Product Assessment Report

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

MAKI GRAIN'TECH

LIPHATECH S.A.S.

November 2012

Internal registration/file no:	PB-11-00057
R4BP no:	2011/4329/10510/FR/AA/20485
Authorisation n°	FR-2013-0035 (Pro) / FR-2013-1025 (General users)
Granting date/entry into force of authorisation/ registration:	2013-07-24
Expiry date of authorisation/ registration:	2016-06-30
Active ingredient:	BROMADIOLONE
Product type:	14

Competent Authority in charge of delivering the product authorisation:
French Ministry of Ecology
Department for Nuisance Prevention and Quality of the Environment
Chemical Substances and Preparation Unit
Grande Arche, Paroi Nord
92 055 La Défense cedex – FRANCE
autorisation-biocide@developpement-durable.gouv.fr

Authority in charge of the efficacy and risk assessment:
Anses – French agency for food, environmental and occupational health and safety
Regulated Products Directorate
253 Avenue du Général Leclerc
94 701 Maisons-Alfort Cedex - FRANCE
biocides@anses.fr

Contents

1 GENERAL INFORMATION ABOUT THE PRODUCT APPLICATION

1.1 Applicant

Company Name:	LIPHATECH SAS
Address:	Bonnel BP3
City:	Pont du Casse
Postal Code:	47480
Country:	FRANCE
Telephone:	+ 33 5 53 69 35 70
Fax:	+ 33 553 479 501
E-mail address:	corg@liphatech.fr

1.1.1 Person authorised for communication on behalf of the applicant

Name:	Gabrielle COR
Function:	Regulatory affairs manager
Address:	Bonnel BP3
City:	Pont du Casse
Postal Code:	47480
Country:	FRANCE
Telephone:	+33 5 53 69 36 37
Fax:	+ 33 553 479 501
E-mail address:	corg@liphatech.fr

1.2 Current authorisation holder[1]

Company Name:	LIPHATECH SAS
Address:	Bonnel BP3
City:	Pont du Casse
Postal Code:	47480
Country:	FRANCE
Telephone:	+ 33 5 53 69 35 70
Fax:	+ 33 553 479 501
E-mail address:	corg@liphatech.fr
Letter of appointment for the applicant to represent the authorisation holder provided (yes/no):	yes

[1] Applies only to existing authorisations

1.3 Proposed authorisation holder

Company Name:	LIPHATECH SAS
Address:	Bonnel BP3
City:	Pont du Casse
Postal Code:	47480
Country:	FRANCE
Telephone:	+ 33 5 53 69 35 70
Fax:	+ 33 553 479 501
E-mail address:	corg@liphatech.fr
Letter of appointment for the applicant to represent the authorisation holder provided (yes/no):	yes

1.4 Information about the product application

Application received:	27/06/2011
Application reported complete:	26/07/2011
Type of application:	Product authorisation
Further information:	New product

1.5 Information about the biocidal product

1.5.1 General information

Trade name:	MAKI GRAIN'TECH
Manufacturer's development code number(s), if appropriate:	BROBL0,0050_05F_LR0234-00
Product type:	PT14 - Rodenticide
Composition of the product (identity and content of active substance(s) and substances of concern; full composition see confidential annex):	Active substance's identity and content: Bromadiolone 0.005% w/w No substance of concern
Formulation type:	VIII.3.1 Granular 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); If yes: authorisation/registration no. and product name: or Has the product the same identity and	No No

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):	

1.5.2 Information on the intended use(s)

Overall use pattern (manner and area of use):	TP14 - Rodenticide Bromadiolone grains baits are used in areas in and around buildings, open areas and waste dumps. Grain products containing bromadiolone are not used in sewers. Products can be supplied with and without sachets. Grain bait products containing bromadiolone are used to protect human food and animal feedstuffs and for general hygiene purposes.
Target organisms:	I.1.1 Murids : *Muridae* I.1.1.1 Brown rat: *Rattus norvegicus* I.1.1.2 Black rat: *Rattus rattus* I.1.1.3 House mouse: *Mus musculus* I.1.1.4 Other murids : *Apodemus sp* I.1.2 Microtids : *Microtus arvalis, Arvicola terrestris*
Category of users:	V1 Non professional / general public V.2 Professional
Directions for use including minimum and maximum application rates, application rates per time unit (e.g. number of treatments per day), typical size of application area:	VI.2 Covered application VI.2.1 in bait stations VI.2.2 other covering **1) For use in and around buildings** The product is typically used in response to an infestation. Firstly, the size and extent of the infestation can be determined by placing bait points containing bait only and observing the locations and amounts where bait is consumed (assume a rat consumes 25 g bait per day and a mouse 3.5 g per day). This is known as a pre-treatment baiting census. Also the target organism is identified. A pre-baiting census is less likely to be conducted by non-professionals (amateur) conducting small control campaigns indoors and more likely to be conducted by professionals conducting large scale control campaigns in and around farms and industrial areas. The purpose of the baiting census is to control the deployment of rodenticides in higher risk situations. The second phase involves replacing the bait

	with the rodenticide product. Depending on the infestation, over the area identified, the product is deployed in bait points containing up to 200 g every 4 to 5 m for rat infestations (or up to 50 g every 1 to 1.5 m for mice infestations). The bait points are visited on a regular basis (for example 1, 3, 5, 7 14, 21 days) and any consumed or spoilt rodenticide is replenished or replaced. Once the consumption of rodenticide has diminished sufficiently the second phase is deemed complete and any rodenticide not consumed is collected for disposal. A third phase can be conducted where bait points are again deployed with bait to determine the size of the population after the treatment. During the visits to bait points, any dead rodents visible are collected for disposal. **2) For use in open areas.** A pre-treatment baiting census is not always conducted. Product is deployed in burrows, up to 200 g per burrow on typically two occasions. After the control campaign any rodenticide not consumed is collected for disposal. During the visits to the treated areas, any dead rodents visible are collected for disposal. **3) For use in waste dumps.** For treatments in waste dumps, the product is always used in sachets. The product is typically used in response to an infestation. A pre-treatment baiting census may be conducted as described for use in and around buildings. Depending on the infestation, over the area identified, the product is deployed in bait points containing up to 200 g every 4 to 5 m for rat infestations (or up to 50 g every 1 to 1.5 m for mice infestations) around the perimeter of the waste dump. The bait points are visited on a regular basis and any consumed or spoilt rodenticide is replenished or replaced. Once the consumption of rodenticide has diminished sufficiently the control is deemed complete and any rodenticide not consumed is collected for disposal. Bait points may again be deployed with bait to determine the size of the population after the treatment. During the visits to bait points, any dead rodents visible are collected for disposal. The product is essentially little more than a food source (bait) and a means to deliver the

	active substance to the target populations. As such the amounts of product used depend on the estimated size and extent of the target population (sufficient bait is used to ensure adequate uptake for each target rodent) rather than the product type. As such the wax block and grain baits are used in similar ways. One of the factors affecting the uptake of a product is its attractiveness compared to other available food sources at a given location. Where food is not abundant, wax blocks are perfectly adequate. However, where natural food sources are plentiful, the product must be sufficiently attractive (i.e a grain bait) to ensure it is consumed. Therefore it is necessary to have various product types to ensure effectiveness is maintained in any particular situation. However, the patterns of actual use of the products are not prescriptive and the usage patterns we have attempted to describe are considered to be realistic worst-cases in terms of amounts used. For smaller target populations less product will be used.
Potential for release into the environment (yes/no):	yes
Potential for contamination of food/feedingstuff (yes/no)	no
Proposed Label:	To be used against domestic rodents: Brown rats *(Rattus novegicus*), Black rats *(Rattus rattus*), Mice (*Mus musculus* spp.), Voles (e.g. *Microtus arvalis*, *Arvicola terrestris*) and Field mice (*Apodemus sylvaticus*). Rat : up to 200 g every 4 to 5 meters, up to 200 g per burrow and quantities can be double if consumption is complete Mice : up to 50 g every 1 to 1.5 meters
Use Restrictions:	There are no specific use related restrictions.

For full details of the intended uses claimed by the applicant, please see annex 0a.

1.5.3 Information on active substance(s)[2]

Active substance chemical name:	Bromadiolone
CAS No:	28772-56-7
EC No:	249-205-9
Purity (minimum, g/kg or g/l):	> 96.9 % w/w
Inclusion directive:	2009-92-CE
Date of inclusion:	01/07/2011

[2] Please insert additional columns as necessary

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:	LiphaTech S.A.S.
Address:	Chemie Park Trostberg, Dr Albert Frank strasse 32
City:	Trostberg
Postal Code:	83308
Country:	Germany
Telephone:	+33 5 53 69 36 37
Fax:	+33 5 53 47 95 01
E-mail address:	corg@liphatech.fr

1.5.4 Information on the substance(s) of concern[3]

There is no substance of concern.

1.6 Documentation

1.6.1 Data submitted in relation to product application

Identity, physicochemical and analytical method data

Physico-chemical properties studies and analytical methods on the biocidal product SUPERCAID GRAIN'TECH and on other formulation R216 (SUPERCAID AS APPAT, one of the representative products used for inclusion) were provided by Liphatech.

No study was submitted on MAKI GRAINTECH. As the only difference between the MAKI GRAINTECH and SUPERCAID GRAIN'TECH is the change of dye, this is acceptable.

Efficacy data

The following efficacy studies were submitted:

- Two series of tests with and without competition to R216 formulation were carried out in rats (wild-strain coumafene-sensitive *Rattus norvegicus*) with exposure to either freshly manufactured impregnated red oat bait or bait aged for 2 years.
- A free-choice laboratory test was carried out with mice (wild-strain warfarin-sensitive *Mus musculus*), with exposure to R216 formulation (used 1 month after manufacture) for 4 days.
- A free-choice laboratory test was carried out with rats (wild-strain warfarin-sensitive *Rattus norvegicus*), with exposure to MAKI GRAIN'TECH (used 9 months after manufacture) for 4 days.
- A free-choice laboratory test was carried out with mice (wild-strain warfarin-sensitive *Mus musculus*), with exposure to MAKI GRAIN'TECH (used 9 month after manufacture) for 4 days.

[3] Please insert additional columns as necessary

- A free-choice laboratory test was carried out with rats (wild-strain warfarin-resistant *Rattus norvegicus*), with exposure to SUPERCAID GRAIN'TECH (used 1 month after manufacture) for 4 days.
- A free-choice laboratory test was carried out with mice (wild-strain warfarin-resistant *Mus musculus*), with exposure to SUPERCAID GRAIN'TECH (used just after manufacture) for 4 days.
- A free-choice laboratory test was carried out with rats (wild-strain warfarin-sensitive *Rattus rattus*), with exposure to SUPERCAID GRAIN'TECH (used 2 months after manufacture) for 4 days.
- A free-choice laboratory test was carried out with rats (wild-strain warfarin-sensitive *Rattus rattus*), with exposure to SUPERCAID (used 20 months after manufacture for 4 days.
- A single feeding laboratory test was carried out with mice (wild-strain warfarin-sensitive *Mus musculus*), with exposure to SUPERCAID GRAIN'TECH (used just after manufacture) for 1 day.
- A single feeding laboratory test was carried out with rats (wild-strain warfarin-sensitive *Rattus norvegicus*), with exposure to SUPERCAID GRAIN'TECH (used 1 month after manufacture) for 4 days.
- A field test was carried out with rats (*Rattus norvegicus*) at two separate farm sites in France, with exposure to SUPERCAID.
- A field test was carried out with mice (*Mus musculus*) at two separate farm sites in France, with exposure to SUPERCAID GRAIN'TECH.
- A free-choice laboratory test was carried out with voles (wild-strain *Microtus arvalis*), with exposure to SUPERCAID GRAIN'TECH (used 15 months after manufacture for 4 days.
- A free-choice laboratory test was carried out with voles (wild-strain *Arvicola terrestris*), with exposure to SUPERCAID GRAIN'TECH (used 15 months after manufacture for 4 days.
- A field test was carried out with common voles and mice (*Microtus arvalis* and *Mus musculus*) at an electric distribution factory (RTE) in France, with exposure to impregnated red oat bait.
- A field test was carried out with common voles and field mice (*Microtus arvalis*, and *Apodemus sp.*) at a cheese factory in France, with exposure to impregnated red oat bait.
- A study on the impact of denatonium benzoate variation concentration on the palatability of rodenticide placebo blocks formula in the rat, *Rattus norvegicus*, wild strain.
- A study on the impact of packaging on the attractivity of placebo blocks in the rat, *Rattus norvegicus*, wild strain.
- A free-choice laboratory test was carried out with rats (wild-strain warfarin-resistant *Rattus norvegicus*), with exposure to SUPERCAID GRAIN'TECH (used 45 months after manufacture) for 4 days.

The above efficacy studies were conducted using wheat grain baits: MAKI GRAIN'TECH, SUPERCAID GRAIN'TECH or, oat grain baits: SUPERCAID, R216 formulation. The differences between the compositions of these products are slight; it consists on a change in cereal support and/or dye or addition of a lubricant. RMS France considered that substitution of wheat with oat, or a change of dye, has no influence on efficacy and palatability. Therefore, results from these studies can be extrapolated to the current formulation of MAKI GRAIN'TECH.

Toxicology data

The applicant submitted toxicological data on another formulation. The results of these data can be extrapolated to the biocidal product MAKI GRAIN'TECH.

Residue data

No new study has been submitted for the biocidal product authorisation.

Ecotoxicology data

No new study has been submitted for the biocidal product authorisation.

1.6.2 Access to documentation

No letter of access submitted, as Liphatech S.A.S. is the applicant that deposited the active substance bromadiolone for annex I inclusion.

2 Summary of the product assessment

The product is to be used in tamper-resistant bait boxes or covered bait stations, and into burrows without protection.

"Tamper-resistant bait boxes" are meant to be tamper-resistant devices, that prevent the access to the baits for children and non-target animals, and that protect the baits from bad weather.

"Covered bait stations" are meant to be devices with the same level of security for the human beings and the environment than the security provided by tamper-resistant bait boxes, fastened to prevent any removal, made in order to avoid direct contact of the bait with the environment. This device must be designed to keep baits out of reach of the general public and non-target animals, and to protect the bait from bad weather

It is considered that professional users only (on the contrary to the general public) are able to design such covered bait stations.

2.1 Identity related issues

The source of the active substance used in the biocidal product MAKI GRAIN'TECH is the source used for annex I inclusion.

2.2 Classification, labelling and packaging

2.2.1 Classification of the biocidal product

Classification - Directive 67/548/EEC	
Class of danger	Xn
R phrases	R48/20/21/22 R20

S phrases (proposed by the RMS)	Non professional user: S2: Keep out of the reach of children S46: If swallowed, seek medical advice immediately and show this container or label

Classification - Regulation (EC) 1272/2008	
Hazard statement	STOT RE 2; H373
Precautionary statements (proposed by the RMS)	Prevention P260: Do not breathe dust/fume/ gas/mist/vapours/spray. Response: P314: Get medical advice/attention if you feel unwell. Disposal: P501: Dispose of contents/container to the appropriated collection circuit

2.2.2 Packaging of the biocidal product

The primary packagings of the biocidal product as deposited by the notifier are:

For professional users:

MAKI GRAIN'TECH is supplied in opaque packaging in sachet or loose.

PE or PP sachets (opaque or transparent) (20-100g) are packed in:
- Opaque metal box (0.5-1 kg)
- Opaque Plastic lockable pouch (PE or PP) (0.5-20kg)
- Opaque plastic bucket (PP) with lid (up to 25 kg)
- Opaque cardboard carton (0.5-25 kg)
- Opaque plastic container (PE or PP) (0.5-4kg)
- Opaque paper laminate bag (0.5-25 kg)

Loose baits are packed in:
- Opaque Plastic lockable pouch (PE or PP) (0.5-20kg)
- Opaque plastic bucket (PP) with lid (0.5- 25 kg)
- Opaque cardboard carton with an integral PE bag (0.5-25 kg)
- Opaque plastic container (PE or PP) (0.5-4kg)
- Paper laminate bag (nature not submitted) (0.5-25 kg)

For non professional users:

MAKI GRAIN'TECH is supplied in opaque packaging in sachet or loose.

PE or PP sachets (opaque or transparent) (20-100g) are packed in:

- Opaque metal box (0.04-1 kg)
- Opaque Plastic lockable pouch (PE or PP) (0.04-4kg)
- Opaque plastic bucket (PP) with lid (0.04-4kg)
- Opaque cardboard carton with an integral PE bag (0.04-4kg)
- Opaque plastic container (PE or PP) (0.04-4kg)

Loose baits are packed in:

- Opaque Plastic lockable pouch (PE or PP) (0.04-4kg)
- Opaque plastic bucket (PP) with lid (0.04-4kg)
- Opaque cardboard carton with an integral PE bag (0.04-4kg)
- Opaque plastic container (PE or PP) (0.04-4kg)

2.3 Physico/chemical properties and analytical methods

2.3.1 Active ingredient

2.3.1.1 Identity, origin of active ingredient

The source of the active substance used in the biocidal product MAKI GRAIN'TECH is the source used for annex I inclusion.

2.3.1.2 Physico-chemical properties and Analytical method for determination of active ingredient and impurities in the technical active ingredient

Physical and chemical properties of the active substance and analytical methods for determination of active ingredient in the technical active ingredient have already been evaluated at EU level and are presented in the CAR of the active substance Bromadiolone (2007). The notifier of the product MAKI GRAIN'TECH is the applicant that supported the annex I inclusion dossier of the active substance.

2.3.2 Biocidal product

2.3.2.1 Identity, composition of the biocidal product

The biocidal product is not the same as the one assessed for the inclusion of the active substance in annex 1 of directive 98/8/EC.

Trade name: MAKI GRAIN'TECH
Code number: BROBL0,0050_01E_F00506-01

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

2.3.2.2 Physico-chemical properties

No study was submitted on MAKI GRAINTECH.

Some studies have been performed on the formulation R216 (SUPERCAID AS APPAT (one of the representative products used for inclusion)), results from these studies could be extrapolated to the product MAKI GRAIN'TECH, formulation F00506-01 on a case by case basis. When the read-across is accepted, it is indicated in the table.

All other properties were submitted on SUPERCAID GRAIN'TECH (LR0234) As the only difference between the MAKI GRAINTECH and SUPERCAID GRAIN'TECH is the change of dye, the read across is acceptable for all study except colour and will not be reported in the table below.

Subsection (Annex Point IIB. 3/TNsG)	**Method**	**Purity/ Specification**	**Results**	**Reference**
3.1 Appearance (IIB3.1/Pt. I-B3.1)				
3.1.1 Physical state and nature	Visual	Product Batch 8086. Specification LR0234.	Homogeneous whole wheat	Caruel, H. (2007a) IIIB 3.1.3-01 Non-GLP
	NFV03-719 NFV03-702	Product Batch 8086. Specification LR0234.	Specific weight: 70.20 kg/hectolitre Weight of 1000 grains 44.57g	Caruel, H. (2007a) IIIB 3.1.3-01 Non-GLP
3.1.2 Colour	Visual		Blue wheat formulation	Document III
3.1.3 Odour	Olfactory	Product Batch 8086. Specification LR0234.	Cereal odour	Caruel, H. (2007a) IIIB 3.1.3-01 Non-GLP
3.2 Explosive properties	assessment based on EEC A14	Batch E8639 Specification	There are no chemical groups that would imply explosive properties in active substance, and none of the components	Tremain, S.P. (2003)

Subsection (Annex Point IIB. 3/TNsG)	Method	Purity/ Specification	Results	Reference
(IIB3.2/Pt. I-B3.2)		R216.	suggest explosive properties, therefore the result has been predicted negative. Read across acceptable for the product MAKI GRAIN'TECH MAKI GRAIN'TECH is not explosive.	IIIB 3.2-01 GLP
3.3 Oxidising properties (IIB3.3/Pt. I-B3.3)	EEC A17 (oxidising properties)	Batch E8639 Specification R216.	There are no chemical groups that would imply oxidising properties in active substance, and none of the components suggest oxidising properties, therefore the result has been predicted negative. Read across acceptable for the product MAKI GRAIN'TECH MAKI GRAIN'TECH does not have oxidizing properties.	Tremain, S.P. (2003) IIIB 3.3-01 GLP
3.4 Flash-point and other indications of flammability or spontaneous ignition (IIB3.4/Pt. I-B3.4)				
Flammability	EEC A10 (flammability- solids)	Batch E8639 Specification R216.	The test material has been determined to be not highly flammable as it did not propagate combustion over the 200 mm of the preliminary screening test. Read across acceptable for the product MAKI GRAIN'TECH MAKI GRAIN'TECH is not highly flammable.	Tremain, S.P. (2003) IIIB 3.4-01 GLP
Self ignition temperature of solids	EEC A16 (relative self ignition temperature of solids)	Batch E8639 Specification R216.	The test material has been determined not to have a relative self-ignition temperature below 400°C. Read across acceptable for the product MAKI GRAIN'TECH Self ignition temperature of MAKI GRAIN'TECH is > 400°C.	Tremain, S.P. (2003) IIIB 3.4-01 GLP
3.5 Acidity/Alkalinity (IIB3.5/Pt. I-B3.5)	CIPAC MT75	Batch F463 Specification LR234.	pH of 1% dispersion 6.27.	Caruel, H. (2009b) IIIB 3.5-01 GLP
3.6 Bulk density (IIB3.6/Pt. I-B3.6)	CIPAC MT159	Batch not specified. Specification	Read across **not acceptable** for the product MAKI GRAIN'TECH as nature of grains is different.	Woolley, A.J. Mullee, D.M. (2005) IIIB 3.6-01

<table>
<tr><th>Subsection (Annex Point IIB. 3/TNsG)</th><th>Method</th><th>Purity/ Specification</th><th>Results</th><th>Reference</th></tr>
<tr><td></td><td></td><td>R216.</td><td></td><td>GLP</td></tr>
<tr><td></td><td>NFV03-719
NFV03-702</td><td>Product Batch 8086.
Specification LR0234.</td><td>Specific weight: 70.20 kg/hectolitre
This value of specific weight is sufficient for characterisation of density of biocidal product.</td><td>Caruel, H. (2007a)
IIIB 3.1.3-01
Non-GLP</td></tr>
<tr><td>3.7 Storage stability - (IIB3.7/Pt. I-B3.7)</td><td>Storage at 54 for 14 days
CIPAC MT 46.3

pH : CIPAC MT 75.3

Dust content: CIPAC MT 171
Flowability CIPAC MT 172</td><td>Batch F463
Specification LR234.</td><td>After 2 weeks at 54 °C in glass beaker :
<table><tr><td></td><td>T0</td><td>2W 54°C</td></tr><tr><td>Appearance</td><td colspan="2">No change</td></tr><tr><td>Content of AS (ppm)</td><td>53.5 ppm</td><td>57.15 ppm</td></tr><tr><td>pH</td><td>6.78</td><td>6.71</td></tr></table>Concentration of a.s. increases by 6% during storage.

MAKI GRAIN’TECH is not stable after 2 weeks at 54°C in glass beaker.
See comments below the table</td><td>Caruel, H. (2006)
IIIB 3.7-01
GLP</td></tr>
<tr><td></td><td>Storage at 54°C for 2 weeks</td><td>Specification LR234.</td><td>After 2 weeks at 54°C in PE sachet, PP sachet and laminate paper sachet in the dark:
The appearance of packaging and of biocidal product did not change.
Other properties (AI content, pH, physico chemical characterization…) are not measured in this study.

This study demonstrates that biocidal product is compatible with PE, PP and laminate paper packagings.</td><td>R. Deslux (2012)
IIIB 3.7-09
GLP</td></tr>
<tr><td>Shelf life study</td><td>Storage at 25ºC for 2</td><td>Batch F581
Specification</td><td>After 2 years at ambient temperature in white plastic box (polyethylene):</td><td>Caruel, H. (2009b)</td></tr>
</table>

<table>
<tr><th>Subsection (Annex Point IIB. 3/TNsG)</th><th>Method</th><th>Purity/ Specification</th><th>Results</th><th>Reference</th></tr>
<tr><td></td><td>years</td><td>LR234.</td><td>
<table>
<tr><td></td><td>T0</td><td>1Y RT</td><td>2Y RT</td></tr>
<tr><td>Appearance</td><td colspan="3">No change</td></tr>
<tr><td>Content of AS (ppm)</td><td>56.3 ppm</td><td>51.9 ppm (-8%)</td><td>45.3 ppm (-20%)</td></tr>
<tr><td>pH</td><td>6.27</td><td></td><td>5.65</td></tr>
</table>
Concentration of a.s. decreases by 20% during storage.

MAKI GRAIN’TECH is not stable after 2 years in white PE box.
See comments below the table</td><td>IIIB 3.7-07
GLP</td></tr>
<tr><td></td><td>GIFAP
Monograph No.17
Storage for 60 months at 25ºC</td><td>Batch 6986
Specification
LR234.</td><td>After 5 years at ambient temperature in white plastic box (polypropylene):
<table>
<tr><td></td><td>T0</td><td>3Y RT</td><td>5Y RT</td></tr>
<tr><td>Appearance</td><td colspan="3">No change</td></tr>
<tr><td>Content of AS (ppm)</td><td>53.1 ppm</td><td>42.8 ppm (-20%)</td><td>44.7 ppm (-16%)</td></tr>
<tr><td>pH</td><td>ND</td><td>6.69</td><td>6.21</td></tr>
</table>
Concentration of a.s. decreases by 16% during storage.
MAKI GRAIN’TECH is not stable after 5 years in white PP box.
See comments below the table</td><td>Caruel, H. (2010a)
IIIB 3.7-04
GLP</td></tr>
<tr><td>Effects of light</td><td></td><td></td><td>No data submitted. Bromadiolone is known to be light sensitive. No more data required as MAKI GRAIN’TECH is conditioned only in opaque packaging.
See comments below the table</td><td></td></tr>
<tr><td colspan="5">3.8 Technical characteristics</td></tr>
</table>

Subsection (Annex Point IIB. 3/TNsG)	Method	Purity/ Specification	Results	Reference
(IIB3.8/Pt. I-B3.8)				
Wettability			Data not required as the product is a ready to use grain bait	
Persistent foaming			Data not required as the product is a ready to use grain bait	
Suspensibility			Data not required as the product is a ready to use grain bait	
Spontaneity of dispersion			Data not required as the product is a ready to use grain bait	
Dilution stability			Data not required as the product is a ready to use grain bait	
Dry sieve test			see particle size distribution	
Wet sieve test			Data not required as the product is a ready to use grain bait	
Dustiness	CIPAC MT171	Batch F2910. Specification LR0234.	The dust content was found to be 0.2 mg The material was classified as “nearly dust free”	FERRON N. (2012) IIIB 3.8-04 GLP
Attrition/friability of granules; integrity of tablets	CIPAC MT 178	Batch F2910. Specification LR0234.	The attrition resistance of the test item was: 99.2%	FERRON N. (2012) IIIB 3.8-04 GLP
Emulsifiability / Emulsion stability / Re-emulsifiability			Data not required as the product is a ready to use grain bait	
Stability of dilute emulsions			Data not required as the product is a ready to use grain bait	
Flowability	CIPAC MT172	Batch F2910. Specification LR0234.	The flowability was not spontaneous through the 5-mm sieve. All material passed through 5 mm sieve screen after 5 drops.	FERRON N. (2012) IIIB 3.8-04 GLP
Pourability (including rinsed residue)			Data not required as the product is a ready to use grain bait	
3.9 Compatibility			MAKI GRAIN’TECH is not intended to be used or mixed with other products.	

Subsection (Annex Point IIB. 3/TNsG)	Method	Purity/ Specification	Results	Reference
with other products (IIB3.9/Pt. I-B3.9)				
3.10 Surface tension (Pt. I-B3.10)			Data not required as the product is a ready to use grain bait	
3.11 Viscosity (Pt. I-B3.10)			Data not required as the product is a ready to use grain bait	
3.12 Particle size distribution (Pt. I-B3.11)	CIPAC MT58.3	Batch E8639 Specification R216.	Read across **not acceptable** for the product MAKI GRAIN'TECH as nature of grains is different. Particle size distribution of grains is according to CIPAC method MT 170 with seives adapted to biocidal product required in post registration.	Woolley, A.J. Mullee, D.M. (2006) IIIB 3.12-01 GLP

Storage stability:

-Shelf life study

The following table summarises the available storage stability and efficacy data for MAKI GRAIN'TECH grain product.

