Product Assessment Report

RATIBROM 2 PASTE

March 2013

Internal registration/file no:	DGDFSC/I.5.i.d.2/2011/213
Authorisation/Registration no:	IT/2013/00169
Granting date/entry into force of authorisation/ registration:	06/12/2013
Expiry date of authorisation/ registration:	30/06/2016
Active ingredient:	Bromadiolone
Product type:	PT14

Biocidal product assessment report related to product authorisation under Directive 98/8/EC

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1 General information about the product application

1.1 Applicant

Company Name:	KOLLANT S.r.l.
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Country:	Italy
Telephone:	+39 049 9983000
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1.1.1 Person authorised for communication on behalf of the applicant

Name:	Martina CARPANESE
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1.2 Current authorisation holder[1]

Company Name:	
Address:	
City:	
Postal Code:	
Country:	
Telephone:	
Fax:	
E-mail address:	
Letter of appointment for the applicant to represent the authorisation holder provided (yes/no):	

[1] Applies only to existing authorisations

1.3 Proposed authorisation holder

Company Name:	KOLLANT S.r.l.
Address:	Via Trieste, 49/53
City:	Padova
Postal Code:	35121
Country:	Italy
Telephone:	+39 049 9983000
Fax:	+39 049 9986005
E-mail address:	martina.carpanese@kollant.it
Letter of appointment for the applicant to represent the authorisation holder provided (yes/no):	No

1.4 Information about the product application

Application received:	05/07/2011
Application reported complete:	29/09/2011
Type of application:	First authorization of a biocidal product
Further information:	

1.5 Information about the biocidal product

1.5.1 General information

Trade name:	RATIBROM 2 PASTE
Manufacturer's development code number(s), if appropriate:	
Product type:	PT14
Composition of the product (identity and content of active substance(s) and substances of concern; full composition see confidential annex):	**Components** / **CAS-No** / **Function** / **Content (% w/w)** Bromadiolone: / 28772-56-7 / Active Ingredient / 0.005 Denatonium benzoate / 3734-33-6 / Human taste deterrent / 0.001 Other components: / Confidential information / Up to 100
Formulation type:	Paste bait
Ready to use product (yes/no):	Yes
Is the product the very same (identity and content) to another product already authorised under the regime of directive 98/8/EC (yes/no);	No

If yes: authorisation/registration no. and product name: **or** **Has the product the same identity and composition like the product evaluated in connection with the approval for listing of active substance(s) on to Annex I to directive 98/8/EC (yes/no):**	No

1.5.2 Information on the intended use(s)

Overall use pattern (manner and area of use):	Covered application by bait stations. RATIBROM 2 PASTE is a ready-to-use fresh pasta bait furnished in sealed food paper bags. It is not intended to be mixed with other products, diluted in any medium, sprayed or dusted. Place the bait inside appropriate container (bait box with access only for rodents) in order to reduce the risk of ingestion by non target animals. Avoid to touch barehanded the product. Utilize the appropriate gloves. Place the container in place of major presence in and around buildings, waste dumps, open areas, store, gardens, etc. and fixed in order to avoid dispersion of bait in the environment.
Target organisms:	Brown rat (*Rattus norvegicus)* House mouse (*Mus musculus)*
Category of users:	Professional and non-professional
Directions for use including minimum and maximum application rates, application rates per time unit (e.g. number of treatments per day), typical size of application area:	The amount of product used per application is 40 g per 10m^2 for *Mus musculus* and 60 - 100 g per 10m^2 for R*attus norvegicus*. Bait points are placed typically every 2 to 5 m for mouse infestation and 5 to 10 m for rat infestation. Closer placement is required for heavier infestations. The duration of the program is at maximum up to 6 weeks. Permanent, preventive treatments are possible under the supervision of a pest control operator or other competent operator. In case of permanent baiting, a minimum dose shall be applied (60 g) and the baiting points are inspected 4-6 times per year. The bait must be placed in appropriate bait stations, protected from atmospheric agents, in order to avoid accidental swallowing of infants, non target species and undesired dispersion of bait in the environment.

	Rodents eat the bait over one or more days and die typically 4-10 days later. If all bait is consumed quickly in a particular area, increase the number of baiting points in that area. Dead rodents are removed for disposal as soon as possible according to local rules. At the end of treatment bait stations and residual bait must be disposed of according to local rules.
Potential for release into the environment (yes/no):	Yes
Potential for contamination of food/feedingstuff (yes/no)	No
Proposed Label:	S1/2 Keep locked up and out of the reach of children S13 Keep away from food, drink and animal feedingstuffs. S20/21 When using do not eat or drink and do not smoke. S24 Avoid contact with skin S37 Wear suitable gloves (only for professionals) S46 If swallowed, seek medical advice immediately and show this container or label S61 Avoid release to the environment. Refer to special instructions/Safety data sheet.
Use Restrictions:	Non professionals baits should be supplied as inner packs or units containing at most enough bait for one bait point (either rat or mouse) and used only in refillable tamper-resistant bait stations. Individual packs for non-professional use should not exceed 500 g. RATIBROM 2 PASTE for professional use should not be available to the general public.

1.5.3 Information on active substance(s)

Active substance chemical name:	Bromadiolone
CAS No:	28772-56-7
EC No:	249-205-9
Purity (minimum, g/kg or g/l):	969 g/kg (relates to the mixture of two racemic diastereomers; 70-90% syn-isomer (1RS,3RS) 10-30% anti-isomers (1RS,3SR))
Inclusion directive:	2009/92/EC
Date of inclusion:	1 July 2011
Is the active substance equivalent to the active substance listed in Annex I to 98/8/EC (yes/no):	Yes

Manufacturer of active substance(s) used in the biocidal product:	
Company Name:	Activa S.r.l.
Address:	Viale Lombardia, 22
City:	Milano
Postal Code:	20131
Country:	Italy
Telephone:	+39 02 70637301
Fax:	+39 02 70637228

1.5.4 Information on the substance(s) of concern

Substance chemical name	-
CAS No:	-
EC No :	-
Purity (minimum, g/kg or g/l):	-
Typical concentration (minimum and maximum, g/kg, or g/l):	-
Relevant toxicological/ecotoxicological information:	-
Original ingredient (trade name):	-

1.6 Documentation

1.6.1 Data submitted in relation to product application

A full product dossier was submitted by KOLLANT s.r.l. in support of the product RATIBROM 2 PASTE containing Bromadiolone.

New data has been submitted in support of the evaluation of the biocidal product. Refer to Annex 2 for the list of new studies reviewed.

1.6.2 Access to documentation

A Letter of Access from ACTIVA has been submitted for the active substance Bromadiolone.

The ACTIVA is owner of all the data on the active substance as it was part of the “Bromadiolone Task Force”, which submitted the Annex II complete dossier to RMS Sweden.

2 Summary of the product assessment

2.1 Identity related issues

A Letter of Access from ACTIVA has been submitted for the active substance Bromadiolone.

ACTIVA S.r.l. as a member of the Bromadiolone Task Force supported Bromadiolone inclusion into Annex I of BPD. Since the manufacturer of the active substance in RATIBROM 2 PASTE is not different, technical equivalence is not to be addressed.

Composition of the biocidal product

	Function	**CAS No.**	**Content % w/w**
Bromadiolone	Active ingredient	28772-56-7	0.005 (0.05 g/kg)
Denatonium benzoate	Human taste deterrent	3734-33-6	0.001 (0.01 g/kg)
Other components:	Confidential information, please to refer to Annex 1 (SPC)		Up to 100

For detailed quantitative and qualitative information on the composition of the biocidal product, please refer to confidential data in Annex 1 (Summary of Product Characteristics).

2.2 Classification, labelling and packaging

The current classification and labelling of the biocidal product according to Directive 99/45/EC (with amendments and adaptation) is provided in the table below.

Not classified in accordance with the Directive 1999/45/EC (with amendments and adaptation)

Classification	Not classified (as in Directive 1999/45/EC)
Symbol(s):	None
Indication(s) of danger:	None
Risk phrases:	None
Safety phrases:	S1/2 Keep locked up and out of the reach of children. S13 Keep away from food, drink and animal feeding stuffs. S20/21 When using, do not eat, drink or smoke S24 Avoid contact with skin S37 Wear suitable gloves (professionals only) S46 If swallowed, seek medical advice immediately (show the label where possible) S61 Avoid release to the environment. Refer to special

	instructions/Safety data sheet

Further, the content of the label is added with precautionary phrases recommended at national level.

If a separate leaflet is attached to or supplied with the product, add the following information to the front label:

- Read attached instructions before use

Active substance Bromadiolone is not currently classified according to Annex VI of Regulation (EC) no 1907/2006 (REACH). Once the harmonised classification for the active substance has been concluded the IT CA will re-examine the classification and labelling of Bromadiolone products.

2.2.1 Harmonised classification of the biocidal product

The current classification and labelling according to Regulation (EC) 1272/2008 is provided in the table below.

Not classified in accordance with the Regulation EC 1272/2008.

Pictogram(s):	None
Signal word(s):	None
Hazard statements:	None
Precautionary statements	P102: Keep out of reach of children. P103: Read label before use. P270: Do not eat, drink or smoke when using this product. P273: Avoid release to the environment. P301+310: IF SWALLOWED: Immediately call a poison centre or doctor/physician. P501: Dispose of contents/container to hazardous waste facilities in accordance with national regulations.

2.2.2 Labelling of the biocidal product

See section 2.2

2.2.3 Packaging of the biocidal product

Considering that anticoagulants used as rodenticides are highly toxic substances, it is considered appropriate to restrict packaging for non professional users as a risk mitigation measure.

Non professional baits should be supplied as units containing at most enough bait for one bait point (either rat or mouse) and used only in refillable tamper-resistant bait stations.

Individual packs for non-professional use should not exceed 500 g.

The packaging details are provided in the table below.

Users	Material	Pack size
Professional	PET bag	Up to 25 kg (containing edible paper sachets of pasta bait 20 g each)

Non-professional	PET bag	Up to 500 g (containing edible paper sachets of pasta bait 20 g each)

2.3 Physico/chemical properties and analytical methods

RATIBROM is a ready-to-use bait in the form of a dark red solid pasta with a characteristic odour, containing Bromadiolone as active substance at 0.005 % w/w concentration.

