Product Assessment Report

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

FAAR AVOINE

TRIPLAN S.A.

November 2012

Internal registration/file no:	PB-11-00070
Authorisation/Registration no:	Prof: FR-2013-0032
R4BP no:	2011/4289/12826/FR/AA/21625
Granting date/entry into force of authorisation/ registration:	18th June 2013
Expiry date of authorisation/ registration:	30th June 2016
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
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1 GENERAL INFORMATION ABOUT THE PRODUCT APPLICATION

1.1 Applicant

Company Name:	TRIPLAN SA
Address:	BP 258 La Poste Française
City:	Andorra La Vella
Postal Code:	AD500
Country:	Andorre
Telephone:	+ 376741445
Fax:	+ 376741450
E-mail address:	saida.triplan@andorra.ad

1.1.1 Person authorised for communication on behalf of the applicant

Name:	Fredy LACROUX
Function:	Director
Address:	BP 258 La Poste Française
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Postal Code:	AD500
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1.2 Current authorisation holder[1]

Company Name:	TRIPLAN SA
Address:	BP 258 La Poste Française
City:	Andorra La Vella
Postal Code:	AD500
Country:	Andorre
Telephone:	+ 376741445
Fax:	+ 376741450
E-mail address:	saida.triplan@andorra.ad
Letter of appointment	yes

[1] Applies only to existing authorisations

for the applicant to represent the authorisation holder provided (yes/no):	

1.3 Proposed authorisation holder

Company Name:	TRIPLAN SA
Address:	BP 258 La Poste Française
City:	Andorra La Vella
Postal Code:	AD500
Country:	Andorre
Telephone:	+ 376741445
Fax:	+ 376741450
E-mail address:	saida.triplan@andorra.ad
Letter of appointment for the applicant to represent the authorisation holder provided (yes/no):	yes

1.4 Information about the product application

Application received:	30/06/2011
Application reported complete:	29/07/2011
Type of application:	Product authorisation
Further information:	

1.5 Information about the biocidal product

1.5.1 General information

Trade name:	FAAR AVOINE
Manufacturer's development code number(s), if appropriate:	SOFAR
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	No

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 composition like the product evaluated in connection with the approval for listing of active substance(s) on to Annex I to directive 98/8/EC (yes/no):	No

1.5.2 Information on the intended use(s)

Overall use pattern (manner and area of use):	FAAR AVOINE is intended to be used for control of mice, brown rats and black rats in buildings included farm buildings. The treatment with FAAR AVOINE is applied by trained professional users and by non-professional users.
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*
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 The product is ready-to-use (cereal grains) so with no dilution and no other substances added for application. It is supplied in sachets or in bulk and manually applied in bait boxes or bait stations with a shovel in the case where the baits are supplied in bulk. Rats : 180-200 g grains/secured bait point separated by 5-10 m. Mice: 30-40 g grains/secured bait point separated by 1-2 m. Over a period of 28 days for application, cleaning, refilling and collect of dead rodents. The control of rats and mice is carried out inside buildings, so the environmental conditions in which rodents are found tend to be similar relating to geographical areas.

Potential for release into the environment (yes/no):	No
Potential for contamination of food/feedingstuff (yes/no)	No
Proposed Label:	Control of rats (black rats and brown rats) and mice indoors.
Use Restrictions:	Use only indoors in secured bait stations out of reach of children and domestic animals.

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
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:	Activa
Company Name:	Dr Tezza S.r.l.
Address:	Viale del lavoro, 326
City:	Angiari vr
Postal Code:	37050
Country:	Italy
Telephone:	0456069004
Fax:	0442660041
E-mail address:	pier@drtezza.eu

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, physico-chemical and analytical method data

[2] Please insert additional columns as necessary
[3] Please insert additional columns as necessary

Physico-chemical properties studies and analytical methods on the biocidal product FAAR AVOINE were provided by TRIPLAN. Complementary data for the validation of the analytical method performed on another formulation (FAAR BLOCK SP) have also been provided.

Efficacy data

The following efficacy studies were submitted:

- Efficacy and palatability laboratory study of FAAR AVOINE rodenticide containing 0.005% bromadiolone on albino house mice (*Mus musculus*).
- Efficacy field study of FAAR AVOINE rodenticide containing 0.005% bromadiolone and 0.001 % denatonium benzoate on albino wild mice (*Mus musculus*). The test is performed in a farm (food storage room and cellar).
- Efficacy field study of FAAR BLE rodenticide containing 0.005% bromadiolone on black rats (*Rattus rattus*). The test is performed in a pig farm.
- Efficacy field study of FAAR BLOC SP, rodenticide containing 0.005% bromadiolone on brown rats (*Rattus norvegicus*). The test is performed in pheasant's aviaries.

The field study on black rats (*R. rattus*) has been done on the product FAAR BLE. The differences between the compositions of the products FAAR BLE and FAAR AVOINE are slight, it consists on a change in cereal support (whole wheat instead oat) and an addition of a stabilisant agent. So we can consider that the difference of composition between the two formulations doesn't have any influence on efficacy. Therefore, results from this study can be extrapolated to the current formulation of FAAR AVOINE.

The field study on brown rats (*R. norvegicus*) has been done with the product FAAR BLOC SP. This product is a block bait containing the same amount of active substance bromadiolone. Since block baits are less palatable than grain baits (this was confirmed by the lab test on albino mice) and efficacy of the product FAAR AVOINE has been confirmed on mice and black rats, results from this field study can be extrapolated to the current formulation FAAR AVOINE.

Toxicology data

The applicant submitted toxicological data on another formulation (FAAR BLOC SP). The results of these data can be extrapolated to the biocidal product FAAR BLE.

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

A letter of access from Activa Srl has been submitted. Access is granted for all the data generated by the bromadiolone task force for the inclusion of bromadiolone into annex I.

2 Summary of the product assessment

The product is to be used in tamper-resistant bait boxes or covered bait stations.

”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 FAAR BLE is different from the source used for annex I inclusion. However, a technical equivalence was assessed by RMS (SE) in 2010 between the used source and the reference source.

2.2 Classification, labelling and packaging

2.2.1 Harmonised classification of the biocidal product

Classification - Directive 67/548/EEC	
Class of danger	Xn
R phrases	R20 R48/20/21/22
S phrases (proposed by the RMS)	none

Classification - Regulation (EC) 1272/2008	
Hazard statement	STOT RE 2; H373
Precautionary statements (proposed by the RMS)	P260 P314 P501

2.2.2 Labelling of the biocidal product

If the proposed classification and specific concentration limits for “active substance” is agreed at the ECHA level, the following labelling according to Directive 67/548/EEC should apply:

Symbols:	Xn
Indications of danger:	Harmful
Risk phrases:	Xn R20 Xn R48/20/21/22
Safety phrases:	none

No classification was proposed by the Applicant. Nevertheless, due to specific concentration limits for bromadiolone, FAAR AVOINE has to be classified as mentioned above.

If the proposed classification and specific concentration limits for “active substance” is agreed at the ECHA level, the following labelling according to the CLP regulation should apply:

Pictograms:	
Signal words:	Warning
Hazard statements:	STOT RE 2; H373

2.2.3 Packaging of the biocidal product

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

For professional users:

FAAR Avoine is supplied in opaque packaging in sachet or loose.

PE sachets (25-100g) are packed in:
- Bags (paper/PE) (20-25 kg)
- Bucket (PE) (5-20kg)
- Carton box (carton) (5-20 kg)

Loose baits are packed in:
- Bags (paper/PE) (20-25 kg)
- Bucket (PE) (5-20kg)
- Carton box (carton) (5-20 kg)

For non professional users:

FAAR BLE is supplied in sachet (PE) sachets (25-100g) are packed in:
- Bucket (PE) (0.5-1.5 kg)
- Carton box (carton) (0.2-1.5kg)
- Metal box (0.2- 1.5kg)
- Bait box
- Jug (PEHD) (0.2-1.5kg)

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 FAAR Avoine is different from the source used for annex I inclusion. However, a technical equivalence was assessed by RMS (SE) in 2010 between the used source and the reference source.

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 and impurities in the technical active substance have already been evaluated at EU level and are presented in the CAR (2011) of the active substance Bromadiolone. The notifier of the product FAAR avoine is part of a task force that deposited a complete dossier for homologation of his source of Bromadiolone.

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: FAAR Avoine
Code number: SOFAR

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

All studies were performed with biocidal product FAAR avoine.

Subsection (Annex Point IIB. 3/TNsG)	Method	Purity/ Specification	Results	Reference
3.1 Appearance (IIB3.1/Pt. I-B3.1)		FAAR avoine 0.056 g/kg bromadiolone		10-920010-30
3.1.1 Physical state and nature	Cereal grains Bait ready for use (AB)			
3.1.2 Colour	Visual inspection at room temperature		Blue/green hulled oat grains (heterogeneous colour)	
3.1.3 Odour	*Not determined.* – Acceptable as an odour should only be recorded if it is very apparent.			
3.2 Explosive properties (IIB3.2/Pt. I-B3.2)	Preliminary study - Determination of exothermic reactions - DSC	FAAR avoine 0.056 g/kg bromadiolone	No exothermic peak greater than 500 J/g was detected during DSC. This thermodynamic information allows knowing that a test on explosive properties with EC A14 method should not be performed. Not explosive	10-920010-29
3.3 Oxidising properties (IIB3.3/Pt. I-B3.3)	Literature survey on oxidizing properties of the ingredient of the product FAAR AVOINE		None of the components of FAAR AVOINE is considered to have oxidizing properties. No oxidizing properties	10-920010-29
3.4 Flash-point and other indications of flammability or spontaneous ignition (IIB3.4/Pt. I-B3.4)				

<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>Flammability

Self ignition temperature of solids</td><td>EC A10

EC A16</td><td>FAAR avoine 0.056 g/kg bromadiolone
FAAR avoine 0.056 g/kg bromadiolone</td><td>The test item was not considered as highly flammable under the experimental conditions

No self ignition temperature of the test item was observed up to 400 °C (corrected value).</td><td>10-920010-29

10-920010-29</td></tr>
<tr><td>3.5 Acidity/Alkalinity (IIB3.5/Pt. I-B3.5)</td><td>CIPAC MT 75.3</td><td>FAAR avoine 0.056 g/kg bromadiolone</td><td>The pH mean value of the test item at 1% m/v in standard water D is:
5.85 at 21.9°C after 1 min.
6.33 at 21.9°C after 10 min.
The pH of the test item being higher than 4 and lower than 10, CIPAC MT 191 the test was not performed.</td><td>10-920010-30</td></tr>
<tr><td>3.6 Relative density (IIB3.6/Pt. I-B3.6)</td><td>EC A3 method
OECD n° 109</td><td>FAAR avoine 0.056 g/kg bromadiolone</td><td>The relative density mean value of the test using the gas comparison method with the stereopycnometer was:
D (20.2°C/4.0°C) = 1.396 ± 0.001.

Bulk and Tap density were required but have not been provided. Data are still required</td><td>10-920010-29</td></tr>
<tr><td>3.7 Storage stability - stability and shelf life (IIB3.7/Pt. I-B3.7)</td><td>Storage study 14 days at 54°C:
CIPAC MT 46.3

pH : CIPAC MT 75.3

particlue size distribution: CIPAC MT 58.3</td><td>FAAR avoine 0.056 g/kg bromadiolone</td><td>After 2 weeks at 54°C in plastic flask:
<table><tr><td></td><td>T0</td><td>2W 54°C</td></tr><tr><td>Bag weight</td><td>103.8g</td><td>97.6g</td></tr><tr><td>Appearance</td><td colspan="2">No change</td></tr><tr><td>Content of AS</td><td>56ppm</td><td>48ppm</td></tr><tr><td>pH</td><td>5.85</td><td>5.94</td></tr><tr><td>Particles <150 µm</td><td>0.0%</td><td>0.0%</td></tr></table>• pH and particle size distribution are stable after 14 days at 54°C.
• Nature of plastic flask is not submitted.
• Variation of active ingredient content after storage : -14.3%</td><td>10-920010-30</td></tr>
</table>

Subsection (Annex Point IIB. 3/TNsG)	Method	Purity/ Specification	Results	Reference
			Biocidal product is not demonstrated stable after 14 days at 54°C.	
Shelf life study			The shelf life study is in progress. The results will be available at the end of November 2012. The results of this study after one year of storage were supposed to be submitted at the end of March 2012. No data submitted in july 2012 Data are still required	
Effects of light			Not required since the product will be stored protected from light. See comments below the table	
3.8 Technical characteristics (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			Data required. No data submitted	
Attrition/friability of granules; integrity of tablets			Data required. No data submitted	
Emulsifiability / Emulsion			Data not required as the product is a ready to use grain bait	

<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>stability / Re-emulsifiability</td><td></td><td></td><td></td><td rowspan="4"></td></tr>
<tr><td>Stability of dilute emulsions</td><td></td><td></td><td>Data not required as the product is a ready to use grain bait</td></tr>
<tr><td>Flowability</td><td></td><td></td><td>Data required. No data submitted</td></tr>
<tr><td>Pourability (including rinsed residue)</td><td></td><td></td><td>Data not required as the product is a ready to use grain bait</td></tr>
<tr><td>3.9 Compatibility with other products (IIB3.9/Pt. I-B3.9)</td><td></td><td></td><td>FAAR avoine is not intended to be used or mixed with other products.</td><td></td></tr>
<tr><td>3.10 Surface tension (Pt. I-B3.10)</td><td></td><td></td><td>Data not required as the product is a ready to use grain bait</td><td></td></tr>
<tr><td>3.11 Viscosity (Pt. I-B3.10)</td><td></td><td></td><td>Data not required as the product is a ready to use grain bait</td><td></td></tr>
<tr><td>3.12 Particle size distribution (Pt. I-B3.11)</td><td>CIPAC MT 58.3</td><td>FAAR avoine 0.056 g/kg bromadiolone</td><td><table><tr><td>Test seive</td><td>% of residues</td></tr><tr><td>850 µm</td><td>100%</td></tr><tr><td>710 µm</td><td>0%</td></tr><tr><td>500µm</td><td>0%</td></tr><tr><td>425µm</td><td>0%</td></tr><tr><td>355µm</td><td>0%</td></tr><tr><td>250µm</td><td>0%</td></tr><tr><td>150µm</td><td>0%</td></tr><tr><td>pan</td><td>0%</td></tr></table>Size distribution of biocidal product was not measured above</td><td>10-920010-30</td></tr>
</table>

Subsection (Annex Point IIB. 3/TNsG)	Method	Purity/ Specification	Results	Reference
			850 µm. The test item should have been tested up to 5 mm. Complete data up to 5mm is required.	

