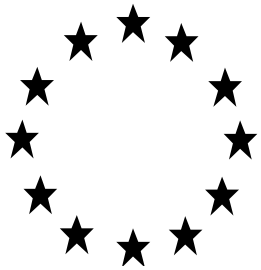
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

PRODUCT ASSESSMENT REPORT OF A BIOCIDAL PRODUCT FOR THE MAJOR CHANGE OF A NATIONAL AUTHORISATION (NA-MAC)



Product identifier in R4BP	**Ratimor Plus Grain Bait**
Product type:	14 (Rodenticide)
Active ingredient(s):	Bromadiolone
Case No. in R4BP	BC–XK038645-17
Asset No. in R4BP	SBP/Original 50 ppm SI-0017955-0000
Evaluating Competent Authority	Slovenia – Chemicals Office of the Republic of Slovenia
Date	May 2019 (NA-MAC Major Change)

Overview of applications

Application type	refMS	Case number in the refMS	Decision date	Assessment carried out (i.e. first authorisation / amendment /renewal)	Page
NA-APP	UK	n/a (Asset number: UK-0000381-0000)	03/12/2012	Initial assessment	-
NA-MRP	UK	n/a (Asset number: SI-0004368-0000)	4/2/2014	/	-
SBP	SI	BC-KH031667-37 (Asset number: SI-0017955-0000)	24/10/2017	/	-
NA-MAC	SI	BC–XK038645-17	5/6/2019	major change	3

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Conclusion

The Slovenian CA for the authorisation of biocidal products has processed an application for major change (NA-MAC) for the biocidal product Ratimor Plus Grain Bait, which contains the active substance bromadiolone (0.0029 % w/w).

In addition to major change, an administrative change of the name of the biocidal product in line to the Annex to Regulation (EU) No 354/2013 has been made as there is no risk of confusion with the names of other biocidal products. A new main trade name is Ratimor Plus Grain Bait. An additional trade name Ratimor Plus žitna vaba has been also added.

The assessment presented in this report represents an Addendum to the Product Assessment Report of a biocidal product Ratimor Grain Bait (UK CA, 2012).

Following evaluation of the major change (to reduce the amount of active substance bromadiolone in the biocidal product Ratimor Plus Grain Bait to 0.0029%) it was decided that:

- Sufficient efficacy had been demonstrated to support authorisation of the biocidal product containing 0.0029% bromadiolone.
- The proposed change doesn't adversely affect the conclusions previously reached within the initial application for authorisation of the biocidal product concerning the compliance with the conditions set out in Article 19 of Regulation (EU) No 528/2012.

Relating the major change of Ratimor Plus Grain Bait the following amendments to the initial authorisation have been made:

- CLP in accordance with the ATP (Commission Regulation (EU) 2016/1179 of 19 July 2016) has been applied.
- Acceptable storage stability for the claimed shelf life based on read-across approach has been demonstrated.
- Additionally requested validation data for determination of the active substance content at the reduced level of 0.0029 % w/w has been evaluated and found sufficient.
- New field trials have been provided by the applicant in order to assess the efficacy of the biocidal product with the reduced content of the active ingredient. The field trial data provided with mice (*Mus musculus)* and rats *(Rattus norvegicus* and *Rattus rattus*) endorses the lowering of the active substance from 50 ppm to 29 ppm since the attractiveness and the effectiveness of the bait is proven unaffected by such action.
- Dermal absorption has been re-evaluated in accordance with the Guidance on Dermal Abortion (EFSA Journal 2012; 10(4):2265. As a result, the dermal absorption has been changed from 0.36 % at first authorisation to 7 % for this major change. A revised human health exposure assessment and risk assessment for human health have therefore been conducted.

1 Summary of the product assessment

1.1 Administrative information

1.1.1 Identifier in R4BP

Ratimor Plus Grain Bait Ratimor Plus žitna vaba

1.1.2 Authorisation holder

Name and address of the authorisation holder	**Name**	Unichem d.o.o.
	Address	Sinja Gorica 2 SI-1360 Vrhnika Slovenia
Authorisation number		
Date of the authorisation	5.6.2019	
Expiry date of the authorisation	31.8.2020	

1.1.3 Manufacturer(s) of the product

Name of manufacturer	Unichem d.o.o.
Address of manufacturer	Sinja Gorica 2 SI-1360 Vrhnika Slovenia
Location of manufacturing sites	Sinja Gorica 2 SI-1360 Vrhnika Slovenia

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

Active substance	Bromadiolone
Name of manufacturer	PelGar International Limited
Address of manufacturer	Unit 13 Newman Lane Industrial Estate Alton, Hampshire GU34 2QR UK

Location of manufacturing sites	Prazska 54 28002 Kolin Czech Republic

1.2 Product composition and formulation

1.2.1 Qualitative and quantitative information on the composition

Common name	IUPAC name	Function	CAS number	EC number	Content (%)
Bromadiolone	3-[3-(4'-Bromo[1,1'-biphenyl]-4-yl)-3-hydroxy-1-phenylpropyl]-4-hydroxy-2H-1-benzopyran-2-one	Active substance	28772-56-7	249-205-9	0.0029

- The product contains a bittering agent and a dye.
- Information on the full composition is provided in the separate confidential[1] annex.
- According to the information provided the product contains no nanomaterials as defined in Article 3 paragraph 1 (z) of Regulation No. 528/2012.

1.2.2 Information on the substance(s) of concern

No substance of concern was identified upon initial assessment (the application for authorisation was submitted and the assessment took place before the Biocidal Products Regulation 528/2012 entered into force). No new substance(s) of concern were identified upon this major change.

1.2.3 Candidate(s) for substitution

Bromadiolone meets the following exclusion criteria according to Article 5(1) BPR:

- toxic for reproduction category 1B,
- persistent and very persistent, bioaccumulative and toxic.

Therefore bromadiolone meets the conditions laid down in Article 10 BPR, and is consequently a candidate for substitution.

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

1.2.4 Type of formulation

Ready-to-use bait: Grain Bait

1.3 Classification and Labelling according to the Regulation (EC) No 1272/2008[2]

Classification **Hazard classes, Hazard categories**	**Hazard statements**
STOT RE 2	H373: May cause damage to organs (blood) through prolonged or repeated exposure.

Labelling	**Code**	**Pictogram / Wording**
	GHS08	
Signal word		Warning
Hazard statements	STOT RE 2	H373: May cause damage to organs (blood) through prolonged or repeated exposure.
Supplemental label elements	/	/
Precautionary statements	P260	Do not breath dust.
	P314	Get medical advice/attention if you feel unwell.
	P501	Dispose of contents/container in accordance with local requirements.
Note	EUH208	Contains 1,2-benzisothiazol-3(2H)-one. May produce an allergic reaction.

1.4 Use(s) appropriate after major change to the authorisation

No.	**Use**
1	House mice – general public – indoor
2	Rats – general public – indoor
3	Rats – general public – outdoor around buildings

[2] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006.

1.4.1 Use 1 appropriate after major change to the authorisation – House mice – general public – indoor

Product Type(s)	PT14 - Rodenticides (Pest control)
Where relevant, an exact description of the use	Not relevant for rodenticides
Target organism(s) (including development stage)	House mouse (*Mus musculus*)
Field(s) of use	Indoor
Application method(s)	Ready-to-use bait [in sachets for loose bait] to be used in tamper-resistant bait stations.
Application rate(s) and frequency	For mouse infestations use 10 g up to 40 g per bait point. Place bait stations 5 m apart reducing to 2 m in case of high infestations.
Category(ies) of users	Non-professional (general public)
Pack sizes and packaging material	1. Edible paper tea-bag sachets (10 g - 20 g) packed in: - polyethylene (PE) or polypropylene (PP) or PE/PP or paper/PE outer sachet packed in cardboard or fibreboard outer pack up to 50g - polyethylene (PE) or polypropylene (PP) packs up to 50 g - natron bag up to 50 g - sachet (PE or PE/PP or PP or paper/PE) packed in cardboard outer pack/carton box or natron bag or PP/HDPE buckets with lid up to 50 g - PE or PP buckets with lid up to 50 g - cardboard or fibre-board boxes with PE or PP bag or liner up to 50 g - cardboard or fibre-board boxes up to 50 g - pre-filled or refillable tamper-resistant HDPE or polypropylene mouse or rat bait station. Bait stations packed in cardboard outer or plastic heat-sealed container or thermo seal foil up to 50 g 2. Bait in PP/paper film sachets, PET/PE film sachets, PE/paper film sachets or PE/aluminised film sachets (10 g - 50 g) packed in: - polyethylene (PE) or polypropylene (PP) or PE/PP or paper/PE outer sachet packed in cardboard or fibreboard outer pack up to 50g - PE or PP packs up to 50 g - HDPE container up to 50 g - Natron bag up to 50 g - Packs up to 50 g - PP woven sack or multi-ply paper sack up to 50 g - Pail (PP) or bucket (PP or PE) with lid up to 50 g - PP or PE tub up to 50 g - Prefilled or refillable tamper-resistant HDPE or PP rat or mouse bait station. Bait stations packed in carboard outer or plastic heat-sealed container or thermo seal foil up to 50 g - PET/PE, PP/PE or paper/PE pouch up to 50 g

	- Cardboard or fibre-board pack with PE or PP bag or liner up to 50 g - Cardboard or fibre-board box up to 50 g - sachet (PE or PE/PP or PP or paper/PE) packed in cardboard outer pack/carton box or natron bag or PP/HDPE buckets with lid up to 50 g 3. Other packaging: - loose bait in prefilled or refillable tamper-resistant mice or rat bait station, packed in carboard outer or plastic heat-sealed container or thermo seal foil up to 50g - loose bait in tray (PVC or polystyrene or polypropylene or PET) with heat sealed lid (PET/polypropylene or PET/polyethylene or polypropylene) to be used with bait station up to 50 g

1.4.1.1 Use-specific instructions for use

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

1.4.1.2 Use-specific risk mitigation measures

See section 1.5.2

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

See section 1.5.3

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

See section 1.5.4

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

See section 1.5.5

1.4.2 Use 2 appropriate after major change to the authorisation – Rats – general public – indoor

Product Type(s)	PT14 - Rodenticides (Pest control)
Where relevant, an exact description of the use	Not relevant for rodenticides
Target organism(s) (including development stage)	Brown rats (*Rattus norvegicus*) Roof rats (*Rattus rattus*)
Field(s) of use	Indoor
Application method(s)	Ready-to-use bait [in sachets for loose bait] to be used in tamper-resistant bait stations.
Application rate(s) and frequency	For rat infestations use 10 g up to 200 g per bait point. Place bait stations 10 m apart reducing to 5 m in case of high infestations.
Category(ies) of users	General Public
Pack sizes and packaging material	1. Edible paper tea-bag sachets (10 g - 20 g) packed in: - polyethylene (PE) or polypropylene (PP) or PE/PP or paper/PE outer sachet packed in cardboard or fibreboard outer pack up to 150g - polyethylene (PE) or polypropylene (PP) packs up to 150 g - natron bag up to 150 g - sachet (PE or PE/PP or PP or paper/PE) packed in cardboard outer pack/carton box or natron bag or PP/HDPE buckets with lid up to 150 g - PE or PP buckets with lid up to 150 g - cardboard or fibre-board boxes with PE or PP bag or liner up to 150 g - cardboard or fibre-board boxes up to 150 g - pre-filled or refillable tamper-resistant HDPE or polypropylene mouse or rat bait station. Bait stations packed in cardboard outer or plastic heat-sealed container or thermo seal foil up to 150 g 2. Bait in PP/paper film sachets, PET/PE film sachets, PE/paper film sachets or PE/aluminised film sachets (10g - 150 g) packed in: - polyethylene (PE) or polypropylene (PP) or PE/PP or paper/PE outer sachet packed in cardboard or fibreboard outer pack up to 150g - PE or PP packs up to 150 g - HDPE container up to 150 g

