of this report “Toxicology – biocidal product”.

New data:

Acute oral and dermal toxicity, skin and eye irritation and skin sensitisation studies have been submitted on the product NYNA D+ BLOC SP. Since it is not expected that the differences of composition between NYNA D+ BLOC SP and NYNA D+ PATE impact the toxicity, the extrapolation of study results from NYNA D+ BLOC SP was accepted.

* Acute oral and dermal toxicity

No mortality, systemic or local effects were observed in these studies. The only reported effect was a slight blue coloration (probably due to the colorant present in the product), in the acute dermal study, noted at 24 hours post-dose on the treated area of all animals and totally reversible on day 2.

Based on the results, no classification is required for these endpoints.

* Irritation and corrosivity

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

* Sensitisation

A Magnusson and Kligman sensitisation test was submitted. Due to deviations (such as first induction phase performed by topical route) from the OECD guideline 406, the FR CA does not accept this study. However, based on the composition of NYNA D+ PATE, no ingredients were listed as skin sensitizers.

* Therefore, it is expected that NYNA D+ PATE is not a skin sensitizer.

Justification for non-submission:

* Dermal absorption:

According to the Competent Autority Report on difenacoum (Doc IIIB6.4), a dermal absorption of 0.047% for wax blocks and pastes containing 0.005 % of difenacoum was considered, based on an *in vitro* study with human skin (8 hours of exposure)[[13]](#footnote-14). Read-across from this study is considered acceptable since NYNA D+ PATE is also a paste bait containing 0.005 % of difenacoum.

* Acute inhalation toxicity:

As the product is a solid bait, the generation of inhalable particle is not expected. Additionally, the vapor pressure of difenacoum is very low (< 5x10-5 Pa at 45°C based on an Activa/Pelgar estimation). Therefore, an acute toxicity test by inhalation is not required.

The current harmonised classification of the active substance is the following:

|  |  |
| --- | --- |
| Classification under directive 67/548/EEC | Classification under regulation (EC) 1272/2008 |
| T+ R28  T R48/25  N, R50/53  No specific concentration limit | Acute Tox. 2 H300  STOT Rep. 1 H372  Aquatic. Acute 1 H400  Aquatic Chronic 1 H410  No specific concentration limit |

Based on the results of the studies, the concentration of the active substance and of other components contained in the product and according to the above classification, NYNA D+ PATE is not classified.

* **Renewal application (2017)**

|  |
| --- |
| **Classification under regulation (EC) 1272/2008 for human health** |
| Acute Tox 1 – H300 ; H310 ; H330  STOT RE 1 – H372 (blood)  Repr. 1B – H360D  Repr. 1B; H360D: C ≥ 0,003 % STOT RE 2; H373: 0,002 % ≤ C < 0,02 % STOT RE 1; H372: C ≥ 0,02 % |

Based on the results of the studies, the concentration of the active substance and of other components contained in the product and according to the above classification, the following classification for human health is required for NYNA PATAPPAT:

* Repr. 1B - H360D: May damage the unborn child
* STOT RE 2 - H373: May cause damage to organs through prolonged or repeated exposure
* Other studies

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

The product is a solid bait only used indoors in secured bait points. Collecting unconsumed baits and dead rodents must be done every week during the treatment so in these recommended conditions, no contamination is expected for feeding stuffs. Finally, according to the Assessment report on difenacoum, “*difenacoum baits should not be placed where food, feedingstuffs or drinking water could be contaminated*”. Therefore, no data on residue was submitted.

### Exposure – PAR 2012

NYNA D+ PATE (PT14) is a ready-to-use paste rodenticide containing 0.005% of difenacoum (pure: 960 g/kg) intended to be applied by professionals and non-professionals. The baits are placed in bait stations (bait boxes or secured bait stations) out of reach of children and domestic animals. Baits are packaged wrapped individually in heat-sealed plastic film sachet for professional and non-professional uses.

#### Exposure of professional users

**Primary exposure**

During professional use, the major route of primary exposure is dermal. The inhalation exposure could be considered as negligible considering the low vapour pressure of difenacoum (< 5x10-5 Pa at 45°C based on an Activa/Pelgar estimation), the physical state of the product and because the baits are individually wrapped in sachet.

Based on all the measured exposure data (75th percentile) in the CEFIC study, the amount of exposure to product **during loading** of 5 wax blocks of 20 g per one manipulation was 27.79 mg (value adopted by the HEEG[[14]](#footnote-15)). The following parameters were taken into account:

* Active substance in product: 0.005%
* Number of pastes (considered as similar to wax blocks) per bait site[[15]](#footnote-16): 18 for control of rats and 3 for control of mice
* Dermal absorption: 0.047%
* Body weight: 60 kg

Thus, the systemic dose of difenacoum per placing of one bait site is 3.92 x10-8 mg/kg bw/event for control of rats and 6.53 x10-9 mg/kg bw/event for control of mice.

Based on all the measured exposure data (75th percentile) in the CEFIC study, the amount of exposure to product is 5.70 mg **during the cleaning** of one bait site (value adopted by the HEEG5). Considering a content of 0.005% of difenacoum in the product, a dermal absorption of 0.047% and a body weight of 60 kg, the systemic dose of difenacoum per cleaning of one bait site is 2.23x10-9 mg/kg bw/event (for rats and mice because the amount of disposed bait is not taken into account).

Although Triplan considers that 30 bait points are treated and 30 bait points are collected per day, FR CA has used the harmonized number of manipulations for rodenticides anticoagulant set in the HEEG opinion agreed at TM III 2010. Considering that 60 loadings and 15 cleaning are done per day for paste bait in sachets, the overall systemic dose via skin (loading + cleaning) is 2.38x10-6 mg a.s/kg bw/day without gloves and 2.38x10-7 mg a.s/kg bw/day (penetration factor of 10)[[16]](#footnote-17) for control of rats. For control of mice, the systemic dose via skin is 4.25x10-7 mg a.s/kg bw/day without gloves.

This scenario considering exposure during loading and cleaning represents a very worst case since NYNA D+ PATE is only supplied in sachets. As a reasonable case, no exposure is expected during loading as the sachet prevents dermal contacts and the exposure can be reduced to 3.35x10-8 mg/kg bw/day (without gloves) for both rats and mice because the amount of disposed bait is not taken into account during cleaning.

**Secondary exposure**

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

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

#### Exposure of non-professional users and the general public

**Primary exposure**

During non-professional use, the major route of primary exposure is dermal. The inhalation exposure could be considered as negligible considering the low vapour pressure of difenacoum (< 5x10-5 Pa at 45°C based on an Activa/Pelgar estimation), the physical state of the product and because the baits are individually wrapped in sachet.

As a worst case, the same assumptions as for professional exposure was considered except for the number of manipulations set at 5 loadings and 5 cleaning per day for non-professional according to the HEEG opinion document[[17]](#footnote-18) and in the absence of PPE. The overall systemic exposure via skin (loading + cleaning) is therefore at 2.08x10-7 mg a.s/kg bw/day for control of rats and 4.38x10-8 mg a.s/kg bw/day for control of mice.

As a reasonable case, since NYNA D+ PATE is only supplied in sachets, no exposure is expected during loading as the sachet prevents dermal contacts. Therefore, the exposure can be reduced to 1.1x10-8 mg/kg bw/day for both rats and mice because the amount of disposed bait is not taken into account during cleaning.

**Secondary exposure**

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

For the scenario “*oral exposure by ingesting bait*”, a reverse scenario was calculated. Based on the AEL of 1.1x10-6 mg a.s/kg bw/day, a body weight of 10 kg and an oral absorption of 68% (as stated in the Assesment report of difenacoum [Activa/Pelgar Study]), ingestion of more than 0.3 mg of product per day (corresponding to about 0.003 % of a 10g paste of NYNA D+ PATE) is needed to exceed the AEL.

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

* **Renewal application (2017)**

General public uses are no longer claimed for the renewal of authorisation.

#### Exposure to residues in food

Based on the intended uses, no residue assessment was performed (Annex 8 “Residue behaviour”).

### Risk characterisation – PAR 2012

#### Risk for professional users

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

**Primary exposure**

Based on the risk assessment of the active substance, the risk for professional users resulting from the intended uses is acceptable. The %AEL is set at 3% (without gloves) when exposure is only considered during cleaning since NYNA D+ PATE is supplied in sachet (see Annex 6 for detailed calculations). However, gloves are recommended to help prevent rodent-borne disease. Moreover, the mention “do not open the sachet” has to be added in the label of the product.

**Secondary exposure**

No relevant secondary exposure is expected for professional users, thus no unacceptable risk has been identified.

* **Renewal application (2017)**

The conclusions of the risk assessment remain unchanged. The RMMs required by the risk assessment remain also unchanged.

* **NA-MAC application (2022)**

The risk assessment performed for the use of the product in buildings (against rats and mice) is considered to cover the exposure assessment for outdoor uses since the claimed application doses are the same (180 g for rats and 30 g for mice) and no change in the size of the packaging is requested.

#### Risk for non-professional users and the general public

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

**Primary exposure**

Based on the risk assessment of the active substance, the risk for non-professional users resulting from the intended uses is acceptable. The %AEL is set at 1% when exposure is only considered during cleaning since NYNA D+ PATE is only supplied in sachet (see Annex 7 for detailed calculations).

**Secondary exposure**

Based on a reverse scenario, more than 0.3 mg of product per day (corresponding to 0.003% of a 10 g paste NYNA D+ PATE) should be ingested by infant to exceed the AEL. This indicates that infants are at significant risk of poisoning. Therefore, even if NYNA D+ PATE contains a bittering agent which reduces the likelihood of ingestion, the baits should be placed in bait boxes which do not allow access to children in secured areas. Product label (“do not open the sachet”) and good practice advise users to prevent access to bait by children and infants.

* **Renewal application (2017)**

General public uses are no longer claimed for the renewal of authorisation.

#### Risk for consumers via residues

Based on the intended uses, no food risk assessment was performed.

**Table 2.7.3-1: Summary of risk characterisation for professional and non-professional users**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Scenario** | **AEL (mg/kg bw/d)** | **Exposure (mg/kg bw/d)** | **%AEL** | **Risk** |
| **Exposure only during cleaning (NYNA D+ PATE supplied and applied in sachet)** | | | | |
| Professional  (without gloves) | 1,1x10-6 | 3,4x10-8 | 3 | **Acceptable** |
| Non-professional  (without gloves) | 1,1x10-6 | 1,1x10-8 | 1 | **Acceptable** |

* **Renewal application (2017)**

The conclusions of the risk assessment remain unchanged for professional users considering the RMMs required by the risk assessment and described in the summary of product characteristics (SPC). The use of PATAPPAT by general public was not considered as it is no longer claimed for the renewal of authorisation.

* **NA-MAC application (2022)**

Exposure of general public (secondary exposure) is still relevant and unchanged.

## Risk assessment for the environment (2012, updated 2017)

### Fate and distribution of the active substance, difenacoum, in the environment – PAR 2012, updated 2017

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

#### Biodegradation of difenacoum

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

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

#### Hydrolysis as a function of pH

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

#### Photolysis in water

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

#### Photodegradation in air

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

#### Distribution

##### Adsorption/desorption

The experimentally derived Koc values are not supported by the physical and chemical properties of difenacoum. Difenacoum is a large aromatic molecule with two polar groups which can potentially ionise at environmental relevant pH. Difenacoum has also a low water solubility and a high log Kow.

According to the Technical Guidance Document (TGD) Part 3, Table 4, the QSAR equation used to calculate log Koc from log Kow (7.62, a QSAR estimation) is:

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

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

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

##### Accumulation

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

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

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

* **Renewal application (2017)**

Based on calculation according to the regulation 1272/2008/EC, no classification is required for the product PATAPPAT.

### Effects of the active substance on environmental organisms – PAR 2012

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

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

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

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

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

#### Atmosphere

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

#### Terrestrial compartment

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

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

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

#### PBT assessment

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

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

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

The primary concern is from predators eating the rodent carcasses and earthworms which have ingested the active substance absorbed to soil. In guidance document for PT14, the active substance is considered to be placed in protected bait point. Therefore, a risk should be taken into account for primary poisoning mainly for birds and mammals of equal or smaller size than the target rodents. Also when target animals carry bait away from e.g. bait stations, non-target animals may be exposed. For the risk characterization of primary poisoning, the PNECoral described in section 2.8.2.7 will be used.