Storage stability:

Stability of FAAR avoine after storage is not demonstrated either by accelerated storage test or by shelf life study. Complete stability tests (shelf life and accelerated) are required in post registration along with compatibility with packaging materials: PE sachet, Bags (paper/PE) and Carton box (carton)

Considering that efficacy test of aged test item demonstrated efficacy of FAAR avoine product after 14 months, a shelf life of 14 month is granted.

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 requirement:

The product and its physico-chemical properties are not characterised sufficiently. Following studies are still required:
Bulk and tap density according to CIPAC MT 186
Accelerated storage stability study according to CIPAC MT 46
Compatibility study of biocidal product with deposited packaging (PE sachet) .
Dustiness of biocidal product according to CIPAC MT 171
Attrition resistance of biocidal product according to CIPAC MT178
Flowability of biocidal product according to CIPAC MT 172
Particle size distribution of grains according to CIPAC MT 170 with sieves adapted to biocidal product.

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

A method to determine bromadiolone in the biocidal product FAAR Bloc sp by HPLC – UV (265nm) was submitted.
Reference: Ricau H, 2011, Report n° 10-920010-042

Validation data:

Linearity	Precision	Recovery rate (%) range	Specificity
50-150% of nominal value n=5 r^2= 0.998	At 52 ppm: RSD = 1.29%	At 100% mean of recovery = 101.5% (n=4) At 50% mean of recovery = 100.5% (n=4)	No interference in chromatograms. Specific to bromadiolone in FAAR Bloc sp

The specificity and accuracy of the previously validated method was tested on biocidal product FAAR avoine.
Reference: Ricau H, 2011, Report n° 10-920010-032

Validation data on FAAR avoine:

Linearity	Precision	Recovery rate (%) range	Specificity
Performed on FAAR Bloc	Performed on FAAR Bloc	At 100% mean of recovery = 101% (n=4) At 50% mean of recovery = 100% (n=4)	No interference in chromatograms. Specific to bromadiolone in FAAR avoine

The process of validating linearity and precision on FAAR block and recovery and specificity on FAAR avoine is acceptable.
The provided method is acceptable for the product FAAR avoine

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, surface and drinking water, blood, liver and food and feedstuff) provided in the CAR of the active substance) provided in the CAR of the active substance are presented in annex I of this document.

2.4 Risk assessment for Physico-chemical properties

FAAR AVOINE 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.
Compatibility with packaging materials and stability of FAAR AVOINE after storage and effect of temperature are not demonstrated by shelf life study and accelerated storage test.
Missing data are required in post registration.

Measures linked to assessment of physico-chemical properties

- Store away from light.

Required information linked to assessment of physico-chemical properties

- Bulk and tap density according to CIPAC MT 186 ;
- Accelerated storage stability study according to CIPAC MT 46 ;
- Compatibility study of biocidal product with deposited packaging (PE sachet) ;
- Dustiness of biocidal product according to CIPAC MT 171 ;
- Attrition resistance of biocidal product according to CIPAC MT178 ;
- Flowability of biocidal product according to CIPAC MT 172 ;
- Particle size distribution of grains according to CIPAC MT 170 with sieves adapted to biocidal product.

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, FAAR AVOINE is intended to be used to control rodents. The target organisms to be controlled are brown rat (*Rattus norvegicus*), black rat (*Rattus rattus*) and house mouse (*Mus musculus*).

The products, organisms or objects to be protected are indoor environments (public, private buildings and farms).

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	Frequency and method of controls	Distance between 2 bait points, for high and low infestation	Methods of application of the bait
Professional users						
Brown rat *Rattus norvegicus*	indoor only	180-200 g / secured bait point	3 to 10 days	4 refilling of bait stations over 28 days Interval between applications (min) : 1 week	5-10 meters	Manual application in bait stations
Black rat *Rattus rattus*	indoor only	180-200 g / secured bait point	3 to 10 days		5-10 meters	
House mouse *Mus musculus*	indoor only	30-40 g / secured bait point	3 to 10 days		1-2 meters	
Non professional users						
Brown rat *Rattus norvegicus*	indoor only	180-200 g / secured bait point	3 to 10 days	4 refilling of bait stations over 28 days Interval between applications (min) : 1 week	5-10 meters	Pre-filled secured boxes Manual application of baits in bait stations
Black rat *Rattus rattus*	indoor only	180-200 g / secured bait point	3 to 10 days		5-10 meters	
House mouse *Mus musculus*	indoor only	30-40 g / secured bait point	3 to 10 days		1-2 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 11 days of ingesting a lethal dose and animals often die out of sight in their nest or burrow.

Efficacy and choice feeding tests were conducted with 2 month-aged baits FAAR AVOINE on albino house mice and the results are presented in the dossier. The studies show that the product is palatable (average treated bait intake at least 70.5 % of the total food consumption) and effective (100% mortality between 3 to 11 days).

A field test was conducted on 14 month-aged baits FAAR AVOINE on mice and the results are also presented in the dossier. This study was performed in a farm with an estimated population size of about 150 mice. The assessed efficacy on mice was of 100%.

A field study was conducted to assess the efficacy of 2 month-aged baits FAAR BLE (whole wheat containing 0.005% bromadiolone) against black rats. The differences between the compositions of the products FAAR BLE and FAAR AVOINE are slight. The active substance and most of the components are at exactly the same concentration in both formulations. FAAR BLE contains also a stabilisant and his support is whole wheat grains instead of hulled oat grains Therefore, results from this study could be extrapolated to the current formulation FAAR AVOINE because differences don't have any influence on the efficacy. The rats ate satisfactorily during the baiting phase, which lead to a satisfying efficacy rate (80.2%). The arrival of young rats consuming in bait stations during post-baiting stage has probably distorted the efficacy assessment or, the baiting phase was not long enough. The operator should have gone on the poisoning and this would have probably led to a higher efficacy rate. This field study has been conducted according to the standard, the acceptability and efficacy on *Rattus rattus* in field was sufficient.

A field study was conducted to assess the efficacy of 7 month-aged baits FAAR BLOC SP (block bait containing 0.005% bromadiolone) against brown rats (*R. norvegicus*). The active substance and some of the components are at exactly the same concentration in FAAR BLOC SP and FAAR AVOINE. A choice feeding tests proceeded with FAAR BLOC SP and FAAR AVOINE on albino mice confirmed that FAAR BLOC SP is less palatable than FAAR AVOINE, i.e. 47.4% against 70.5% respectively. A lab study has also shown that FAAR AVOINE is efficient on albino house mice (mice are less sensitive to anticoagulants than brown rats). Thus, results from this study could be extrapolated to the current formulation of FAAR AVOINE. This field study conducted according to the standard, has given very good results, 92.8 % for a very large population (> 1000 individuals). The efficacy of FAAR BLOC SP against *Rattus norvegicus* in field was well demonstrated.

All efficacy studies are presented in annex 3.

The product is applied in bait stations by professional and non-professional users in discrete locations within the infested area. Distances between each bait station, so as the number and timings of application and the amount of product depends of several factors: 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 FAAR AVOINE for the intended uses presented in the table below is acceptable.

Target organisms	Dosage claimed	Distance between 2 bait points, for high and low infestation	Time delay of the action of the product	Frequency and method of controls	Area of use	Methods of application of the bait
Professional users						
Rats *Rattus norvegicus* *Rattus rattus*	200 g / secured bait point	High infestation: 5 meters Low infestation: 10 meters	3 to 11 days	Inspect and resupply the bait stations, 3 days after application then once a week as long as the bait is consumed.	indoor only	Manual application in bait stations
House mice *Mus musculus*	40 g / secured bait point	High infestation: 1 meter Low infestation: 2 meters				
Non professional users						
Rats *Rattus norvegicus* *Rattus rattus*	200 g / secured bait point	High infestation: 5 meters Low infestation: 10 meters	3 to 11 days	Inspect and resupply the bait stations, 3 days after application then once a week as long as the bait is consumed.	indoor only	Pre-filled secured boxes Manual application of baits in bait stations
House mice *Mus musculus*	40 g / secured bait point	High infestation: 1 meter Low infestation: 2 meters				

The field study has been done with a 14 month-aged bait so we can conclude that FAAR AVOINE can be considered as effective after a 14 months storage period.
The 24 months storage period claimed by the applicant must be demonstrated with a field study realized with a 24 month-aged product.

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

[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.

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]).

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 bromadionone (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.

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[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

- 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.
- 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 FAAR AVOINE has shown a sufficient efficacy for the control of mice and rats for an indoor use in domestic, industrial and commercial buildings including farm buildings.

The application rates validated are presented in annex 0b.

In addition to the bulk packaging, FAAR AVOINE is also supplied in sachets and pre-filled bait stations of different amounts. The applicant has to adapt the amount per sachet and bait boxes to the efficient doses. The amount of bait per bait station must not exceed the recommended application rates.

In order to reflect the efficacy data of the product, labels has to be revised as following:
- Inspections of bait points have to be made three days after the first application then weekly
- The time delay of the product 's action should be added on the basis of efficacy tests (3 to 11 days).
- The application rates must be mentioned as authorized (see above).
- It should be precised that the shelf life of the product is 14 months.

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 FAAR AVOINE has shown a sufficient efficacy and can be used for the control of mice *(Mus musculus)* and rats (*Rattus norvegicus* and *Rattus rattus*) inside domestic, industrial and commercial buildings including farm buildings. Nevertheless, 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 FAAR AVOINE can be considered as effective after a 14 months storage period. The 24 months storage period claimed by the applicant shall be demonstrated.

Conditions of use :

- 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.

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

Further required information:

Concerning the efficacy of the product, the 24 month storage period claimed by the applicant must be demonstrated with a field study realized with a 24 month-aged product at latest 2 years after the authorization of the product.

The authorization holder has to report any observed resistance to bromadiolone to the Competent Authorities (CA) 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 the following:

Target organisms	Dosage claimed	Distance between 2 bait points, for high and low infestation	Time delay of the action of the product	Frequency and method of controls	Area of use	Methods of application of the bait
Professional users						
Rats *Rattus norvegicus* *Rattus rattus*	200 g / secured bait point	High infestation: 5 meters Low infestation: 10 meters	3 to 11 days	Inspect and resupply the bait stations, 3 days after application then once a week as long as the bait is consumed.	indoor only	Manual application in bait stations
House mice *Mus musculus*	40 g / secured bait point	High infestation: 1 meter Low infestation: 2 meters				
Non professional users						
Rats *Rattus norvegicus* *Rattus rattus*	200 g / secured bait point	High infestation: 5 meters Low infestation: 10 meters	3 to 11 days	Inspect and resupply the bait stations, 3 days after application then once a week as long as the bait is consumed.	indoor only	Pre-filled secured boxes Manual application of baits in bait stations
House mice *Mus musculus*	40 g / secured bait point	High infestation: 1 meter Low infestation: 2 meters				

The product FAAR AVOINE is intended to be used for control of mice *(Mus musculus)*, brown rats *(Rattus norvegicus)* and black rats *(Rattus rattus)* indoor. The control of mice and rats 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. Pre-filled secured bait boxes are also available for non-professional users.

2.7 Risk assessment for human health

No new human exposure studies have been submitted. In the dossier, Triplan assessed the human exposure based on the TNsG on human exposure, section 7.2 of part 3 – June 2002. This document only contains a series of examples for human exposure assessment and should not be considered as reference data. Therefore, since Triplan provided a letter of access for the unpublished CEFIC study "*Chambers J.G. and Snowdon P.J. Study to determine potential exposure to operators during simulated use of anticoagulant rodenticide baits*", the FR CA decided to base the human exposure assessment for professionals on this study as done by the RMS (Finland) of the active substance in the Assessment report on bromadiolone. This study examined the inhalation and dermal exposures associated with all activities involved in using a grain bait (decanting material from a large container to a pail, filling and placing bait points, and clean-up and disposal of bait points). The used grain bait containing coumatetralyl was selected as a worst case representative product of all cereal-based rodenticide baits. In this study, 10 replicates were performed at 1, 5 and 10 manipulations. Therefore, the FR CA decided to use the exposure estimations issued from the CEFIC study for the assessment of FAAR AVOINE.

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

Additionally, the Human Exposure Expert Group (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 Human health effects assessment

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.

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*", FAAR AVOINE does not contain any substance of concern.

2.7.1.3. Toxicology of the biocidal product

New data:
Acute oral and dermal toxicity, skin and eye irritation and skin sensitisation studies have been provided on the product FAAR BLOC SP.

- Acute oral and dermal toxicity

In the acute oral toxicity study, no mortality occurred up to 2000 mg/kg bw/day (daily examination during 14 days) and no systemic clinical signs related to the administration of FAAR BLOC SP were observed. The body weight evolution of the animals remained normal throughout the study. In addition, the macroscopically examination of the animals at the end of the study did not reveal treatment-related changes.
No mortality was observed in the dermal acute toxicity study (LD_{50} > 2000 mg/kg bw/day). A depilation was noted on the treatment site on day 1 in two males (2/5). Erythema was noted on the treatment site in two females on day 2 and in all females on day 3 (5/5) associated with dryness. These cutaneous reactions were totally reversible on day 7.
Based on these results, no classification is required either for FAAR BLOC SP or for FAAR AVOINE.

Route	Species Strain Sex No/group	Dose levels Duration of exposure	Value LD_{50}/LC_{50}	Remarks
Oral	Rat Sprague Dawley (SPF Caw) 6 female/group	Single dose at 2000 mg/kg bw Post exposure period: 14 days	At 2000 mg/kg bw: no death LD_{50}>2000 mg/kg bw	FAAR BLOC SP
Dermal	Rat Sprague Dawley (SPF Caw) 5/sex/group	Single dose of 2000 mg/kg bw, applied to 10% body surface for	At 2000 mg/kg bw: no death LD_{50}>2000 mg/kg bw	

		24 hours	Dermal irritation consisted of depilation on day 1 (2/5 males) and erythema on day 2 (2/5 females) and on day 3 (all females) associated with dryness, except in one female. These cutaneous reactions were totally reversible on day 7.	

- Irritation and corrosivity

No cutaneous reactions (erythema, eschar and oedema) were observed in the skin irritation study, whatever the examination times (i.e. 1, 24, 48 and 72 hours after the patch removal). However, the validity of this study is questioned since it was not specified in the study report whether the powder was moistened with water. Nevertheless, since FAAR BLOC SP does not contain skin irritant ingredient above 1%, no classification with regard to skin irritation is warranted.
FAAR BLOC SP was slightly irritant to the eye of rabbit.
Based on the results of the irritation assays on rabbit's skin and eye, no classification is required either for FAAR BLOC SP or for FAAR AVOINE.

