Product Assessment Report

Biocidal product assessment report related to product authorisation under regulation 528/2012

FANGA B+

TRIPLAN S.A.

December 2015

Internal registration/file no:	BC-RQ006542-27
Authorisation/Registration no:	National authorisation
Granting date/entry into force of authorisation/ registration:	
Expiry date of authorisation/ registration:	
Active ingredient:	Brodifacoum (CAS: 56073-10-0)
Product type:	14

Competent Authority in charge of delivering the product authorization:
French Ministry of Ecology
Department for Nuisance Prevention and Quality of the Environment
Chemical Substances and Preparation Unit
Tour Séquoia
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
14 rue Pierre-Marie Curie
94 701 Maisons-Alfort Cedex - FRANCE

biocides@anses.fr

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1 General information about the product application

1.1 Applicant

Company Name:	TRIPLAN SA
Address:	BP258 La Poste Française
City:	Andorre la Vieille
Postal Code:	AD500
Country:	Principauté d'Andorre
Telephone:	+376 741 454
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E-mail address:	triplan@andorra.ad

1.1.1 Person authorised for communication on behalf of the applicant

Name:	Fredy Lacroux
Function:	Managing director
Address:	BP258 La Poste Française
City:	Andorre la Vieille
Postal Code:	AD500
Country:	Principauté d'Andorre
Telephone:	+376741 454
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E-mail address:	triplan@andorra.ad

1.1.2 Proposed authorisation holder

Company Name:	**TRIPLAN** :	**TRIPLAN-** BUREAU DE LIAISON FRANCE
Address:	BP258 La Poste Française	1, place Saint-Silain
City:	Andorre la Vieille	Périgueux
Postal Code:	AD500	24000
Country:	Principauté d'Andorre	FRANCE
Telephone:	+33 1 76 74 1 4 54	+33 1.76 741 454
Fax:		
E-mail address:	triplan@andorra.ad	triplan@andorra.ad
Letter of appointment for the applicant to represent the authorisation holder provided (yes/no):	No	

1.2 Information about the product application

Application received:	01/7/2014
Application reported complete:	26/08/2014
Type of application:	National authorization
Further information:	

1.3 Information about the biocidal product

1.3.1 General information

Trade name:	FANGA B+
Manufacturer's development code number(s), if appropriate:	
Product type:	TP14, Rodenticide
Composition of the product (identity and content of active substance(s) and substances of concern; full composition see confidential annex):	Brodifacoum 0.001% w/w
Formulation type:	pasta bait
Ready to use product (yes/no):	Bait ready for use (RB)
Is the product the very same (identity and content) to another product already authorised under the regime of directive 98/8/EC (yes/no); If yes: authorisation/registration no. and product name: or Has the product the same identity and 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):	YES FANGA PATE PRO

1.3.2 Information on the intended use(s)

Overall use pattern (manner and area of use):	Rodenticide against wild mice, brown rats and black rats. In and around buildings and open areas by professional and non-professional users. In waste dumps and landfills by professional users. Baits are placed in bait boxes or in secured bait stations.
Target organisms:	Scientific name: *Rattus rattus*, common name: roof rat (syn.), development stage: adults/juveniles Scientific name: *Rattus norvegicus*, common name: brown rat, development stage: adults/juveniles Scientific name: *Mus musculus*, common name: house mouse, development stage: adults/juveniles
Category of users:	Professional and non-professional users
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:	Professionals: Rat - 200 g of product / bait station; 5 to 10 meters between bait stations. Mice: - 40 g of product / bait station; 1 to 2 meters between bait stations.

	Non professional Rat - 200 g per bait station 5 -10m/bait station - 4 bait stations for non-professionals Mice: - 40 g per bait station 1-2m/bait station - 4 bait stations for professionals Do not open the sachet. The number of sachets per bait stations must be adapted to the effective dose. Respect the distance between 2 bait stations. The number of bait stations is function of the area of treatment and the infestation rate. Distances between bait stations must be respected. Inspect and refill the bait stations few days after the first application then once in a week as long as the bait is consumed. The biocidal effect appears between 4 and 9 days after ingestion of the baits
Potential for release into the environment (yes/no):	Yes
Potential for contamination of food/feedingstuff (yes/no)	Yes
Proposed Label:	Yes
Use Restrictions:	

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

1.3.3 Information on active substance

Active substance chemical name:	Brodifacoum	
CAS No:	56073-10-0	
EC No:	259-980-5	
Purity (minimum, g/kg or g/l):	950 g/kg	
Inclusion directive:	2010/10/UE	
Date of inclusion:	9 February 2010	
Is the active substance equivalent to the active substance listed in Annex I to 98/8/EC (yes/no):	yes	
Manufacturer of active substance(s) used in the biocidal product:		
Company Name:	PM TEZZA SRL	ACTIVA/PM TEZZA SRL
Address:	Via Tre Ponti 22	Via Feltre 32
City:	S. Maria di Zevio (VR)	Milan
Postal Code:	37050	20132

Country:	Italy	Italy
Telephone:	+39 02 70 63 73 01	
Fax:		Fax: 0039 02-70637228
E-mail address:	sara.lodini@activa.it	sara.lodini@activa.it

1.3.4 Information on the substance(s) of concern

There is no substance of concern. However,the product contains the preservative bronopol which is currently assessed as PT6.

1.4 Documentation

1.4.1 Data submitted in relation to product application

Identity, physico-chemical and analytical method data

Physico-chemical properties studies and analytical methods on the biocidal product FANGA B+ RONGEUR and FANGA RONGEUR PRO were provided by Triplan. Read across is acceptable (see confidential part).

A letter of access has been provided by Activa to Triplan for physico-chemical properties studies and analytical methods on the active substance.

Efficacy data

The following efficacy studies were submitted:

- A free-choice laboratory test was carried out with mice (***Mus musculus***), with exposure to a one year aged formulation of **FANGA B+** (0.001 % w/w brodifacoum) for 4 days.
- A free-choice laboratory test was carried out with rats (***Rattus norvegicus***), with exposure to a one year aged formulation of **FANGA B+** (0.001 % w/w brodifacoum) for 4 days.
- A free-choice laboratory test was carried out with rats (***Rattus rattus***), with exposure to a one year aged formulation of **FANGA B+** (0.001 % w/w brodifacoum) for 4 days.
- A free-choice laboratory test was carried out with house mice (***Mus musculus***), brown and black rats (***Rattus norvegicus*** and ***Rattus rattus***), with exposure to a fresh formulation of **FANGA B+** (0.001 % w/w brodifacoum) for 20 days.
- A field test was carried out with house mice (***Mus musculus***), with exposure to a one year aged formulation of **FANGA B+** (0.001 % w/w brodifacoum).
- A field test was carried out with brown rats (***Rattus norvegicus***), with exposure to a fresh formulation of **FANGA B+** (0.001 % w/w brodifacoum).
- 2 field tests were carried out with black rats (***Rattus rattus***), with exposure respectively to a two and three year aged formulation of **FANGA B+** (0.001 % w/w brodifacoum).

Toxicology data

The applicant submitted new toxicological data on active substance and studies for the product (see corresponding sections). A new percutaneous absorption study (*in vitro*) has been submitted by TRIPLAN for difenacoum and results were extrapolated to brodifacoum.

Residue data

No specific residue data were submitted in the context of this dossier. The product FANGA B+ is intended to be used in bait station indoor and outdoor. It will not get in contact with food or feed. Residue in food or feed are not expected. Considering the intended uses no data is required.

Ecotoxicology data

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

1.4.2 Access to documentation

As stated in the letter of access granted by Activa to Triplan:

Activa S.r.l, (via Feltre 32, Milano-Italy), as Notifier and having rights on all the data included in the Dossier for Brodifacoum (CAS No: 56073-10-0) presented by The Activa/Pelgar Brodifacoum and

Difenacoum Task Force (composed by: Activa/Tezza S.r.l and Pelgar International Ltd) for Annex I listing to RMS Italy ***authorises*** *the France competent authorities to use these data for authorisation purpose TRIPLAN (BP 258 Poste Francaise - AD500 Andorre la Vieille - PRINCIPAT D'ANDORRA) for the product* ***FANGA B+*** *(PT14).*

Please refer to the letter of access for the complete list of studies for which access has been granted.

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 FANGA B+ is Activa, source not used for annex I inclusion. According to the combined CAR (2010), the technical equivalence between Pelgar source and Activa source has been performed and accepted by Italy in August 2013 by IT.

Therefore the source ACTIVA used for the biocidal product FANGA B+ is accepted.

Refer to the confidential annex for more details.

2.2 Classification, labelling and packaging

2.2.1 Harmonised classification of the active substance

Classification - Regulation (EC) 1272/2008		
Hazard statement	Acute Tox. 1	
	Acute Tox. 2	
	STOT RE 1	
	Aquatic Acute 1	
	Aquatic Chronic 1	
Precautionary statements	H310	Fatal in contact with skin.
	H300	Fatal if swallowed.
	H372	Causes damage to organs through prolonged or repeated exposure.
	H400	Very toxic to aquatic life.
	H410	Very toxic to aquatic life with long lasting effects.

2.2.2 Classification of the biocidal product

Classification - Regulation (EC) 1272/2008	
Hazard statement	None
Precautionary statements	None

2.2.3 Labelling of the biocidal product

Labelling - Regulation (EC) 1272/2008	
Pictograms:	None
Signal words:	None
Hazard statements:	None

2.2.4 Packaging of the biocidal product

For professional users:

- 10 g and 20 g sachets in paper packed in 5-10-15-18-20 kg PE bucket or 5-10-12-15-20-50 kg carton box with PE liner

For non-professional users:

- 10 g and 20 g sachets in paper packed in PE bucket or carton box with PE liner or metal box without lacquer or HDPE containers (0.1; 0.2; 0.3; 0.4; 0.5; 0.6; 0.7; 0.8; 0.9; 1; 1.2; 1.3; 1.4; 1.5kg) or bait box in PET/PP/PE/PVC (135cm^3, 235cm^3)

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 FANGA B+ is the Activa source used for annex I inclusion according to the combined CAR (2010). Technical equivalence between Pelgar source and Activa source has been performed and accepted in August 2013 by IT.

2.3.1.2 Physico-chemical properties

Physical and chemical properties of the active substance have already been evaluated at EU level and are presented in the CAR of the active substance brodifacoum (2010). The applicant TRIPLAN has a letter of access to these data.