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

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

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

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

#### Summary of PNEC

##### PNEC for aquatic organisms:

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

**PNECwater = 0.06 μg/L**

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

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

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

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

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

**PNECSTP = 0.48 mg/L**

##### PNEC for terrestrial organisms:

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

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

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

PNECsoil = 2.04 mg/kg wet weight

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

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

##### PNEC for birds and mammals

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

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

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

PNECoral for mammals is derived from the NOAEL of 0.03 mg/kg bw/d origin from the 90-day subchronic test in rat (Doc IIIA6.4.1 of the CAR of difenacoum). The NOAEL is transformed to NOEC (concentration in food) by multiplying with the conversion factor of 20 (TGD, Table 22). The appropriate assessment factor according to the TGD is 90. The PNECoral value kept for the risk assessment is:

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

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

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

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Table 2.8.2-1: summary of the difenacoum PNECs | | | | |
| **Compartment** | | **Test Value** | **AF** | **PNEC Unit** |
| Aquatic | PNECwater | LC50 =0.064 mg/L | 1000 | 0.064 µg/L |
| PNECsediment | PNECwater in eq. 70 (TGD) | | 2.51 mg/kg wet weight |
| PNECSTP | Water solubility= 0.48 mg/L | | 0.48 mg/L |
| Terrestre | PNECsoil | LC50 >994 mg/kg | 1000 | 0.994 mg/kg dry weight  0.877 mg/kg wet weight |
| PNECoral for birds | LC50 =1.4 mg/kg food  LD50= 0.3 mg/kg bw/d | 3000 | 0.5 μg/kg food eq. to  0.1 μg/kg bw/d |
| PNECoral for mammals | NOEC= 0.6 mg/kg food  NOAEL=0.03 mg/kg bw/d | 90 | 7 μg/kg food eq. to  0.3 μg/kg bw/d |

### Effects on environmental organisms for biocidal product NYNA D+ PATE – PAR 2012

It is important to notice that the applicant did not provide ecotoxicological data about the biocidal product NYNA D+ PATE. So all the environment risk assessment of NYNA D+ PATE is based on data obtained from the active substance, difenacoum.

Bronopol is used in the biocidal product as preservative. This substance is classified as ”Very toxic for aquatic organisms” according to the Directive 67/548/CEE. Moreover, the substance is also notified in the frame of biocidal directive and evaluated by Spanish Competent Authority to be included in the Annex I of the Directive 98/8/CE.

Therefore, as no data with the biocidal product is available, FR CA considered that the environmental risk assessment should take into account bronopol.

Data of the acute toxicity of bronopol on aquatic organisms are available in the material safety data sheet:

EC50 (72 h) = 0.4 mg/L (*Algae*)

EC50 (48 h) = 1.4 mg/L (*Daphnia magna*)

LC50 (96 h) = 41.2 mg/L (*Oncorhynchus mykiss*)

EC50 > 50 mg/L (Bacteria)

According to the Directive 67/548/CEE, bronopol is classified R50: Very toxic to aquatic organisms with a specific concentration limit: C>2.5%.

Based on CLP regulation 1272/2008, the classification of bronopol is Aquatic Acute 1 – H400: Very toxic to aquatic life.

Nevertheless, in the concentration used in NYNA D+ PATE, the substance does not contribute to the classification of the biocidal product.

As no enough data is available to carry out a complete risk assessment with the substance bronopol, this assessment should be reviewed after the inclusion of bronopol in the Annex I of the Directive 98/8/CE.

### Environmental exposure assessment – PAR 2012, updated 2017

Exposure scenarios are defined as a set of conditions about sources, pathways and use patterns that quantify the release of the substance from processing, use and disposal into soil, water, air and waste. To describe the possible release of rodenticides from its use and disposal, the exposure scenarios for PT14 introduced in EUBEES ESD (2003), with an addendum endorsed at the 23rd CA meeting Nov. 2006 are used.

In accordance with EUBEES ESD (2003) and TGD for Risk Assessment (2003), a quantitative approach is used in the risk assessment for NYNA D+ PATE biocidal product. Quantitative PEC estimations are performed for the relevant environmental compartments for difenacoum. The different PEC values are derived from model calculations, but available measured data (e.g. difenacoum metabolism in rat) are also taken into consideration.

The product NYNA D+ PATE is a ready-to-use impregnated paste product with 0.005% of difenacoum, the active substance, and bronopol as preservative. The product is used as 10 g paste portions packed in paper sachet. The packed impregnated paste is placed in secured bait stations. According to the applicant, the product is intended to be used in bait boxes inside industrial, commercial and residential buildings. Bait points are inspected and replenished once a week when bait taken is observed.

The available data about the treatment campaign are extracted from the applicant’s dossier:

* Duration of a treatment campaign: 28 d,
* Rat application rates: up to 180 g of product / bait point separated by 5-10 meters,
* Mouse application rates: up to 30 g of product / bait point separated by 1-2 meters
* The NYNA D+ PATE baits are placed only in bait stations,
* The product is used inside buildings only,
* Number of bait stations: 20 inside, 5 meters apart for rats, 1 meter for mice,
* Day 1: Treatment with 18 x 10 g product per box for rat, 3 x 10 g per box for mouse,
* Day 7, 14 and 21: bait refilling.

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

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

#### PEC in surface water and sediment

Exposure of surface water and sediment after the treatment with rodenticides is only relevant for indoor application of liquid poisons, residues from mixing and cleaning (ESD PT14) when a release is foreseen via the STP. As NYNA D+ PATE is a solid form and is intended to be used indoor only, no indirect or direct exposure to surface water and sediment is expected.

#### PEC in air

Difenacoum is not expected to partition to the atmosphere to any significant extent due to low vapour pressure and Henry's Law constant. Difenacoum has a potential for rapid photo-oxidative degradation in the air (half-life about two hours). The exposure of air is therefore considered negligible for the application of NYNA D+ PATE biocidal product.

#### PEC in soil and groundwater

As NYNA D+ PATE is intended to be used indoor only, no exposure to soil and groundwater is expected.

#### Non compartment specific exposure relevant to the food chain (primary and secondary poisoning)

##### Primary poisoning

The risk assessment for the primary poisoning presented below was extracted from the Annex I inclusion dossier for the active substance considering that difenacoum concentration is identical in the product NYNA D+ PATE and in the representative product presented for the Annex I inclusion. Primary poisoning calculations are carried out considering the ‘in and around buildings’ scenario from the EUBEES ESD PT14 as a worst case scenario in view of the fact that the product is applied inside buildings only.

According to ESD (Larsen, 2003), primary poisoning hazard to mammals and birds (both wild and domestic) can be considered small in the scenario “in and around buildings”. In use scenarios where difenacoum is placed in protected bait point, there is the risk for primary poisoning mainly for birds and mammals of equal size or smaller as the target rodents, which may be able to enter the bait stations. Also when target animals carry bait away from e.g. bait stations, non-target animals may be exposed.

Worst case exposure estimations are based on the equations and default values proposed by the ESD (Larsen, 2003). Some defaults parameters may be replaced by product-specific properties.

The Tier 1 assessment assumes that there is no bait avoidance by the non-target animals and that they obtain 100% of their diet in the treated area and has access to difenacoum product. **The worst case Tier 1 PECoral is 50 mg/kg** (difenacoum present at 0.005% w/w in NYNA D+ PATE) and is used in quantitative risk assessment for the long-term situation.

According to ESD (Larsen, 2003) a Tier 2 assessment can be done estimating daily uptake of a compound (ETE) by non-target animals according to the equation 19 of ESD:

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

FIR: food intake rate of the indicator species,

BW: indicator species body weight,

C: concentration of the active substance in fresh diet,

AV: avoidance factor,

PT: fraction of diet obtained in treated area and

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

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

When elimination of active substance is taken into account, the expected concentration of active substance (EC) in animal is calculated with equation **EC = ETE x (1-El),** where El is fraction of daily uptake eliminated (number between 0 and 1, default 0.3). According to the toxicokinetic study (section 2.8.2.6) the total daily elimination in rats taking into account excretion through faeces and metabolism of difenacoum in rat liver, is approximately 40% (elimination factor 0.4), which is used in calculations also for non-target animals as there is no other data available. Calculations for ETE and EC values for worst case and realistic worst case situations are presented in the table below. According to the guidance agreed at 23rd Competent Authority meeting, these values are used for qualitative risk assessment of primary poisoning in acute situation.

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| --- |
| **Table 2.8.4.4‑1 : Expected concentrations of difenacoum in non-target animals in the worst case (Step 11) and realistic worst case (Step 22) for acute situations with and without elimination** |
|  |

Calculations of the expected concentrations (EC) for 5 days exposure considering elimination are calculated according to ESD equation 21 as a worst case i.e. AV, PT and PD are set to 1. According to the guidance agreed at 23rd CA meeting, EC5 values are used for quantitative risk assessment of primary poisoning in the long-term situation.

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| --- |
| **Table 2.8.4.4‑2 : Expected concentrations of difenacoum (EC5) in non-target animals for the long-term situations (worst case).** |
|  |
| Among the anticoagulant poisoning incidents, dogs are common victims. The intoxication of dogs is easily detected as they live together with man. Intoxication incidents of wild animals may often remain unobserved. Small non-target rodents, such as voles, and small, granivorous birds can feed on rodenticidal baits because they can pass through the entrance hole of a bait station. Exposure may also arise if target animals carry bait away from the bait station. The domestic animals at risk are dog, pig and hen. Birds eating cereal and weed seeds like sparrows, pigeons and pheasants are possible wild species that may be at risk of primary poisoning. |

##### Secondary poisoning

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

As no exposure of the aquatic compartment is foreseen with the use of NYNA D+ PATE inside buildings, no risk assessment for secondary poisoning through the aquatic food chain is required.

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

As no exposure of the terrestrial compartment is foreseen with the use of NYNA D+ PATE inside buildings, no risk assessment for secondary poisoning through the terrestrial food chain is needed.

***Secondary poisoning for the rodent-eating mammal or the rodent-eating bird***

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

The risk assessment for the secondary poisoning presented below was extracted from the Annex I inclusion dossier for the active substance considering that difenacoum concentration is identical in the product NYNA D+ PATE and in the representative product presented for the Annex I inclusion. Secondary poisoning calculations are carried out considering the ‘in and around buildings’ scenario from the EUBEES ESD PT14 as a worst case scenario in view of the fact that the product is applied inside buildings only.

According to ESD (Larsen, 2003) document, for uses in and around buildings it is assumed that predators among mammals and birds may occur inside buildings or they may hunt rats in the immediate vicinity of buildings (parks and gardens or further away), also scavengers may search for food close to buildings and thus secondary poisoning through poisoned rats exists. Secondary poisoning hazard can only be ruled out completely when the rodenticide is used in fully enclosed spaces so that rodents cannot move to outdoor areas or to (parts of) buildings where predators may have access.

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

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

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

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

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

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| --- |
| **Table 2.8.4.4‑3 : Estimated concentration (EC) of difenacoum in target rodents (rats) in mg a.s./kg bw at different times during a control operation** |
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Tier 1 PECoral for short term situation is calculated according to the equation 22 in ESD (Larsen, 2003):

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

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

where:

Frodent; fraction of poisoned rodents in predator's diet

ECn: expected concentration of a.s. in the rodent on day 'n' before the last meal

n; the number of days the rodent is eating rodenticide until caught, default 5.

These values, presented in Table 2.8.4.4-4 below, are used for qualitative risk assessment of secondary poisoning in acute situation.

* Tier 1 PECoral for long term situation is calculated similar way, but the Frodent is set to 0.5, which means that it is assumed that non-target animal consume 50 % of their daily intake on poisoned rodents. These values, presented in Table 2.8.4.4-4 below, are used for Tier 1 quantitative risk assessment of secondary poisoning in the long-term situation.

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| --- |
| **Table 2.8.4.4‑4 : Predicted environmental concentrations of difenacoum in food of predator (PECoral) for acute and long-term situations.** |
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* Tier 2 for long-term exposure: according to the CAR of difenacoum, the PECoral is the concentration in non-target animals after a single day of exposure (mg/kg bw) using values PD of 1 (100% bait consumption by rodent) and Frodent of 0.5. PECoral values presented in the table 2.8.4.4-5 below are used for Tier 2 quantitative risk assessment of secondary poisoning in the long-term situation.