On the basis of the physical-chemical properties the product can be considered not explosive, not oxidising and not flammable/highly flammable. The measurement of the pH of a 1% w/v aqueous dispersion is 6.50 at 22°C. The density is proved to be 1.204 g/mL.

As regards the studies submitted on accelerated storage stability, the study at 35°C for 12 weeks and at 40°C for 8 weeks are complete and it can be assumed that the product is stable. A shelf life study is ongoing. On the basis of the presented study it can be assumed that the product is provisional stable at room temperature for at least two years.

2.3.1 Physico-chemical properties

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

	Method	**Purity/Specification**	**Results**	**Reference**
Physical state and nature	EPA Guidelines OPPTS 830.6303	0.00533% w/w Batch No. 2310773	Solid pasta (22°C)	Paronuzzi Ticco S. (2010a)
Colour	EPA Guidelines OPPTS 830.6302	0.00533% w/w Batch No. 2310773	Dark red (22°C)	Paronuzzi Ticco S. (2010a)
Odour	EPA Guidelines OPPTS 830.6302	0.00533% w/w Batch No. 2310773	Characteristic odour (22°)	Paronuzzi Ticco S. (2010a)
Explosive properties	--	---	Not explosive. None of the components is classified as explosive under directive 67/548/EC	
Oxidizing properties	--	---	Not oxidising. None of the components is classified as oxidiser under directive 67/548/EC	
Flash point	--	--	No ignition temperature The test article is a solid pasta therefore a flash-point study is not required.	
Autoflammability	--	--	Not flammable. No evidence of	

	Method	Purity/Specification	Results	Reference
			flammability in use. None of the components of the product is classified as flammable under the directive 67/548/EC.	
Other indications of flammability	--	--	--	--
Acidity / Alkalinity	CIPAC MT 75.3	0.00533% w/w / Batch No.: 2310773	pH = 6.5 (1% aqueous dispersion) (mean of two experiments) T = 22 °C	Paronuzzi Ticco S. (2010a)
Relative density / bulk density	CIPAC MT 33	0.00533% w/w / Batch No.: 2310773	1.204 g/mL (mean of three experiments)	Paronuzzi Ticco S. (2010a)
Storage stability – stability and shelf life	GIFAP No. 17 CH114/2010 (analytical method supply by the sponsor)	0.00533% w/w / Batch No.: 2010661	A test of storage stability at room temperature for two years is in progress and the final report will be available on October 2012.	Paronuzzi Ticco S. (2010b)
Effects of temperature (35°C for 12 weeks	CIPAC MT 46 CH114/2010 (analytical method supply by the sponsor)	0.00533% w/w / Batch No.: 2310773	From the data reported it can be concluded that the test article is stable in its commercial packaging after 12 weeks at 35 °C.	Paronuzzi Ticco S. (2011a)
Effects of temperature (40°C for 8 weeks	CIPAC MT 46 CH114/2010 (analytical method supply by the sponsor)	0.00505% w/w / Batch No.: 4910813	From the data reported it can be concluded that the test article is not stable in its commercial packaging after 8 weeks at 40 °C, therefore a study with an increase period and lower temperature was submitted. See above (35°C for 12 weeks).	Paronuzzi Ticco S. (2011a)
Effects of light		A statement	Exposure of the product to sunlight is limited if it is correctly stored and used. In fact the use, exposure is limited to the time it takes to place the bait and cover it or to close the bait box. Due to the	

	Method	Purity/Specification	Results	Reference
			very short length of time of exposure it is considered that further information is unnecessary.	
Reactivity towards container material	No guidelines	0.00533% w/w / Batch No.: 2310773	The container did not present any deformation in either bottom or lateral layers, or loss of sample or evident corrosion phenomena.	Paronuzzi Ticco S. (2011a) Paronuzzi Ticco S. (2011b)
Technical characteristics in dependence of the formulation type	None	None	Not relevant to solid pasta baits which are not mixed with water.	
Compatibility with other products	None	None	Not required since the product is ready-to-use and it is not intended to be added to or mixed with any other product.	
Surface tension	None	None	Not required since the product is a ready-to-use solid paste.	
Viscosity	None	None	Not required since the product is a ready-to-use solid paste.	
Particle size distribution	None	None	Not required since the product is a ready-to-use solid paste.	

2.3.2 Analytical methods

Analytical methods to determine the active substance are described in the analytical methods of Bromadiolone (Annex I CAR) and are presented in the List of endpoints for Bromadiolone.

Formulation analysis

The validation analytical method performed by Paronuzzi Ticco S. (2010) is suitable for the determination of Bromadiolone in the formulation RATIBROM 2 PASTE. The content of Bromadiolone in RATIBROM 2 PASTE sample was determined by HPLC with UV detection at 270 nm. Quantitation was performed using an external standard. Bromadiolone was extracted by ethanol. The resulting solution was placed in a sonication bath for 15 minutes and stirred overnight. The extract was centrifuged at 8000 rpm for 10 minutes; the supernatant was injected into HPLC. The method for the determination of the active ingredient Bromadiolone in the bait RATIBROM 2 PASTE was validated with respect to specificity, linearity of detector response, precision and accuracy following guideline SANCO/3030/rev. 4.

Specificity: No interferences with the blank formulation

Linearity: concentration range 5 – 15 µg/mL (corrsponding to 0.0025% w/w – 0.0075% w/w)
Linearity: $R^2 > 0.9999$.

Repeatability (precision): 0.0049 % w/w ± 0.0005 % w/w (49 ± 5 mg/kg); S.D. 0.0004; RSD% = 7.20%.

Accuracy: Three fortification levels – 75%, 100%, 125%; Mean recoveries 95.2%

Mean recovery range: 93.2% – 97.0%

	Principle of method
Technical active substance as manufactured:	HPLC/UV
Impurities in technical active substance:	Confidential data
Active substance in the formulation:	Extraction with ethanol. Determination by HPLC/UV-Vis at 270 nm.

2.4 Risk assessment for Physico-chemical properties

On the basis of the available data, it can be conclude that RATIBROM 2 PASTE does not pose any physical-chemical hazard.

2.5 Effectiveness against target organisms

The formulation RATIBROM 2 PASTE consists in a "fresh paste" intended for both professional and domestic use to control rodent pests in and around industrial, commercial and residential buildings, in open areas and waste dumps. It is effective against all rodents in civil and industrial field and it is particularly attractant and palatable to house mice (Mus musculus) and brown rats (Rattus norvegicus).

Bromadiolone is a second generation anticoagulant which prevents blood clotting in the target organisms by inhibiting regeneration of the active form of vitamin K1 and it is used as a rodenticide. The efficacy of RATIBROM 2 PASTE (bromadiolone content of 0.005%) has been assessed both through laboratory (on brown rats and mouse with aged and fresh paste bait) and field studies (2 studies: one on brown rats and one on mice). The results of laboratory studies with fresh and aged paste bait evidenced as RATIBROM 2 PASTE is palatable and effective (100%) on brown rats (Rattus norvegicus) and house mice (Mus musculus). In addition, two field studies were performed on brown rats (Rattus norvegicus) and house mice (Mus musculus).

According to the results of field studies, the product RATIBROM 2 PASTE showed a good acceptance and provided a complete effectiveness (100 %) against brown rat and house mice populations present in the trial sites.

2.5.1 Dose / mode of action / known limitations / resistance

The formulation is a ready to use bait containing 0.005 % w/w of the anticoagulant active ingredient bromadiolon and the product is supplied in heat sealed food paper bags of 20 g each. The treatments last at maximum 6 weeks and the amount of used product per application 40 g per 10 square meters for house mice and 60 - 100 g per 10 square meters for rats, depending on the severity of the infestation. Bait points are placed typically every 5-10m. The product is placed in a bait station or fixed to a structure such that rats and mice can eat them. In situations where bait boxes cannot be used, the bait is covered such that non-target organisms cannot reach them. Baiting points are inspected at least weekly and replenished when bait has been eaten. Dead rodents are removed for disposal in order to prevent them being eaten by non-target animals and birds.

Repeated use of coumarin-like anticoagulant rodenticides such as bromadiolone may lead to development of resistance. Bromadiolone resistance does not display the same pattern as the more widespread and better known warfarin resistance.

2.6 Exposure assessment

Exposure values have been calculated using the paper "HEEG opinion on a harmonized approach for the assessment of rodenticides (anticoagulants)" agreed at TM II 2011.

2.6.1 Description of the intended use(s)

The product RATIBROM 2 PASTE takes the form of a solid paste containing 0.005% w/w bromadiolone. RATIBROM 2 PASTE baits are furnished in heat sealed filter paper bags and weights 20 g each, the product RATIBROM 2 PASTE is intended for professional use to control rodent pests in and around industrial, commercial and residential buildings, open areas and waste dumps; a non-professional use in and around buildings is also envisaged. The product is placed in plastic bait boxes such that rats and mice can eat it or, in situations where bait boxes cannot be used, the bait is covered such that non-target organisms cannot reach it. The amount of used product per application is 40 g per 10 square meters for mice and 60-100 g for rats. Baiting points are placed typically every 2-5 m for mice and 5-10 m for rats.

2.6.2 Assessment of exposure to humans and the environment

2.6.2.1 Main paths of human exposure towards difenacoum from its use in biocidal products

Exposure path	Industrial use	Professional use	General public	Via the environment
Inhalation	No	No	No	No
Dermal	No	Yes	Yes	No
Oral	No	No	Yes	No

Inhalation exposure
According to TNsG Human Exposure to Biocidal Products (Part 3, pag 55) and to Assessment Report on bromadiolone, the risk of exposure by inhalation is negligible (10-5 mg/m3). Therefore, inhalation exposure for professionals and non-professionals placing paste bait is considered to be negligible due to the very low volatility of the active substance. Likewise, for non-users the risk due to the inhalation exposure to residues during or after application via environment is considered to be negligible.

Dermal exposure
Paste baits are put into the place by hand. For users dermal exposure is limited to the hands only. Exposure of other parts of the body can be discharged as negligible. For non-users, the risk of dermal exposure to residues during application is considered not relevant. Children could potentially be the group most at risk as they may play inside or around buildings where baits have been placed. However, product labels and good practice advise users to prevent access to bait by children. Consequently, risk of dermal exposure to bromadiolone for non-users is considered to be negligible.