Source CAR 2010 (Document I):

Brodifacoum is an off-white powder at 20 °C and atmospheric pressure, with a relative density of 1.53. It was observed to darken and decompose at 235.8 °C, whereas no decomposition or transformation occurred below 150 °C.

Brodifacoum is non-volatile, with a Henry's Law Constant value of 2.35E-18 Pa.m^3.mol^{-1}. It is essentially insoluble in water at pH 5, but its solubility proved to increase with pH, due to the variation of the ionisation degree of the 4-hydroxycoumarin group in pH range under investigation (5-9). Brodifacoum also turned out to be soluble in organic solvents; results showed that solubility did not vary with temperature, except for dichloromethane.

Brodifacoum dissociation constant was estimated to be 4.50. Log Pow was found to be 4.92 at pH 7 and 20 °C. As expected, Log Pow decreased with higher temperature and pH.

Brodifacoum is not highly flammable. Besides, it does not show explosive or oxidising properties. Reaction with container materials (mild steel) has not been observed, either. All results considered, it can be concluded that brodifacoum does not exhibit hazardous physical-chemical properties.

2.3.1.3 Analytical method for determination of active ingredient and impurities in the technical active ingredient

Analytical method for the determination of pure active substance brodifacoum in the technical active substance as manufactured has already been performed and validated at EU level in the CAR of brodifacoum (2010). The applicant TRIPLAN has a letter of access to these data.

Summary: (source AR November 2010)

	Principle of method
Technical active substance as manufactured:	Brodifacoum is analysed in the technical material by reversed-phased HPLC/UV (254nm) Purity : 96.2-99.4% w/w (mean: 98.1 % w/w)

2.3.1.4 Analytical method for determining relevant components and/or residues in different matrices

Analytical methods for the determination of residues of the active substance brodifacoum in the different matrices (plants, soil, drinking, ground and surface water, human and animal body fluids and tissues) have already been performed and validated at EU level in the CAR of brodifacoum (2010). No method in air is required since the active substance is non-volatile.

Analytical methods are presented in Annex of this document.

The applicant TRIPLAN has a letter of access to these data.

2.3.2 Biocidal product

2.3.2.1 Identity, composition of the biocidal product, packaging.

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	FANGA B+	
Ingredient of preparation	Function	Content
brodifacoum (CAS No.56073-10-0)	Active substance	0.01 g/kg (0.001 %w/w)
Formulants	Details on the composition of the product are included in the Confidential part	
Physical state of preparation	solid	
Nature of the preparation	pasta	

The composition of the product is confidential and is presented in a confidential annex. The product contains 0.001% w/w of pure active substance brodifacoum.

2.3.2.2 Physico-chemical properties

The tested product is FANGA B+. Some properties have already been described for FANGA PATE PRO. Read across of the two compositions allow to accept this justification.

Table 2.3.2-1: Physico-chemical properties of the biocidal product

Properties	Method	Purity/ Specification	Results	Reference	Acceptable Yes/no
B3 – Physical, chemical and technical properties					
B3.1 Appearance					
B3.1.1 – Physical state and nature **B3.1.2 – Colour** **B3.1.3 – Odour**	Visual control	FANGA B+ 0.00938 g/kg Brodifacoum 11/308/02	Translucid greasy paper bags containing about 9-10 g piece of paste Blue sky Strong chemical odour	22776-Interim report[1]	**Acceptable**
B3.2 Acidity/alkalinity					
pH 1% dilution	CIPAC MT 75.3	FANGA PATE PRO (brodifacoum 0.0055%) Batch: 308/11/01	The pH mean value of the test item at 1% m/v in standard water D is: 5.22 at 19.4 °C after 1 min. 5.43 at 19.5°C after 2 min. 5.83 at 19.7°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.	11-920010-17[2]	**Acceptable.** **Read across is acceptable.**
B3.3 Relative density and bulk, tap density					
Relative density	EU A3 method (2008) OECD guideline 109 (1995)	FANGA PATE PRO (brodifacoum 0.0055%) Batch: 308/11/01	The relative density mean value of the test item using the gas comparison method with the stereopycnometer was: $D^{4\text{-}20°C}$ = 1.322 ± 0.001	11-920010-016	**Acceptable** **Read across is acceptable.**
B3.4 Storage stability, stability and shelf-life					
B3.4.1 Storage stability tests					

[1]De Ryckel B. 2012. Physical and chemical properties and storage stability of FANGA B+ FIRST INTERIM REPORT Analysis on the test item as received and after 14 days at 54°C ± 2°C. Centre Wallon de Recherches Agronomiques, Report 22776 of 6 September 2012, GLP.

[2]Demangel B. 2012. Physico-chemical tests and chemical stability before and after an accelerated storage procedure for 14 days at 54 ± 2 °C on FANGA PATE PRO In compliance with CIPAC MT 46.3 (CIPAC Handbook J - 2000). DEFITRACES Report 11-920010-017 of 12 March 2012.

Properties	Method	Purity/ Specification	Results	Reference	Acceptable Yes/no
B3 – Physical, chemical and technical properties					
B3.1 Appearance					
B3.4.1.1 – Accelerated storage study (2 weeks at 54°C)	CIPAC MT 46.3	FANGA B+ 0.00938 g/kg Brodifacoum 11/308/02	**Aspect** Before the accelerated storage for 14 days at 54°C: Physical state at ambient temperature: intact translucent greasy paper bags containing about 9 g of piece of paste. Colour of paste: blue sky. Odour: strong chemical odour After the procedure of storage for 14 days at 54°C: Physical state at ambient temperature: intact translucent greasy paper bags containing about 9 g of piece of paste. Colour of paste: blue sky. Odour: strong chemical odour. No modification of appearance. **Appearance and stability of the commercial type package** Before the accelerated storage for 14 days at 54°C: polypropylene bucket of 1 kg closed with a white PE lid to clip. Ø :± 19.5 cm, h : ± 13.5 cm. Well closed bucket without deterioration or special anomaly. No observable sign of test item contamination on the outer surface, no leak during shaking or turning, no noticeable odour before opening of the package. Weight =769.6 g After the procedure of storage for 14 days at 54°C: polypropylene bucket of 1 kg closed with a	22776-First Interim report	**Acceptable. Packaging (polypropylene) is stable after accelerated storage** **Acceptable Variation of brodifacoum: -6.4%** **Variations are above 5%. The applicant states that they may be due to the heterogeneity of the product and to the adsorption of the a.i on the matrix. A study is in progress to demonstrate it and is required in post authorization.** **The method used for the determination of brodifacoum is validated.**

Properties	Method	Purity/ Specification	Results	Reference	Acceptable Yes/no
B3 – Physical, chemical and technical properties					
B3.1 Appearance					
	HPLC Defitraces Report n°11-920010-019 AMD		white PE lid to clip. Ø :± 19.5 cm, h : ± 13.5 cm. Well closed bucket without deterioration or special anomaly. No observable sign of test item contamination on the outer surface, no leak during shaking or turning, no noticeable odour before opening of the package. Weight =765.9g DW= -0.5% No modification of appearance or significant pack weight change. **Quantitative analysis of Brodifacoum:** The content of Brodifacoum before accelerated storage procedure was: 0.000938% ± 0.000027% w/w. The content of Brodifacoum after accelerated storage procedure was: 0.000878% ± 0.000036% w/w. A slight change was observed (-6.4% deviation from T=0 value) after the accelerated storage procedure for 14 days at 54°C±2°C. The applicant states: FANGA B+ is a paste essentialy made of cereal. Content of active substance brodifacoum in the product is very low (0.01g/kg, 10ppm). The product is considered heterogeneous and variations of active substance content (>5%) cannot be explained as a degradation. A study is in progress to demonstrate it.		

Properties	Method	Purity/ Specification	Results	Reference	Acceptable Yes/no
B3 – Physical, chemical and technical properties					
B3.1 Appearance					
B3.4.1.1 – Accelerated storage study (8 weeks at 40°C))	CIPAC MT 46.3 HPLC Defitraces Report n°11-920010-019 AMD	FANGA B+ 0.0099 g/kg Brodifacoum 15-024	**Aspect** Before and after accelerated storage: blue paste, thermofused plastic bags in an aluminium can. No change of weight. **Active substance content** Before accelerated storage: 0.00099 After accelerated storage: 0.00096 (-3%)	Report 15-920010-005 (2015)	**Acceptable. The product is considered stable in metal can.**
B3.4.1.2 – Ambient shelf life study	Technical Monograph n°17, 2nd edition, 2009	FANGA B+ 0.00938 g/kg Brodifacoum 11/308/02	**Aspect:** Before storage: Physical state at ambient temperature: intact translucent greasy paper bags containing about 9 g of piece of paste. Colour of paste: blue sky. Odour: strong chemical odour After the procedure of storage for 16 months: No modification of appearance. After the procedure of storage for 2 years: No modification of appearance. **Appearance and stability of the commercial type package** *Before* the accelerated storage: polypropylene bucket of 1 kg closed with a white PE lid to clip. Ø :± 19.5 cm, h : ± 13.5 cm. Well closed bucket without deterioration or special anomaly. No observable sign of test item contamination on the outer surface, no leak	22776-Final report[3]	**Acceptable. The product is stable 2 years at ambient temperature in polypropylene packaging. A variation of a.i > 10% has been noted. The applicant states it is due to the heterogeneity of the product and of the adsorption of the a.i on the matrix. A study to demonstrate the variations of the active**

[3] De Ryckel B. 2012. Physical and chemical properties and storage stability of FANGA B+ - Final Report - Analysis on the test item as received after 14 days at 54°C ± 2°C and after 16 months and 2 years at 20°C ± 2°C. Centre Wallon de Recherches Agronomiques, Report 22776 of 29 April 2014, GLP

Properties	Method	Purity/ Specification	Results	Reference	Acceptable Yes/no
B3 – Physical, chemical and technical properties					
B3.1 Appearance					
	HPLC Defitraces Report n°11-920010-019 AMD		during shaking or turning, no noticeable odour before opening of the package. Mass=1183.1 g *After* the procedure of storage for 16 months: No change in the appearance of the packaging Mass (product + packaging): 1181.6 g. Difference : **-0.1%** *After* the procedure of storage for 2 years: No change in the appearance of the packaging Mass before storage for the second year: 1105.4 g Mass at sampling (product + packaging): 1105.0 g. Difference : **0.0%** **Quantitative analysis of Brodifacoum** Initial active substance content: 9.38 ± 0.27 mg/kg After the procedure of storage for 16 months: Active substance content: 8.24 ± 0.31 mg/kg Difference: **-12.1%** After the procedure of storage for 2 years: Active substance content: 7.65 ± 0.39 mg/kg Difference : **-18.4%** The applicant states: FANGA B+ is a paste essentialy made of cereal. Content of active substance brodifacoum in the product is		**substance content or an appropriate shelf life study is required in post authorization.** **The method used for the determination of brodifacoum is validated.**

<table>
<tr><th>Properties</th><th>Method</th><th>Purity/ Specification</th><th>Results</th><th>Reference</th><th>Acceptable Yes/no</th></tr>
<tr><td colspan="6">B3 – Physical, chemical and technical properties</td></tr>
<tr><td colspan="6">B3.1 Appearance</td></tr>
<tr><td></td><td></td><td></td><td>very low (0.01g/kg, 10ppm). The product is considered heterogeneous and variations of active substance content (>5%) cannot be explained as a degradation. For other product (FANGA B+ rongeur (mainly made of wheat) and FANAG B+ SOURIS RAT (mainly made of oat), variations of active substance brodifacoum with time were not linear. Therefore for these products, it can be assumed that the variations are not related to a degradation of the active substance.
A study is in progress to demonstrate it with the product FANGA B+.