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| --- |
| **Table 2.8.4.4‑5 : Expected concentrations of difenacoum in non-target animals due to secondary poisoning after a single day exposure (concentration of difenacoum in rodenticide bait 0.005%); rodents caught by predators on day 5 and 14 (after feeding), PD 1, Frodent 0.5.** |
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|  |

### Risk characterisation for the environment – PAR 2012, updated 2017

Risk characterization for the environment is done quantitatively by comparing predicted environmental concentrations (PEC) and the concentrations below which effects on organism will not occur (PNEC) according to the guidance in Technical guidance document (TGD, 2003) and 'Emission scenario document for biocides used as rodenticides' (Larsen, 2003, ESD PT14).

The environmental risk characterization has been carried out for difenacoum.

#### Primary poisoning

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

|  |  |  |  |
| --- | --- | --- | --- |
| **Table 2.8.5.1‑1 : Tier 1 risk characterisation of primary poisoning.** | | | |
|  | PEC mg/kg food | PNEC mg/kg food | PEC/PNEC |
| Birds | 50 | 0.0005 | 100 000 |
| Mammals | 50 | 0.007 | 7 143 |

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

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

|  |
| --- |
| **Table 2.8.5.1‑2 : Tier 2 risk characterisation of primary poisoning.** |
|  |

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

The risk characterisation indicates a very high risk to non-target mammals and birds from direct eating of bait. Primary poisoning incidents can be minimised by preventing the access of non-target animals to the baits. It is assumed in the ESD that if the rodenticide baits are used according to the label instructions, the risk for primary poisoning is negligible. However, it is stated at the EU level that it may not be possible to exclude exposure of all non-target animals, as the baits have to be accessible to target rodents, they may as well be accessible to non-target mammals and birds of equal or smaller size than the target rodents.

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

#### Secondary poisoning

The only relevant scenario of secondary poisoning in the case of an indoor application only is for the rodent-eating mammal or bird.

***Rodent eating birds and mammals***

A qualitative assessment of the acute secondary poisoning is made by comparing the concentration in the rodents to LD50 values from acute oral studies. Rodents are assumed to eat entirely on bait containing difenacoum and the non-target animals are assumed to consume entirely poisoned rodents. The qualitative assessment indicates that birds are likely to survive and mammals are likely to die if they eat poisoned rats (Table 2.8.5.2-1). The species specific sensitivity differences or other aspects normally covered by the assessment factors are not taken into account in the qualitative assessment.

|  |
| --- |
| **Table 2.8.5.2‑1 : Qualitative assessment of acute secondary poisoning.** |
|  |

###### ***Tier 1 assessment of secondary poisoning***

The Tier 1 assessment of secondary poisoning is based on the concentration in the predator's or scavenger's food, i.e. poisoned rodents. The rodents are assumed to consume entirely the bait (PD = 1), while half of the predator's or scavenger's daily food intake is poisoned rodents (Frodent = 0.5). The rodents are assumed to eat the baits in five or fourteen successive days, whereas the predator or the scavenger is assumed to eat the poisoned rodents during one day. The predator is assumed to catch the rodent after last meal on day 5 or day 14. Only resistant rodents are assumed to eat bait 14 day. The calculation of concentrations in rodents is explained in detail in Section 2.8.4.4.2. The PNECoral is based on the highest concentration causing no effects in the test with long-term exposure. The derivations of PNECs are explained in Section 2.8.2.7.5.

|  |
| --- |
| **Table 2.8.5.2‑2 : Tier 1 risk characterization of secondary poisoning.**  Expected concentration in target rodents is compared to the PNECoral expressed as concentration in food. Rodents are assumed to consume entirely bait (PD=1). Half of the predator's diet is poisoned rodents (Frodent=0.5). |
| The Tier 1 risk characterization shows that there is an unacceptable risk for secondary poisoning and birds are at higher risk due to lower PNECoral (Table 2.8.5.2-2).  Resistant rodents can feed on the poisoned baits longer and accumulate higher difenacoum residues than non-resistant rodents. Resistant rodents can continue to feed difenacoum up to two weeks, while the non-resistant rodents stop feeding after 5 days. Based on the calculations, the resistant rodents cause about 1.5 times higher risk for secondary poisoning of birds and mammals than non-resistant rodents. |

###### ***Tier 2 assessment of secondary poisoning***

In the Tier 2 assessment of long-term secondary poisoning the expected concentration in predators is compared to PNECoral expressed as a daily dose. The predators accumulate difenacoum by feeding on poisoned target rodents during one day. The rodents are assumed to eat entirely the bait (PD = 1), whereas half of the predator's or scavenger's daily food intake is poisoned rodents (Frodent = 0.5). The rodents are assumed to eat the baits in five or fourteen successive days. The susceptible rodents are assumed to stop feeding after 5 days, but resistant rodents are assumed to continue feeding until day 14. The calculation of expected concentrations is explained in detail in Section 2.8.4.4.2.

|  |
| --- |
| **Table 2.8.5.2‑3: Tier 2 risk characterization of secondary poisoning.**  The difenacoum expected concentrations in predatory birds and mammals are compared to the PNECoral expressed as daily dose. |
|  |

The Tier 2 risk characterization shows a high risk for secondary poisoning (Table 2.8.5.2-3). The PNECoral expressed as a dose is approximately equal for birds and mammals, and the sensitivity of the species used in calculations is determined predominantly by the ratio of daily food consumption to body weight so that the higher ratio results in the higher risk. No data are available on the sensitivity of the example species (the species listed in Table 12 of the ESD) to difenacoum. Only one day exposure of predators is assumed in the ESD, but it is mentioned that predators could be exposed over several days. This would mean higher accumulation in predators, because daily elimination of difenacoum from the predators is assumed to be less than the ingested amount. On the other hand, it is unlikely that all worst case assumptions would materialize simultaneously in nature. It is likely that in the long-term exposure, the prey rodents do not eat only the bait and also the fraction of poisoned rodents in the predator's diet can be lower than 50%. The resistant rodents cause somewhat higher risk for predators than non-resistant rodents, but the difference is smaller than in the Tier 1 assessment.

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

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

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

Nevertheless, in order to reduce the risk of secondary poisoning, it is very important to follow the use instructions of the rodenticide baits (see section 3). The risk reduction measures are considered in the section 2.9.

|  |
| --- |
| * **Renewal application (2017)**   New information was submitted at the renewal stage of the approval of difenacoum :   * A bioaccumulation tests in fish lead to a new BCF of 1100 L//kg which was lower than the predicted BCF of 9010 L/kg and 35645 L/kg. It was assumed in the original risk assessment that secondary poisoning via the aquatic food chain would not be significant due to low water solubility and high adsorption tendency of difenacoum. Even though risk is identified in the terrestrial food chain for birds, the risk via poisoned rodents is considered significantly higher compared to risk via earthworms or other invertebrates. Thus, conclusion from the original assessment is not changed. * An earthworm reproduction test: this test permits to revise the PNECsoil which could have an impact only for open area uses (not intended for this dossier). Therefore, this new PNECsoil has no impact on the previous conclusion for NYNA D+ PATE   Regarding this new information, the conclusion of the environmental risk assessment performed for the first authorization (PAR 2012) remains unchanged. |

* **NA-MAC application (2022)**

The risk assessments presented in 2012 and 2017 do not cover the outdoor uses added during the major change of 2022. Therefore, a new exposure assessment is conducted for the new uses, taking into account the latest updates of the active substance Difenacoum endpoints.

## Risk assessment for the environment (2022)

The product PATAPPAT is a rodenticide in paste form individually packaged in sachet containing 0.005% w/w Difenacoum (0.05 g/kg).

As for the authorisation of 2012 and 2017, the following risk assessment is carried out for the active substance (Difenacoum Renewal of approval AR, July 2016).

### Effects assessment on the environment

No new environmental studies have been carried out with the product PATAPPAT. All data pertaining to the active substance are therefore derived from the revised AR of Difenacoum (Renewal of approval, July 2016) and AR of September 2009.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Summary table on PNEC values of Difenacoum** | | | | | |
| **Compartments** | | **Parameters** | **Values** | **Units** | **Reference** |
| **Aquatic** | | PNECSTP | 4.80E-01 | [mg/L] | AR 2009 |
| PNECwater | 6.00E-05 | [mg/L] |
| PNECsediment | 2.51E+00 | [mg/kgww] | EPM –Log Kow < 5 but log Koc > 5. RCRsediment = RCRsw x 10\* |
| **Terrestrial** | | PNECsoil | 5.53E-01 | [mg/kgww] | RNL AR 2016 |
| **Primary and secondary poisoning** | **Acute** | NAETbirds, TIER I | 1.33E-02 | [mg/kg food] | Calculated according the revised ESD for PT14 (2018) – see explanations below |
| NAETmammals, TIER I | 1.20E-01 | [mg/kg food] |
| NAETbirds, TIER II | 1.67E-03 | [mg/kg bw] |
| NAETmammals, TIER II | 6.00E-03 | [mg/kg bw] |
| **Chronic** | PNECoral,birds, TIER I | 5.00E-04 | [mg/kg food] | AR 2009 |
| PNECoral,mammals, TIER I | 7.00E-03 | [mg/kg food] |
| PNECoral,birds, TIER II | 1.00E-04 | [mg/kg bw] |
| PNECoral,mammals, TIER II | 3.00E-04 | [mg/kg bw] |

*PNEC determination for primary and secondary poisoning:*

Acute/chronic poisoning:

In the revised ESD for PT14 (2018), a quantitative approach is proposed for acute and chronic exposure of non-target birds and mammals. Since the PNECoral is generally based on chronic effect concentrations, another threshold values were defined for the acute poisoning situation, named “NAET”, or “No acute Effect Threshold”.

The available acute data from the AR (2016) are:

A NOEC of 0.40 mg/**kg food** from a dietary toxicity test on *Japanese Quail* (IIIA Activa/Pelgar, A7.5.3.1.2) and thus, a **NAETbirds of 1.33E-02** (=0.40/30) **mg/kg food**is calculated.

A LD50 of 1.8 mg/**kg bw** from an acute oral toxicity test on *Rattus norvegicus* (IIIA SOREX A6.1.1/01), and therefore, a **NAETmammals of 6.00E-03** (=1.8/300) **mg/kg bw** is calculated.

In Tier I, the PECoral represents the concentration of the active substance in bait (for primary poisoning) or the concentration in the rodent/slug eaten by the predator/scavenger (for secondary poisoning) in mg/kg food. In Tier II, the PECoral are in mg/kg bw, therefore, they can be compared with NAET/PNECoral calculated in mg/kg bw.

In the Volume IV Part B+C (2017), conversion between mg/kg food and mg/kgbw is possible for birds and mammals according to equations 96 and 97:

|  |
| --- |
| NOECbirds/mammals (in mg/kg food) = NOAELbirds/mammals (in mg/kg bw/d) x CONVbird/mammals |

Therefore, for Difenacoum:

|  |  |
| --- | --- |
| **Parameters** | **Values** |
| **BIRDS** | |
| NAETbirds(in mg/kg food) | 1.33E-02 mg/kg food |
| CONVbirds | 8 (reference for *Gallus domesticus,* as no value is available for *Japanese Quail*) |
| NAETbirds(in mg/kg bw/d) | 1.67E-03 |
| **MAMMALS** | |
| NAETmammals(in mg/kg bw/d) | 6.00E-03 |
| CONVmammals | 20 (*Ratus norvegicus* > 6 weeks) |
| NAETmammals(in mg/kg food) | 1.20E-01 mg/kg food |

***Foreseeable routes of entry into the environment on the basis of the use envisaged***

According to the new intended uses (application against mice and rats around buildings, in waste dumps, in open areas), two types of releases are taken into account:

* Direct releases to soil (including groundwater) relevant for:
  + The treatment around buildings,
  + The treatment of open areas and waste dumps.
* Direct releases to surface water (including sediments) relevant for:
  + The treatment around buildings,
  + The treatment of open areas.