Oral exposure
Paste baits are not likely to reach the mouth of professional or non-professional users. Therefore, the risk during use is considered to negligible. Equally, for non-users, risk of oral exposure to residues during or after application is considered to be negligible. Children or infants may play inside or around buildings where baits have been placed. However, product labels and good practice advise users to prevent access to bait by children. Paste baits also contain a bittering agent (denatonium benzoate) that in some cases may help to prevent infants chewing and ingesting bait.

2.6.2.2 Primary exposure

2.6.2.2.1 Professional use

The exposure values have been estimated by using the most appropriate reference for the evaluation of rodenticide products which is the HEEG harmonisation paper (based on Chambers, 2009) agreed at TM II 2011. No specific data for trays have been made available in the HEEG opinion, however, it is indicated that the data for wax blocks can reasonably be used for sachets.

For professional use, the agreed number of manipulations has been set at 60 and 15 for loadings (application phase) and cleanings (post-application phase), respectively. For the application of rodenticides in sewage systems no cleaning phase is required.

Application phase – securing blocks into bait stations

The Chambers study determined the following scenario: 5 operators secured 5 compressed wax blocks (each 20 g, in total 100 g bait per box) into a bait station by pushing bait mounting pegs in the stations through holes in wax blocks. Three trials were conducted with 1, 5 and 10 times securing of wax blocks. Since the results of 1, 5 and 10 securing are similar, all trials are included in the calculation of the 75th percentile. The indicative exposure of 27.79 mg b.p. is valid for loading of one bait box with block bait (i.e., per 5 blocks). For dermal exposure HEEG opinion states that the number of contacts of the operator and the number of handled wax blocks (*i.e.*, paste bait) is essential. Consequently, the number of contacts during one manipulation should be taken into account in the dermal exposure assessment.

The product RATIBROM 2 PASTE is a solid (paste) formulation containing 0.005% of active ingredient. The product is a ready to use paste bait furnished in heat sealed food paper bags (tea-bags) of 20 g each which, according to label instructions, should be applied, at maximum, at the dose of 100 g per bait site.

For dermal absorption of 0.36%, estimated for powdered products, was used.

Professional users are assumed to wear protective gloves when handling the products. Gloves are assumed to reduce the exposure of hands by 90%.

Operator exposure during placing 20 g paste sachets into bait point

No PPE (gloves)	
Amount of exposure to product (75th percentile) during securing of 5 sachets (100g) per one manipulation	27.79 mg b.p.
Potential dermal exposure for 60 manipulations	27.79 mg b.p. x 60 = **1667.4 mg b.p.**
Amount of a.s. on fingers/hands (a.s. concentration 0.005% w/w)	1667.4 mg × (0.005 / 100) = **8.3×10^{-2} mg a.s**.
Systemic dose (dermal absorption 0.36%, bw 60kg) per placing 5 sachets	(8.3×10^{-2} mg x (0.36 / 100)) / 60kg = **5.0×10^{-6} mg/kg bw**
PPE (gloves)	
Systemic dose (dermal absorption 0.36%, bw 60kg) per placing 5 sachets	**5.0×10^{-7} mg/kg bw**

Post-application phase – clean-up and disposal of partly consumed paste sachets

The Chambers study determined the following scenario: 5 operators emptied a loaded bait station by sliding the wax block off the mounting pegs into a 10 L plastic bucket. This is done 1, 5 and 10 times. The following table summarizes the different approaches. The recommended value of **5.7 mg b.p**. is valid for the cleaning of one bait box. This value derived for the wax block can be also used for the paste in sachets.

For the post-application-phase, the agreed number of 15 manipulations should be taken into account. Therefore, the resulting potential dermal exposure is **15 x 5.70 = 85.5 mg b.p.**

Dermal exposure for professional operator during the cleaning out phase

No PPE (gloves)	
Amount of exposure to product (75th percentile) during clean-up and disposal per one manipulation.	**5.70 mg b.p.**
Potential dermal exposure for 15 manipulations	5.7 mg b.p. x 15 = **85.5 mg b.p.**
Amount of a.s. on fingers/hands (a.s. concentration 0.005% w/w)	85.5 mg × (0.005 / 100) = **4.3 x 10^{-3} mg a.s**.
Systemic dose (dermal absorption 0.36%, bw 60kg) per clean-up	(4.3 x 10^{-3} mg x (0.36 / 100)) / 60kg = **2.6×10^{-7} mg/kg bw**
PPE (gloves)	
Systemic dose (dermal absorption 0.36%, bw 60kg) per clean-up	**2.6×10^{-8} mg/kg bw**

Total dermal exposure for professional users:

No PPEs
5.0 × 10^{-6} mg/kg/day + 2.6 × 10^{-7} mg/kg/day = **5.3 × 10^{-6} mg/kg/day**

With PPEs
5.0 × 10^{-7} mg/kg/day + 2.6 × 10^{-8} mg/kg/day = **5.3 × 10^{-7} mg/kg/day**

2.6.2.2.2 Non-professional use

The application of RATIBROM 2 PASTE by non-professional users differs from the professional uses due to the fact that the product is supplied as sealed units which cannot be refilled. Therefore, there will be neither dermal nor inhalation exposure to the general public from use of the baits in rodent control. Ready-to-use bait stations already containing the baits are available, reducing exposure to almost negligible levels. However, in accordance with the CARs on various rodenticides, fewer manipulations as compared to professionals are considered. Hence, 5 loading and 5 cleaning manipulations are assumed for a non-professional user. For non-professional users, no protection by gloves is to be considered due to the fact that general public may not either be informed on the measures to control exposure or accurately follow instructions for use of product.

Non-professional exposure during placing 5 x 20 g paste sachets into bait point

No PPE (gloves)	
Amount of exposure to product (75th percentile) during securing of 5 sachets (100g) per one manipulation	27.79 mg b.p.
Potential dermal exposure for 5 manipulations	27.79 mg b.p. x 5 = **138.9 mg b.p.**
Amount of a.s. on fingers/hands (a.s. concentration 0.005% w/w)	138.9 mg × (0.005 / 100) = **6.9 x 10^{-3} mg a.s**.
Systemic dose (dermal absorption 0.36%, bw 60kg) per placing 5 sachets	(6.9 x 10^{-3} mg x (0.36 / 100)) / 60kg = **4.1×10^{-7} mg/kg bw**

Post-application phase – clean-up and disposal of partly consumed paste sachets
For the resulting potential dermal exposure of post-application-phase 5 manipulations has been used as proposed by applicant. For the post-application phase the resulting potential dermal exposure is **5 x 5.70 mg b.p. = 28.5 mg b.p.**

Dermal exposure for non-professional user during cleaning out phase

No PPE (gloves)	
Amount of exposure to product (75th percentile) during clean-up and disposal per one manipulation.	**5.70 mg b.p.**
Potential dermal exposure for 5 manipulations	5.7 mg b.p. x 5 = **28.5 mg b.p.**
Amount of a.s. on fingers/hands (a.s. concentration 0.005% w/w)	28.5 mg × (0.005 / 100) = **1.4×10^{-3} mg a.s**.
Systemic dose (dermal absorption 0.36%, bw 60kg) per clean-up	(1.4×10^{-3} mg x (0.36 / 100)) / 60kg = **8.4×10^{-8} mg/kg bw**

Total dermal exposure for non-professional users
4.1×10^{-7} mg/kg/day + 8.4×10^{-8} mg/kg/day = **4.9×10^{-7} mg/kg/day**

2.6.2.3 Indirect exposure as a result of use of the active substance in biocidal product

During application of RATIBROM 2 PASTE in rodent control, secondary exposure to the rodenticide baits may occur. The scenario considers incidental ingestion of baits by infants.
The TNsG (2002) Part 3 (Appendix 7.2.1) provides algorithms and assumptions for the secondary exposure assessment.

Ingestion of bait by children
The TNsG on Human Exposure (2007) has identified an indirect scenario for oral exposure from transient mouthing of baits whereby a child eats a 10mg and a 5 g portion of the bait.
Assuming 70% oral absorption and an infant's body weight of 10 kg, systemic exposure is equal to: (5 g x 0.005% a.s.*70%)/10 kg = 0.018 mg/kg bw
However, ingestion of 5 g represents a high overestimate of exposure, since baits contain a repellent (denatonium benzoate as bitter agent), which will most likely urge the children to spit the baits.
Applying the general assumption of ingestion of 10 mg of bait (TNsG default for a bait with repellent), systemic exposure is 3.5×10^{-5} mg/kg bw.

Results are summarized in the table below:

Scenario	**Estimated systemic exposure [mg/kg bw/d]**
Ingestion of bait (5 g)	1.8×10^{-2}
Ingestion of bait (10 mg)	3.5×10^{-5}

2.7 Risk assessment for human health

2.7.1 Hazard potential

2.7.1.1 Toxicology of the active substance

The toxicology of the active substance was examined extensively according to standard requirements. The results of this toxicological assessment can be found in the CAR and in particular in the "Combined Assessment Report of the active substance Bromadiolone-Product type 14 (Rodenticides)", revised version August 2010, RMS Sweden. The threshold limits and labelling regarding human health risks listed in Annex 4 „Toxicology and metabolism" must be taken into consideration.

Bromadiolone is a second-generation single-dose anticoagulant rodenticide, structurally similar to vitamin K. It disrupts the normal blood clotting mechanisms resulting in increased bleeding tendency and, eventually, profuse haemorrhage and death.

In acute oral toxicity studies, bromadiolone was very toxic to rats with a LD_{50} to the rat of between 0.56 and 1.31 mg/kg bw. Bromadiolone was acutely toxic by dermal administration, with an LD_{50} of 1.71 mg/kg bw in rabbits and with a combined sexes dermal LD_{50} value of 23.3 mg/kg in rats.
The LC_{50} by inhalation, in rats was 0.43 µg/L. Waiving of inhalation studies has been accepted, since operator exposure through inhalation is unlikely to occur based in the information presented concerning production procedures and based on the physical-chemistry data showing low vapour pressure. However, a classification as R26 'Very toxic by inhalation' is warranted based on the available data.