<table>
<tr><td>Product tested</td><td>determination T1</td><td>determination T2</td><td>determination T3</td></tr>
<tr><td rowspan="2">FANGA B+ (pasta made of cereal mixture)</td><td>14 days</td><td>16 months</td><td>24 months</td></tr>
<tr><td>-6,4</td><td>-12,1%</td><td>-18,4%</td></tr>
<tr><td rowspan="2">FANGA B+ rongeur (cereal :wheat)</td><td>14 days</td><td>16 months</td><td>24 months</td></tr>
<tr><td>-8,8%</td><td>+0,1%</td><td>-27,8%</td></tr>
<tr><td rowspan="2">FANGA B+ SOURIS RAT (cereal : oat)</td><td>14 jrs</td><td>16 mois</td><td>24 mois</td></tr>
<tr><td>-25,4 %</td><td>+ 16,5 %</td><td>-13%</td></tr>
</table>
</td><td></td><td></td></tr>
</table>

Properties	Method	Purity/ Specification	Results	Reference	Acceptable Yes/no
B3 – Physical, chemical and technical properties					
B3.1 Appearance					
B3.4.1.3 – Low temperatures stability test (liquids)			Not applicable		**Not applicable**
B3.4.2 Effects on content of the active substance and technical characteristics of the biocidal product					
B3.4.2.1 – Light			No data provided. The active substance is sensitive to light (DT50: photolysis in water<1day). According to the label, the product must be stored away from light.		**The product must be stored away from light.**
B3.4.2.2 – Temperature and humidity	-	-			
B3.4.2.3 – Reactivity towards container material	-	-			
B3.5 Technical characteristics of the biocidal product					
B3.5.1 – Wettability	-	-	Not applicable	-	**Not applicable**
B3.5.2 – Suspensibility, spontaneity and dispersion stability	-	-	Not applicable	-	**Not applicable**
B3.5.3 – Wet sieve analysis and dry sieve test	-	-	Not applicable	-	**Not applicable**
B3.5.4 – Emulsifiability, re-	-	-	Not applicable	-	**Not applicable**

Properties	Method	Purity/ Specification	Results	Reference	Acceptable Yes/no
B3 – Physical, chemical and technical properties					
B3.1 Appearance					
emulsifiability and emulsion stability					
B3.5.5 – Disintegration time	-	-	Not applicable	-	**Not applicable**
B3.5.6 – Particle size distribution, content of dust/ fines attrition, friability	-	-	Not applicable	-	**Not applicable**
B3.5.7 – Persistent foaming	-	-	Not applicable	-	**Not applicable**
B3.5.8 – Flowability/ Pourability/ Dustability	-	-	Not applicable	-	**Not applicable**
B3.5.9 – Burning rate – smoke generators	-	-	Not applicable	-	**Not applicable**
B3.5.10 – Burning completeness – smoke generators	-	-	Not applicable	-	**Not applicable**
B3.5.11 – Composition of smoke – smoke generator	-	-	Not applicable	-	**Not applicable**

Properties	Method	Purity/ Specification	Results	Reference	Acceptable Yes/no
B3 – Physical, chemical and technical properties					
B3.1 Appearance					
B3.5.12 – Spraying pattern - aerosols	-	-	Not applicable	-	**Not applicable**
B3.5.13 – Other technical characteristics	-	-	Not applicable	-	**Not applicable**
B3.6 Physical and chemical compatibility with other products including other biocidal products with which its use is to be authorised					
B3.6.1 – Physical compatibility	-	-	Not applicable	-	**Not applicable**
B3.6.1 – Chemical compatibility	-	-	Not applicable	-	**Not applicable**
B3.7 Degree of dissolution and dilution stability					
Dilution stability	-	-	Not applicable	-	**Not applicable**
B3.8 Surface tension					
Surface tension	-	-	Not applicable	-	**Not applicable**
B3.9 Viscosity					
Viscosity	-	-	Not applicable	-	**Not applicable**
B4 – Physical hazards and respective characteristics					

Properties	Method	Purity/ Specification	Results	Reference	Acceptable Yes/no
B3 – Physical, chemical and technical properties					
B3.1 Appearance					
B4.1 – Explosives	Differential Scanning Calorimetric method (DSC). Literature survey on explosive properties and oxidizing properties of the ingredients of the product FANGA PATE PRO.	FANGA PATE PRO (brodifacoum 0.0055%) Batch: 308/11/01	One assay with four phases was performed during the test. During the first phase, one exothermic peak was observed at 243.1 °C with an enthalpy difference of 210.1 J/g which was lower than the limit of 500 J/g specified in the guideline. Neither endothermic nor exothermic peak was observed up to 500 °C under the experimental conditions used during the second phase. During the third phase, neither endothermic nor exothermic peak was observed up to 500 °C under the experimental conditions used. This thermodynamic information allows knowing that a test on explosive properties with EC A14 method should not be performed. Based on most recent approach of structural formulas, the components of the product are not classified as explosive. In addition, the DSC graph shows an exothermic effect with decomposition energy lower than 500 J/g which confirms that FANGA PATE PRO is not likely to be explosive.	11-920010-016[4]	**Acceptable. According to the composition and the DSC results, the product does not contain explosive compounds. Read across is acceptable.**
B4.2 – Flammable gases	-	-	Not applicable	-	**Not applicable**

[4] Demangel B. 2012. Physico chemical tests on FANGA PATE PRO. DEFITRACES, Report 11-920010-016 of 22 February 2012, GLP.

Properties	Method	Purity/ Specification	Results	Reference	Acceptable Yes/no
B3 – Physical, chemical and technical properties					
B3.1 Appearance					
B4.3 – Flammable aerosols	-	-	Not applicable	-	**Not applicable**
B4.4 – Oxidising gases	-	-	Not applicable	-	**Not applicable**
B4.5 – Gases under pressure	-	-	Not applicable	-	**Not applicable**
B4.6 – Flammable liquids	-	-	Not applicable	-	**Not applicable**
B4.7 – Flammable solids	EU A10 (2008)	FANGA PATE PRO (brodifacoum 0.0055%) Batch: 308/11/01	Preliminary test: the test was performed twice. Conditions of the test: Humidity: About 39% Room temperature: About 19.5 °C Atmospheric pressure: 97.9 kPa Assay 1: A consumption of the paste was observed at the contact of the flame. Neither propagation nor ignition was observed. Assay 2: The same observations as for the assay 1 were recorded. Main test: Taking in account the results obtained during the preliminary test, no main test was performed. The test item was not considered as highly flammable under the experimental conditions of the test.	11-920010-016	**Acceptable. The product is not auto-flammable and not flammable.**
B4.8 – Self-reactive substances and mixtures	-	-	No data provided.	-	**The product does not contain self reactive substances.**

Properties	Method	Purity/ Specification	Results	Reference	Acceptable Yes/no
B3 – Physical, chemical and technical properties					
B3.1 Appearance					
B4.9 – Pyrophoric liquids	-	-	Not applicable	-	**Not applicable**
B4.10 – Pyrophoric solids	-	-	Not applicable	-	**Not applicable**
B4.11 – Self heating substances and mixtures	EU A16 (2008)	FANGA PATE PRO (brodifacoum 0.0055%) Batch: 308/11/01	No self ignition temperature of the test item was observed up to 400°C (corrected value).	11-920010-016	**Acceptable. The product is not auto-flammable up to 400°C. Read across is acceptable.**
B4.12 – Substances and mixtures which in contact with water emit flammable	-	-	Not applicable	-	**Not applicable**
B4.13 – Oxidising liquids	-	-	Not applicable	-	**Not applicable**
B4.14 – Oxidising solids	Literature survey on explosive properties and oxidizing properties of the ingredients of the product FANGA PATE PRO		Based on most recent approach of structural formulas, the product does not contain oxidizing compound, or they are in low content (<1%). Accordingly, the biocidal product is not expected to present a significant hazard, and testing is considered as unnecessary.	11-920010-016	**Acceptable. According to the composition and the type of formulation, the product is not expected to have oxidizing properties. Read across is acceptable.**

Properties	Method	Purity/ Specification	Results	Reference	Acceptable Yes/no
B3 – Physical, chemical and technical properties					
B3.1 Appearance					
B4.15 – Organic peroxides	-	-	Not applicable	-	**Not applicable**
B4.16 – Corrosive to metals	-	-	Not applicable	-	**Not applicable**
B4.17 Additionnal physical indications of hazard					

Conclusion:

FANGA B+ is a paste ready-to-use rodenticide. It is presented as 10 g piece of paste in individual sachet in paper.

Considering the small changes of composition and the non-physico-chemical classification of formulants, physico-chemical properties can be considered as similar between FANGA PATE PRO and FANGA B+.
FANGA B+ is not flammable, not autoflammable, has no explosive properties and no oxidizing properties. No change appeared in the appearance of the biocidal product or the packaging after storage procedures for 14 days at 54°C and 2 years at ambient temperature in polypropylene and metal box packaging. The product is therefore compatible with all claimed packaging.