### Exposure assessment

The product PATAPPAT is a rodenticide in paste form individually packaged in sachet containing 0.005% w/w Difenacoum (CAS n° 56073-07-5) and placed in secured bait box. The product is used at a maximum of 30 g for mouse and 180 g for rat / bait point. The following table is a summary of the claimed uses.

|  |  |  |  |
| --- | --- | --- | --- |
| Claimed uses | Field of use | Targets | Covered by |
| Use 1 | Indoor (trained professional) | Mice/Rats | Already validated in the RNL (2012/2017) |
| Use 2 | Indoor (professional) | Mice | Already validated in the RNL (2012/2017) |
| Use 3 | Indoor (professional) | Rats | Already validated in the RNL (2012/2017) |
| Use 4 | Outdoor – Around building (trained professional) | Mice/Rats | Scenario 1 / Scenario 4 |
| Use 5 | Outdoor – Around building (professional) | Mice/Rats | Scenario 1 / Scenario 4 |
| Use 6 | Outdoor – Open area/Waste dumps (trained professional) | Mice/rats | Scenario 2 / Scenario 3 / Scenario 4 |

Scenario 1: Around buildings - Emission to soil due to the use around building on unpaved ground,

Scenario 2: Open area,

Scenario 3: Waste dumps/landfills,

Scenario 4: Bank slopes.

**General information**

|  |  |
| --- | --- |
| Assessed PT | PT 14 |
| Assessed scenarios | Scenario 1: Around buildings - Emission to soil due to use around building on unpaved ground,  Scenario 2: Open area,  Scenario 3: Waste dumps/landfills,  Scenario 4: Bank slopes. |
| ESD(s) used | Revised Emission Scenario Document for Product Type 14: Rodenticides, August 2018 |
| Approach | Scenario 1: Consumption based  Scenario 2: Consumption based  Scenario 3: Consumption based  Scenario 4: Consumption based |
| Distribution in the environment | Calculated based on Guidance for BPR IV Part B+C (2017).  Assessment report: Difenacoum (Renewal of approval, July 2016)  Technical Agreements for Biocides of November, 2021 |
| Groundwater simulation | No |
| Confidential Annexes | No |
| Life cycle steps assessed | Scenarios 1/2/3/4:  Production: No  Formulation No  Use: Yes  Service life: No |
| Remarks |  |

***Emission estimation***

The local emissions for each scenario were assessed according to the Revised Emission Scenario Document for Product Type 14: Rodenticides, August 2018. Updates of the Technical agreement for Biocides (November, 2021) were also taken into account.

*Worst-case target and packaging of product:*

As the product PATAPPAT is not intended to be used directly in burrows, the highest emissions to the environment are due to the treatment of rats with bagged baits placed in tamper bait station. Therefore, only this worst-case situation is assessed.

##### Scenario 1: Around building - Emission to soil due to use around building on unpaved ground

The following input parameters are used to calculate the local emissions to soil.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Input parameters for calculating the local emission** | | | | |
| **Input** | **Symbol** | **Value** | **Unit** | **Remarks** |
| Scenario 1: Exposure scenario for areas around building - Emission to soil due to use around building on unpaved ground | | | | |
|  |  |  |  |  |
| Worst-case rodent to be controlled | *-* | Rats | [-] | S |
| Type of bait formulation (worst-case) | - | Bagged baits | [-] | S |
| Amount of product used at each refill for one bait station/box | Qprod | 180 | [g] | S |
| Fraction of substance in product | Fcproduct | 5E-05 | [-] | S |
| Number of application sites | Nsites | 10 | [-] | D |
| Number of applications (initial baiting+refillings) | Nappl | 5 | [-] | D |
| Fraction of substance released directly to soil | Frelease-D,soil | 0.01 | [-] | D  bagged bait |
| Fraction of substance metabolised | Fmetab | 0.6 | [-] | S  IIB Difenacoum, 2008 |
| Fraction of substance released indirectly to soil | Freleased-ID,soil | 0.36 | [-] | O  0.9 x (1 - Fmetab) |
| Soil area exposed directly | AREAexposed-D | 0.09 | [m²] | D |
| Soil area exposed indirectly | AREAexposed-ID | 550 | [m²] | D |
| Depth of exposed soil | DEPTHsoil | 0.1 | [m] | D |
| **Output** | | | | |
| **Local direct emission of substance to soil from a campaign** | **Elocalsoil-D-campaign** | **4.50E-04** | [g] | O |
| **Local indirect emission of substance to soil from a campaign** | **Elocalsoil-ID-campaign** | **1.62E-01** | [g] | O |
| **Elocal total (Tier II)** | **Elocaltotal Tier II** | **1.67E-01** | [g] | **Nsites x Elocalsoil-D + Elocalsoil-ID** |

The total concentration resulting from Indirect + Direct emissions will be presented as it is proposed in the ESD (Tier I). The refined total concentration (Tier II), resulting from Indirect and Direct emissions emitted to the entire zone indirectly exposed (550 m²) is also presented as this seems more relevant for groundwater and secondary poisoning via the terrestrial compartment.

##### Scenario 2: Open area

As the product is applied only in tamper bait station, the scenario ”Outdoor around building” covers the scenario ”Open area” (Revised ESD for PT14 (2018).

##### Scenario 3: Waste dumps/landfills

The following input parameters are used to calculate the local emissions to soil.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Input parameters for calculating the local emission** | | | | |
| **Input** | **Symbol** | **Value** | **Unit** | **Remarks** |
| Scenario 3:Exposure scenarios for waste dumps/landfills | | | | |
|  |  |  |  |  |
| Worst-case rodent to be controlled | - | Rats | [-] | S |
| Type of bait formulation | - | Bagged baits | [-] | S |
| Amount of product used at each application for one bait station/box | Qprod | 180 | [g] | S |
| Fraction of substance in product | Fcproduct | 5E-05 | [-] | S |
| Number of application sites | Nsites | 121 | [-] | D |
| Number of applications | Nappl | 7 | [-] | D |
| Fraction of substance released directly to soil | Frelease-D,soil | 0.01 | [-] | D |
| Fraction of substance metabolised | Fmetab | 0.6 | [-] | S  IIB Difenacoum, 2008 |
| Fraction of substance released indirectly to soil | Freleased-ID,soil | 0.36 | [-] | O  0.9 x (1 - Fmetab) |
| Soil area exposed directly | AREAexposed-D | 0.14 | [m²] | D |
| Soil area exposed indirectly | AREAexposed-ID | 10000 | [m²] | D |
| Depth of exposed soil | DEPTHsoil | 0.1 | [m] | D |
| **Output** | | | | |
| **Local direct emission of substance to soil from a campaign** | **Elocalsoil-D-campaign** | **6.30E-04** | [g] | O |
| **Local indirect emission of substance to soil from a campaign** | **Elocalsoil-ID-campaign** | **2.74E+00** | [g] | O |
| **Local total (Tier II)** | **Elocaltotal Tier II** | **2.82E+00** | [g] | **Nsites x Elocalsoil-D + Elocalsoil-ID** |

The total concentration resulting from Indirect + Direct emissions will be presented as it is proposed in the ESD (Tier I). The refined total concentration (Tier II), resulting from Indirect and Direct emissions emitted to the entire zone indirectly exposed (10 000 m²) will be also presented as it seems more relevant for groundwater and secondary poisoning via the terrestrial compartment.

##### Scenario 4: Bank slopes

As the uses “Open area” as well as “Outdoor around building” are claimed, the scenario “Bank slope” is also evaluated (TAB, November, 2021, ENV180).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Input parameters for calculating the local emission** | | | | |
| **Input** | **Symbol** | **Value** | **Unit** | **Remarks** |
| Scenario 4: Exposure scenario for bank slopes: | | | | |
|  |  |  |  |  |
| Amount of product used at each application for one bait station/box | Qprod | 180 | [g] | S |
| Fraction of substance in product | Fcproduct | 5E-05 | [-] | S |
| Number of application sites | Nsites | 12 | [-] | D |
| Number of applications | Nappl | 1 | [-] | D |
| Fraction of substance released directly to water | Frelease-D,water | 0.4 | [-] | D |
| Water volume of channel | Vchannel | 450000 | [L] | D |
| **Output** | | | | |
| **Local direct emission of substance to water** | **Elocalwater-D-** | **4.32E-02** | [g] | O |

***Fate and distribution in exposed environmental compartments***

|  | STP | Freshwater | Sediment | Soil | Ground-water | Secondary poisoning |
| --- | --- | --- | --- | --- | --- | --- |
| Scenario 1: Around building | - | - | - | ++ | + | + |
| Scenario 2: Open areas | Covered by scenario 1 | | | | | |
| Scenario 3: Waste dumps | - | - | - | ++ | + | + |
| Scenario 4: Bank slopes | - | ++ | + | - | - | + |

*++: direct exposure +: indirect exposure -: no exposure*

Input parameters for calculating the fate and distribution of the active substance in the environment were selected from the revised Difenacoum RNL assessment report (2016).

|  |  |  |  |
| --- | --- | --- | --- |
| **Input parameters (only set values) for calculating the fate and distribution in the environment** | | | |
| Input | Value | Unit | Remarks |
| Molecular weight | 444.5 | g/mol | RNL AR Difenacoum (2016) |
| Vapour pressure (at 20°C) | 6.70E-09 | Pa | RNL AR Difenacoum (2016) |
| Water solubility (at 20°C) | 1.7 | mg/L | RNL AR Difenacoum (2016) |
| Log Octanol/water partition coefficient | 4.78 | Log 10 | RNL AR Difenacoum (2016) |
| Organic carbon/water partition coefficient (Koc) | 1 803 018 | L/kg | RNL AR Difenacoum (2016) |
| Biodegradability | No |  | RNL AR Difenacoum (2016) |
| DT50 for degradation in soil | 833 | d (at 12ºC) | RNL AR Difenacoum (2016) |
| BCFfish | 1100 | L/kgww | RNL AR Difenacoum (2016) |
| BCFearthworms | 1.32 | L/kgww | RNL AR Difenacoum (2016) |
| BMF | 1 | - | RNL AR Difenacoum (2016) |

The fractioning of the actives substance between air, water, sludge and degradation is indicated in the following table.

|  |  |  |
| --- | --- | --- |
| **Calculated fate and distribution in the STP** | | |
| **Compartment** | **Percentage [%]** | **Remarks** |
| Air | 0.0000000128 | Simple Treat v4.0, considering a concentration suspended solids effluents (Css) of 30 mg/L or 0.03 kg/m3 (TAB 2021, ENV9) |
| Water | 7.63 |
| Sludge | 92.37 |
| Degraded in STP | 0 |

#### Calculated PEC values

A summary of the calculated PEC values for each scenario and each environmental compartment is indicated in the following table.

For scenarios 1 and 3, the total concentration resulting from Indirect + Direct emissions is presented as it is proposed in the ESD (Tier I). The refined total concentration (Tier II), resulting from Indirect and Direct emissions emitted to the entire zone indirectly exposed (550 m² for scenario 1 and 10000 m² for scenario 3) is also presented as this seems more relevant for groundwater and secondary poisoning via the terrestrial compartment.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Elocal and PEC values summary** | | | | | |
|  | | **Elocal**  [g/campaign] | **PECwater\*** | **PECsoil** | **PECGW\*\*** |
| [mg/l] | [mg/kg ww] | [μg/l] |
| Scenario 1: Around building | Direct emissions | 4.50E-04 | - | 2.94E-02 | 9.25E-04 |
| Indirect emissions | 1.62E-01 | - | 1.73E-03 | 5.45E-05 |
| Total Tier I | - | - | 3.11E-02 | 9.79E-04 |
| Total Tier II | 1.67E-01 | - | 1.78E-03 | 5.60E-05 |
| Scenario 2: Open areas | | Covered by scenario 1 | | | |
| Scenario 3: Waste dumps | Direct emissions | 6.30E-04 | - | 2.65E-02 | 8.32E-04 |
| Indirect emissions | 2.74E+00 | - | 1.61E-03 | 5.07E-05 |
| Total Tier I | - | - | 2.81E-02 | 8.83E-04 |
| Total Tier II | 2.82E+00 | - | 1.66E-03 | 5.22E-05 |
| Scenario 4: Bank slopes | | 4.32E-02 | 9.60E-05 | - | - |

*\*PECsediment:* The PNECsediment was derived through the Equilibrium Partitioning Method, therefore, the risk for the sediment compartment is covered by the Risk assessment for Surface water with an additional factor or 10.

*\*\*PECGW:* Considering the very low AEL derived during the substance assessment of Difenacoum, much lower threshold value for groundwater is considered (**0.01 µg/L**) to prevent risks for humans via contaminated water (France proposal for specific References Values in groundwater for rodenticides, December 2012).