Species Strain No/group	Average score 24, 48, 72h		Reversibility?	Result
	erythema	oedema		
Rabbit Albino New Zealand 3 females	0.00	0.00	No (no cutaneous reactions)	FAAR BLOC SP

Species Strain No/group	Average score				Reversibility?	Result
	cornea	iris	Conjunctiva			
			Redness	Chemosis		
Rabbit Albino New Zealand 3 females	0.00	0.00	0.43	0.00	Yes. Slight to moderate chemosis, noted 1 hour after the test item instillation and totally reversible on day 1.	FAAR BLOC SP

- Sensitisation

A Magnusson and Kligman sensitisation test was submitted. Due to deviations from the OECD guideline 406 (use of SLS not clearly specified, no skin reaction observed at MNNC in the main test, dryness and scab at MNIC, choice of the pre-MNIC, controle positive older than 6 months), the validity of this study is questionned. However, based on the composition of FAAR BLOC SP and of FAAR

AVOINE, no ingredients were listed as skin sensitisers. Therefore, it is expected that FAAR BLOC SP and FAAR AVOINE, are not skin sensitisers.

Species Strain Sex	Method	Number of animals sensitized/total number of animals	Result
Albino Guinea pig Dunkin-Hartley Males	GPMT assay	Controls:16 males Test group: 11 males	No evidence for inducing delayed contact hypersensitivity FAAR BLOC SP

Justification for non submission:

- Dermal absorption:

A dermal absorption of 3.1% was determined for cereal grains (value based on the results of *in vitro* study with rat skin after 24 hours of exposure – FAAR BLE_ac-PH-10-0247-amended[9]). As this study was not a GLP one and had several deficiencies, and although the absorption rate of the product must be considered as lower than or equal to 3.1%, a default value of 10% was considered for FAAR AVOINE, as mentioned in the bromadiolone assessment report (Final CAR, Avril 2011, Task Force).

- Acute inhalation toxicity:

Since the generation of inhalable particle is considered as possible for FAAR AVOINE, FAAR AVOINE should be classified Xn, R20 – Harmful by inhalation, according to the specific concentration limits set for bromadiolone.

- Repeated toxicity

According to the specific concentration limits set for bromadiolone, FAAR AVOINE should be classified Xn, R48/20/21/22. Classification with regard to the inhalation route is required since professionals and non-professionals may be exposed by inhalation to dust when handling FAAR AVOINE.

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.

Classification under directive 67/548/EEC	Classification under regulation (EC) 1272/2008
T+ R26/27/28 T R48/23/24/25 Repr.Cat. 1; R61	Acute Tox. 1 H300, H310, H330 STOT RE 1 H372 Repr. 1A; H 360D
Specific concentration limits for human health:	Specific concentration limits for human health:

[9] Colas S. 2011. FAAR BLE evaluation of skin absorption: *in vitro* method (non GLP study). Phycher Bio-Développement, Study AC-PH-10/0247-amended of the 6 June 2011.Non GLP, (unpublished).

C ≥ 0.5% 0.25% ≤ C < 0.5% 0.025% ≤ C < 0.25% **0.0025% ≤ C < 0.025%**	T+; R61-26/27/28 – T;R48/23/24/25 T+; R26/27/28 – T; R48/23/24/25 T; R23/24/25 – T; R48/23/24/25 **Xn; R20/21/22 – R48/20/21/22**	C ≥ 0.01% **0.001%≤C<0.01%**	STOT RE 1; H372 **STOT RE 2; H373**

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, FAAR AVOINE is classified as follows:

Classification under directive 1999/45/EC	Classification under regulation (EC) 1272/2008
Xn R20 Xn R48/20/21/22	STOT RE 2; H373

- Other studies

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

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

2.7.2 Human exposure assessment

FAAR AVOINE (PT14) is a ready-to-use rodenticide containing 0.005% of bromadiolone. Baits are packaged in sachets for professional and non-professional users or in bulk for professional users.The baits are placed in bait stations in buildings (bait boxes or secured bait stations) out of reach of children and domestic animals.

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

Exposure path	Industrial use	Professional use	General public	*via* the environment
Inhalation	Not applicable	For non professionals: negligible (baits in sachets). For professionals: Exposure only during the phase of decanting from	Negligible. Bromadiolone is not volatile; its vapor pressure is low ($2.3E^{-8}$ Pa at 25℃)	Not applicable

		25 kg bags.		
Dermal	Not applicable	Direct exposure	Indirect exposure: only children and infant	Not applicable
Oral	Not applicable	Unrealistic exposure	Indirect exposure: only children and infants	Not applicable

2.7.2.2 Exposure of professional users

FAAR AVOINE is intended to be used as a ready-to-use rodenticidal bait for rodent control by professional users inside buildings.

Primary exposure

Dermal exposure

Based on a CEFIC study (Chambers *et al*., 2004[10]) and taking into account the *HEEG opinion on an harmonised approach for the assessment of rodenticides (anticoagulants)* agreed at TMII 2011, the amount of product on fingers/hands **during the decanting** was 93 mg per 3 kg of decanted product, when considering 1 to 4 decanting times per day and 52.3 mg per 3 kg of decanted product when considering more than 4 decanting times per day.
Since for the control of mice, the quantity of decanted product is 1.9 kg corresponding to one decanting time, 93 mg of product was considered. In contrast, for the control of rats, the quantity of decanted product is 12.6 kg corresponding to more than 4 decanting times, leading therefore to consider 52.3 mg of product on fingers/hands.

The following parameters were taken into account:

- Active substance in product: 0.005%,(w/w)
- Quantity of decanted product: 12.6 kg for rat (200 g of grains per bait boxes; 63 loading of bait boxes[11]) and 1.9 kg for mouse (40 g of grains per bait boxes; 63 loading of bait boxes),
- Dermal absorption: 10%,
- Body weight: 60 kg.

The quantities of 200 g for the control of rats and 40 g for the control of mice correspond to the validated efficient doses.

Therefore, the systemic dose of bromadiolone on fingers/hands during decanting is

- For the control of rats: 1.8×10^{-5} mg/kg bw/day,
- For the control of mice: 3.7×10^{-6} mg/kg bw/day.

Based on the CEFIC study and taking into account the *HEEG opinion on an harmonised approach for the assessment of rodenticides (anticoagulants)* agreed at TMII 2011, the amount of product on fingers/hands **during the loading** was 2.04 mg for the assessment of more than 4 manipulations per day (the agreed number is 63 manipulations in professional use based on the HEEG opinion on

[10] 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

[11] HEEG opinion on harmonising the number of manipulations in the assessment of rodenticides (anticoagulant), agreed at TMII2010

harmonising the number of manipulations in the assessment of rodenticides (anticoagulant) agreed at TMIII 2010). Therefore, considering 63 manipulations per day, the systemic dose of bromadiolone on fingers/hands during loading is $1.1x10^{-5}$ mg/kg bw/day for the control of rats and mice because the amount of disposed bait is not taken into account during loading.

Based on the CEFIC study and taking into account the *HEEG opinion on an harmonised approach for the assessment of rodenticides (anticoagulants)* agreed at TMII 2011, the amount of product on fingers/hands **during the cleaning** was 3.79 mg/manipulation for the assessment of more than 4 manipulations per day (the agreed number is 16 cleanings in professional use based on the HEEG opinion on harmonising the number of manipulations in the assessment of rodenticides (anticoagulant) agreed at TMIII 2010). Therefore, considering 16 cleanings per day, the systemic dose of bromadiolone on fingers/hands during loading is $5.1x10^{-6}$ mg/kg bw/day for the control of both rats and mice because the amount of disposed bait is not taken into account during cleaning.

In conclusion, the total systemic dermal exposure is set at $3.4x10^{-5}$ mg/kg bw/day and $1.9x10^{-5}$ mg/kg bw/day without PPE for the control of rats and mice, respectively. When gloves are worn (10% gloves penetration factor), the exposure is reduced by a factor of 10 down to $3.4x10^{-6}$ mg/kg bw/day and $1.9x10^{-6}$ mg/kg bw/day for the control of rats and mice, respectively. According to the HEEG opinion agreed at TM I10 (default protection factors for protective clothing and gloves), a further refinement is possible considering a glove penetration factor of 5% for solids. In this case, the total systemic dermal exposure is $1.7x10^{-6}$ mg/kg bw/day and $9.7x10^{-7}$ mg/kg bw/day for the control of rats and mice, respectively.

Inhalation exposure

Exposure by inhalation route is relevant **during the decanting** of the product. Based on the CEFIC study and taking into account the HEEG opinion on an harmonised approach for the assessment of rodenticides (anticoagulants) agreed at TMII 2011, the air concentration is 9.62 mg product/m^3.
The following parameters were considered:

- Duration of manipulation: 15 minutes per day for rats (3 minutes per decanting; 12.6 kg decanted in 3 kg buckets per day) and 3 minutes per day for mice (3 minutes per decanting; 1 decanting per day)
- Inhalation rate: 1.25 m^3/hour
- Inhalation absorption: 100%
- Active substance in product: 0.005%(w/w)
- Body weight: 60 kg

Based on these assumptions, the systemic concentration of bromadiolone is $2.5x10^{-6}$ mg/kg bw/day for the control of rats and $5.0x10^{-7}$ mg/kg bw/day for the control of mice.

Total exposure

The total systemic exposure resulting from inhalation and dermal contacts with the product is $3.7x10^{-5}$ mg a.s/kg bw/day and $2.0x10^{-5}$ mg a.s/kg bw/day without gloves for the control of rats and mice, respectively. The systemic exposure is reduced to $5.9x10^{-6}$ mg a.s/kg bw/day and $2.4x10^{-6}$ mg a.s/kg bw/day for the control of rats and mice, respectively, with gloves, considering a 10% penetration factor or $4.2x10^{-6}$ mg a.s/kg bw/day and $1.5x10^{-6}$ mg a.s/kg bw/day for the control of rats and mice with gloves, considering a 5% penetration factor.

The estimations above are representative for exposure to FAAR AVOINE in bulk but they represent a very worst case when the product is supplied and applied in sachets. In this case, it can be assumed that there is no decanting phase and no exposure is expected during loading in bait points as the sachet prevents dermal contacts and exposure by inhalation. Therefore, only exposure during cleaning can be considered: $5.1x10^{-6}$ mg a.s/kg bw/day without gloves and $5.1x10^{-7}$ mg a.s/kg bw/day

with gloves (10% penetration factor) for the control of both rats and mice because the amount of disposed bait is not taken into account during cleaning.

	Component	**CAS**	**Inhalation internal exposure [mg/kg/d]**		**Dermal internal exposure [mg/kg/d]**		**Total exposure [mg/kg/d]**		**Model**
			Rats	Mice	Rats	Mice	Rats	Mice	
Bulk formulation (exposure during decanting, loading and cleaning phases)									
Tier 1 (without PPE)	Bromadiolone	28772-56-7	$2.5x10^{-6}$	$5.0x10^{-7}$	$3.4x10^{-5}$	$1.9x10^{-5}$	$3.7x10^{-5}$	$2.0x10^{-5}$	Cefic study
Tier 2 a (gloves penetration factor: 10%)	Bromadiolone	28772-56-7	$2.5x10^{-6}$	$5.0x10^{-7}$	$3.4x10^{-6}$	$1.9x10^{-6}$	$5.9x10^{-6}$	$2.4x10^{-6}$	Cefic study
Tier 2 b (gloves penetration factor: 5%)	Bromadiolone	28772-56-7	$2.5x10^{-6}$	$5.0x10^{-7}$	$1.7x10^{-6}$	$9.7x10^{-7}$	$4.2x10^{-6}$	$1.5x10^{-6}$	Cefic study
Sachet formulation (exposure during cleaning phase)									
Tier 1 (without PPE, dermal exposure expected only during the cleaning phase)	Bromadiolone	28772-56-7	Not applicable	Not applicable	$5.1x10^{-6}$	$5.1x10^{-6}$	$5.1x10^{-6}$	$5.1x10^{-6}$	Cefic study
Tier 1 (with gloves, dermal exposure expected only during the cleaning phase)	Bromadiolone	28772-56-7	Not applicable	Not applicable	$5.1x10^{-7}$	$5.1x10^{-7}$	$5.1x10^{-7}$	$5.1x10^{-7}$	Cefic study

Secondary exposure

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

In Annex 4 “Safety for professional operators”, results of the exposure calculations for the active substance for the professional user are laid out.

2.7.2.3 Exposure of non-professional users and the general public

FAAR AVOINE is intended to be used as a ready-to-use rodenticidal bait for rodent control by non-professionals inside buildings.

Primary exposure

FAAR AVOINE is only supplied and applied in sachets for non professional users. As a worst case, exposure has been assessed in a first step approach considering FAAR AVOINE supplied as loose grains. In a second step, the protection of a sachet has been considered. In this case, it can be assumed that there is no decanting phase and no exposure is expected during loading in bait points as the sachet prevents dermal contacts and exposure by inhalation.
This approach is to assess the necessity of the sachet packaging related to risks.

Based on the CEFIC study and taking into account the *HEEG opinion on an harmonised approach for the assessment of rodenticides (anticoagulants)* agreed at TMII 2011, the amount of product on fingers/hands **during the cleaning** was 4.52 mg/manipulation for the assessment of 1 to 4 cleanings per day and 3.79 mg/manipulation for the assessment of 1 to 4 cleanings per day. According to the HEEG opinion on harmonising the number of manipulations in the assessment of rodenticides (anticoagulant) agreed at TMIII 2010, 5 cleanings per day is considered for non-professional use. However, since the CEFIC study was designed for professional users and that the agreed number of cleanings for non-professionals is closed to 4, the amount of 4.52 mg/manipulation was used for exposure assessment. Therefore, the systemic exposure is $1.9x10^{-6}$ mg a.s/kg bw/day for the control of both rats and mice because the amount of disposed bait is not taken into account during cleaning.