	- Natron bag up to 150 g - Packs up to 150 g - PP woven sack or multi-ply paper sack up to 150 g - Pail (PP) or bucket (PP or PE) with lid up to 150 g - PP or PE tub up to 150 g - Prefilled or refillable tamper-resistant HDPE or PP mouse or rat bait station. Bait stations packed in carboard outer or plastic heat-sealed container or thermo seal foil up to 150 g - PET/PE, PP/PE or paper/PE pouch up to 150 g - Cardboard or fibre-board pack with PE or PP bag or liner up to 150 g - Cardboard or fibre-board box up to 150 g - sachet (PE or PE/PP or PP or paper/PE) packed in cardboard outer pack/carton box or natron bag or PP/HDPE buckets with lid up to 150 g 3. Other packaging: - loose bait in prefilled or refillable tamper-resistant mice or rat bait station, packed in carboard outer or plastic heat-sealed container or thermo seal foil up to 150g - loose bait in tray (PVC or polystyrene or polypropylene or PET) with heat sealed lid (PET/polypropylene or PET/polyethylene or polypropylene) to be used with bait station up to 150 g

1.4.2.1 Use-specific instructions for use

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

1.4.2.2 Use-specific risk mitigation measures

See section 1.5.2

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

See section 1.5.3

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

See section 1.5.4

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

See section 1.5.5

1.4.3 Use 3 appropriate after major change to the authorisation – Rats – general public – outdoor around buildings

Product Type(s)	PT14 - Rodenticides (Pest control)
Where relevant, an exact description of the use	Not relevant for rodenticides
Target organism(s) (including development stage)	Brown rats (*Rattus norvegicus*) Roof rats (*Rattus rattus*)
Field(s) of use	Outdoor around buildings
Application method(s)	Ready-to-use bait [in sachets for loose bait] to be used in tamper-resistant bait stations.
Application rate(s) and frequency	For rat infestations use 10 g up to 200 g per bait point. Place bait stations 10 m apart reducing to 5 m in case of high infestations.
Category of users	General Public
Pack sizes and packaging material	1. Edible paper tea-bag sachets (10 g - 20 g) packed in: - polyethylene (PE) or polypropylene (PP) or PE/PP or paper/PE outer sachet packed in cardboard or fibreboard outer pack up to 150g - polyethylene (PE) or polypropylene (PP) packs up to 150 g - natron bag up to 150 g - sachet (PE or PE/PP or PP or paper/PE) packed in cardboard outer pack/carton box or natron bag or PP/HDPE buckets with lid up to 150 g - PE or PP buckets with lid up to 150 g - cardboard or fibre-board boxes with PE or PP bag or liner up to 150 g - cardboard or fibre-board boxes up to 150 g - pre-filled or refillable tamper-resistant HDPE or polypropylene mouse or rat bait station. Bait stations packed in cardboard outer or plastic heat-sealed container or thermo seal foil up to 150 g

	2. Bait in PP/paper film sachets, PET/PE film sachets, PE/paper film sachets or PE/aluminised film sachets (10 g - 150 g) packed in: - polyethylene (PE) or polypropylene (PP) or PE/PP or paper/PE outer sachet packed in cardboard or fibreboard outer pack up to 150g - PE or PP packs up to 150 g - HDPE container up to 150 g - Natron bag up to 150 g - Packs up to 150 g - PP woven sack or multi-ply paper sack up to 150 g - Pail (PP) or bucket (PP or PE) with lid up to 150 g - PP or PE tub up to 150 g - Prefilled or refillable tamper-resistant HDPE or PP mouse or rat bait station. Bait stations packed in carboard outer or plastic heat-sealed container or thermo seal foil up to 150 g - PET/PE, PP/PE or paper/PE pouch up to 150 g - Cardboard or fibre-board pack with PE or PP bag or liner up to 150 g - Cardboard or fibre-board box up to 150 g - sachet (PE or PE/PP or PP or paper/PE) packed in cardboard outer pack/carton box or natron bag or PP/HDPE buckets with lid up to 150 g 3. Other packaging: - loose bait in prefilled or refillable tamper-resistant mouse or rat bait station, packed in carboard outer or plastic heat-sealed container or thermo seal foil up to 150g - loose bait in tray (PVC or polystyrene or polypropylene or PET) with heat sealed lid (PET/polypropylene or PET/polyethylene or polypropylene) to be used with bait station up to 150 g

1.4.3.1 Use-specific instructions for use

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

1.4.3.2 Use-specific risk mitigation measures

See section 1.5.2

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

See section 1.5.3

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

See section 1.5.4

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

See section 1.5.5

1.5 General directions for use

1.5.1 Instructions for use

- Read and follow the product information as well as any information accompanying the product or provided at the point of sale before using it. - Prior to the use of rodenticide products, non-chemical control methods (e.g. traps) should be considered. - Remove food which is readily attainable for rodents (e.g. spilled grain or food waste). Apart from this, do not clean up the infested area just before the treatment, as this only disturbs the rodent population and makes bait acceptance more difficult to achieve. - Bait stations should be placed in the immediate vicinity where rodent activity has been observed (e.g. travel paths, nesting sites, feedlots, holes, burrows etc.). - Where possible, bait stations must be fixed to the ground or other structures. - Do not open the sachets containing the bait. - Place bait stations out of the reach of children, birds, pets, farm animals and other non-target

animals.

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

- Do not place bait stations near water drainage systems where they can come into contact with water.

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

- Remove the remaining bait or the bait stations at the end of the treatment period.

1.5.2 Risk mitigation measures

- Consider preventive control measures (plug holes, remove potential food and drinking as far as possible) to improve product intake and reduce the likelihood of reinvasion.

- Do not use anticoagulant rodenticides as permanent (e.g. for prevention of rodent infestation or to detect rodent activity) or pulsed baits.

- The product information (i.e. label and/or leaflet) shall clearly show that:

  - the product shall be used in adequate tamper resistant bait stations (e.g. "use in tamper resistant bait stations only"),

  - users shall properly label bait stations with the information referred to in section 5.3 of the SPC (e.g. "label bait stations according to the product recommendations").

- Using this product should eliminate rodents within 35 days.

- The product information (i.e. label and/or leaflet) shall clearly recommend that in case of suspected lack of efficacy by the end of the treatment (i.e. rodent activity is still observed), the user should seek advice from the product supplier or call a pest control service.

- Search for and remove dead rodents during treatment, at least as often as bait stations are inspected.

- Dispose dead rodents in accordance with local requirements.

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

- This product contains an anticoagulant substance. If ingested, symptoms, which may be delayed, may include nosebleed and bleeding gums. In severe cases, there may be bruising and blood present in the faeces or urine.
- Antidote: Vitamin K1 administered by medical/veterinary personnel only.
- In case of:
  - Dermal exposure, wash skin with water and then with water and soap.
  - Eye exposure, rinse eyes with eyes-rinse liquid or water, keep eyes lids open at least 10 minutes.
  - Oral exposure, rinse mouth carefully with water. Never give anything by mouth to unconscious person. Do not provoke vomiting. If swallowed, seek medical advice immediately and show the product's container or label.
- Contact a veterinary surgeon in case of ingestion by a pet.
- 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, get a medical attention or call 112 ".

Hazardous to wildlife.

1.5.4 Instructions for safe disposal of the product and its packaging

- At the end of the treatment, dispose uneaten bait and the packaging in accordance with local requirements.
- Use of gloves is recommended.
- Do not touch dead rodents with bare hands, but use gloves or tools, such as claws, when removing them. Pack the killed rodents into a plastic bag and remove them as municipal waste.

1.5.5 Conditions of storage and shelf-life of the product under normal conditions of storage

- Store in a dry, cool and well ventilated place. Keep the container closed and away from direct sunlight.
- Store locked up.
- Store in places prevented from the access of children, birds, pets and farm animals.
- Shelf life: 2 years

1.5.6 Other information

- Because of their delayed mode of action, anticoagulant rodenticides take from 4 to 10 days to be effective after consumption of the bait.
- Rodents can be disease carriers. Do not touch dead rodents with bare hands, use gloves or use tools such as claws when disposing them.
- This product contains a bittering agent and a dye.
- In case of common packaging for mice and rats, for non-professional users, maximum packaging size is 150 g.
- For mice and rats: Make frequent inspections of the bait points during the first 10 – 14 days and replace any bait eaten by rodents or that has been damaged by water or contaminated by dirt.

1.5.7 Documentation

The applicant has a full letter of access to the data from the active substance dossier and associated [redacted] (a member of Bromadiolone Task Force) [redacted] products. Letter of Access grants the permission to Unichem to all studies that were made on 50 ppm formulations (before 2012) and access is limited for authorisation purposes of rodenticide products in the EU only.

2 Assessment of the product

2.1 Proposed Uses

2.1.1 Use 1 – House mice – general public – indoor

Product Type(s)	PT14 - Rodenticides (Pest control)
Where relevant, an exact description of the use	Not relevant for rodenticides
Target organism(s) (including development stage)	House mouse (*Mus musculus*) – adults and juveniles
Field(s) of use	Indoors
Application method(s)	Ready-to-use bait [in sachets for loose bait] to be used in tamper-resistant bait stations.
Application rate(s) and frequency	For mouse infestations use 10 g up to 40 g per bait point. Place bait stations 5 m apart reducing to 2 m in case of high infestations. 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.
Category(ies) of users	General Public
Pack sizes and packaging material	1. Edible paper tea-bag sachets (10 g - 20 g) packed in: - polyethylene (PE) or polypropylene (PP) or PE/PP or paper/PE outer sachet packed in cardboard or fibreboard outer pack up to 50g - polyethylene (PE) or polypropylene (PP) packs up to 50 g - natron bag up to 50 g - sachet (PE or PE/PP or PP or paper/PE) packed in cardboard outer pack/carton box or natron bag or PP/HDPE buckets with lid up to 50 g - PE or PP buckets with lid up to 50 g - cardboard or fibre-board boxes with PE or PP bag or liner up to 50 g - cardboard or fibre-board boxes up to 50 g - pre-filled or refillable tamper-resistant HDPE or polypropylene mouse or rat bait station. Bait stations packed in cardboard outer or plastic heat-sealed container or thermo seal foil up to 50 g 2. Bait in PP/paper film sachets, PET/PE film sachets, PE/paper film sachets or PE/aluminised film sachets (10 g - 50 g) packed in: - polyethylene (PE) or polypropylene (PP) or PE/PP or paper/PE outer sachet packed in cardboard or fibreboard outer pack up to 50g - PE or PP packs up to 50 g - HDPE container up to 50 g - Natron bag up to 50 g

	- Packs up to 50 g - PP woven sack or multi-ply paper sack up to 50 g - Pail (PP) or bucket (PP or PE) with lid up to 50 g - PP or PE tub up to 50 g - Prefilled or refillable tamper-resistant HDPE or PP rat or mouse bait station. Bait stations packed in carboard outer or plastic heat-sealed container or thermo seal foil up to 50 g - PET/PE, PP/PE or paper/PE pouch up to 50 g - Cardboard or fibre-board pack with PE or PP bag or liner up to 50 g - Cardboard or fibre-board box up to 50 g - sachet (PE or PE/PP or PP or paper/PE) packed in cardboard outer pack/carton box or natron bag or PP/HDPE buckets with lid up to 50 g 3. Other packaging: - loose bait in prefilled or refillable tamper-resistant mice or rat bait station, packed in carboard outer or plastic heat-sealed container or thermo seal foil up to 50g - loose bait in tray (PVC or polystyrene or polypropylene or PET) with heat sealed lid (PET/polypropylene or PET/polyethylene or polypropylene) to be used with bait station up to 50 g