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

On the basis of these results, Bromadiolone requires labelling with the symbol T+ and the risk phrases R28 'Very toxic if swallowed'; R27 'Very toxic in contact with the skin' and R26 'Very toxic by inhalation'. Bromadiolone is not classified as a skin irritant, eye irritant or a skin sensitiser.

Repeated dose oral studies showed that at doses as low as 20 µg/kg/day in the dog, lethal effects developed after 64 to 85 days administration.
In the 90-day oral exposure study in rabbits, a significant increase in prothrombin time was seen in the 1 µg/kg dose group. The overall NOAEL for repeat dose effects is 0.5 µg/kg/day based on the absence of adverse effects in this dose group.

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

Bromadiolone was not mutagenic in a standard range of in vitro and in vivo tests. Considering the lack of genotoxicity potential and the high toxicity of the substance both carcinogenicity and chronic toxicity study were waived.

Reproductive effects of bromadiolone can not be excluded by the submitted two-generation reproduction toxicity study. A teratogenicity study on rabbit showed severe fetal malformations following exposure to maternally toxic levels of bromadiolone. In rabbits, the lowest LOAEL for maternal toxicity was determined at 0.002 mg/kg bw/d based on haemorrhages in the kidneys. However, the possibility that the effects seen may have been due to non-specific influences such as generalised toxicity cannot be excluded. Bromadiolone was not embryotoxic or teratogenic in guideline studies in rat and rabbit. However, based on the structural similarity to and the same mode of action as warfarin, bromadiolone is considered as a possible developmental toxicant and therefore requires the classification as Reprotoxic with the labelling R61, may cause harm to the unborn child.

The toxicological studies do not indicate any neurotoxic effects.

Regarding the assessment of risks associated with exposure to a rodenticidal bait, two reference doses for the systemic toxicity of Bromadiolone were defined.

With regard to short-term (acute) exposure an **AEL_{acute} = 0.0023 µg/kg bw/d** based on the LOAEL of the developmental toxicity study in rabbit is proposed with a safety factor of 600.

With regard to long-term (chronic) exposure an **$AEL_{medium/long-term}$ = 0.0012 µg/kg bw/d** based on the NOAEL of the 90day-toxicity study in rabbit is proposed with a safety factor of 300.

Data are corrected for bioavailability in respect to an oral absorption of 70%.

Reference dose	Value (µg/kg bw/d)	Study	Effect level (µg/kg bw/d)	Relevance for risk assessment
AEL $_{acute}$	0.0023*	Developmental toxicity study in rabbits	2 (LOAEL) SF 600	acute exposure (single dose or a few days of exposure)
AEL $_{medium/long-term}$	0.0012*	90-day rabbit study	0.5 (NOAEL) SF 300	repeated exposure (few weeks per year or frequent exposure)

*corrected for 70% oral absorption

2.7.1.2 Toxicology of the substance(s) of concern

No ingredients are included in the formulated product, which are considered to be of toxicological concern in view of their toxicity profile and concentration in the product.

2.7.1.3 Toxicology of the biocidal product

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

New GLP complaint studies using RATTIBROM 2 containing 0.005% Bromadiolone as pasta bait, have been submitted to address acute oral and dermal toxicity, skin and eye irritation. Until now, no skin sensitisation toxicity test has been available on the formulation RATIBROM 2.

The product RATTIBROM 2, is not acutely toxic by the oral (LD_{50}>2000 mg/kg bw) and dermal (LD_{50}>2000 mg/kg bw) routes.

RATTIBROM 2 is formulated as a highly viscous paste, using mostly food grade materials, which are solid and of low vapour pressure. The formulation is not a powder and as stated by the Applicant, it is not applied in a manner that generates respirable aerosol, particles or droplet. The formulation is therefore not respirable, does not produce respirable particles, and does not produce respirable vapours. Due to the low vapour pressure of the a.s and the physical state of the product, the amount of potential exposure through inhalation is most likely at very low level. Therefore the Applicant considered that a study on acute inhalation toxicity of the product is not required. The RMS IT agrees with this conclusion.

The results of the GLP complaint skin and eye irritation tests conducted on the product showed that RATTIBROM 2 is non-irritating to the skin and eyes and does not meet the EU and GSH classification criteria for these end-points.

As stated by the Applicant, a study on RATIBROM 2 PASTEis ongoing. It has to be underlined that the a.s. Bromadiolone is not classified as sensitizer (Assessment Report, 2010) and there are no other components in the RATIBROM 2 PASTE formulation which are of skin sensitizing relevance. However, being in progress a new skin sensitization study on RATIBROM 2, in order to come to a final conclusion, a complete evaluation of these results is required.

Regarding dermal absorption, an in vitro dermal absorption study through human skin is already available, within the active substance dossier, on two formulations, e.g. saline (0.00255% bromadiolone) and a wax block formulation (0.005% bromadiolone). Considering the experimental conditions used in the present study, in terms of formulation, active substance content and values used for the dermal absorption calculation (sum of the absorbed dose and the exposed skin, including tape strip 1-20) as a worst case, following a conservative approach, RMS IT considers acceptable the read-across of these results to RATIBROM 2. Overall, RMS IT concludes that **a dermal absorption value of 0.36%** (as a worst case) has to be used in the risk characterization, when calculating the potential human systemic dose of bromadiolone following exposure to this product. Moreover, the Applicant states that the biocidal product will not come into contact with food (and it is not applied by spraying or dusting such that food or feedingstuffs could be contaminated): therefore, there is no requirement to assess potential residues on foodstuffs. Based on intended uses and proper baiting practices of the biocidal product, contamination of food/feedingstuffs is considered highly unlikely to occur. The RMS IT accepts these justifications.

2.7.2 Exposure

The biocidal product contains the active substance (pure: 50 mg/kg) and no substance of concern.

2.7.2.1 Exposure of professional users

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

2.7.2.2 Exposure of non-professional users and the general public

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

2.7.2.3 Exposure to residues in food

In Annex 8 “Residue behaviour”, the results of the residue assessment are laid out.

2.7.3 Risk Characterisation

Commento [CR1]: Dermal Absorption e AELs da confermare

With proper use in accordance with regulations harmful effects on the health of users and third parties are not expected. The estimated exposures for the intended use are compared to the respective systemic AEL.

2.7.3.1 Risk for Professional Users

Risk characterisation is performed on basis of the “margin of exposure” approach and by calculation of the percentage of the corresponding AEL. Risk characterization for professionals has been assessed by using chronic AEL and chronic NOAEL.

Margin of Exposure (MoE): MoE = NOAEL/calculated systemic exposure

Results of the comparison of the estimated total systemic exposure levels to the respective health-based limit values as derived for Bromadiolone for professional users are summarized below:

Workplace operation	PPE	Exposure route	Systemic dose (mg/kg bw)	% AEL [1]	MoE [2]
Professional loading block bait, clean-up	None	Dermal	5.3×10^{-6}	**442**	**94.3**
Professional loading block bait, clean-up	Gloves	Dermal	5.3×10^{-7}	44.2	943

[1)] based on $AEL_{medium/long-term}$ of 1.2×10^{-6} mg/kg bw/d; AF = 300

[2)] based on NOAEL of the 90day-toxicity study in rabbit of 5.0×10^{-4} mg/kg bw/d; MOE_{ref} = 300

Conclusion: for professional users, a safe use is only predicted when the use of PPEs is prescribed.

2.7.3.2 Risk for non-professional users and the general public

For non-professional users, no protection by gloves is to be considered due to the fact that general public may not either be informed on the measures to control exposure or accurately follow instructions for use of product.

Results of the comparison of the estimated total systemic exposure levels to the respective health-based limit values as derived for Bromadiolone for non-professional users are summarized below:

Workplace operation	PPE	Exposure route	Systemic dose (mg/kg bw)	% AEL [1]	MoE [2]
Non-professional Loading block bait, clean-up	None	Dermal	4.9×10^{-7}	41.2	1012

[1)] based on $AEL_{medium/long-term}$ of 1.2×10^{-6} mg/kg bw/d; AF = 300

[2)] based on NOAEL of the 90day-toxicity study in rabbit of 5.0×10^{-4} mg/kg bw/d; MOE_{ref} = 300

Conclusion: for non-professional users, a safe use is predicted also not considering the use of PPE.
Potential secondary exposure route from application of RATIBROM in rodent control include ingestion of pellets by infants. The relevant scenarios are not considered to result in long-term exposure, whereas acute exposure may occur.

As incidental exposure is predicted, comparison to acute exposure limit values is considered appropriate.

			LOAEL = 2.0 x 10^{-3} mg/kg bw/d AF = 600 AEL = 2.3 x 10^{-6} mg/kg bw/d	
Exposure scenario	**Exposure route**	**Systemic dose (mg/kg bw/d)**	**MOE (MOE_{ref}= 600)**	**AEL%=(Exp x 100) /AEL**
Infant – ingestion of poison bait (5g)	Oral	1.8×10^{-2}	0.11	782609
Infant – ingestion of poison bait (10mg)	Oral	3.5×10^{-5}	57.1	1522

Conclusion
Based on default exposure values assuming infants will ingest poison bait there is a significant risk of poisoning. As such concern is raised for these scenarios.

2.7.3.3 Risk for consumers via residues

The acute or chronic exposure to residues in food resulting from the intended uses is unlikely to cause a risk to consumers. Regarding consumer health protection, there are no objections against the intended uses.

2.8 Risk assessment for the environment

Active substance

The overall environmental fate profile reported in the assessment report of the Bromadiolone indicates that Bromadiolone is not readily biodegradable under environmentally relevant conditions or during sewage treatment processes. Hydrolysis of the active substance is not expected to be a significant process in the environment. Laboratory soil column leaching and aged leaching studies indicate that the active substance and any potential degradation products, even if released indirectly to soil in small quantities, are not likely to move through the soil profile and are unlikely to reach groundwater in significant quantities. The active substance is not expected to volatilize to or persist in air in significant quantities.

Biocidal product

The product takes the form of a solid paste containing 0.005% w/w bromadiolone. Other than the active ingredient, it is composed of food-grade materials forming a bait base. Baits are dyed red to make them unattractive to wildlife and to help detection of accidental ingestion or manipulation.