Scenario	**Component**	**CAS**	**Inhalation internal exposure [mg/kg/d]**	**Dermal internal exposure [mg/kg/d]**	**Total exposure [mg/kg/d]**	**Model**
Control of rats and mice - Sachet considered (exposure only during cleaning)						
Non professional	Bromadiolone	28772-56-7	Not applicable	$1.9x10^{-6}$	$1.9x10^{-6}$	Cefic study

Secondary exposure

Exposure of non users could result from the handling of dead rodents or ingesting poison baits. The "*handling of dead rodents*" scenario is excluded due to unrealistic assumptions (very low amount of bromadiolone is expected on the fur because FAAR AVOINE is an oral bait and toxicokinetics data showed that urine is a minor route of excretion for bromadiolone).

For the scenario "*oral exposure by ingesting bait*", a reverse scenario was calculated. Based on the 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 (Task Force)], ingestion of more than 0.66 mg of product per day by an infant is needed to exceed the AEL.

In Annex 5 "Safety for non-professional operators and the general public", the results of the exposure calculations for the active substance and the substance of concern for the non-professional user and the general public are laid out.

2.7.3 Risk assessment for human health

2.7.3.1 Risk for Professional Users

The estimated exposures for the professional users are compared to the systemic $AEL_{long\text{-}term}$ of bromadiolone set in the Assessment report ($1.2x10^{-6}$ mg/kg bw/day for long-term exposure).

Primary exposure

The risk for professional users resulting from the intended use is unacceptable when FAAR AVOINE is supplied in bulk, even if gloves are worn (%AEL at 351% and 123% for the control of rats and mice, respectively, with a gloves penetration factor of 5%).

For FAAR AVOINE supplied and applied in sachet, the risk resulting from the intended use is acceptable when professionals are wearing gloves with a penetration factor of 10% (%AEL at 42% for the control of rats and mice). Gloves are anyway recommended to help prevent rodent-borne disease. Moreover, the mention “do not open the sachet” has to be added in the label of the product.

Summary of risk characterisation for professionals for the control of rats

Scénario	**AEL (mg/kg bw/d)**	**Exposure (mg/kg bw/d)**	**%AEL**	**Risk**
Bulk formulation (exposure during decanting, loading and cleaning phases)				
Professional (without gloves)	$1.2x10^{-6}$	$3.7x10^{-5}$	3048	Unacceptable
Professional (with gloves ; penetration factor of 10 %)	$1.2x10^{-6}$	$5.9x10^{-6}$	493	Unacceptable
Professional (with gloves ; penetration factor of 5 %)	$1.2x10^{-6}$	$4.2x10^{-6}$	351	Unacceptable
Sachet formulation (exposure during cleaning phase)				
Professional (without gloves)	$1.2x10^{-6}$	$5.1x10^{-6}$	421	Unacceptable
Professional (with gloves ; penetration factor of 10 %)	$1.2x10^{-6}$	$5.1x10^{-7}$	42	**Acceptable**

Summary of risk characterisation for professionals for the control of mice

Scénario	**AEL (mg/kg bw/d)**	**Exposure (mg/kg bw/d)**	**%AEL**	**Risk**
Bulk formulation (exposure during decanting, loading and cleaning phases)				
Professional (without gloves)	$1.2x10^{-6}$	$2.0x10^{-5}$	1661	Unacceptable
Professional (with gloves ; penetration factor of 10 %)	$1.2x10^{-6}$	$2.4x10^{-6}$	204	Unacceptable
Professional (with gloves ; penetration factor of 5 %)	$1.2x10^{-6}$	$1.5x10^{-6}$	123	Unacceptable
Sachet formulation (exposure during cleaning phase)				
Professional (without gloves)	$1.2x10^{-6}$	$5.1x10^{-6}$	421	Unacceptable
Professional (with gloves ; penetration factor of 10 %)	$1.2x10^{-6}$	$5.1x10^{-7}$	42	**Acceptable**

Secondary exposure

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

2.7.3.2 Risk for non-professional users and the general public

The estimated exposure for the non-professional users is compared to the systemic $AEL_{long\text{-}term}$ of bromadiolone set in the Assessment report ($1.2x10^{-6}$ mg/kg bw/day for long-term exposure).

Primary exposure

The risk for non-professional users resulting from the intended use is unacceptable (% AEL at 157% for the control of rats and mice). However, the risk calculation is based on a default dermal absorption of 10% for bromadiolone. This value is likely lower as demonstrated in an *in vitro* dermal absorption study performed with FAAR BLE (a dermal absorption of 3.1% was determined). But, due to deficiencies, this study was not considered as valid.

Summary of risk characterisation for non professionals for the control of rats and mice

Scénario	**AEL (mg/kg bw/d)**	**Exposure (mg/kg bw/d)**	**%AEL**	**Risk**
Sachet formulation (exposure during cleaning phase)				
Non-professional (without gloves)	$1.2x10^{-6}$	$1.9x10^{-6}$	157	Unacceptable

Secondary exposure

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 FAAR AVOINE 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.

2.7.3.3 Risk for consumers via residues

Considering the intended uses no dietary risk assessment is necessary.

2.7.3.4 Risk for combined exposure

Not relevant.

2.7.3.5 Conclusion of the risk assessment for human health

The risk resulting from the intended use is acceptable when professionals are wearing gloves and when FAAR AVOINE is supplied and applied in sachet.
The risk for non-professional users resulting from the intended use is unacceptable. Consequently, the use is restricted to professionals.
Finally, there is a significant risk of poisoning for infants, thus, the baits should be unattainable for children.

Measures to protect man

- Wear protective gloves when handling the product and dead rodents.
- 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.

2.8 Risk assessment for the environment

2.8.1 Fate and distribution in the environment

The summary of information about the active substance bromadiolone is carried out with the data from the CAR of bromadiolone supplied by the notifier Task Force (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). No new ecotoxicological information on the active substance bromadiolone has been submitted in the product dossier.

2.8.1.1 Degradation

2.7.1.1. Abiotic degradation

2.8.1.1.1.1 Hydrolysis in function of pH

According to the test OECD 111 bromadiolone is considered stable to hydrolysis with a $DT_{50\ hydrolysis}$ value > 1 year at environmentally relevant temperatures for all pH. Hydrolytic degradation is not expected to be a significant process in the environment.

2.8.1.1.1.2 Photolysis in water

Photolysis of bromadiolone in water is rapid and follows a biphasic pattern. Complete photolysis occurs within two hours. Several metabolites are observed in the photolysis study. Nevertheless, it was stated that they were not identified because of limited exposure of the aquatic compartment by bromadiolone and since it is not likely that a substance with a specific mode of action will have metabolite more toxic than the parent compound. It is stated in the CAR of bromadiolone that it should be considered that in natural waters photolysis will have only a minor impact on the degradation of bromadiolone, and in accordance with TGD II, the impact of photodegradation will be considered as negligible in the risk assessment.

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 bromadiolone were estimated using EPIWIN v 3.12. The indirect photolysis half-life of bromadiolone reacting with OH radicals is 2.090 hours with a rate constant of $61.422*10^{-12}$ cm^3/molecule/s and 2.015 hours with a rate constant of 13.650 cm^3/molecule/s when reacting with ozone. This shows that bromadiolone photodegrades rapidly in air. Moreover, the vapour pressure of bromadiolone at 25° C is $1*10^{-7}$ Pa and Henr's law constant is $4.25*10^{-4}$ Pa*m^3/mol. Hence, bromadiolone is not expected to volatilise to, or persist in, air in significant quantities.

2.7.1.2. Biotic degradation

2.8.1.1.2.1 Aquatic compartment

According to the OECD tests bromadiolone is not readily or inherently biodegradable.
In addition, no degradation of bromadiolone occurred in a test for anaerobic degradation ISO 11734 but 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 aerobic degradation in STP or further degradation studies in water and sediments have been performed. 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 a half-life is over 365 days.

2.8.1.1.2.2 Terrestrial compartment

Degradation studies in soil have not been performed with the justification that bromadiolone will be degraded by light and that the release of bromadiolone is only local. The justification has been found acceptable in the CAR of bromadiolone regarding its second part at active substance level. Nevertheless, soil degradation studies are required at the product authorisation stage because the effect of sunlight on degradation of bromadiolone in soil has not been shown and the degradation in soil has not been quantified for the active substance inclusion. However due to the intended use of FAAR AVOINE, which is only as rodenticide inside buildings, the exposure of the soil is limited and no risk assessment for soil is conducted for this product. Subsequently no soil degradation studies including degradation rates and formation of major metabolites is required for the product FAAR AVOINE.

It is stated in the CAR of bromadiolone that risk assessment for soil is based on that bromadiolone is not degraded according to ready and inherently biodegradability tests.

2.8.1.2 Distribution

Bromadiolone is strongly adsorbed to soil and the experimentally determined Koc values (OECD 106) are ranged between 3530 and 41600 mL/g. On the basis of this study bromadiolone is practically 'non mobile' in soil.

Therefore it is assumed that bromadiolone will not reach groundwater in significant quantities.

This assessment is considered sufficient at active substance level. However, it is stated in the CAR of bromadiolone that in order to clarify the distribution properties of bromadiolone soil degradation studies including degradation rates and formation of major metabolites are required at the product authorisation stage. Due to the intended use of FAAR AVOINE, which is only as rodenticide inside buildings, the exposure of the soil is limited. Subsequently no soil degradation studies including degradation rates and formation of major metabolites is required for the product FAAR AVOINE.

2.8.1.3 Accumulation

Bromadiolone has a high Log Kow (3.8), it does not degrade and its molecular weight indicates no hindrance for uptake by organisms.

The aquatic BCF has been estimated with calculation method because the fish bioconcentration test was not reliable. The measured value of log Kow value (3.8) allows to calculate an estimated BCF for fish :

$$\mathbf{BCF_{fish} = 339\ L/kg}$$

(according to Equation 74, TGD).

In conclusion bromadiolone has potential for bioaccumulation in organisms.

2.8.1.4 Behaviour in air

Volatilisation

The vapour pressure of bromadiolone at 25°C is $1*10^{-7}$ Pa and Henry's law constant is $4.25*10^{-4}$ $Pa*m^3/mol$. These figures show that bromadiolone not is expected to volatilise to air in significant quantities.

Global warming

Bromadiolone (with absorption at 263 nm) is not likely to contribute to global warming since it has no absorption in the atmospheric window.

Stratospheric - Tropospheric ozone

Bromadiolone, which has a short atmospheric half-life, will not have any negative effects on stratospheric and tropospheric ozone.

Acidification
Due to low expected emissions to air and due to the fact that bromadiolone does not contain any of the acidifying substances mentioned in TGD II, section 3.7.2 it is not likely that bromadiolone will have any effect on acidification of the receiving soil or surface water.

In summary, bromadiolone is not expected to volatilise to air from soil or water, and no negative effects of bromadiolone are expected in the air compartment.

2.8.2 Effects on environmental organisms for active substance

The summary of information about the active substance bromadiolone is carried out with the data from the CAR of bromadiolone owned by the Task Force (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). No new ecotoxicological information on the active substance bromadiolone has been submitted in the product dossier.

2.8.2.1 Aquatic compartment (including water, sediment and STP)

2.8.2.1.2. Aquatic organisms

Bromadiolone is acutely toxic to fish (*Oncorhynchus mykiss*) with an LC50 of 2.86 mg/L in nominal concentration as the measured concentrations of bromadiolone were all within the range 95-102 % of nominal. EC50 for *Daphnia magna* was 5.79 mg/L (nominal concentration), i.e. the same order of magnitude as that for fish. The alga *Pseudokirchneriella subcapitata* was found to be the most sensitive of the three aquatic organisms tested, with an ErC50 of 1.14 mg/L. Due to the rapid photolysis of the test substance, the test concentrations used to express the results were calculated according to the OECD Guidance document on aquatic toxicity testing of difficult substances and mixtures. However, it is very likely that the degradation is much faster than what can be seen as a disappearance in 72 h, so it was considered in the CAR of substance active bromadiolone owned by Task Force that the resulting effect value (ErC50) is most probably an underestimation of toxicity. Therefore, an extra assessment factor of 3 was applied to the ErC50 to compensate for this uncertainty. The Technical Meeting has earlier (TM II-07, CAR based on the other notifier of bromadiolone, LiphaTech S.A.S) agreed to use an extra assessment factor of 3 based on a similar uncertainty. DMSO was used to increased the solubility of bromadiolone in invertebrate and algae studies.
The table below summarise the results of these tests.

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}	2.86*	CAR a.s. III-A 7.4.1.1
OECD 202 / static system	*D. magna* aquatic invertebrate	48 hour EC_{50}	5.79*	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}	0.66** 1.14**	CAR a.s. III-A 7.4.1.3

* Nominal concentration

** Geometric mean of the initial concentration and LOQ/2

Justification of $PNEC_{water}$:

On the basis of acute toxicity data of the active ingredient bromadiolone for fish, invertebrates and algae, the PNEC is derived from the lowest L/EC50 value (algae ErC50 = 1.14 mg/l). An assessment factor of 1000 is appropriate when only results from acute studies are available (TGD II, section 3.3 table 16). As discussed above, an additional assessment factor of 3 is introduced due to uncertainties regarding photolytic degradation of bromadiolone in the light conditions used in the test.
This gives a PNECfreshwater of 1.14/1000/3 = $3.8*10^{-4}$ mg/L.

PNECfreshwater = 3.8 10^{-4} mg a.s./L.

Additional endpoints: The PNEC values for freshwater from the final CA report of another notifier 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 lower: **PNECfreshwater = 1.7 10^{-5} mg a.s./L** than the PNEC derived in the final CAR of bromadiolone of the notifier Task Force. Therefore, as the data set are considered equivalent, the worst case PNEC from the other notifier final CAR is used in the risk assessment.

2.8.2.4.2. Sediment dwelling organisms

No ecotoxicological data for sediment-dwelling organisms are available in the Task Force dossier. As the exposure to the aquatic compartment is low, it was stated that no tests on these organisms was requested.

Justification of $PNEC_{sediment}$
The PNEC for sediment dwelling organisms was calculated with the equilibrium partitioning method according to TGD II, section 3.5.2.3., equation 70 as no tests are available. The average Koc value of **14770 mL/g** was calculated using the experimentally determined Koc values (OECD 106) ranging between **3530 and 41600 mL/g.**

PNECsediment = 0.83 mg a.s./kg ww

Additional endpoints: Not relevant.

2.8.2.4.3. STP micro-organisms

The toxicity to microorganisms in a sewage treatment plant (STP) was estimated by a respiration inhibition test (OECD 209) and an EC_{50} was found to be 132.8 mg/L.