The active substance content was considered as stable after accelerated storage procedure. A decrease in active substance content was observed after 2 years of storage (- 18.4%). The variation of active ingredient can be due to the heterogeneity of the product. A study to demonstrate that the variations of brodifacoum content in the product after storage 2 years are not due to a degradation of the active substance or a new storage stability study including intermediate results is required in post authorization.

The active substance is sensitive to light. Therefore, the product must be stored away from light.

FANGA B+ is not classified for physico-chemical properties.

Shelf life: 2 years based on the results of the accelerated storage stability results

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

Analytical method for the determination of brodifacoum in the product has been provided.
Principle of the method: brodifacoum is analyzed after extraction from the product with methanol, filtered and quantified by reverse phase HPLC-UV.

Chromatographic conditions:
Colum: Zorbax SB Phenyl, length: 25cm, internal diameter: 3.0mm, granulometry: 5.0µm, Agilent.

Detector: UV, 265nm.
Mobile phase: Eluent A acetonitrile, Eluent B water/acetic acid 34/1.

Time (min)	Eluent% A	Eluent %B	Rate (mL/min)
0	70	30	1.0
15	70	30	1.0

Rate: 1(mL/min).
Oven temperature: 30°C.
Volume injected: 20µL.
Retention times (min): 4.9 for brodifacoum I and 5.4 for brodifacoum II.

Linearity was performed with 5 calibration standards, prepared in methanol, from 0.51to 1.50mg/L. The same linearity was used for the determination of active substance in the product FANGA PATE PRO and FANGA BLOC SP PRO.

Precision was performed by analyzing twice five samples of FANGA BLOC SP PRO. The extraction is the same as for FANGA PATE PRO.

Specificity and accuracy were performed with the formulation FANGA PATE PRO:
Test item: FANGA PATE PRO, Batch 308/11/01.
Blank formulation: (FANGA PATE PRO): Batch 311/11.
Reference item : brodifacoum, purity 99.3%, batch SZB8324XV (supplier: SIGMA Aldrich).

Results are summarized in the following table.

Table 2.3.2-2: Analytical method for the determination of brodifacoum (reverse phase HPLC-UV)

Sample	Test substance	Analytical method	Fortification range/ number of measurements	Linearity	Specificity	Recovery rate (%)	Repeatability			Reference
						range	Mean	St dev.		
FANGA PATE PRO Batch 308/11/01 Blank formulation Batch 311/11	Brodifacoum	reverse phase HPLC-UV	Fortification levels: reconstituted sample at 1 concentration level (0.005%, 1mg/L in solution after dilution) two samples prepared and analysed in duplicate	0.51-1.50mg/L Y= 1.4717x - 0.09 R^2=0.9965	No interference observed	100-102% two reconstituted sample in duplicate at 0.005% of active substances (1mg/L)	101%	SD: 0.8 RSD: 0.8 %	5 samples (FANGA BLOC PRO) in duplicate Mean: 0.0045% (w/w) SD:0.0001 RSD: 2.90% Horwitz value: 6.04	RICAU hélène, report No. 11-920010-015, May 2012 RICAU Hélène, report No. 11-920010-019, May 2012

Chromatograms were provided for the formulation blank, reference item and test item (at 0.005%). No interference has been observed at the retention time of brodifacoum. Specificity of the method is acceptable.

Linearity has been demonstrated with 5 calibration standards.
According to Sanco/3030/99 rev.4, recoveries should be between 80-120% for active substances with nominal content below 0.01%. Accuracy is acceptable.
RSD is below Horwitz value. Repeatability is acceptable.
It is concluded that the provided method is validated and acceptable for the product FANGA PATE PRO.

Extrapolation with FANGA B+
Specificity of the method with the formulation FANGA B+ has been demonstrated in the report CRA-W Study n° 22776. Chromatograms of the blank formulation, calibration standard and test item have been provided. No interference at the retention time of brodifacoum was observed. Nevertheless, a complementary analytical method for the determination of brodifacoum in FANGA B+ by definition of the accuracy of the method was required since the content of brodifacoum is lower (0.001%w/w) than in FANGA PATE PRO.

Additional validation data on accuracy were provided in report No. R15-920010-004. A blank formulation of FANGA B+ was fortified with brodifacoum at a content of 0.001% (10ppm). Two samples were prepared and injected twice. Mean recovery was 98%. Results are in acceptable range (80-120%). The method is considered suitable for the determination of brodifacoum in the product FANGA B+.

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

A letter of access has been provided by Activa to TRIPLAN for analytical methods in the different matrices.
The analytical methods for determination of residues of active substance in different matrices (soil, air, drinking and surface water, body fluids and tissues, in food and feedstuff) provided in the CAR of the active substance are presented in annex of this document.
Since there is no risk of contact with alimentation, no analytical method is required for the determination of brodifacoum residues in food and feedstuff.

2.4 Risk assessment for Physico-chemical properties

FANGA B+ is a ready-to-use paste bait. The product is not flammable, not auto-flammable (up to 400°C), not explosive and does not have oxidizing properties.

The product is stable 14 days at 54°C and 2 years at ambient temperature in polypropylene packaging and 8 weeks at 40°C in metal can. Therefore, the product is considered compatible with all claimed packaging.

Variations of active substance in the product are higher than 10 % and can be due to the heterogeneity of the product. A study to demonstrate that the variations of brodifacoum content in the product after storage 2 years are not due to a degradation of the active substance is required in post authorization. Alternatively, an appropriate long term storage stability study could be provided.

Risk mitigation measures linked to assessment of physico-chemical properties
- Store away from light.

Required information linked to assessment of physico-chemical properties
A study to demonstrate that the variations of brodifacoum content in the product after storage 2 years are not due to a degradation of the active substance or a new storage stability study including intermediate results is required in post authorization.

2.5 Effectiveness against target organisms

Function: MG 03: Pest Control.
Product Type 14: Rodenticide.

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

According to the uses claimed by the applicant, the product FANGA B+ is intended to be used to control rats and mice. The target organisms to be controlled are *Mus musculus*, *Rattus norvegicus* and *Rattus rattus*.

FANGA B+ is used in and around buildings, and in open areas by professional and non-professional users, in waste dumps by professional users only.

The products, organisms or objects to be protected are public and private buildings, farms, opens areas and waste dump sites.

The application rates recommended by the applicant are the following (see also Annex 0a):

- Rats: 180-200 g /secured bait point separated by 5-10 m.
- Mice: 30-40 g /secured bait point separated by 1-2 m.

2.5.2 Effects on target organisms and efficacy

The applicant submitted the following studies, all performed with the product FANGA B+ (0.001 % w/w brodifacoum):

Efficacy and palatability laboratory studies

- Study n° ROD 201201:

This trial has been conducted with a fresh formulation of **FANGA B+** (0.001 % w/w brodifacoum).

For house mice (*Mus musculus*), the mean palatability percentage is very low with 14 % and the mortality percentage is 100 % within 6 to 15 days.
For brown rats (*Rattus norvegicus*), the mean palatability percentage is very low with 14 % and the mortality percentage is 100 % within 5 to 10 days.

For black rats (*Rattus rattus*), the mean palatability percentage is 27 % and the mortality percentage is 100 % within 6 to 21 days.

It has to be noted that the duration of exposure was 20 days instead of 4, and palatability was under the criteria of 20 % according tot he TNsG on product evaluation for rodenticides. Therefore, others tests have been performed to prove the efficacy of the product FANGA B+

- Study n°: 12-TOX024-4:

This trial has been conducted with a one year aged formulation of **FANGA B+** (0.001 % w/w brodifacoum).
For house mice (*Mus musculus*), the mean palatability percentage is 61 % and the mortality percentage of 100 % within 3 to 9 days.

- Study n° 12 TOX024-3:

This trial has been conducted with a one year aged formulation of **FANGA B+** (0.001 % w/w brodifacoum).
For brown rats (*Rattus norvegicus*), the mean palatability percentage is 43 % and the mortality percentage is 90 % within 4 to 6 days.

- Study n° 13 TOX025:

This trial has been conducted with a one year aged formulation of **FANGA B+** (0.001 % w/w brodifacoum).

For black rats (*Rattus rattus*), the mean palatability percentage is 59 % and the mortality percentage is 100 % within 3 to 10 days.

Field studies:

- Study n°13TOX019:

This trial has been conducted in a farm in France with a fresh formulation of **FANGA B+** (0.001 % w/w brodifacoum).
For house mice (*Mus musculus*), the assessed bait has been very well accepted and the efficacy is estimated at 100 %.

- Study n°13TOX020:

This trial has been conducted in a farm in France with a fresh formulation of **FANGA B+** (0.001 % w/w brodifacoum).
For brown rats (*Rattus norvegicus*), the assessed bait has been very well accepted and the efficacy is estimated at 100 %.

- Studies n°2008.BCD.SAG13 and 2001.BCD.SAG15

These trials have been conducted in a farm in Italy with respectively a two and a three year aged formulation of **FANGA B+** (0.001 % w/w brodifacoum).
For black rats (*Rattus rattus*), the assessed bait has been very well accepted and the efficacy is estimated at 100 %.

French competent authorities (FR CA) consider that the elements presented in the dossier are sufficient to demonstrate the efficacy of the product against mice (*Mus musculus*) and rats (*Rattus norvegicus* and *Rattus rattus*).

All efficacy studies are presented in annex 9.

2.5.3 Mode of action including time delay

Brodifacoum acts as a vitamin K 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.

Brodifacoum works by blocking the regeneration of vitamin K 2,3-epoxide to vitamin K hydroquinone. Since the amount of vitamin K in the body is finite, the progressive block of the regeneration of vitamin K will lead to an increasing probability of a fatal haemorrhage.

Taking into account the results of the submitted laboratory studies, death of target animals occurs 3 to 21 days after ingestion.

2.5.4 Occurrence of resistance – resistance management / Unacceptable Effect

Resistance to the first generation anticoagulants has been widely reported in both *Rattus norvegicus* and *Mus domesticus* since the late 1950's. The incidence of resistance to first generation anticoagulants in areas in which it is established is commonly 25-85%. 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[5]; Lund, 1984[6]; Pelz *et al*. 1995[7]). The resistance factor tells how much the anticoagulant dose has to be multiplied to kill resistant

[5]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
[6] 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
7 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

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[8]). 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[9]).