RATIBROM 2 PASTE baits are furnished in heat sealed filter paper bags and weights 20 g each.

RATIBROM 2 PASTE is intended for professional use to control rodent pests in and around industrial, commercial and residential buildings, open areas and waste dumps; a domestic use in and around buildings is also envisaged.

The product is placed in plastic bait boxes such that rats and mice can eat it or, in situations where bait boxes cannot be used, the bait is covered such that non-target organisms cannot reach it. The amount of used product per application is 40 g per 10 square meters for mice and 60-100 g for rats. Baiting points are placed typically every 2-5 m for mice and 5-10 m for rats.

Dead rodents are removed for disposal as soon as possible, in order to prevent them being eaten by non-target animals and birds. When no more bait is eaten and rodent activity stops, the remains of all bait are removed for disposal.

Access to active substance data is granted by Activa s.r.l. Letter of Access. Therefore, when applicable, reference is made to the active substance data.

The environmental compartment reached by application of the product will be soil.
Considering the low vapour pressure of bromadiolone (2.13×10^{-8} Pa at 25°C) and considering that the active substance is embedded in a fat matrix the product is not expected to volatilize to or persist in air insignificant quantities.
No release in soil is expected since waste and residue of a mixture batch are usually recycled in new production batches.
No water emissions containing the substance arise from the formulation process.
Environmental exposure may result from the release of rodenticides from its use and disposal. Direct environmental exposure may take place when rodenticides are applied outdoors on public and private areas around buildings or constructions, on water banks, waste disposal sites and waste

dumps. The product is a ready to use formulation in the form of bait sachets or bait trays to be placed into bait stations. The use of bait station increase the safety of rodenticides and reduce the primary poisoning hazards of non-target animal. It is assumed that bait boxes minimizes environmental releases, in addition the use of boxes clearly improves the safety of bait placements and permits easy retrieval of uneaten bait at the end of a treatment

PEC in surface water, ground water and sediment

In and around buildings application.
Direct emission in surface water is not considered relevant for in and around buildings application of the product placed in bait boxes.
Open areas.
Direct emission in surface water is not considered relevant for open areas application of the product placed in bait boxes.
Waste dumps/landfills.
Direct emission in surface water is not considered relevant for landfills application of the product placed in bait boxes.

PEC in air compartment

In and around buildings application.
Direct emission in air is not considered relevant for in and around buildings application of the product placed in bait boxes.

Open areas
Direct emission in air is not considered relevant for open areas application of the product placed in bait boxes.

Waste dumps/landfills
Direct emission in air is not considered relevant for landfills application of the product placed in bait boxes.

PEC in soil compartment

In and around buildings application
The main exposure of the environment during in and around buildings application is expected to be soil contaminated by spills during application, refilling and disposal operations. However, the contributions from disperse release of rodenticide via urine and faeces should also be considered. The rodents may disperse the substance during its use period and spread it in the surroundings either directly by rats carrying the bait away from the bait boxes or through urine and faeces.
On a farm with a rat problem, the bait boxes are assumed to be distributed around the walls of the barn, stable and fodder buildings and at the manure collection areas
According to Emission Scenario Document for Biocides used as Rodenticides, a farm, which has a rat problem, presents a realistic worst case example. In this case it is assumed that 10 bait stations is used each filled with 250 g of baits, inspected and replenished 5 times. It is an assumption that all of the bait has been eaten. The duration of a rodenticide campaign is assumed to be 21days.

A summary of the input parameters used in the calculation is provided in the table below:

	Symbol	**Variable/parameters**	**Worst case (default values)**	**Realistic use**
INPUT	$Q_{prod:}$	amount of product used in control operation for each bait box [g]	250	60
	$Fc_{product}$:	fraction of active substance in product	0,00005	0,00005
	Nsites:	number of application sites	10	10
	N_{refil}:	number of refilling times	5	6
	$F_{release\text{-}D,\ soil}$:	fraction of product released directly to soil	0,01	0,01

	$F_{release\text{-}ID,\ soil}$:	fraction released indirectly to soil	0,9	0,2[1]
	$F_{metabolised:}$	fraction of active ingredient metabolised		
INPUT	$AREA_{exposed}$:	area directly exposed to rodenticide originating from bait box [m^2]	0,09	0,09
	$DEPTH_{soil}$:	depth of exposed soil [m]	0,1	0,1
	RHO_{soil}:	density of exposed soil [kg/m^3]	1700	1700
	$Elocal_{soil\text{-}campaign,\ direct}$:	direct emission to soil from a campaign [g/camp]	0,006	0,002
	$Elocal_{soil\text{-}campaign,\ indirect}$:	indirect emission to soil from a campaign [g/camp]	0,557	0,036
	$Elocal_{soil\text{-}campaign}$:		0,563	0,037
	$AREA_{exposed\text{-}ID}$:	area indirectly exposed to rodenticide [m^2]	550	550
OUTPUT	$Elocal_{soil\text{-}D\text{-}campaign}$	Local direct emission rate of active substance to soil from a campaign: [g/camp]	0,0063	0,002
	$Clocal_{soil\text{-}D}$	Local concentration in soil due to direct release after a campaign: [mg/kg]	0,0408	0,012
	$Clocal_{soil\text{-}ID}$	Concentration in soil due to indirect (disperse) release after a campaign: [mg/kg]	0,0060	0,000
	$Clocal_{soil}$	Total concentration in soil [**mg/kg]**	**0,0468**	0,012

[1] Refinements: as a worst case assumption 20 % of ingested active substance is released via urine and faeces as unchanged bromadiolone and bromadiolone-based metabolites.

Form this scenario the local PEC in industrial/application soil estimated is 0.0468 mg/kgwwt (wwt=wetweight) considering worst case and 0.012 mg/kgwwt considering a realistic use.

Open areas

This scenario covers control of rats and water voles in open areas such as around farmland, parks and golf courses where the aim is to prevent "nuisance" from burrows or "soil heaps" or due to public hygiene reasons. Rodenticides are also used to reduce impacts on game rearing or outside food stores. The product is placed in bait stations applied on the surface. According to Emission Scenario Document for Biocides used as Rodenticieds, direct emission in soil during open area application is considered to be the same estimated for the in and around buildings application.

Waste dumps/landfills

In some instances, applications of rodenticides to refuse dumps take place. Mostly this use is limited to occasions of population outbreaks of rats. Often the rodenticides are deployed around the perimeter of the dump, more than in the disposal area itself. The bait stations may be placed at regular places. The dumps are visited 4 to 6 times per year by a rodent control service and rodenticide baits are applied to the dump. A summary of the input parameters used in the calculation is provided in the table below:

	Symbol	**Variable/parameter**	**Worst case (default values)**	**Realistic use**
INPUT	Q_{prod}	amount of product used in control operation [kg]	300	40
	$Fc_{product}$	fraction of active substance in product	0,00005	0,00005

	N_{app}	number of applications	7	7
	$F_{release, soil}$	fraction of product released to soil	0,9	0,9
	$AREA_{exposed}$	area exposed to rodenticida[m^2]	10000	10000
	$DEPTH_{soil}$	depth of exposed soil [m]	0,1	0,1
	RHO_{soil}	density of wet exposed soil [kg/m^3]	1700	1700
OUTPUT	$Elocal_{soil\text{-}campaign}$	Local emission of active substance to soil from a campaign [g]	0,0945	0,0126
OUTPUT	**$Clocal_{soil}$**	Local concentration in soil after a campaign [**mg/kg +**	**0,0000556**	**0,0000074**

Form this scenario the local PEC (worst case) in industrial/application soil estimated is 5.56 x 10^{-5} mg/kgwwt and a realistic value of 7.4 x 10^{-6} mg/kgwwt.

Commento [o2]: Bromadiolone has been evaluated as a rodenticide against rats and mice for the following use patterns: sewers (professional use only) and in and around buildings (professional and non-professional use). CAR a.s.

Effect assessment

The BCF value was derived by calculation from the log Kow, resulting in a BCF of 575. It can be concluded that bromadiolone has a low to moderate potential to bioconcentrate in fish tissues.
Based on the results of acute toxicity studies, bromadiolone is toxic to fish.
Algae represented the most sensitive of the three aquatic trophic levels tested, in spite of the fact that the conditions necessary in algal growth inhibition tests are the ones most likely of all the aquatic acute toxicity tests to result in lowering of exposure concentrations, based on the photo-instability of bromadiolone in aqueous solution. The effect of bromadiolone on aerobic biological sewage treatment processes was assessed by determining inhibition of respiration of the micro-organisms present in activated sludge following three-hour contact and the resulting calculated EC50 was 31.6 mg/L (nominal). The effect of bromadiolone on earthworms was assessed in an acute toxicity test in which E. foetida were exposed in artificial soil to a liquid formulation containing 10.34 g bromadiolone/L. The 14-day LC50 of bromadiolone was greater than 9.48 mg/kg dry soil, the highest concentration applied. If this value is normalized with respect to moisture content of the soil, the resulting LC50 is 8.4 mg/kg soil. Bromadiolone is toxic to birds, based on acute oral and short-term dietary toxicity tests conducted with two species. Three studies have been presented that were conducted to simulate the secondary poisoning of non-target predatory birds and mammals that may potentially occur following intake of poisoned target rodents containing bromadiolone residues. In conclusion, the intake of poisoned rats may cause severe effects including death to predatory birds. The effect on wild mammals seems to be less severe, but the submitted study comprised a limited number of animals and the concentration of bromadiolone in the mice fed to the martens was not known.

No risk for the aquatic compartment is foreseen.

No risk for the atmospheric compartment is foreseen.
The PNECsoil is set to 0.0885 mg/kg soil according to the assessment report of the active substance. The terrestrial PEC/PNEC ratio is smaller than 1, indicating an acceptable risk for the terrestrial ecosystem.

Primary and secondary poisoning

Due to the highly toxic nature of Bromadiolone, primary and secondary poisoning presents a hazard to non target mammals and birds following use in and around buildings. The quantitative risk assessments shows that there are, in some cases very high, unacceptable risks to non-target vertebrates via primary and secondary poisoning. Therefore, it would seem more appropriate to develop and validate risk management procedures than to refine the risk assessment procedures.