Table 2.8.2.1.3: Toxicity to STP micro-organisms

Guideline / Test method	Species / Inoculum	Endpoint / Type of test	Exposure		Results (mg a.s/l)*				Reference
			design	duration	EC_{20}	EC_{50}	EC_{80}	NOEC (EC_{15})	
OECD 209	Activated sludge	Respiration inhibition	static	3 hours	c.a.25 *	132.8	NA**	NA	CAR a.s. Doc. III-A 7.4.1.4

* Not calculated but estimated to be approximately 25 mg/L
** NA: Not Available

Justification of $PNEC_{microorganisms:}$
Since no NOEC or EC10 was available an assessment factor of 100 was used on the EC_{50} in accordance with TGD II section 3.4 table 17. This gives a PNEC of 132.8/100 = 1.33 mg/L.

PNECSTP microorganisms = 1.33 mg a.s./L

Additional endpoints: The PNEC values for sewage treatment microorganisms from the final CA report of another notifier 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 lower: **PNEC STP microorganisms = 0.32 mg a.s./L** than the PNEC derived in the final CA of bromadiolone of the notifier Task Force. Therefore, as the data set are considered equivalent, the worst case PNEC from the other notifier final CAR is used in the risk assessment.

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

No effects of bromadiolone, in soil concentration ranging up to 1331 mg/kg dw, were found on earthworms in a test conducted according to the guideline OECD 207. LC50 was determined to be >918 mg/kg dw, when corrected for soil humidity.

Table 2.8.2.3: Toxicity to soil organisms

Guideline / Test method	Species	Endpoint / Type of test	Exposure		Results (mg a.s/kg wwt soil)		Reference
			design	duration	NOEC	LC_{50}	
OECD 207	*Eisenia foetida*	LC_{50}	soil exposure	13days	918 (standardised)	> 918 (standardised)	CAR a.s. Doc. III-A 7.5.1.2

Justification of $PNEC_{soil}$

Since LC50 was determined to be >918 mg/kg ww, when corrected for soil humidity, an assessment factor of 1000 was used in accordance with TGD part II section 3.6 table 20 for calculation of PNEC. This would give a PNECsoil of 918 mg/kg ww/1000 = 0.918 mg/kg ww.

$PNEC_{soilDATA}$ = 0.918 mg/kg wet weight

According to TGD II section 3.6.2.1, if results from only one terrestrial study are available the PNEC should also be calculated from the aquatic toxicity data using equilibrium partitioning calculations. These calculations should be performed according to equation 72 in the TGD II.

$PNEC_{soilEPM}$ = 0.099 mg/kg wet weight

The calculations above indicate that effects may be found at concentrations higher than 0.099 mg/kg, but empirically in the study submitted by the notifier no effects were found in tests with earthworm at concentrations of 918 mg/kg ww. In the TGD II section 3.6.2 and 3.6.2.1 it is stated that equilibrium partitioning calculations can never replace toxicity data for soil organisms but should only be used for screening and that toxicity data for aquatic organisms cannot replace data for soil dwelling organisms. However, the difference between the empirical and modelled figures is notable, especially when taking into account the PNECsoil value from the final CA report of the other notifier 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). This value was derived empirically (also in this case there was no effect at the highest tested concentration) and is considerably lower, being 0.0084 mg/kg wet soil. Due to that only one soil organism was tested and also considering the uncertainties arising from the differing data of the two applicants, the PNEC soil value derived from the equilibrium partitioning calculations may be considered as the more realistic value.

Additional endpoints:

The PNEC values for terrestrial organisms from the final CA report of another notifier 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 lower: **PNECsoil= 0.0084 mg/kg wet weight** than the PNEC derived in the final CA of bromadiolone of the notifier Task Force. Therefore, as the data set are considered equivalent, the worst case PNEC from the other notifier final CAR is used in the risk assessment.

2.8.2.4 Non compartment specific effects relevant to the food chain

The exposure of bromadiolone directly to non-target birds and mammals (primary poisoning) and indirectly via target rodent carcasses (secondary poisoning) is considered a critical aspect of the risk assessment

Table 2.8.2.4: Toxicity to birds and mammals (key studies)

Guideline / Test method	Species	Endpoint / Type of test / Duration	Results		Reference
			NOEC/NO(A)EL	LD/C_{50}	
OPPTS 850.2100	Japanese quail (*Coturnix coturnix japonica*)	LD_{50}/ acute oral 1 day and 14 days oservation	31.3 mg a.s/kg bw/day	**LD_{50} = 134 mg a.s/kg bw LC_{50}=1070 mg a.s/kg food**	CAR a.s. Doc. A-III 7.5.3.1.1-03
OECD 206	Japanese quail (*Coturnix coturnix japonica*)	Reproduction test 42 days	**NOEC = 0.039 mg a.s/kg bw/day Equivalent to NOEC= 0.26 mg/L drinking water**		CAR a.s. Doc. III-A 7.5.3.1.3
OECD 401	Rat	Acute toxicity to mammals	NOEL = 0.0025 mg a.s/kg bw/day -	**LD_{50} = 1.31 mg a.s/kg bw LC_{50}=26 mg a.s/kg food**	CAR a.s. Doc. III-A 6.1.1
OECD 409	Rabbit	Repeated dose toxicity 90 days	**NO(A)EL=0.0005 mg a.s/kg bw/day NOEC= (0.0005*33.3)=0.017 mg a.s/kg food**	-	CAR a.s.Doc.III-A 6.4.1

2.8.3.1.1. Primary poisoning

Acute/short-term qualitative assessment

Acute primary toxicity for birds and mammals is assessed only qualitatively in accordance with the decision from TMIII-06 as stated in the CAR of bromadiolone (owned by the Task Force).

For mammals the acute toxicity to rat: **LD50 = 1.31 mg a.s. /kg bw** is the lowest value for acute toxicity.

Additional endpoints:

The LD50 value for mammals from the final CA report of another notifier 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 lower: **LD50 = 0.56-0.84 mg a.s. /kg bw** than the value used in the final CA of bromadiolone of the notifier Task Force. Therefore, as the data set are considered equivalent, the worst case value from the other notifier final CAR is used in the qualitative risk assessment for comparisons with estimated daily uptakes of bromadiolone (ETE, mg a.s. /kg bw).

For birds the acute toxicity to Japanese quail: **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).

Additional endpoints:
No additional endpoints were used for birds.

Long-term quantitative 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**

For birds the $PNEC_{oral}$ was determined by the NOEC value calculated from the 42-day 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) = 0.039/30 = 0.0013 mg/kg bw/ day
equivalent to
$PNEC_{oral}$ for birds (conc. In food) = 0.26/30 = 0.0087 mg/L drinking water

Additional endpoints:
The PNEC values for bird from the final CA report of another notifier 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 lower: **$PNEC_{oral}$ for birds (dose) = 0.00038 mg/kg bw/ day** (equivalent to $PNEC_{oral}$ for birds (conc. in food) =0.0033 mg/kg food) than the PNEC derived in the final CA of bromadiolone of the notifier Task Force. Subsequently, the worst case PNEC from the other notifier final CAR is used in the risk assessment.

2.8.3.1.2. Secondary poisoning

Acute/short-term qualitative assessment
Acute primary toxicity for birds and mammals is assessed only qualitatively in accordance with the decision from TMIII-06 as stated in the CAR of bromadiolone (owned by the Task Force).

For mammals the acute toxicity to rat: LD50 = 1.31 mg a.s. /kg bw recalculated into **LC50 = 26 mg/kg food**, using the conversion factor bw/dfi of 20 from table 22 in the TGD II is the lowest value for the acute toxicity.

Additional endpoints:
The recalculated LC50 value for mammals from the final CA report of another notifier 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 lower: **LC50 = 11.2-16.8 mg a.s. /kg food** than the value used in the final CA of bromadiolone of the notifier Task Force. Therefore, as the data set are considered equivalent, the worst case value from the other notifier final CAR is used in the qualitative assessment for comparisons with estimated daily uptakes of bromadiolone (PEC mg a.s. /kg food).

For birds the acute toxicity to Japanese quail: LD50 = 134 mg a.s. /kg bw recalculated into **LC50 = 1070 mg/kg food**, using equation 77 in the TGD II and the conversion factor bw/dfi of 8 (domestic hen) from table 22 in the TGD II is the lowest value for the acute toxicity.

Additional endpoints:
The recalculated LC50 value for birds from the final CA report of another notifier 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 lower: **LC50 = 207 mg a.s. /kg food** than the value used in the final CA of bromadiolone of the notifier Task Force. Therefore, as the data set are considered equivalent, the worst case value from the other notifier final CAR is used in the qualitative risk assessment for comparisons with estimated daily uptakes of bromadiolone (PEC mg a.s. /kg food).

These recalculations were considered acceptable in the CAR of bromadiolone owned by the Task Force.

Long-term quantitative 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 = 0.017/90 = 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 42-day 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 = 0.26/30 = 0.0087 mg/L drinking water

equivalent to $PNEC_{oral}$ for birds = 0.039/30 = 0.0013 mg/kg bw/ day

Additional endpoints:
The PNEC values for bird for secondary poisoning from the final CA report of another notifier 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 lower: **$PNEC_{oral}$ for birds = 0.00075 mg/kg food (**equivalent to $PNEC_{oral}$ for birds = 0.00019 mg/kg bw/day) than the PNEC derived in the final CA of bromadiolone of the notifier Task Force. Subsequently, the worst case PNEC from the other notifier final CAR is used in the risk assessment.

2.8.2.5 Summary of PNECs of the active substance bromadiolone

Table 2.8.2.5: Summary of the bromadiolone (a.s.) PNECs used for risk assessment

Compartment		Test Value	AF	PNEC	CAR
Aquatic	PNECwater	LC_{50} =0.17 mg a.s. /L	10 and 1000	1.7×10^{-5} mg a.s. /L	LT
	$PNEC_{sediment}$	Not available		0.83 mg a.s. /kg ww sediment (Equilibrium partioning Method)	TF
	$PNEC_{STP}$	EC_{50} = 31.6 mg a.s. /L	100	0.32 mg a.s. /L	LT
Terrestrial	$PNEC_{soil}$	LC_{50} >8.4 mg a.s. /kg ww soil	1000	0.0084 mg a.s. /kg ww soil	LT

Primary and secondary poisoning	$PNEC_{oral\ for\ birds}$	NOEC = 0.1 mg/kg food NOEL = 0.01138 mg/kg bw/day	30	0.0033 mg a.s. /kg food 0.00038 mg/kg bw/day	LT
	$PNEC_{oral\ for\ mammals}$	NO(A)EL=0.0005 mg a.s/kg bw/day NOEC= (0.0005*33.3)=0.017 mg a.s/kg food Rabbit repeated dose toxicity 90 days	90	0.00019 mg/kg food 0.0000056 mg/kg bw/day	TF

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 is used in the risk assessment.

2.8.2.6 PBT and ED assessment

Due to the properties of persistence, of toxicity and to uncertainties with regard to the B-criterion, the substance bromadiolone is considered as a potential PBT.
According to the CAR of the notifier Task Force, the active substance bromadiolone is not an endocrine disruptor.

2.8.3 Effects on environmental organisms for biocidal product FAAR AVOINE

It is important to notice that the applicant did not provide ecotoxicological data about the biocidal product FAAR AVOINE. So all the effects assessment is based on the data obtained from the active substance 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).

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 the product FAAR AVOINE, the substance does not contribute to the classification of the biocidal product.

2.8.3.1 Aquatic compartment (including water, sediment and STP)

2.8.4.5.1. Aquatic organisms

Refers to section 2.8.2.1

2.8.4.5.2. Sediment dwelling organisms

Refers to section 2.8.2.1

2.8.4.5.3. STP micro-organisms

Refers to section 2.8.2.1

2.8.3.2 Atmosphere

Refers to section 2.8.2.2

2.8.3.3 Terrestrial compartment

Refers to section 2.8.2.3

2.8.3.4 Non compartment specific effect relevant to the food chain

Refers to section 2.8.2.4

2.8.3.5 Summary of PNECs

Refers to section 2.8.2.5

2.8.4 Environmental exposure assessment

2.8.4.1 Assessment of exposure in the environment

As the product contains no substances of concern, it is considered that risks posed to environment following the use of FAAR AVOINE 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.

The product FAAR AVOINE is a ready-to-use rodenticidal bait containing 0.005% bromadiolone. The product is constituted by cereal grains supplied in sachet or in bulk for professional and non professional users. The product is used as 40 g for mouse and 200 g for rat / bait point. The impregnated grains is placed in secured bait stations. According to the applicant, the product is intended to be used in bait boxes or bait stations inside domestic, industrial, and farm buildings. Baits are placed in secured bait point and refilled 4 times over 28 days. Dead rodents and unconsumed baits are removed each week.

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

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

2.8.4.2 Aquatic compartment (including water, sediment and STP)

Exposure of the aquatic compartment *via* the STP after the treatment with rodenticides is only relevant for indoor application of liquid poisons, residues from mixing and cleaning (ESD PT14). As FAAR AVOINE is a solid form and is intended to be used indoor only, indirect or direct exposure of the aquatic compartment may be considered negligible.

2.8.4.3 Atmospheric compartment

Due to its physico-chemical properties (low vapour pressure of $1x10^{-7}$ Pa and low Henry’s law constant), bromadiolone is not expected to be present in the atmosphere in significant quantities. The exposure of air is therefore considered negligible for the application of FAAR AVOINE biocidal product.

2.8.4.4 Terrestrial compartment

As FAAR AVOINE is intended to be used indoor only, no exposure to soil and groundwater is expected.

2.8.4.5 Non-compartmental specific effects relevant to the food chain (secondary poisoning)

2.8.4.5.1. Primary poisoning

As stated in the ESD (Larsen, 2003), primary poisoning hazard to mammals and birds (both wild and domestic) can be considered small when rodenticides are applied according to the label instructions. In the scenario "in and around buildings" when the product is placed in protected bait point, the risk for primary poisoning is mainly for birds and mammals of equal size or smaller as the target rodents, which may be able to enter into the bait stations. Another exposure of non-target animals may arise when target rodents carry bait away from bait stations.

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

Primary poisoning - Tier 1 assessment

The Tier 1 assessment assumes that the whole day's food requirement is satisfied by consumption of bait blocks 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 FAAR AVOINE).
Hence, **the worst case Tier 1 PEC_{oral} is 50 $mg.kg^{-1}$**.

Primary poisoning - Tier 2 assessment, acute

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

ETE = (FIR/BW) * C * AV * PT * PD ($mg.kg^{-1}_{bw}.d^{-1}$); with

FIR: food intake rate of the indicator species ($g.d^{-1}$),
BW: indicator species body weight (g),
C: concentration of the active substance in fresh diet ($mg.kg^{-1}$),
AV: avoidance factor (-),
PT: fraction of diet obtained in treated area (-) and
PD: the fraction of the food type in the diet (-).