2.1.2 Use 2 – Rats – general public – indoor

Product Type(s)	PT14 - Rodenticides (Pest control)
Where relevant, an exact description of the use	Not relevant for rodenticides
Target organism(s) (including development stage)	Brown rats (*Rattus norvegicus*) – adults and juveniles Roof rats (*Rattus rattus*) – adults and juveniles
Field(s) of use	Indoors
Application method(s)	Ready-to-use bait [in sachets for loose bait] to be used in tamper-resistant bait stations.
Application rate(s) and frequency	For rat infestations use 10 g up to 200 g per bait point. Place bait stations 10 m apart reducing to 5 m in case of high infestations. 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.
Category(ies) of users	General Public
Pack sizes and packaging material	1. Edible paper tea-bag sachets (10 g - 20 g) packed in: - polyethylene (PE) or polypropylene (PP) or PE/PP or paper/PE outer sachet packed in cardboard or fibreboard outer pack up to 150g - polyethylene (PE) or polypropylene (PP) packs up to 150 g - natron bag up to 150 g

	- sachet (PE or PE/PP or PP or paper/PE) packed in cardboard outer pack/carton box or natron bag or PP/HDPE buckets with lid up to 150 g - PE or PP buckets with lid up to 150 g - cardboard or fibre-board boxes with PE or PP bag or liner up to 150 g - cardboard or fibre-board boxes up to 150 g - pre-filled or refillable tamper-resistant HDPE or polypropylene mouse or rat bait station. Bait stations packed in cardboard outer or plastic heat-sealed container or thermo seal foil up to 150 g 2. Bait in PP/paper film sachets, PET/PE film sachets, PE/paper film sachets or PE/aluminised film sachets (10g - 150 g) packed in: - polyethylene (PE) or polypropylene (PP) or PE/PP or paper/PE outer sachet packed in cardboard or fibreboard outer pack up to 150g - PE or PP packs up to 150 g - HDPE container up to 150 g - Natron bag up to 150 g - Packs up to 150 g - PP woven sack or multi-ply paper sack up to 150 g - Pail (PP) or bucket (PP or PE) with lid up to 150 g - PP or PE tub up to 150 g - Prefilled or refillable tamper-resistant HDPE or PP mouse or rat bait station. Bait stations packed in carboard outer or plastic heat-sealed container or thermo seal foil up to 150 g - PET/PE, PP/PE or paper/PE pouch up to 150 g - Cardboard or fibre-board pack with PE or PP bag or liner up to 150 g - Cardboard or fibre-board box up to 150 g - sachet (PE or PE/PP or PP or paper/PE) packed in cardboard outer pack/carton box or natron bag or PP/HDPE buckets with lid up to 150 g 3. Other packaging: - loose bait in prefilled or refillable tamper-resistant mice or rat bait station, packed in carboard outer or plastic heat-sealed container or thermo seal foil up to 150g - loose bait in tray (PVC or polystyrene or polypropylene or PET) with heat sealed lid (PET/polypropylene or PET/polyethylene or polypropylene) to be used with bait station up to 150 g

2.1.3 Use 3 – Rats – general public – outdoor around buildings

Product Type(s)	PT14 - Rodenticides (Pest control)
Where relevant, an exact	Not relevant for rodenticides

description of the use	
Target organism(s) (including development stage)	Brown rats (*Rattus norvegicus*) – adults and juveniles Roof rats (*Rattus rattus*) – adults and juveniles
Field(s) of use	Outdoor around buildings
Application method(s)	Ready-to-use bait [in sachets for loose bait] to be used in tamper-resistant bait stations.
Application rate(s) and frequency	For rat infestations use 10 g up to 200 g per bait point. Place bait stations 10 m apart reducing to 5 m in case of high infestations. • Place the bait stations in areas not liable to flooding. • Replace any bait in a bait station in which bait has been damaged by water or contaminated by dirt. • The bait stations should be visited only 5 to 7 days after the beginning of the treatment and at least weekly afterwards, in order to check whether the bait is accepted, the bait stations are intact and to remove rodent bodies. Re-fill bait when necessary.
Category(ies) of users	General Public
Pack sizes and packaging material	1. Edible paper tea-bag sachets (10 g - 20 g) packed in: - polyethylene (PE) or polypropylene (PP) or PE/PP or paper/PE outer sachet packed in cardboard or fibreboard outer pack up to 150g - polyethylene (PE) or polypropylene (PP) packs up to 150 g - natron bag up to 150 g - sachet (PE or PE/PP or PP or paper/PE) packed in cardboard outer pack/carton box or natron bag or PP/HDPE buckets with lid up to 150 g - PE or PP buckets with lid up to 150 g - cardboard or fibre-board boxes with PE or PP bag or liner up to 150 g - cardboard or fibre-board boxes up to 150 g - pre-filled or refillable tamper-resistant HDPE or polypropylene mouse or rat bait station. Bait stations packed in cardboard outer or plastic heat-sealed container or thermo seal foil up to 150 g 2. Bait in PP/paper film sachets, PET/PE film sachets, PE/paper film sachets or PE/aluminised film sachets (10 g - 150 g) packed in: - polyethylene (PE) or polypropylene (PP) or PE/PP or paper/PE outer sachet packed in cardboard or fibreboard outer pack up to 150g - PE or PP packs up to 150 g - HDPE container up to 150 g - Natron bag up to 150 g - Packs up to 150 g - PP woven sack or multi-ply paper sack up to 150 g - Pail (PP) or bucket (PP or PE) with lid up to 150 g - PP or PE tub up to 150 g - Prefilled or refillable tamper-resistant HDPE or PP mouse or rat bait station. Bait stations packed in carboard outer or plastic heat-sealed container or thermo seal foil up to 150 g

	- PET/PE, PP/PE or paper/PE pouch up to 150 g - Cardboard or fibre-board pack with PE or PP bag or liner up to 150 g - Cardboard or fibre-board box up to 150 g - sachet (PE or PE/PP or PP or paper/PE) packed in cardboard outer pack/carton box or natron bag or PP/HDPE buckets with lid up to 150 g 3. Other packaging: - loose bait in prefilled or refillable tamper-resistant mouse or rat bait station, packed in carboard outer or plastic heat-sealed container or thermo seal foil up to 150g - loose bait in tray (PVC or polystyrene or polypropylene or PET) with heat sealed lid (PET/polypropylene or PET/polyethylene or polypropylene) to be used with bait station up to 150 g

2.2 Physical, chemical and technical properties

The formulation change requested by the applicant to reduce the bromadiolone content of the product from 0.005 % to 0.0029 % is not considered to impact the physical chemical properties. The data considered for the original 0.005 % bromadiolone formulation composition are considered appropriate to support the 0.0029 % bromadiolone product.

As it is was agreed at March 2016 Working Group of the Biocidal Products Committee that new storage stability tests are necessary following formulation change to reduce the concentration of active substance in anticoagulant rodenticides, a new storage stability test was required during validation in order to check if the active substance remains stable after storage for the proposed shelf life. The applicant submitted a justification that existing data are sufficient to address the shelf life at lower concentration of the active substance. In line with the discussion at the Working Group – Analytical methods and Physical-Chemical Properties (APCP) to the Biocidal Products Committee in November 2018 on a possibility to bridge for shelf life data (from a chemistry view point) between PT14 products that only differ in active substance content, a scientifically sound justification was required since a read-across was applied. Due to the revised scientifically sound justification for bridging to previous product was received from the applicant, eCA finds bridging plausible and expects the stability of the product for two years at room temperature.
Accordingly, the conclusion on initial assessment on physical, chemical and technical properties remains valid.

2.3 Physical hazards and respective characteristics

Ratimor Plus Grain Bait has almost identical formulation as [redacted], differing only in lower concentration of active substance (from 50 ppm to 29 ppm), consequently not influencing the physical hazards and respective characteristics of the product.

No new data was provided, nor had new guidance to be taken into account for the major change evaluation.

Accordingly, the conclusion from the former assessment regarding physical hazards and respective characteristics remains valid.

2.4 Methods for detection and identification

In the initial authorisation the applicant provided a validated method capable of measuring the active substance in bait samples which can be used for their product analysis:

Approximately 10 g of the homogenised formulation is accurately weighed out into a 250 ml flask and 50 ml dichloromethane/methanol (20 vol %:80 vol %) is added along with 1 ml of formic acid. After sonication for 15 mins the sample solution was centrifuged at 8000 rpm for 10 mins. The supernatant was transferred into a 50 ml conical flask and 0.5 ml of the internal standard was added (1,3,5-triphenylbenzene). Final determination was by HPLC-UV (gradient elution on a C18 column). Quantification was achieved at 270 nm using external standards. Validation data supporting the method are outlined in the table below.

In this application, further considerations have been made as to whether these data remain appropriate, considering the reduction in the active content from 0.005 % to 0029 % w/w.

The applicant submitted partial validation of the method of analysis of bromadiolone, to prove that the method is suitable for the determination of bromadiolone in the product with lower concentration. Partial validation included only linearity study. For the linearity study, 24 injections were made e.g. duplicate injections of 11 reference standards and 1 blank. The concentration of reference standards was between 0.5 µg/mL and 20 µg/mL. The calibration line equation is $y = 0.0000317x-0.0176628$ with $r^2 = 0.9991$. The expected concentration of bromadiolone, in case 10 g of sample were prepared in the final volume of 50 mL, would be 5.8 µg/mL, which is within linearity range.

Analytical methods for the determination of bromadiolone in the product

Sample	Test Substance	Analytical method	Recovery fortification level (%w/w)	Recoveries (%)	Repeatability % RDS	Linearity	Specificity	Reference
[redacted]	bromadiolone	HPLC/MS/DAD	0.00375 0.005	99.1 96.4	1.67 (6)	5.04 – 15.12	Yes – retention time match	B4.1 Garofani,

[redacted]		UV detector	0.00625	99.6		µg/ml, r>0.99 (approx: 50 –150 % of nominal content) 5 standards over concentration range	with standard and no interference seen in chromatogram of blank formulation	2007b
Standard solution in DCM	bromadiolone	HPLC-PDA	Not needed	Not needed	Not needed	R^2 = 0.9991, 11 points in duplicate from 0.5 to 20 µg/mL	Not needed	Norris, 2019

New data were provided to prove linearity and limit of quantification.

The conclusion from the former assessment regarding methods for detection and identification remains valid, except for the limit of quantification and linearity. LOQ can be set to the lowest calibration point, e.g. 0.5 µg/mL.

The additional partial validation of linearity proved that the method for the determination of bromadiolone in the product, assessed in the CAR, is fit-for-purpose although the concentration of bromadiolone has decreased.

For the environmental matrices, the initial authorisation references the CAR for bromadiolone – these methods remain appropriate to support the product.

2.5 Efficacy against target organisms

Ratimor Plus Grain Bait is a ready-to-use cereal bait formulation for the control of mice, brown rats and roof rats indoor and outdoor around buildings. The product is intended for use by general public.

It functions as a second-generation ‘single-dose’ anticoagulant rodenticide. Anticoagulant rodenticides are vitamin K antagonists. They disrupt the normal blood clotting mechanisms resulting in increased bleeding tendency and, within a relatively short time frame (typically 2-4 days), profuse haemorrhage and death.

Palatability

As part of the initial authorisation, the applicant addressed the standard efficacy data requirements for the biocidal product containing 50 ppm bromadiolone. Palatability studies using *Mus musculus* and *Rattus norvegicus* were accepted showing overall 61.1 % and 50% palatability, respectively. The SI CA considers that these studies remain relevant as a reduction to 29 ppm active substance concentration is not likely to reduce the palatability of the product. It is agreed that when ≥ 20% palatability is

demonstrated in the initial authorisation of the product, only new field trials are required for the application for a major change.