	T0	3 month	6 month	9 month	12 month	24 month	36 month	48 month	60 month	Reference
bromadiolone content in stability study (mg/kg)	53.07 (100.0 %)	--	--	--	--	--	42.79 (80.1%)	40.79 (76.9%)	44.70 (84.2%)	Caruel, (2010a)
	56.31 (100.0 %)	55.86 (99.0%)	54.55 (97.0%)	53.25 (95.0%)	51.88 (92.0%)	45.28 (80.0%)	--	--	--	Caruel, (2009b)
Efficacy	LR 234: efficacy remained with wheat bait stored for 45 months									--

Analytical measurements of content of bromadiolone in MAKI GRAIN'TECH demonstrate a decrease of content of 20% after 2 years and 3 years and 24% after 4 years and 16 % after 5 years of storage. Overall the decrease appears to be continuous and reaches a plateau around -20%. These decreases are higher than the allowed variation of 10%.

The explanation submitted by the notifier :

- Bromadiolone adsorbs to the matrix (see atempt to extract more with dimethyl formamide in Woolley, A.J, Mullee, D.M. (2005) study). The decrease of bromadiolone content observed could be atributed to this adsorbtion.
- The variation of active substance content may be due to the heterogeneity of grains within batches (grains within a batch may have different contents of active substance).
- Efficacy data show that product is effective following storage of the bait for 45 months.

RMS agrees with explanation from the applicant and, based on the results of the long term storage test considers MAKI GRAIN'TECH stable in its packaging for 3years and 6 months.

- 14 days at 54°C study:

The variation of active substance content after 14 days at 54°C is +6%. The difference in active substance content is higher than 5% which is the accepted variation according to the FAO manual (§4.6.2). Aspect of the test item during the storage has not changed and no significant changes were observed for pH measures after storage 14 days at 54 °C. Moreover Bromadiolone is thermically stable (melting point at 198 °C and decomposition started at 260 °C). The same heterogeneity and adsorption questions arise. The effect of temperature should be demonstrated by the submission of a new accelerated storage stability study (14 days at 54°C or at a lower temperature) with acceptable results.

The compatibility of the product MAKI GRAINTECH with the PE, PP and paper laminate sachet has been demonstrated and covers all the claimed packagings.

The effect of light has not been provided and FR recommends to store away from light due to the sensitivity of the active substance to light. All the claimed packagings are opaque.

Data requirements

Particle size distribution of grains is according to CIPAC method MT 170 with seives adapted to biocidal product required in post registration.
An accelerated storage stability study (14 days at 54°C or at a lower temperature) is required with CIPAC MT46.

2.3.3 Analytical methods for detection and identification

2.3.3.1 Analytical method for determining the active substance and relevant component in the biocidal product

Instead of validation of a method of determination of bromadiolone in MAKI GRAIN'TECH, the applicant submitted a method to determine bromadiolone in 3 different formulations by HPLC – UV (260nm).

Reference: Caruel, H. (2005)., Report n° BRO0502H
Validation data (linearity, precision and recovery) on SUPERCAID (LR216):

Linearity	Precision	Recovery rate (%) range	Specificity
27.5-106 ppm n=6 r^2=0.999	At 57 ppm: RSD = 0.83%	At 100% mean of recovery = 99.7% (n=6)	No interference in chromatograms. Specific to bromadiolone in : Blue Wheat LR0233 Red Oat LR0216 (MAKI) Red Semolina LR0218

Conclusion:
Validation data (linearity, precision and recovery) on SUPERCAID (LR216) are acceptable for MAKI GRAIN'TECH (LR234)

Demonstration of applicability of the method to MAKI GRAIN'TECH is required in the form of chromatograms of placebo, of test sample and of a reference sample.

2.3.3.2 Analytical methods for determining relevant components and/or residues in different matrices

The analytical methods for determination of residues of active substance in different matrices (soil, air, blood, liver and food and feedstuff) provided in the CAR of the active substance are presented in annex I of this document.

The analytical method for determination of Bromadiolone in surface and drinking water is not considered as highly specific. A confirmatory method must be submitted in post registration

2.4 Risk assessment for Physico-chemical properties

MAKI GRAIN'TECH is a ready-to-use grain rodenticide. It is not highly flammable, not auto-flammable at ambient temperature, does not have explosive and oxidizing properties.
An accelerated storage stability study is required in post registration. The Biocidal product is stable 42 months at ambient temperature and is compatible with PE sachet, PP sachet, paper laminate sachet and PE box.

Professional & non professional users

Measures linked to to assessment of physico-chemical properties

- Store away from light.
- Store at maximum 40℃.

Required information linked to assessment of physico-chemical properties

- Particle size distribution of grains is according to CIPAC method MT 170 with seives adapted to biocidal product required in post registration.
- An accelerated storage stability study (14 days at 54℃ or at a lower temperature) is required with CIPAC MT46.
- Demonstration of applicability of the method to MAKI GRAIN'TECH in the form of chromatograms of placebo, of test sample and of a reference sample.
- The analytical method for determination of Bromadiolone in surface and drinking water is not considered as highly specific. A confirmatory method must be submitted in post registration.

2.5. Effectiveness against target organisms

2.5.1 Function

MG 03: Pest Control
Product Type 14: Rodenticide

2.5.2 Organisms to be controlled and products, organisms or objects to be protected

According to the uses claimed by the applicant, **MAKI GRAIN'TECH** is intended to be used to control rodents. The target organisms to be controlled are brown rats (***Rattus norvegicus***), black rats (***Rattus rattus***), house mice (***Mus musculus***), common voles (***Microtus arvalis***), field mice (***Apodemus sp.***) and water voles (***Arvicola terrestris***).

MAKI GRAIN'TECH is used in areas in and around buildings, open areas and waste dumps. Products can be supplied with and without sachets. The products, organisms or objects to be protected are human food and animal feedstuffs and for general hygiene purposes.

The application rates recommended and uses claimed by the applicant are the following (see also annex 0a):

Target organisms	Area of use	Dosage claimed	Time delay of the action of the product	Distance between 2 bait points, for high and low infestation	Frequency and method of controls	Methods of application of the bait
PROFESSIONAL USERS						
Rats *Rattus norvegicus* *Rattus rattus*	In and around buildings	Up to 200 g	4 to 6 days	High infestation: 4-5 meters Low infestation: 8-10 meters	High infestation: 3 days after first application then ideally every week or 15 days Low infestation: 1 week after first application then ideally every week or 15 days	Manual application in bait stations, bait points, loose but inaccessible and burrows
House mice *Mus musculus*	In and around buildings	Up to 50 g		High infestation: 1-1,5 meters Low infestation: 2-3 meters		
Voles *Microtus arvalis* *Arvicola terrestris*	In and around buildings	Up to 100 g		High infestation: 3 meters Low infestation: 6 meters		
Field mice *Apodemus sp.*	In and around buildings	Up to 50 g		High infestation: 1-1,5 meters Low infestation: 2-3 meters		
Rats *Rattus norvegicus* *Rattus rattus*	Open areas	Up to 200 g	4 to 6 days	In each burrow or High infestation: 3-5 meters Low infestation: 10-15 meters	High infestation: 3 days after first application then ideally every month Low infestation: 1 week after first application then	Manual application in bait stations and burrows
House mice *Mus musculus*	Open areas	Up to 50 g				
Voles *Microtus arvalis* *Arvicola terrestris*	Open areas	Up to 100 g				

Field mice *Apodemus sp.*	Open areas	Up to 50 g			ideally every month	
Rats *Rattus norvegicus* *Rattus rattus*	Waste dumps	Up to 200 g	4 to 6 days		Application every 2 to 3 months	Manual application in bait stations, bait points and burrows
NON PROFESSIONAL USERS						
Rats *Rattus norvegicus* *Rattus rattus*	In and around buildings	Up to 200 g	4 to 6 days	<u>High infestation:</u> 4-5 meters <u>Low infestation:</u> 8-10 meters	**<u>High infestation:</u>** 3 days after first application then ideally every week or 15 days **<u>Low infestation:</u>** 1 week after first application then ideally every week or 15 days	Manual application in bait stations, bait points, loose but inaccessible
House mice *Mus musculus*	In and around buildings	Up to 50 g		<u>High infestation:</u> 1-1,5 meters <u>Low infestation:</u> 2-3 meters		
Voles *Microtus arvalis* *Arvicola terrestris*	In and around buildings	Up to 100 g		<u>High infestation:</u> 3 meters <u>Low infestation:</u> 6 meters		
Field mice *Apodemus sp.*	In and around buildings	Up to 50 g		<u>High infestation:</u> 1-1,5 meters <u>Low infestation:</u> 2-3 meters		

2.5.3 Effects on target organisms and efficacy

Anticoagulants rodenticides disrupt the blood-cutting mechanisms. Signs of poisoning in rodents are those associated with an increased tendency to bleed, leading ultimately to profuse haemorrhage. After feeding on bait containing the active substance for 2-3 days the animal becomes lethargic and slow moving. Signs of bleeding are often noticeable and blood may be seen around the nose and anus. As symptoms develop, the animal will lose its appetite and will remain in its burrow or nest for increasingly long periods of time. As the active substance has a long acting action, death will usually occur within 3 to 21 days of ingesting a lethal dose and animals often die out of sight in their nest or burrow.

Laboratory and field studies have been conducted with mice, field mice, voles and rats using grain baits containing 50 mg/kg bromadiolone: **MAKI GRAIN'TECH**, **SUPERCAID GRAIN'TECH**, **SUPERCAID**, **R216 formulation**. The differences between the compositions of these products are slight; it consists on a change in cereal support and/or dye, or addition of a lubricant. RMS France considered that substitution of wheat with oat, or a change of dye, has no influence on efficacy and palatability. Therefore, results from these studies can be extrapolated to the current formulation of **MAKI GRAIN'TECH**.

- Efficacy on brown rats (*Rattus norvegicus*)

Two series of tests with and without competition to the reference bait **R216 formulation** (Lorgue, 2002a) were carried out with rats (wild-strain coumafene-sensitive ***Rattus norvegicus***) with exposure to either freshly manufactured impregnated red oat bait or bait aged for 2 years. The studies show that the product is palatable (average treated fresh bait intake at least 49 % of the total food consumption and 43% after 2 years storage) and effective (100 % mortality between 4 to 11 days).

A free-choice laboratory test (Berny, 2008a) was carried out with rats (wild-strain warfarin-sensitive ***Rattus norvegicus***) with exposure to impregnated blue wheat bait **MAKI GRAIN'TECH** (used 9 months after manufacture) for 4 days. The efficacy (mortality) was 90 % within 7 to 11 days where bait was consumed in

competition with the reference bait. The study shows that the product is palatable (average treated bait intake at least 66 % of the total food consumption) and effective (90 % mortality between 7 to 11 days).

A free-choice laboratory test (Berny, 2005a) was carried out with rats (wild-strain warfarin-resistant ***Rattus norvegicus***), with exposure to impregnated red wheat bait **SUPERCAID GRAIN'TECH** (used 1 month after manufacture) for 4 days. The study shows that the product is palatable (average treated bait intake at least 44 % of the total food consumption) and effective (84% mortality between 7 to 18 days).

A no-choice laboratory test (Berny, 2007b) was carried out with rats (wild-strain warfarin-sensitive ***Rattus norvegicus***) with exposure to impregnated red wheat bait **SUPERCAID GRAIN'TECH** (used 1 month after manufacture) for 4 days. The study shows that the product is effective (100 % mortality between 5 to 11 days).

A field test (Berny, 2010b) was carried out with rats (***Rattus norvegicus***) at two separate farm sites in France. The product, **SUPERCAID** was highly effective, achieving 100 % of control at the two sites.

A free-choice laboratory test (Berny, 2012) was carried out with rats (wild-strain warfarin-resistant ***Rattus norvegicus***), with exposure to **SUPERCAID GRAIN'TECH** (used 45 months after manufacture) for 4 days. The study shows that the product is palatable (average treated bait intake at least 58 % of the total food consumption) and effective (100 % mortality between 7 to 14 days).

- Efficacy on black rats (*Rattus rattus*)

A free-choice laboratory test (Berny, 2009a) was carried out with rats (wild-strain warfarin-sensitive ***Rattus rattus***), with exposure to impregnated red wheat bait **SUPERCAID GRAIN'TECH** (used 27 months after manufacture) for 4 days. The study shows that the product is palatable (average treated bait intake at least 41 % of the total food consumption) and effective (90 % mortality between 7 to 11 days).

A free-choice laboratory test (Berny, 2010a) was carried out with rats (wild-strain warfarin-sensitive ***Rattus rattus***), with exposure to impregnated red oat bait **SUPERCAID** (used 20 months after manufacture for 4 days). The study shows that the product is palatable (average treated bait intake at least 55 % of the total food consumption) and effective (95 % mortality between 7 to 16 days).

- Efficacy on house mice (*Mus musculus*)

A free-choice laboratory test (Berny, 2003a) was carried out with mice (wild-strain warfarin-sensitive ***Mus musculus***), with exposure to impregnated red oat bait **R216 formulation** (used 1 month after manufacture) for 4 days. The study shows that the product is palatable (average treated bait intake at least 48 % of the total food consumption) and effective (90 % mortality between 4 to 21 days).

A free-choice laboratory test (Berny, 2008b) was carried out with mice (wild-strain warfarin-sensitive ***Mus musculus***), with exposure to impregnated blue wheat bait **MAKI GRAIN'TECH** (used 9 month after manufacture) for 4 days. The study shows that the product is palatable (average treated bait intake at least 84 % of the total food consumption) and effective (100 % mortality between 7 to 14 days).

A free-choice laboratory test (Berny, 2005b) was carried out with mice (wild-strain warfarin-resistant ***Mus musculus***), with exposure to impregnated red wheat bait **SUPERCAID GRAIN'TECH** (used just after manufacture) for 4 days. The study shows that the product is palatable (average treated bait intake at least 40 % of the total food consumption) and effective (93 % mortality between 7 to 15 days).

A no-choice laboratory test (Berny, 2007a) was carried out with mice (wild-strain warfarin-sensitive ***Mus musculus***), with exposure to impregnated red wheat bait **SUPERCAID GRAIN'TECH** (used just after manufacture) for 1 day. The study shows that the product is effective (100 % mortality between 7 to 17 days).

A field test (Berny, 2010c) was carried out with mice (***Mus musculus***) at two separate farm sites in France. The product, **SUPERCAID GRAIN'TECH** was highly effective, achieving 100% control at the two sites.

- Efficacy on common voles (*Microtus arvalis*), water voles (*Arvicola terrestris*) and field mice (*Apodemus sp.*)

A free-choice laboratory test (Berny, 2009b) was carried out with voles (wild-strain ***Microtus arvalis***) with exposure to impregnated red wheat bait **SUPERCAID GRAIN'TECH** (used 15 months after manufacture) for 4 days. The study shows that the product is palatable (average treated bait intake at least 59 % of the total food consumption) and effective (100 % mortality between 3 to 7 days).

A free-choice laboratory test (Berny, 2009c) was carried out with water voles (wild-strain ***Arvicola terrestris***) with exposure to impregnated red wheat bait **SUPERCAID GRAIN'TECH** (used 15 months after manufacture for 4 days). The study shows that the product is palatable (average treated bait intake at least 51 % of the total food consumption) and effective (90% mortality between 3 to 9 days).

A field test (Bourret, 2008a) was carried out with common voles and mice (***Microtus arvalis*** and ***Mus musculus***) at an electric distribution factory (RTE) in France. The product, a red oat cereal bait containing bromadiolone, was highly effective, achieving 100% control at site. Nevertheless, there is no indication about mice and voles proportions. No census by trapping has been done. As there is a lab study with *Microtus arvalis,* this use is validated.

A field test (Bourret, 2008b) was carried out against common voles and field mice (***Microtus arvalis***, and ***Apodemus sp.***) at a cheese factory in France. The product, a red oat cereal bait containing bromadiolone, was highly effective, achieving 100% control. Nevertheless, there is no indication about field mice and voles proportions. No census by trapping has been done. As there is no other study with *Apodemus sp.* a field study with this specie has to be provided within the framework of a post-authorization monitoring to validate this use.

Nevertheless, common voles (Microtus arvalis) and water voles (Arvicola terrestris) are essentially devastating cultures and meadows, where they dig galleries and eat away at vegetables, with important consequences on the production of herbs and feeds and the decay of plantations. The water vole is besides the object, in France, of a preventive and reasoned control within the framework of the pesticide regulation, with in particular the establishment of a threshold of population of voles above which the chemical treatments are forbidden. In this context, Anses considers that the use "control of voles" is more relevant within the framework of the pesticide regulations.

A study shows that denatonium benzoate variation concentration (10 to 100 ppm) has no impact on the palatability of rodenticide placebo blocks formula in the rat, ***Rattus norvegicus***, wild strain (Berny, 2005c).
Another study shows that packaging has no impact on the attractivity of placebo blocks in the rat, ***Rattus norvegicus***, wild strain (Berny, 2005d).
The composition of these placebo baits tested in the two latter studies are different from the composition of bromadiolone baits tested in efficacy studies. But this doesn't affect the results of these studies that can be extrapolated to the current formulation of MAKI GRAIN'TECH.

The results of these studies are described in Section IIIB 5.10.2 and are summarised in annex 3.

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

On the basis of the efficacy data submitted, the level of efficacy of the product MAKI GRAIN'TECH for the intended uses presented in the table below is acceptable.
In the absence of supporting data on *Apodemus sp.*, suitable information (as a field test) demonstrating the efficacy of MAKI GRAIN'TECH against field mice, will need to be provided in support of the authorisation.

Target organisms	Area of use	Dosage claimed	Time delay of the action of the product	Distance between 2 bait points, for high and low infestation	Frequency and method of controls	Methods of application of the bait
PROFESSIONAL USERS						
Rats *Rattus norvegicus* *Rattus rattus*	In and around buildings	200 g	3 to 21 days	High infestation: 4-5 meters Low infestation: 8-10 meters	Inspect and resupply the bait stations, 3 days after application then once a week as long as the bait is consumed.	Manual application in bait stations, bait points, loose but inaccessible and burrows
House mice *Mus musculus*		50 g		High infestation: 1-1,5 meters Low infestation: 2-3 meters		
Field mice *Apodemus sp.*		50 g		High infestation: 1-1,5 meters Low infestation: 2-3 meters		
Voles *Microtus arvalis* *Arvicola terrestris*		100 g		High infestation: 3 meters Low infestation: 6 meters		
Rats *Rattus norvegicus* *Rattus rattus*	Open areas	200 g		In each burrow or High infestation: 3-5 meters Low infestation: 10-15 meters		Manual application in bait stations and burrows
House mice *Mus musculus*		50 g				
Field mice* *Apodemus sp.*		50 g				
Voles *Microtus arvalis* *Arvicola terrestris*		100 g				
Rats *Rattus norvegicus* *Rattus rattus*	Waste dumps	200 g	3 to 21 days	In each burrow or High infestation: 3-5 meters Low infestation: 10-15 meters	Inspect and resupply the bait stations, 1 week after application then once a month as long as the bait is consumed.	Manual application in bait stations, bait points and burrows
NON PROFESSIONAL USERS						
Rats *Rattus norvegicus* *Rattus rattus*	In and around buildings	200 g	3 to 21 days	High infestation: 4-5 meters Low infestation: 8-10 meters	Inspect and resupply the bait stations, 3 days after application	Manual application in bait stations, bait

House mice *Mus musculus*		50 g		High infestation: 1-1,5 meters Low infestation: 2-3 meters	then once a week as long as the bait is consumed.	points, loose but inaccessible
Field mice* *Apodemus sp.*		50 g		High infestation: 1-1,5 meters Low infestation: 2-3 meters		
Voles *Microtus arvalis* *Arvicola terrestris*		100 g		High infestation: 3 meters Low infestation: 6 meters		

** A field trial against Apodemus sp. should be provided within two years after the authorisation*

It should also be noted that the uses related to the open areas exclude golf courses, national parks, and islands, considered as not agricultural areas recovering from the pesticide regulation.

The submitted studies permit to conclude that MAKI GRAIN'TECH can be considered as effective after a 45 month storage period.

2.5.4 Mode of action including time delay

Bromadiolone acts as a vitamin K1 antagonist. It interferes with the regeneration of prothrombin disturbing the normal blood clotting mechanisms and increasing tendency to bleed. The main site of its action is the liver, where several of the blood coagulation precursors under vitamin K dependent post translation processing take place before they are converted into the respective procoagulant zymogens. Bromadiolone acts as an inhibitor of K1 epoxide reductase, preventing the regeneration of vitamin K and preventing activation of clotting factors.

2.5.5 Occurrence of resistance

Resistance to the first generation anticoagulants has been widely reported for both *Rattus norvegicus* and *Mus domesticus* since the late 1950's. The incidence of resistance to first generation anticoagulants in areas in which it is established is commonly 25-85%. Some degree of resistance to difenacoum has been reported in the UK, Denmark, France and Germany but this is usually found in certain populations of rodents highly resistant to first generation anti-coagulants (Greaves et al., 1982[4]; Lund, 1984[5]; Pelz et al. 1995[6]). The resistance factor tells how much the anticoagulant dose has to be multiplied to kill resistant individuals compared to sensitive ones. The resistant factors for difenacoum in the brown rats ranged from 1.1 to 8.6 (Greaves and Cullen-Ayres 1988[7]). The study included rats resistant to warfarin and difenacoum. Resistance factors for warfarin ranged from approx. 50 to 2300. Greaves et al. (1982) reported a fivefold difenacoum dose needed to kill difenacoum resistant rats. Considerable doubt exists as to the significance of reports in UK of resistance to second-generation anticoagulants and in the UK control failures with the second-generation products are increasingly being attributed to baiting problems rather than physiological resistance (Greaves and Cullen Ayres, 1988; Quy et al. 1992a,b[8]).

[4] Greaves J. H.; Shepherd D. S.; Gill, J. E. (1982): An investigation of difenacoum resistance in Norway rat populations in Hampshire. *Annals of Applied Biology* 100, 581–587.
[5] LUND, M. (1984): Resistance to the second generation anticoagulant rodenticides. *In Proceedings of 11th vertebrate pest conference*, Sacramento, Ca. March 6-8, 1984: 89-94.
[6] Pelz H-J, Ha¨nisch D, Lauenstein G (1995) Resistance to anticoagulant rodenticides in Germany and future strategies to control *Rattus norvegicus. Pestic Sci* 43, 61–67
[7] Greaves J. H.; Cullen-Ayres P. B. (1988): Genetics of difenacoum resistance in the rat. In: J. W. Suttie (Ed.), Current advances in vitamin K research, Elsevier, N.Y., 381–388.
[8] Quy R.J., Shepherd D.S., Inglis I.R. (1992): Bait avoidance and effectiveness of anticoagulant rodenticides against warfarin- and difenacoum-resistant populations of Norway rats (Rattus norvegicus). *Crop Protection*, Volume 11, Issue 1, February 1992, Pages 14-20

Recent studies carried out in different European countries, in the UK more particularly (Kerins *et al*, 2001; see annex 1) revealed the occasional occurrence of cross-resistances to second-generation anticoagulants, such as difenacoum and bromadiolone on resistant brown rats (*Rattus norvegicus*) populations to coumafene. Moreover, a recent publication (Baer *et al.*, 2012) has demonstrated that the majority (91%) of warfarin resistant rat trapped in East and West parts of Belgium were also resistant to bromadiolone. The rats trapped in the region of Flanders (northern Belgium) carried mutation Y139F. This mutation is found extensively in France where it also confers resistance to bromadiolone (Grandemange et al., 2009). More recently, the same mutation was also found in UK (Prescott *et al.*, 2011) where applications of bromadiolone had been unsuccessful. Difenacoum is also thought to be partially resisted by rats which carry Y139F. So, resistance to second generation anticoagulant rodenticides should not be minimized.

Only an exhaustive study carried out at the French and European levels could enable to point-out resistant areas with first-generation anticoagulants and potential cross-resistances to second-generation anticoagulants. It is one of the actions undertaken since 2010 in France by a group of scientists (Rodent program "*impacts of anticoagulants rodenticides on ecosystems-adaptations of target rodents and effects on their predators*").

Resistance management strategies

The immediate aim of resistance management is to prevent or retard the development of resistance to a given anticoagulant while, as far as is not counterproductive, permitting its continued use. The ultimate aim is to reduce or eliminate the adverse consequences of resistance.

CropLife International has published a strategy for resistant management of rodenticides (RRAC 2003). The habitat management is addressed in the strategy in addition to chemical control. The access of rodents should be restricted by physical barriers and no food should be available for rodents. Rotation between different anticoagulants is not a reliable means of managing the anticoagulant resistance, as all anticoagulants have the same mode of action and the nature of resistance is also similar. The resistant individuals can be identified by conducting a blood clotting response (BCR) test (Gill et al. 1993, RRAC 2003). The problem with the BCR test is that it has proven difficult to standardise and it produces both false positives and negatives (Pelz et al. 2005). In order to follow the occurrence and spread of difenacoum resistance, wild rats should be continuously monitored for resistance in the rodent controlled area. The recommendations of CropLife International are quoted below.

To avoid the development of resistance in susceptible rodent populations:

- When anticoagulant rodenticide is used, ensure that all baiting points are inspected weekly and old bait replaced where necessary.
- Undertake treatment according to the label until the infestation is completely cleared.
- On completion of the treatment remove all unused baits.
- Do not use anticoagulant rodenticides as permanent baits routinely. Use permanent baits only where there is a clear and identified risk of immigration or introduction or where protection is afforded to high-risk areas.
- Monitoring of rodent activity should be undertaken using visual survey, through the use of non-toxic placebo monitors or by other effective means.
- Record details of treatment.
- Where rodent activity persists due to problems other than resistance, use alternative baits or baiting strategies, extend the baiting programme or apply alternative control techniques to eliminate the residual infestation (acute or sub-acute rodenticides, gassing or trapping).
- Ensure that complete elimination of the infestation is achieved. In case of suspected resistance, testing for genetic resistance has to be performed by molecular biological methods.
- As appropriate during the rodenticide treatment, apply effective Integrated Pest Management measures (remove alternative food sources, water sources and harbourage and, proof susceptible areas against rodent access).

Treatment of rodent infestations containing resistant individuals:

- Where rodent infestations containing resistant individuals are identified, immediately use an alternative anticoagulant of higher potency. If in doubt, seek expert advice on the local circumstances.
- Alternatively use an acute or sub-acute but non-anticoagulant rodenticide.
- In both cases it is essential that complete elimination of the rodent population is achieved. Where residual activity is identified apply intensive trapping to eliminate remaining rodents. Gassing or fumigation may be useful in specific situations.
- Apply thorough Integrated Pest Management procedures (environmental hygiene, proofing and exclusion).
- Do not use anticoagulant rodenticides as permanent baits as routine. Use permanent baits only where there is a clear and identified risk of immigration or introduction or where protection is afforded to high risk areas.
- Record details of treatment.

Application of area or block rodent control to eliminate resistance:

- Where individual infestations are found to be resistant or contain resistant individuals it is possible that the resistance extends further to neighbouring properties.
- Where there are indications that resistance may be more extensive than a single infestation, apply area or block control rodent programmes.
- The area under such management should extend at least to the boundaries of the area known resistance and ideally beyond.
- These programmes must be effectively coordinated and should encompass the procedures identified above.

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

2.5.6 Evaluation of the Label Claims

French Competent Authorities (FR CA) assessed that the product MAKI GRAIN'TECH has shown a sufficient efficacy for the control of mice, voles and rats for use in and around buildings, in open areas use and in waste dumps. The use “field mouse” is also accepted but a field study with *Apodemus sp.* has to be provided within the framework of a post-authorisation monitoring to validate this use.