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

Table 2.8.4.5-1: Expected concentrations of bromadiolone in non-target animals in the worst case (Step 1) and realistic worst case (Step 2) for acute situations

Non-target animal	BW = Typical bodyweight (g)[a]	FIR = Daily mean food intake (g dry weight.day^{-1})	C = Concentration of bromadiolone in bait ($mg.kg^{-1}$)	ETE, conc. of bromadiolone after one meal ($mg.kg^{-1}$ bw.d^{-1})	
				Step 1	Step 2
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)

Primary poisoning - Tier 2 assessment, long-term

The long-term risks of bromadiolone are determined by the expected concentrations (EC) in the animal after metabolism and elimination, which is regarded as PEC. The EC is calculated by using the actual dose of the substance consumed by a non-target animal each day (ETE) using the realistic worst case scenario (Step 2), calculated above. 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)

According to the ESD, a default value of 0.3 for daily uptake eliminated (El) can be used if no studies are submitted. The EC values are the expected concentration of active substance bromadiolone in non-target animals in primary poisoning scenarios after one meal followed by 24 hour elimination period.

Table 2.8.4.5-2: Expected concentrations of bromadiolone in non-target animals in realistic worst case (Step 2) for long-term situation

Non-target animal	EC, conc. of bromadiolone after one day of elimination (mg.kg^{-1} bw)
	Step 2
Dog	1.15
Pig	0.19
Pig young	0.60
Tree sparrow	8.71
Chaffinch	7.56
Wood pigeon	2.73
Pheasant	2.72

2.8.4.5.2. Secondary poisoning

Secondary poisoning via the aquatic food chain

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

Secondary poisoning via the terrestrial food chain

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

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

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

Secondary poisoning - Tier 1 assessment, acute

Calculations of the risk for secondary poisoning of scavengers and predators are done by determining the concentration of bromadiolone in their food, i.e. the poisoned rodents. This PEC_{oral} is then compared to the LC_{50} values for a qualitative risk assessment in accordance with the decision from TM III-06. According to the ESD section 3.3.1, the consumption of rodenticides makes up at least 20 % of total consumptions in a choice test and could in a worst case be up to 100 %, whilst 50 % would be considered as the normal situation. Therefore, in the calculations the fractions of the food type in the diet (PD) are set to 0.2, 0.5 and 1.0. The FIR/BW quotient (food intake rate of the indicator species/indicator species body weight) is a default value set to 0.1, i.e. it is assumed that the rats eat 10 % of their bodyweight each day. The avoidance factor (AV) is 1, which means no avoidance, since rats is their natural prey, and the fraction of diet (PT) obtained in the area is set to 1.

The calculation is done according to equation 19 in the ESD:

$ETE = (FIR/BW)*C*AV*PT*PD$ ($mg.kg^{-1}$ $bw.day^{-1}$)

This equation gives the concentration of bromadiolone in the rat (PEC_{oral}) after a meal the first day. Considering the elimination rate and that the mean time to death is seven days the concentration in the rodents each day can be calculated by the equation 21 in the ESD:

$EC_n = \Sigma_{n-1}\ ETE * (1\text{-}El)_n$

For the active substance bromadiolone, the default value of 0.3 is used for elimination (El) in accordance with the CAR of bromadiolone from the Bromadiolone Task Force.

Table 2.8.4.5-3: Residues of bromadiolone in target animals at specific point in times and varying bait consumption

	Residues in target animal ($mg.kg^{-1}$bw)		
	20%	**50%**	**100%**
Day 1 after the first meal	1.0	2.5	5.0
Day 2 before new meal	0.7	1.8	3.5
Day 5 after the last meal	**2.8**	**6.9**	**13.9**
Day 7 mean time to death	1.4	3.4	6.8

According to the ESD, the concentrations of bromadiolone in rats are at peak after consuming bait for 5 days; thereafter the concentrations in rodents are decreasing until day 7 due to excretion and metabolism of the rodenticide. The values from day 5 are used as PEC_{oral}.

Secondary poisoning - Tier 1 assessment, long-term

To assess the risk of long-term secondary poisoning to birds and mammals, the PEC in rodents after 5 days is used considering that the consumption of rodenticides makes up 100 % of total consumptions (refer to Table 2.8.4.5-3).

Table 2.8.4.5-4: Residues of bromadiolone in target animals at specific point in times and varying bait consumption used in the long term assessment

	PEC_{oral} Bromadiolone conc. in target rodent ($mg.kg^{-1}$ bw), ESD default values
Birds	13.9
Mammals	13.9

Secondary poisoning - Tier 2 assessment, long-term

For the Tier 2 assessment the average food intake for each species and the average weight of the species have been considered, according to the Table 3.5 in the ESD. The calculations are based on the expected values for uptake of active substance by a mammal predator or a bird of prey after a single day of exposure presented as an illustrative example in the ESD, as no specific values were reported in the final CAR of bromadiolone from the Bromadiolone Task Force.

The amount of a.i. consumed by the non-target animal is 13.9 $mg.kg^{-1}$ bw for rodents caught on day 5 and 16.6 $mg.kg^{-1}$ bw for resistant rodents caught on day 14, also assuming that the non-target animals feed to 50 % on the rodents, all in accordance with the ESD. By knowing the amount of a.i. consumed by the non-target animal and the weight of the animal, the PEC (concentration in non-target animal) after one day consumption of rodents can be calculated. The results are presented in Table 2.8.4.5-5.

Table 2.8.4.5-5: Expected concentrations of bromadiolone in non-target animals (predators/carnivores) due to secondary poisoning after a single day of exposure (concentration of bromadiolone in rodenticide bait 0.005%). Rodents fed 100% on rodenticide and predators/carnivores fed 50% on poisoned rodents.

			Normal susceptible rodents caught on day 5		Resistant rodents caught on day 14	
Species	**Body weight (g)**	**Daily mean food intake ($g.d^{-1}$)**	**Amount a.i. consumed by non-target animal (mg)**	**Conc.in non-target animal ($mg.kg^{-1}$)**	**Amount a.i. consumed by non-target animal (mg)**	**Conc.in non-target animal ($mg.kg^{-1}$)**
Barn owl *(Tyto alba)*	295	72.9	0.51	1.7	0.60	2.1
Kestrel *(Falco tinnunculus)*	209	78.7	0.55	2.6	0.65	3.1
Little owl *(Athene noctua)*	164	46.4	0.32	2.0	0.38	2.3
Tawny owl *(Strix aluco)*	426	97.1	0.67	1.6	0.80	1.9
Fox *(Vulpes vulpes)*	5700	520.2	3.61	0.6	4.31	0.8
Polecat *(Mustela putorius)*	689	130.9	0.91	1.3	1.08	1.6
Stoat *(Mustela erminea)*	205	55.7	0.39	1.9	0.46	2.3
Weasel *(Mustela nivlis)*	63	24.7	0.17	2.7	0.20	3.3

2.8.5 Risk characterisation 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 and/or LD_{50}) according to the guidance in Technical guidance document (TGD, 2003) and 'Emission scenario document for biocides used as rodenticides' (Larsen, 2003, ESD PT14).
The environmental risk characterization has been carried out for bromadiolone.

2.8.5.1 Primary poisoning

Tier 1 assessment

The PEC value for Tier 1 assessment is compared to the long-term PNECs for birds and mammals. The PNECoral birds and mammals from the final CAR of the notifier Task Force represent the worst case value in comparison with values presented in final CAR from other notifier so they are used in the risk assessment.

Table 2.8.5.1-1: Tier 1 risk characterization of primary poisoning

	PEC (conc. of bromadiolone in food ($mg.kg^{-1}$))	PNEC (conc. of bromadiolone in food ($mg.kg^{-1}$))	PEC /PNEC
Long-term			
Birds	50	0.0033 mg/kg	15152
Mammals	50	0.00019 mg/kg	263000

The resulting PEC/PNEC ratios reveal a high risk for both birds and mammals of long-term primary poisoning.

Tier 2 assessment, acute

For the acute situation of primary poisoning only a qualitative risk assessment is carried out in accordance with the decision from TM III-06.

For the Tier 2 acute qualitative assessment, the PEC values are compared to the LD50 values in the table.

The worst case LD50 values between the final CAR from the notifier Task Force (TF) and from the notifier Liphatec S.A.S. (LT) are used for the qualitative risk assessment.

Table 2.8.5.1-2: Tier 2 acute qualitative risk characterization of primary poisoning

Non-target animal	PECoral = ETE, conc. of bormadiolone after one meal ($mg.kg^{-1}$)		LD50 dose ($mg.kg^{-1}$ bw d^{-1})	PEC oral higher than LD50 (y/n)	
	Step 1	Step 2		Step 1	Step 2
Dog	2.28	1.64	1.3 (TF)	**y**	**y**
Pig	0.38	0.27	0.56-0.84 (LT)	n	n
Pig young	1.20	0.86	0.56-0.84 (LT)	**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

This comparison indicates that birds are not at risk for acute primary poisoning; while the situation for mammals is more uncertain. Dogs are at risk and pigs are at not at risk but very close to being at risk.

Tier 2 assessment, long-term

The PEC values are compared to the worst case PNEC value between the final CAR from the notifier Task Force (TF) and from the notifier Liphatec S.A.S. (LT).

Table 2.8.5.1-3: Tier 2 long-term risk characterization of primary poisoning

Non-target animal	PECoral = EC, conc. of bormadiolone after one day of elimination (mg.kg^{-1}) Step 2	PNEC (mg.kg^{-1} bw.d^{-1})	PEC /PNEC Step 2
Dog	1.15	0.0000056 (TF)	205 000
Pig	0.19	0.0000056 (TF)	33 900
Pig young	0.60	0.0000056 (TF)	107 000
Tree sparrow	8.71	0.00038 (LT)	22 909
Chaffinch	7.56	0.00038 (LT)	19 895
Wood pigeon	2.73	0.00038 (LT)	7 186
Pheasant	2.72	0.00038 (LT)	7 147

Very high risk of primary poisoning at long-term are identified for both birds and mammals.

The risk characterisation indicates a very high risk to non-target mammals and birds from direct eating of bait. Primary poisoning incidents can be minimised by preventing the access of non-target animals to the baits. It is assumed in the ESD that if the rodenticide baits are used according to the label instructions, the risk for primary poisoning is negligible. However, it is stated at the EU level that it may not be possible to exclude exposure of all non-target animals, as the baits have to be accessible to target rodents, they may as well be accessible to non-target mammals and birds of equal or smaller size than the target rodents.
Nevertheless, as the product FAAR AVOINE is intended to be used indoor and in bait stations only, primary poisoning can therefore be considered negligible as domestic animals can be kept away from the product, and wild animals other than rats and mice are not expected to be found inside buildings.

2.8.5.2 Secondary poisoning

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

Tier 1 assessment, acute

The PECoral are compared to the LC50 values presented in the section above for qualitative risk assessment in accordance with the decisions taken at the TMIII-06. The worst case LC50 values between the final CAR from the notifier Task Force (TF) and from the notifier Liphatec S.A.S. (LT) are used for the qualitative risk assessment.

Table 2.8.5.2-1: Tier 1 acute qualitative risk assessment of secondary poisoning

Non-target animal	PECoral Expected concentration in rodent (mg.kg^{-1}) caught on day 5 after meal			LC50 dose (mg.kg^{-1} food)	PEC oral higher than LD50 (y/n)
	PD=0.2	PD=0.5	PD=1		PD=0.2;0.5 and 1
Birds	2.8	6.9	13.9	207 (LT)	n
Mammals	2.8	6.9	13.9	11.2-16.8 (LT)	n

This qualitative risk assessment indicates no risk for birds and mammals in acute situations.

Tier 1 assessment long-term

To assess the risk of long-term secondary poisoning, the PEC in rodents after 5 days is used and compared to the long-term PNECoral for birds and mammals. The worst case PNEC values between the final CAR from the notifier Task Force (TF) and from the notifier Liphatec S.A.S. (LT) are used for the qualitative risk assessment.

Table 2.8.5.2-2: Tier 1 long-term risk assessment of secondary poisoning

Non-target animal	PECoral Expected concentration in rodent ($mg.kg^{-1}$) caught on day 5 after meal	PNECoral (mg/kg food)	PEC /PNEC
	PD=1		PD=1
Birds	13.9	0.00075 (LT)	18 500
Mammals	13.9	0.00019 (TF)	73 200

The tier 1 long-term assessment indicates very high risks of long-term secondary poisoning for birds and mammals.

Tier 2 assessment, long-term

Table 2.8.5.2-3: Tier 2 long-term risk assessment of secondary poisoning

Species	PEC (mg/kg bw)		PNEC (mg/kg bw)	PEC/PNEC	
	day 5	day 14		day 5	day 14
Barn owl *(Tyto alba)*	1.7	2.1	0.00019 (LT)	9 070	10 832
Kestrel *(Falco tinnunculus)*	2.6	3.1	0.00019 (LT)	13 776	16 447
Little owl *(Athene noctua)*	2.0	2.3	0.00019 (LT)	10 349	12 359
Tawny owl *(Strix aluco)*	1.6	1.9	0.00019 (LT)	8 338	9 957
Fox *(Vulpes vulpes)*	0.6	0.8	0.0000056 (TF)	110 000	140 000
Polecat *(Mustela putorius)*	1.3	1.6	0.0000056 (TF)	180 000	290 000
Stoat *(Mustela erminea)*	1.9	2.3	0.0000056 (TF)	340 000	410 000
Weasel *(Mustela nivlis)*	2.7	3.3	0.0000056 (TF)	480 000	590 000

The tier 2 risk characterisation shows very high risks for secondary poisoning at long-term for birds and mammals.

It is stated in the final assessment report for bromadiolone of the notifier Task Force, that comparison with monitoring data from the literature indicates that the very high risks of secondary poisoning emerging from the calculations according to the ESD are confirmed.

However, considering the fact that FAAR AVOINE is intended to be used indoor only, it can be assumed that, applying use restrictions (such as collecting dead rodents), the risk for secondary poisoning will be lower.
Nevertheless, in order to reduce the risk of secondary poisoning, it is very important to follow the use instructions of the rodenticide baits. The risk reduction measures are considered in the section 2.9.

2.8.5.3 Conclusion of the risk assessment for the environment

No studies were conducted with the product FAAR AVOINE 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 indoor use by professionals and 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.