During the initial authorisation it was sufficient to perform tests only with one species of rats to prove the efficacy of the biocidal product. Consequently, efficacy (palatability) data from studies with *R. norvegicus* are available.

Effectiveness

Efficacy of Ratimor Plus Grain Bait was confirmed in three field trials carried out in Italy in 2017 and conducted in-line with EPPO guideline PP 1/114(2) and Transitional Guidance on Efficacy Assessment for Product Type 14 Rodenticides, published in December 2016 by ECHA. Field tests were performed against wild populations of synanthropic rodents (*Mus musculus, Rattus norvegicus and Rattus rattus*) infesting agricultural warehouses and animal stables. In all three field trials complete control (100%) of the target populations was achieved, demonstrating the attractiveness and effectiveness of the bait product. It is concluded that the product, when used in accordance with label instructions, can provide effective control of the target organisms.

Data from the field trials are summarised in the annex.

The label reference to pulsed baiting must be removed from each of the general public users proposed labels in accordance with the BPC opinion. Label should state that the product should not be used for permanent or pulsed baiting for the general public use.

For the general public use, product is allowed to be used only indoor and outdoor around buildings and bait stations should be placed in areas not liable to flooding.

Occurrence of resistance

In areas where resistance is suspected, care should be taken with the selection of rodenticides. Where resistance has been confirmed, active substances to which the population is resistant should not be used.

The control of rodent populations should never rely upon the use of chemical control measures alone, and it is essential that an integrated pest management (IPM) programme is implemented.

In addition to the use of chemical control methods, an IPM programme against resistant rodents will include trapping, environmental and habitat modification (restriction of access to food, water and harbourage), and proofing, exclusion and restriction of movement.

2.6 Risk assessment for human health

For the risk assessment for human health we refer to the Product Assessment Report (PAR) of the initial authorisation that was done for grain bait formulation containing 0.005 % w/w bromadiolone. PAR was prepared by the UK eCA. No new studies have been performed for the major change application. Ratimor Plus Grain Bait is virtually identical to Ratimor Grain Bait product. The main difference between the two products is lower concentration of active substance – lowered concentration of bromadiolone from 50 ppm to 29 ppm for Ratimor Plus Grain Bait. For other constituents of the grain bait formulation the differences between formulations (50 ppm and 29 ppm formulations) are none or very small (the differences are intended to compensate for the reduced concentration of the active substance; please see confidential annex for further details). Therefore, the applicant proposed read-across to studies conducted with [redacted] baits containing bromadiolone for skin corrosion and irritation, eye irritation, respiratory tract irritation, respiratory sensitization (ADS) and acute toxicity (oral, inhalation, dermal). The eCA SI agrees that the studies submitted for the first authorisation and presented again below are still considered valid.

From the initial assessment regarding effects of the product on human health following exceptions were considered:

- CLP in accordance with the 9th ATP (Commission Regulation (EU) 2016/1179 of 19 July 2016) was applied to this major change.
- Dermal absorption has been re-evaluated in accordance with the Guidance on Dermal absorption (EFSA Journal 2012;10(4):2665). The dermal absorption value was raised from 0.36 % to 7 %. A revised human health exposure assessment has therefore been conducted.

2.6.1 Assessment of effects of the active substance on human health

As above.

2.6.2 Assessment of effects of the product on human health

2.6.2.1 Percutaneous absorption

No new data on the dermal absorption of the biocidal product have been submitted, but the applicant proposes to read across to the in vitro dermal absorption study (Toner F, 2008) that is available in the active substance dossier. Detailed results can be found in the final CAR.

Summary table of in vitro studies on dermal absorption					
Method, Guideline, GLP status, Reliability	**Species, Number of skin samples tested per dose, Other relevant information about the study**	**Test substance, Doses**	**Absorption data for each compartment and final absorption value**	**Remarks** *(e.g. major deviations)*	**Reference**
OECD Guideline 428, GLP: yes Reliability: 1	10 samples of human skin per dose, obtained from 5 different donors (female)	Test preparation 1: bait:saline (1:1, w/w), 0.0025 % bromadiolone Test preparation 2: wax block, 0.005 % bromadiolone	Test preparation 1: 0.36 % ± 0.30 % Test preparation 2: 0.04 % ± 0.04 %	/	Toner F (2008)

The applicant has provided the following justification to read across to dermal absorption data obtained in the Toner (2008) dermal absorption study assessed at Annex I inclusion of bromadiolone dossier, and to which [redacted] has access:

"A dermal absorption study was performed in vitro on human split-thickness skin (5 donors). The exposure time was 8h and monitoring was for a total of 24h (including 16h post exposure sampling). The rate and extent of absorption was investigated following topical application of [14C]-Bromadiolone incorporated into bait:saline (1:1, w/w) formulation (0.0025 % w/w bromadiolone) – *test preparation 1* and a representative wax block formulation (0.005 % w/w bromadiolone) – *test preparation 2*. Approximately 0.36 % were absorbed of the bait:saline formulation and 0.04% and were absorbed of the wax block formulation, respectively (calculated as dermal delivery, including tape strip 1 to 20). In the case of the bait:saline application, the block bait was ground to a powder and applied to the skin as a 1:1 bait:saline mix, to mimic the presence of the material on a sweating skin surface. This is an extreme worse case, which gives maximum contact of the active substance in the bait to the skin surface. This is a clear worst-case application, when compared to the standard non-dusty solid baits that are actually used. Therefore, we propose that these worst-case data are used in the exposure calculations for all formulated products."

Applicant has provided additional justification for read across: Tested wax blocks formulation, which was used for dermal absorption testing, contains more than 50% of grain raw material (in shape of cut wheat, rolled oats and whole wheat flour). Tested material was taken out of the middle, which was composed mostly from grain parts. Wax in blocks formulation or fats in pasta bait formulation improve the contact of bait with skin. Besides that, since active substance is lipophilic, wax or fats are better media for attracting/dissolving active substance. This way it is more possible the active substance diffuses on to the skin, than in case of grain or pellets, where 'hydrophilic barrier' between bait and skin is present. By 'hydrophilic barrier' it is meant the lower and limited solubility of bromadiolone in water,

that even decreases with lowering of pH. It is very unlikely the dermal absorption value is higher in grain bait or pellets, than in wax blocks or pasta bait.

Taking into account the difference in formulation types and concentrations of active substance, the applicant proposes that dermal absorption value of 0.36% obtained with the 0.0025% bromadiolone bait: saline formulation (Bromadiolone Test Preparation 1) will provide a worst-case dermal absorption value for the grain bait from human skin, and should therefore be taken forward to the human health risk assessment for the biocidal product.

eCA SI used EFSA Guidance on dermal absorption (EFSA Journal 2012;10(4):2665) for re-assessment of the Toner (2008) dermal absorption study. In section 6.2 of the guidance is a list of criteria that must be met for a formulation to be considered sufficiently similar to a reference formulation. In last paragraph is written that it is considered unlikely that the criteria will be met when moving from one formulation type to another. In Toner (2008) study Test preparation 1 was prepared in a way that bromadiolone (0.0025 %) was incorporated into bait:saline (1:1, w/w) formulation. No exact composition of wax bait block is provided in Toner (2008) study report, neither is clear the composition of material that was taken from the middle of the wax block for preparation of Test preparation 1. Co-formulant content is therefore unlikely to be within +/- 25 % w/w of that in the reference formulation as required under section 6.2. Because in this case the product is grain bait and the reference product is wax block / saline bait the eCA SI considers that the formulations are not sufficiently similar.

The default dermal absorption value should be used instead. A 4 % default value for grain formulations was agreed for second generation anticoagulant rodenticides on BPC TOX WG V 2016 meeting. This value was based on the available information for second generation anticoagulant rodenticides that contained 0.005 % of active substance. Since the active substance in Ratimor Plus Grain Bait product is more diluted (0.0029 %), a *pro-rata* calculation would be required, resulting in an adjusted refined value of 7 %.

2.6.2.2 Acute toxicity

The applicant has not submitted data on the acute oral and dermal toxicity for the biocidal product, but proposes to read-across to studies that were conducted with [redacted] product for the end-points of acute oral and dermal toxicity (studies were used at initial authorisation). The resulting conclusions remain the same as in the initial authorisation.

Summary table of animal studies on acute oral toxicity conducted with [redacted] (containing 0.005% bromadiolone) (Doc IIB-4 of PAR [redacted]).

Route	Method, Guideline	Species, strain, sex, No./Group	Dose levels Duration of exposure	Values LD_{50}/LC_{50}	Remarks	Reference
Oral	OECD 420 Method B1 GLP	Rat (Sprague-Dawley CD (Crl:CD® (SD) IGS BR) 5 female animals treated	2000 mg/kg, Single dose	Females: estimated to be > 2000 mg/kg bodyweight	No deaths. No signs of systemic toxicity. Expected gains in bodyweight over the study period. No abnormalities noted at necropsy.	B6.1.1 Bradshaw, 2008a
Dermal	OECD 402 Method B3 GLP	Rat (Sprague-Dawley CD (Crl:CD® (SD) IGS BR) 5 male and 5 female animals treated	2000 mg/kg, 24 hours	Males and Females: > 2000 mg/kg bodyweight	No deaths. No signs of systemic toxicity. No signs of dermal irritation. Expected gains in bodyweight over the study period. No abnormalities noted at necropsy.	B6.1.2 Bradshaw, 2008b

Specific acute toxicity studies on the biocidal product [redacted] showed the acute oral toxicity to be > 2000 mg/kg bw and the acute dermal toxicity to be > 2000 mg/kg be to the rat. On the basis of these studies and a consideration of data supplied for the active substance in the Annex I dossier, the eCA SI considers that the biocidal product Ratimor Plus Grain Bait has a low acute toxicity by oral and dermal routes. No classification of the product according to CLP for these end-points is required.

For the end-point of acute inhalation toxicity no product data has been provided. eCA SI agrees with the decision made by UK CA at initial authorisation of the product. The acute inhalation toxicity of the biocidal product can be extrapolated from data obtained for the active substance in document IIA of the Annex I dossier. The LC_{50} in rat is 0.43 µg/l. The LC_{50} for the product is expected to be larger than 5 mg/l . No classification of the product according to CLP for inhalation toxicity is required.

2.6.2.3 Irritation and corrosivity

The applicant has not submitted data on the skin and eye irritation/corrosivity. As in initial authorisation the applicant proposes to read -across to studies that were conducted with [redacted] product for

the end-points of skin and eye irritation. The resulting conclusions remain the same as in the original authorisation.

Summary table of animal studies on skin irritation conducted with [redacted] (containing 0.005% bromadiolone) (Doc IIB-4 of PAR [redacted]).

Species	Method (Test formulation)	Average score		Reversibility	Result	Remark	Reference
		24, 48, 72 h		(yes/no)			
		Erythema	Oedema				
Rabbit	OECD 404 Method B4 GLP	0.45 (0.67-0.67-0)	0 (0-0-0)	Yes	Slightly irritating	Not classified for irritation or corrosivity	B6.2.1 Bradshaw, 2007

Summary table of animal studies on skin irritation conducted with [redacted] (containing 0.005 % bromadiolone) (Doc IIB-4 of PAR [redacted]).

Species	Method	Average Score					Reversibility Yes/No	Result	Reference
		Cornea	Iris	Conjunctiva					
				Discharge	Redness	Chemosis			
Rabbit	OECD 405 Method B5 GLP	0 (0-0-0)	0 (0-0-0)	0.3 (1-0-0)	0.3 (1-0-0)	0 (0-0-0)	Yes, within 2 days	Minimal irritant Not classified for irritation	B6.2 (2) Bradshaw, 2008c

On the basis of these studies and considering of data supplied for the active substance in the Annex I dossier, the eCA considers that the biocidal product Ratimor Plus Grain Bait is not irritating to the skin or eyes. No classification of the product according to CLP for these end-points is required.