The application rates validated are presented in annex 0b.

The applicant has to adapt the amount per sachet to the efficient doses. The amount of bait per bait station or bait points must not exceed the recommended application rates.

In order to reflect the efficacy data of the product, labels has to be revised as following:
- Inspections of bait must be mentioned as authorized (see above).
- The time delay of the product‘s action should be added on the basis of efficacy tests (3 to 21 days).
- The application rates must be mentioned as authorized (see above).
- The target species should be precisely identified.
- Golf courses are excluded from open areas

Because of cross-resistances occurrence to second-generation anticoagulants, the product label has to contain information on resistance management for rodenticides **(**see *Specific use restriction and issues accounted for product labelling* below).

2.5.7 Conclusion of the efficacy assessment

The product MAKI GRAIN'TECH has shown a sufficient efficacy and can be used for the control of mice *(Mus musculus),* voles *(Microtus arvalis, Arvicola terrestris)* and rats (*Rattus norvegicus* and *Rattus rattus*) in and around buildings, in open areas and waste dumps. The product MAKI GRAIN'TECH can also be used for the control of field mice, nevertheless, a field study with *Apodemus sp.* has to be provided within the framework of a post-authorization monitoring to validate this use. Furthermore, a monitoring of the resistance phenomenon of rodent populations toward the active substance bromadiolone and resistant strategies management must be put in place. The collected information must be sent every 2 years to Anses within the framework of a post-authorization monitoring. Furthermore, it can be concluded that the product MAKI GRAIN'TECH can be considered as effective after a 45 month storage period.

Conditions of use :

For professional users:

- Adapt the number of bait station to the infestation level.
- Inspect and resupply the bait stations, 3 days after application then once a week as long as the bait is consumed.
- Remove all bait points after the end of treatment.
- The amount of bait per bait point and distances between bait points must be respected. Products have always to be used in accordance with the label.
- The users should inform if the treatment is ineffective and report straightforward to the registration holder any alarming signals which could be assumed to be resistance development.
- To avoid resistance:
    - The treatment has to be alternated with other kinds of active substances having different modes of action.
    - Adopt integrated pest management methods such as the combination of chemical, physical control methods and other public health measures.
    - The level of efficacy have to be monitored (periodic check), and the case of reduced efficacy has to be investigated for possible evidence of resistance.
    - Do not use the product in areas where resistance is suspected or established.

For non professional users:

- Adapt the number of bait station to the infestation level.
- Inspect and resupply the bait stations, 3 days after application then once a week as long as the bait is consumed.
- Remove all bait points after the end of treatment.
- To avoid resistance:

- The amount of bait per bait point and distances between bait points must be respected. Products have always to be used in accordance with the label.
- The users should inform if the treatment is ineffective and report straightforward to the registration holder any alarming signals which could be assumed to be resistance development.

The authorization holder has to report any observed resistance to bromadiolone to Anses or other appointed bodies involved in resistance management every two years.

Required information linked to efficacy assessment
Concerning the efficacy of the product, a new field study is awaited to confirm the efficacy against field mice (*Apodemus sylvaticus*) at latest 2 years after the authorization of the product.

The authorization holder has to report any observed resistance to bromadiolone to Anses or other appointed bodies involved in resistance management every two years.

2.6. Description of the intended use(s)

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

The validated application rates and intended uses are detailed in section 2.5.3. (see table).

The efficacy of the product MAKI GRAIN'TECH has been proved for the control of mice *(Mus musculus)*, field mice (*Apodemus sp.),* voles *(Microtus arvalis, Arvicola terrestris),* brown rats *(Rattus norvegicus)* and black rats *(Rattus rattus)* in and around buildings, in open areas and in waste dumps. The control is based on the principle of applying baits in infested areas with obvious tracking of faeces, and smears next to holes and harbourages.

The product is a ready-to-use grain bait with no dilution nor other substances added for application. It is manually applied by trained professional users and by non-professional users in bait stations, bait points. It is also applied in burrows or as loose baits but inaccessible by professional users.

2.7. Risk assessment for human health

No new human exposure studies have been submitted.
In the dossier, Liphatech assessed the human exposure based on the studies of Chambers *et al.* and Snowdon and the Human Exposure Expert Group (HEEG) opinion on an Harmonised approach for the assessment of rodenticides (anticoagulants). However, contrary to use the 75th percentile over all at it is recommended in the HEEG opinion, Liphatech used the geometric mean.

For non professional users, the same studies and assumptions were used for the estimation of human exposure since the values available in the TNsG and User Guidance (Human exposure to biocidal products – TNsG June 2002 – version 1) are considered as unrealistic.

Additionally, the HEEG opinion on harmonising the number of manipulations in the assessment of rodenticides (anticoagulant), agreed at TMIII 2010 and the HEEG opinion on an harmonised approach for the assessment of rodenticides (anticoagulants) agreed at TMII 2011 were taken into account for the estimation of exposure for professionals and non professionals.

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 **combined** CAR.
Bromadiolone (CAS no. 28772-56-7) was notified as an existing active substance, by a first applicant LiphaTech S.A.S, hereafter referred to as LiphaTech, and by a second applicant Bromadiolone Task Force, hereafter referred to as Task Force, in product-type 14. A combined assessment report was available on December 2010.

The following corresponds to the summary of the effect assessment available in the combined assessment report of bromadiolone.

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

No dermal absorption study were performed on the active substance alone (it was only provided for the formulated product or mixed with bait), but a default value of 10% could be used if considered necessary.
Dermal penetration in humans was estimated as < 1.6% for a powdered product.
Based on data from in vitro human skin studies with two representative products containing bromadiolone, the dermal absorption was less than 0.3% for the wax block formulations.

In acute oral toxicity studies, bromadiolone was very toxic to rats with a LD_{50} to the rat of between 0.56 and 1.31 mg/kg bw. Bromadiolone is slightly less toxic to dogs with a LD_{50} value of 8.1 mg/kg bw. The symptoms were observed 1-2 days prior to death and included signs of internal haemorrhage, which were confirmed at necropsy.

Bromadiolone was also acutely toxic by dermal administration, with an LD_{50} of 1.71 mg/kg bw in rabbits (LiphaTech) and with a combined sexes dermal LD_{50} value of 23.3 mg/kg in rats (Task Force).

The LC_{50} by inhalation, in rats was 0.43 µg/L (LiphaTech). Waiving of inhalation studies has been accepted for Task Force, since operator exposure through inhalation is unlikely to occur based in the information presented concerning production procedures and based on the physical chemistry data showing low vapour pressure. However, a classification as R26 'Very toxic by inhalation' is warranted based on the other applicant's data (LiphaTech).

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

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

A non-guideline study in the dog submitted by LiphaTech demonstrated that after ingestion of a single lethal dose or repeated administration of sublethal doses of bromadiolone on five occasions at 48 hour intervals, antidotal therapy consisting of slow intravenous injection of vitamin K followed by 7 days of oral administration of vitamin K resulted in rapid and complete recovery.
A study in rat with bromadiolone pellets (50 ppm end use product) submitted by LiphaTech also showed that vitamin K can reverse the effects. However, the effectiveness varied with the duration of exposure to bromadiolone.

Bromadiolone was not mutagenic in a standard range of in vitro and in vivo tests.

The carcinogenicity study and the chronic toxicity study were waived.
Performing long-term exposure studies is technically difficult when studying highly toxic substances such as bromadiolone, since dose levels, at which toxicity is identifiable but without rendering high levels of lethality, are hard to predict. The waiving is accepted, also considering the lack of genotoxicity.

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

In addition, evidence is presented to show that it would not be possible to perform a meaningful long-term study in any species because of the accumulative nature and high toxicity of the active substance.

Reproductive effects of bromadiolone can not be excluded by the submitted two-generation reproduction toxicity study (Task Force), but since long term exposure studies are technically hard to perform for such highly toxic substances as bromadiolone, no new study will be required. As with carcinogenicity, the primary reason for not requiring such a study is the long term use of the structurally similar molecule warfarin in humans without association with adverse effects on fertility.
The 2-generation study is therefore accepted as waived for both applicants.

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

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

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

The derivation of an acceptable level of exposure value for single use (AELacute) is based on the teratogenicity study in rabbits submitted by Task Force. It is based on the LOAEL of 2 µg/kg bw, using a safety factor of 600 (10 for interspecies and 10 for intraspecies variability, 2 for using LOAEL instead of NOAEL and an extra factor of 3 for severity of effects) and with correction of 70% oral absorption, resulting in an **AELacute of 0.0023 µg/kg bw**.
It was decided at TM III, 2006 that an extra AF of 3 will be used for all AVKs, while it was recognised that this factor is not scientifically derived. At TM I, 2007 it was further decided that a factor of 3 is considered sufficient to provide safe margins to cover for the use of subchronic studies for chronic exposure scenarios.
To derive an AELmedium, for repeated exposure, the subchronic study in rabbit submitted by Task Force is used, since it was performed in the most sensitive species. The NOAEL in this study is 0.5 µg/kg bw based on the prolonged prothrombin time seen at 1 µg/kg bw. With a safety factor of 300 and with correction of of 70% oral absorption, this would lead to an **AELmedium of 0.0012 µg/kg bw**.

To set an AELchronic the same NOAEL as for AELmedium will be used as no chronic studies have been performed. An extra safety factor of 3 will cover for the differences in exposure time.

The threshold limits and labelling regarding human health risks listed in Annex 2 „Toxicology and metabolism" must be taken into consideration.

2.7.1.2 Toxicology of the substance(s) of concern

Considering the following definition of a substance of concern set in the TNsG on data requirement chapter 4 (2000), "*the substance is regarded as a substance of concern if [...] it is classified as dangerous **and** its concentration in the product exceeds the classification limit set in the Council Directive 88/379/EEC, as amended by Directive 1999/45/EC, for a particular dangerous property **or** the other classification limit*

indicated for the substance in a preparation set in Annex I of Council Directive 67/548/EEC ***or*** *causes that the overall sum of the concentrations of dangerous substances in the product exceeds the limit for classification of the preparation set in Council Directive 88/379/EEC, as amended by Directive 1999/45/EC, for a particular dangerous property*",

MAKI GRAIN'TECH does not contain any substance of concern.

The basis for health assessment of the substance of concern is laid out in Annex 3 "Toxicology – biocidal 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.

Percutaneous absorption

No data on the product was provided by applicant.
It was proposed to use the *in vitro* dermal absorption of bromadiolone through human split thickness skin membranes of radiolabelled bromadiolone of two test preparations (red impregnated oat and Green Block) containing 50mg/kg and with a composition considered as extrapolable to MAKI GRAIN'TECH.

The dislogeable (unabsorbed) dose for ^{14}C-bromadiolone in red impregnated oat formulation applied to human split thickness skin membrane was 94.57% of applied dose. Total radioactivity available for absorption (perfusate + tapestrips+skin membrane) was 1.59% of applied dose. After 24 hours the total amount of ^{14}C-bromadiolone in red impregnated oat formulation absorbed through skin into to the perfusate was only 0.7%.

The dislogeable (unabsorbed) dose for ^{14}C-bromadiolone in red paste formulation applied to human split thickness skin membrane was 107.94% of applied dose. Total radioactivity available for absorption (perfusate + tapestrips + skin membrane) was 0.27% of applied dose. After 24 hours the total amount of ^{14}C-bromadiolone in red paste formulation absorbed through skin into to the perfusate was only 0.7%. Human *in vivo* dermal absorption can be estimated at < 1%.

In the exposure assessment, absorption of 1.6% is used as a worst case (remark: this approach was accepted in the CAR of Liphatech bromadiolone for a similar product (SUPERCAID AS appat)).

Acute toxicity

No studies have been performed with MAKI GRAIN'TECH.

For oral and dermal acute toxicity, a read across with a comparable formulation (Maki Rat and Mouse Meal Bait) containing the same concentration of bromadiolone is proposed.
Since it is not expected that the differences of composition between Maki Rat and Mouse Meal Bait formulation and MAKI GRAIN'TECH formulation impact the toxicity, the extrapolation of studies results was accepted (remark: this approach was accepted in the CAR of Liphatech bromadiolone for a similar product (SUPERCAID AS appat)).

Route	Species Strain Sex No/group	Dose levels Duration of exposure	Value LD_{50}/LC_{50}	Remarks
Oral	Rat	Single dose at	At 5000 mg/kg	Maki Rat and

	Crl:CD.BR 5/sex/group	5000 mg/kg bw Post exposure period: 21 days	bw: no death LD_{50}>5000 mg/kg bw	Mouse Meal Bait
Dermal	Rabbit Hra:(NZW)SPF 5/sex/group	Single dose of 0.05 g/cm^2 equivalent to 2000 mg/kg bw, applied to 10% body surface for 24 hours	At 2000 mg/kg bw: no death LD_{50}>2000 mg/kg bw Dermal irritation consisted of slight erythema for 6 of 10 rabbits on day 1 only. All reactions resolved by day 2	Maki Rat and Mouse Meal Bait

A justification for non-submission of data was provided by applicant for the acute inhalation toxicity based on the physical nature of the product (inhalation of volatiles from the grains is highly improbable and inhalation of dust also). Additionally, the vapor pressure of bromadiolone is low ($2.13x10^{-8}$ Pa at 25°C)

The justification for non-submission based on the physical nature of the product, is not acceptable considering that exposure by dust could be not negligible. In this context, the classification of the product for this endpoint will be based on the directive 99/45/EEC.

Irritation and corrosivity

No studies have been performed with MAKI GRAIN'TECH.

A read across with a comparable formulation (Maki Rat and Mouse Meal Bait) containing the same concentration of bromadiolone is proposed.
Since it is not expected that the differences of composition between Maki Rat and Mouse Meal Bait formulation and MAKI GRAIN'TECH formulation impact the toxicity, the extrapolation of studies results was accepted (remark: this approach was accepted in the CAR of Liphatech bromadiolone for a similar product (SUPERCAID AS appat)).

Skin irritation

Species	Average score 24, 48, 72h		Reversibility?	Result
	erythema	oedema		
Rabbit	0.28	0.00	Slight erythema evident in first 24-48 hours had reversed within 72 hours	Maki Rat and Mouse Meal Bait

Eye irritation

Species	Average score				Reversibility?	Result
	cornea	iris	Conjunctiva			
			Redness	Chemosis		
Rabbit	0.00	0.00	0.94	0.39	Yes. Initial slight conjunctival reactions had resolved within 96 hours of	Maki Rat and Mouse Meal Bait

					treatment	

Based on these data, the product should not be classified for irritation.

Sensitisation

No studies have been performed with MAKI GRAIN'TECH.

A read across with a comparable formulation (Maki Rat and Mouse Meal Bait) containing the same concentration of bromadiolone is proposed.
Since it is not expected that the differences of composition between Maki Rat and Mouse Meal Bait formulation and MAKI GRAIN'TECH formulation impact the toxicity, the extrapolation of studies results was accepted (remark: this approach was accepted in the CAR of Liphatech bromadiolone for a similar product (SUPERCAID AS appat)).

Species	Method	Number of animals sensitized/total number of animals	Result
Guinea pig	Buehler test	Controls:10 males Test group: 10 males Positive controls: 4 males	No evidence for inducing delayed contact hypersensitivity Maki Rat and Mouse Meal Bait

Based on these data, the product should not be classified for sensitisation.

Other

No harmonised classification is currently available but a classification according the criteria in directive 67/548/ECC with specific concentration limits is proposed in the combined assessment report. A classification proposal has been also submitted to ECHA in August 2010.

<u>Proposed classification according to the criteria in directive 67/548/EEC:</u>
T+; R26/27/28
T; R48/23/24/25
Repr. Cat. 1; R61

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

<u>Proposed classification according to the criteria in Regulation (EC) 1272/2008:</u>
Acute tox. 1; H300, H310, H330
Repr. 1A; H360D
STOT RE 1; H372

Specific concentration limits
C≥0.01% STOT RE 1; H372
0.001%≤C<0.01% STOT RE 2; H373

In the absence of harmonised classification, this proposal is used to determine the classification of the product.

Based on the results of the studies, the concentration of the active substance and of other components contained in the product and according to the above classification, MAKI GRAIN'TECH required a classification:

Xn ; R48/20/21/22 R20

STOT RE2; H373

The basis for the health assessment of the biocidal product is laid out in Annex 5 "Toxicology – biocidal product"

2.7.2 Human exposure assessment

MAKI GRAIN'TECH is a cereal grain baits that contains 50 mg/kg bromadiolone as the active substance. It is supplied ready to use in sachet or not for professionals and amateur user.

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

The potential for exposure to bromadiolone is summarised in the table below:

Exposure path	Industrial use	Professional use	General public	*via* the environment
Inhalation	Not relevant	Potentially significant	Negligible	Negligible
Dermal	Not relevant	Potentially significant	Potentially significant	Negligible
Oral	Not relevant	Negligible	Negligible	Negligible

Professional and non-professional users may be potentially exposed by skin contact either when dispensing the product or when cleaning-up and disposing of unused product.

Professional users may be potentially exposed by inhalation during decanting of grain bait
Oral exposure is considered to be negligible as the product is unlikely to reach the mouth directly.

2.7.2.2 Exposure of professional users

Assessment of exposure was based on the studies of Chambers[9] *et al.* and Snowdon[10] and the HEEG opinion on an Harmonised approach for the assessment of rodenticides (anticoagulants).

MAKI GRAIN'TECH (in sachet or not) is used:

- In and around building and open areas against rats (200 g/bait point), voles (100 g/bait point) and mice/field mice (50 g/bait point)

[9] J.G. chambers, P.J. Snowdown « study to determine potential exposure to operators during simulated use of anticoagulant rodenticide baits ». Synergy LABORATORIES limited, Thaxted, UK, laboratory report number SYN/1302, 8 March 2004 Sponsor CEFIC/EBPF Rodenticides Data Development Group

[10] P.J. Snowdon "Pilot study to determine primary sources of exposure to operators during simulated use of anticoagulant rodenticide baits". Synergy LABORATORIES limited, Thaxted, UK, laboratory report number SYN/1301, 27 November 2003, Sponsor CEFIC/EBPF Rodenticides Data Development Group

- Waste dump against rats (200 g/bait point)

The data of exposure used for “in and around building “covered the scenario “waste dump“ and “open areas”. In this scenario, 3 steps are taken in consideration: Mixing and loading-decanting of grain bait, application – loading and placing bait boxes and post-application –cleaning of bait boxes.

Exposure by dermal and inhalation were considered.

The assessment of exposure was assessed by tier approach:
Grain without sachet:
- Tier 1: no protective gloves
- Tier 2: protective gloves with a protection of 95%

Grain with sachet
- Tier 1: no protective gloves

In case of grain in sachet, it can be assumed that no exposure is expected during decanting and placing in bait point as the sachet prevents dermal contacts and inhalation. Therefore, only exposure during cleaning could be considered and therefore, exposure will be the same for treatment against rats, voles and mice/field mice.

The following points have been taken in consideration:
- For dermal absorption, a value of 1.6 % is used
- Active substance in product: 0.005 % (w/w)
- Operator body weight is assumed to be 60 kg
- A protection factor of 95 % for protective gloves was used, based on HEEG opinion “Default protection factors for protective clothing and gloves, agreed at TMI 2010.

Based on the studies of Chambers *et al.* and Snowdon and the HEEG opinion on an Harmonised approach for the assessment of rodenticides

Scenario in and around building:
For decanting, dermal exposure assessment is based on the amount of product on hand exposure during the decanting of 3 kg of grain bait: 52.3 mg bp.
The corresponding value will be 219.66 mg product for 12.6 kg.
It was considered that operator will be loaded 63 points per day.
Inhalation exposure assessment is based on the amount of product in air during the decanting of 3 kg of grain bait: 9.62 mg bp/m^3.
The amount of inhaled product will be 2.53 mg product for 12.6 kg.
It was considered that operator will be loaded 63 points per day.

For loading, exposure assessment is based on the amount of product on fingers/hands during the loading of 200 g of product per one manipulation: 2.04 mg.
It was considered that operator will be loaded 63 points per day.

For cleaning, exposure assessment is based on the amount of product on fingers/hands during the cleaning of one bait point: 3.79 mg.
It was considered that operator will be cleaned 16 points per day.

Summary of exposure

Tier	Scenario	Inhalation	Dermal

		exposure mg	exposure mg
In and around building			
Without sachet			
RATS : 200 g			
Tier 1	Without gloves	$1.3x10^{-4}$	$3.3x10^{-4}$
Tier 2	With gloves	$1.3x10^{-4}$	$1.6x10^{-5}$
VOLES: 100 g			
Tier 1	Without gloves	$6.3x10^{-5}$	$2.4x10^{-4}$
Tier 2	With gloves	$6.3x10^{-5}$	$1.2x10^{-5}$
MICE/FIELD MICE: 50 g			
Tier 1	Without gloves	$3.2x10^{-5}$	$1.9x10^{-4}$
Tier 2	With gloves	$3.2x10^{-5}$	$9.8x10^{-6}$
With sachet			
RATS : 200 g ; VOLES: 100 g; MICE/FIELD MICE: 50 g			
Tier 1	Without gloves	negligible	$4.9x10^{-5}$

For grain in sachet, the assessment of exposure during use against rats in and around building is a worst case for the treatment against voles and mice/field mice as the efficient dose is inferior.

2.7.2.3 Exposure of non-professional users and the general public

MAKI GRAIN'TECH (in sachet or not) is used against rats (200 g/bait point), voles (100 g/bait point) and mice/field mice (50 g/bait point):

- In and around building

In this scenario, 3 steps are taken in consideration: Mixing and loading-decanting of grain bait, application – loading and placing bait boxes and post-application –cleaning of bait boxes.

The assessment of exposure was assessed considering without gloves and without sachet.

In case of grain in sachet, it can be assumed that no exposure is expected during placing in bait point as the sachet prevents dermal contacts. Therefore, only exposure during cleaning could be considered. In this context if risk characterization is acceptable without sachet, it is not necessary to assess exposure with sachet.

The following points have been taken in consideration:

- For dermal absorption, a value of 1.6 % is used
- Active substance in product: 0.005 % (w/w)
- Operator body weight is assumed to be 60 kg
- Agreed with the TNsG on human exposure 2007, no PPE is taken in consideration for non-professional

Based on the studies of Chambers *et al.* and Snowdon and the HEEG opinion on an Harmonised approach for the assessment of rodenticides.

Scenario in and around building:

For decanting, dermal exposure assessment is based on the amount of product on hand exposure during the decanting of 3 kg of grain bait: 93.1 mg bp.
The corresponding value will be 31 mg product for 1 kg.
It was considered that non professional will be loaded 5 points per day.
Inhalation exposure assessment is based on the amount of product in air during the decanting of 3 kg of grain bait: 9.62 mg bp/m^3.
The amount of inhaled product will be 0.2 mg product for 1 kg.
It was considered that non professional will be loaded 5 points per day.

For loading, exposure assessment is based on the amount of product on fingers/hands during the loading of 200g of product per one manipulation: 3.57 mg.
It was considered that operator will be loaded 5 points per day.

For cleaning, exposure assessment is based on the amount of product on fingers/hands during the cleaning of one bait point: 4.52 mg.
It was considered that operator will be cleaned 5 points per day.

Summary of exposure

Tier	**Scenario**	**Inhalation exposure**	**Dermal exposure mg**	**Oral exposure**
In and around building				
Without sachet				
Rat : 200 g				
Tier 1	Without gloves	$1x10^{-5}$	$5.7x10^{-5}$	negligibe

The assessment of exposure of non professional for the treatment against rats covers the exposure for the treatment against voles and mice/field mice.

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

Secondary exposure of users and non users could result in the handling of dead rodents. However, this scenario is excluded due to unrealistic assumptions (very low amount of bromadiolone is expected on the fur)

Exposure of non users can occur during ingestion of poison baits.
For the scenario "*oral exposure by ingesting bait*", a reverse scenario was calculated. Based on the acute AEL of $2.3x10^{-6}$ mg a.s/kg bw/day, a body weight of 10 kg and an oral absorption of 70% (as stated in the Assessment report of bromadiolone), ingestion of more than 0.66 mg of product per day by an infant is needed to exceed the AEL.

2.7.3 Risk assessment for human health

The estimated exposures for the professional and non professionnel users are compared to the systemic AEL of bromadiolone set in the combined Assessment report:

AEL long-term	$1.2x10^{-3}$ µg/kg/d
AEL medium-term	
AEL acute	$2.3x10^{-3}$ µg/kg/d

2.7.3.1 Risk for Professional Users

Table 2.7.3-1: Summary of risk characterisation for professionals

Tier	Scenario	AEL (µg/kg bw/d)	Exposure (µg/kg bw/d)	% AEL	Risk
In and around building					
Without sachet					
RATS: 200 g					
Tier 1	Without gloves	$1.2x10^{-3}$	$7.6x10^{-3}$	629	unacceptable
Tier 2	With gloves	$1.2x10^{-3}$	$2.4x10^{-3}$	198	unacceptable
VOLES: 100 g					
Tier 1	Without gloves	$1.2x10^{-3}$	$5x10^{-3}$	419	unacceptable
Tier 2	With gloves	$1.2x10^{-3}$	$1.2x10^{-3}$	104	unacceptable
MICE/FIELD MICE: 50 g					
Tier 1	Without gloves	$1.2x10^{-3}$	$3,8x10^{-3}$	315	unacceptable
Tier 2	With gloves	$1.2x10^{-3}$	$6,9x10^{-4}$	57.4	**acceptable**
With sachet					
RATS: 200 g; VOLES: 100 g; MICE/FIELD MICE:50 g					
Tier 1	Without gloves	$1.2x10^{-3}$	$8x10^{-4}$	67.4	**acceptable**

The risk for professional user is acceptable “in and around building” and consequently for the scenario “waste dump“ and “open areas” :

- Without sachet with gloves only for the treatment against mice/field mice;
- With sachet without gloves for the treatment against rats, voles and mice/field mice.

Considering the results and to maintain coherence between the intended uses, French Agency proposes to keep only the packaging with sachet.

2.7.3.2 Risk for non-professional users and the general public

Table 2.7.3-2: Summary of risk characterisation for non-professionals

Tier	Scenario	AEL (µg/kg bw/d)	Exposure (µg/kg bw/d)	% AEL	Risk
In and around building					
Without sachet					

RATS : 200 g					
Tier 1	Without gloves	$2.3x10^{-3}$	$1.1x10^{-3}$	48.6	**acceptable**

The risk for non-professionnal is acceptable “in and around building” for treatment against rats,voles and mice/field mice without sachet and by extrapolation with sachet.

But considering the results and to maintain coherence between the intended uses, French Agency proposes to keep only the packaging with sachet.

2.7.3.3 Indirect exposure as a result of use

Based on a reverse scenario, more than 0.66 mg of product per day should be ingested by an infant to exceed the AEL.
This indicates that infants are at significant risk of poisoning. Therefore, even if MAKI GRAIN’TECH contains a bittering agent which reduces the likelihood of ingestion, the baits should be unattainable for children.
Product label (“do not open the sachet”) and good practice advise users to prevent access to bait by children and infants.

2.7.3.4 Risk for consumers via residues

Considering the intended uses no dietary risk assessment is necessary.

2.7.3.5 Risk for combined exposure

Not relevant.

2.7.3.6 Conclusion of the risk assessment for human health

No unacceptable risk has been observed for professionals and non-professionals using MAKI GRAIN’TECH in individual plastic sachets, without gloves.

For the indirect scenario “Infant ingesting bait”, an unacceptable risk was observed. Therefore, even if MAKI GRAIN’TECH contains a bittering agent which reduces the likelihood of ingestion, the baits should be unattainable which do not allow access to children. Product label (“do not open the sachet”) and good practice advise users to prevent access to bait by children and infants.

Professional users

Measures to protect man

- Gloves have to be worn to help prevention against rodent-borne disease.
- Do not open the sachets.
- Apply strict hygiene measures: do not eat, drink or smoke during handling of the product and wash hands after use of the product.
- Tamper-resistant bait boxes should be clearly marked to show that they contain rodenticides and that they should not contain other products than rodenticides.