##### Primary and secondary poisoning

As outdoor uses such as in scenarios “Around building”, “Open area”, “Waste dumps” are claimed, both primary and secondary poisoning are relevant (Table 40 from the Revised ESD for PT14, 2018).

**Primary poisoning**

Non-target birds and mammals may encounter bait containing Difenacoum if they are small enough to be able to reach the bait, or because the bait is inadequately safeguarded or a secured bait point has become damaged, or by finding pieces of bait which have been removed by target rodents. The scenarios assessed are taken from the Revised ESD for PT14 (2018) and the worst-case concentration of active substance in the bait (50 mg/kg) is used in the calculations.

TIER I (acute/chronic)

In Tier I, it is assumed that the whole day’s food requirement of the non-target species consists in the consumption of the rodenticide. Avoidance is not considered to be relevant. Therefore, the concentration in the food is the same as the concentration of the active substance in the bait.

**Tier 1 PECoral = 5.00E+01 mg/kg food**

TIER II

In Tier II, a more realistic feeding behaviour of defined generic focal species is taken into account, considering parameters such as their food intake rate (FIR), the fraction of diet obtained in the treated area (PT), an avoidance factor…

* For acute poisoning: Risk is quantified using the estimated daily intake of a compound (ETE) by general focal species,
* For chronic poisoning: Risk is quantified using the estimated intake of a compound for 5 consecutive days (immediately after the last meal).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Input parameters for calculating the PEC values (Primary poisoning, Tier I and Tier II)** | | | | |
| **Input** | **Symbol** | **Value** | **Unit** | **Remarks** |
| Primary poisoning: Acute/Chronic PEC calculations | | | | |
| Concentration of the active substance (bait) | C | 50 | [mg/kg] | S |
| Avoidance factor | AV | 1 | [-] | D |
| Fraction of diet obtained in treated area | PT | 1 | [-] | D |
| Composition of diet obtain from treated area | PD | 1 | [-] | D |
| ADME factor | ADME | 0 | [-] | D |
| Number of days the not-target species is consuming rodenticide baits | n | 1 to 4 | [-] | D |
| Food intake rate:  -House sparrow  -Shrew  -Woodpigeon | FIR | 0.23  0.55  0.1 | [g/g bw per day] | D |
| Rodenticide product consumption:  -Dogs  -Young pigs | RPC | 0.06  0.024 | [g/g bw per day] | D |
| **Output** | | | | |
| **Primary poisoning – Tier I** | | | | |
| Acute - Concentration of the active substance (bait) | PECoral, acute | 5.00E+01 | [mg/kg food] | O  PECoral, acute = C |
| Chronic - Concentration of the active substance (bait) | PECoral, chronic | 5.00E+01 | [mg/kg food] | O  PECoral, chronic = C |
| **Primary poisoning – Tier II** | | | | |
| Acute - Estimated daily uptake of a compound (=PECoral,acute): | | | | |
| House sparrow | ETE | 1.15E+01 | [mg/kg bw] | O |
| Shrew | ETE | 2.75E+01 | [mg/kg bw] | O |
| Woodpigeon | ETE | 5.00E+00 | [mg/kg bw] | O |
| Dogs | ETE | 3.00E+00 | [mg/kg bw] | O |
| Young Pigs | ETE | 1.20E+00 | [mg/kg bw] | O |
| Chronic - Expected concentration of an active substance in the non-target species on day 5 immediately after the 5th meal (=PECoral,chronic): | | | | |
| House sparrow | PECoral,5-d | 5.75E+01 | [mg/kg bw] | O |
| Shrew | PECoral,5-d | 1.38E+02 | [mg/kg bw] | O |
| Woodpigeon | PECoral,5-d | 2.50E+01 | [mg/kg bw] | O |
| Dogs | PECoral,5-d | 1.50E+01 | [mg/kg bw] | O |
| Young Pigs | PECoral,5-d | 6.00E+00 | [mg/kg bw] | O |

**Secondary poisoning**

Different types of secondary poisoning are considered in the Revised ESD for PT14 (2018):

* From consuming primarily exposed target and non-target organisms (Secondary poisoning - Tier I).
* From consuming secondary exposed non-target organisms (Secondary poisoning - Tier II).
* From consuming organisms (terrestrial or aquatic) that have been exposed to rodenticides via emissions to the environment (Secondary poisoning via environmental emissions).
  + Secondary poisoning via contaminated rodents and slugs Tier I and II

For secondary poisoning (Tier I and II), the worst-case concentration of active substance in the bait (50 mg/kg) is used in the calculations. Scenarios taken from the Revised ESD for PT14 (2018) are assessed below.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Input parameters for calculating the PEC values (Secondary poisoning Tier I and II)** | | | | |
| **Input** | **Symbol** | **Value** | **Unit** | **Remarks** |
| Secondary poisoning Tier I and II, Acute/Chronic PEC calculations: | | | | |
| Concentration of the active substance (bait) | C | 50 | [mg/kg] | S |
| Avoidance factor | AV | 1 | [-] | D |
| Fraction of diet obtained in treated area | PT | 1 | [-] | D |
| Composition of diet obtain from treated area | PD | 1 | [-] | D |
| ADME factor | ADME | 0 | [-] | D |
| Number of days the not-target species is consuming rodenticide baits | n | 1 to 4 | [-] | D |
| Food intake rate / body weight rodent | FIR/BWrodent | 0.1 | [-] | D |
| Food intake rate / body weight slug | FIR/BWslug | 0.4 | [-] | D |
| Fraction of poisoned rodents in predators’ diet | Frodent acute | 1 | [-] | D |
| Fraction of poisoned slugs in predators’ diet | Fslug acute | 1 | [-] | D |
| Fraction of poisoned rodents in predators’ diet | Frodent chronic | 0.5 | [-] | D |
| Fraction of poisoned slugs in predators’ diet | Fslug chronic | 0.5 | [-] | D |
| **Intermediate calculations** | | | | |
| Concentration in food (rodent) after one day | Cfood,rodent | 5.00E+00 | [mg/kg food/d] | O |
| Concentration in food (slug) after one day | Cfood,slug | 2.00E+01 | [mg/kg food/d] | O |
| **Output** | | | | |
| **Secondary poisoning – Tier I** | | | | |
| Acute - Predicted environmental concentration of an active substance in food of a predator/scavenger: | | | | |
| If the food is a rodent | PECoral,rodent acute | 2.50E+01 | [mg/kg food] | O |
| If the food is slugs | PECoral,slug, acute | 1.00E+02 | [mg/kg food] | O |
| Chronic - Predicted environmental concentration of an active substance in food of a predator/scavenger: | | | | |
| If the food is a rodent | PECoral,rodent chronic | 1.25E+01 | [mg/kg food] | O |
| If the food is slugs | PECoral,slug, chronic | 5.00E+01 | [mg/kg food] | O |
| **Secondary poisoning – Tier II** | | | | |
| Acute - Predicted environmental concentration of an active substance in a rodent predator: | | | | |
| Barn owl (*Tyto alba*) | PECoral,rodent,birds, acute | 6.25E+00 | [mg/kg bw/d] | O |
| Kestrel (*Falco tinnunculus*) | PECoral,rodent,birds, acute | 9.50E+00 | [mg/kg bw/d] | O |
| Carrion crow (*Corvus corone*) | PECoral,rodent,birds, acute | 7.00E+00 | [mg/kg bw/d] | O |
| Red fox (*Vulpes vulpes*) | PECoral,rodent,mammals, acute | 2.50E+00 | [mg/kg bw/d] | O |
| Weasel (*Mustela nivalis*) | PECoral,rodent,mammals, acute | 9.75E+00 | [mg/kg bw/d] | O |
| Domestic cat (*Felix silvestris catus*) | PECoral,rodent,mammals, acute | 1.25E+00 | [mg/kg bw/d] | O |
| Shrew (*Sorexp ssp*) | PECoral,slug,mammals, acute | 5.50E+01 | [mg/kg bw/d] | O |
| European starling (*Sturnus vulgaris*) | PECoral,slug,birds, acute | 6.30E+01 | [mg/kg bw/d] | O |
| Chronic - Predicted environmental concentration of an active substance in a rodent predator: | | | | |
| Barn owl (*Tyto alba*) | PECoral,rodent,birds, chronic | 3.13E+00 | [mg/kg bw/d] | O |
| Kestrel (*Falco tinnunculus*) | PECoral,rodent,birds, chronic | 4.75E+00 | [mg/kg bw/d] | O |
| Carrion crow (*Corvus corone*) | PECoral,rodent,birds, chronic | 3.50E+00 | [mg/kg bw/d] | O |
| Red fox (*Vulpes vulpes*) | PECoral,rodent,mammals, chronic | 1.25E+00 | [mg/kg bw/d] | O |
| Weasel (*Mustela nivalis*) | PECoral,rodent,mammals, chronic | 4.88E+00 | [mg/kg bw/d] | O |
| Domestic cat (*Felix silvestris catus*) | PECoral,rodent,mammals, chronic | 6.25E-01 | [mg/kg bw/d] | O |
| Shrew (*Sorexp ssp*) | PECoral,slug,mammals, chronic | 2.75E+01 | [mg/kg bw/d] | O |
| European starling (*Sturnus vulgaris*) | PECoral,slug,birds, chronic | 3.15E+01 | [mg/kg bw/d] | O |

* + Secondary poisoning via the environment

Secondary poisoning via the food chain earthworms-non target mammals or birds is calculated considering PEC values of scenarios where soil compartment exposure are foreseen (scenarios 1, 2 and 3). Secondary poisoning via the food chain fish-non target mammals or birds is calculated considering PEC values of scenarios where aquatic compartment exposure are foreseen (scenario 4). For these scenarios, PECoral,predator for soil and surface water are calculated according to Volume IV Part B+C (2017) equations and it is considered that 50% of the diet comes from a local area and 50% comes from the regional area. Thus, when the PEClocalsoil is used in calculation, the PECoral,predator,soil to be used in risk assessment is x 0.5.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Input parameters for calculating the PEC values (Secondary poisoning via the environment)** | | | | |
| **Input** | **Symbol** | **Value** | **Unit** | |
| Secondary poisoning *via* surface water contamination: | | | | |
| Bioconcentration factor for fish on wet weight basis | BCF fish | 1100 | [L/kg wet fish]] | |
| Biomagnification factor in fish | BMF | 1 | [-] | |
| Fraction of diet sourced locally | Fdiet,local | 0.5 | [-] | |
|  | | | | |
| Secondary poisoning *via* soil contamination: | | | | |
| Bioconcentration factor for earthworms on net weight basis | BCF worms | 1.32 | [L/kg wet earthworms] | |
| Conversion factor for soil concentration wet-dry weight soil | CONVsoil | 1.13 | [kg ww/kg dw] | |
| Fraction of gut loading in worm | Fgut | 0.1 | [kg dw/kg ww] | |
| Fraction of diet sourced locally | Fdiet,local | 0.5 | [-] | |
|  | | | | |
| **Output for Secondary poisoning via soil/water contamination:** | | | | | |
| **Scenarios** | | **PECoral,predator,SW** [mg/kg wet fish] | | **PECoral,predator,soil** [mg/kgww earthworms] | |
| **EMISSIONS TO SOIL** | | | | | |
| Scenario 1: Around building (Outdoor application) | Direct emissions | n.r | | 1.50E-03 | |
| Indirect emissions | n.r | | 8.82E-05 | |
| Total Tier I | n.r | | 1.59E-03 | |
| Total Tier II | n.r | | 9.07E-05 | |
| Scenario 2: Open areas | | Covered by scenario 1 | | | |
| Scenario 3: Waste dumps | Direct emissions | n.r | | 1.35E-03 | |
| Indirect emissions | n.r | | 8.22E-05 | |
| Total Tier I | n.r | | 1.43E-03 | |
| Total Tier II | n.r | | 8.45E-05 | |
| **EMISSIONS TO SURFACE WATER** | | | | | |
| Scenario 4: Bank slopes | | 5.28E-02 | | n.r | |

n.r: not relevant

### Risk characterisation

##### Atmosphere

Difenacoum is a non-volatile substance (vapour pressure 6.70E-09 Pa and Henry’s Law constant <1.11E-06 Pa.m3/mol) presenting a half-life of several hours in air. Therefore, it is not expected to contaminate air and no PNEC value were calculated. The atmosphere is not considered to be an environmental compartment of concern.