No specific study has been performed to address potential respiratory irritation. Inhalational exposure of the product is considered negligible for non-professionals, because bait is packed in small bags or sachets and non-professional users will not decant the product, therefore dusting and inhalation of the product is considered negligible. The product contains denatonium benzoate and triethanolamine that are potential substances of concern, but these substances are not present in a biocidal product at sufficient concentrations to trigger a human health classification, and are not considered further in the human health risk assessment. There are no other substances classified as irritants or respiratory irritants.

2.6.2.4 Sensitisation

The applicant has not submitted the data on skin and respiratory sensitisation of the biocidal product. Studies on the active substance have not identified any indication of sensitizing properties and no other

ingredients of the product are expected to cause skin sensitization. In the Ratimor Plus Grain Bait is present co-formulant 1,2-benzisothiazoli-3-one which is classified as Skin Sensitiser Category 1 at a concentration over one tenth of its specific concentration limit (see confidential annex for details). It can elicit the response in individuals who are already sensitised to this co-formulant. According to CLP the label on packaging shall bear the following statement: “EUH208 – Contains 1, 2- benzisothiazolin-3-one. May produce an allergic reaction.”

No specific studies have been performed to address potential respiratory sensitisation. Inhalational exposure to the product is considered negligible. The product does not contain any substances classified as respiratory sensitizers. No classification in accordance with CLP is required.

2.6.2.5 Other

No other tests to reveal the toxicological properties of the biocidal product are necessary.

2.6.3 Exposure assessment

This application is for major change to Ratimor Plus Grain Bait with a decrease of the active substance content from 50 ppm to 29 ppm (0.0029 % w/w).
Ratimor Plus Grain Bait is a ready-to-use bait (in sachets for loose bait) to be used in tamper-resistant bait stations containing 0.0029 % w/w bromadiolone for use to control mice and rats indoors, and rats outdoors around buildings.

The number and timing of application is summarised below.
1. For mice control, the recommended dose is up to 40 g of bait every 2 - 5 meters.
2. For rat control, the recommended dose is up to 200 g of bait every 5 – 10 meters.

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

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

List of scenarios

Summary table: scenarios			
Scenario number	**Scenario** (e.g. mixing/ loading)	**Primary or secondary exposure** **Description of scenario**	**Exposed group**
1.	Loading and placing bait boxes	Primary exposure: Loading of grain bait in sachets and placing bait boxes	Non-Professionals
2.	Cleaning of bait boxes	Primary exposure: Clean-up and emptying of loaded bait stations	Non-Professionals
3.	Oral ingestion of bait	Secondary exposure: Toddler transient mouthing of bait	General public

Non-professional exposure

Description of Scenario 1: Loading of grain bait in sachets and placing bait boxes		
The product is supplied in bags/sachets/trays with maximum weight of 150 g and not as loose bait. The 200 g of the product is loaded per station using 10 g sachets. There is no specific exposure data available for grain bait in sachets therefore the indicative exposure values for loose grain bait are used. The loose grain bait data is considered to represent a worst case comparing to grain bait in sachets. According to the HEEG opinion 10 (Harmonising the number of manipulations in the assessment of rodenticides (anticoagulants)) the maximum number of manipulations is 5 for loading and 5 for clean-up. Due to the non-linearity of the data from the CEFIC study, the indicative exposures per manipulation are higher for 1-4 manipulations than for 5 or more. Whilst the total exposure for 5 cleaning operations is similar to that for 4 cleaning operations, the total exposure for 4 loading operations is higher than that for 5 loading operations. Consequently, as a precautionary measure for this evaluation higher indicative values for loading 4 manipulations are considered for the exposure estimation. The indicative exposure during loading of bait boxes is 3.57 mg b.p per loading manipulation.		
	Parameters	Value
Tier 1	Adult body weight	60 kg
	Concentration of active substance	0.0029 % w/w
	Dermal penetration	7 %
	Dermal exposure (indicative 75th percentile for 4 manipulations) (HEEG Opinion 12)	3.57 mg b.p. / manipulation
	Number of loading bait stations per day and person (application phase) ((HEEG Opinion 10)	5
	Dermal exposure to the product	3.57 mg b.p/manipulation x 5 =17.85 mg of product/person/day

Calculations for Scenario 1

Summary table: systemic exposure from non-professional uses					
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake**	**Estimated dermal uptake (mg/kg bw/d)**	**Estimated oral uptake**	**Estimated total uptake (mg/kg bw/d)**
Scenario 1	1 (no PPE)	-	6.04×10^{-7}	-	6.04×10^{-7}

Description of Scenario 2: Clean-up and emptying of loaded bait stations		
Post-application a non-professional user may be required to clean-up and empty partly loaded bait stations into a bucket. Dermal exposure is likely to be limited to the hands only when emptying loaded bait stations into a bucket. Inhalation exposure during clean-up/disposal of grain bait is not expected. According to the HEEG opinion 10 (Harmonising the number of manipulations in the assessment of rodenticides (anticoagulants)) the maximum number of manipulations is 5 for clean-up. Due to the non-linearity of the data from the CEFIC study, the indicative exposures per manipulation are higher for 1-4 manipulations than for 5 or more. Whilst the total exposure for 5 cleaning operations is similar to that for 4 cleaning operations, the total exposure for 4 loading operations is higher than that for 5 loading operations. Consequently, as a precautionary measure for this evaluation higher indicative values for loading 4 manipulations are considered for the exposure estimation. The indicative exposure during clean-up/emptying of bait boxes is 4.52 mg b.p per cleaning manipulation.		
	Parameters	Value
Tier 1	Adult body weight	60 kg
	Concentration of active substance	0.0029 % w/w
	Dermal penetration	7 %
	Dermal exposure (indicative 75th percentile for 4 manipulations) (HEEG Opinion 12)	4.52 mg b.p/manipulation
	Number of loading bait stations per day and person (application phase) ((HEEG Opinion 10)	5
	Dermal exposure to the product	4.52 mg b.p/manipulation x 5 = 22.6 mg of product/person/day

Calculations for Scenario 2

Summary table: systemic exposure from non-professional uses					
Exposure scenario	**Tier/PPE**	**Estimated inhalation uptake**	**Estimated dermal uptake (mg/kg bw/d)**	**Estimated oral uptake**	**Estimated total uptake (mg/kg bw/d)**
Scenario 2	1 (no PPE)	-	7.65×10^{-7}	-	7.65×10^{-7}

Combined scenarios

Summary table: combined systemic exposure from non-professional uses				
Scenarios combined	**Estimated inhalation uptake**	**Estimated dermal uptake (mg/kg bw/d)**	**Estimated oral uptake**	**Estimated total uptake (mg/kg bw/d)**

Scenarios 1: Loading of grain bait in sachets and placing bait boxes (no PPE)	-	6.04×10^{-7}	-	1.37×10^{-6}
Scenarios 2: Clean-up and emptying of loaded bait stations (no PPE)	-	7.65×10^{-7}	-	

Exposure of the general public

Description of Scenario 3: Secondary exposure of a toddler transient mouthing of bait		
The worst case scenario for secondary exposure to rodenticide baits is the ingestion of the formulation by infants/toddler. The likelihood of this is reduced by the positioning of the bait in stations and boxes which have been designed to prevent access to the contents. The formulation also contains a human aversive agent that in some cases may help to prevent infants chewing and ingesting bait. However, instances of exposure could occur. The TNsG and the User Guidance indicate that an estimate of exposure can be made by assuming that either 10mg (TNsG 2002, part 2, p.58) or 5 g (TNsG User Guidance, version 1, p 73) of bait is swallowed by a 10 kg toddler. It should be noted that the TNsG User Guidance states that there is a risk of ingestion "if no bait box is used". Exposure can be calculated as follows, assuming 100% oral absorption:		
	Parameters[1]	Value
Tier 1	Toddler body weight	10 kg
	Concentration of active substance in b.p.	0.0029 % w/w
	Oral absorption	100 %
	Amount of bait ingested by toddler (considering no presence of bittering agent)	5 g

Scenario 3: The dose of bromadiolone an infant is expected to receive from the transient mouthing of bait (User guidance, assuming bittering effect of taste deterrent) is based on ingesting 10 mg of bait and is 2.9×10^{-5} mg/kg bw (10 mg x 0.000029 ÷10 kg).

Combined scenarios

There are no combined scenarios foreseen for the general public.

Dietary exposure

Not applicable.

2.6.4 Risk characterisation for human health

2.6.4.1 Risk for professional users

Not applicable.

2.6.4.2 Risk for non-professional users

For the calculation of risk to non-professional users, the AEL_{acute} of bromadiolone was used. According to the Annex I CAR for bromadiolone the derivation of an acceptable level of exposure value for single use (AEL_{acute}) is based on the teratogenicity study in rabbits. AEL_{acute} of 2.3×10^{-6} mg/kg bw/day is based on the maternal LOAEL from a teratogenicity study in rabbits of 2 µg/kg bw/d, using safety factor of 600 and with correction of 70% for oral absorption.

Risk for non-professional users from the different scenarios can be found in the following tables.

Systemic effects

Task/Scenario	Tier	AEL mg/kg bw/d	Estimated uptake mg/kg bw/d	Estimated uptake/ AEL (%)	Acceptable (yes/no)
Scenario 1: Loading of grain bait in sachets and placing bait boxes	1 (no PEE)	2.3×10^{-6}	6.04×10^{-7}	26.3 %	yes
Scenario 2: Clean-up and emptying of loaded bait stations	1 (no PEE)	2.3×10^{-6}	7.65×10^{-7}	33.2 %	yes

Combined scenarios

Task/Scenario	Tier	AEL mg/kg bw/d	Estimated uptake mg/kg bw/d	Estimated uptake/ AEL (%)	Acceptable (yes/no)
Scenario 1 + 2: Loading of grain bait in sachets and placing bait boxes + clean-up and emptying of loaded bait stations	1 (no PEE)	2.3×10^{-6}	1.37×10^{-6}	59.5 %	yes

Local effects

The product Ratimor Plus Grain Bait does not have any local effects. A risk assessment for local effects is not considered relevant.

In the Ratimor Plus Grain Bait co-formulant 1,2-benzisothiazoli-3-one is present which is classified as Skin Sensitiser Category 1, with specific concentration limit 0.05 % (see confidential annex for details). At a concentration over one tenth of its specific concentration limit it can elicit the response in individuals who are already sensitised to this co-formulant. According to CLP the label shall bear the following statement: “EUH208 – Contains 1, 2- benzisothiazolin-3-one. May produce an allergic reaction.”

Conclusion

The calculation presented above shows that the risk for non-professional user is within the acceptable limit without use of PPE.

2.6.4.3 Risk for the general public

Systemic effects

Task/Scenario	Tier	AEL mg/kg bw/d	Estimated uptake mg/kg bw/d	Estimated uptake/ AEL (%)	Acceptable (yes/no)
Scenario 3: Loading of grain bait in sachets and placing bait boxes	1 (no PEE)	2.3×10^{-6}	2.9×10^{-5}	1261 %	no

Conclusion

The secondary exposure of a toddler was estimated for transient mouthing of grain bait. The estimated exposure is predicted to result in systemic exposure over 100 % of the AEL of bromadiolone and therefore there is a potential risk for general public. However, the design of the rat bait boxes will incorporate a tamper-proof seal system to prevent easy access to internal compartments. As a result of

incorporating a tamper proof seal system infants are not expected to be able to gain access to the rodenticides and subsequent mouthing scenarios are deemed unlikely.
To mitigate the risk of secondary human exposure the product has to be labelled with additionally phrases:

- “Place product out of the reach of children, birds, pets, farm animals and other non-target animals.”
- “Where possible, bait stations must be fixed to the ground or other structures.”
- "Store locked up."