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.
- 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.

2.9 Measures to protect man, animals and the environment

See Summary of Product Characteristics (SPC).

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3 PROPOSAL FROM 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)

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 FAAR AVOINE is to be used in tamper-resistant bait boxes or covered bait stations.

”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

FAAR AVOINE 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.
Compatibility with packaging materials and stability of FAAR AVOINE after storage and effect of temperature are not demonstrated by shelf life study and accelerated storage test.
Missing data are required in post registration.

Summary of efficacy assessment

The product FAAR AVOINE has shown a sufficient efficacy and can be used for the control of mice (Mus musculus) and rats (Rattus norvegicus and Rattus rattus) inside domestic, industrial and commercial buildings including farm buildings. Nevertheless, 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 FAAR AVOINE can be considered as effective after a 14 months storage period. The 24 months storage period claimed by the applicant shall be demonstrated.

Summary of risks characterisation of the product for human health

The risk resulting from the intended use is acceptable when professionals are wearing gloves and when FAAR AVOINE is supplied and applied in sachet.

The risk for non-professional users resulting from the intended use is unacceptable. Consequently, the use is restricted to professionals.

Finally, there is a significant risk of poisoning for infants, thus, the baits should be unattainable for children.

Summary of risks characterisation of the product for the environment

No studies were conducted with the product FAAR AVOINE 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 indoor use by professionals and 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.

Risk mitigation measures and conditions of use

Measures linked to assessment of physico-chemical properties

- Store away from light.

Conditions of use linked to efficacy assessment

- Adapt the number of bait stations 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.

Recommendations to be taken into account by the applicant

- Adapt the amount of bait per bait point to the validated effective dose.
- The product label has to contain information on resistance management for rodenticides.

Measures to protect man

- Wear protective gloves when handling the product and dead rodents.
- 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.
- 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.

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

- Bulk and tap density according to CIPAC MT 186 ;
- Accelerated storage stability study according to CIPAC MT 46 ;
- Compatibility study of biocidal product with deposited packaging (PE sachet) ;
- Dustiness of biocidal product according to CIPAC MT 171 ;
- Attrition resistance of biocidal product according to CIPAC MT178 ;
- Flowability of biocidal product according to CIPAC MT 172 ;
- Particle size distribution of grains according to CIPAC MT 170 with sieves adapted to biocidal product.

Required information linked to efficacy assessment

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

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
FAAR AVOINE Formulation: grains	Brown rat :*Rattus norvegicus*	Professional	Indoor only	Rats : 180-200 g/secured bait point	3 to 10 days	4 refilling of bait stations Over 28 days Interval between applications (min) : one week	25 – 50 – 100 g sachet	5-10 meters	Manual application of baits in bait stations	yes	Sachet	Bag (paper bag several layers and one plastic film in PE) – 25kg 20kg; bucket (PE) 5 kg – 10kg - 15kg – 18kg – 20kg ; carton box (carton) 5 kg - 10kg – 15kg- 20kg.
	Brown rat :*Rattus norvegicus*	Professional	Indoor only	Rats : 180-200 g/secured bait point	3 to 10 days	4 refilling of bait stations Over 28 days Interval between applications (min) : one week	bulk	5-10 meters	Manual application of baits in bait stations	no	bulk	Bag (paper bag several layers and one plastic film in PE) – 25kg 20kg; bucket (PE) 5 kg – 10kg - 15kg – 18kg – 20kg ; carton box (carton) 5 kg - 10kg – 15kg- 20kg
	Brown rat :*Rattus norvegicus*	Non professional	Indoor only	Rats : 180-200 g/secured bait point	3 to 10 days	4 refilling of bait stations Over 28 days Interval between applications (min) : one week	25 – 50 – 100 g sachet	5-10 meters	Pre-filled secured boxes Manual application of baits in bait stations	yes	sachet	Bucket (PE) 500g – 1kg - 1,5kg carton box (carton) from 200g to 1.5kg; metal box from 200g to 1.5kg; bait box ; jug (PEHD) from 200 to 1.5kg
	Black rat : *Rattus rattus*	Professional	Indoor only	Rats : 180-200 g/secured bait point	3 to 10 days	4 refilling of bait stations Over 28 days Interval between	25 – 50 – 100 g sachet	5-10 meters	Manual application of baits in bait stations	yes	sachet	Bag (paper bag several layers and one plastic film in PE) – 25kg 20kg; bucket (PE) 5 kg – 10kg - 15kg – 18kg – 20kg ;

					applications (min) : one week						carton box (carton) 5 kg - 10kg – 15kg- 20kg
	Black rat : *Rattus rattus*	Professionnal	Indoor only	Rats : 180-200 g/secured bait point	3 to 10 days	4 refilling of bait stations Over 28 days Interval between applications (min) : one week	bulk	5-10 meters	Manual application of baits in bait stations	no	bulk	Bag (paper bag several layers and one plastic film in PE) – 25kg 20kg; bucket (PE) 5 kg – 10kg - 15kg – 18kg – 20kg ; carton box (carton) 5 kg - 10kg – 15kg- 20kg
	Black rat : *Rattus rattus*	Non professionnal	Indoor only	Rats : 180-200 g/secured bait point	3 to 10 days	4 refilling of bait stations Over 28 days Interval between applications (min) : one week	25 – 50 – 100 g sachet	5-10 meters	Pre-filled secured boxes Manual application of baits in bait stations	yes	sachet	Bucket (PE) 500g – 1kg - 1,5kg carton box (carton) from 200g to 1.5kg; metal box from 200g to 1.5kg; bait box ; jug (PEHD) from 200 to 1.5kg.
	Mice : *Mus musculus*	Professionnal	Indoor only	Mice : 30-40 g/secured bait point	3 to 10 days	4 refilling of bait stations Over 28 days Interval between applications (min) : one week	25 – 50 – 100 g sachet	1-2 meters	Manual application of baits in bait stations	yes	sachet	Bag (paper bag several layers and one plastic film in PE) – 25kg 20kg; bucket (PE) 5 kg – 10kg - 15kg – 18kg – 20kg ; carton box (carton) 5 kg - 10kg – 15kg- 20kg
	Mice : *Mus musculus*	Professionnal	Indoor only	Mice : 30-40 g/secured bait point	3 to 10 days	4 refilling of bait stations Over 28 days Interval between applications (min) : one week	bulk	1-2 meters	Manual application of baits in bait stations	no	bulk	Bag (paper bag several layers and one plastic film in PE) – 25kg 20kg; bucket (PE) 5 kg – 10kg - 15kg – 18kg – 20kg ; carton box (carton) 5 kg - 10kg – 15kg- 20kg
	Mice : *Mus musculus*	Non professionnal	Indoor only	Mice : 30-40 g/secured bait point	3 to 10 days	4 refilling of bait stations Over 28 days Interval between applications (min) : one week	25 – 50 – 100 g sachet	1-2 meters	Pre-filled secured boxes Manual application of baits in bait stations	yes	sachet	Bucket (PE) 500g – 1kg - 1,5kg carton box (carton) from 200g to 1.5kg; metal box from 200g to 1.5kg; bait box ; jug (PEHD) from 200 to 1.5kg

* 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 chart 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	Dosage claimed	Distance between 2 bait points, for high and low infestation	Time delay of the action of the product	Frequency and method of controls	Area of use	Methods of application of the bait
Professional users						
Rats *Rattus norvegicus* *Rattus rattus*	200 g / secured bait point	High infestation: 5 meters Low infestation: 10 meters	3 to 11 days	Inspect and resupply the bait stations, 3 days after application then once a week as long as the bait is consumed.	indoor only	Manual application in tamper-resistant bait boxes or covered bait stations
House mice *Mus musculus*	40 g / secured bait point	High infestation: 1 meter Low infestation: 2 meters				

Annex 1: Summary of product characteristics

See separated file.

Annex 2: List of studies reviewed

List of <u>new data</u>[12] 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	B3.2, 3.3, 3.4, 3.6	Demangel B	2011	Physico chemical tests on FAAR AVOINE. DEFITRACES, Report n°10-920010-029 of 13 May 2011, GLP (unpublished).	Triplan	☐	☒	☒	☐
B3	B3.1, 3.5, 3.7, 3.12	Demangel B	2011	Physico-chemical tests before and after an accelerated storage procedure for 14 days at 54 ± 2℃ on FAAR AVOINE. DEFITRACES, Report n°10-920010-30 of 24 February 2011, GLP (unpublished).	Triplan	☐	☒	☒	☐

[12] 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	
B4	B4.1.1	Ricau H	2011	Analytical method validation for the determination of bromadiolone in the FAAR BLOC SP in compliance with SANCO/3030/99 rev. 4 from 11/07/00. DEFITRACES, Report 10-920010-042 of 11 February 2011, GLP (unpublished).		☐	☒	☒	☐
B4	B4.1.2	Ricau H	2011	Analytical method validation for the determination of bromadiolone in the FAAR AVOINE in compliance with SANCO/3030/99 rev. 4 from 11/07/00. DEFITRACES, Report 10-920010-032 of 8 April 2011, GLP (unpublished).	Triplan	☐	☒	☒	☐
B5	B5.10.2.1/01	Barbieux S Grolleau G	2011	Efficacy laboratory study of FAAR BLE rodenticide containing 0.005% bromadiolone with albino house mice (*Mus musculus*). Cabinet Barbieux, report SB-2011-003 of 23 May 2011, not GLP (unpublished).	**Triplan**	☐	☒	☒	☐
B5	B5.10.2.1	Barbieux S Grolleau G	2011	Efficacy laboratory study of FAAR BLOC SP, rodenticide containing 0.005% bromadiolone with albino house mice (Mus musculus) Cabinet BARBIEUX, report SB-2011-002 of 23 May 2011, not GLP (unpublished).	**Triplan**	☐	☒	☒	☐
B5	B5.10.2.1/02	Barbieux S Grolleau G	2011	Efficacy field study of FAAR BLE rodenticide containing 0.005% bromadiolone with black rats *(Rattus rattus),* Cabinet BARBIEUX, report SB-2011-004 of 3 May 2011, not GLP (unpublished).	**Triplan**	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
B5	B5.10.2.1/01	Barbieux S Grolleau G	2011	Efficacy laboratory study of the rodenticide FAAR AVOINE containing 0.005% bromadiolone with albino house mice (Mus musculus). Cabinet BARBIEUX, Report SB-2011-001 of 23 May 2011, not GLP (unpublished).	**Triplan**	☐	☒	☒	☐
B5	B5.10.2.1	Barbieux S Grolleau G	2011	Efficacy laboratory study of FAAR BLOC SP, rodenticide containing 0.005% bromadiolone with albino house mice (Mus musculus) Cabinet BARBIEUX, report SB-2011-002 of 23 May 2011, not GLP (unpublished).	**Triplan**	☐	☒	☒	☐
B6	B6.1.1	Colas S	2011	FAAR BLOC SP evaluation of acute oral toxicity in rats – acute toxic class method. PHYCHER BIO DEVELOPPEMENT, study n°: TAO423-PH-10/0422 of 19 April 2011, GLP (unpublished).	Triplan	☐	☒	☒	☐
B6	B6.1.2	Colas S	2011	FAAR BLOC SP assessment of acute dermal toxicity in rats. PHYCHER BIO DEVELOPPEMENT, study n°: TAD-PH-10/0422 of 19 April 2011, GLP (unpublished).	Triplan	☐	☒	☒	☐
B6	B6.2.1	Colas S	2011	FAAR BLOC SP assessment of acute dermal irritation. PHYCHER BIO DEVELOPPEMENT, study n°: IC-OCDE-PH-10/0422 of 19 April 2011, GLP (unpublished).	Triplan	☐	☒	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
B6	B6.2.2	Colas S	2011	FAAR BLOC SP assessment of acute eye irritation. PHYCHER BIO DEVELOPPEMENT, study n°: IO-OCDE-PH-10/0422 of 19 April 2011, GLP (unpublished).	Triplan	☐	☒	☒	☐
B6	B6.3	Colas S	2011	FAAR BLOC SP assessment of sensitizing properties on albino Guinea pigs, maximisation test according to Magnusson and Kligman. PHYCHER BIO DEVELOPPEMENT, study n°: SMK-PH-10/0422 of 19 April 2011, GLP (unpublished).	Triplan	☐	☒	☒	☐
B6	B6.4	Colas S	2011	FAAR BLE evaluation of skin absorption: *in vitro* method (non GLP study). PHYCHER BIO-DEVELOPPEMENT, study n°AC-PH-10/0247-amended of 6 June 2011, non GLP (unpublished).	Triplan	☐	☒	☒	☐

Annex 3 : Analytical methods residues – active substance

Bromadiolone

Date: 2012

Matrix, action levels, relevant residue and reference

Summary taken from final CAR of task force of bromadiolone (2011):

Soil (principle of method and LOQ)	HPLC-MS (LOQ 0.22 µg/kg) LC-MS/MS (LOQ 0.01 mg/kg)
Air (principle of method and LOQ)	HPLC-UV (LOQ 0.5 µg/m^3) No confirmatory method available-not considered needed due to the low vapour pressure
Water (principle of method and LOQ)	HPLC-FD (LOQ 0.05 µg/l), HPLC-MS (LOQ 0.05 µg/l) confirmation: LC-MS/MS
Body fluids and tissues (principle of method and LOQ)	LC-MS/MS (LOQs 0.05 mg/l blood, 0.05 mg/kg liver) LC-MS/MS (LOQs 0.01 mg/l blood, 0.01 mg/kg liver)
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Multi residue method: LC-MS/MS (LOQ 0.01 mg/kg cucumber and wheat) Single method: LC-MS/MS (LOQ 0.01 mg/kg lemon and oilseed rape)
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	LC-MS/MS (LOQ 0.01 mg/kg meat)

Methods suitable for the determination of residues (monitoring methods)