##### Aquatic (including sediment compartment, STP), terrestrial, groundwater compartments and secondary poisoning via the environment

A summary of the calculated PEC/PNEC values and PECGW values for each scenario and all other environmental compartments are indicated in the following table. For secondary poisoning via the environment, only birds are presented as they represent the worst-case and PECoral fish and earthworm are compared with PNECoral birds Tier I (in mg/kg food).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **PECGW and RCR for aquatic, terrestrial compartments and secondary poisoning via the environment calculations** | | | | | | |
|  | | **RCR water\*** | **RCR soil** | **PECGW** [μg/l] | **Secondary poisoning via the environment** | |
| **RCR predator,SW** | **RCR predator,soil** |
| Birds as worst case | Birds as worst case |
| **DIRECT EMISSIONS TO SOIL** | | | | | | |
| Scenario 1: Around building (Outdoor application) | Direct emissions | - | 5.32E-02 | 9.25E-04 | - | **3.00E+00** |
| Indirect emissions | - | 3.13E-03 | 5.45E-05 | - | 1.76E-01 |
| Total Tier I | - | 5.63E-02 | 9.79E-04 | - | **3.17E+00** |
| Total Tier II | - | 3.22E-03 | 5.60E-05 | - | 1.81E-01 |
| Scenario 2: Open areas | | Covered by scenario 1 | | | | |
| Scenario 3: Waste dumps | Direct emissions | - | 4.79E-02 | 8.32E-04 | - | **2.70E+00** |
| Indirect emissions | - | 2.92E-03 | 5.07E-05 | - | 1.64E-01 |
| Total Tier I | - | 5.08E-02 | 8.83E-04 | - | **2.86E+00** |
| Total Tier II | - | 3.00E-03 | 5.22E-05 | - | 1.69E-01 |
| **DIRECT EMISSIONS TO SURFACE WATER** | | | | | | |
| Scenario 4: Bank slopes | | **1.60E+00** | - | - | **1.06E+02** | - |

*\*RCRsediment:* The PNECsediment was derived through the Equilibrium Partitioning Method, therefore, the risk for the sediment compartment is covered by the Risk assessment for Surface water with an additional factor or 10. As risks are already foreseen for surface water, risks for sediment compartment are not presented.

All scenarios lead to acceptable risks for all environmental compartments except Scenario 4 – Bank slopes, for which unacceptable risks are foreseen for the aquatic compartment and for the secondary poisoning *via* the ingestion of contaminated fish. A RMM should be applied for the use around building and open area for which the scenario is relevant.

Concerning secondary poisoning *via* the environment for scenario 1 and 3, unacceptable risks are foreseen for every scenarios in Tier I. Neverthless, no risk are foreseen in Tier II which is considered to be more realistic.

##### Primary and Secondary Poisoning Tier I and II

Acute/chronic poisoning:

In the revised ESD for PT14 (2018), a quantitative approach is proposed for acute and chronic exposure of non-target organisms. Since the PNECoral is generally based on chronic effect concentrations, another threshold values were defined for the acute poisoning situation, named “NAET”, or “No acute Effect Threshold”.

Therefore, NAET values are compared with PECoral,acute and PNECoral are compared with PECoral,chronic.

Tier I/Tier II calculations:

In Tier I, the PECoral represents the concentration of the active substance in bait (for primary poisoning) or the concentration in the rodent/slug eaten by the predator/scavenger (for secondary poisoning) in mg/kg food. Therefore, this value should be compared with a NAET (for acute poisoning) or PNECoral (for chronic poisoning) converted inmg/kg food.

In Tier II, the PECoral are in mg/kg bw, therefore, they can be compared with NAET/PNECoral calculated in mg/kg bw.

A summary of the calculated PEC/PNEC values for primary and secondary poisoning (Tier I and II) are indicated in the following table.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **RCR calculations (Primary and Secondary poisoning Tier I and II)** | | | | |
|  | **Acute** | | **Chronic** | |
|  | **Birds** | **Mammals** | **Birds** | **Mammals** |
| Primary poisoning Tier I and II, Acute/Chronic RCR calculations: | | | | |
| **Primary poisoning – Tier I** | | | | |
| RCR | **3.76E+03** | **4.17E+02** | **1.00E+05** | **7.14E+03** |
| **Primary poisoning – Tier II** | | | | |
| RCR - House sparrow | **6.89E+03** | n.r | **5.75E+05** | n.r |
| RCR - Shrew | n.r | **4.58E+03** | n.r | **4.58E+05** |
| RCR - Woodpigeon | **2.99E+03** | n.r | **2.50E+05** | n.r |
| RCR - Dogs | n.r | **5.00E+02** | n.r | **5.00E+04** |
| RCR - Young Pigs | n.r | **2.00E+02** | n.r | **2.00E+04** |
| Secondary poisoning Tier I and II, Acute/Chronic RCR calculations: | | | | |
| **Secondary poisoning – Tier I** | | | | |
| RCR calculated with the active substance in food (=rodent) of a predator/scavenger | **1.88E+03** | **2.08E+02** | **2.50E+04** | **1.79E+03** |
| RCR calculated with the active substance in food (=slug) of a predator/scavenger | **7.52E+03** | **8.33E+02** | **1.00E+05** | **7.14E+03** |
| **Secondary poisoning – Tier II** | | | | |
| RCR - Barn owl (*Tyto alba*) | **3.74E+03** | n.r | **3.13E+04** | n.r |
| RCR - Kestrel (*Falco tinnunculus*) | **5.69E+03** | n.r | **4.75E+04** | n.r |
| RCR - Carrion crow (*Corvus corone*) | **4.19E+03** | n.r | **3.50E+04** | n.r |
| RCR - Red fox (*Vulpes vulpes*) | n.r | **4.17E+02** | n.r | **4.17E+03** |
| RCR - Weasel (*Mustela nivalis*) | n.r | **1.63E+03** | n.r | **1.63E+04** |
| RCR - Domestic cat (*Felix silvestris catus*) | n.r | **2.08E+02** | n.r | **2.08E+03** |
| RCR - Shrew (*Sorexp ssp*) | n.r | **9.17E+03** | n.r | **9.17E+04** |
| RCR - European starling (*Sturnus vulgaris*) | **3.77E+04** | n.r | **3.15E+05** | n.r |

Unacceptable risks are foreseen with very high RCRs for primary and secondary poisoning (Tier I and II). In order to mitigate the risk of poisoning, specific use instructions and risk mitigation measures must be put in place.

***Conclusion***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Field of use** | **Targets** | **Covered by** | **Acceptable risks for the environment** |
| Use 1 | Indoor (trained professional) | Mice/Rats | Validated in the RNL (2012/2017) | |
| Use 2 | Indoor (professional) | Mice | Validated in the RNL (2012/2017) | |
| Use 3 | Indoor (professional) | Rats | Validated in the RNL (2012/2017) | |
| Use 4 | Outdoor – Around building (trained professional) | Mice/Rats | Scenario 1 / Scenario 4 | **YES (except for primary and secondary poisoning, and if releases to the aquatic compartment are prevented)** |
| Use 5 | Outdoor – Around building (professional) | Mice/Rats | Scenario 1 / Scenario 4 | **YES (except for primary and secondary poisoning, and if releases to the aquatic compartment are prevented)** |
| Use 6 | Outdoor – Open area/Waste dumps (trained professional) | Mice/rats | Scenario 2 / Scenario 3 / Scenario 4 | **YES (except for primary and secondary poisoning, and if releases to the aquatic compartment are prevented)** |

***Mixture toxicity***

As no substance of concern was identified in the product, mixture toxicity assessment is not relevant.

***Aggregated exposure (combined for relevant emission sources)***



*Figure 1: Decision tree on the need for estimation of aggregated exposure*

Conclusion: Emission *via* the STP is the only way that could lead to combined exposure of the different uses. However, no use leads to emission to the STP, aggregated exposure is not relevant.

|  |
| --- |
| **Overall conclusion on the risk assessment for the environment of the product** |
| The risk assessment has been conducted for the active substance only. No substance of concern has been defined for the environment.  For the new outdoor uses around building (uses 4 and 5), in open area and waste dump (use 6), unacceptable risks are foreseen for the aquatic compartment and the secondary poisoning via the eating of contaminated fish if baits are used near water bodies. The following risk mitigation measure must be applied:  “*Do not use the product close to surface waters (e.g. rivers, ponds, water channels, dykes, irrigation ditches).”*  Moreover, for all uses, the risk for primary and secondary poisoning of non-target animals (especially via the contaminated rodents) cannot be excluded. Specific use restrictions must be applied to mitigate these risks.  - 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 open the sachets containing the bait. |

## Measures to protect man, animals and the environment – PAR 2012

The measures to protect man, animals and the environment are extracted from the Doc IIIB8 and updated according to the information submitted in the NYNA D+PATE dossier.

### Recommended methods and precautions concerning handling, use, storage, transport or fire

Bait stations are provided to avoid the possibility for children and domestic animals to be in contact with the biocidal product.For professionals and non-professionals, the product is wrapped individually in heat-sealed paper sachet for preventing dermal and inhalation exposure.Size of containers is appropriate to intended uses to be done.Professional users have to be trained before using the biocidal product.

Handling and use

The product must be used in accordance with the label.

Appropriate protective clothes and gloves are recommended for users during handling and cleaning. Placing the baits in secured bait station out of the reach of children and domestic animals is necessary. The bait station must be secured with no possibility for children and domestic animals to open the bait boxes or to access to the bait stations. The bait station must not offer the possibility for rodents to take baits away in the nests. Collecting unconsumed baits and dead rodents must be done every week during the treatment.

Avoid exposure to high temperature and strong oxidizing agents.

Storage

Keep out of the reach of children and domestic animals; store away from food, drink and animal feeding stuff, and away from light. Keep container tightly closed in fresh and dry places.

Methods and precaution concerning transport

Not regulated.

Methods and precautions concerning fire

Suitable extinguishing media: foam and chemical powders. Water must not be used for environmental safety reasons.

Special protective equipment for fire-fighters: wear protective clothing and self-contained breathing apparatus.

Risk of toxic gases in fumes (carbon monoxide, carbon dioxide…)

### Emergency measures in case of an accident

Personal precautions

Inhalation: no action should be necessary.

Ingestion: if swallowed, seek medical advice immediately and show container or leaflet. A treatment with vitamin K1 should be necessary during a long period.

Skin or eye contact: wash immediately with plenty of water.

Environmental precautions

Avoid uncontrolled disposal into the environment because of danger for non-target animals.

Do not throw the product on the ground, into a water course, into the sink or down the drain.

Any spillage should be cleared up immediately

### Disposal considerations

Unconsumed products and packaging should be disposed according to national or local regulation.

Empty containers must not be reused.

The product is ready-to-use and applied directly in bait stations indoors only. The baits which have not been consumed by rodents and dead rodents are kept away by operators.

It is not expected that any direct release to soil compartment would occur as a direct result of the indoor application of NYNA D+ PATE. However, if a spill occurs, baits must be collected with a shovel and stored in hermetic containers and eliminated according to national or local regulation.