2.6.4.4 Risk for consumers via residues in food

Exposure to Ratimor Plus Grain Bait via residues in food is not considered to be relevant.

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

The biocidal product does not contain other substances in quantities that would be of toxicological concern in the production formulation.

2.6.5 Risk assessment for animal health

Neither new data were provided, nor a new guidance to be taken into account for re-assessment of effects on animal health. Accordingly, the conclusion from the former assessment regarding animal health remains valid.

The product is formulated as grain bait that has to be placed into bait boxes where exposure of non-target animals can be prevented. Product label also indicates that the product may be applied only at places where children and domestic animals have no access to the placed bait. These measures ensure that risk for non-target animals will be appropriately controlled. For further consideration of effects on non-target animals, see the following section on the risk assessment for the environment.

2.7 Risk assessment for the environment

SI CA: The following section has been submitted by the applicant and reviewed by the SI CA. The applicants’ assessment was found to be acceptable, and any comments made by the SI CA have been added to each section in the green boxes to differentiate from the applicant's submission.

SI CA: The following scenario is similar to the one assessed in the PAR (UK CA, 2012) where products are used in bait stations in and around buildings. However, according to the conservative worst-case

scenario in the PAR (UK CA, 2012), 29 mg rather than 50 mg bromadiolone/kg product is assumed. Since an acceptable risk assessment was shown for the baiting rates higher than those proposed here, the SI CA considers it appropriate to simply reference the existing PAR (UK CA, 2012) assessments. Effectively the SI CA proposes to use the acceptable risk envelope set in the CAR assessment to address the risk posed by the lower application rates requested for these specific uses of this product without further detailed consideration of the applicant's submission.

The change in active substance concentration from 0.005% to 0.0029% w/w will result in a lower environmental exposure. Therefore the exposure assessment carried out in 2013 is still valid. Regarding groundwater, the recent CG decision requires this now be assessed:

Groundwater assessment for rodenticides

As required by Article 31(3) of the BPR and Article 2(1)(f) of Regulation 492/2014, when carrying out their assessment of whether the conclusions of the first authorisation regarding Article 19(1)(iv) remain valid, applicants will have to address the groundwater assessment. Since no new guidance was agreed in the past that could become applicable at the time of the completion of the applications for renewal by 28/02/2017, the guidance of reference are the existing methods that are applied since years as standard tools for the assessment of active substances:

- Tier I according to Vol. IV Part B (the former TGD), as provided in chapter 2.3.8.6 of this guidance document.

- Tier II using the FOCUS models PEARL or PELMO for refinements in case Tier I would lead to an exceedance of the relevant trigger values.

The previous exposure assessment contained a Tier 1 assessment of groundwater PECs. The following is an extract from the report:

Exposure of groundwater may occur as a result of soil exposure which occurs via residues present in sewage sludge after using the product in sewers and via direct (spillages) and disperse release (urine and faeces) after the use of the product in and around buildings. As an indication for potential groundwater levels, the concentration in soil pore-water in the various scenarios was examined. The calculated values do not exceed the EU trigger value of 0.1 µg/L.

<u>In and around building scenario</u>

The worst case application is for the rat. Bait points for rats are set 5 – 10 m apart with 10 bait points per farm containing 200g bait per bait point. The bait stations are regularly inspected, re-filled, and dead rodents are removed. In the ESD worst case scenario 10 bait stations 5 m apart around a farm building are used, each filled with 250 g of wax blocks, and it is assumed that the rodenticide campaign will last for 21 days. It is also assumed that all of the bait is replenished 5 times. In the so-called typical scenario the replenishment is done only 1.5 times. The scenario presented by the applicant differs from the ESD worst case scenario only regarding the amount of bait in each station, i.e. 200 g instead of 250 g, and the other parameters are considered as equal to the worst case scenario.

In the ESD it is estimated that the total direct release to the environment is 1 %, which gives a direct release of (10*250*5*0.01)/21= 6 g product/day averaged over 21 days (worst case). In the normal use

scenario according to CEFIC (2002) it is assumed that not all of the bait is eaten, that the bait is supposed to have been refilled 1.5 times and that the direct release would be 1.8 g product / day at average.

According to the ESD the terrestrial environment is exposed via direct release at application and indirect release from the target animals' urine and faeces. The fraction released to soil has been calculated (Ref.: [redacted]) as 0.73. Since the toxicity of possible metabolites is unknown they will be assumed to be of similar toxicity as bromadiolone.

Local direct emission to soil of the active substance is calculated by considering the total amount of the product used and the fraction of active substance in product, the number of application sites and refilling times and the fraction of the product released directly to soil. This is calculated according to following equation in the ESD.

$C\ local_{soil\text{-}D} = E\ local_{soil\text{-}D\text{-}campaign} * 1000 / (Area_{exposed\text{-}D} * Depth_{soil} * RHO_{soil} * N_{sites})$

The local concentration in soil was calculated by dividing the local direct emission with the soil volume assumed to be polluted by the direct release, according to the ESD. The soil volume as-sumed to be directly exposed is 0.009 m^3. The weight of wet soil according to TGD is 1700 kg / m^3. The weight of the polluted soil around each bait box will according to these calculations be 153 kg.

The local concentration in soil due to indirect release was calculated according to following equation in the ESD. A calculation of the worst-case soil concentrations with the assumptions made above would then give;

$Clocal_{soil\text{-}ID}=(Q_{prod}*Fc_{prod}*N_{sites}*N_{refill}*10^3*F_{release\text{-}ID,soil}*(1-F_{release\text{-}D,soil}))/Area_{exposed\text{-}ID}*Depth_{soil}*RHO_{soil}$

Total soil concentrations around the bait boxes are the sum of the soil concentrations caused by direct and indirect pollution of the soil. The majority of the soil around the buildings will have a concentration equal to the concentration caused by indirect release:

$Clocal_{soil} = Clocal_{soil\text{-}D} + Clocal_{soil\text{-}ID}$

PEC groundwater was calculated according to equation 67 in TGD II, where it is assumed that PEC local groundwater equals to PEC local pore water in agricultural soils. The concentration in the soil pore waters is determined by the predicted bromadiolone concentration in local soil, the bulk density of the soil and the soil-water partitioning coefficient.

$PEClocal_{soil,\ porewater} = PEClocal_{soil} * RHO_{soil} / (k_{soil\text{-}water}*1000)$

An average Koc value of 14770 ml/g was used in the calculations for derivation of $k_{soil\text{-}water}$. However, due to the limited use of bromadiolone in campaigns that last for a limited time, usually three weeks, and that good management practice prescribes that both leftover feed and dead rodents are collected and disposed of in a secure way, the exposure to groundwater is likely to be negligible.

Scenario	***In and around buildings***		
	Worst case	***Worst case (applicant)***	***Realistic***
$Clocal_{soil\text{-}D}$ (mg/kg)	***0.0237***	***0.0190***	***0.0057***
$Clocal_{soil\text{-}ID}$ (mg/kg)	***0.0028***	***0.0022***	***0.0007***
$Clocal_{soil\text{-}total}$ (mg/kg)	***0.0265***	***0.0212***	***0.0064***
PEC groundwater (ng/l)	*101.6*	*81.3*	*24.4*

As the major change will lead to a lower PEC_{gw} a new assessment is not necessary here.

Primary and Secondary Poisoning

SI CA: The calculations of PEC/PNEC ratios for primary and secondary poisoning below have not been checked by the SI CA. The approaches used are in line with those in the CAR, however the following

calculations provided by the applicant are for primary poisoning, Tier 2 not relevant: PECoral/PNECoral for acute assessment and ECoral calculated from ETE (Step 1) for long-term assessment. As result of the EU assessment concern was raised regarding the primary and secondary risk to birds and mammals. On the basis of the similarity in approaches no further work regarding the above calculations and associated PEC are considered necessary. The risk of primary and secondary poisoning is common to all second-generation anticoagulant rodenticides and as a result the issue of mitigation is being considered as a generic issue both at the SI and EU level. The SI assessment of the primary and secondary poisoning can be found in section "Discussion on risks of primary and secondary poisoning in comparison to monitoring data and proposal for risk mitigation measures" of this PAR.

The concentration in the final product is 0.0029% w/w for the active substance bromadiolone. The assessments were carried out according to the ESD PT14 (CA-Jun03-Doc.8.2-PT14 and the TGD (2003). It involves tiered approaches for assessing the risks through both primary and secondary poisoning.

Primary Poisoning

In the first tier scenario, the risk is characterised by the ratio between PEC_{oral} and $PNEC_{oral}$. The ratios PEC/PNEC are above 1 for both short and long term exposure. This indicates a potential risk, which must be refined.

	PEC (conc. in food, mg/kg)	**PNEC (conc. in food)**	**PEC/PNEC**
Long-term			
Birds	29	0.0087 mg/L	3340
Mammals	29	0.00019 mg/kg	153000

Acute risk assessment for primary poisoning of a non-target organism:

Tier 2:

In the refined risk assessment the daily uptake (ETE) is compared to the PNEC for birds and mammals. The PNEC values for each representative animal are compared with the ETE values to provide an indication of the risk to non-target animals ingesting a daily dose of the product.

Non-target animal	**Typical bodyweight (g)**	**Daily mean food intake (g dw/day)**	**Concentration of bromadiolone in bait (mg/kg)**	**ETE (mg/kg bw)**	
				Step 1	**Step 2**
Dog	10 000[a]	456[b]	29	1.32	0.95
Pig	80 000[a]	600[a]	29	0.22	0.16
Pig, young	25 000[a]	600[a]	29	0.70	0.50
Tree sparrow	22[a]	7.6[a]	29	10.02	7.21
Chaffinch	21.4[a]	6.42[a]	29	8.7	6.3
Wood pigeon	490[a]	53.1[a]	29	3.14	2.26
Pheasant	953[a]	102.7[a]	29	3.12	2.25

[a] According to table 3.1 in the ESD
[b] Calculated from log FIR=0.822 log BW-0.629 according to equation on page 50 ESD

Non-target animal	PECoral = ETE, concentration of bromadiolone after one meal (mg/kg)		LD50 (mg/kg bw/d)	PECoral higher than LD50 (y/n)	
	Step 1	Step 2		Step 1	Step 2
Dog	1.32	0.95	10	n	n
Pig	0.22	0.16	3	n	n
Pig, young	0.70	0.50	3	n	n
Tree sparrow	10.02	7.21	134	n	n
Chaffinch	8.7	6.3	134	n	n
Wood pigeon	3.14	2.26	134	n	n
Pheasant	3.12	2.25	134	n	n

Tier 2 acute risk assessment: $PEC_{oral}/PNEC_{oral}$ for non-target animals accidentally exposed to bait containing bromadiolone after one meal

Non-target animals	ETE, concentration of bromadiolone after one meal (one day) (mg/kg b.w.)		$PNEC_{oral}$ (dose, mg/kg b.w./d)	PEC/PNEC	
	Step 1	Step 2		Step 1	Step 2
Dog	1.32	0.95	0.0000056	236000	170000
Pig	0.22	0.16	0.0000056	39000	29000
Pig, young	0.70	0.50	0.0000056	125000	89000
Tree sparrow	10.02	7.21	0.0013	7700	5600
Chaffinch	8.7	6.3	0.0013	7000	5000
Wood pigeon	3.14	2.26	0.0013	2400	1700
Pheasant	3.12	2.25	0.0013	2400	1700

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

Long-risk assessment for primary poisoning of a non-target organism:

Tier 2:

In the long-term risk assessment, the EC (expected concentration of active substance in the animal) after metabolism and other elimination is calculated and used to calculate the $EC_{oral/}PNEC_{ratio}$after 1-day and 5-day elimination of Brodifacoum. The $EC_{oral/}PNEC_{ratio}$ are above 1 after 1-day elimination of Brodifacoum indicating a potential risk (data not shown). The $EC_{oral/}PNEC_{ratio}$ for the 5-day elimination of Brodifacoum are shown below.