However, the target rodents are vermin and thus constitute a danger to public health. Moreover, it has not yet been established that adequate alternatives to bromadiolone exist, which are both equally effective and less damaging to the environment.

To minimise the likelihood of target rodents developing resistance to second-generation anticoagulant rodenticides, long-term deployment of baits as a preventative control measure is not recommended. Product labels additionally instruct users to retrieve and securely dispose of all unconsumed baits at the end of control programmes. Both these factors limit the opportunity for exposure and reduce the primary poisoning risk to small non-target animals. Provided that baits are deployed in accordance with the product labelling and other approved guidance on good practice, the primary poisoning risk to non-target mammals may be considered to be negligible.

2.9 Measures to protect man, animals and the environment

The instructions for use must contain the following indications:

- Always read the label before use and follow the instructions provided.
- Keep out of reach of children.
- Keep away from food, drink and animal feeding stuffs.
- Avoid contact with skin.
- Wear suitable gloves during use (professionals only).
- If swallowed, seek medical advice immediately (show the label where possible).
- Do not smoke eat or drink while handling this product.
- Baits must be secured in tamper resistant bait boxes to minimise the risk of consumption and poisoning to children, companion animals and other non-target animals.
- Bait boxes must be placed in areas inaccessible to children, companion animals and non-target animals.
- Bait boxes must always be clearly labelled “Do Not Touch” and warn of the contents.
- In public areas (such as business premises, schools, hospitals etc) it must be clearly signed that rodenticide control is in operation. Signage must provide information on the risks of interfering with the product and dead rodents.
- Do not use in agriculture.
- Dead rodent bodies must be collected during all control operations to minimise the risk of consumption and poisoning to children, companion animals and other non-target animals.
- Wear suitable gloves during dead rodent collection.
- Wash hands and face after application and use of the product, and before eating, drinking or smoking.

Methods and precautions concerning storage

The product is not affected by the variation of temperature normally reached in a warehouse owing to seasonality. However, it should be stored in a closed, dry and well-ventilated area, only in those adopted by the supplier.

Keep away from children. Keep away from food, drinks or animal feedingstuffs. Protect from light, heat and naked flames.

Methods and precautions concerning transport

Normal precautions for stable and non-reactive products should be adopted.

Methods and precautions concerning fire

Suitable extinguishing agents: carbon dioxide, foam, powders.
Non-suitable extinguishing media: none in particular

Special Protective equipment: Wear self-contained respiratory apparatus; wear protective clothing in order to avoid contact with the skin and the eye.

Special exposure risks: bromadiolone may release toxic fumes.

Specific treatment in case of an accident, e.g. first-aid measures, antidotes, medical treatment if available
General advice: In the case of accident or if you feel unwell, seek medical advice immediately (show the label where possible and report the authorisation number).
Prevent the access of children and domestic animals. Do not contaminated foodstuffs with the product.
First aid measures:

- Inhalation: None
- Skin contact: Flush skin immediately and thoroughly with soap and water. Seek medical advice.
- Eye contact: Flush immediately and thoroughly with soap and water. Seek medical advice.
- Ingestion: Seek medical advice immediately and show the container or label.

ADVICE FOR DOCTORS:

Pharmaceutical-dynamic action: the active substance contained in the product is a competitive antagonist of Vitamin K and reduces the hepatic synthesis of K-dependent factors.

Symptoms: heavy poisoning by ingestion inhibits the vitamin K, causing skin and mucous aemorrhages. The symptomatology of the other systems and apparatus is prevailingly haemorrhagic.

Therapy: in case of ingestion of big quantities, provoke vomiting, perform gastric lavage and monitor the protrombinic activity; if it reduces, give vitamin K.

Controindications: anticoagulants.

Emergency measures to protect the environment

The product must not penetrate the sewers, surface water, ground water and neighbouring areas.

Methods for cleaning up: collect the product with mechanical means, store it in tight containers and dispose according to local legislation.

Procedures, if any, for cleaning application equipment
No application equipment used.

Identity of relevant combustion products in cases of fire
Special exposure hazards in a fire: as for all organic materials, combustion may lead to formation of hazardous oxides of carbon, nitrogen and other toxic fumes.

Procedures for waste management of the biocidal product and its packaging and where relevant, treated waste material for industry, professional users and the general public (nonprofessional users), e.g. *p*ossibility of reuse or recycling, neutralisation, conditions for controlled discharge, and incineration.
Product: Dispose the product waste in accordance with the local rules. Reuse or recycle the unused product when possible.
Empty packaging: empty containers are considered wastes of the same class of the contents and should be disposed of in accordance with the relevant local rules.
Carcasses of dead rodents collected during campaign should be disposed safely.

Possibility of destruction or decontamination following accidental release in or on the following: (a) Air; (b) Water, including drinking water; (c) Soil

Air: Bromadiolone has a very low vapour pressure, and decomposes at around 220°C and therefore and therefore the risk of release of the active ingredient to the atmosphere is negligible.

Water (including drinking water) in or on soil: Avoid soil and water contamination. If the product gets into water, it should be removed mechanically and disposed of according to local rules. In the case of environmental contamination, inform the authorities.

Observations on undesirable or unintended side-effects, e.g. on beneficial and other non-target organisms

The product is palatable to non-target species in sufficient quantity to produce toxic effects. The active substance will have the same toxic effect in non-target species as in target species.

In case of ingestion by non-target species seek for veterinary showing the container or label.

Specify any repellents or poison control measures included in the preparation that are present to prevent action against non-target organisms

Denatonium benzoate, at low concentrations, is used as repellent for non-target organism, specially children.

3 Proposal for decision

It is considered that the evaluation has shown that sufficient data have been provided to verify the outcome and conclusions, and permit the proposal for granting an authorisation of the biocidal product RATIBROM 2 PASTE.

All the elements listed in Doc I, section 3.3, of the CAR on Bromadiolone (Sweden, 2010) have been taken into account when authorising RATIBROM 2 PASTE.

Due to the unacceptable risk calculated for infants ingesting the product, it is considered appropriate to limit aspects of the packaging for non professional use as a further risk mitigation measure.

Non-professional baits are to be used in refillable tamper-resistant bait stations and supplied as inner packs or units containing at most enough bait for one bait-point (either rat or mouse) with a maximum pack-size of 500g.

Annex:

1. **Summary of product characteristics**
2. **List of studies reviewed**
3. **Analytical methods residues – active substance**
4. **Toxicology and metabolism –active substance**
5. **Toxicology – biocidal product**
6. **Safety for professional operators**
7. **Safety for non-professional operators and the general public**
8. **Residue behaviour**

Annex 1: Summary of product characteristics

(a) Product trade name: RATIBROM 2 PASTE

(b) (i) Qualitative and quantitative information on the composition of the biocidal product

NB: This information is confidential and should not be disclosed to third parties

Active substance(s)				Contents				
Common name	IUPAC name	CAS number	EC number	Concentration	Unit[2]	w/w (%)	Minimum purity (% w/w)	Same source as for Annex I inclusion
Bromadiolone	3-[(1RS,3RS;1RS,3SR)-3-(4´-bromobiphenyl-4-yl)-3-hydroxy-1-phenylpropyl]-4-hydroxycoumarin	28772-56-7	249-205-9	0.050	g/kg	0.0050	96.9	☒ yes ☐ no
Add rows as necessary								

Co-formulants					Contents				
Common name	IUPAC name	Function	CAS number	EC number	Concentration	Unit	w/w (%)	Classification	Substance of concern
Denatonium benzoate	benzyldiethyl(2,6-xylylcarbamoylmethyl)ammonium benzoate	Human taste deterrent	3734-33-6	223-095-2	0.01	g/kg	0.001	Xn; R20/22 Xi; R41, R38 R52/53	☐ yes ☒ no
Triethanol amine	2.2´,2”-nitriloethanol	Emulsifying agent	102-71-6	203-049-8	3.00	g/kg	0.300	-	☐ yes ☒ no
Polyethylene glycol 200	Poly(oxy-1,2-ethanediyl),α-hydro-ω-hydroxy-Ethane-1,2-diol, ethoxylated	Solvent	25322-68-3	500-038-2	1.50	g/kg	0.150	-	☐ yes ☒ no
Propylene glycol	1,2-propanediol	Solvent	57-55-6	200-338-0	18.50	g/kg	1.850	-	☐ yes ☒ no
Pigment Red 49:1	Not available	Colorant	1103-38-4	2141606	0.50	g/kg	0.050	-	☐ yes ☒ no

2 g/l, g/kg, other. For biological products, the concentration should state the number of activity units/units of potency (as appropriate) per defined unit of formulation (e.g. per gramme or per litre).

Milk powder	**Not available**	**Bait**	**-**	**-**	**1.50**	**g/kg**	**0.150**	**-**	☐ **yes** ☒ **no**
Sugar	**Sucrose, pure**	**Bait**	**57-50-1**	**200-334-9**	**10.00**	**g/kg**	**1.000**	**-**	☐ **yes** ☒ **no**
Talcum CM3	**Not available**	**Bait**	**14807-96-6**	**238-877-9**	**30.00**	**g/kg**	**3.000**	**-**	☐ **yes** ☒ **no**
Vegetable Oil (soy oil)	**Not available**	**Bait**	**8002-13-9**	**232-299-0**	**210.05**	**g/kg**	**21.005**	**-**	☐ **yes** ☒ **no**
Wheat flour	**Not available**	**Bait**	**-**	**-**	**722.59**	**g/kg**	**72.259**	**-**	☐ **yes** ☒ **no**
Bronopol	**2-bromo-2-nitro-1,3-propanediol**	**Preservative**	**52-51-7**		**0.50**	**g/kg**	**0.050**	**Xn; R21/22 Xi; R37/38-41 N; R50**	☐ **yes** ☒ **no**
BHA	**Phenol,(1,1-dimethylethyl)-4-methoxy-**	**Antioxidant**	**25013-16-5**	**246-563-8**	**0.60**	**g/kg**	**0.060**	**Xn; R22 Xi; R36/37/38 R40**	☐ **yes** ☒ **no**
BHT	**2,6-Di-tert-butyl-4-methylphenol**	**Antioxidant**	**128-37-0**	**204-881-4**	**0.60**	**g/kg**	**0.060**	**Xn; R22 Xi; R36//38 N; R51/53**	☐ **yes** ☒ **no**
Liquid Lecithins (Lecitin 100)	**Not available**		**8002-43-5**	**232-307-2**	**0.60**	**g/kg**	**0.060**	**-**	☐ **yes** ☒ **no**
Add rows as necessary									

Sum	**1000.0**		**100.0**

(b) (ii) Is the product identical to the representative product, assessed for the purpose of the Annex I inclusion?