Annex 1: List of studies reviewed

##### List of new data[[18]](#footnote-19) submitted in support of the evaluation of the active substance – PAR 2012

| **Section No** | **Reference No** | **Author** | **Year** | **Title** | **Owner of data** | **Letter of Access** | | **Data protection claimed** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  | **Yes** | **No** | **Yes** | **No** |
| A2 | CH-299-2009 | Garofani S. | 2009 | Difenacoum technical: complete analysis of five batch samples | Activa |  |  |  |  |
| A2.7 | CH-297-2009 | Garofani S. | 2009 | Difenacoum technical: validation of the analytical method for the determination of the active ingredient content | Activa |  |  |  |  |
| A2.8 | CH-298-2009 | Garofani S. | 2009 | Difenacoum technical: validation of the analytical method for the determination of significant impurities content | Activa |  |  |  |  |
| A3.3 | CH – 082/2010 | Garofani S. | 2010 | Difenacoum technical: determination of the colour, odour and physical state | Activa |  |  |  |  |
| A4.2 (c) | CEMR-4470 | Marshall L. | 2009 | Validation of a method for the determination of Difenacoum residues in sediment | Activa / PelGar Brodifacoum and Difenacoum Task Force |  |  |  |  |
| A4.2 (c) | CEMR-4469 | Marshall L. | 2009 | Validation of a method for the determination of Difenacoum residues in animal Matrices (Liver and Muscle) and Crop matrix | Activa / PelGar Brodifacoum and Difenacoum Task Force |  |  |  |  |
| A4.2 (e) | CEMR-4469 | Marshall L. | 2009 | Validation of a method for the determination of Difenacoum residues in animal Matrices (Liver and Muscle) and Crop matrix | Activa / PelGar Brodifacoum and Difenacoum Task Force |  |  |  |  |

##### List of new data submitted in support of the evaluation of the biocidal product – PAR 2012, updated 2017

| **Section No** | **Reference No** | **Author** | **Year** | **Title** | **Owner of data** | **Letter of Access** | | **Data protection claimed** | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  | **Yes** | **No** | **Yes** | **No** | |
| B3.1, 3.4, 3.6 | 10-920010-009 | Demangel B. | 2010 | Physico chemical tests on NYNA D+ PATE | Triplan |  |  |  |  |
| B3.2, 3.3 | 09-920010-001 | Da Costa C, Teiche A. | 2010 | Physico chemical tests on NYNA D+ PATE | Triplan |  |  |  |  |
| B3.5, 3.7 | 10-920010-010 | Ferron N. | 2010 | Physico-chemical tests before and after accelerated storage procedure for 14 days at 54 ± 2°C on NYNA D+ PATE in compliance with CIPAC MT 46.3 (CIPAC Handbok J – 2000) | Triplan |  |  |  |  |
| B4.1.1 | 10-920010-008 | Ricau H | 2010 | Validation of an analytical method for the determination of difenacoum in NYNA D+ BLOC SP in compliance with CIPAC/3807R | Triplan |  |  |  |  |
| B4.1.2 | 10-920010-012 | Ricau H | 2010 | Validation of an analytical method for the determination of difenacoum in NYNA D+ PATE in compliance with CIPAC/3807R | Triplan |  |  |  |  |
| B5.10.2./01 | XXX | XXX | 2010 | Efficacy laboratory study of NYNA D+, paste rodenticide containing 0.005% difenacoum with albino house mice (*Mus musculus*). | Triplan |  |  |  |  |
| B5.10.2./03 | XXX | XXX | 2010 | Efficacy field study for NYNA D+, paste rodenticide containing 0.005% difenacoum with black rats (*Rattus rattus*). | Triplan |  |  |  |  | |
| B5.11 | Published data | Pelz HJ *et al* | 2005 | The genetic basis of resistance to anticoagulants in rodents. | Published data |  |  |  |  | |
| B5.11 | Published data | Lasseur R et *al* | 2006 | Les rongeurs font de la résistance. Nuisibles et parasites | Published data |  |  |  |  | |
| B5.11 | Published data | Myllymäki A | 1995 | Anticoagulant resistance in Europe: Appraisal of the data from the 1992 EPPO questionnaire | Published data |  |  |  |  | |
| B5.11 | Published data | Kerins G M et al | 2001 | The interaction between the indirect Anticogulant Coumatetralyl and Calciferol (vitamin D3) in Warfarin-resistant rats (*Rattus norvegicus*) | Published data |  |  |  |  | |
| B5.11 | Published data | Desideri D *et al* | 1978 | Note préliminaire sur la mise en évidence à Marseille d'une résistance au coumafène chez *Rattus rattus*. | Published data |  |  |  |  | |
| B6.1.1 | XXX | XXX | 2010 | NYNA D+ BLOC SP evaluation of acute oral toxicity in rats – acute toxic class method. | Triplan |  |  |  |  | |
| B6.1.2 | XXX | XXX | 2010 | NYNA D+ BLOC SP evaluation of acute dermal toxicity in rats. | Triplan |  |  |  |  | |
| B6.2.1 | XXX | XXX | 2010 | NYNA D+ BLOC SP assessment of acute dermal irritation. | Triplan |  |  |  |  | |
| B6.2.2 | XXX | XXX | 2010 | NYNA D+ BLOC SP assessment of acute eye irritation. | Triplan |  |  |  |  | |
| B6.3 | XXX | XXX | 2010 | NYNA D+ BLOC SP Assessment of sensitizing properties on albino Guinea pigs maximization test according to Magnusson and Kligman. | Triplan |  |  |  |  | |
| - | 09-920010-002 | Demangel B | 2010 | Physico-chemical tests before and after an accelerated storage procedure for 14 days at 54 +/- 2°C on NYNA D+ PATE, DEFITRACES, Report n° 09-920010-009, 18/01/2010 | Triplan |  | X | X |  | |
| - | 10-920010-011 | Demangel B | 2012 | Physico-chemical tests and chemical stability after a storage procedure for 2 years at 20 +/- 2 °c on NYNA D+ PATE, DEFITRACES, Report n° 10-920010-011, 06/12/2012 | Triplan |  | X | X |  | |

Annex 2: Analytical methods residues – active substance – PAR 2012

**Difenacoum**

Date: 12/2011

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

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

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

**Methods for products of plant origin**

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

**Methods for foodstuffs of animal origin**

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

**Methods for soil**

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

**Methods for sediment**

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

**Methods for drinking water and surface water**

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

**Methods for air**

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

**Methods for body fluids/tissue**

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

# Annexe 3a: Efficacy of the Active Substance from its Use in the Product NYNA D+ PATE – PAR 2012

Note that this table have been summarized by the applicant and FR CA had assessed it.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Test substance | Test organism(s) | Test conditions/concentration applied exposure time | Test results: effects, mode of action, resistance | Reference |
| NYNA D+  0.005% difenacoum | Albino house mice  (*Mus musculus)*  5 males and 5 females per lot  (3 lots) | **Laboratory CEB n°1**  Lot efficacy (no-choice food),  Lot acceptance (free-choice food)  Lot control animals.  Intoxication duration: 3 days with daily measurements of mortality and consumption.  Acclimation: 3 days in individual cage.  At D0:  - Control lot: - 25 g per animal of usual food  - Acceptance lot: - 3 paste sachets (21.5 to 28.5 g) + 25 g of usual food per animal,  - Efficacy lot :- 3 paste sachets (21.5 to 28.5 g) per animal  3 consecutive days with daily consumption measurements.  Mortality was observed during 21 days from the first day of intoxication and noted every 24 hours. | In this study, the control animals’ lot has been a good reference because operators noticed the increase of body weight within 21 days of food consumption.  The efficacy lot’s bait consumption is 25% to 55% lower than the controls’ one.  But in the acceptance lot we noticed that the bait was overwhelmingly preferred to usual food even the overall consumptions were close to the acceptance lot’s ones.  In both cases, **100% mortality** has been reached (average of 7.4 days for the no-choice test and 6.7 days for the free-choice one).  Difenacoum efficacy has been confirmed and we think that the obtained results can be extrapolated to rats.  No resistance is observed in this trial | Barbieux S  Grolleau G  SB-2010-005  (B5.10.1) |
| NYNA D+  0.005% difenacoum | Black rats (*Rattus rattus)* | **Field study CEB n° 2**  The used method is relative and allows knowing the bait biocidal product efficacy on a rat’s population without knowing the precise population size.  Daily food consumptions are measured.  56 stations have been placed in a pig farm.  Acclimation phase of mice to their new environment. Then:  - Pre-baiting phase: 500 g grains per day per station (67 days).  - Poisoning phase: 500 g baits per day and per bait station (5 days).  - Post-baiting phase: 500 g grains oat per station and per day (11 days).  Daily consumptions were recorded at interval of 24 hours at the beginning and the end of pre-baiting stage, at the end of post-baiting phase and during the two first days during poisoning phase. | A field study conducted in a pig farm with black rats using paste sachets, containing 50 ppm difenacoum, has given excellent results:   * - Pre-baiting stage: 3734.7 g * - Post-baiting stage : 211.7 g   within 8 days of intoxication.  **The assessed efficacy is 94.3%.**  Because of the great rats’ mistrust and high food competition (pig farm), the pre-baiting duration has been exceptionally long (67 days instead of 18 to 21 days for the brown rats).  The tested bait has proven very effective; however we cannot assess its acceptance because the rats stored the blocks.  **Despite this low mortality rate, it is in adequacy with the results assessed in the laboratory with albino house mice and** **confirms the efficacy of the product**  No resistance is observed in this trial | Barbieux S  Grolleau G  SB-2010-007  (B5.10.2) |

# Annex 4: Toxicology and metabolism –active substance – PAR 2012, updated 2017

**Difenacoum**

Threshold Limits and other Values for Human Health Risk Assessment

Date: 12/2011

| **Summary** | | | | | |
| --- | --- | --- | --- | --- | --- |
|  | Value | | Study | SF | |
| AEL long-term | 0.0000011 mg/kg bw/day | | Teratogenicity in rabbit | 600 | |
| AEL medium-term | 0.0000011 mg/kg bw/day | | Teratogenicity in rabbit | 600 | |
| AEL acute | 0.0000011 mg/kg bw/day | | Teratogenicity in rabbit | 600 | |
|  | | | | | |
| Inhalative absorption: 100% | | | | |  |
| Oral absorption: 68 % | | | | |  |
| Dermal absorption: 0.047 % for wax block bait (Activa Pelgar study) – 3 % for pellet and grain baits (Sorex study) | | | | |  |
| **Classification** | | | | | |
| with regard to toxicological data (according to the criteria in Dir. 67/548/EEC) | | Current classification: T+ ; R28, R48/25 - N; R50/53  Proposed classification by the RMS: T+; R26/27/28, Repr. Cat. 1, R61 - T; R48/23/24/25 - N ; R50/53 | | | |
| with regard to toxicological data (according to the criteria in Reg. 1272/2008) | | Current classification: Acute Tox 2, H300; STOT RE 1, H372 ; Aquatic Acute 1, H400; Acute chronic 1, H410 | | | |
|  | | Proposed classification by the RMS: Acute Tox 2, H330, H310, H300; Repr. 1A, H360D; STOT RE 1, H372; Aquatic Acute 1, H400; Acute chronic 1, H410 | | | |

* **Renewal application (2017)**

| **Classification** | |
| --- | --- |
|  |  |
| with regard to toxicological data (according to the criteria in Reg. 1272/2008) | Acute Tox 1 – H300 ; H310 ; H330  STOT RE 1 – H372 (blood)  Repr. 1B – H360D  Repr. 1B; H360D: C ≥ 0,003 % STOT RE 2; H373: 0,002 % ≤ C < 0,02 % STOT RE 1; H372: C ≥ 0,02 % |
|  |  |

Annex 5: Toxicology – biocidal product – PAR 2012, updated 2017

**NYNA D+ PATE**

Date: 12/2011

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

| **Acute toxicity, irritancy and skin sensitisation of the preparation (Annex IIIB, point 6.1, 6.2, 6.3)** | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Rat LD50 oral (OECD 420) > 2000 mg/kg bw |  | | | |  | |  |  | |
| Rat LD50 dermal (OECD 402) > 2000 mg/kg bw |  | | | |  | |  |  | |
| Rat LC50 inhalation (OECD 403): no study submitted |  | | | |  | |  |  | |
| Skin irritation (OECD 404): non irritant |  | | | |  | |  |  | |
| Eye irritation (OECD 405): non irritant |  | | | |  | |  |  | |
| Skin sensitisation (OECD 406; Maximisation test): Study submitted but not acceptable | |  |  |  | |  | | |

Acute toxicity tests:

| Route | Method Guideline | Species Strain Sex no/group | dose levels  duration of exposure | Value LD50/LC50 | Remarks | Reference |
| --- | --- | --- | --- | --- | --- | --- |
| Oral | OECD 423 | Sprague Dawley  6 Females | 2000mg/kg bw | > 2000mg/kg bw | No mortality | Colas S. 2010 |
| Dermal | OECD 402 | Sprague Dawley  5/sex | 2000mg/kg bw | > 2000mg/kg bw | No mortality  Neither cutaneous nor systemic effects | Colas S. 2010 |

Skin irritation test:

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Species | Method | Average score 24 and 72 h | | Reversibility yes/no | Result | Reference |
| Erythema | Oedema |
| Albinos NZ rabbit  3 males | OECD 404  Semi-occlusive, 4h | 0 | 0 | na | Not irritant | Colas S. 2010 |