- For professional users, covered bait stations could be used. These stations must be placed only in areas not accessible to the general public and non-target animals.
- Baits must be unattainable to children, pets or other non-target animals in order to minimize the risk of poisoning.
- Do not place tamper-resistant bait boxes and covered bait stations on surfaces in contact with food, feed or drinks and beverages.
- Collect uneaten bait, bait fragments dragged away from the tamper-resistant bait boxes or covered bait stations and dead rodents, during and after treatment.
- Remove all bait points after the end of treatment.

Non professional users

Measures to protect man

- Do not open the sachets.
- Apply strict hygiene measures: do not eat, drink or smoke during handling of the product and wash hands after use of the product.
- Use only in tamper-resistant bait boxes.
- Tamper-resistant bait boxes should be clearly marked to show that they contain rodenticides and that they should not contain other products than rodenticides.
- Baits must be unattainable to children, pets or other non-target animals in order to minimize the risk of poisoning.
- Do not place tamper-resistant bait boxes and covered bait stations on surfaces in contact with food, feed or drinks and beverages.
- Collect uneaten bait, bait fragments dragged away from the tamper-resistant bait boxes or covered bait stations and dead rodents, during and after treatment.
- Remove all bait points after the end of treatment.

2.8. Risk assessment for the environment

2.8.1 Fate and distribution of the active substance, bromadiolone, in the environment

The summary of information about the active substance bromadiolone is carried out with the data from the Competent Authority Report (CAR) of bromadiolone owned by the notifier Liphatech S.A.S (Liphatech S.A.S, Competent Authority Report According to Directive 98/8/EC, Active substance in Biocidal Products, Bromadiolone CAS 28772-56-7, Product Type 14 (Rodenticides), RMS Sweden, March 2008). No new ecotoxicological information on the active substance bromadiolone has been submitted in the product dossier.

2.8.1.1 Degradation

2.8.1.1.1 Abiotic degradation

2.8.1.1.1.1 Hydrolysis as function of pH

According to the test US EPA 161-1, bromadiolone is considered stable to hydrolysis at pH 5, 7 and 9 with no significant degradation products. The hydrolytic degradation of bromadiolone is not expected to be a significant process in the environment.

2.8.1.1.1.2 Photolysis in water

The active substance undergoes rapid photodegradation with a mean half-life time (DT_{50}) value of 12.5 minutes at 25°C. Photolysis of bromadiolone led to the formation of carbon dioxide and significant levels (>10% of the applied radioactivity) of six unidentified degradation products which had either reached plateau levels or were declining at the end of the study (15 days). These metabolites are supposed to be transient since they were past their maximum levels after the end of the study. The exposure to the aquatic compartment according to the recommended use of bromadiolone was considered as low, therefore it was stated that no further characterisation of metabolites was requested for the inclusion of the active substance.

2.8.1.1.1.3 Photolysis in soil

Not relevant for bromadiolone

2.8.1.1.1.4 Photodegradation in air

Photodegradation characteristics of the active substance have been estimated using the Atmospheric Oxidation Program v1.90 (AOPWIN) program. Bromadiolone has an estimated half-life of 2.1 hours and the ozone reaction in air is estimated to 2.0 hours. This shows that bromadiolone photodegrades rapidly in air.It is predicted not to be a potential greenhouse gas. Finally, bromadiolone is not expected to volatilise (low Henry's law constant = 8.99 x 10^{-7} $Pa.m^3.mol^{-1}$) or to persist in air in significant quantities as emissions to the air compartment are expected to be low.

2.8.1.1.2 Biotic degradation

2.8.1.1.2.1 Aquatic compartment

According to the available data and the OECD test 301B, bromadiolone is not readily or inherently biodegradable.

The effect of bromadiolone on aerobic biological sewage treatment plant (STP) processes was assessed by determining inhibition of respiration of the micro-organisms present in activated sludge following 3 hour contact. The study indicated that bromadiolone inhibits microbial activity, and therefore it can possibly have a negative impact on microorganisms in an STP. No studies on biodegradation in sewage treatment plants and in water and sediment systems are available, so bromadiolone is considered not degraded under such conditions. The applicants justifications referring to the limited exposure of these compartments for bromadiolone have been found acceptable in the CAR of the bromadiolone.
Hence, for the aquatic compartment, bromadiolone is assumed to be not biodegradable under environmentally relevant conditions. So the risk assessment in aquatic compartment is based on the assumption that bromadiolone is not biodegradable and the half-life (DT_{50}) is over 365 days.

2.8.1.1.2.2 Terrestrial compartment

Bromadiolone is quickly degraded in soil under aerobic conditions in laboratory according to two studies conducted with the US EPA Pesticide Assessment Guidelines, Subdivision N, Paragraph 162-1 and BBA guideline Part IV, 4-1 (1986). Calculated DT_{50} values are between 4 and 53 days (at 12°C, extrapolated from 20 and 25°C). Mean value has been calculated to 16 days. Degradation led to the formation of unidentified soil metabolites which persisted in significant quantities for > 1570 days.

So the risk assessment is based on the assumption that bromadiolone is not readily biodegradable and a half life in soil is over 16 days. Moreover, the active substance degradation in soil leads to the formation of five major metabolites (exceeding 10 % of active rate). One of the metabolites was identified as bromadiolone ketone with an estimated half-life between 162 and 474 days at 12°C. The four remaining metabolites (Unk 1, Unk 3, M4 and M5) were not identified but their half-lives were estimated. DT_{50} varied between 86 and 387 days at 12°C. For one of the metabolites (Unk 3) it was not possible to calculate a DT_{50} since a decline profile was not established during the study. For the same reason, it was not possible to calculate a DT_{50} for another unknown metabolite, M9 (probably corresponding to Unk 3). It should be noted that the levels of Unk3/M9 increased steadily and reached 24 and 24.8 % of AR, respectively, at the end of the studies (365 and 154 d, respectively). Finally, the level of soil non-extractable residues (NER) reached a level of 9 to 21 % of AR after *ca* 100 days.
No further studies were submitted by the applicant. It was accepted that the environmental exposure of bromadiolone is limited to very strict areas when used as recommended for the inclusion of the active substance.

2.8.1.2 Distribution

The active substance is adsorbed to soil. The determined K_{oc} for bromadiolone from the combined assessment report (including data for both applicants) is between 1563 to 41600 mL/g (mean value 14770 mL/g). No pH dependence observed. On the basis of this data, bromadiolone is practically ’non mobile” in soil.

2.8.1.3 Accumulation

The aquatic BCF has been estimated with calculation method (according to Equation 74, TGD) because the fish bioconcentration tests were only used as supportive data in the CAR of the bromadiolone. The measured value of log Kow (4.07) allows to calculate an estimated BCF for fish : 575 L/kg.

For the terrestrial compartment, an estimation of the BCF for bromadiolone has been done using equation 82d of the TGD with a log K_{ow} of 4.07, resulting in a $BCF_{earthworm}$ of 142 L/kg.

The calculations show that bromadiolone has a low bioaccumulation potential in aquatic and terrestrial organisms.

2.8.1.4 Behaviour in air

The vapour pressure of bromadiolone at ambient temperature has been determined to be 2.13 x 10^{-8} Pa (OECD 104). Furthermore, Henry's law constant for bromadiolone has been calculated to 8.99 x 10^{-7} Pa·m^3/mol (based on a water solubility of 12.5 mg/L). Based on these data bromadiolone is not considered volatile and is not expected to partition into air in significant quantities.

In addition, the photochemical oxidative degradation half-life of bromadiolone in air is estimated to 2.1 hours and the ozone reaction in air is estimated to 2.0 hours.

Considering the above information, bromadiolone is not expected to volatilise to or persist in air in significant quantities.

2.8.2 Effects on environmental organisms

The summary of information about the active substance bromadiolone is carried out with the data from the Competent Authority Report (CAR) of bromadiolone owned by the notifier Liphatech S.A.S (Liphatech S.A.S, Competent Authority Report According to Directive 98/8/EC, Active substance in Biocidal Products, Bromadiolone CAS 28772-56-7, Product Type 14 (Rodenticides), RMS Sweden, March 2008). No new ecotoxicological information on the active substance difenacoum has been submitted in the product dossier.

2.8.2.1 Aquatic compartment (including water, sediment and STP)

2.8.2.1.1 Aquatic organisms

Bromadiolone is very toxic to aquatic organisms. Algae are the most sensitive of the three trophic levels tested (E_bC_{50} =0.17 mg a.s/L). Bromadiolone is also toxic to fish (LC_{50}= 8 mg a.s/L) and invertebrates (EC_{50} = 2 mg a.s/L).

Table 2.8.2.1-1: Toxicity to freshwater aquatic organisms

Guideline / Test method	Species	Endpoint	Results (mg a.s/l)	Reference
OECD 203 / semi-static system	*O. mykiss* fish	96 hour LC_{50}	> 8.0 (nominal./measured.)	CAR a.s. III-A 7.4.1.1-01

OECD 202 / static system	*D. magna* aquatic invertebrate	48 hour EC_{50}	2.0 (measured)	CAR a.s. III-A 7.4.1.2
OECD 201 / static system	*Pseudo-kirchneriella subcapitata* algae	72 hour E_bC_{50} 72 hour E_rC_{50}	0.17 >1.0	CAR a.s. III-A 7.4.1.3

Justification of $PNEC_{water}$:
The $PNEC_{water}$ is derived from the lowest available LC_{50} value = 0.17 mg/L (algae). An additional assessment factor of 10 has been added to the assessment factor of 1000, due to the large uncertainty and likely underestimation of toxicity that is the case for the actual endpoint growth inhibition of algae as only data on acute toxicity is available. Therefore,

$$\mathbf{PNEC_{water} = 1.7 \times 10^{-5}\ mg/L.}$$

2.8.2.1.2 Sediment dwelling organisms

No ecotoxicological data for sediment-dwelling organisms are available in the Liphatech S.A.S.dossier. As the exposure to the aquatic compartment is low, therefore it was stated that no test on these organisms was requested.

Justification of $PNEC_{sediment}$:
No ecotoxicological data for sediment-dwelling organisms are available in the Liphatech S.A.S.dossier. However a PNEC for the sediment dwelling organisms is calculated with the equilibrium partitioning method accoding to TGD II, taking into account the average Koc value of 14770 mL/g.
Therefore,

$$\mathbf{PNEC_{sediment} = 0.83\ mg/kg\ ww.}$$

2.8.2.1.3 STP micro-organisms

Concerning microbial activity in water an EC50(3h) of 31.6 mg/L (nominal concentration) and an EC20 of approximately 10 mg/L were determined for bromadiolone according to OECD 309, inhibition of microorganisms present in activated sludge.

Justification of $PNEC_{STP}$:
The $PNEC_{microorganisms}$ is derived from the available LC_{50} value = 31.6 mg/L divided by an assessment factor of 100.Therefore,

$$\mathbf{PNEC_{microorganims} = 0.316\ mg/L}$$

2.8.2.2 Atmosphere

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

2.8.2.3 Terrestrial compartment

Bromadiolone caused no acute toxic effects on earthworms up to 9.48 mg/kg dry soil, the highest concentration applied (OECD 207). After normalization, the resulting moisture-corrected 14-day LC50 of bromadiolone is 8.4 mg/kg dry weight No further studies on the toxicity to terrestrial organisms have been available with the argument that exposure of the terrestrial compartment is very localized and limited to small areas.

Justification of $PNEC_{soil}$:
The $PNEC_{soil}$ is derived from the experimental data. An assessment factor of 1000 was applied to the LC_{50} > 8.4 mg/kg issued from an earthworms study to derive the $PNEC_{soil}$.

$PNEC_{soil}$ = 0.0084 mg/kg wet weight

The $PNEC_{soil}$ value wasn't calculated according to the equilibrium partitioning method (EPM) because it was not considered suitable for highly hydrophobic substances like bromadiolone.

2.8.2.4 Non compartment specific effects relevant to the food chain

2.8.2.4.1 Primary poisoning

2.8.2.4.1.1 Acute/short-term qualitative assessment

Acute primary toxicity for birds and mammals is assessed only qualitatively in accordance with the decision from TMIII-06.

For mammals the LD_{50} value for mammals from the final CA report of bromadiolone (LiphaTech S.A.S, Competent Authority Report According to Directive 98/8/EC, Active substance in Biocidal Products, Bromadiolone CAS 28772-56-7, Product Type 14 (Rodenticides), RMS Sweden, March 2008) is the lowest value. Therefore, **LD50 = 0.56-0.84 mg a.s. /kg bw** is used in the qualitative risk assessment for comparisons with estimated daily uptakes of bromadiolone (ETE, mg a.s. /kg bw).

Bromadiolone is toxic **for birds**, based on acute oral and short-term dietary toxicity tests conducted with two species. For bobwhite quail and mallard duck the LD_{50} values were 138 and 1,293 mg/kg bw, respectively. The lowest LC50 value for birds is the acute toxicity to Japanese quail from the final CA report of another notifier of bromadiolone (Task Force, Competent Authority Report According to Directive 98/8/EC, Active substance in Biocidal Products, Bromadiolone CAS 28772-56-7, Product Type 14 (Rodenticides), RMS Sweden, April 2011): LD50 = 134 mg a.s. /kg bw is used in the qualitative assessment for comparisons with estimated daily uptakes of bromadiolone (ETE, mg a.s. /kg bw).

2.8.2.4.1.2 Long term quantitative assessment

Justification of $PNEC_{oral\ mammals}$ and $PNEC_{oral\ birds}$:

Table 2.8.2.4-2: PNEC for birds and mammals, Lipha Tech data (from the Assessment Report)

Organism group	Species/ test	Results	Assess -ment factor	PNEC (conc. in food)	PNEC (dose)

Birds	Japanese quail/ reproduction test 140 days (20 weeks)	NOEC = 0.1 mg/kg food NOEL = 0.01138 mg/kg bw/day	30	0.0033 mg/kg food	0.00038 mg/kg bw/day
Mammals	Rat/ subchronic 90 days (difethialone)	NOAEL =2 µg/kg bw/day	90	0.00044 mg/kg food	0.000022 mg/kg bw/day
	Dog/ subchronic 90 days	NOAEL =8 µg/kg bw/day	30	0.011 mg/kg food	0.00027 mg/kg bw/day

For birds the $PNEC_{oral}$ was determined by the NOEC value calculated from the 20week reproduction test. According to the TGD section 3.8.3.5, the NOEC value is divided by an assessment factor of 30 which results in a:

$PNEC_{oral}$ for birds (dose) = 0.01138/30 = 0.00038 mg/kg bw/ day
equivalent to
$PNEC_{oral}$ for birds (conc. In food) = 0.1/30 = 0.0033 mg/kg food

Additional endpoint:

The $PNEC_{oral\ mammals}$ from the final CA report of another notifier of bromadiolone (Task Force, Competent Authority Report According to Directive 98/8/EC, Active substance in Biocidal Products, Bromadiolone CAS 28772-56-7, Product Type 14 (Rodenticides), RMS Sweden, April 2011) is lower than the $PNEC_{oral\ mammals}$ calculated above and is thus used in the risk assessment. For mammals, the most sensitive organism is the rabbit in the 90 days subchronic test with a NO(A)EL of 0.0005 mg/kg bw. According to the TGD section 3.8.3.5, the NOAEL is transformed into a NOEC using a conversion factor of 33.3, and the AF_{oral} of 90 is applied to this NOEC, which results in a

$PNEC_{oral}$ for mammals = 0.0005/90 = 0.0000056 mg/kg bw/day
equivalent to
$PNEC_{oral}$ for mammals = 0.017/90 = 0.00019 mg/kg food

A PNECoral for dog was derived from a subchronic 90-days study with an AF of 30 which results to:

$PNEC_{oral}$ for dog = 0.0011 mg/kg bw/day
equivalent to
$PNEC_{oral\ for}$ dog = 0.008/30 = 0.00027 mg/kg food

2.8.2.4.2 Secondary poisoning

2.8.2.4.2.1 Acute/short-term qualitative assessment

For mammals, the value of the acute toxicity to rat: LD_{50} = **11.2-16.8 mg a.s. /kg food** (Lipha Tech data) is used as the worst case value for bromadiolone in the qualitative assessment for comparisons with estimated daily uptakes of bromadiolone (PEC mg a.s. /kg food).

For birds, the lowest **LC50** is **207 mg a.s. /kg food** (Lipha Tech data). Subsequently, and is used in the qualitative risk assessment for comparisons with estimated daily uptakes of bromadiolone (PEC mg a.s. /kg food).

2.8.2.4.2.2 Long term quantitative assessment

From the data submitted by the participant, it has not been possible to derive a specific PNEC for secondary poisoning of mammals due to the limited numbers of animals and lack of information of the concentration in fed. However, in the final CA report of another notifier of bromadiolone (Task Force, Competent Authority Report According to Directive 98/8/EC, Active substance in Biocidal Products, Bromadiolone CAS 28772-56-7, Product Type 14 (Rodenticides), RMS Sweden, April 2011) data are available: for mammals, the most sensitive organism is the rabbit in the 90 days subchronic test with a NO(A)EL of 0.0005 mg/kg bw. According to the TGD section 3.8.3.5, the NOAEL is transformed into a NOEC using a conversion factor of 33.3, and the AF_{oral} of 90 is applied to this NOEC, which results in a

$PNEC_{oral}$ for mammals = 0.017/90 = 0.00019 mg/kg food

equivalent to $PNEC_{oral}$ for mammals = 0.0005/90 = 0.0000056 mg/kg bw/day

For birds the $PNEC_{oral}$ was determined by the NOEC value calculated from the 7-day dietary test. According to the TGD section 3.8.3.5, the NOEC value is divided by an assessment factor of 300 which results in a

$PNEC_{oral}$ for birds = 0.056/300 = 0.00019 mg/Kg bw/day

equivalent to $PNEC_{oral}$ for birds = 0.00075 mg/Kg food

2.8.2.5 Summary of PNECs

PNEC values from the final CA report of other notifier of bromadiolone are indicated when they represent worst-case value in comparison with the PNEC values presented in the CA report of the notifier Task Force.
The lowest PNEC values are used in the risk assessment.

Table 2.8.2.5-1: summary of the bromadiolone PNECs used for risk assessment

Compartment		Test Value	AF	PNEC Unit	CAR
Aquatic	$PNEC_{water}$	LC_{50} =0.17 mg/L	1000*10	0.000017 mg/L	Liphatech
	$PNEC_{sediment}$	Not available		0.83 mg/kg ww sediment (EPM)	Liphatech
	$PNEC_{STP}$	EC_{50} = 31.6	100	0.316 mg/L	Liphatech
Terrestrial	$PNEC_{soil}$	LC_{50} >8.4 mg/kg	1000	0.0084 mg/kg	Liphatech
Primary and secondary poisoning	$PNEC_{oral\ for\ birds}$	NOEC = 0.1 mg/kg food NOEL = 0.01138 mg/kg bw/day Japanese quail/ reproduction test 140 days (20 weeks)	30	**0.0033 mg/kg food** **0.00038 mg/kg bw/day**	Liphatech
		NOEC = 0.056 mg/kg bw/d Great horned owl/dietary 7 days	300	0.00075 mg/kg food 0.00019 mg/kg bw/d	Liphatech
	$PNEC_{oral\ for\ mammals}$	NO(A)EL=0.0005 mg a.s/kg bw/day NOEC= (0.0005*33.3)=0.017 mg a.s/kg food	90	**0.00019 mg/kg food** **0.0000056 mg/kg bw/day**	Task Force The PNEC oral for mammals is lower with the Task Force data

		Rabbit repeated dose toxicity 90 days			than for the Liphatech one so this PNEC is used for the risk assessment.
		NOAEL =8 µg/kg bw/day Dog/ subchronic 90 days	30	0.011 mg/kg food 0.00027 mg/kg bw/day	Liphatech

2.8.2.6 PBT and endocrine disruption assessment

The P/vP screening criteria are fulfilled and the soil P criterion of REACH is fulfilled when taking the toxic and persistent metabolites into account.
The B/vB screening criteria may be fulfilled.
The T criterion is fulfilled.

The TC NES Subgroup on Identification of PBT and vPvB Substances was consulted on the PBT properties of bromadiolone. The conclusion reached at the meeting on 5 March 2008 is that bromadiolone is considered a potential PBT substance.

According to the CAR of the notifier Liphatech S.A.S., the active substance bromadiolone is not an endocrine disruptor.

2.8.3 Effects on environmental organisms for biocidal product

The applicant did not provide ecotoxicological data about the biocidal product MAKI GRAIN'TECH. So the risk assessment is based on the data obtained from the active substance bromadiolone (LiphaTech S.A.S, Competent Authority Report According to Directive 98/8/EC, Active substance in Biocidal Products, Bromadiolone CAS 28772-56-7, Product Type 14 (Rodenticides), RMS Sweden, March 2008).

Denatonium benzoate is used in the biocidal product as bittering agent. This substance is classified as "Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment" in the frame of the Directive 91/414/EEC. Nevertheless in the concentration used in MAKI GRAIN'TECH, the substance does not contribute to the classification of the biocidal product according to the Directive 1999/45/EC.

No other substance used in the biocidal product is classified for the environment.

2.8.4 Environmental exposure assessment

In accordance with EUBEES ESD (2003) and TGD for Risk Assessment (2003), a quantitative approach is used in the risk assessment for MAKI GRAIN'TECH biocidal product. Quantitative PEC estimations are performed for the relevant environmental compartments.

As the product contains no substances of concern, it is considered that risks posed to environment following the use of MAKI GRAIN'TECH can adequately be assessed based on the evaluation conducted for the active substance. Therefore the exposure assessment is based on the data obtained from the active substance bromadiolone only.

MAKI GRAIN'TECH as bait contains 50 mg/kg bromadiolone as the active substance. The product is intended to be used to control rodents. Bromadiolone bait formulations are composed of dry solid cereal grains. The bait formulations are available ready to use either as loose bait or in sachets for both professional and non-professional use

MAKI GRAIN'TECH is used in the following areas:

- In and around buildings (professional and non-professional use);
- Waste dump (landfill) area (professional use only);
- Open areas (professional use only).

For the intended uses, the terrestrial compartment is the only relevant compartment of release. The risks are also calculated for primary and secondary poisoning.

2.8.4.1 PEC in surface water, sediment and STP

Contamination of surface water, STP or sediment with bromadiolone from the placing of bait in and around buildings, in open area or in waste dump is considered negligible according to the ESD. No exposure assessment is conducted for the aquatic compartment.

2.8.4.2 PEC in air

For bromadiolone, the estimated half-life for the hydroxyl reaction in air is 2.1 hours. With a vapour pressure value as determined by OECD 104 of 2.13 x 10^{-8} Pa and a Henry's law constant of 8.99 x 10^{-7} $Pa.m^3.mol^{-1}$, bromadiolone is not expected to volatilize to air in significant quantities following use in and around buildings, in open area or in waste dump. Finally, the potential concentration of bromadiolone in air is considered to be negligible.

2.8.4.3 PEC in soil (including groundwater)

2.8.4.3.1 In and around buildings

The exposure assessment has been carried out according to the EUBEES ESD for rodenticides (ESD PT14)[11] and the TGD[12]. As the ESD PT14 indicates, the only primary compartment to be exposed during a use around buildings is the terrestrial compartment. Emission calculations to soil and groundwater were conducted with the default parameters of the ESD PT14 as well as the specific information on the product provided by the applicant:

- A bromadiolone concentration in the baits of 0.005% (w/w),
- The protection of baits in bait stations or in other coverings,
- Maximal dose rates: 200 g for rats and 50 g for mice. These dose rates cover the treatment for voles and field mice
- Minimal distance between two bait points: 4 m for rats and 1 m for mice.

Exposure of the terrestrial compartment (soil) will occur when bromadiolone bait is deployed outdoors. EUBEES considers a scenario that entails outdoor baiting with bait boxes around a farm building. In this

[11] EUBEES 2 Emission scenario document for biocides used as rodenticides (Larsen, 2003)
[12] Technical Guidance Document on Risk Assessment (ECB, 2003)

situation, exposure is assumed to arise through a combination of transfer (direct release) and deposition *via* urine and faeces (disperse release) onto soil. In the scenario with the applicant parameters, the active substance metabolism is taken into account. EUBEES 2 considers that, in general, 90% of the total amount of rodenticide consumed by the target rodents over the duration of the outdoor baiting campaign enters soil via urine and faeces. In the case of bromadiolone, however, this is reduced in view of the extensive metabolism seen in a study with rats. Since no information is available on the toxicity of metabolites, it was assumed for the inclusion that these are as toxic as the a.s. and therefore the total value for excretion via faeces and urine (54.2% of dosed radioactivity excreted) will be used. This includes both the a.s. and the metabolites. The fraction of bromadiolone that enters soil via urine and faeces is thus 0.542.

EUBEES 2 considers two levels of baiting. In the first, described as the "realistic worst-case" with default values, the campaign lasts 21 days and secured bait points (initially filled on day 1 and repeatedly and completely emptied by the target rodents) are refilled on days 3, 7, 14 and 21, so 5 replenishments of the bait stations are considered. In the other, "typical" scenario, bait consumption progressively declines as the campaign proceeds, such that the replenishments made on days 3, 7, 14 and 21 represent 100%, 25-50%, 10% and 0%, respectively, of the quantity initially deployed on day 1 (=1.5 replenishments).

In both scenarios, the direct and disperse bromadiolone releases ($Elocal_{soil}$, mg) to the relevant soil surfaces may be calculated according to the input values presented in the table below. The different PEC values are calculated using the TDG equations. The degradation in soil was not considered in the calculation.