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

2.5.5 Evaluation of the Label Claims

French competent authorities (FR CA) assessed that the product FANGA B+ has shown a sufficient efficacy for the control of *Rattus norvegicus, Rattus rattus* and *Mus musculus*.

<u>The application rates validated are the following:</u>

[8] 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.
9 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

- Rats (*Rattus norvegicus* and *Rattus rattus*): 180-200 g /secured bait point separated by 5-10 m.
- House mice (*Mus musculus*): 30-40 g/secured bait point separated by 1-2 m.
- Bait points should be controlled and resupply as long as the bait is consumed:
    - 3 days after the first application then weekly for use in and around building and open areas;
    - 1 week after the first application then monthly for use in waste dump.

The product FANGA B+ is supplied in sachets of different amounts. The applicant has to adapt the sachets sizes to the efficient doses. The amount of bait per bait station or bait points must not exceed the recommended application rates.

2.5.6 Summary of efficacy assessment

French competent authorities (FR CA) assessed that the product product FANGA B+ SOURIS RAT has shown a sufficient efficacy for the control of *Rattus norvegicus, Rattus rattus and Mus musculus*, in and around building, , in open areas and in waste dump.

Conditions of use linked to efficacy assessment (professional users)
- Adapt the number of bait stations to the infestation level.
- Products have always to be used in accordance with the label.
- Inspect and resupply the bait stations as long as the bait is consumed:
    - 3 days after the first application then weekly in and around building and in open areas.
    - 1 week after the first application then monthly for use in waste dump.
- Remove all bait stations after the end of treatment.
- The amount of bait per bait point and distances between bait points must be respected.
- The users should inform is 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.

Conditions of use linked to efficacy assessment (non-professional users)
- 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.
- Inspect and resupply the bait stations as long as the bait is consumed, 3 days after the first application then weekly, in and around building and in open areas.
- Remove all bait stations after the end of treatment.
- 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.

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.

Required information linked to efficacy assessment
- The authorisation holder has to monitor the resistance phenomenon of rodent populations toward the active substance brodifacoum, and resistance strategies management must be put in place. Results of the resistance monitoring must be submitted to the Competent Authorities (CA) or other appointed bodies involved in resistance management every 2 years.

2.6 Description of the intended use(s)

The product FANGA B+ is intended to be used for the control of rats (*Rattus rattus* and *Rattus norvegicus*) and mice (*Mus musculus*) in and around buildings, and in open areas by professional and non-professionnal users; in waste dumps by professional users only.

The application rates validated are the following:

- Rats (*Rattus norvegicus* and *Rattus rattus*): 180-200 g /secured bait point separated by 5-10 m.
- House mice (*Mus musculus*): 30-40 g/secured bait point separated by 1-2 m.

The product is a ready-to-use paste bait with no dilution nor other substances added for application. The mode of application claimed by the applicant is a manual application in secured bait stations.

2.7 Risk assessment for human health

2.7.1 Hazard potential

2.7.1.1 Toxicology of the active substance

The toxicology of the active substance was examined extensively according to standard requirements.
The results of this toxicological assessment can be found in the **combined** AR.

Brodifacoum (CAS no. 56073-10-0) was notified as an existing active substance, by Syngenta Limited and Activa / Pelgar brodifacoum and difenacoum Task Force, hereafter referred to as the applicants, 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 brodifacoum.

A (data from Syngenta) and B (data from Activa/PelGar)

- **Toxicokinetics**

A:
Brodifacoum (0.21 mg/kg bw) administered orally to rats was rapidly absorbed (T_{max} =8h; C_{max} 16.1 ng/ml whole blood). The levels declined slowly and about 10% (1.3 ng/ml) was still present at 10 days after dosing. Almost all (82.5 %) the radioactivity in whole blood was found to be associated with the plasma. Based on the radioactivity still associated to the animal tissues, 10 days after the treatment, the **oral absorptionwas >75 %.** After a single oral dose of 10 mg/kg of *Brodifacoum* about 64.0% was absorbed and could be accounted for in the liver, carcass and bile 48h after dosing. The rest was recovered in the faeces, as unabsorbed material.

After absorption the product was widely distributed. 10 days after dosing the proportion of the retained dose was highest in the liver (22.8 %), followed by the pancreas (2.3 %), and then the kidney (0.8 %), heart (0.1 %) and spleen (0.2 %). The remainder of the dose (≅50%) was in the carcass and skin.
Brodifacoum was only partially metabolised. 31.3% and 19.6% of the residues in the carcass and liver, respectively, was unchanged *Brodifacoum*. Two more polar metabolites were detected in the bile, the major one being identified as the glucuronide.

Brodifacoum shows a high potential for bioaccumulation: in all studies undertaken and at all dose levels tested, the liver retained the largest % of the dose, even very long time after dosing.
Analyses of the rat livers from the 90 day feeding study, indicate a non-linear accumulation of *Brodifacoumvs* dose and time.

A small amount (11 – 14%) of the radioactivity was slowly eliminated in urine and faeces over 10 days following a single oral dose of 0.25 mg/kg. Biliary and renal routes are of equal significance in the elimination of *Brodifacoum*. The rate of elimination as given by the biological half-life, was calculated to be 150 – 200 days.

The elimination from the liver was biphasic at higher doses. There was a rapid phase (days 1-4) which also corresponded to a reduction in clotting factor synthesis, followed by a slower terminal phase (days 28-84) during which blood clotting function was normal. The half-life of elimination from the liver during

the rapid and the slow phase was ≅4 and 128 days, respectively. At low dose levels, clotting factor synthesis was unaffected indicating that probably only the slow elimination phase was present in the liver. The half-life of *Brodifacoum* in the liver was calculated in the range of 282-350 days.

Dermal absorption was assessed by using a formulation (ready-for-use pellet bait) containing 0.0048% *Brodifacoum* w/w tested in vitro test on human skin samples. Over the entire 24 h exposure *Brodifacoum* (determined by LC-MS-MS) was found below the LOQ in the receptor fluid (<3.53% of the applied dose) and in the epidermis (<1.64%), after tape stripping. The applied dose was readily removed by mild skin washing and recovered (108 ±6.25%) in the washing fluid. **A 'surrogate value' of 5% dermal absorption was calculated** by summing up the amount in the receptor fluid and in the epidermis after tape stripping, which can be considered as systemically available material. This value has been taken forward to the risk characterization as the worst case, also taking into account that the exposure period exceeds the usual time (*i.e.* 8 hours) of professional handling.

B:
Read across to data from some related 2nd generation anticoagulants (*i.e.Difenacoum*, *Flocoumafen*) is requested for ADME data, including dermal absorption, and has been applied for other end-points by the RMS.

Beside the similar mode of action, the read across is supported by bridging studies demonstrating the similarity in physico-chemical and toxicological properties of these substances which are presented up-front to Doc. IIA- Section 3.

Anticoagulant rodenticides including *Brodifacoum* are rapidly absorbed via the gastro-intestinal tract and oral absorption is assumed to be 100 %, on the basis of amount of radioactivity recovered in the excreta and retained in the tissues. The major route of elimination after oral administration is via the faeces, both as polar metabolites and parent compound. *Brodifacoum* is widely distributed and bioaccumulates in the liver with minor concentrations in the kidney.

Elimination processes are very slow with 50-75 % of the administered dose being retained in the liver ($t_{1/2}$ for hepatic residues more than 200 days).

The metabolism of *Brodifacoum* is limited, although in repeated dose studies evidence of induction of metabolism was reported, with increasing levels of radioactivity associated to polar metabolites recovered in the urine. The toxicologically relevant chemical species is the parent compound.

No study on dermal absorption of *Brodifacoum* has been presented. *Brodifacoum* is expected to be slowly absorbed through the skin, due to the lipophylicity of the molecule, allowing passive transport through the membrane. The read across principle can be applied, based on the close structural relationship, the similar physico-chemical properties and the same mode of action displayed by *Brodifacoum* towards other 2nd generation anticoagulants, such as *Difethialone* and *Difenacoum*. A dermal absorption value =4% has been adopted for *Difethialone*, whereas in the case of *Difenacoum* twodifferent values have been used for risk characterisation depending on the type of formulation, that is 3% (pellets and grains) or 0.047% (wax block bait).

In the CAR, by applying the read across from data on a structurally related 2nd generation anticoagulant *Difenacoum*, a 3% dermal absorption value was adopted for the exposure calculation (below reported under Section 2.2.1.8). This value was calculated from a dermal absorption study testing a pellet formulation containing *Difenacoum* as active substance.

Conclusion on toxicokinetics: An almost complete oral absorption can be considered, on the basis of amount of radioactivity recovered in the excreta and retained in the tissues. *Brodifacoum* is widely distributed and bioaccumulates mainly in the liver with lower concentrations in the kidney. Hepatic bioaccumulation of *Brodifacoum* is a non-linear *vs* dose and time. The elimination kinetic from the liver was biphasic, with an half-life in the range of 282-350 days. The excretion after oral administration is very slow (11 – 14% in 10 days), occurring via the urine and the bile, both as polar metabolites (glucuronide) and parent compound. The metabolism of *Brodifacoum* is limited and the toxicologically relevant chemical species is the parent compound.

Concerning the dermal absorption value to be used in the risk characterization for wax block bait, in the Combined Assessment Report for d*ifenacoum* (September 2009) a value of 0.047% was proposed. Therefore, on the basis of the available study and reading across from data on other 2nd generation anticoagulant rodenticides, two different values should be used for risk characterization depending on the type of formulation: 5% (pellets and grains) or 0.047 % (wax block bait).

- **Acute effects**

A:
Brodifacoum was very toxic to rats and mice with similar oral LD_{50} of about 0.4 mg/kg bw to the male rat and mouse. *Brodifacoum* is also acutely toxic by the dermal and inhalation routes. Death was the result of internal haemorrhage.
Brodifacoum does not fulfil the EU criteria for classification as a skin or eye irritant, but is able to cause skin sensitization in guinea pig and fulfils the EU criteria for classification as a skin sensitizer.

B:
Brodifacoum is very toxic if swallow (oral LD_{50}<5 mg/kg bw) or in contact with skin (dermal LD_{50}= 7.48 mg/kg bw in rat females; even lower in males).

The waiving for the inhalation toxicity study has been accepted due to low vapour pressure of *Brodifacoum* and data on dustiness and particle size, indicating that the potential for inhalation is limited in addition to ethical and animal welfare reasons. However, based on data with structurally related compounds with the same mechanism of action (*i.e.* 2nd generation anticoagulants), it is expected that the substance is also highly toxic after inhalation.