☐ **yes** ☒ **no** ☐ **unknown**

If not, briefly describe the difference.

MINOR DIFFERENCES IN NON-ACTIVE INGREDIENTS

(b) (iii) Does the biocidal product contain or consist of Genetically Modified Organisms (GMOs) within the meaning of Directive 2001/18/EC?

☐ **yes** ☒ **no**

If yes, does the product comply with Directive 2001/18/EC?

☐ **yes** ☐ **no**

A copy of any written consent(s) of the competent authorities to the deliberate release into the environment of the GMOs for research and development purposes where provided for by Part B of the above-mentioned Directive was provided.

(c) Manufacturer(s) of the active substance(s) (name(s) and address(es) including location of plant(s))[3]

Name of the active substance: Bromadiolone

Manufacturer

Company Name: Activa S.r.l.
Address: Viale Lombardia, 22
City: Milano Postal Code: 20131 Country: Italy
Telephone: +39 02 70637301 Fax: +39 02 70637228 E-Mail:

Intra-Community VAT number or, for non EU companies, company registration number:

Manufacturing site(s) (if different)

Company Name: Dr Tezza S.r.l.
Address: Via Tre Ponti, 22
City: S.Maria de Zevio (VR) Postal Code: 37050 Country: Italy
Telephone: +39 45 6069004 Fax: + 39 45 6069118 E-Mail: dr.tezza@tin.it

Intra-Community VAT number or, for non EU companies, company registration number:

(d) Formulator(s) of the biocidal product (name(s) and address(es) including location of plant(s))[3]

Formulator

Company Name: Kollant S.r.l.
Address: Via Trieste, 49/53
City: Padova Postal Code: 35121 Country: Italy
Telephone: +39 049 9983000 Fax: +39 049 9986005
E-Mail: martina.carpanese@kollant.it

Intra-Community VAT number or, for non EU companies, company registration number: IT 03346320967

Formulation site(s) (if different)

Company Name: Kollant S.r.l.
Address: Via C. Colombo, 7/7A
City: Vigonovo (VE) Postal Code: 30030 Country: Italy
Telephone: + 39 049 9983001 Fax: + 39 049 9983005 E-Mail:

Intra-Community VAT number or, for non EU companies, company registration number: IT 03346320967

3 All sites involved in the manufacturing process of each active substance and of the product must be listed.

Physical state and nature of the biocidal product:

(e) Type of formulation: Paste bait

(f) Ready-to-use product: ☐no ☒ yes

Classification and labelling statements of the biocidal product:

(g) Product classification: Not classified

(h) Risk and Safety Phrases:

Risk Phrases: None

Safety Phrases:

S1/2 Keep locked up and out of the reach of children.

S13 Keep away from food, drink and animal feeding stuffs.

S20/21 When using, do not eat, drink or smoke

S24 Avoid contact with skin

S37 Wear suitable gloves (professionals only)

S46 If swallowed, seek medical advice immediately (show the label where possible)

S61 Avoid release to the environment. Refer to special instructions/Safety data sheet

(i) Product classification according to GHS: Not classified

(j) Hazard statement according to GHS: None

Intended uses and efficacy:

(k) PT: 14

(l) Target harmful organisms: Brown rat (*Rattus norvegicus*); House mouse (*Mus musculus*)

(m) Development stage of target organisms: Juveniles; Adults

(n) Function/mode of action: Rodenticide/Anticoagulant

(o) Field of use: In and around buildings; open areas (professional use only)

(p) Application aim: Stored product protection/food protection; Health protection

(q) User category: Professional and non-professional/general public

(r) Application method[4]: Covered application (in bait stations, other covering)

Directions for use[5]:

4 Indicate how the product will be applied (e.g. brush, spray, dipping, bait, etc). Where the product is to be used by more than one user category, indicate the application method(s) intended for each user category.
5 Provide in the following sections the information as it is proposed to appear on the product label or appropriate product literature.

(s) M*a*nner and area of use[6]:

RATIBROM 2 PASTE is used for the control of brown rat (*Rattus norvegicus*) and house mouse (*Mus musculus*).

The active substance Bromadiolone is an anticoagulant rodenticide/Vitamin K antagonist.

RATIBROM 2 PASTE can be used in and around buildings, open areas and waste dumps (only professional use).

RATIBROM 2 PASTE can be used by professionals and non-professionals/general public.

RATIBROM 2 PASTE is applied via tamper resistant bait stations. Bait is deposited and fixed in the bait stations. Stations and baiting points are controlled in an interval of 7 days and consumed bait is replaced.

Non professionals baits should be supplied as inner packs or units containing at most enough bait for one bait point (either rat or mouse) and used only in refillable tamper-resistant bait stations.

(t) Conditions of use7:

The amount of product used per application is 40 g per $10m^2$ for *Mus musculus* and 60 - 100 g per $10m^2$ for *Rattus norvegicus*.

Bait points are placed typically every 2 to 5 m for mouse infestation and 5 to 10 m for rat infestation. Closer placement is required for heavier infestations. The duration of the program is at maximum up to 6 weeks. Permanent, preventive treatments are possible under the supervision of a pest control operator or other competent operator. In case of permanent baiting, a minimum dose shall be applied (60 g) and the baiting points are inspected 4-6 times per year.

(u) Instructions for safe use of the product:[8]

The bait must be placed in appropriate bait stations, protected from atmospheric agents, in order to avoid accidental swallowing of infants, non target species and undesired dispersion of bait in the environment.

Avoid to touch barehanded the product. Utilize the appropriate gloves (professionals only).

Rodents eat the bait over one or more days and die typically 4-10 days later.

Place the container in place of major presence and fixed in order to avoid dispersion of bait in the environment.

(v) Particulars of likely direct or indirect adverse effects and first aid instructions:

MECHANISM OF ACTION: the active ingredient of RATIBROM 2 PASTE is a long lasting anticoagulant chemical and decreases the hepatic synthesis of k-dependent factors.

SYMPTONS: Severe poisoning by ingestion causes Vitamin K inibithion , causing dermal and mucous haemorrhages. Symptoms to occur in other systems is mainly haemorrhagic. TERAPY: if large quantities

6 Indicate information on the target organisms, the mode of action, the field of use, the application aim, the user category and the application method. All efficacy claims should be reflected.
7 Include the details of the directions for use. This should be expressed in terms of amount of product per unit area or a length of application (e.g. dip for 3 minutes). For aerosols and sprays a discharge rate should be included. If the product is a concentrate, indicate the dilution rate(s) here (e.g. *dilute 1 part of product with x parts of water*).
8 Where appropriate, indicate here the period of time needed for the biocidal effect, the interval to be observed between applications of the biocidal product or between application and the next use of the product treated, or the next access by man or animals to the area where the biocidal product has been used, including particulars concerning decontamination means and measures and duration of necessary ventilation of treated areas; particulars for adequate cleaning of equipment; particulars concerning precautionary measures during use, storage and transport (e.g. personal protective clothing and equipment, measures for protection against fire, covering of furniture, removal of food and feedingstuff and directions to prevent animals from being exposed).

are ingested, induce vomiting, perform gastric lavage and monitor prothrombin activity, if decreased Vitamin K1 should be administered. Follow the appropriate medical protocol.

(w) Instructions for safe disposal of the product and its packaging:

Keep out of the reach of children. Keep container tightly closed. Keep away from food, drink and animal feed stuffs. Store in original container, tightly closed, in a safe place. The product should not be re-used or recycled. Unconsumed product should be collected and disposed in accordance with local requirements.

(x) Conditions of storage and shelf-life of the product under normal conditions of storage: two years

(y) Additional information:

Packaging details are provided in the table below.

Users	Material	Pack size
Professional	PET bag	Up to 25 kg (containing edible paper sachets of pasta bait 20 g each)
Non-professional	PET bag	Up to 500 g (containing edible paper sachets of pasta bait 20 g each)

Annex 2: List of studies reviewed

List of new data[9] submitted in support of the evaluation of the active substance

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
						Yes	No	Yes	No
						☐	☐	☐	☐
Add rows as necessary									

List of new data submitted in support of the evaluation of the biocidal product

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
						Yes	No	Yes	No
B3	B3.1/01 & B3.5/01 & B3.6/01	Paronuzzi Ticco S.	2010	RATIBROM 2: Determination of the Physico-chemical Properties ChemService s.r.l., Study No. CH - 330/2010 GLP, Unpublished.	Kollant S.r.l.		☒	☒	☐
B3	B3.7.1/01	Paronuzzi Ticco S., Ravetta G.	2010	RATIBROM 2: Two Years Storage Stability and Corrosion Characteristics ChemService s.r.l., Study No. CH - 115/2010 GLP, Unpublished.	Kollant S.r.l.		☒	☒	☐