Table 2.8.4.3-1: PEC bromadiolone in soil and groundwater for uses in and around buildings

		ESD Default parameters: realistic worst-case		**Refined and specific parameters: typical scenario**		
Symbol	**Variable/parameters**	**Rat**	**Mouse**	**Rat**	**Mouse**	**Unit**
INPUTS						
$Q_{prod:}$	**Amount of product used in control operation for each bait box**	**200**	**50**	**200**	**50**	**[g]**
$Fc_{product}$:	**Concentration of active substance in product**	**0.05**	**0.05**	**0.05**	**0.05**	**[g.kg^{-1}]**
Nsites:	**Number of application sites**	**10**	**10**	**10**	**10**	**[-]**
N_{refil}:	**Number of refilling times**	**5**	**5**	**1.5**	**1.5**	**[-]**
$F_{release-D,\ soil}$:	**Fraction of product released directly to soil**	**0.01**	**0.01**	**0.01**	**0.01**	**[-]**
$F_{release-ID,\ soil}$:	**Fraction released indirectly to soil**	**0.9**	**0.9**	**0.542**	**0.542**	**[-]**
Koc	**Organic carbon adorption coefficient**	**14770**	**14770**	**14770**	**14770**	**[L.kg-1]**
Distance	**Distance between 2 bait points**	**4**	**1**	**4**	**1**	**[m]**
$AREA_{exposed-D}$:	**Area directly exposed to rodenticide originating from one**	**0.09**	**0.09**	**0.09**	**0.09**	**[m^2]**

	bait box					
$AREA_{exposed-ID}$:	**Area indirectly exposed to rodenticide**	**440**	**110**	**440**	**110**	**[m^2]**
$DEPTH_{soil}$:	**Depth of exposed soil**	**0.1**	**0.1**	**0.1**	**0.1**	**[m]**
RHO_{soil}:	**Density of exposed soil**	**1700**	**1700**	**1700**	**1700**	**[$kg.m^{-3}$]**
OUTPUTS						
$Elocal_{soil-campaign, direct}$:	***Direct emission to soil from a campaign***	**5.00E-03**	**1.25E-03**	**1.50E-03**	**3.75E-04**	**[$g.camp^{-1}$]**
$Elocal_{soil-campaign, indirect}$:	***Indirect emission to soil from a campaign***	**4.46E-01**	**1.11E-01**	**8.05E-02**	**2.01E-02**	**[$g.camp^{-1}$]**
$Elocal_{soil-campaign}$:	***Total emission to soil from a campaign***	**4.51E-01**	**1.13E-01**	**8.20E-02**	**2.05E-02**	**[$g.camp^{-1}$]**
$Clocal_{soil-D}$	***Local concentration in soil due to direct release ($AREA_{exposed-D}$) after a campaign:***	**3.27E-02**	**8.17E-03**	**9.80E-03**	**2.45E-03**	**[$mg.kg^{-1}_{wwt}$]**
$Clocal_{soil-ID}$	***Concentration in soil due to indirect (disperse= $AREA_{exposed-ID}$) release after a campaign:***	**5.96E-03**	**5.96E-03**	**1.08E-03**	**1.08E-03**	**[$mg.kg^{-1}_{wwt}$]**
$Clocal_{soil}$	***Worst case total concentration in soil = PECsoil***	**3.86E-02**	**1.41E-02**	**1.09E-02**	**3.53E-03**	**[$mg.kg^{-1}_{wwt}$]**
$Clocal_{soil\ mean\ concentration}$	***Mean concentration in soil. The total amount of product release (=$Elocal_{soil-campaign}$) is divided by the whole area exposed(=$AREA_{exposed-ID}$)***	**6.02E-03**	**6.02E-03**	**1.10E-03**	**1.10E-03**	**[$mg.kg^{-1}_{wwt}$]**
Kp_{soil}	***Partition coefficient solid-water in soil***	**2.95E+02**	**2.95E+02**	**2.95E+02**	**2.95E+02**	**[$L.kg^{-1}$]**
$K_{soil\ water}$	***Soil-water partitioning coefficient***	**4.43E+02**	**4.43E+02**	**4.43E+02**	**4.43E+02**	**[$m^3.m^{-3}$]**
PEClocal soil, porew	***Worst case concentration in groundwater (based on the total concentration in soil)***	**1.48E-04**	**5.42E-05**	**4.17E-05**	**1.35E-05**	**[$mg.L^{-1}$]**
PEClocal soil, porew	***Mean concentration in groundwater (based on mean concentration in soil)***	**2.31E-05**	**2.31E-05**	**4.20E-06**	**4.20E-06**	**[$mg.L^{-1}$]**

2.8.4.3.2 Open areas

MAKI GRAIN'TECH is applied in open areas by inserting inside or near the openings of the tunnels of the target rodents. According to the EUBEES 2 scenario, the use near the openings of the tunnels is covered by the assessment of the scenario "in and around buildings" with bait box. Thus this section "Open areas" only

assesses the use inside the tunnels during which, according to the scenario presented in EUBEES 2, two treatments would typically be applied in the interval of six days. Bait deployment comprises 200 g of product against rats and 50 g against mice per application and per tunnel entrance. These dose rates cover the treatment for voles and field mice. Based on a tunnel of 8 cm diameter, worst-case soil exposure is assumed to occur to a depth of 10 cm from the contact half (*i.e.* the burrow floor) of a 30 cm tunnel section in which the bait is placed. This section of tunnel floor is assumed to receive an input corresponding to 5% of the product during application and a further 20% as the bait is consumed.

Considering the localised treated area, the risk for groundwater from this use was not considered relevant.

Table 2.8.4.3-2: PEC of bromadiolone in soil and groundwater for uses in open area

			Rat treatment	Mice treatment	unit
INPUTS	**Qprod:**	**Amount of product used in control operation**	**200**	**50**	**[g.burrow^{-1}]**
	Fc$_{product}$:	**Fraction of active substance in product**	**0.05**	**0.05**	**[g a.i. kg^{-1}]**
	N$_{app}$:	**Number of application sites**	**1**	**1**	**[-]**
	N$_{refil}$:	**Number of refilling times**	**2**	**2**	**[-]**
	F$_{release, soil, appl}$:	**Fraction of product released to soil during application**	**0.05**	**0.05**	**[-]**
	F$_{release, soil, use}$:	**Fraction of product released to soil during use**	**0.2**	**0.2**	**[-]**
	Vsoil$_{exposed}$:	**Soil volume exposed to rodenticide**	**0.0085**	**0.0085**	**[m^3]**
	RHO$_{soil}$:	**Density of wet exposed soil**	**1700**	**1700**	**[kg.m^{-3}]**
	Koc	**Organic carbon adorption coefficient**	**14770**	**14770**	**[L.kg^{-1}]**
OUTPUTS	**Elocal$_{soil-campaign}$**	***Local emission of active substance to soil during a campaign***	**5.00E-03**	**1.25E-03**	**[g.camp]**
	Clocal$_{soil}$	***Local concentration in soil after a campaign***	**3.46E-01**	**8.65E-02**	**[mg.kg^{-1}$_{wwt}$]**

The predicted concentration of 0.346 mg bromadiolone/kg soil for application against rats represents the worst-case in the immediate vicinity of each bait application. However, since the target rodents will eat and spread portions of edible baits, and since much of the active substance will subsequently be excreted over a wide area outside the tunnel network, soil concentrations elsewhere will be considerably lower.

2.8.4.3.3 Waste Dumps

Bromadiolone bait is deployed around the perimeter of waste-dumps and land-fill sites to control populations of rats. EUBEES 2 suggests a scenario (with default values) in the event of an infestation outbreak that entails

40 kg of grain protected inside bait boxes distributed over an area of 1 ha, with a total of seven applications per year. In this situation, soil exposure is assumed to arise through a combination of deposition via urine and faeces combined with rodenticide contained in the carcasses of poisoned target rodents. In general, ninety percent of the total amount of rodenticide consumed by the target rodents over the duration of each baiting campaign is assumed to enter soil over the 1 ha surface.

However, the application doses claimed by the applicant are expressed as amount of biocidal product with a distance between two bait points and not over a surface. So to predict the concentration of bromadiolone in soil and groundwater for the uses in waste dump, the intended doses are calculated for the 1 ha surface as below:

Q_{prod} = (length of the waste dump of 1ha/distance between bait**) + 1) x (**length of the waste dump of 1ha/distance between bait**) x (**amount of product per bait point**)**

Example of calculation for rat treatment:

Q_{prod} = ((100 m /3 m) + 1) x (100 m / 3 m) x 0.2 $kg_{product}$

Q_{prod} = 229 kg/ha

In the scenario with the applicant parameters, the active substance metabolism is taken into account. EUBEES 2 considers that, in general, 90% of the total amount of rodenticide consumed by the target rodents over the duration of the outdoor baiting campaign enters soil via urine and faeces. In the case of bromadiolone, however, this is reduced in view of the extensive metabolism seen in a study with rats. Since no information is available on the toxicity of metabolites, it was assumed for the inclusion that these are as toxic as the a.s. and therefore the total value for excretion via faeces and urine (54.2% of dosed radioactivity excreted) will be used. This includes both the a.s. and the metabolites. The fraction of bromadiolone that enters soil via urine and faeces is thus 0.542.

Table 2.8.4.3-3: PEC of bromadiolone in soil and groundwater for uses in waste dump

			Anticoagulant-Rat- ESD default values	Dose for rat intended by the applicant	Unit
INPUT	Q_{prod}	Amount of product used in control operation / ha	40.0	229 (= 200g / 3m)	[$kg.ha^{-1}$]
	$Fc_{product}$	Fraction of active substance in product	0.05	0.05	[g $a.i.kg^{-1}$
	N_{app}	Number of applications	7	7	[-]
	$F_{release, soil}$	Fraction of product released to soil	0.9	0.542	[-]
	$AREA_{exposed}$	Area exposed to rodenticide	10 000	10 000	[m^2]
	$DEPTH_{soil}$	Depth of exposed soil	0.1	0.1	[m]
	RHO_{soil}	Density of wet exposed	1700	1700	[$kg.m^{-3}$]

		soil			
	Koc	**Organic carbon adsorption coefficient**	**14 770**	**14 770**	**[L.kg^{-1}]**
OUTPUT	**Elocal$_{soil\text{-}campaign}$**	***Local emission of active substance to soil from a campaign***	**12.6**	**43.4**	**[g.camp]**
	Clocal$_{soil}$	***Local concentration in soil after a campaign***	**0.0074**	**0.0255**	**[mg.kg^{-1}$_{wwt}$]**
	Kp$_{soil}$	***Partition coefficient solid-water in soil***	**2.95E+02**	**2.95E+02**	**[L.kg^{-1}]**
	K$_{soil\ water}$	***Soil-water partitioning coefficient***	**4.43E+02**	**4.43E+02**	**[m^3.m^{-3}]**
	PEClocal $_{soil,\ porew}$	***Concentration in groundwater***	**2.84E-05**	**9.79E-05**	**[mg.L^{-1}]**

The worst-case deposition scenario is unrealistic for different reasons. First, it assumes that the 1 ha baited surface (where the deposition occurs) remains static, whereas in reality it is likely to shift as areas that become filled up with waste are capped with soil. Secondly, it assumes that the rodenticide used in every baiting campaign contains the same active substance and, thirdly, penetration is limited to a depth of 10 cm from the soil surface, despite the fact that the management of waste dump and landfill sites commonly involves the mechanical disturbance and movement of considerable quantities of soil.

2.8.5 Risk characterization for the environment

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

2.8.5.1 Aquatic compartment (including water, sediment, STP)

2.8.5.1.1 In and around building

Exposure scenario is not considered relevant in the EUBEES 2 ESD for rodenticides. Bromadiolone is not expected to occur to any significant extent following the use of MAKI GRAIN'TECH in and around buildings. Therefore, PEC values for bromadiolone in surface water and sediment are assumed to be negligible and have not been further considered.

2.8.5.1.2 Open areas

Exposure of surface water arising from the use of MAKI GRAIN'TECH bait in open areas is not expected to be significant or widespread for open area uses. Therefore, estimates of bromadiolone concentrations in surface water have not been calculated and aquatic PEC/PNEC ratios are not presented. Since the scope for exposure is negligible, the risks presented to aquatic biota by bromadiolone are expected to be very low. No further assessment of risk is necessary.

2.8.5.1.3 Waste dump

Exposure of surface water arising from the use of MAKI GRAIN'TECH bait is not expected to be significant or widespread for waste dump uses. Therefore, estimates of bromadiolone concentrations in surface water have not been calculated and aquatic PEC/PNEC ratios are not presented. Since the scope for exposure is negligible, the risks presented to aquatic biota by bromadiolone deployed in waste dumps are expected to be very low. No further assessment of risk is necessary.

2.8.5.2 Atmospheric compartment

For bromadiolone, the estimated half-life for the hydroxyl reaction in air is 2.1 hours, the vapour pressure as determined by OECD 104 is 2.13 x 10^{-8} Pa and the Henry's law constant is 8.99 x 10^{-7} $Pa.m^3.mol^{-1}$ (based on a water solubility of 12.5 mg a.s/l). Therefore bromadiolone is not expected to volatilize to air in significant quantities.

2.8.5.3 Terrestrial compartment

Soil exposure occurs both through a combination of direct and indirect releases from the use of MAKI GRAIN'TECH bait in the scenario "in and around buildings", "open areas" and "waste dump".

2.8.5.3.1 In and around building

Exposure of the terrestrial compartment (soil) will occur when MAKI GRAIN'TECH is deployed outdoors. Realistic worst case and typical case predicted soil concentrations (PECs) have been calculated for the use scenario in and around buildings, for application in control campaign. The resulting PEC/PNEC ratios for the soil are summarized in the Table below:

Table 2.8.5.3-1: PECsoil/PNECsoil for soil-dwelling invertebrates exposed to bromadiolone following outdoor use of bait around buildings

Baiting scenario (EUBEES 2)	**PECsoil (mg bromadiolone/kg wwt soil)**	**PNECsoil (mg bromadiolone/kg wwt soil)**	**PEC/PNEC ratio**
Realistic worst case considering 5 replenishments of the bait points per campaign			
Rat treatment	3.86E-02	8.4E-03	**4.60**
Mice treatment:	1.41E-02		**1.68**
Typical scenario considering 1.5 replenishments of the bait points per campaign and the metabolisation of the substance in rodents – Worst case concentration in soil in the area just around the bait point.			
Rat treatment	4.17E-05	8.4E-03	**1.30**
Mice treatment	1.35E-05		0.42
Typical scenario considering 1.5 replenishments of the bait points per campaign and the metabolisation of the substance in rodents – Mean concentration in soil considering the area for indirect release			
Rat treatment	1.10E-03	8.4E-03	0.13

Mice treatment	1.10E-03		0.13

The risk is unacceptable for soil when the exposure assessment takes into account the default parameters of the EUBEES 2 scenario or for the typical scenario for rat treatment in the area considered for the direct release of the substance. However, the PEC/PNEC ratios shown above are, for the typical scenario and both treatments (rat and mice), less than 1.0 for the area of indirect release and indicate that there no unacceptable risks to the terrestrial compartment when the product MAKI GRAIN'TECH is used in and around building.

The risk is acceptable in groundwater for the use of MAKI GRAIN'TECH in and around building according to the typical case even in considering the worst case total concentration just around the bait station as presented below:

Table 2.8.5.3-2: PEC groundwater due to use of MAKI GRAIN'TECH in and around building

Baiting scenario (EUBEES 2)	**PECgroundwater (µg bromadiolone/L)**	**Threshold value in groundwater (µg/L)**	**Risk characterization**
Realistic worst case considering 5 replenishments of the bait points per campaign			
Rat treatment	0.148	0.1	**Non acceptable**
Mice treatment:	0.054	0.1	Acceptable
Typical scenario considering 1.5 replenishments of the bait points per campaign and the metabolisation of the substance in rodents – Worst case concentration in soil in the area just around the bait point.			
Rat treatment	0.042	0.1	Acceptable
Mice treatment:	0.014	0.1	Acceptable
Typical scenario considering 1.5 replenishments of the bait points per campaign and the metabolisation of the substance in rodents – Mean concentration in soil considering the area for indirect release			
Rat treatment	0.004	0.1	Acceptable
Mice treatment:	0.004	0.1	Acceptable

2.8.5.3.2 Open areas

Exposure of the terrestrial compartment (soil) will occur when MAKI GRAIN'TECH bait is applied in open areas by inserting inside the openings of the tunnels of the target rodents.

Predicted soil concentrations (PECs) have been calculated for the use scenario in open areas, for application in rats/rodents control campaign according to the doses claimed by the applicant. The resulting PEC/PNEC ratios for the soil are summarized in the Table below:

Table 2.8.5.3-3: PECsoil/PNECsoil for soil-dwelling invertebrates exposed to bromadiolone following use of bait in open area

Baiting scenario (EUBEES 2)	**PEC_{soil} (mg /kg wwt)**	**$PNEC_{soil}$ (mg /kg wwt)**	**PEC/PNEC**
Typical use (rat treatment)	3.46E-01	8.4E-03	**41**
Typical use (mice treatment)	8.65E-02		**10**

The PEC/PNEC ratios are above 1.0 and indicate that there are unacceptable risks to the terrestrial compartment when the product MAKI GRAIN'TECH is used in the tunnels of open areas. However, the PEC/PNEC ratios calculated indicate a marginal risk based on the PEC that represents a localised "hotspot" of contamination near the entrance of each baited tunnel. According to the EUBEES 2 scenario, the use near the openings of the tunnels is covered by the assessment of the scenario "in and around buildings" with bait box. As argued above (section 2.8.4.3.1), there is no unacceptable risk for the terrestrial compartment (including groundwater) when the MAKI GRAIN'TECH is used near the openings of the tunnels of the target rodents.

Considering the localised treated area in the tunnels, the risk for groundwater was not considered relevant.

2.8.5.3.3 Waste dump

Predicted soil concentrations (PECs) have been calculated for the use scenario in waste dump, for application against rats control campaign. The resulting PEC/PNEC ratios for the soil are summarized in the Table below:

Table 2.8.5.3-4: PECsoil/PNECsoil for soil-dwelling invertebrates exposed to bromadiolone following use of bait at waste dumps and landfill sites

Baiting scenario (EUBEES 2)	PECsoil (mg/kg wwt soil)	PNECsoil (mg/kgwwt soil)	PEC/PNEC ratio
Realistic worst case: ESD default values considering an application rate of 40 $kg_{Product}$/ha			
Default parameters	7.41E-03	8.4E-03	0.9
Typical scenario: specific parameters taking into account the application rates from the product instructions			
Rat treatment (229 kg/ha)	2.55E-02	8.4E-03	**3**

The PEC/PNEC ratio shown above is smaller than 1.0 for the EUBEES dose indicating that there no unacceptable risks to the terrestrial compartment when the product MAKI GRAIN'TECH is used in waste dump. However, for the dose claimed by the applicant, for rat treatment, the risks are unacceptable.

Table 2.8.5.3-5: PEC groundwater due to use of MAKI GRAIN'TECH in waste dump

Baiting scenario (EUBEES 2)	Maximum PECgroundwater (µg bromadiolone/L)	Threshold value in groundwater (µg/L)	Risk characterization
Realistic worst case: ESD default values considering an application rate of 40 $kg_{Product}$/ha			
Default treatment	2.84E-02	0.1	Acceptable
Typical scenario: specific parameters taking into account the application rates from the product instructions			
Rat treatment (229 kg/ha)	9.79E-02	0.1	Acceptable

The risk for groundwater is acceptable for the EUBEES default dose and for the rat treatment.

Therefore the application dose rate must be limited to remain below the usual practice referred in the ESD which is equivalent to 40 kg/ha.

2.8.6 Non-compartmental specific effects relevant to the food chain

Non-target vertebrates may be exposed to bait containing bromadiolone either directly by ingestion of exposed blocks or grains (primary poisoning) or indirectly by ingestion of the carcasses of target rodents that contain bromadiolone residues (secondary poisoning).

Bait containing bromadiolone contains also 10 mg denatonium benzoate per kg, a powerful bittering agent that is intended to deter accidental ingestion of blocks or gains by humans. It may also deter some non-target mammals.

2.8.6.1 Primary poisoning

Non-target birds and mammals may encounter bait containing bromadiolone if they are small enough to be able to reach the bait, or because the bait is inadequately safeguarded or a secured bait point has become damaged, or by finding pieces of bait which have been removed by target rodents. The quantities of bromadiolone potentially accessible to non-target mammals can be calculated based on the size and number of bait at each secured bait point and an estimate of the amount of bait removed from them.

2.8.6.1.1 Tier1

The Tier 1 assessment assumes that the whole day's food requirement is satisfied by consumption of bait and therefore the concentration in food will be the same as the concentration of the active substance in the bait: 50 $mg.kg^{-1}$ (0.005% w/w of bromadiolone in MAKI GRAIN'TECH).
Hence, **the worst case Tier 1 PEC_{oral} is 50 $mg.kg^{-1}$**.

Table 2.8.6.1-1: Tier 1 risk assessment of bromadiolone in bait potentially accessible to non-target vertebrates following deployment at secured bait points in and around buildings

	PEC (conc. in food, mg/kg)	PNEC (conc. in food, mg/kg)	PEC/PNEC
Bird	50	0.0033	**15151**
Mammal	50	0.00019	**263158**
Dog	50	0.011	**4546**

The table above provides a clear indication of high risk to birds and non-target mammals. It is, however a conservative risk assessment approach and represents a worst case.

For birds, a separate, graded assessment of long-term risks of primary poisoning by bait has been done. It is based on different intakes of bromadiolone-treated bait in relation to untreated food, depending on to which extent bromadiolone bait is accessible to birds. The PNEC for birds from the table above has been used in the calculations.

Table 2.8.6.1-2: PECoral/PNECoral for non-target, birds exposed to bromadiolone in bait removed from secured bait points in and around buildings

Proportion of bait point contents accessible, expressed as fraction of ingested food (%)	Bromadiolone conc. potentially ingested by non-target vertebrates (mg/kg) ≡ PECoral	PNEC (conc. in food, mg/kg)	PEC/PNEC (long-term)
100	50	0.0033	15151

50	25		7576
40	20		6061
30	15		4546
20	10		3030
10	5		1515
5	2.5		758
2	1		303
1	0.5		152

The long-term assessment indicates clearly unacceptable risk even if only 1% of the food is constituted of bait. The risk is, however, mitigated by the prerequisite that good practice requires that secured bait points, containing bait in a chamber not directly accessible from the access hole, be used in locations where a potential for avian exposure exists.

2.8.6.1.2 Tier 2, acute

In the tier 2 acute qualitative risk assessment the daily uptake (ETE) of bromadiolone is compared with the effect data for birds and mammals. Domestic animals may accidentally ingest parts of baits discarded outside the secured bait points. The body weights, daily food intakes and estimates of bromadiolone ingestion, based on sufficient bait being accessible to satisfy a day's food intake requirement, are presented below for a representative non-target mammal based on the equation:

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

where

- ETE is the estimated daily uptake of the active substance ($mg.kg^{-1}_{bw}.d^{-1}$),
- FIR is the non-target mammal food intake (fresh weight) ($g.d^{-1}$),
- BW is the indicator species body weight (g),
- C is the concentration of active substance in the fresh diet (bait) ($mg.kg^{-1}$),
- AV is the avoidance factor (default 1.0 = no avoidance; 0.9 for typical case),
- PT is the fraction of diet obtained in the treated area (default 1.0; 0.8 for typical case)
- and PD is the fraction of food type in the diet (default 1.0), first tier (worst case).

Table 2.8.6.1-3: ETE for non-target animals ingesting bait containing bromadiolone

Non-target mammal	Typical bodyweight (g)a	Daily mean food intake (g dry weight/day)	Concentration of bromadiolone in bait (mg/kg)	ETE, concentration of bromadiolone after one meal (one day) (mg/kg bw)	
				Default values	Typical case
Dog	10 000	456[b]	50	2.28	1.64
Pig	80 000	600[a]	50	0.38	0.27
Pig, young	25 000	600[a]	50	1.20	0.86
Tree sparrow	22	7.6[a]	50	17.27	12.44
Chaffinch	21.4	6.42[a]	50	15.00	10.80
Wood pigeon	490	53.1[a]	50	5.42	3.90
Pheasant	953	102.7[a]	50	5.39	3.88

[a] From EUBEES 2, Table 3.1, Section 3.2.1.
[b] From EUBEES 2, using the equation log FIR = 0.822 log BW – 0.629 (for mammals)

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

Table 2.8.6.1-4: Tier 2 acute qualitative risk assessment for non-target animals accidentally exposed to bait containing bromadiolone in and around building

Non-target animal	PECoral: ETE, concentration of bromadiolone after one meal (one day) (mg/kg)		LD_{50} (dose, mg/kg bw/d)	PECoral higher than LD_{50} (y/n)	
	Worst case	Typical case		Worst case	Typical case
Dog	2.28	1.64	0.56-0.84	y	y
Pig	1.38	0.27	0.56-0.84	y	n
Pig, young	1.20	0.86	0.56-0.84	y	y
Tree sparrow	17.27	12.44	134 (TF)	n	n
Chaffinch	15.00	10.80	134 (TF)	n	n
Wood pigeon	5.42	3.90	134 (TF)	n	n
Pheasant	5.39	3.88	134 (TF)	n	n

The qualitative risk assessment indicates that ingestion by a non-target animal of an amount of bromadiolone bait equivalent to one day's food intake requirement will result in risk for dogs and pigs.

2.8.6.1.3 Tier 2, long term

The expected concentrations (EC) of bromadiolone in non-target species are calculated from the respective ETE values using an elimination factor. When calculating the long-term risks, elimination and metabolism of the substance (El) have to be considered. Calculations are performed according to the equation 20 of the ESD:

$$EC = ETE*(1-El)$$

An EUBEES default value of 0.3 for daily uptake eliminated (El) can be used if no studies are submitted.

Table 2.8.6.1-5: Tier 2 long-term risk assessment: PECoral/PNECoral for non-target animals exposed to bait containing bromadiolone in and around buildings after one day elimination, calculated with typical case values for AV (=0.9) and PT (=0.8)

Non-target animal	PEC: EC, concentration of bromadiolone after one day elimination (mg/kg)	PNEC (dose, mg/kg bw/d)	PEC/PNEC
Dog	1.10	0.00027	4 074
Pig	0.18	0.0000056	33 750
Pig, young	0.58	0.0000056	108 000
Tree sparrow	8.71	0.00038	22 909
Chaffinch	7.56	0.00038	19 895
Wood pigeon	2.73	0.00038	7 186
Pheasant	2.72	0.00038	7 147

This assessment provides indication of very high risks to both mammals and birds, but, as mentioned above, it should be noted that consumption of these quantities of bromadiolone bait is generally not realistic and should be regarded strictly as worst case.

2.8.6.2 Secondary poisoning

2.8.6.2.1 Secondary poisoning via the aquatic food chain

As no exposure of the aquatic compartment is foreseen with the use of MAKI GRAIN'TECH for the uses in and around buildings, in open areas and in waste dumps, no risk assessment for secondary poisoning through the aquatic food chain is required.

2.8.6.2.2 Secondary poisoning via the terrestrial food chain

2.8.6.2.2.1 The earthworm-eating mammal or bird

According to the TGD secondary poisoning through the terrestrial route is soil → terrestrial organisms (earthworm) → earthworm-eating mammal or bird. Since birds and mammals consume worms with their gut contents and the gut of earthworms can contain substantial amounts of soil, the exposure of the predators may be affected by the amount of substance that is in the soil. The risk assessment for secondary poisoning for earthworm-eating mammals and birds has been carried out for the in and around use and for the waste dump application. As the use in open area is quite localised, the exposure of earthworm was deemed negligible in this case.

$PECoral_{predator}$ is calculated as an example for rat treatment application for the in and around (typical scenario), taking into account the concentration of bromadiolone in soil based on mean concentration in the whole exposed area, as:

$PEC\ oral_{,predator} = C_{earthworm}$ (eq 80, TGD, 2003)

$C_{earthworm} = (BCF_{earthworm} * C_{porewater(based\ on\ mean\ concentration\ in\ soil)} + Clocal_{soil\ mean\ concentration} * F_{gut} * CONV_{soil}) / (1 + Fg_{ut\ kgdwt/kgwwt} * CONV_{soil\ kgwwt/kgdwt})$ (eq 82c, TGD 2003).

No measured BCF for earthworm is available and the calculated BCF of 142 $L/kg_{wet\ earthworm}$ is used in the calculations.

$C_{earthworm}$ = (142 $L/kg_{wet\ earthworm}$ x 4.2E-06 mg/L + 1.1E-03 mg/kg_{wwt} x 0.1 kg_{dwt}/kg_{wwt} x 1.13 kg_{wwt}/kg_{dwt})/(1+0.1 *1.13) = *6.47E-04 $mg/kg_{wet\ earthworm}$*.

According to the TGD, the most appropriate scenario is that 50% of the diet comes from a local area and 50% comes from the regional area, thus when the $PEClocal_{,soil}$ is used in calculation, the $PECoral_{,predator}$ to be used in risk assessment is $C_{earthworm}$ x 0.5 = **3.24E-04 $mg/kg_{wet\ earthworm}$**.

	$PECoral_{,predator}$ ($mg/kg_{wet\ earthworm}$)	**$PNEC_{oral}$ mg/kg food**	**PEC/PNEC (mammals)**	**PEC/PNEC (birds)**
In and around building – Mean concentration				
Rat treatment:	**3.24E-04**	**PNEC oral mammal:0.00019** **PNEC oral bird:0.00075**	**1.7**	**0.4**
Mice treatment:	**3.24E-04**		**1.7**	**0.4**

Realistic worst case: ESD default values considering an application rate of 40 $kg_{Product}$/ha				
Default parameters	**3.24E-04**	**PNEC oral mammal:0.00019 PNEC oral bird:0.00075**	**6.9**	**1.8**
Typical scenario: specific parameters taking into account the application rates from the product instructions				
Rat treatment (229 kg/ha)	**7.50E-03**	**PNEC oral mammal:0.00019 PNEC oral bird:0.00075**	**39**	**10**

Whatever the scenario, the PEC/PNEC ratio exceeds 1 for both earthworm eating birds and mammals for the except in the in and around scenario for rat taking into account the concentration in soil based on the whole exposed area.

Despite of the calculated risk, the RMS considers the secondary poisoning via earthworms less important than secondary poisoning via the food chain bait → rodent → rodent-eating birds or mammals.