Brodifacoum is not irritant to the skin or eyes of rabbits and showed no sensitizing potential in a LLNA study in mice.

Conclusion on acute effects: *Brodifacoum* is very toxic after oral administration and also via the dermal and inhalation routes. Death was the result of internal haemorrhage. Classification with T+; R26/27/28; 'Very toxic by inhalation, in contact with skin and if swallowed' is warranted.

Brodifacoum does not fulfil the EU criteria for classification as a skin or eye irritant. Although showed no sensitizing potential in a LLNA study in mice, it was able to cause skin sensitization in guinea pig and fulfils the EU criteria for classification as a skin sensitizer.

- **Repeated Dose Effects**

A:
Repeated dose oral studies show that in the rat and in the dog, the clinical signs, haematological and post mortem data were consistent with the known pharmacological action of *Brodifacoum*: impairment of the clotting cascade and increased prevalence of haemorrhage leading to death. There were no indications of other secondary toxicities: any of the other parameters including histopathological analysis revealed no treatment related alterations.

The subchronic 90-day oral toxicity allowed the derivation of the lowest repeated toxicity NOEL= 0.001 mg/kg bw/day. In this study, no treatment related effects on haematological parameters were evidenced at any dose, after 45 days, but statistically significant increases in both the kaolin-cephalin time (KCT) and the prothrombin time (PT) were measured at the highest dose level, 0.004 mg/kg bw/day after 90 days. Based upon this effect on prothrombin times and based on haemorrhagic changes seen at necropsy, the NOEL was set at the next lowest dose, 0.001 mg/kg bw/day.

Classification with T; R48/23/24/25 "Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed" is warranted based on these data plus extrapolation from the acute data for the dermal and inhalation route of exposure.

B:
Repeated oral exposure to *Brodifacoum* resulted in clinical signs and toxicity consistent with the mode of action of the rodenticide and its properties of anti-coagulant agent (lethal haemorrhages). The overall NOAEL for subchronic oral toxicity is 0.04 mg/kg/day.

No data have been submitted on dermal repeated toxicity On the basis of both physico-chemical properties and b*rodifacoum* mode of action it can be anticipated that subchronic effect due to prolonged skin contact should not be disregarded.

No data on repeated inhalation toxicity have been submitted. As indicated by the low vapour pressure, dustiness and particle size, the potential for inhalation is low and the request for a repeated dose inhalation toxicity study is not considered justified also based on ethical and animal welfare reasons.
However, based on the results of the acute dermal and inhalation toxicity studies, route-to-route extrapolation, consistently with the decision adopted for *Difenacoum* (being the read across accepted for other end-points), it is justified to assume a similar concern for serious damage to health by prolonged exposure through dermal and inhalation routes also.

- **Genotoxicity**

A:
Brodifacoum was tested in *Salmonella typhimurium* strains TA 1535, TA 1537,TA 98, TA 100, TA 1538. with and without S9-mix, up to 5000 mg/plate, with negative results. No clastogenic activity was observed in the *in-vitro* cytogenetic assay in human lymphocytes, performed with and without metabolic activation, up to cytotoxic doses. The *in vitro* mammalian cell mutation assay in mouse lymphoma L5178Y cells also resulted negative, with and without S9-mix, while cytotoxic effects was observed at the highest doses. The applicants submitted also an *in vitro* UDS test and in an *in vitro* cell transformation assay, but because of several methodological and reporting shortcomings, they were considered of limited scientific significance. An *in vivo* mouse micronucleus test gave negative results. The studies submitted were rather dated, therefore they were not always compliant with the current guidelines. However a genotoxic potential of the active substance can be reliably ruled out.

B:
Brodifacoum was tested for genotoxic activity in the bacterial reverse mutation test in *Salmonella thyphimurium* in strains TA 98, TA 100, TA 102, TA 1535 and TA 1537, up to 5000 g/plate, with and without metabolic activation (S9-mix). No genotoxic activity was observed in any bacterial strain. The substance resulted negative up to cytotoxic concentration also in the gene mutations assay in L5178Y mouse lymphoma cells, with and without S9-mix, and in the *in vitro* mammalian chromosome aberration test in human lymphocytes (50% mitotic inhibition at the maximum dosage tested).

- **Carcinogenicity/chronic toxicity**

A, B:
Carcinogenicity and long-term toxicity studies were waived as infeasible and unnecessary.

- **Reproductive and developmental toxicity**

A:
Brodifacoum did not induce developmental effects in two adequate prenatal toxicity studies in the rat and rabbit, respectively.

In particular, in the rat studies maternal hemorrhages were observed at dose levels > 0.01 mg/kg bw (NOEL 0.001 mg/kg bw) whereas no effects on conceptuses were detected up to the top dose level of 0.02 mg/kg bw. In the rabbit study, the top dose of 0.005 mg/kg b.w caused a high proportion of maternal deaths, whereas no significant effects on litters were observed. In spite of these findings, a provisional decision has been made at the Technical Meeting of Classification and Labelling that [R61] should be applied to all anticoagulant active substances on the basis of analogy to *Warfarin*.

B:
There was no evidence of developmental toxicity effects up to the dose levels of 0.04 and 0.004 mg/kg bw in rats and rabbits, respectively. In rabbit dams an increase in kaolin-cephalin and prothrombin time was present at 0.004 mg/kg bw (NOAEL 0.002 mg/kg).

Whereas it is suggested that two-generation studies may not be need for anticoagulant rodenticides, a two-generation study on rat was submitted: findings confirmed those of developmental toxicity, both qualitatively (parental toxicity with haemorrhages, no reproductive or developmentakl effects in the absence of general toxicity) and quantitatively (NOAEL: 0.001 mg/kg bw).

Since the conventional OECD Guideline 414 may have limitations in the detection of possible developmental effects of coumarin related compounds, and in spite of these findings, a provisional decision has been made at the Technical Meeting of Classification and Labelling that [R61] should be applied to all anticoagulant active substances on the basis of analogy to *Warfarin.*

- **Neurotoxicity**

A:
None of the acute or subchronic performed tests gave any indication for a potential neurotoxic effect of

Brodifacoum
B:
The toxicological studies do not indicate any neurotoxic effects.

Conclusion on repeated dose effects: Repeated oral exposure to b*rodifacoum* resulted in clinical signs and toxicity consistent with the mode of action of the rodenticide and its properties of anti-coagulant agent (lethal haemorrhages). The NOEL for subchronic oral toxicity is in the range 0.04 -0.001 mg/kg/day (the lowest values identified with sensitive end-points, such as increases in both the kaolin-cephalin time and the prothrombin time). Based on results from the acute dermal and inhalation toxicity studies, route-to-route extrapolation, consistently with the decision adopted for b*ifenacoum*, it is justified to assume serious damages associated to prolonged exposure through dermal and inhalation routes also. Therefore, classification with T; R48/23/24/25 "Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed" is warranted.

Conclusion on Genotoxicity and Carcinogenicity: *brodifacoum* displayed no mutagenic activity in a standard range of genotoxicity tests. No long-term carcinogenicity study was submitted by the two applicants. In fact, chronic toxicity studies were not considered to be technically feasible due to the specific action of the active substance on the test/target species. However, the anticoagulant action is apparently the only pharmacological action of *brodifacoum*. The active substance has no structural alerts for carcinogenicity and no concern about possible non-genotoxic carcinogenic potential can be derived from the toxicological studies. Therefore the justifications of both the applicants for not-submission of carcinogenicity data was considered acceptable.

Conclusion on Reproductive toxicity: Reproductive and developmental toxicity studies on *brodifacoum* did not reveal any specific effects. General toxicity effects were consistent with the mode of action of the rodenticide and its properties of anti-coagulant agent. The lowest NOAELs for rabbits and rats were 0.002 and 0.001 mg/kg bw.

In spite of these findings, a provisional decision has been made at the Technical Meeting of Classification and Labelling that [R61] should be applied to all anticoagulant active substances on the basis of analogy to *Warfarin*.

None of the acute or subchronic performed tests gave any indication for a potential neurotoxic effect of *Brodifacoum*.

The harmonised classification of the active substance is the following:

Classification under directive 67/548/EEC	Classification under regulation (EC) 1272/2008
T+ R27/28 T ;R48/24/25 No specific limit concentrations	Acute Tox1 H310 Acute Tox 2 H300 STOT RE Cat 1 H372 No specific limit concentrations

The following corresponds to the summary of the derivation of the AELs from the combined Assessment Report of brodifacoum:

A: The Acceptable Exposure Level for acute exposure (AEL_{acute}) was based on the maternal NOEL from developmental study of 0.001 mg/kg bw/day (rat, maternal effect). A safety factor of 300 (10 for intra-

species variability x 10 for inter-species variability x 3 additional factor for severity of effects). The AEL_{acute}resultsto be of 3.3 x 10^{-6} mg/kg/day.

The Acceptable Exposure Level for repeated exposure (AEL_{chr}) was based on a subchronic NOEL from a 90-day oral rat study of 0.001 mg/kg bw/day. A safety factor of 300 (10 for intra-species variability x 10 for inter-species variability x 3 additional factor for severity of effects). The AEL_{chr} resultsto be of 3.3 x 10^{-6} mg/kg/day.

B: The Acceptable Exposure Level for acute exposure (AEL_{acute}) was based on NOAEL from a developmental study(female rabbit) of 0.002 mg/kg bw/day. A safety factor of 300 (10 for intra-species variability x 10 for inter-species variability x 3 additional factor for severity of effects). The AEL_{acute}resultsto be of 6.7 x 10^{-6} mg/kg bw/d.

The Acceptable Exposure Level for repeated exposure (AEL_{chr}) was based on NOAEL for females from the reproductive 2-generation study in rat of 0.001 mg/kg bw/day. A safety factor of 300 (10 for intra-species variability x 10 for inter-species variability x 3 additional factor for severity of effects). The AEL_{chr} resultsto be of 3.3 x 10^{-6} mg/kg bw/day.

TMIII09 agreed to derive $AEL_{medium\ term}$ consistently with what decided for the other AVK rodenticides. Therefore, $AEL_{medium\ term}$ was calculated from the NOAEL of 0.002 mg/kg bw/day (developmental oral toxicity study in rabbit) divided by an Assessment Factor of 300 (10 for interspecies x 10 for intraspecies x 3 additional factor for severity of effects). The $AEL_{medium\ term}$ results to be of 6.7 x 10^{-6} mg/kg bw/day.