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

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
						Yes	No	Yes	No
B3	B3.7.1/02 & B3.7.2/01	Paronuzzi Ticco S., Zacchello G.	2011	RATIBROM 2: Determination of the Accelerated Storage Stability and Corrosion Characteristics ChemService s.r.l., Study No. CH - 331/2010 GLP, Unpublished.	Kollant S.r.l.		☒	☒	☐
B3	B3.7.1/03 & B3.7.2/02	Paronuzzi Ticco S.	2011b	RATIBROM 2: Determination of the Accelerated Storage Stability and Corrosion Characteristics at 40°C ChemService s.r.l., Study No. CH - 334/2010 GLP, Unpublished.	Kollant S.r.l.		☒	☒	☐
B4	B4.1/01	Paronuzzi Ticco S.	2010	RATIBROM 2: Validation of the analytical method for the determination of the active ingredient content ChemService s.r.l., Study No. CH-114/2010 GLP, Unpublished.	Kollant S.r.l.		☒	☒	☐
B5	B5.10/01	Freli V.	2011	Rodenticide Efficacy Evaluation and Palatability on Ratibrom 2 in accelerated aging conditions Eurofin Biolab S.r.l. Assay Center., Study ID: 2010/1266 SAM Unpublished	Kollant S.r.l.		☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
						Yes	No	Yes	No
B5	B5.10/05	Rovetto I.	2010	Efficacy evaluation of RATIBROM 2 (bromadiolone 0,005% a.i. pasta bait) against Norway rat (Rattus norvegicus Berk.) in Italy. Sagea Centro di Saggio S.r.l., Trial code: 1017.BCD.SAG09 Unpublished	Kollant S.r.l.		☒	☒	☐
B5	B5.10/06	Rovetto I.	2010	Efficacy evaluation of RATIBROM 2 (bromadiolone 0,005% a.i. pasta bait) against House mouse (Mus musculus L.) in Italy. Sagea Centro di Saggio S.r.l., Trial code: 1018.BCD.SAG09 Unpublished	Kollant S.r.l.		☒	☒	☐
B6	B6.1.1/01	Shegar S.	2011	Acute oral toxicity study of RATIBROM 2 in rats. Jai Research Foundation, Study N° 401-1-01-2069 GLP, Unpublished	Kollant S.r.l.		☒	☒	☐
B6	B6.1.2/01	Shegar S.	2011	Acute dermal toxicity study of RATIBROM 2 in rats. Jai Research Foundation, Study N° 403-1-01-2070 GLP, Unpublished	Kollant S.r.l.		☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
						Yes	No	Yes	No
B6	B6.2.1/01	Shegar S.	2011	Acute dermal irritation study of RATIBROM 2 in rabbits. Jai Research Foundation, Study N° 406-1-01-2071 GLP, Unpublished	Kollant S.r.l.		☒	☒	☐
B6	B6.2.2/01	Shegar S.	2011	Acute eye irritation study of RATIBROM 2 in rabbits. Jai Research Foundation, Study N° 407-1-01-2072 GLP, Unpublished	Kollant S.r.l.		☒	☒	☐
Add rows as necessary									

Annex 3: Analytical methods residues – active substance

Bromadiolone

Matrix, action levels, relevant residue and reference

matrix	limit	relevant residue	reference or comment
plant products			
food of animal origin			
soil			
drinking water			
surface water			
air			
body fluids / tissues			

Methods suitable for the determination of residues (monitoring methods)

Methods for products of plant origin

reference	matrix	LOQ (mg/kg)	principle	comment	owner
Annex IIIA, point IV.1	cucumber, wheat,	0.01	LC/MS/MS	Multiresidue method	
Annex IIIA, point IV.1	oilseed rape, lemon	0.01	LC/MS/MS	Single method	

Methods for foodstuffs of animal origin

reference	matrix	LOQ (mg/kg)	principle	comment	owner
Annex IIIA, point IV.1	bovine meat and liver	0.01	LC/MS/MS	None	

Methods for soil

reference	LOQ (mg/kg)	principle	comment	owner
AnnexIIA, point 4.2	0.01	HPLC/MS/MS	None	

Methods for drinking water and surface water

reference	matrix	LOQ (µg/l)	principle	comment	owner
Annex IIA, point 4.2	water	0.05	HPLC/MS	LC/MS/MS confirmatory	

Methods for air

reference	LOQ (µg/m3)	principle	comment	owner
Annex IIA, Point 4.2	0.5	HPLC/UV	No confirmatory method available-not considered needed due to the low vapour pressure	

Methods for body fluids/tissue

reference	matrix	LOQ (mg/kg)	principle	comment	owner
Annex IIA, point 4.2	Blood, liver	0.01	LC-MS/MS	None	

Annex 4: Toxicology and metabolism –active substance

Bromadiolone

Threshold Limits and other Values for Human Health Risk Assessment

Date: xx.xx.xxxx

Summary			
	Value (µg/kg bw/day)	Study	SF
AEL long-term	0.0012*	90-day rabbit	300
AEL medium-term	0.0012*	90-day rabbit	300
AEL acute	0.0023*	Developmental toxicity study rabbit	600

*corrected for 70% oral absorption

Inhalative absorption	No data available. Exposure via inhalation is expected to be negligible both during production and during the use of the baits.
Oral absorption	>70% (71-77% based on carcass, urinary- and biliary excretion, Task Force data)
Dermal absorption	10% default value for the pure active substance. No study on the pure active substance is available. Default value agreed on the basis of MW (>500) and log Pow (>4) . 0.36% agreed as a worst case value, based on an in vitro study of formulated active (bait:saline incorporated bromadiolone 0.00255 w/w) and a representative wax block formulation (0.005 % w/w).

Classification	
with regard to toxicological data (according to the criteria in Dir. 67/548/EEC)	T+; N; R26/27/28, T; R48/23/24/25, Repr.Cat. 1 or 2; R61; 50-53
with regard to toxicological data (according to the criteria in Reg. 1272/2008)	Acute tox. 1; H300, H310, H330 Repr. 1A; H360D STOT RE 1; H372 Aquatic Acute 1; H400 Aquatic Chronic 1; H410 C≥0.01% STOT RE 1; H372 0.001%≤C<0.01% STOT RE 2; H373 M-factor 1

Annex 5: Toxicology – biocidal product

Ratibrom 2 Paste

Date: xx.xx.xxxx

General information

Formulation Type	Solid paste
Active substance(s) (incl. content)	Bromadiolone (0.005% w/w)
Category	

Acute toxicity, irritancy and skin sensitisation of the preparation (Annex IIIB, point 6.1, 6.2, 6.3)	
Rat LD50 oral (OECD 420)	>2000 mg/kg bw
Rat LD50 dermal (OECD 402)	>2000 mg/kg bw
Rat LC50 inhalation (OECD 403)	not required
Skin irritation (OECD 404)	Not irritant
Eye irritation (OECD 405)	Not irritant
Skin sensitisation (OECD 429; LLNA)	Not sensitizer, on the basis of the classification of both the active substance and the other components. However, since the Applicant stated that a new skin sensitization study on RATIBROM 2 was ongoing, a complete evaluation of these results is required.

Additional toxicological information (e.g. Annex IIIB, point 6.5, 6.7)	
Short-term toxicity studies	Not required
Toxicological data on active substance(s) (not tested with the preparation)	No other active substances (not tested with the preparation)
Toxicological data on non-active substance(s) (not tested with the preparation)	No other non-active substances (not tested with the preparation)
Further toxicological information	Not required

Classification and labelling proposed for the preparation with regard to toxicological properties (Annex IIIB, point 9)	
Directive 1999/45/EC	Not classified S(1/2) Keep locked up and out of the reach of children S13 Keep away from food, drink and animal feed stuffs S20/21 When using, do not eat, drink or smoke S24 Avoid contact with skin and eye S37 Wear suitable gloves (only for professionals) S46 If swallowed, seek medical advice immediately (show label where possible) S61 Avoid release to the environment. Refer to special instructions/safety data sheet
Regulation 1272/2008/EC	Not classified

Annex 6: Safety for professional operators

Ratibrom 2 Paste

Date: xx.xx.xxxx

Exposure assessment

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

Primary exposure of professionals

Component	**CAS**	**Potential Dermal Total [mg/day]**	**Potential Dermal Total [mg/kg/d]**	**Actual Dermal Total [mg/day]**	**Actual Dermal Total [mg/kg/d]**	**Inhalation Exposure [mg/m³]**	**Model**
Bromadiolone	28772-56-7	-	5.3×10^{-6}	-	5.3×10^{-7}	n.a.	HEEG harmonisation paper (based on Chambers, 2009)

Risk assessment

Component	**CAS**	**AEL [mg/kg/d]**	**Absorption**		**Inhal ext [mg/m3]**			**Derm ext [mg/kg/d]**		
			inh	derm	Act. Expo	**% AEL**	**MoE**	Act. Expo	**% AEL**	**MoE**
Bromadiolone	28772-56-7	1.2×10^{-6}	-	0.36%	-	-	-	5.3×10^{-7}	44.2	943

The risk assessment for the substance(s) of concern has to be carried out in almost the same manner.

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

Ratibrom 2 Paste

Date:xx.xx.xxxx

General information	
Formulation Type	Solid paste
Active substance(s) (incl. content)	Bromadiolone (50 mg/kg)
Category	PT14
Authorisation number	

Bromadiolone

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

Exposure scenarios for intended uses (Annex IIIB, point 6.6)	
Primary exposure	Placing and clean-up of solid paste baits furnished in heat sealed filter paper bags
Secondary exposure, acute	Infant – ingestion of poison bait (5g; 10mg)
Secondary exposure, chronic	-

Conclusion:
Exposure of non-professionals and the general public to the biocidal product containing 50mg/kg as active substance is considered acceptable, if the biocidal product is used as intended and all safety advices are followed.

Details for the exposure estimates: none

Annex 8: Residue behaviour

Bromadiolone

Intended Use: professional and domestic use
Active substance(s):Bromadiolone
Formulation of biocidal product: Ready to use Bait (RB)
Place of treatment: in and around buildings, in open areas and waste dumps
Pest: brown rat (*Rattus norvegicus*) and house mouse (*Mus musculus/domesticus*)
The formulation is a ready to use bait containing 0.005 % w/w of the anticoagulant active ingredient bromadiolone. The product is supplied in heat sealed food paper bags of 20 g each. The treatments last at maximum 6 weeks. The amount of used product per application 40 g per 10 square meters for house mice and 60 - 100 g per 10 square meters for rats, depending on the severity of the infestation. Bait points are placed typically every 5-10m. The product is placed in a bait station or fixed to a structure such that rats and mice can eat them. In situations where bait boxes cannot be used, the bait is covered such that non-target organisms cannot reach them. Baiting points are inspected at least weekly and replenished when bait has been eaten. Dead rodents are removed for disposal in order to prevent them being eaten by non-target animals and birds.

The intended use descriptions of the Bromadiolone – contained in biocidal products for which authorisation is sought indicate that these uses are not relevant in terms of residues in food and feed. The product is to be used against Brown rat, Black rat and House mouse. No further data are required concerning the residue behaviour.

The intended uses are not relevant in terms of consumer health protection.