2.8.6.2.2.2 The rodent-eating mammal and the rodent-eating bird

Rodents targeted by indoor and outdoor baiting campaigns are likely to roam outdoors and within the hunting ranges of predatory birds and mammals. Target animals that succumb to the effects of anticoagulant rodenticides and die whilst foraging outdoors may be found and ingested by scavenging vertebrates. A potential for secondary poisoning of birds and mammals therefore exists.

The bromadiolone residue concentration in rodents is based on the following equation:

$$EC_n = \sum_{n=1}^{n-1} ETE * (1 - EL)^n$$

- Where
  - EC_n is the estimated residue concentration in the rodent on day n,
  - ETE is the estimated theoretical exposure as defined above for primary poisoning for mammals
  - and EL is the fraction of residue eliminated from the target rodent per day.

The ETE values for rodents (mice and rats) are based on three theoretical levels of ingestion of bait constituting 100%, 50% and 20% of the daily food intake (to allow for various intakes of alternative foods), a FIR/bw rate of 0.1 for rats and mice and a concentration of bromadiolone in bait equal to 50 mg/kg. The ETE values are therefore 5.0, 2.5 and 1.00 mg bromadiolone/kg bw for levels of bait consumption equivalent to 100%, 50% and 20% of daily food intake, respectively.

According to EUBEES 2, the default rate of elimination of residues from the bodies of target rodents is 30% per day (faecal route only). According to the Competent Authority report of the bromadiolone, this default daily elimination rate of 30% for anticoagulant rodenticides prescribed by EUBEES 2 is in general accordance with the mean values measured for bromadiolone, which averaged 32.7% over the first three days and ranged from 12.0% for day 1 to 53.3% for day 2.

The residue levels are also based on an assumption that ingestion of bromadiolone in bait occurs consistently during the first five days of baiting and that feeding (including bait ingestion) ceases on day 6, followed by death on day 7. However, the time to death under more realistic conditions may differ from that observed in the laboratory if the target rodents have unrestricted access to alternative food(s). EUBEES 2 considers three levels of bait consumption by target rodents, expressed in terms of bait ingestion as a percentage of total daily food intake. A level of 20% is regarded as the minimum for an effective bait formulated to appeal to target rodents, whilst 100% represents the realistic worst-case view. In the presence of other, competing food sources (presumed to be present to allow a population of target rodents to become established), an intake of around 50% may be more likely.

Table 2.8.6.2-1: Residues of bromadiolone in target rodents from the ingestion of bait at different times during a control campaign, calculated according to EUBEES 2

Time	Residues of bromadiolone in target rodent (mg/kg bw)		
	20% bait consumption	**50% bait consumption**	**100% bait consumption**
Day 1, after first meal	1.000	2.500	5.000
Day 2 before new meal	0.700	1.750	3.500
Day 5 after last meal	**2.773**	**6.933**	**13.866**
Day 7 (mean time to death)	1.359	3.397	6.794

Calculated residue patterns suggest that levels increase following each daily intake until day 5, after which the rodents are assumed to eat no more bait blocks or treated grain, but to continue to excrete residues at approximately 30% per day, resulting in a reduction of residues by approximately 50% between the last intake on day 5 and death on day 7.

A semi-field data shows the calculated above values to be overestimated. In a study of the effects of secondary exposure to bromadiolone on *Bubo virginianus*, measured cumulative bait consumption by male rats during the three-day exposure period was equivalent to bromadiolone intakes ranging from 4.9 to 15.5 mg/kg, with a mean of 11.02 mg/kg bw, or 3.67 mg bromadiolone/kg bw/day. The data tabulated below show the levels of bromadiolone residues predicted according to EUBEES 2, based on the mean daily intake regime described above.

Table 2.8.6.2-2: Residues of bromadiolone in rats, predicted according to EUBEES 2, based on a mean measured bait intake equivalent to 3.67 mg bromadiolone/kg bw/day and 30% daily elimination.

Time	Residues of bromadiolone in rats (mg/kg bw)
Day 1, after first meal (bait)	3.67
Day 2, before new meal	2.57
Day 2, after second meal (bait)	6.24
Day 3, before new meal	4.37
Day 3, after third meal (bait)	8.04
Day 4, before new meal (uncontaminated feed)	5.63
Day 5, at termination of study	3.94

The predicted mean bromadiolone residue in male rat carcasses at termination on day 5 is 3.94 mg/kg bw. By contrast, the measured concentrations of bromadiolone in five whole male rats ranged from 0.35 to 1.55 mg/kg bw (mean: 0.9 mg/kg bw). The mean measured residue concentration at termination on day 5 corresponds to just 23% of the value predicted for the same timepoint according to EUBEES 2. For comparison, the calculated actual concentration in rats at day 3 (which would be the actual worst case was 3.0 mg/kg bw, or 37% of EUBEES default. Since these figures will not in any decisive way affect the risk assessment, they will not be included in the calculations. In the table below and in the following assessments,

the various concentrations of bromadiolone in target rodents on day 5 and day 7 have been lowered using the figure 23% to better reflect real, measured residues based on the study mentioned above from the CAR of bromadiolone.

Table 2.8.6.2-3: Residues of bromadiolone in target rodents from the ingestion of bait blocks or grain bait at different times during a control campaign, based on the mean residue level measured in rats

Time	Residues of bromadiolone in target rodent (mg/kg bw)		
	20% bait consumption	50% bait consumption	100% bait consumption
Day 5 after last meal1	0.638	1.595	3.189
Day 7 (mean time to death)[2]	0.325	0.781	1.563

[1] Based on values calculated according to EUBEES 2 and corrected by × 23%;

[2] Based on excretion of 30% per day and a reduction of approximately 50% between days 5 and 7.

2.8.6.2.2.2.1 Rodent-eating birds - Tier 1, acute

For the first tier qualitative assessment of acute secondary poisoning to birds, the maximum residue levels in target rodents that arise on day 5 after the last meal are compared to the effect value expressed as concentration in food. **For birds** the lowest **LC50** is **207 mg a.s. /kg food** (Lipha Tech data). The first tier assessment also assumes the following three levels of bromadiolone bait consumption: 20%, 50% and 100% of the daily food intake of the target rodents. Two scenarios are described, one based on default bromadiolone residue values in target rodents derived from the EUBEES ESD document and one based on measured residue values reported by the applicant.

Table 2.8.6.2-4: Tier 1 qualitative estimate of acute risk for predatory or scavenging birds ingesting target rodents, on day 5 of a control campaign, containing bromadiolone obtained from areas in and around buildings (maximum rodent residue levels), two different scenarios

	LD_{50} (mg/kg food)	PEC_{oral} - residues of bromadiolone in target rodent (mg/kg bw)			PECoral higher than LD_{50} (y/n)		
bait, % of rodents' food intake/day (PD)		20%	50%	100%	20%	50%	100%
EUBEES 2, default	207	2.773	6.933	13.866	n	n	n
Measured residue levels	207	0.638	1.595	3.189	n	n	n

Table 2.8.6.2-5: Tier 1 estimate of acute PECoral/PNECoral for predatory or scavenging birds ingesting target rodents, on day 7 of a control campaign, containing bromadiolone obtained from areas in and around buildings, two different scenarios.

	LD_{50} (mg/kg food)	PECoral - residues of bromadiolone in target rodent (mg/kg bw)			PECoral higher than LD_{50} (y/n)		
bait, % of rodents' food intake/day (PD)		20%	50%	100%	20%	50%	100%
EUBEES 2, default	207	1.359	3.397	6.794	n	n	n

Measured residue levels	207	0.325	0.781	1.563	n	n	n

The above estimates assume that rodents containing bromadiolone residues are wholly ingested by predatory or scavenging birds which feed exclusively on target rodents (F_{rodent} = 1). No account has been taken of the daily food intakes of different predatory birds. The tier 1 qualitative assessment does not indicate any acute risk for secondary poisoning of birds.

2.8.6.2.2.2.2 Rodent-eating birds - Tier 1, long-term

For the first tier assessment of long-term secondary poisoning to birds, the maximum residue levels in target rodents that arise on day 5 after the last meal are compared to the long-term PNEC value for concentration in food. In this case the specific PNEC value for secondary poisoning as described in section 2.8.2.4 is used. In tier 1 long-term assessment it is assumed that 100% of the target rodents' food intake constituted of bromadiolone bait and that 50% of the predator's diet is poisoned rodents (F_{rodent} = 0.5). Also here two scenarios are described; one based on default bromadiolone residue values from the EUBEES ESD document and one based on measured values reported by the applicant.

Table 2.8.6.2-6: Tier 1 estimate of long-term secondary poisoning of predatory or scavenging birds ingesting target rodents, on day 5 of a control campaign, containing bromadiolone obtained from areas in and around buildings, two different scenarios.

	PNEC (conc. in food, mg/kg)	**Residues of bromadiolone in target rodent (mg/kg bw)**	**PECoral/PNECoral**
EUBEES 2, default	0.00075	13.866	18500
Measured residue levels	0.00075	3.189	4250

According to this assessment the risk for poisoning of non-target predator birds, particularly owls, during long-term exposure via rodents poisoned with bromadiolone is very high. Therefore, a refined tier 2 assessment is set out below, based on representative avian species.

2.8.6.2.2.3 Rodent-eating birds - Tier 2

The refined tier 2 estimate of risk considers exposure of relevant species of avian predators, based on their bodyweights and food intakes (table below). The bodyweights and food intake data of raptorial species (other than red kite, *Milvus milvus*) are drawn from the EUBEES 2 guidance document. The mean bodyweight of *M. milvus* is from standard texts on this species and its food intake rate is estimated using the default values given in SANCO/4145/2000. In the following two tables it is assumed that 50% of the diet of each bird species on a single day consists of rodents containing bromadiolone and that they are caught on day 5, just after their last meal. In each case, bromadiolone bait has contributed 100% of the daily food intake of the rodents eaten by the birds.

Table 2.8.6.2-7: Estimated intakes and concentrations (EUBEES scenario) of bromadiolone (BDN) in raptorial avian predators and scavengers of rodents, assuming poisoned rodents comprise 50% of a bird's diet and that bait contributed 100% of the target rodents' daily food intake.

Non-target avian predator	Mean body weight (g)	Daily food intake (g/day)	Normal susceptible rodents caught on day 5, before their last meal[b]		Normal susceptible rodents caught on day 5, just after their last meal[c]		Resistant rodents caught on day 14, just after their last meal[d]	
			BDN consumed (mg)	BDN in predator (mg/kg bw)	BDN consumed (mg)	BDN in predator (mg/kg bw)	BDN consumed (mg)	BDN in predator (mg/kg bw)
Tyto alba	294	72.9	0.32	1.1	0.51	1.7	0.61	2.1
Athene noctua	164	46.4	0.21	1.2	0.32	2.0	0.39	2.3
Strix aluco	426	97.1	0.43	1.0	0.67	1.6	0.81	1.9
Falco tinnunculus	209	78.7	0.35	1.7	0.55	2.6	0.65	3.1
Milvus milvus	1 138	195a	1.36	0.76	0.87	1.19	1.62	1.42

[a] Daily energy expenditure of 1,089 kJ/day, energy content of a small mammal 21.7 kJ/g, moisture content of a small mammal 68.6% and assimilation efficiency 82%.

[b] Based on a rodent containing 8.9 mg bromadiolone/kg (according to Table 3.5 in the EUBEES ESD).

[c] Based on a rodent containing 13.9 mg bromadiolone/kg (according to Table 3.5 in the EUBEES ESD).

[d] Based on a rodent containing 16.6 mg bromadiolone/kg (according to Table 3.5 in the EUBEES ESD).

Table 2.8.6.2-8: Estimated intakes and concentrations (experimental data) of bromadiolone (BDN) in raptorial avian predators and scavengers of rodents, assuming poisoned rodents comprise 50% of a bird's diet and that bait contributed 100% of the target rodents' daily food intake.

Non-target avian predator	Mean bodyweight (g)	Daily food intake (g/day)	Normal susceptible rodents caught on day 5, just after their last meal[d]		Normal susceptible rodents caught on day 7, two days after their last meal	
			BDN consumed (mg)	BDN in predator (mg/kg bw)	BDN consumed (mg)	BDN in predator (mg/kg bw)
Tyto alba	294	72.9	0.116	0.395	0.057	0.194
Athene noctua	164	46.4	0.074	0.451	0.036	0.221
Strix aluco	426	97.1	0.155	0.363	0.076	0.178
Falco tinnunculus	209	78.7	0.125	0.600	0.062	0.294
Milvus milvus	1,138	195[a]	0.311	0.273	0.152	0.134

[a] Daily energy expenditure of 1,089 kJ/day, energy content of a small mammal 21.7 kJ/g, moisture content of a small mammal 68.6% and assimilation efficiency 82%.

[d] Based on a rodent containing 3.189 mg bromadiolone/kg.

[e] Based on a rodent containing 1.563 mg bromadiolone/kg.

In the next two tables, the concentrations of bromadiolone in the avian predators are compared to the specific PNEC value for secondary poisoning expressed as daily dose (PNEC = 0.00019 mg/kg bw/d).

Table 2.8.6.2-9: Tier 2 estimates of PECoral/PNECoral (EUBEES scenario) for predatory and scavenging birds ingesting target rodents (as 50% of their diet) containing bromadiolone obtained from areas in and around buildings. It is assumed that bait contributed 100% of the target rodents' daily food intake.

Non-target avian predator	Normal susceptible rodents caught on day 5, before their last meal		Normal susceptible rodents caught on day 5, just after their last meal		Resistant rodents caught on day 14, just after their last meal	
	PEC	PEC/PNEC	PEC	PEC/PNEC	PEC	PEC/PNEC
Tyto alba	1.1	5807	1.7	9070	2.1	10832
Athene noctua	1.3	6626	2.0	10349	2.4	12359
Strix aluco	1.0	5338	1.6	8338	1.9	9957
Falco tinnunculus	1.7	8819	2.6	13774	3.1	16450
Milvus milvus	0.76	4013	1.2	6268	1.4	7485

Table 2.8.6.2-10: Tier 2 estimates of PECoral/PNECoral (experimental data) for predatory and scavenging birds ingesting target rodents (as 50% of their diet) containing bromadiolone obtained from areas in and around buildings. It is assumed that bait contributed 100% of the target rodents' daily food intake.

Non-target avian predator	Normal susceptible rodents caught on day 5, just after their last meal		Normal susceptible rodents caught on day 7, two days after their last meal	
	PEC	PEC/PNEC	PEC	PEC/PNEC
Tyto alba	0.395	2081	0.194	1020
Athene noctua	0.451	2374	0.221	1164
Strix aluco	0.363	1913	0.178	938
Falco tinnunculus	0.600	3160	0.294	1549
Milvus milvus	0.273	1438	0.134	705

Based on the assumption that 50% of a predatory bird's diet consists of rodents that contain the maximum estimated quantity of bromadiolone residues, the risk assessment indicates high risk, *i.e.* the PECoral/PNECoral by far exceeds 1.0 for all the raptorial bird species considered. To obtain acceptable risk levels, the intakes of bromadiolone must be at least 2-3 orders of magnitude lower than those of the above scenarios.

2.8.6.2.2.4 Rodent-eating mammals - Tier 1, acute

For the first tier qualitative assessment of acute secondary poisoning to mammals, the maximum residue levels in target rodents that arise on day 5 after the last meal are compared to the mammal effect value expressed as concentration in food. The LD_{50} for rat of 0.56-0.84 mg/kg bw is recalculated, using conversion factor from Table 22 in the TGD (bw/dfi = 20) to 11.2-16.8 mg/kg food. The first tier assessment also assumes the following three levels of bromadiolone bait consumption: 20%, 50% and 100% of the daily food intake of the target rodents. Two scenarios are described, one based on default bromadiolone residue values in target rodents derived from the EUBEES ESD document and one based on measured residue values reported by the applicant.

Table 2.8.6.2-11: Tier 1 qualitative estimate of acute risk for predatory or scavenging mammals ingesting target rodents, on day 5 of a control campaign, containing bromadiolone obtained from areas in and around buildings (maximum rodent residue levels), two different scenarios.

	LD_{50} (mg/kg food)	PECoral - residues of bromadiolone in target rodent (mg/kg bw)			PECoral higher than LD_{50} (y/n)		
bait, % of rodents' food intake/day (PD)		20%	50%	100%	20%	50%	100%
EUBEES 2, default	11.2-16.8	2.773	6.933	13.866	n	n	y
Measured residue levels	11.2-16.8	0.638	1.595	3.189	n	n	n

Table 2.8.6.2-12: Tier 1 estimate of acute PECoral/PNECoral for predatory or scavenging mammals ingesting target rodents, on day 7 of a control campaign, containing bromadiolone obtained from areas in and around buildings, two different scenarios.

	LD_{50} (mg/kg food)	PECoral - residues of bromadiolone in target rodent (mg/kg bw)			PECoral higher than LD_{50} (y/n)		
bait, % of rodents' food intake/day (PD)		20%	50%	100%	20%	50%	100%
EUBEES 2, default	11.2-16.8	1.359	3.397	6.794	n	n	n
Measured residue levels	11.2-16.8	0.325	0.781	1.563	n	n	n

The above estimates assume that rodents containing bromadiolone residues are wholly ingested by predatory or scavenging mammals which feed exclusively on target rodents (F_{rodent} = 1).

The tier 1 qualitative assessment does not indicate acute risk for secondary poisoning of mammals except for PD = 1 when ingesting rodents caught on day 5 of a campaign, where there may be risk. In view of these uncertainties a quantitative tier 2 assessment is set out below, based on representative mammal species.

2.8.6.2.2.5 Mammals - Tier 1, long-term

For the first tier assessment of long-term secondary poisoning to mammals, the maximum residue levels in target rodents that arise on day 5 after the last meal are compared to the long-term mammal PNEC value for concentration in food. In tier 1 long-term assessment it is assumed that 100% of the target rodents' food intake constituted of bromadiolone bait and that 50% of the predator's diet is poisoned rodents (F_{rodent} = 0.5). Also here two scenarios are described, one based on default bromadiolone residue values from the EUBEES ESD document and one based on measured values reported in the CAR.

Table 2.8.6.2-13: Tier 1 estimate of long-term secondary poisoning of predatory or scavenging mammals ingesting target rodents, on day 5 of a control campaign, containing bromadiolone obtained from areas in and around buildings, two different scenarios.

	PNEC (conc. in food, mg/kg)	Residues of bromadiolone in target rodent (mg/kg bw)	PECoral/PNECoral

EUBEES 2, default	0.00019	13.866	72979
Measured residue levels	0.00019	3.189	16784

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

2.8.6.2.2.6 Mammals - Tier 2

The refined, tier 2 estimate of risk is based on exposure to non-target predators taking into account relevant species, their bodyweights and food intakes (table below). The bodyweights and food intakes are based on the EUBEES 2 guidance and on documents referred to therein (SANCO/4145/2000). The following two tables assume that 50% of the diet of each mammal species on a single day consists of rodents containing bromadiolone. In each case, bromadiolone bait has contributed 100% of the daily food intake of the rodents eaten by the mammals.

Table 2.8.6.2-14: Estimated intakes and concentrations (EUBEES scenario) of bromadiolone (BDN) in mammalian predators and scavengers of rodents, assuming poisoned rodents comprise 50% of a predator/scavenger's diet and that bait contributed 100% of the target rodents' daily food intake

Non-target mammalian predator	Mean body weight (g)	Daily food intake (g/day)	Normal susceptible rodents caught on day 5, before their last meala		Normal susceptible rodents caught on day 5, just after their last mealb		Resistant rodents caught on day 14, just after their last mealc	
			BDN consumed (mg)	BDN in predator (mg/kg bw)	BDN consumed (mg)	BDN in predator (mg/kg bw)	BDN consumed (mg)	BDN in predator (mg/kg bw)
Vulpes vulpes	5 700	520.2	2.31	0.41	3.62	0.63	4.32	0.76
Mustela putorius	689	130.9	0.58	0.85	0.91	1.32	1.09	1.58
Mustela erminea	205	55.7	0.25	1.21	0.39	1.89	0.46	2.26
Mustela nivalis	63	24.7	0.11	1.74	0.17	2.72	0.21	3.25

[a] Based on a rodent containing 8.9 mg bromadiolone/kg (according to Table 3.5 in the EUBEES ESD).

[b] Based on a rodent containing 13.9 mg bromadiolone/kg (according to Table 3.5 in the EUBEES ESD).

[c] Based on a rodent containing 16.6 mg bromadiolone/kg (according to Table 3.5 in the EUBEES ESD).

Table 2.8.6.2-15: Estimated intakes and concentrations of bromadiolone (BDN) in mammalian predators and scavengers of rodents, assuming poisoned rodents comprise 50% of a predator/scavenger's diet and that bait contributed 100% of the target rodents' daily food intake

Non-target mammalian predator	Mean body weight (g)	Daily food intake (g/day)	Normal susceptible rodents caught on day 5 just after their last meald		Normal susceptible rodents caught on day 7 two days after their last meale	
			BDN consumed (mg)	BDN in predator (mg/kg bw)	BDN consumed (mg)	BDN in predator (mg/kg bw)
Vulpes vulpes	5 700	520.2	0.829	0.146	0.407	0.071
Mustela putorius	689	130.9	0.209	0.303	0.102	0.148
Mustela erminea	205	55.7	0.089	0.433	0.044	0.212

Mustela nivalis	63	24.7	0.039	0.625	0.019	0.306

[d] Based on a rodent containing 3.189 mg bromadiolone/kg.

[e] Based on a rodent containing 1.563 mg bromadiolone/kg.

Table 2.8.6.2-16: Tier 2 estimate of long-term PECoral/PNECoral (EUBEES scenario) for predatory mammals ingesting target rodents (as 50% of their diet) containing bromadiolone obtained from areas in and around buildings. It is assumed that bait contributed 100% of the target rodents' daily food intake.

Non-target mammalian predator	Normal susceptible rodents caught on day 5, before their last meal		Normal susceptible rodents caught on day 5, just after their last meal		Resistant rodents caught on day 14, just after their last meal	
	PEC	PEC/PNEC	PEC	PEC/PNEC	PEC	PEC/PNEC
Vulpes vulpes	0.41	73214	0.63	112500	0.76	135714
Mustela putorius	0.85	151786	1.32	235714	1.58	282143
Mustela erminea	1.21	216071	1.89	337500	2.26	403571
Mustela nivalis	1.74	310714	2.72	485714	3.25	580357

Table 2.8.6.2-17: Tier 2 estimate of long-term PECoral/PNECoral (experimental data) for predatory mammals ingesting target rodents (as 50% of their diet) containing bromadiolone obtained from areas in and around buildings. It is assumed that bait contributed 100% of the target rodents' daily food intake.

Non-target mammalian predator	Normal susceptible rodents caught on day 5, just after their last meal		Normal susceptible rodents caught on day 7, two days after their last meal	
	PEC	PEC/PNEC	PEC	PEC/PNEC
Vulpes vulpes	0.146	26071	0.071	12679
Mustela putorius	0.303	54107	0.148	26429
Mustela erminea	0.433	77321	0.212	37857
Mustela nivalis	0.625	111607	0.306	54643

The tier 2 risk assessment using the long-term mammalian PNEC data expressed as daily dose (0.0000056 mg/kg bw/day) results in very high risks to non-target mammalian predators.

2.8. 7 Conclusion

No studies were conducted with the product MAKI GRAIN'TECH for the environment part; therefore the environmental risk assessment has been carried out with data from the CAR of bromadiolone. The environmental risk is considered as limited for the use in and around buildings by professional and for indoor use by non-professionals, in strict compliance with the specific use instructions of rodenticidal baits and the use restrictions to reduce the risk for primary and secondary poisoning.

Nevertheless, the Authority in charge of the efficacy and risk assessment is not able to assess the applicability of the specific use instructions and restrictions for the outdoor applications by non-professionals and the uses by professionals in waste dump and around burrows in open areas.

Professional users

Measures to protect environment

- Dispose of the tamper-resistant bait boxes and covered bait stations, uneaten baits and dead rodents in accordance with local requirements.
- Never wash the tamper-resistant bait boxes and covered bait stations with water.
- Place the tamper-resistant bait boxes and covered bait stations in areas non-liable to floodings and sites sheltered from rain.
- Do not throw the product on the ground, into a water course, into the sink or down the drain and into the environment.
- Collect uneaten bait, bait fragments dragged away from the tamper-resistant bait boxes or covered bait stations and dead rodents, during and after treatment.
- Tamper-resistant bait boxes should be clearly marked to show that they contain rodenticides and that they should not contain other products than rodenticides.
- For professional users, covered bait stations could be used. These stations must be placed only in areas not accessible to the general public and non-target animals.
- Baits must be unattainable to children, pets or other non-target animals in order to minimize the risk of poisoning.
- Remove all bait points after the end of treatment.

Non professional users

Measures to protect environment

- Dispose of the tamper-resistant bait boxes and covered bait stations, uneaten baits and dead rodents in accordance with local requirements.
- Never wash the tamper-resistant bait boxes and covered bait stations with water.
- Place the tamper-resistant bait boxes and covered bait stations in areas non-liable to floodings and sites sheltered from rain.
- Do not throw the product on the ground, into a water course, into the sink or down the drain and into the environment.
- Collect uneaten bait, bait fragments dragged away from the tamper-resistant bait boxes or covered bait stations and dead rodents, during and after treatment.
- Use only in tamper-resistant bait boxes.
- Tamper-resistant bait boxes should be clearly marked to show that they contain rodenticides and that they should not contain other products than rodenticides.
- Baits must be unattainable to children, pets or other non-target animals in order to minimize the risk of poisoning.
- Remove all bait points after the end of treatment.

Required information linked to risk assessment for environment

An identification of the bromadiolone major metabolites from the photolysis in water study as well as those from the degradation in soil study has to be provided at the latest 3 years after the authorization of the product.

2.9. Measures to protect man, animals and the environment

See Summary of Product Characteristics (SPC).

3 PROPOSAL FOR DECISION TO BE ADOPTED BY THE FRENCH CA (Ministry of Ecology)

This section is a proposal from the authority in charge of the risk assessment (ANSES) for the decision to be adopted by the competent authority in charge of the decision (French Ministry of Ecology).

In case of inconsistency between the risk assessment and the decision, only the original and signed decision has a legal value. The decision specifies the terms and conditions to the making available on the market and use of the biocidal product.

The product is to be used in tamper-resistant bait boxes or covered bait stations, and into burrows without protection.

”Tamper-resistant bait boxes” are meant to be tamper-resistant devices, that prevent the access to the baits for children and non-target animals, and that protect the baits from bad weather.

”Covered bait stations” are meant to be devices with the same level of security for the human beings and the environment than the security provided by tamper-resistant bait boxes, fastened to prevent any removal, made in order to avoid direct contact of the bait with the environment. This device must be designed to keep baits out of reach of the general public and non-target animals, and to protect the bait from bad weather

It is considered that professional users only (on the contrary to the general public) are able to design such covered bait stations.

Conclusions of efficacy and risk assessment

Risk assessment for physico-chemical properties

MAKI GRAIN’TECH is a ready-to-use grain rodenticide. It is not highly flammable, not auto-flammable at ambient temperature, does not have explosive and oxidizing properties.
An accelerated storage stability study is required in post registration. The biocidal product is stable 42 months at ambient temperature and is compatible with PE sachet, PP sachet, paper laminate sachet and PE box which covers all the claimed packagings.

Summary of efficacy assessment

The product MAKI GRAIN'TECH has shown a sufficient efficacy for the control of mice *(Mus musculus),* voles *(Microtus arvalis, Arvicola terrestris)* and rats (*Rattus norvegicus* and *Rattus rattus*) in and around buildings, in open areas and waste dumps. The product MAKI GRAIN'TECH can also be used for the control of field mice, nevertheless, a field study with *Apodemus sp.* has to be provided within the framework of a post-authorization monitoring to validate this use. Furthermore, a monitoring of the resistance phenomenon of rodent populations toward the active substance bromadiolone and resistant strategies management must be put in place. The collected information must be sent every 2 years to Anses within the framework of a post-authorization monitoring. Furthermore, it can be concluded that the product MAKI GRAIN'TECH can be considered as effective after a 45 month storage period.