Conclusions:

The following AELs should be considered in the risk characterization for *brodifacoum*:

- $AEL_{acute\ and\ medium\ term}$of 6.7 x 10^{-6} mg/kg bw/day based on the NOAEL from a developmental study(female rabbit) of 0.002 mg/kg bw/day;
- AEL_{chr} of 3.3 x 10^{-6} mg/kg bw/day based on the NOAEL for females from the reproductive 2-generation study in rat of 0.001 mg/kg bw/day.

2.7.1.2 Toxicology of the substance(s) of concern

The biocidal product FANGA B+ contains no substances of concern.

2.7.1.3 Toxicology of the biocidal product

The toxicology of the biocidal product was examined appropriately according to standard requirements. The product was a dummy product in the EU- review program for inclusion of the active substance in Annex I of Directive 98/8/EC.
The basis for the health assessment of the biocidal product is laid out in Annex 5 ”Toxicology – biocidal product”

Acute oral and dermal toxicity, skin and eye irritation and skin sensitisation studies have been realized with the product FANGA BLOC SP PRO, a block formulation containing 0.005% of brodifacoum. The compositions of FANGA BLOC SP PRO and FANGA B+ are considered similar.

2.7.1.3.1 Percutaneous absorption

A default value of 0.047% was considered for product containing 0.005% of brodifacoum, as mentioned in the brodifacoum assessment report. This value has been considered relevant for the product FANGA B+ containing 0.001%. Indeed, no major increase in the dermal absoprtion value is expected with such very low concentrations of active substance in products and considering that the concentrations are in the same order of magnitude.

2.7.1.3.2 Acute toxicity

Oral route
No mortality occurred during the study (daily examination during 14 days).
No clinical signs related to the administration of the test item were observed.
The body weight evolution of the animals remained normal throughout the study.
The macroscopically examination of the animals at the end of the study did not reveal treatment-related changes.
LD50 of the test item is higher than 2000 mg/kg/bw.

Route	Method	Species	Dose level	LD50
Oral	OECD 423	Rat 3 males and 3 females	2000mg/kg bw	>2000 mg/kg bw

Dermal route

No mortality occurred during the study.
The body weight evolution of the animals remained normal throughout the study.
Neither cutaneous reactions nor systemic clinical signs related to the administration of the test item were observed.
The macroscopically examination of the animals at the end of the study did not reveal treatment-related changes.

LD50 of the test item is higher than 2000 mg/kg/bw.

Route	Method	Species	Dose level	LD50
Dermal	OCDE 402	Rat 5 males and 5 females	2000 mg/kg bw	>2000 mg/kg bw

Based on the above-mentioned results, no classification is required for FANGA B+.

2.7.1.3.3 Irritation and corrosivity

Based on the results of the irritation assays on rabbit's skin and eye, no classification is required for FANGA B+.

Route	Method	Species	Dose level	
skin	OECD 404	Rabbit NZ 3 females	0.5 g	No irritant
eye	OCDE 405	Rabbit NZ 3 females	0.1 g	No irritant

2.7.1.3.4 Sensitization

Based on the results of the irritation assays on rabbit's skin and eye (LLNA), no classification is required for FANGA B+.

Route	Method	Species	Dose level	
skin	OECD 429	Mice16 (12 for the treated groups)	Topical way of induction: 5, 10, 25% of the test item	No skin sensitizing

2.7.1.3.5 Other studies

No other studies are performed on FANGA B+

2.7.2 Human exposure assessment

FANGA B+ (PT14) is a ready-to-use rodenticide containing 0.001 % of brodifacoum (pure: 950 g/kg). Baits are packaged in bulk and in sachet for professional users, only in sachet for non professional users.The baits are placed in bait stations (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

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

Table 2.7.2-1: Main paths of human exposure
:

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

2.7.2.2 Direct exposure as a result of use of the active substance in biocidal product

2.7.2.2.1 Exposure of professional users

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

FANGA B+ is used for the control of rats and mice for use indoor and outdoor, with the purpose of protecting human food and animal feedstuffs, and for human hygiene.
The product is only supplied in sachets. Considering the nature of sachet (paper), a dermal exposure during loading is taken into account. Exposure assessment has been realized with the dose of 200 g of product for the control of rats. This assessment covers the assessment for mice as the intended doses are lower.

Based on the CEFIC study and taking into account the *HEEG opinion on an harmonised approach for the assessment of rodenticides (anticoagulants)* agreed at TMII2011, the amount of product on fingers/hands **during the loading** of 5 wax blocks of 20g per one manipulation was 27.79 mg. The following parameters were taken into account:

- active substance in product: 0.001 %,(w/w);
- Number of blocks per bait site[10]: 20 for control of rats
- dermal absorption: 0.047 %,
- body weight: 60kg.

Thus, the systemic dose of brodifacoum per placing of one bait site is $8.7x10^{-9}$mg/kg bw/event for control of rats and mice (because the amount of disposed bait is not taken into account).

The harmonized number of manipulations for rodenticides anticoagulant set in the HEEG opinion agreed at TM III 2010 was used to assess the overall exposure systemic dose. Considering 60loading are done per day, the systemic dose via skin is 5.2 $x10^{-7}$ mg a.s/kg bw/day for the control of rats.

Based on the CEFIC study and taking into account the *HEEG opinion on an harmonised approach for the assessment of rodenticides (anticoagulants)* agreed at TMII2011, the amount of product on fingers/hands **during the cleaning** of one bait site is 5.70mg. The following parameters were taken into account:

[10]Although the block weights 10 g and not 20 g as in the CEFIC study, it was considered that the important parameter is the number of blocks loaded rather than the weight of the block

- active substance in product: 0.001 %,(w/w);
- dermal absorption: 0.047 %,
- body weight: 60kg.

Thus, the systemic dose of brodifacoum per cleaning of one bait site is 4.47 $x10^{-10}$mg/kg bw/event for control of rats and mice (because the amount of disposed bait is not taken into account).

The harmonized number of manipulations for rodenticides anticoagulant set in the HEEG opinion agreed at TM III 2010 was used to assess the overall exposure systemic dose. Considering 15 cleaning are done per day, the systemic dose via skin is 6.7 $x10^{-9}$ mg a.s/kg bw/day for the control of 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 5.3 $x10^{-7}$ mg/kg bw/day without PPE for the control of rats and mice.

2.7.2.2.2 Exposure of non-professional users

The product is also supplied in sachets for non-professional users. Considering the nature of sachet (paper), a dermal exposure during loading is taken into account. Exposure assessment has been realized with the dose of 200 g of product for the control of rats. This assessment covers the assessment for mice as the intended doses are lower.

Based on the CEFIC study and taking into account the *HEEG opinion on an harmonised approach for the assessment of rodenticides (anticoagulants)* agreed at TMII2011, the amount of product on fingers/hands **during the loading** of 5 wax blocks of 20g per one manipulation was 27.79 mg. The following parameters were taken into account:

- active substance in product: 0.001 %,(w/w);
- Number of blocks per bait site[11]: 20 for control of rats
- dermal absorption: 0.047 %,
- body weight: 60kg.

Thus, the systemic dose of brodifacoum per placing of one bait site is 8.7 $x10^{-9}$mg/kg bw/event for control of rats and mice (because the amount of disposed bait is not taken into account).

The harmonized number of manipulations for rodenticides anticoagulant set in the HEEG opinion agreed at TM III 2010 was used to assess the overall exposure systemic dose. Considering 5loading are done per day, the systemic dose via skin is 4.35 $x10^{-8}$ mg a.s/kg bw/day for the control of rats.

Based on the CEFIC study and taking into account the *HEEG opinion on an harmonised approach for the assessment of rodenticides (anticoagulants)* agreed at TMII2011, the amount of product on fingers/hands **during the cleaning** of one bait site is 5.70mg. The following parameters were taken into account:

- active substance in product: 0.001 %,(w/w);
- dermal absorption: 0.047 %,
- body weight: 60kg.

Thus, the systemic dose of brodifacoum per cleaning of one bait site is 4.47 $x10^{-10}$mg/kg bw/event for control of rats and mice (because the amount of disposed bait is not taken into account).

The harmonized number of manipulations for rodenticides anticoagulant set in the HEEG opinion agreed at TM III 2010 was used to assess the overall exposure systemic dose. Considering 5 cleaning are done per day, the systemic dose via skin is 2.23 $x10^{-9}$ mg a.s/kg bw/day for the control of 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 4.6 $x10^{-8}$ mg/kg bw/day without PPE for the control of rats and mice.

[11]Although the block weights 10 g and not 20 g as in the CEFIC study, it was considered that the important parameter is the number of blocks loaded rather than the weight of the block

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

Exposure can occur during handling of dead rodents by professionnal and general public.
However, this scenario is excluded and considered of low relevance due to unrealistic assumptions (TNsG on human exposure (2007)).

Besides, exposure of non users can occur during ingestion of poison baits. For the scenario "*oral exposure by ingesting bait*", a reverse scenario was calculated. Based on the acute AEL of 6.7 x 10^{-6} mg a.s/kg bw/day, a body weight of 10kg and an oral absorption of 75% (as stated in the Assessment report of brodifacoum), ingestion of more than 4.4 mg of product per day by an infant is needed to exceed the AEL.

2.7.2.4 Exposure to residues in food

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

The biocidal product will not come into contact with food and it is not applied by spraying or dusting such that food or feeding stuffs could be contaminated. Therefore there is no requirement to assess potential residues on foodstuffs. Based on intended uses and proper baiting practices of the biocidal product, contamination of food/feedingstuffs is considered highly unlikely to occur.

Brodifacoum baits should not be placed where food, feedingstuffs or drinking water could be contaminated

2.7.2.5 Combined exposure

Not relevant.

2.7.3 Risk assessment for human health

The estimated exposures for the professional users are compared to the systemic AEL of brodifacoum set in the Assessment Report (3.3x10^{-6} mg/kg bw/day for long-term exposure and 6.7 x10^{-6} mg/kg bw/day for short term exposure).

2.7.3.1 Risk for direct exposure

2.7.3.1.1 Professional users

Based on the risk assessment of the active substance, the risk for professional users resulting from the intended use is acceptable for FANGA B+, even if gloves are not worn (%AEL at 16%) for the control of rats and, by extension, of 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.