Tier 2 long-term risk assessment: $EC_{oral}/PNEC_{oral}$ ratio after 5-day elimination

Non-target animals	EC_{oral} AV = 1, PT = 1 (mg/kg bw)	EC_{oral} AV = 0.9, PT = 0.8 (mg/kg bw)	$PNEC_{oral}$ (mg/kg bw/day)	Ratio $EC_{oral}/PNEC_{oral}$
Dog	0.92	0.67	0.0000056	119000
Pig	0.15	0.11	0.0000056	19600
Pig, young	0.49	0.35	0.0000056	62600
Tree sparrow	7.01	5.05	0.0013	4000
Chaffinch	6.1	4.4	0.0013	3400
Wood pigeon	2.2	1.6	0.0013	1200
Pheasant	2.2	1.6	0.0013	1200

[a] calculation according to equation 21 in the ESD; 30% of a.s. is eliminated

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

Conclusion:

Overall, all acute and long-term $PEC_{oral}/PNEC_{oral}$ ratios are still above the trigger value of 1 indicating acute and long-term unacceptable risks.

Secondary Poisoning

A Tier 1 risk assessment was carried out to assess the risk for poisoning of non-target predator birds and mammals during acute and long-term exposure via rodents poisoned. The $PEC_{oral}/PNEC_{oral}$ values exceeded the trigger value of 1 (data not shown). Therefore, a refined tier 2 assessment was carried out, based on representative species. The refined tier 2 risk assessment considers exposure of relevant species of predators, based on their bodyweights and food intakes. The bromadiolone concentrations in non-target mammals and birds consuming contaminated rodents is calculated ($ETE_{oral\ predators}$) and compared to the $PNEC_{oral}$

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

Species	Exposure	$ETE_{oral\ predators}$ (mg a.s./kg/d)	$PNEC_{oral}$ (mg a.s./kg/d)	Ratio $ETE_{oral\ predators}$ / $PNEC_{oral}$
Barn owl (*Tyto alba*)	Day 5 before the last meal	0.638	0.0013	490
	Day 5 after the last meal	1.000		770
	Day 14 after the last meal	1.19		915
Kestrel (*Falco tinnunculus*)	Day 5 before the last meal	0.970	0.0013	750
	Day 5 after the last meal	1.51		1160
	Day 14 after the last meal	1.81		1400

Species	Exposure	ETE $_{oral\ predators}$ (mg a.s./kg/d)	PNEC$_{oral}$ (mg a.s./kg/d)	Ratio ETE $_{oral\ predators}$ / PNEC$_{oral}$
Little owl (*Athene noctua*)	Day 5 before the last meal	0.729	0.0013	560
	Day 5 after the last meal	1.14		880
	Day 14 after the last meal	1.36		1050
Tawny owl (*Strix aluco*)	Day 5 before the last meal	0.586	0.0013	450
	Day 5 after the last meal	0.916		705
	Day 14 after the last meal	1.09		840
Fox (*Vulpes vulpes*)	Day 5 before the last meal	0.235	0.0000056	42000
	Day 5 after the last meal	0.366		65000
	Day 14 after the last meal	0.438		78000
Polecat (*Mustela putorius*)	Day 5 before the last meal	0.488	0.0000056	87000
	Day 5 after the last meal	0.763		136000
	Day 14 after the last meal	0.920		164000
Stoat (*Mustela erminea*)	Day 5 before the last meal	0.698	0.0000056	125000
	Day 5 after the last meal	1.09		195000
	Day 14 after the last meal	1.30		232000
Weasel (*Mustela nivalis*)	Day 5 before the last meal	1.00	0.0000056	179000
	Day 5 after the last meal	1.58		282000
	Day 14 after the last meal	1.88		336000

All ratios ETE$_{oral\ predators}$ / PNEC$_{oral}$ are above the trigger value of 1 indicating an unacceptable risk of secondary poisoning.

Calculations based on monitoring data

Monitoring data for Barn owls (Newton et al, 1997) provides a basis for calculations to determine what relevance the worst case calculations above, which indicate large implications on non-target bird and mammal populations, may have in the environment. The data based on 1100 collected birds shows that 30 % of the birds collected the recent decades have residues of second generation rodenticides. It also shows that cca. 1 % of the collected birds had died of rodenticide poisoning (Table 5.3.10). We do not know if all birds killed by rodenticides were retrieved or how the more detailed picture for each year looks.

Table 5.3.10 Rodenticide residues in livers of Barn owls killed by rodenticides (from Newton et al, 1997)

Owl no.	Rodenticide	Rodenticide concentration (mg/kg liver)
1	Bromadiolone	0.13

2	Bromadiolone Brodifacoum Flocoumafen	0.05 0.002 0.003
3	Difenacoum	0.17
4	Bromadiolone	1.07
5	Brodifacoum	0.87
6	Bromadiolone Brodifacoum	1.72 0.07
7	Bromadiolone	0.33
8	Brodifacoum	0.42

To assess the lethal dose the report by Ramell et al, (1984) submitted by the applicant (IIIA 7.5.7.1.1) is also considered. In this study brodifacoum was used to eradicate rabbits in the field. After the treatment dead rabbits, cats and birds of different species were collected and the concentrations of rodenticides in their bodies and livers were measured. Among the collected birds were two hawks which had died by secondary poisoning and the concentration in their livers was 0.12 and 0.34 mg/kg. Another study submitted by the applicant (IIIB 7.8.7.1-02) showed that a concentration of approximately 0.6-1.25 mg/kg liver killed owls in an acute study after consumption of mice which had consumed brodifacoum. Using this data, it may be concluded that the lowest lethal dose of bromadiolone is 0.13 mg/kg liver for Barn owls, and if liver concentrations were kept below this level all of the barn owls in the study by Newton et al. (1997) would probably have been protected with the exception for owl number two, but the liver of this owl also contained two other, more potent anticoagulants.

What is then the maximum body concentration of rodenticide in a rat in order to avoid that the rodenticide concentration in the predatory bird's liver reaches 0.13 mg/kg? First of all it is assumed that the liver constitutes about 4 % of the total body weight which then for a Barn owl is 0.04*0.294 kg = 0.012 kg liver. According to the ESD, a campaign lasts for 21 days and the daily feed intake (DFI) of the owl is 0.075 kg.

The lowest amount of rodenticide in the liver which will cause lethality is equal to the liver weight multiplied by the lowest lethal concentration in liver; 0.012 kg * 0.13 mg/kg = 0.00156 mg. Thus, the lowest total amount of bromadiolone that will cause lethality in a Barn owl, if reaching the liver, is 0.00156 mg or 1.56 µg.

To determine the maximum daily bromadiolone consumption during a campaign that may be lethal for a barn owl, the lowest lethal bromadiolone amount is divided by the number of days for a normal treatment period, i.e. 0.00156 mg/21 days = 0.000074 mg/d. Thus, less than 0.074 µg bromadiolone may be consumed daily during the campaign.

The limit concentration in rats is then calculated as the maximum daily consumption divided by the body weight of rat consumed each day, i.e. 0.074 µg/0.075 kg = 0.99 µg kg bw. Thus, 0.99 µg/kg bw is the maximum bromadiolone concentration in rats that would not cause lethality according to monitoring data. This value must not directly be compared to a PNEC value, since it does not have any safety component (assessment factor) to account for uncertainties regarding other effects than lethality and variations in sensitivity between different individuals.

Bearing this in mind, if this effect value is compared to the PEC in rats of 13.9 mg/kg bw, which is worst case according to the ESD, a risk for secondary poisoning of barn owls is identified with a risk quotient calculated as 13.9/(0.99*10-3)= 14000.
This assessment could be refined further since the monitoring data reveals that 30 % of the population is affected by rodenticides and consequently, the PD+PF could be assumed to be 0.3. However, these figures seems to be increasing and therefore it is assumed that PD+PF = 0.5. After such refinement the risk quotient would be halved, i.e. $6.95/(0.99*10^{-3}) = 7000$. The data used for these calculations is mainly based on five individuals and therefore it might be necessary to apply assessment factors for intraspecies variations. Moreover, it could be argued that barn owl may not be the most sensitive species and that an assessment factor also for variation between species would be needed.
In conclusion, this example based on monitoring data confirms that there is a very high risk of secondary poisoning for predatory birds and mammals, and the risk quotient obtained this way even exceeds the high PEC/PNEC ratios obtained from the tier 2 calculations based on the ESD worst case. This is notable and a more thorough investigation into monitoring data and comparison with modelled data should be carried out in conjunction with the future comparative assessment of second generation rodenticides.

Discussion on risks of primary and secondary poisoning in comparison to monitoring data and proposal for risk mitigation measures

According to the calculations in accordance with the ESD and TGD II, the biocidal product with bromadiolone will cause unacceptable risks both for acute and long-term exposure and both for primary and secondary poisoning. The very high risk quotients indicate that birds and mammals that have rodents as prey or feed on carcasses of rodents are significantly threatened by the use of bromadiolone and probably also by other second generation anticoagulant rodenticides. A study that demonstrates this is that of Balcomb (1986) in which 62-92% of small birds put dead in agricultural fields had disappeared within 24 h.
It may be argued that these rodenticides have been used for a couple of decades and if the risk were as severe as indicated by the calculations performed according to the ESD, effects would have been observed in nature on population level or at least in the amount of poisoned individuals. There have been some investigations on the concentrations of bromadiolone and other rodenticides in predators, both birds and mammals, and the figures from these investigations clearly show that predators are exposed and, as stated above, around 30 % of birds and mammals have been/are exposed to second generation anticoagulants. In an attempt to refine the risk assessment the result indicated that rodents could have rodenticide concentrations in their livers of ca 1 µg/kg before causing lethality to barn owls. When analysing the effect of rodenticides it is motivated to describe the effect from all second generation anticoagulant rodenticides together, since the effect on non-target animals will probably be additive from these substances or even higher due to compound effects. It seems from monitoring data published on

barn owls that 1% of the owls had died from secondary poisoning by rodenticides (Newton et al, 1997). The question is whether this 1% lethality will have any effect on population level. It is difficult to predict the effect of rodenticides on the size of predator populations since the effect on a population depends on the size of the population, the mating behaviour, the normal average age of the population, and what animals of a population are killed by the rodenticide i.e. adult or young, females or males. Moreover, the effect may not necessarily be death but could also be decreased fertility or altered behaviour. Abnormal behaviour may e.g. lead to that more birds are killed by cars. Consequently, even a 1 % increased death rate could have an impact on the size of the population (Broman, 2003), but, looking at the barn owl population in England it seems as it has stabilised during the two last decades after a 60-70 % decline between 1930 and 1980. Figures for mammals are more uncertain, especially since many mammals may hide before they die.

The possibility of primary and secondary poisoning of non-target animals by bromadiolone campaigns on infested farms will depend on number of factors. Since risk is a combination of hazard and probability, the probability of poisoning non-target organisms has to be reduced. The probability of poisoning will depend on the duration of the treatment campaign, since the longer the campaign the higher is the probability for long-term toxic effects. Moreover, the frequency of campaigns in a specific area has to be considered, which means that campaigns have to be coordinated locally or regionally, taking into consideration the size of the hunting grounds of the species to protect. Otherwise predatory birds may catch rats with abnormal behaviour on one farm for a week and then on the next farm the next week and so forth. If the hunting grounds for a barn owl cover something like five farms the length of the exposure period to owls for poisoned rats could theoretically increase from 3 to 15 weeks. The frequency and length of the campaigns should be recorded by the professional users and could also be connected to monitoring programmes, e.g. monitoring of dead birds regarding cause of death and liver concentrations of rodenticides where the pattern of rodenticide use could be related to the variation over time of the recorded liver concentrations.