The shelf-life of the product is 45 months.

Summary of risks characterisation of the product for human health

No unacceptable risk has been observed for professionals and non-professionals using MAKI GRAIN'TECH in individual plastic sachets, without gloves.

For the indirect scenario "Infant ingesting bait", an unacceptable risk was observed. Therefore, even if MAKI GRAIN'TECH contains a bittering agent which reduces the likelihood of ingestion, the baits should be unattainable which do not allow access to children. Product label ("do not open the sachet") and good practice advise users to prevent access to bait by children and infants.

Summary of risks characterisation of the product for the environment

No studies were conducted with the product MAKI GRAIN'TECH for the environment part; therefore the environmental risk assessment has been carried out with data from the CAR of bromadiolone. The environmental risk is considered as limited for the use in and around buildings by professional and for indoor use by non-professionals, in strict compliance with the specific use instructions of rodenticidal baits and the use restrictions to reduce the risk for primary and secondary poisoning.

Nevertheless, the Authority in charge of the efficacy and risk assessment is not able to assess the applicability of the specific use instructions and restrictions for the outdoor applications by non-professionals and the uses by professionals in waste dump and around burrows in open areas.

The treshold value of 0.1 µg/L in groundwater, taken into account for the risk assessment of groundwater contamination, is an historical value of water quality. As part of the assessment of rodenticides products applications, taking into account the very low toxicological reference values of active substances for this type of product, Anses believes it is necessary, for some of them, including bromadiolone, to revise downward the threshold value of 0.1 µg / L.

Anses is currently working on new proposals for threshold values in groundwater for some of these active substances, and a position paper is going to be submitted for discussion at European level in the context of a forthcoming Technical Meeting.

It should be noted that these proposals do not challenge the conclusion of already issued assessments for rodenticides products.

Risk mitigation measures and conditions of use

Professional users

Measures linked to assessment of physico-chemical properties

- Store away from light.
- Store at maximum 40°C.

Conditions of use linked to efficacy assessment

- Adapt the number of bait station to the infestation level.
- Inspect and resupply the bait stations, 3 days after application then once a week as long as

the bait is consumed.

- Remove all bait points after the end of treatment.
- The amount of bait per bait point and distances between bait points must be respected. Products have always to be used in accordance with the label.
- The users should inform if the treatment is ineffective and report straightforward to the registration holder any alarming signals which could be assumed to be resistance development.
- To avoid resistance:
    - The treatment has to be alternated with other kinds of active substances having different modes of action.
    - Adopt integrated pest management methods such as the combination of chemical, physical control methods and other public health measures.
    - The level of efficacy have to be monitored (periodic check), and the case of reduced efficacy has to be investigated for possible evidence of resistance.
    - Do not use the product in areas where resistance is suspected or established.

Measures to protect man

- Gloves have to be worn to help prevention against rodent-borne disease.
- Do not open the sachets.
- Apply strict hygiene measures: do not eat, drink or smoke during handling of the product and wash hands after use of the product.
- Tamper-resistant bait boxes should be clearly marked to show that they contain rodenticides and that they should not contain other products than rodenticides.
- For professional users, covered bait stations could be used. These stations must be placed only in areas not accessible to the general public and non-target animals.
- Baits must be unattainable to children, pets or other non-target animals in order to minimize the risk of poisoning.
- Do not place tamper-resistant bait boxes and covered bait stations on surfaces in contact with food, feed or drinks and beverages.
- Collect uneaten bait, bait fragments dragged away from the tamper-resistant bait boxes or covered bait stations and dead rodents, during and after treatment.
- Remove all bait points after the end of treatment.

Measures to protect environment

- Dispose of the tamper-resistant bait boxes and covered bait stations, uneaten baits and dead rodents in accordance with local requirements.
- Never wash the tamper-resistant bait boxes and covered bait stations with water.
- Place the tamper-resistant bait boxes and covered bait stations in areas non-liable to floodings and sites sheltered from rain.
- Do not throw the product on the ground, into a water course, into the sink or down the drain and into the environment.
- Collect uneaten bait, bait fragments dragged away from the tamper-resistant bait boxes or covered bait stations and dead rodents, during and after treatment.

- Tamper-resistant bait boxes should be clearly marked to show that they contain rodenticides and that they should not contain other products than rodenticides.
- For professional users, covered bait stations could be used. These stations must be placed only in areas not accessible to the general public and non-target animals.
- Baits must be unattainable to children, pets or other non-target animals in order to minimize the risk of poisoning.
- Remove all bait points after the end of treatment.

Non professional users

Measures linked to assessment of physico-chemical properties

- Store away from light.
- Store at maximum 40℃.

Conditions of use linked to efficacy assessment

- Adapt the number of bait station to the infestation level.
- Inspect and resupply the bait stations, 3 days after application then once a week as long as the bait is consumed.
- Remove all bait points after the end of treatment.
- To avoid resistance:
    - The amount of bait per bait point and distances between bait points must be respected. Products have always to be used in accordance with the label.
    - The users should inform if the treatment is ineffective and report straightforward to the registration holder any alarming signals which could be assumed to be resistance development.

Measures to protect man

- Do not open the sachets.
- Apply strict hygiene measures: do not eat, drink or smoke during handling of the product and wash hands after use of the product.
- Use only in tamper-resistant bait boxes.
- Tamper-resistant bait boxes should be clearly marked to show that they contain rodenticides and that they should not contain other products than rodenticides.
- Baits must be unattainable to children, pets or other non-target animals in order to minimize the risk of poisoning.
- Do not place tamper-resistant bait boxes and covered bait stations on surfaces in contact with food, feed or drinks and beverages.
- Collect uneaten bait, bait fragments dragged away from the tamper-resistant bait boxes or covered bait stations and dead rodents, during and after treatment.
- Remove all bait points after the end of treatment.

Measures to protect environment

- Dispose of the tamper-resistant bait boxes and covered bait stations, uneaten baits and dead rodents in accordance with local requirements.
- Never wash the tamper-resistant bait boxes and covered bait stations with water.
- Place the tamper-resistant bait boxes and covered bait stations in areas non-liable to floodings and sites sheltered from rain.
- Do not throw the product on the ground, into a water course, into the sink or down the drain and into the environment.
- Collect uneaten bait, bait fragments dragged away from the tamper-resistant bait boxes or covered bait stations and dead rodents, during and after treatment.
- Use only in tamper-resistant bait boxes.
- Tamper-resistant bait boxes should be clearly marked to show that they contain rodenticides and that they should not contain other products than rodenticides.
- Baits must be unattainable to children, pets or other non-target animals in order to minimize the risk of poisoning.
- Remove all bait points after the end of treatment.

Directions for safe disposal of the product and its packaging

Directions linked to risk assessment for human health

- Collect uneaten bait, bait fragments dragged away from the tamper-resistant bait boxes or covered bait stations and dead rodents, during and after treatment.
- Remove all bait points after the end of treatment.

Directions linked to risk assessment for environment

- Collect uneaten bait, bait fragments dragged away from the tamper-resistant bait boxes or covered bait stations and dead rodents, during and after treatment.
- Dispose of the tamper-resistant bait boxes and covered bait stations, uneaten baits and dead rodents in accordance with local requirements.
- Never wash the tamper-resistant bait boxes and covered bait stations with water.
- Do not throw the product on the ground, into a water course, into the sink or down the drain and into the environment.
- Remove all bait points after the end of treatment.

Information required post-authorisation

Required information linked to assessment of physico-chemical properties

- Particle size distribution of grains is according to CIPAC method MT 170 with seives adapted to biocidal product required in post registration.
- An accelerated storage stability study (14 days at 54℃ or at a lower temperature) is required with CIPAC MT46.
- Demonstration of applicability of the method to MAKI GRAIN'TECH in the form of chromatograms of placebo, of test sample and of a reference sample.

- The analytical method for determination of Bromadiolone in surface and drinking water is not considered as highly specific. A confirmatory method must be submitted in post registration.

Required information linked to efficacy assessment
Concerning the efficacy of the product, a new field study is awaited to confirm the efficacy against field mice (*Apodemus sylvaticus*) at latest 2 years after the authorization of the product.

The authorization holder has to report any observed resistance to bromadiolone to Anses or other appointed bodies involved in resistance management every two years.

Required information linked to risk assessment for environment
An identification of the bromadiolone major metabolites from the photolysis in water study as well as those from the degradation in soil study has to be provided at the latest 3 years after the authorization of the product.

Annex 0a : Intended uses claimed by the applicant

Name of the product and type of formulation (grains, powder, paste, block…)	Target organism (rat, mice…)*	User category (professional/non professional)*	Area of use (sewers, in and around buildings, indoor only, open areas, waste dumps,…)*	Dosage claimed expressed in g/bait point, for high and low infestation (if appropriate)	Time delay of the action of the product	Frequency and method of controls	Size(s) of the bait (g/bloc, g/grain, g/sachet, g/paste …)	Distance between 2 bait points, for high and low infestation (if appropriate)	Methods of application of the bait (ex: pre-filled secured bait box)	Package details : Individual packaging (yes/no)**	Primary packaging : type : bulk, individual wrapping…/ nature: bucket, bottle, sachet…/ material: paper, polyethylene…/ sizes	Secondary packaging
MAKI GRAIN TECH **Formulation: F00506-01**	Rats	Professional	In and around buildings	Up to 200 g *This level is adapted according to the size of the sachet*	4 to 6 days after the first consumption	High infestation 3 days after first application then ideally every week or 15 days Low infestation 1 week after first application then ideally every week or 15 days If consumption is complete, repeat the treatment without exceeding the dose of 200g	Loose, or in sachets 20g to 100g	4 to 5 meters High infestation 8 to 10 meters low infestation	Grain baits are manually placed in the rodent infested area. Methods of deployment for professional users are bait stations (tamper proof boxes), bait points (a makeshift arrangement which uses materials and/or the local environment to restrict access to the bait), loose but inaccessible (an arrangement which uses the local environment only to restrict	Yes	Packaging: sachet Material: PE or PP (Opaque or transparent)	Opaque Metal box 500g to 1 kg Opaque Plastic lockable pouch PE or PP 500g to 20 kg Opaque Plastic bucket (PP) with lid Up to 25 kg Opaque Cardboard carton 500g to 25 kg Opaque plastic container (PE or PP) 500g to 4 kg Opaque Paper laminate bag 500g to 25 kg
										No	Opaque Plastic lockable pouch PE or PP 500g to 20 kg Opaque Plastic bucket (PP) with lid 500g to 25 kg Opaque Cardboard carton with an with integral PE bag 500g to 25 kg Opaque plastic container (PE or PP)	

									access to the bait), burrows		500g to 4 kg Paper laminate bag 500g 25 kg	
	Mice	Professional	In and around building	Up to 50 g *This level is adapted according to the size of the sachet*	4 to 6 days after the first consumption	High infestation 3 days after first application then ideally every week or 15 days Low infestation 1 week after first application then ideally every week or 15 days every week or 15 days If consumption is complete, repeat the treatment without exceeding the dose of 50g	Loose, or in sachets 20g to 50g	1 to 1.5 meters in high infestation 2 to 3 meters in low infestation	Grain baits are manuallyplaced in the rodent infested area. Methods of deployment for professional users are bait stations (tamper proof boxes), bait points (a makeshift arrangement which uses materials and/or the local environment to restrict access to the bait), loose but inaccessible (an arrangement which uses the local environment only to restrict access to the bait), burrows	YES	Packaging: sachet Material: PE or PP (Opaque or transparent)	Opaque Metal box 500g to 1 kg Opaque Plastic lockable pouch PE or PP 500g to 20 kg Opaque Plastic bucket (PP) with lid 500g to 25 kg Opaque Cardboard carton with an with integral PE bag 500g to 25 kg Opaque plastic container (PE or PP) 500g to 4 kg Opaque Paper laminate bag 500g to 25 kg
										NO	Opaque Plastic lockable pouch PE or PP 500g to 20 kg Opaque Plastic bucket (PP) with lid 500g to 25 kg Opaque Cardboard carton with an with integral PE bag 500g to 25 kg Opaque plastic container (PE or PP) 500g to 4 kg Opaque Paper laminate bag 500g to 25 kg	
	Voles	Professional	In and around building	Up to 100 g *This level is adapted according to the size of the sachet*	4 to 6 days after the first consumption	High infestation 3 days after first application then ideally every week or 15 days Low infestation 1 week after first application then ideally every week or 15 days If consumption is complete,	Loose, or in sachets 20g to 100g	3 meters high infestation Every 6 meters in low infestation	Grain baits are manually placed in the rodent infested area. Methods of deployment for professional users are bait stations (tamper proof boxes), bait	YES	Packaging: sachet Material: PE or PP (Opaque or transparent)	Opaque Metal box 500g to 1 kg Opaque Plastic lockable pouch PE or PP 500g to 20 kg Opaque Plastic bucket (PP) with lid 500g to 25 kg Opaque Cardboard carton with an with integral PE bag 500g to 25 kg Opaque plastic container (PE or PP)

						repeat the treatment without exceeding the dose of 100g			points (a makeshift arrangement which uses materials and/or the local environment to restrict access to the bait), loose but inaccessible (an arrangement which uses the local environment only to restrict access to the bait), burrows			500g to 4 kg Opaque Paper laminate bag 500g to 25 kg
										NO	Opaque Plastic lockable pouch PE or PP 500g to 20 kg	
											Opaque Plastic bucket (PP) with lid 500g to 25 kg	
											Opaque Cardboard carton with an with integral PE bag 500g to 25 kg	
											Opaque plastic container (PE or PP) 500g to 4 kg	
											Opaque Paper laminate bag 500g to 25 kg	
	Field Mice	Professional	In and around building	Up to 50 g *This level is adapted according to the size of the sachet*	4 to 6 days after the first consumption	High infestation 3 days after first application then ideally every week or 15 days Low infestation 1 week after first application then ideally every week or 15 days If consumption is complete, repeat the treatment without exceeding the dose of 50g	Loose, or in sachets 20g to 50g	1 to 1.5 meters in high infestation 2 to 3 meters in low infestation	Grain baits are manually placed in the rodent infested area. Methods of deployment for professional users are bait stations (tamper proof boxes), bait points (a makeshift arrangement which uses materials and/or the local environment to restrict access to the bait), loose but inaccessible (an arrangement which uses the local environment	YES	Packaging: sachet Material: PE or PP (Opaque or transparent)	Opaque Metal box up to 1 kg
												Opaque Plastic lockable pouch PE or PP 500g to 20 kg
												Opaque Plastic bucket (PP) with lid 500g to 25 kg
												Opaque Cardboard carton with an with integral PE bag 500g to 25 kg
												Opaque plastic container (PE or PP) 500g to 4 kg
												Opaque Paper laminate bag 500g to 25 kg
										NO	Opaque Plastic lockable pouch PE or PP 500g to 20 kg	
											Opaque Plastic bucket (PP) with lid 500g to 25 kg	

									only to restrict access to the bait), burrows		Opaque Cardboard carton with an with integral PE bag 500g to 25 kg	
											Opaque plastic container (PE or PP) 500g to 4 kg	
											Opaque Paper laminate bag 500g to 25 kg	
	Rats	Professional	Open areas	Up to 200 g *This level is adapted according to the size of the sachet*	4 to 6 days after the first consumption	High infestation 3 days after first application then ideally every month Low infestation 1 week after first application then ideally every month If consumption is complete, repeat the treatment without exceeding the dose of 200g	Loose, or in sachets 20g to 100g	NA in each burrows 10-15 m low infestation 3-5 m high infestation (depends also on the configuration of the site)	Grain baits are manually placed in the rodent infested area. Methods of deployment for professional users are bait stations (tamper proof boxes) or in burrow	YES	Packaging: sachet Material: PE or PP (Opaque or transparent)	Opaque Metal box 500g to 1 kg
												Opaque Plastic lockable pouch PE or PP 500g to 20 kg
												Opaque Plastic bucket (PP) with lid 500g to 25 kg
												Opaque Cardboard carton with an with integral PE bag 500g to 25 kg
												Opaque plastic container (PE or PP)) 500g to 4 kg
												Opaque Paper laminate bag 500g to 25 kg
										NO	Opaque Plastic lockable pouch PE or PP 500g to 20 kg	
											Opaque Plastic bucket (PP) with lid 500g to 25 kg	
											Opaque Cardboard carton with an with integral PE bag 500g to 25 kg	
											Opaque plastic container (PE or PP) 500g to 4 kg	
											Opaque Paper laminate bag 500g to 25 kg	
	Mice	Professional	Open areas	Up to 50 g *This level is adapted according to the size of the sachet*	4 to 6 days after the first consumption	High infestation 3 days after first application then ideally every month Low infestation 1 week after first application then	Loose, or in sachets 20g to 50g	NA in each burrows 10-15 m low infestation 3-5 m high infestation	Grain baits are manually placed in the rodent infested area. Methods of deployment for	YES	Packaging: sachet Material: PE or PP (Opaque or transparent)	Opaque Metal box up to 1 kg
												Opaque Plastic lockable pouch PE or PP 500g to 20 kg
												Opaque Plastic bucket (PP) with lid 500g to 25 kg
												Opaque Cardboard

						ideally every month If consumption is complete, repeat the treatment without exceeding the dose of 50g		(depends also on the configuration of the site)	professional users are bait stations (tamper proof boxes) or in burrow			carton with an with integral PE bag 500g to 25 kg
												Opaque plastic container (PE or PP) 500g to 4 kg
												Opaque Paper laminate bag 500g to 25 kg
										NO	Opaque Plastic lockable pouch PE or PP 500g to 20 kg	
											Opaque Plastic bucket (PP) with lid 500g to 25 kg	
											Opaque Cardboard carton with an with integral PE bag 500g to 25 kg	
											Opaque plastic container (PE or PP) 500g to 4 kg	
											Opaque Paper laminate bag 500g to 25 kg	
	Voles	Professional	Open areas	Up to 100 g *This level is adapted according to the size of the sachet*	4 to 6 days after the first consumption	High infestation 3 days after first application then ideally every month Low infestation 1 week after first application then ideally every month If consumption is complete, repeat the treatment without exceeding the dose of 100g	Loose, or in sachets 20g to 50g	NA in the burrow 10-15 m low infestation 3-5 m high infestation (depends also on the configuration of the site)	Grain baits are manually placed in the rodent infested area. Methods of deployment for professional users are bait stations (tamper proof boxes) or in burrow	YES	Opaque Packaging: sachet Material: PE or PP (Opaque or transparent)	Opaque Metal box 500g to 1 kg
												Opaque Plastic lockable pouch PE or PP 500g to 20 kg
												Opaque Plastic bucket (PP) with lid 500g to 25 kg
												Opaque Cardboard carton with an with integral PE bag 500g to 25 kg
												Opaque plastic container (PE or PP) 500g to 4 kg
												Opaque Paper laminate bag 500g to 25 kg
										NO	Opaque Plastic lockable pouch PE or PP 500g to 20 kg	
											Opaque Plastic bucket (PP) with lid 500g to 25 kg	
											Opaque Cardboard carton with an with integral PE bag 500g to 25 kg	
											Opaque plastic	

											container (PE or PP) 500g to 4 kg	
											Opaque Paper laminate bag 500g to 25 kg	
	Field Mice	Professional	Open areas	Up to 50 g *This level is adapted according to the size of the sachet*	4 to 6 days after the first consumption	High infestation 3 days after first application then ideally every month Low infestation 1 week after first application then ideally every month If consumption is complete, repeat the treatment without exceeding the dose of 50 g	Loose, or in sachets 20g to 50g	NA in each burrows 10-15 m low infestation 3-5 m high infestation (depends also on the configuration of the site)	Grain baits are manually placed in the rodent infested area. Methods of deployment for professional users are bait stations (tamper proof boxes) or in burrow	YES	Packaging: sachet Material: PE or PP (Opaque or transparent)	Opaque Metal box up to 1 kg
												Opaque Plastic lockable pouch PE or PP 500g to 20 kg
												Opaque Plastic bucket (PP) with lid 500g to 25 kg
												Opaque Cardboard carton with an with integral PE bag 500g to 25 kg
												Opaque plastic container (PE or PP) 500g to 4 kg
												Opaque Paper laminate bag 500g to 25 kg
										NO	Opaque Plastic lockable pouch PE or PP 500g to 20 kg	
											Opaque Plastic bucket (PP) with lid 500g to 25 kg	
											Opaque Cardboard carton with an with integral PE bag 500g to 25 kg	
											Opaque plastic container (PE or PP) 500g to 4 kg	
											Opaque Paper laminate bag 500g to 25 kg	
	Rats	Professional	Waste dump	Up to 200 g *This level is adapted according to the size of the sachet*	4 to 6 days after the first consumption	Application every 2 to 3 months If consumption is complete, repeat the treatment without exceeding the dose of 200g	Loose, or in sachets 20g to 100g	NA in the burrow 10-15 m low infestation 3-5 m high infestation (depends also on the configuration of the site)	Grain baits are manually placed in the rodent infested area. Methods of deployment for professional users are bait stations (tamper proof boxes), bait points (a	YES	Packaging: sachet Material: PE or PP (Opaque or transparent)	Opaque Metal box 500g to 1 kg
												Opaque Plastic lockable pouch PE or PP 500g to 20 kg
												Opaque Plastic bucket (PP) with lid 500g to 25 kg
												Opaque Cardboard carton with an with integral PE bag 500g to 25 kg
												Opaque plastic container (PE or PP) 500g to 4 kg

									makeshift arrangement which uses materials and/or the local environment to restrict access to the bait), burrows			Opaque Paper laminate bag 500g to 25 kg
										NO	Opaque Plastic lockable pouch PE or PP 500g to 20 kg	
											Opaque plastic bucket (PP) with lid 500g to 25 kg	
											Opaque Cardboard carton with an with integral PE bag 500g to 25 kg	
											Opaque plastic container (PE or PP) 500g to 4 kg	
											Opaque Paper laminate bag 500g to 25 kg	
	Mice	Amateur	In and around building	Up to 50 g *This level is adapted according to the size of the sachet*	4 to 6 days after the first consumption	High infestation 3 days after first application then ideally every week or 15 days Low infestation 1 week after first application then ideally every week or 15 days If consumption is complete, repeat the treatment without exceeding the dose of 50g	Loose, or in sachets 20g to50g	1 to 1.5 meters in high infestation 2 to 3 meters in low infestation	Grain baits are manually placed in the rodent infested area. Methods of deployment for amateur users are bait stations (tamper proof boxes), bait points (a makeshift arrangement which uses materials and/or the local environment to restrict access to the bait), loose but inaccessible (an arrangement which uses the local environment only to restrict access to the bait).	YES	Packaging: sachet Material: PE or PP (Opaque or transparent)	Opaque Metal box 40g to 1 kg
												Opaque Plastic lockable pouch PE or PP 40g to 4 kg
												Opaque Plastic bucket (PP) with lid 40g to 4 kg
												Opaque Cardboard carton with an with integral PE bag 40g to 4 kg
												Opaque plastic container (PE or PP) 40g to 4 kg
										NO	Opaque Plastic lockable pouch PE or PP 40g to 4 kg	
											Opaque Plastic bucket (PP) with lid 40g to 4 kg	
											Opaque plastic container (PE or PP) 40g to 4 kg	
											Opaque Cardboard carton with an with integral PE bag 40g to 4 kg	

Rats	Amateur	In and around buildings	Up to 200 g *This level is adapted according to the size of the sachet*	4 to 6 days after the first consumption	High infestation 3 days after first application then ideally every week or 15 days Low infestation 1 week after first application then ideally every week or 15 days If consumption is complete, repeat the treatment without exceeding the dose of 200g	Loose, or in sachets 20g to 100g	4 to 5 meters High infestation 8 to 10 meters low infestation	Grain baits are manually placed in the rodent infested area. Methods of deployment for amateur users are bait stations (tamper proof boxes), bait points (a makeshift arrangement which uses materials and/or the local environment to restrict access to the bait), loose but inaccessible (an arrangement which uses the local environment only to restrict access to the bait).	YES	Packaging: sachet Material: PE or PP (Opaque or transparent)	Opaque Metal box 40g to 1 kg Opaque Plastic lockable pouch PE or PP 40g to 4 kg Opaque Plastic bucket (PP) with lid 40g to 4 kg Opaque Cardboard carton with an with integral PE bag 40g to 4 kg Opaque plastic container (PE or PP) 40g to 4 kg
									NO	Opaque Plastic lockable pouch PE or PP 40g to 4 kg Opaque Plastic bucket (PP) with lid 40g to 4 kg Opaque Cardboard carton with an with integral PE bag 40g to 4 kg Opaque plastic container (PE or PP) 40g to 4 kg	
Voles	Amateur	In and around buildings	Up to 100 g *This level is adapted according to the size of the sachet*	4 to 6 days after the first consumption	High infestation 3 days after first application then ideally every week or 15 days Low infestation 1 week after first application then ideally every week or 15 days If consumption is complete, repeat the treatment without exceeding the	Loose, or in sachets 20g to 100g	3 meters high infestation Every 6 meters in low infestation	Grain baits are manually placed in the rodent infested area. Methods of deployment for amateur users are bait stations (tamper proof boxes), bait points (a makeshift arrangement which uses	YES	Packaging: sachet Material: PE or PP (Opaque or transparent)	Opaque Metal box 40g to 1 kg Opaque Plastic lockable pouch PE or PP 40g to 4 kg Opaque Plastic bucket (PP) with lid 40g to 4 kg Opaque Cardboard carton with an with integral PE bag 40g to 4 kg Opaque plastic container (PE or PP)

						dose of 100g			materials and/or the local environment to restrict access to the bait), loose but inaccessible (an arrangement which uses the local environment only to restrict access to the bait).			40g to 4 kg
											Opaque Plastic lockable pouch PE or PP 40g to 4 kg	
											Opaque Plastic bucket (PP) with lid 40g to 4 kg	
											Opaque Cardboard carton with an with integral PE bag 40g to 4 kg	
											Opaque plastic container (PE or PP) 40g to 4 kg	
	Field mice	Amateur	In and around buildings	Up to 50 g *This level is adapted according to the size of the sachet*	4 to 6 days after the first consumption	High infestation 3 days after first application then ideally every week or 15 days Low infestation 1 week after first application then ideally every week or 15 days If consumption is complete, repeat the treatment without exceeding the dose of 50g	Loose, or in sachets 20g to 50g	1 to 1.5 meters in high infestation 2 to 3 meters in low infestation	Grain baits are manually placed in the rodent infested area. Methods of deployment for amateur users are bait stations (tamper proof boxes), bait points (a makeshift arrangement which uses materials and/or the local environment to restrict access to the bait), loose but inaccessible (an arrangement which uses the local environment only to restrict access to the bait).	YES	Packaging: sachet Material: PE or PP (Opaque or transparent)	Opaque Metal box 40g to 1 kg
												Opaque Plastic lockable pouch PE or PP 40g to 4 kg
												Opaque Plastic bucket (PP) with lid 40g to 4 kg
												Opaque Cardboard carton with an with integral PE bag 40g to 4 kg
												Opaque plastic container (PE or PP) 40g to 4 kg
										NO	Opaque Plastic lockable pouch PE or PP 40g to 4 kg	
											Opaque Plastic bucket (PP) with lid 40g to 4 kg	
											Opaque Cardboard carton with an with integral PE bag 40g to 4 kg	
											Opaque plastic container (PE or PP) 40g to 4 kg	

* One option by line

**for more details please fulfill the column related to primary packaging and secondary packaging

Annex 0b : proposed uses for authorisation

This table reflects the results of the risk assessment. In case of differences between the uses suggested by Anses to be authorised and the uses contained in the decision taken by the French ministry, only the original and signed decision has a legal value.