Eye irritation test:

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Species | Method | Average Score (24h, 48h, 72h) | | | | Result | Reversibility yes/no | Remarks | Reference |
| Cornea | Iris | Redness  Conjunctiva | Chemosis |
| Albinos NZ rabbit  3 Males | OECD 405 | 0 | 0 | 1.7  0.7  1 | 1  0.3  0.3 | Not irritant | Redness reversible at Day 3-4  Chemosis reversible at Day 2-3 | Other findings: Slight corneal opacity in 1 animal at 1h, reversible at Day 1  Iris congestion at 1h, reversible at Day 1 | Colas S. 2010 |

Sensitisation test:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Species** | **Method** | **Number of animals sensitized/total number of animals** | **Result** | **Reference** |
| Albino Guinea pig  Treated group : 11 females | OECD 406: Maximization test  Induction phases: 0.5 ml at 40% in distilled water by topic route  Challenge phases: A cup containing the test item at 5 and 2.5% in distilled water | 36 % (4/11) after the first challenge at 5% at 24 and 48 hours. No reaction at 72 hours. No reaction at 2.5 %  9 % (1/11) after the second challenge at 5% at 24 hours. No reaction at 48 hours. No reaction at 2.5 % | No skin sensitizing | Colas S. 2010  Not acceptable |

| **Additional toxicological information (e.g. Annex IIIB, point 6.5, 6.7)** | | | | |
| --- | --- | --- | --- | --- |
| Short-term toxicity studies | None |  |  |  |
| Toxicological data on active substance(s) (not tested with the preparation) | None |  |  |  |
|  |  |  |  |  |
| Toxicological data on non-active substance(s) (not tested with the preparation) | None |  |  |  |
|  |  |  |  |  |
| Further toxicological information | None | | | |

|  |  |
| --- | --- |
| **Classification and labelling proposed for the preparation with regard to toxicological properties (Annex IIIB, point 9)** | |
| Directive 1999/45/EC | None |
| Regulation 1272/2008/EC | None |

* **Renewal application (2017)**

|  |  |
| --- | --- |
| **Classification and labelling proposed for the preparation with regard to toxicological properties (Annex IIIB, point 9)** | |
| Regulation 1272/2008/EC | Repr. 1B - H360D  STOT RE 2 - H373 |

Annex 6: Safety for professional operators – PAR 2012

**NYNA D+ PATE**

Date: 12/2011

**Exposure assessment**

| **Exposure scenarios for intended uses (Annex IIIB, point 6.6 )** |
| --- |

Primary exposure of professionals – Control of rats

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Component** | **CAS** | **Potential Dermal Total**  **[mg/kg/d]** | **Actual Dermal Total**  **[mg/kg/d]** | **Inhalation Exposure**  **[mg/m³]** | **Model** |
| Sachet not considered: exposure during loading and cleaning (worst case) | | | | | | |
| Tier 1 (without gloves) | Difenacoum | 56073-07-5 | 2.4x10-6 | 2.4x10-6 | negligible | Cefic study |
| Tier 2 (with gloves; penetration factor: 10%) | Difenacoum | 56073-07-5 | 2.4x10-6 | 2.4x10-7 | negligible | Cefic study |
| Sachet considered: exposure only during cleaning considered (reasonable case) | | | | | | |
| Tier 1 (without PPE) | Difenacoum | 56073-07-5 | 3.4x10-8 | 3.4x10-8 | negligible | Cefic study |

Primary exposure of professionals – Control of mice

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Component** | **CAS** | **Potential Dermal Total**  **[mg/kg/d]** | **Actual Dermal Total**  **[mg/kg/d]** | **Inhalation Exposure**  **[mg/m³]** | **Model** |
| Sachet not considered: exposure during loading and cleaning (worst case) | | | | | | |
| Tier 1 (without gloves) | Difenacoum | 56073-07-5 | 4.3x10-7 | 4.3x10-7 | negligible | Cefic study |
| Sachet considered: exposure only during cleaning considered (reasonable case) | | | | | | |
| Tier 1 (without PPE) | Difenacoum | 56073-07-5 | 3.4x10-8 | 3.4x10-8 | negligible | Cefic study |

Risk assessment – Control of rats

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Scenario** | **Component** | **CAS** | **AEL [mg/kg/d]** | **Absorption**  **[%]** | | **Inhal ext**  **[mg/m3]** | | **Derm syst**  **[mg/kg bw/d]** | | Risk |
|  |  |  |  | inh | derm | Expo | %AEL | Expo | %AEL |  |
| Sachet not considered: exposure during loading and cleaning (worst case) | | | | | | | | | | |
| Tier 1 (without gloves) | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 0.047 | negligible | n.a | 2.4x10-6 | 217 | Unacceptable |
| Tier 2 (with gloves; penetration factor: 10%) | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 0.047 | negligible | n.a | 2.4x10-7 | 22 | Acceptable |
| Sachet considered: exposure only during cleaning considered (reasonable case) | | | | | | | | | | |
| Tier 1 (without gloves) | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 0.047 | negligible | n.a | 3.4x10-8 | 3 | Acceptable |

Risk assessment – Control of mice

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Scenario** | **Component** | **CAS** | **AEL [mg/kg/d]** | **Absorption**  **[%]** | | **Inhal ext**  **[mg/m3]** | | **Derm syst**  **[mg/kg bw/d]** | | Risk |
|  |  |  |  | inh | derm | Expo | %AEL | Expo | %AEL |  |
| Sachet not considered: exposure during loading and cleaning (worst case) | | | | | | | | | | |
| Tier 1 (without gloves) | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 0.047 | negligible | n.a | 4.3x10-7 | 39 | Unacceptable |
| Sachet considered: exposure only during cleaning considered (reasonable case) | | | | | | | | | | |
| Tier 1 (without gloves) | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 0.047 | negligible | n.a | 3.4x10-8 | 3 | Acceptable |

* **Renewal application (2017)**

The conclusions of the risk assessment remain unchanged. The RMMs required by the risk assessment remain also unchanged.

Annex 7: Safety for non-professional operators and the general public – PAR 2012

**NYNA D+ PATE**

| **General information** | |
| --- | --- |
| Formulation Type: Paste |  |
| Active substance(s) (incl. content): Difenacoum (0.005%) |  |

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

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

| **Exposure scenarios for intended uses (Annex IIIB, point 6.6 )** | |
| --- | --- |
| Primary exposure: non-professional use |  |
| Secondary exposure, acute: child ingesting bait |  |
| Secondary exposure, chronic: none |  |

Conclusion:

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

The accidental ingestion of baits poses a risk to infants since the AEL is exceeded when infant ingests more than 0.3 mg of product per day (about 0.003% of a 10g paste).

Details for the exposure estimates:

Exposure assessment – Control of rats

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Component** | **CAS** | **Potential Dermal Total**  **[mg/kg/d]** | **Actual Dermal Total**  **[mg/kg/d]** | **Inhalation Exposure**  **[mg/m³]** | **Model** |
| Sachet not considered: exposure during decanting, loading and cleaning (worst case) | | | | | | |
| Non professional | Difenacoum | 56073-07-5 | 2.07x10-7 | 2.07x10-7 | negligeable | Cefic study |
| Sachet considered: exposure only during cleaning considered (reasonable case) | | | | | | |
| Non professional | Difenacoum | 56073-07-5 | 1.1x10-8 | 1.1x10-8 | negligeable | Cefic study |

Exposure assessment – Control of mice

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Component** | **CAS** | **Potential Dermal Total**  **[mg/kg/d]** | **Actual Dermal Total**  **[mg/kg/d]** | **Inhalation Exposure**  **[mg/m³]** | **Model** |
| Sachet not considered: exposure during decanting, loading and cleaning (worst case) | | | | | | |
| Non professional | Difenacoum | 56073-07-5 | 4.4x10-8 | 4.4x10-8 | negligeable | Cefic study |
| Sachet considered: exposure only during cleaning considered (reasonable case) | | | | | | |
| Non professional | Difenacoum | 56073-07-5 | 1.1x10-8 | 1.1x10-8 | negligeable | Cefic study |

Risk assessment - Control of rats

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Scenario** | **Component** | **CAS** | **AEL [mg/kg/d]** | **Absorption**  **[%]** | | **Inhal ext**  **[mg/m3]** | | **Derm syst**  **[mg/kg bw/d]** | | **Risk** |
|  |  |  |  | inh | derm | Expo | %AEL | Expo | %AEL |  |
| Sachet not considered: exposure during decanting, loading and cleaning (worst case) | | | | | | | | | | |
| Non-professional | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 0.047 | negligible | n.a | 2.07x10-7 | 19 | Acceptable |
| Sachet considered: exposure only during cleaning considered (reasonable case) | | | | | | | | | | |
| Non-professional | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 0.047 | negligible | n.a | 1.1x10-8 | 1 | Acceptable |

Risk assessment - Control of mice

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Scenario** | **Component** | **CAS** | **AEL [mg/kg/d]** | **Absorption**  **[%]** | | **Inhal ext**  **[mg/m3]** | | **Derm syst**  **[mg/kg bw/d]** | | **Risk** |
|  |  |  |  | inh | derm | Expo | %AEL | Expo | %AEL |  |
| Sachet not considered: exposure during decanting, loading and cleaning (worst case) | | | | | | | | | | |
| Non-professional | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 0.047 | negligible | n.a | 4.4x10-8 | 4 | Acceptable |
| Sachet considered: exposure only during cleaning considered (reasonable case) | | | | | | | | | | |
| Non-professional | Difenacoum | 56073-07-5 | 1.1x10-6 | 100 | 0.047 | negligible | n.a | 1.1x10-8 | 1 | Acceptable |

* **Renewal application (2017)**

General public uses are no longer claimed for the renewal of authorisation.

Annex 8: Residue behaviour – PAR 2012

**Difenacoum**

Date: 12/2011

Intended Use (critical application): Control of mice and rats

Active substance(s): Difenacoum

Formulation of biocidal product: Paste

Place of treatment: inside building (domestic, industrial and farm)

The product is a paste bait only used indoor in secured bait station. Collecting unconsumed baits and dead rodents must be done every week during the treatment so in these recommended conditions; no contamination is expected for feeding stuffs. Finally, according to the Assessment report on difenacoum, “*difenacoum baits should not be placed where food, feedingstuffs or drinking water could be contamined*”.

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

1. See document CA-Nov16-Doc.4.x-Final on the concept of tamper-resistant bait stations. [↑](#footnote-ref-2)
2. See document CA-Nov16-Doc.4.x-Final on the concept of tamper-resistant bait stations. [↑](#footnote-ref-3)
3. See document CA-Nov16-Doc.4.x-Final on the concept of tamper-resistant bait stations. [↑](#footnote-ref-4)
4. See document CA-Nov16-Doc.4.x-Final on the concept of tamper-resistant bait stations. [↑](#footnote-ref-5)
5. See document CA-Nov16-Doc.4.x-Final on the concept of tamper-resistant bait stations. [↑](#footnote-ref-6)
6. Technical guidance document in support of the directive 98/8/ec concerning the placing of biocidal products on the market - Guidance on data requirements for active substances and biocidal products, October 2000. [↑](#footnote-ref-7)
7. Guidance on the Biocidal Products Regulation Volume III Human Health – Part B Risk Assessment, October 2015. [↑](#footnote-ref-8)
8. 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-9)
9. 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-10)
10. 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-11)
11. 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-12)
12. 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-13)
13. It has to be noted that this dermal absorption study has not been re-assessed according to the criteria laid in the EFSA guidance on dermal absorption of 2012. [↑](#footnote-ref-14)
14. HEEG opinion on an harmonised approach for the assessment of rodenticides (anticoagulants) agreed at TMII2011. [↑](#footnote-ref-15)
15. Although the bait weights 10 g and not 20 g as in the CEFIC study, it was considered that the important parameter is the number of pastes loaded rather than the weight. [↑](#footnote-ref-16)
16. HEEG opinion Default protection factors for protective clothing and gloves, agreed at TMI2010 [↑](#footnote-ref-17)
17. HEEG opinion on harmonising the number of manipulations in the assessment of rodenticides (anticoagulant), agreed at TMII2010 [↑](#footnote-ref-18)
18. Data which have not been already submitted for the purpose of the Annex I inclusion. [↑](#footnote-ref-19)