Below we have listed some suggested risk mitigation measures. See also Doc I, section 3 for the complete account for risk mitigation measures suggested for bromadiolone.

- The length of the campaign should be minimised, aiming at an optimal effect on the target rodents.
- Campaigns should be recorded and the time between campaigns should be as long as possible.
- Campaigns should be coordinated regionally to minimise the time of exposure for non-target animals that roam over large areas.
- Site inspections should be made regularly whereby bait points should be checked and dead rodents removed.
- After a campaign remaining bait should be removed.
- Monitoring programmes of dead predatory birds and mammals are recommended, where i.a. liver concentrations of bromadiolone are measured.

An important argument for the benefit of rodenticide use is that bromadiolone and/or other second generation anticoagulants are substances of great importance for the control of rodent populations that otherwise may spread diseases and cause economic loss for the society.

Proposals for risk mitigation measures

SI CA: The SI CA considers it appropriate that risk mitigation measures listed above are the same as in the PAR (UK CA, 2012).

Overall conclusion

According to this risk assessment the risk for poisoning of non-target predator birds and mammals during primary (acute and long-term exposure) and secondary poisoning is high as the trigger value is exceeded in all cases.

No safe use was established for the bromadiolone product at a concentration of 29 ppm in the ecotoxicology risk assessment.

3 General Annexes

3.1 List of studies for the biocidal product

Author	Year	Title	Publication	Report no.	Legal entity owner	Report date	GLP/ GEP	Data Protection Claimed
[redacted]	2017	Efficacy evaluation of Ratimor Grain Bait (bromadiolone 0.029 g/kg a.i., grain bait) against Norway rat (Rattus norvegicus Berk.)	unpublished	Trial Code: 2001.BCD.SAG17	Unichem	05/02/2017	GEP	Y
[redacted]	2017	Efficacy evaluation of Ratimor Grain Bait (bromadiolone 0.029 g/kg a.i., grain bait) against Roof rat (Rattus rattus L.)	unpublished	Trial code: 2002.BCD.SAG17	Unichem	05/02/2017	GEP	Y
[redacted]	2017	Efficacy evaluation of Ratimor Grain Bait (bromadiolone 0.029 g/kg a.i., grain bait) against House mouse (Mus musculus L.)	unpublished	Trial code: 2003.BCD.SAG17	Unichem	05/02/2017	GEP	Y
Norris D.	2019	Partial validation of the methods of analysis of the Active Ingredient bromadiolone within a Whole Wheat Bait Formulation, in compliance with Good Laboratory Practice	unpublished	DNA5046	Unichem	15.3.2019	yes	Y
Ranke J.	2019	Kinetic evaluation and read-across of the storage stability of a certain type of bait products containing bromadiolone	unpublished	Jrwb-139	Unichem	11/2/2017	-	no

3.2 Summaries of the efficacy studies

Summary of efficacy study against black rat infestation (*Rattus rattus*)

Function and field of use envisaged	Ratimor Plus Grain Bait (PT14)
Test substance	A cereal bait formulation containing 29 ppm bromadiolone

<table>
<tr><td>Test organism(s)</td><td>Roof rat (Rattus rattus)

Wild population located in agricultural habitat (breeding stables for pigs, fodder and equipment warehouses) in [redacted].
(resistance status unknown)</td></tr>
<tr><td>Test method, test system/concentrations applied/ exposure time</td><td>Droppings, sightings and activity established these rodents to be roof rats.
No rodenticide treatments were carried out in this site over the previous six months.
Census (unpoisoned) bait and tracking patches were employed to measure rodent populations both quantitatively and qualitatively for a period of 5 days prior to commencement of the test.
A 3-day lag period was used.
The trial was then undertaken using the product as per the proposed label instructions.
29 ppm Ratimor Plus Grain Bait bait was placed into commercially available tamper-proof bait stations, or in protected bait placements. Records of bait consumption were taken daily. Bait points which dropped below 200 g or that had been spoilt were either topped up or swapped with fresh bait.
After a further 4-day lag phase a post-treatment with census bait was undertaken.</td></tr>
<tr><td>Test results; effects</td><td>
<table>
<tr><th>Bait consumption</th><th>Pre-treatment census</th><th>Treatment census</th><th>Post-treatment census</th><th>% control</th></tr>
<tr><td>Total bait consumption (g)</td><td>4129</td><td>5510</td><td>0</td><td>100</td></tr>
<tr><td>Maximum daily bait consumption (g)</td><td>1003 (5th day)</td><td>847 (5rd day)</td><td>0</td><td>100</td></tr>
<tr><td></td><td></td><td></td><td></td><td></td></tr>
<tr><th>Activity over sand patches</th><th>Pre-treatment census</th><th>Treatment census</th><th>Post-treatment census</th><th>% control</th></tr>
<tr><td>Total activity score</td><td>103</td><td>206</td><td>0</td><td>100</td></tr>
<tr><td>Maximum daily activity score</td><td>24</td><td>24</td><td>0</td><td>100</td></tr>
</table>

According to the values recorded on the last 4 days of the Pre-treatment it was calculated an average daily baits consumption of 557 grams. This value was used as an index of the rat population size. Average tracking score values of 16-23 were recorded during the Pre-treatment period.

If conservative assumptions were made that the animals ate only census bait during the census period, and none of their normal food, that rats weighed on average 150 g, and ate approximately 10% of their body weight daily in dry food (Meehan 1984), then an estimate of a population size of a minimum of 35-45 rats was obtained.</td></tr>
</table>

	Total of 5510 g of treated bait was consumed during the 14 day baiting phase. Tracking patch activity dropped to zero on day 12 of the baiting period as did bait consumption. Complete (100%) effectiveness against *Rattus rattus* population across the trial site. No evidence was found during the trial that the use of 29 ppm Ratimor Plus Grain Bait bait when used in accordance to the label guidelines did pose a significant risk to non-target or companion animals.
Reference	[redacted], 2017

Summary of efficacy study against brown rat infestation (*Rattus norvegicus*)

Function and field of use envisaged	Ratimor Plus Grain Bait (PT14)
Test substance	A cereal bait formulation containing 29 ppm bromadiolone
Test organism(s)	Brown Rat (*Rattus norvegicus*) Wild population located in agricultural buildings lodging equipment warehouses in [redacted] (resistance status unknown)
Test method, test system/concentrations applied/ exposure time	Droppings, sightings and activity established these rodents to be brown rats. No rodenticide treatments were carried out in this site over the previous six months. Census (unpoisoned) bait and tracking patches were used to measure rodent populations both quantitatively and qualitatively for a period of 5 days prior to commencement of the test. A 3-day lag period was observed. The trial was then undertaken using the product as per the proposed label instructions. 29 ppm Ratimor Plus Grain Bait bait was placed into commercially available tamper-proof bait stations, or in protected bait placements. Records of bait consumption were taken daily. Bait points which dropped below 200g or that had been spoilt were either topped up or swapped with fresh bait. After a further 6-day lag phase a post-treatment census was undertaken.
Test results; effects	

Bait consumption	**Pre-treatment census**	**Treatment census**	**Post-treatment census**	**% control**
Total bait consumption (g)	4279	4029	0	100
Maximum daily bait consumption (g)	958 (5th day)	699 (8th day)	0	100
Activity over sand	**Pre-treatment**	**Treatment census**	**Post-treatment**	**% control**

	<table><tr><th>patches</th><th>census</th><th></th><th>census</th><th></th></tr><tr><td>Total activity score</td><td>100</td><td>258</td><td>0</td><td>100</td></tr><tr><td>Maximum daily activity score</td><td>24</td><td>24</td><td>0</td><td>100</td></tr></table> According to the values recorded on the last 4 days of the Pre-treatment census, it was calculated an average daily baits consumption of 1045 grams. This value was used as an index of the rat population size. Average tracking score values of 15-24 were recorded during the Pre-treatment period. If conservative assumptions were made that the animals ate only census bait during the census period, and none of their normal food, that rats weighed on average 200 g, and ate approximately 10% of their body weight daily in dry food (Meehan 1984), then an estimate of a population size of a minimum of 50-55 rats was obtained. Total of 4029 g of treated bait was consumed by day 15 of the 18 day baiting phase, started only 3rd day of the treatment phase. Tracking patch activity dropped to zero on day 16 of the baiting period as did bait consumption. Complete (100%) effectiveness against *Rattus norvegicus* population across the trial site. No evidence was found during the trial that the use of 29 ppm bromadiolone grain bait when used in accordance to the label guidelines did pose a significant risk to non-target or companion animals.
Reference	[redacted] 2017

Summary of efficacy study against mouse infestation (*Mus musculus*)

Function and field of use envisaged	Ratimor Plus Grain Bait (PT14)
Test substance	A grain bait formulation containing 29 ppm bromadiolone
Test organism(s)	House mouse (*Mus musculus*) Wild population located in an agricultural buildings lodging horses breeding stables, fodder and equipment warehouses in [redacted] (resistance status unknown)
Test method, test system/concentrations applied/ exposure time	Droppings, sightings and activity established these rodents to be mice. No rodenticide treatments were carried out in this site over the previous six months. Census (unpoisoned) bait and tracking patches were used to measure rodent populations both quantitatively and qualitatively for a period of 5 days prior to commencement of the test. A 3-day lag period was observed. The trial was then undertaken using the product as per the proposed label instructions. 29 ppm Ratimor Plus Grain Bait was placed into commercially available

<table>
<tr><td></td><td>tamper-proof bait stations, or in protected bait placements. Records of bait consumption were taken daily. Bait points which dropped below 40 g or that had been spoilt were either topped up or swapped with fresh bait. After a further 3-day lag phase a post-treatment census was undertaken.</td></tr>
<tr><td>Test results; effects</td><td>
<table>
<tr><th>Bait consumption</th><th>Pre-treatment census</th><th>Treatment census</th><th>Post-treatment census</th><th>% control</th></tr>
<tr><td>Total bait consumption (g)</td><td>1376</td><td>1179</td><td>0</td><td>100</td></tr>
<tr><td>Maximum daily bait consumption (g)</td><td>326 (5th day)</td><td>258 (4th day)</td><td>0</td><td>100</td></tr>
<tr><td></td><td></td><td></td><td></td><td></td></tr>
<tr><th>Activity over sand patches</th><th>Pre-treatment census</th><th>Treatment census</th><th>Post-treatment census</th><th>% control</th></tr>
<tr><td>Total activity score</td><td>91</td><td>175</td><td>0</td><td>100</td></tr>
<tr><td>Maximum daily activity score</td><td>21</td><td>22</td><td>0</td><td>100</td></tr>
</table>
According to the values recorded on the last 4 days of the Pre-treatment census, it was calculated an average daily baits consumption of 185.5 grams. This value was used as an index of the rat population size. Average tracking score values of 13-21 were recorded during the Pre-treatment period.
If conservative assumptions were made that the animals ate only census bait during the census period, and none of their normal food, that mice weighed on average 12-24 grams, and showed an average daily intake of 3.5-4 grams (Macdonald & Barrett, 1993; Berry, 1991), then an estimate of a population size of a minimum of 45-55 mice was obtained.
Total of 1518 g of treated bait was consumed by day 11 of the 14 day baiting phase.
Tracking patch activity dropped to zero by day 11 and no more bait was consumed after day 12.
Complete (100%) effectiveness against Mus Musculus population across the trial site.
No evidence was found during the trial that the use of 29 ppm bromadiolone grain bait when used in accordance to the label guidelines did pose a significant risk to non-target or companion animals.
</td></tr>
<tr><td>Reference</td><td>[redacted], 2017</td></tr>
</table>