Target organisms	Area of use	Dosage claimed	Time delay of the action of the product	Distance between 2 bait points, for high and low infestation	Frequency and method of controls	Methods of application of the bait
PROFESSIONAL USERS						
Rats *Rattus norvegicus* *Rattus rattus*	In and around buildings	200 g	3 to 21 days	High infestation: 4-5 meters Low infestation: 8-10 meters	Inspect and resupply the bait stations, 3 days after application then once a week as long as the bait is consumed.	Manual application in bait stations, bait points, loose but inaccessible and burrows
House mice *Mus musculus*		50 g		High infestation: 1-1,5 meters Low infestation: 2-3 meters		
Field mice* *Apodemus sp.*		50 g		High infestation: 1-1,5 meters Low infestation: 2-3 meters		
NON PROFESSIONAL USERS						
Rats *Rattus norvegicus* *Rattus rattus*	Indoor	200 g	3 to 21 days	High infestation: 4-5 meters Low infestation: 8-10 meters	Inspect and resupply the bait stations, 3 days after application then once a week as long as the bait is consumed.	Manual application in bait stations, bait points, loose but inaccessible
House mice *Mus musculus*		50 g		High infestation: 1-1,5 meters Low infestation: 2-3 meters		

Field mice* *Apodemus sp.*		50 g		<u>High infestation:</u> 1-1,5 meters <u>Low infestation:</u> 2-3 meters		

** A field trial against Apodemus sp. should be provided within two years after the authorisation*

Annex 1: Summary of product characteristics

See separated file.

Annex 2: List of studies reviewed

List of <u>new data</u>[13] submitted in support of the evaluation of the active substance

No <u>new data</u> have been submitted in support of the evaluation of the active substance

List of <u>new data</u> 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	IIIB 3.1.3-01	Caruel, H.	2007a	Bromadiolone Red Wheat 50 mg/kg BROBL0,0050_05F_LR0234_00 Appearance, Colour, Odour Centre R&D De Sangosse, Pont du Casse, France. Study code: BRO0703C. Non-GLP, Unpublished.	Liphatech	☐	☒	☒	☐
B3	IIIB 3.2-01 3.3-01 3.4-01	Tremain, S.P.	2003	Supercaid AS Appat Determination of Hazardous Physico-Chemical Properties. SafePharm Laboratories Ltd, Shardlow, Derbyshire, UK. Study code: 1840/011. GLP, Unpublished.	Liphatech	☐	☒	☒	☐

[13] 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	
B3	IIIB 3.5-01	Caruel, H.	2009b	Bromadiolone Red Wheat 50 mg/kg Storage Stability (25°C – 2 years), BROBL0,0050_05F_LR0234_00. Centre R&D De Sangosse, Pont du Casse, France. Study code: BRO0710E. GLP, Unpublished.	Liphatech	☐	☒	☒	☐
B3	IIIB 3.7-01	Caruel, H.	2006	Bromadiolone Red Wheat 50 mg/kg Accelerated Storage Stability (54°C – 14 days), BROBL0,0050_05F_LR0234_00. Centre R&D De Sangosse, Pont du Casse, France. Study code: BRO0610V. GLP, Unpublished.	Liphatech	☐	☒	☒	☐
B3	IIIB 3.7-04	Caruel, H.	2010a	Bromadiolone Red Wheat 50 mg/kg – Long Term Storage Stability (25°C), BROBL0,0050_05F_LR0234_00. Centre R&D De Sangosse, Pont du Casse, France. Study code: BRO0812F. GLP, Unpublished.	Liphatech	☐	☒	☒	☐
B3	IIIB 3.7-07	Caruel, H.	2009b	Bromadiolone Red Wheat 50 mg/kg – Storage Stability (25°C – 2 years), BROBL0,0050_05F_LR0234_00. Centre R&D De Sangosse, Pont du Casse, France. Study code: BRO0710E. GLP, Unpublished.	Liphatech	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
B3	IIIB 3.12-01	Woolley, A.J. Mullee, D.M.	2006	Supercaid AS Appat Determination of Dust Content and Apparent Density. SafePharm Laboratories Ltd, Shardlow, Derbyshire, UK. Study code: 1840/022. GLP, Unpublished.	Liphatech	☐	☒	☒	☐
B4	IIIB 4.1-01	Caruel, H.	2005	Bromadiolone Cereals 50 mg/kg - Analytical Method Validation. Centre R&D De Sangosse, Pont du Casse, France. Study code: BRO0502H. GLP, Unpublished.	Liphatech	☐	☒	☒	☐
B5	IIIB-5.10.2-01	Lorgue, G.	2002a	Study on the Efficacy and Attractivity of an Oat Bait Impregnated with 50 mg/kg of Bromadiolone in the Rat, Wild Strain, Sensitive to Coumafene. ENVL, Marcy L'Etoile, France. Study code: P 99.04/b. Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐
B5	IIIB-5.10.2-02	Berny, P.	2003a	Study on the Efficacy and Attractivity of a Impregnated Oat Bait with 50 mg/kg of Bromadiolone in the House Mouse, Mus Musculus, Wild Strain, Sensitive to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/0308/BDN/Oat/Mm/S/T0. Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
B5	IIIB-5.10.2-03	Berny, P.	2008a	Study on the Efficacy and Attractivityof a Wheat at 50 mg/kg of Bromadiolone in the Rat, Rattus Norvegicus, Wild Strain, Sensitive to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/0711/BDN/Wheat/Rn/S. Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐
B5	IIIB-5.10.2-04	Berny, P.	2008b	Study on the Efficacy and Palatability of a Wheat at 50 mg/kg of Bromadiolone in the House Mouse, Mus Musculus, Wild Strain, Sensitive to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/0712/BDN/Wheat/Mm/S/T0, Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐
B5	IIIB-5.10.2-05	Berny, P.	2005a	Studyon the Efficacy and Attractivity of a Wheat Bait at 50 mg/kg of Bromadiolone in the Rat, Rattus Norvegicus, Wild Strain, Resistant to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/0503/BDN/Wheat/Rn/R/T0. Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐
B5	IIIB-5.10.2-06	Berny, P.	2005b	Study on the Efficacy and Attractivity of a Wheat Bait with 50 mg/kg of Bromadiolone in the House Mouse, Mus Musculus, Wild Strain, Resistant to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/0504/BDN/Wheat/Mm/R/T0. Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
B5	IIIB-5.10.2-07	Berny, P.	2009a	Study on the Efficacy and Palatability a Wheat at 50 mg/kg of Bromadiolone in the Rat, Rattus Rattus, Wild Strain, Sensitive to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/0911/BDN/Wheat/Rr/S, Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐
B5	IIIB-5.10.2-08	Berny, P.	2010a	Study on the Efficacy and Palatability of an Oat Bait at 50 mg/kg of Bromadiolone in the Rat, *Rattus rattus*, Wild Strain, Sensitive to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/0912/BDN/Oat/Rr/R/S. Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐
B5	IIIB-5.10.2-09	Berny, P.	2007a	Study on the Efficacy of a Red Wheat Bait at 50 mg/kg of Bromadiolone in the House Mouse, Mus Musculus, Wild Strain, Sensitive to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/0702/BDN/Wheat/Mm/S/T0. Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐
B5	IIIB-5.10.2-10	Berny, P.	2007b	Study on the Efficacy of a Red Wheat at 50 mg/kg of Bromadiolone in the Rat, Rattus Norvegicus, Wild Strain, Sensitive to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/0703/BDN/Wheat/Rn/S/T0. Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
B5	IIIB-5.10.2-11	Berny, P.	2010b	Evaluation of the Efficacy of Oat Rodenticide Containing 50 mg/kg Bromadiolone for the Control of Brown Rat Infestations in and Around Agricultural Buildings. ENVL, Marcy L'Etoile, France. Study code: FSR-0906. Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐
B5	IIIB-5.10.2-12	Berny, P.	2010c	Evaluation of the Efficacy of a Wheat Rodenticide Containing 50 mg/kg Bromadiolone for the Control of House Mice Infestations in and Around Urban Buildings. ENVL, Marcy L'Etoile, France. Study code: FSR-0908. Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐
B5	IIIB-5.10.2-13	Berny, P.	2009b	Study on the Eficacy and Palatability of a Bromadiolone Wheat 50 mg/kg in the Common Vole, *Microtus Arvalis*, Wild Strain, ENVL, Marcy L'Etoile, France. Study code: RE/0901/BDN/Wheat/Ma. Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐
B5	IIIB-5.10.2-14	Berny, P.	2009c	Study on the Palatability and Efficacy of a Bromadiolone Wheat 50 mg/kg in the Water Vole, *Arvicola Terrestris*, Wild Strain, ENVL, Marcy L'Etoile, France. Study code: RE/0902/BDN/Wheat/At. Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
B5	IIIB-5.10.2-15	Bourret, A.	2008a	Treatment of Mice and Common Voles Infestation with an Oat Rodenticide Containing 50 mg/kg Bromadiolone in an Electrical Distribution Factory (RTE). Liphatech, Bonnel, France. Study code: 0802. Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐
B5	IIIB-5.10.2-16	Bourret, A.	2008b	Treatment of Common Voles Infestations with an Oat Rodenticide Containing 50 mg/kg Bromadiolone in a Cheese Factory. Liphatech, Bonnel, France. Study code: 0801. Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐
B5	IIIB-5.10.2-17	Berny, P.	2005c	Study on the Impact of Denatonium Benzoate Variation Concentration on the Palatability of a Rodenticide Block Formula in the Rat, *Rattus Norvegicus*, Wild Strain. ENVL, Marcy L'Etoile, France. Study code: RE/0404/BDN/Block/Rn. Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐
B5	IIIB-5.10.2-18	Berny, P.	2005d	Study on the Impact of Packaging on the Attractivity of a Block in the Rat, *Rattus Norvegicus*, Wild Strain. ENVL, Marcy L'Etoile, France. Study code: RE/0314/Pack/R225/Block/Rn. Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
B5	IIIB-5.10.2-19	Berny, P.	2003b	Selection of House Mouse Strains, *Mus Musculus* According to Their Degree of Resistance to an Anticoagulant of 1st Generation: Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/SOU/0202. Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐
B5	IIIB-5.10.2-20	Berny, P.	2002b	Selection of Rat Strains, *Rattus Norvegicus* According to Their Degree of Resistance to an Anticoagulant of 1st Generation: Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/SOU/0201. Non-GLP, Unpublished.	LiphaTech	☐	☒	☒	☐
B5	IIIB-5.10.2-21	Berny, P.	2012	Study on the efficacy and palatability of an oat at 50 mg/kg of Bromadiolone in the rat, Rattus Norvegicus, wild strain, resistant to warfarin. Laboratoire de Toxicologie, ENVL, report number RE/1204/BDN/Oat/Rn/R, May 2012 (unpublished).	LiphaTech	☐	☒	☒	☐
B5	IIIB-5.10.2-22	Berny, P.	2012b	Study on the efficacy and palatability of a wheat at 50 mg/kg of Bromadiolone in the rat, Rattus Norvegicus, wild strain, resistant to warfarin. Laboratoire de Toxicologie, ENVL, report number RE/1206/BDN/Wheat/Rn/R, (unpublished).	LiphaTech	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
B6	IIIB 6.1.1-01	Glaza, S.M.	1993a	Acute oral toxicity study (Limit test) of Maki Rat and Mouse Meal Bait in Rats. Hazleton Wisconsin, Madison, Wisconsin, USA. Laboratory report no. HWI 30702242 GLP/Unpublished	LiphaTech	☐	☒	☒	☐
B6	IIIB 6.1.2-01	Glaza, S.M.	1993b	Acute Dermal Toxicity Study (Limit test) of Maki Rat and Mouse Meal Bait in Rabbits. Hazleton Wisconsin, Madison, Wisconsin, USA. Laboratory report no. HWI 30702243 GLP/Unpublished	LiphaTech	☐	☒	☒	☐
B6	IIIB 6.1.3-01	Duchosal, F. and Biedermann, K	1994	Technical test and 4-hour acute inhalation toxicity study (Limit test) with Bromadiolone (1% powder) in rats. RCC, Research and Consulting Company, Itingen, Switzerland. Laboratory report no. 362518 GLP/Unpublished	LiphaTech	☐	☒	☒	☐
B6	IIIB 6.2-01	Glaza, S.M.	1993c	Primary Dermal Irritation Study of Maki Rat and Mouse Meal Bait in Rabbits. Hazleton Wisconsin, Madison, Wisconsin, USA. Laboratory report no. HWI 30702244 GLP/Unpublished	LiphaTech	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
B6	IIIB 6.2-02	Glaza, S.M.	1993d	Primary Eye Irritation Study of Maki Rat and Mouse Meal Bait in Rabbits. Hazleton Wisconsin, Madison, Wisconsin, USA. Laboratory report no. HWI 30702245 GLP/Unpublished	LiphaTech	☐	☒	☒	☐
B6	IIIB 6.3-01	Glaza, S.M.	1993e	Dermal Sensitisation Study of Maki Rat and Mouse Meal Bait in Guinea Pigs – Closed Patch Technique. Hazleton Wisconsin, Madison, Wisconsin, USA. Laboratory report no. HWI 30702246 GLP/Unpublished	LiphaTech	☐	☒	☒	☐
B6	IIIB 6.4-01	Hassler, S.	2004	Percutaneous Penetration of ^{14}C-Bromadialone formulated as Red Impregnated Oat and Green Blocks through human split thickness skin membrane (*in vitro*). RCC Ltd. Laboratory report number 849290. GLP/Unpublished	LiphaTech	☐	☒	☒	☐
B6	IIIB 6.6-01	Snowdon, P.J.	2003	Pilot study to determine primary sources of exposure to operators during simulated use of anticoagulant rodenticide baits. Synergy Laboratories Limited Laboratory report no. SYN/1301 GLP/Unpublished	LiphaTech	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
B6	IIIB 6.6-02	Chambers, J.G., Snowdon, P.J.	2004	Study to determine potential exposure to operators during simulated use of anticoagulant rodenticide baits. Synergy Laboratories Limited Laboratory report no. SYN/1302 GLP/Unpublished	LiphaTech	☐	☒	☒	☐

Annex 3: Analytical methods residues – active substance

Bromadiolone

Matrix, action levels, relevant residue and reference

Extract from document IIA of final CAR of bromadiolone (LiphaTech S.A.S):

Test substance	Sample	Analytical method	Fortification range / Number of measurements	Linearity	Specificity	Recovery rate (%)			Limit of determination	LOQ required**	Reference
						Range	Mean	RSD%			
Bromadiolone	soil	LC/MS-MS	0.01 to 0.10 mg/kg / 10	r2 = 0.999079	specific	83 - 102	91	6.8	0.01 mg/kg	3.7 mg/kg	A4.2(a)/01
	soil*	HPLC/UV	0.06 to 0.10 mg/kg / 23	-	specific	70 - 110	88	9.3	0.06 mg/kg	3.7 mg/kg	A4.2(a)/02
	air	HPLC/UV	0.5 to 100 µg/m^3 / 19	r2 = 0.9997	specific	69 - 101	85	11.2	0.5 µg/m^3	0.012 µg/m^3	A4.2(b)/01
	drinking water	HPLC/ fluorescence ***	0.05 to 0.50 µg/L /14	r2 = >0.9996	specific	71 - 88	79	6.9	0.05 µg/L	0.1 µg/L	A4.2(c)/01
	surface water	HPLC/ fluorescence ***	0.05 to 0.50 µg/L /15	r2 = >0.9996	specific	72 - 93	85	7.0	0.05 µg/L	0.17 mg/L	A4.2(c)/01
	blood	LC/MS-MS	0.05 to 0.50 mg/L /10	r2 = 0.991	specific	73 - 99	90	9.2	0.05 mg/L	0.05 mg/l	A4.2(d)/01
	liver	LC/MS-MS	0.05 to 0.50 mg/kg /10	r2 = 0.9845	specific	59 - 88	77	11.4	0.05 mg/kg	0.1 mg/kg	A4.2(d)/02
	Cucumber wheat	LC/MS-MS	0.01 to 0.10 mg/kg / 5 per level and matrix	r2= 0.9433 to 0.9963	specific	82-106 72-102	95 85	8.2 11.3	0.01 mg/kg 0.01 mg/kg	-	A4.2(e)/02

	Oil seed rape (seeds) Meat (muscle) Lemon (whole fruit)	LC/MS-MS	0.01 to 0.10 mg/kg / 5 per level and matrix	r2 >0.9983	specific	97-114 71-104 71-98	106 84 81	10 10 10	0.01 mg/kg 0.01 mg/kg 0.01 mg/kg	-	A4.2(e)/03

* This method is not considered acceptable on the basis on the current accessible information.

** Criteria according to SANCO/825/00 rev.7

*** This detector is not considered as highly specific. A confirmatory method is required.

Annex 4 : Toxicology and metabolism –active substance

Bromadiolone

Threshold Limits and other Values for Human Health Risk Assessment

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

- Adjusted for 70% oral absorption in rat (Task Force)

Inhalative absorption	100%
Oral absorption	70% (Task Force data)
Dermal absorption	10% (based on MW (>500) and log Pow (>4))

Classification **No harmonised classification is currently available**	
with regard to toxicological data (according to the criteria in Dir. 67/548/EEC)	<u>Proposed classification according to the criteria in directive 67/548/EEC:</u> T+; R26/27/28 T; R48/23/24/25 Repr. Cat. 1; R61 Specific concentration limits C≥0.5% : T+;R61-26/27/28 - T; R48/23/24/25 0.25%≤C<0.5% :T+; R26/27/28 – T; R48/23/24/25 0.025%≤C<0.25% : T; R23/24/25 – T; R48/23/24/25 **0.0025%≤C<0.025% : Xn; R20/21/22 – R48/20/21/22**
with regard to toxicological data (according to the criteria in Reg. 1272/2008)	<u>Proposed classification according to the CLP Regulation 1272/2008:</u> Acute tox. 1; H300, H310, H330 Repr. 1A; H360D STOT RE 1; H372 Specific concentration limits C≥0.01% STOT RE 1; H372 **0.001%≤C<0.01% STOT RE 2; H373**

A classification proposal has been submitted to ECHA in August 2010

Annex 5 : Toxicology – biocidal product

MAKI GRAIN'TECH

General information
Formulation Type: grain bait
Active substance(s) (incl. content): 0.005%
Category

Acute toxicity, irritancy and skin sensitisation of the preparation (Annex IIIB, point 6.1, 6.2, 6.3)	
Rat LD50 oral (OECD 420)	LD_{50}>5000 mg/kg
Rat LD50 dermal (OECD 402)	LD_{50}>2000 mg/kg
Rat LC50 inhalation (OECD 403)	No study submitted
Skin irritation (OECD 404)	Non irritant
Eye irritation (OECD 405)	Non irritant
Skin sensitisation (OECD 429; LLNA)	Not sensitizing *read across with a comparable formulation

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

Classification and labelling proposed for the preparation with regard to toxicological properties (Annex IIIB, point 9)	
Directive 1999/45/EC	Xn; R20, R48/20/21/22
Regulation 1272/2008/EC	STOT RE 2; H373

Annex 6
Efficacy of the active substance from its use in the biocidal product

Test substance	Test organism(s)	Test system / concentrations applied / exposure time	Test results: effects, mode of action, resistance	Reference	RI
Red impregnated oat R216	*Rattus norvegicus* (wild strain, sensitive to coumafene)	Laboratory study, using either freshly manufactured bait or bait aged for 2 years, two series of tests with 10 mixed sex animals with 3 and 4 day exposures.	Average palatability of the fresh bait was 49% and 43 % after storage for two-years in darkness. Average efficacy was 100 % between 4 and 11 days after initial consumption.	IIIB5.10.2-01	1
Red impregnated oat R216	*Mus musculus* (wild strain, sensitive to warfarin)	Laboratory study, using freshly manufactured bait, two free-choice tests with a total of 20 mixed sex animals, 4 day exposure.	Average palatability of the treated bait was 48 %. Average efficacy was 90 % between 4 and 21 days after initial consumption.	IIIB5.10.2-02	1
MAKI GRAIN'TECH	*Rattus norvegicus* (wild strain, sensitive to warfarin)	Laboratory study, using bait aged for 9 months, two free-choice tests with a total of 22 mixed sex animals, 4 day exposure.	Average palatability of the treated bait was 66 %. Average efficacy was 90 % between 7 and 11 days after initial consumption.	IIIB5.10.2-03	1
MAKI GRAIN'TECH	*Mus musculus* (wild strain, sensitive to warfarin)	Laboratory study, using bait aged for 9 months, two free-choice tests with a total of 22 mixed sex animals, 4 day exposure.	Average palatability of the treated bait was 84 %. Average efficacy was 100 % between 7 and 14 days after initial consumption.	IIIB5.10.2-04	1
SUPERCAID GRAIN'TECH	*Rattus norvegicus* (wild strain, resistant to warfarin)	Laboratory study, using bait aged just after manufacture, two free-choice tests with a total of 20 mixed sex animals, 4 day exposure.	Average palatability of the treated bait was 44 %. Average efficacy was 84 % between 7 and 18 days after initial consumption.	IIIB5.10.2-05	2
SUPERCAID GRAIN'TECH	*Mus musculus* (wild strain, resistant to warfarin)	Laboratory study, using bait just after manufacture, two free-choice tests with a total of 24 mixed sex animals, 4 day exposure.	Average palatability of the treated bait was 40 %. Average efficacy was 93 % between 7 and 15 days after initial consumption.	IIIB5.10.2-06	1

Test substance	Test organism(s)	Test system / concentrations applied / exposure time	Test results: effects, mode of action, resistance	Reference	RI
SUPERCAID GRAIN'TECH	*Rattus rattus* (wild strain, sensitive to warfarin)	Laboratory study, using bait aged for 27 months, two free-choice tests with a total of 20 mixed sex animals, 4 day exposure.	Average palatability of the treated bait was 41 %. Average efficacy was 90 % between 7 and 11 days after initial consumption.	IIIB5.10.2-07	1
SUPERCAID	*Rattus rattus* (wild strain, sensitive to warfarin)	Laboratory study, using bait aged for 20 months, two free-choice tests with a total of 20 mixed sex animals, 4 day exposure.	Average palatability of the treated bait was 55 %. Average efficacy was 95 % between 7 and 16 days after initial consumption.	IIIB5.10.2-08	1
SUPERCAID GRAIN'TECH	*Mus musculus* (wild strain, sensitive to warfarin)	Laboratory study, using bait just after manufacture, no-choice feeding test with a total of 25 mixed sex animals, 1 day exposure.	Average efficacy was 100 % between 7 and 17 days after initial consumption.	IIIB5.10.2-09	1
SUPERCAID GRAIN'TECH	*Rattus norvegicus* (wild strain, sensitive to warfarin)	Laboratory study, using bait just after manufacture, single feeding test with a total of 20 mixed sex animals, 1 day exposure.	Average efficacy was 100 % between 5 and 11 days after initial consumption.	IIIB5.10.2-10	1
SUPERCAID	*Rattus norvegicus*	Field study conducted at 2 farm sites in France. Bait stations contained 150 g at 14 to 24 locations across the test sites.	Based on consumption estimates the efficacy under field conditions was 100 % at each site.	IIIB5.10.2-11	1
SUPERCAID GRAIN'TECH	*Mus musculus*	Field study conducted at 2 urban sites in France. Bait stations contained 40 g at 12 locations for each test sites.	Based on consumption estimates the efficacy under field conditions was 100 % at each site.	IIIB5.10.2-12	1
SUPERCAID GRAIN'TECH	*Microtus arvalis* (wild strain)	Laboratory study, using bait aged for 15 months, one free-choice test with a total of 10 mixed sex animals, 4 day exposure.	Average palatability of the treated bait was 59 %. Average efficacy was 100 % between 3 and 7 days after initial consumption.	IIIB5.10.2-13	1

Test substance	Test organism(s)	Test system / concentrations applied / exposure time	Test results: effects, mode of action, resistance	Reference	RI
SUPERCAID GRAIN'TECH	*Arvicola terrestris* (wild strain)	Laboratory study, using bait aged for 15 months, one free-choice test with a total of 10 mixed sex animals, 4 day exposure.	Average palatability of the treated bait was 51 %. Average efficacy was 90 % between 3 and 9 days after initial consumption.	IIIB5.10.2-14	1
Red impregnated oat	*Microtus arvalis* *Mus musculus*	Field study conducted in an electric distribution factory (RTE) in France. Bait stations contained 25g bait (for mice) and 300g (for voles) at 54 locations for both test species.	Based on consumption estimates the efficacy under field conditions was 100 %. Nevertheless, there is no indication about mice and voles proportions. No census by trapping has been done.	IIIB5.10.2-15	2
Red impregnated oat	*Microtus arvalis* *Apodemus sp.*	Field study conducted in and around a cheese factory in France. Bait stations contained 100 g at 33 locations for both test sites.	Based on consumption estimates the efficacy under field conditions was 100 % at the site. Nevertheless, there is no indication about field mice and voles proportions. No census by trapping has been done. As there is no other study with Apodemus sp. A field study with this specie has to be provided within the framework of a post-authorization monitoring to validate this use.	IIIB5.10.2-16	2
Green placebo blocks containing 10 and 100ppm Bitrex	*Rattus norvegicus* (wild strain)	Laboratory study, conducted to investigate the impact of a bittering agent, denatonium benzoate, on the attractivity of two placebo blocks. Two groups of 10 mixed sex animals. One group given 10 mg/kg bittering agent and the other 100 mg/kg. 4 day exposure.	Average palatability of bait containing 10 ppm bittering agent was 53 %. => equivalent palatability for blocks containing 10 or 100 g/kg of denatonium benzoate	IIIB5.10.2-17	1
Green placebo bloc LR0225	*Rattus norvegicus* (wild strain)	Laboratory study, conducted to investigate the impact on attractivity of two different packaging on the placebo blocks (wrapped either in polypropylene or polyethylene). 10 mixed sex animals, 4 day exposure.	The attractivity index for blocks wrapped in polypropylene was 0.53 indicating no significant difference in consumption of the blocks resulting from different wrappings.	IIIB5.10.2-18	1

Test substance	Test organism(s)	Test system / concentrations applied / exposure time	Test results: effects, mode of action, resistance	Reference	RI
EPPO bait impregnated with 250 mg/kg warfarin	*Mus musculus* (wild strains, sensitive and resistant to warfarin)	Laboratory study - Assessment of strain sensitivity. Two strains of the wild type *Mus musculus* were selected Animals selected for assessment of resistance or sensitivity were either wild caught or born to wild caught individuals. The warfarin resistant strain and the sensitive strain were maintained separately. Warfarin was administered by dietary admixture and treated diet was available for a period (dependent on species; 6 days). Sensitive individuals die within 21 days of dietary consumption, resistant rodents, having consumed adequate levels of treated diet, survive beyond the 21 day period.	Resistant strains – the *Mus musculus* strain has shown greater than 66 % resistance to warfarin. The strain is therefore considered to be resistant. Sensitivity – the tests completed have resulted in mortality of 70 % of higher, confirming the sensitivity of the strain to warfarin.	IIIB5.10.2-19	1
EPPO bait impregnated with 250 mg/kg warfarin	*Rattus norvegicus* (wild strains, sensitive and resistant to warfarin)	Laboratory study - Assessment of strain sensitivity. Two strains of the wild type *Rattus norvegicus* were selected. Animals selected for assessment of resistance or sensitivity were either wild caught or born to wild caught individuals. The warfarin resistant strain and the sensitive strain were maintained separately. Warfarin was administered by dietary admixture and treated diet was available for a period (dependent on species; 6 days for rats). Sensitive individuals die within 21 days of dietary consumption, resistant rodents, having consumed adequate levels of treated diet survive beyond the 21 day period.	Ten studies between 1998 and 2001 confirmed the resistant strains of *Rattus norvegicus* have shown 70-100 % resistance to warfarin. The strain is therefore considered to be resistant. Six sensitivity tests between 1999 and 2002 – the tests completed have resulted in complete mortality in each case, confirming the sensitivity of the strain to warfarin.	IIIB5.10.2-20	1
SUPERCAID GRAIN'TECH	*Rattus norvegicus* (wild strain, resistant to warfarin)	Laboratory study, using bait aged for 45 months, a free-choice test with a total of 10 mixed sex animals, 4 day exposure.	Average palatability of the treated bait was 58 %. Average efficacy was 100 % between 7 and 14 days after initial consumption.	IIIB5.10.2-22	1