Analyte	Matrix	Analytical method	Linearity (range and r^2)	Specificity	Recovery (%)				LOQ	LOQ required[1]	Reference in Doc III
					Fortification level	Range (n=5)	Mean	RSD%			
bromadiolone	soil	HPLC-MS (m/z 509.6-510.7 considered sufficiently specific)	0.066-13.2 µg/mL matrix matched standards (corresponding to 0.66-130.2 µg/kg soil) r^2= >0.997	No interferences shown	0.22 µg/kg	95.9-97.8	97.1	0.7	0.22 µg/kg	50 µg/kg	Morlacchini, 2009 (A4.2(a)/02)
					0.66 µg/kg	77.0-78,0 (n=4)	77.5	0.7			
					1.32 µg/kg	96.8-98.1 (n=4)	97.4	0.6			
					66 µg/kg	91.1-92.4 (n=4)	91.7	0.6			
bromadiolone	Water:	Quantification: HPLC-MS (m/z 527 used in the validation) Confirmation: LC-MS/MS (m/z 527 → 509 proven applicable for confirmation)	0.1-0.5 µg/ml (the fortification levels corresponds to 0.1-0.5 µg/ml injected on the column) r^2= >0.99	No interferences shown					0.05 µg/l		Martinez, 2005 (A4.2(c)/01)
	drinking				0.05 µg/l	80-100	93	9		0.1 µg/l	
					0.5 µg/l	73-85	79	6			
					5.0 µg/l	70-89	80	9			
					50 µg/l	79-105	93	12			
	ground				0.05 µg/l	63-87	70	13		-	
					0.5 µg/l	84-92	87	5			
					5.0 µg/l	81-97	88	6			
					50 µg/l	90-107	97	7			
	surface				0.05 µg/l	89-113	106	9		1.14 mg/l/ 0.38 µg/l[2]	
					0.5 µg/l	80-90	86	5			
					5.0 µg/l	76-84	81	3			
					50 µg/l	107-120	114	5			
bromadiolone	body fluids and tissues:	LC-MS/MS (primary transition m/z 525→250); confirm m/z 527→ 250; validation data available for both transitions but only reported here for the primary)	0.5-25 ng/mL (corresponding to 0.05-0.25 mg/kg or mg/l in the fortified sample) Matrix matched standards for tissues r^2= >0.999	No interferences shown							Marshall, 2010a (A4.2(d)/02)
	blood				0.01 mg/l	89-110	97	9	0.01 mg/l	0.05 mg/L	
					0.1 mg/l	93-105	101	5			
	tissues (liver)				0.01 mg/kg	92-110	101	9	0.01 mg/kg	0.1 mg/kg	
					0.1 mg/kg	102-110	105	3			

Analyte	Matrix	Analytical method	Linearity (range and r^2)	Specificity	Recovery (%)				LOQ	LOQ required[1]	Reference in Doc III
					Fortification level	Range (n=5)	Mean	RSD%			
bromadiolone	food and feeding stuffs:	LC-MS/MS (m/z 527 → 250 used for validation) External calibration relative to internal standard (coumatetralyl or diphacenone) using matrix matched standards	0.03-1.2 µg/ml (corresponding to 30% of LOQ to 120% of 10 x LOQ) r^2= not explicitly given for each matrix (given as 0.9433 to 0.9963 including matrices that are not reported here due to unacceptable data)	No interference shown. Control samples showed residues <30% of LOQ					0.01 mg/kg	-	Turnbull, 2005 (A4.3/01)
	cucumber				0.1 mg/kg 1.0 mg/kg	87-106 82-94	100 91	8 6			
	wheat				0.1 mg/kg 1.0 mg/kg	77-102 (n=4) 72-96	87 83	13 11			
bromadiolone	food and feeding stuffs:	LC-MS/MS (primary transition m/z 525→250); confirm m/z 527→ 250; validation data available for both transitions but only reported here for the primary)	0.5-25 ng/mL (corresponding to 0.05-0.25 mg/kg in the fortified sample) r^2= >0.9992	No interferences shown					0.01 mg/kg	-	Marshall, 2010b (A4.3/02)
	oil-seed rape				0.01 0.1	82-99 89-116	90 98	8 11			
	whole lemon				0.01 0.1	88-89 91-97	94 95	5 3			

Annex 4 : Toxicology and metabolism –active substance

Bromadiolone

Threshold Limits and other Values for Human Health Risk Assessment

Date: xx.xx.xxxx

Summary			
	Value	Study	SF
AEL long-term	0.0012 µg/kg/d	90-day rabbit (Task force) NOAEL = 0.5 µg/kg bw/day	300*
AEL medium-term	0.0012 µg/kg/d	90-day rabbit (Task force) NOAEL = 0.5 µg/kg bw/day	300*
AEL acute	0.0023 µg/kg/d	Developmental toxicity study rabbit (Task Force) LOAEL = 2 µg/kg bw/day	300*
*Adjusted for 70% oral absorption in rat (Task Force)			

Inhalative absorption	100%
Oral absorption	70% (Task Force)
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

Classification	**No harmonised classification is currently available**
	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

FAAR AVOINE

Date: xx.xx.xxxx

General information
Formulation Type cereal grains
Active substance(s) (incl. content) 0.005% bromadiolone
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}>2000 mg/kg *
Rat LD50 dermal (OECD 402)	LD_{50}>2000 mg/kg *
Rat LC50 inhalation (OECD 403)	No study submitted
Skin irritation (calculation rules according to Directive 1999/45/EC)	Non irritant
Eye irritation (OECD 405)	Non irritant *
Skin sensitisation (calculation rules according to Directive 1999/45/EC)	Not sensitizing

*read across from FAAR BLOC SP

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

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

* according to specific concentration limits specified for bromadiolone

Annex 6 : Safety for professional operators

FAAR AVOINE

Date: xx.xx.xxxx

Exposure assessment

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

Exposure of professionals to the biocidal product containing bromadiolone as active substance is considered as acceptable provided the product is supplied in sachet and PPE are worn.

Primary exposure of professionals – FAAR AVOINE in bulk (exposure during decanting, loading and cleaning considered)

	Component	**CAS**	**Inhalation internal exposure [mg/kg/d]**		**Dermal internal exposure [mg/kg/d]**		**Total exposure [mg/kg/d]**		**Model**
			Rats	Mice	Rats	Mice	Rats	Mice	
Tier 1 (without PPE)	Bromadiolone	28772-56-7	$2.5x10^{-6}$	$5.0x10^{-7}$	$3.4x10^{-5}$	$1.9x10^{-5}$	$3.7x10^{-5}$	$2.0x10^{-5}$	Cefic study
Tier 2 a (gloves penetration factor: 10%)	Bromadiolone	28772-56-7	$2.5x10^{-6}$	$5.0x10^{-7}$	$3.4x10^{-6}$	$1.9x10^{-6}$	$5.9x10^{-6}$	$2.4x10^{-6}$	Cefic study
Tier 2 b (gloves penetration factor: 5%)	Bromadiolone	28772-56-7	$2.5x10^{-6}$	$5.0x10^{-7}$	$1.7x10^{-6}$	$9.7x10^{-7}$	$4.2x10^{-6}$	$1.5x10^{-6}$	Cefic study

Primary exposure of professionals – FAAR AVOINE in sachet (exposure only during cleaning) – Control of rats and mice

	Component	**CAS**	**Inhalation internal exposure [mg/kg/d]**	**Dermal internal exposure [mg/kg/d]**	**Total exposure [mg/kg/d]**	**Model**
Tier 1 (without PPE)	Bromadiolone	28772-56-7	Not applicable	$5.1x10^{-6}$	$5.1x10^{-6}$	Cefic study
Tier 2 (gloves penetration factor: 10%)	Bromadiolone	28772-56-7	Not applicable	$5.1x10^{-7}$	$5.1x10^{-7}$	Cefic study

Risk assessment

Control of rats

Scenario	Component	CAS	AEL [mg/kg/d]	Absorption [%]		Total syst exposure [mg/kg bw/d]		Risk
				inh	derm	Expo	%AEL	
FAAR AVOINE in bulk								
Professional (without gloves)	Bromadiolone	28772-56-7	$1.2x10^{-6}$	100	10	$3.7x10^{-5}$	3048	Unacceptable
Professional (gloves penetration factor: 10%)	Bromadiolone	28772-56-7	$1.2x10^{-6}$	100	10	$5.9x10^{-6}$	493	Unacceptable
Professional (gloves penetration factor: 5%)	Bromadiolone	28772-56-7	$1.2x10^{-6}$	100	10	$4.2x10^{-6}$	351	Unacceptable
FAAR AVOINE in sachet								
Professional (without gloves)	Bromadiolone	28772-56-7	$1.2x10^{-6}$	100	10	$5.1x10^{-6}$	421	Unacceptable
Professional (gloves penetration factor: 10%)	Bromadiolone	28772-56-7	$1.2x10^{-6}$	100	10	$5.1x10^{-7}$	42	Acceptable

Control of mice

Scenario	Component	CAS	AEL [mg/kg/d]	Absorption [%]		Total syst exposure [mg/kg bw/d]		Risk
				inh	derm	Expo	%AEL	
FAAR AVOINE in bulk								
Professional (without gloves)	Bromadiolone	28772-56-7	$1.2x10^{-6}$	100	10	$2.0x10^{-5}$	1661	Unacceptable
Professional (gloves penetration factor: 10%)	Bromadiolone	28772-56-7	$1.2x10^{-6}$	100	10	$2.4x10^{-6}$	204	Unacceptable
Professional (gloves penetration factor: 5%)	Bromadiolone	28772-56-7	$1.2x10^{-6}$	100	10	$1.5x10^{-6}$	123	Unacceptable
FAAR AVOINE in sachet								
Professional (without gloves)	Bromadiolone	28772-56-7	$1.2x10^{-6}$	100	10	$5.1x10^{-6}$	421	Unacceptable
Professional (gloves penetration factor: 10%)	Bromadiolone	28772-56-7	$1.2x10^{-6}$	100	10	$5.1x10^{-7}$	42	Acceptable

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

FAAR AVOINE

Date:xx.xx.xxxx

General information
Formulation Type cereal grains
Active substance(s) (incl. content) 0.005% bromadiolone
Category
Authorisation number

Bromadiolone

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

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

Conclusion:
Exposure of non-professionals to the biocidal product containing bromadiolone as active substance is considered unacceptable. However, the risk calculation is based on a default dermal absorption of 10% for bromadiolone. This value is likely lower as demonstrated in an *in vitro* dermal absorption study performed with FAAR BLE (a dermal absorption of 3.1% was determined). But, due to deficiencies, this study was not considered as valid.

The accidental ingestion of baits poses a risk to infants since the AEL is exceeded when infant ingests more than 0.34 mg of product per day.

Details for the exposure estimates:

Scenario	Component	CAS	Inhalation internal exposure [mg/kg/d]	Dermal internal exposure [mg/kg/d]	Total exposure [mg/kg/d]	Model
Control of rats and mice - Sachet considered (exposure only during cleaning)						
Non professional	Bromadiolone	28772-56-7	Not applicable	$1.9x10^{-6}$	$1.9x10^{-6}$	Cefic study

Risk assessment

Scenario	Componen	CAS	AEL	Absorptio	Total syst	Risk

	t		[mg/kg/d]	n [%]		exposure [mg/kg bw/d] [mg/m^3]		
				inh	derm	Expo	%AEL	
Control of rats and mice - Sachet considered (exposure only during cleaning)								
Non-professional	Bromadiolone	28772-56-7	$1.2x10^{-6}$	100	10	$1.9x10^{-6}$	157	Unacceptable

Annex 8
Efficacy of the active substance from its use in the biocidal product

Test substance	Test organisms	Test system / Concentrations applied / exposure time	Test conditions	Test results: effects, mode of action, resistance	Reference	RI
FAAR AVOINE 0.005 % bromadiolone	Albino house mice (*Mus musculus*)	Laboratory test: CEB n°1 5 males and 5 females per lot 3 lots: Lot efficacy (no-choice food), Lot acceptance (free-choice food) Lot control animals. Food or bait biocidal product have been given: - 30 g per animal of usual food for the controls, - 20 g per animal of usual food + 20 g of bait for acceptance lot, - 30 g per animal of bait for the efficacy lot, Intoxication duration: 3 days with daily measurement of mortality and consumption.	Acclimation: 3 days in individual cage. Room temperature was 22°C ± 1°C. Mortality was observed during 11 days (from the first day of intoxication until the death of the last animal at the 11th day) every 24 hours.	Within the free-choice food lot, the bait has been well accepted: 58.5 % to 82.0 % of the overall consumption during 3 days. 100% efficacy has been reached from 5 to 7 days within the acceptance lot and from 3 to 11 days within the efficacy lot. 0 % mortality in the control lot	**IIIB5.10.2-01**	1

Test substance	Test organisms	Test system / Concentrations applied / exposure time	Test conditions	Test results: effects, mode of action, resistance	Reference	RI
FAAR AVOINE 0.005 % bromadiolone	Wild house mice (*Mus musculus*)	Field trial: CEB n°2 18 bait stations Pre-baiting phases (18 days): 50 g or 100 g grains per station Baiting phase (24 days): 50 g baits per station. Post-baiting phases (7 days): 50 g grains per station	Test performed in a farm (food storage room and cellar). Habituation of an isolated wild population of mice to their new environment. Estimated population size: 150. The daily consumption was measured from day 24/09 to day 03/10 then every 2 or 3 days from day 03/10 till the end of poisoning.	The efficacy was total (100 %). Pre-baiting plateau = 286.25 g Post-baiting plateau = 0 g The assessed bait has been well accepted by mice and effective and the results are coherent with laboratory ones.	**IIIB5.10.2-02**	1
FAAR BLE 0.005 % bromadiolone	Wild black rats (*Rattus rattus*)	Field trial: CEB n°2 Pre-baiting phases (36 days): 500 g grains per station. 34 bait stations increased till 65 stations. Baiting phase (8 days): 500 g baits per station. 68 bait stations. Post-baiting phases (6 days): 500 g grains per station	Test performed in a pig farm. Habituation of an isolated wild population of black rats to their new environment. The daily consumption was measured from day 28 to day 50.	The efficacy is acceptable (80.2 %). Pre-baiting plateau = 5636.7 g Post-baiting plateau = 1118.3 g The arrival of young rats consuming in bait stations has probably distorted the efficacy assessment.	**IIIB5.10.2-02**	2
FAAR BLOC SP 0.005 % bromadiolone	Wild brown rats (*Rattus norvegicus*)	Field study CEB n°2 46 bait stations Pre-baiting phase (12 days) : 250 to 750 g of grain were placed daily in each station. Poisoning phase (8 days) : 20 blocks of baits per day and per station. Post-baiting phase (6 days) : 500 g of the pre-baiting grains per station and per day.	Field study conducted in pheasants aviaries 46 empty bait stations have been placed at the beginning of the study (acclimation phase). Daily food consumptions are measured.	The field study with brown rats during 8 days of intoxication has given 92.8 % efficacy for a very large population (> 1000 individuals). Pre-baiting stage = 23581.8 g Post-baiting stage = 1691.0 g	**IIIB5.10.2-02**	2