Table 2.7.3-1: Summary of risk characterisation for professionals for the control of rats

Scénario	**AEL (mg/kg bw/d)**	**Exposure (mg/kg bw/d)**	**%AEL**	**Risk**
Sachet formulation (paper) (exposure during loading and cleaning phases)				
Professionnal (without gloves)	3.3 x10^{-6}	5.3 x 10^{-7}	16%	Acceptable

2.7.3.1.2 *Non-professional users*

Based on the risk assessment of the active substance, the risk for non-professional users resulting from the intended use is acceptable for FANGA B (%AEL at 1%) for the control of rats and, by extension, of mice.

Table 2.7.3-1: Summary of risk characterisation for non-professionals for the control of rats

Scénario	**AEL (mg/kg bw/d)**	**Exposure (mg/kg bw/d)**	**%AEL**	**Risk**

Sachet formulation (paper) (exposure during loading and cleaning phases)				
Non Professionnal	$6.7x10^{-6}$	4.6×10^{-8}	0.7%	Acceptable

2.7.3.2 Risk for indirect exposure

Based on a reverse scenario, more than 8.9 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 FANGA B+ 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

The acute or chronic exposure to residues in food resulting from the intended uses is unlikely to cause a risk to consumers. Regarding consumer health protection, there are no objections against the intended uses. However, the product does not come in direct or indirect contact with food and feedstuff.

2.7.3.4 Risk for combined exposure

Not relevant.

2.7.3.5 Conclusion on health risk assessment

Summary of risks characterisation of the product for human health

Based on the risk assessment of the active substance, the risk for professional and non-professional users resulting from the intended use is acceptable for FANGA B+ for the control of rats and mice.

Risk of secondary poisoning to infants and children is considered as relevant. Therefore, even if FANGA B+ contains a bittering agent which reduces the likelihood of ingestion, the baits should be unattainable for children.

Summary of risks characterisation of the product for consumer

The intended uses description of the product FANGA B+ indicates that these uses are not relevant in terms of residues in food and feed. However, the product does not come in direct or indirect contact with food and feedstuff.

Risk mitigation measures linked to risk assessment for human health

Professional

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

Non- professional

- 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 non-professional users, use only in tamper-resistant boxes.
- 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.

Emergency *(information provided in the product Safety Data Sheet)*

If inhaled: breathe fresh air and keep at rest.

If a contact occurs with skin: Remove contaminated clothes and wash skin with soap and rinse copiously with water. Do not use solvents or thinners.

If a contact occurs with eyes: Wash copiously under a trickle of water (tepid if possible) for several minutes, keeping eyelids open under the trickle of water.

If swallowed, seek medical advice immediately and show this container or label. Do not induce vomiting. Whatever the quantity of the product ingested, do not eat and do not drink. In case of emergency, contact 112.Note to doctor: the product FANGA B+ contains an anticoagulant-rodenticide, treatment with vitamin K1 could be needed for a long time.

Disposal considerations

- 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.

Required information linked to risk assessment for human health

None.

2.8 Risk assessment for the environment

2.8.1 Fate and distribution in the environment of the active substance brodifacoum

The summary of information about the active substance brodifacoum is carried out with the data from the combined Assessment Report (AR) of brodifacoum owned by Syngenta Limited and Activa / Pelgar brodifacoum and difenacoum Task Force[12].

2.8.1.1 Degradation

2.8.1.1.1 Abiotic degradation

2.8.1.1.1.1 Hydrolysis in function of pH

Brodifacoum is considered stable to hydrolysis. It was concluded that the hydrolytic half-life (DT_{50}) was above one year at environmentally relevant pH. The hydrolytic degradation is deemed negligible.

2.8.1.1.1.2 Photolysis in water

Brodifacoum photolytically degrades in aqueous solution with a half-life (DT_{50}) < 1 day. Photolysis of brodifacoum was fast with 38 % of removal in the first hour of exposure. Greater than 89 % of photolysis has occurred by around three hours. No degradation products were detected.

2.8.1.1.1.3 Photolysis in soil

No data on photolysis of the active substance in soil has been submitted in the combined AR of brodifacoum.

2.8.1.1.1.4 Photodegradation in air

[12] Syngeta Limited and Activa / Pelgar Brodifacoum and Difenacoum Task Force Combined Assessment Report according to the procedure of Directive 98/8/EC, active substance in biocidal products, brodifacoum CAS n°56073-10-0, product type 14 (rodenticides), RMS Italy, Revision: 16 december 2010.

The photo-oxidative degradation of brodifacoum in air was estimated by a structural activity relationship (QSAR) method using the Atmospheric Oxidation Program v1.90 (AOPWIN). brodifacoum is predicted to undergo rapid indirect photolysis with OH radicals and ozone (DT_{50}= approximately 2 hours). According to GBPR IV Part B[13], the half-live has been recalculated considering $C_{OH} = 0.5 * 10^6$ molec/cm^3; corresponding to a DT_{50} of 0.217 days). There are no predicted effects on the atmosphere.

2.8.1.1.2 Biotic degradation

2.8.1.1.2.1 Aquatic compartment

- Ready biodegradation / inherent biodegradation

Brodifacoum is not readily biodegradable under OECD 301B Test (0% after 28 days). Brodifacoum is not inherently biodegradable under the conditions of the 'Inherent – Concawe Test' (OECD 302D) performed (0% after 56 days).

- Degradation in water/sediment system

No study on degradation of the active substance in water/sediment system has been submitted in the combined AR of brodifacoum.

2.8.1.1.2.2 Degradation in STP

No study on degradation of the active substance in sewage treatment plant system has been submitted in the combined AR of brodifacoum.

2.8.1.1.2.3 Terrestrial compartment

Brodifacoum is persistent in soil with a DT_{50} value of 157 days at 20°C, corresponding to a DT_{50} value of 298 days à 12°C.

2.8.1.1.3 Distribution

Based on literature data, the Koc value (50 000 L/kg) indicates that the active substance would not be mobile in soil and is not expected to contaminate groundwater. A laboratory study carried out by another applicant shows that with Koc values which ranged from 17.8 (pH 8.46) to 426 579 (pH 3.29), with a Koc value of 9155 L/kg at pH7.1-7.6, brodifacoum can be considered immobile in soil. Under basic conditions (high pH), brodifacoum is not likely to be adsorbed onto soils or sewage sludge due to the ionisation of the molecule; whereas under acidic conditions (low pH), brodifacoum is likely to be adsorbed onto soils or sewage sludge as the molecule is in its neutral or non-ionised form.
brodifacoum is not expected to move from soil into water.

2.8.1.1.4 Accumulation

Brodifacoum has a log Kow > 6 (6.12) and is highly adsorptive; consequently these properties indicate that brodifacoum is likely to bioaccumulate in aquatic or terrestrial species.

The aquatic BCF has been estimated with calculation method for substances with a $K_{ow} > 6$:

BCF_{fish} = 35 645 L/kg (according to Equation 75; GBPR IV Part B).

The terrestrial BCF has been estimated with calculation method:

$BCF_{earthworm}$ = 15 820 L/kg (according to Equation 82d; GBPR IV Part B).

These BCF values confirm the high bioaccumulation potential of brodifacoum in aquatic and terrestrial species.

[13]Guidance on the Biocidal Products Regulation, Volume IV Environment - Part B Risk Assessment (active substances), Version 1.0, April 2015

2.8.1.1.5 Behaviour in air

The vapour pressure of brodifacoum has been determined to be << 1 x 10^{-6} Pa (OECD 104, EC methods A.4). Furthermore, Henry's law constant has been calculated to be << 2.18 x 10^{-3} $Pa.m^3.mol^{-1}$ at pH 7 (based on a water solubility of 0.24 mg/L). Based on these data brodifacoum is not expected to partition into atmosphere to a relevant extent.

In addition, brodifacoum is predicted to undergo rapid indirect photolysis with OH radicals and ozone (DT_{50}= approximately 2 hours) and undergoes rapid direct photodegradation (DT_{50} = 0.217 days).

2.8.2 Effects on environmental organisms for active substance Brodifacoum

The summary of information about the active substance brodifacoum is carried out with the data from the combined AR of brodifacoum owned by Syngenta Limited and Activa / Pelgar brodifacoum and difenacoum Task Force[14].

2.8.2.1 Aquatic compartment (including water, sediment and STP)

2.8.2.1.1 Aquatic organisms

Based on the results of acute toxicity studies submitted in the combined AR by Activa / PelGarbrodifacoum and difenacoum Task Force, brodifacoum is toxic to aquatic organisms at low concentrations. No long-term tests have been performed. Studies are available for the three trophic levels (fish, daphnia and algae). *Selenastrum capricornutum* is the most sensitive species with a 72h E_rC_{50} of 0.04 mg a.s./L.

Table 2.8.2-1 Toxicity to freshwater aquatic organisms (measured concentrations)

Guideline / Test method	Species	Endpoint	Results (mg a.s./L)	Reference
OECD 203	*Oncorhynchus mykiss* - fish	LC_{50} – 96h	0.042	Activa / PelGar Brodifacoum and Difenacoum Task Force CAR a.s. Doc III-A 7.4.1.1
OECD 202	*Daphnia magna* - invertebrate	EC_{50} – 48h	0.25	Activa / PelGar Brodifacoum and Difenacoum Task Force CAR a.s. Doc III-A 7.4.1.2
OECD 201	*Selenastrum capricornutum* - algae	E_bC_{50} – 72h E_rC_{50} – 72h	0.016 0.04	Activa / PelGar Brodifacoum and Difenacoum Task Force CAR a.s. Doc III-A 7.4.1.3

Justification of $PNEC_{water}$

According to the GBPR, the $PNEC_{water}$ is derived from the 72h E_rC_{50} value (0.04 mg a.s./L) for *Selenastrum capricornutum* divided by an assessment factor of 1000. Therefore,

PNECwater = 0.04 µg a.s./L.

[14]Syngeta Limited and Activa / Pelgar Brodifacoum and Difenacoum Task Force Combined Assessment Report according to the procedure of Directive 98/8/EC, active substance in biocidal products, brodifacoum CAS n°56073-10-0, product type 14 (rodenticides), RMS Italy, Revision: 16 december 2010

2.8.2.1.2 Sediment dwelling organisms

No experimental data are available for sediment dwelling organisms. A $PNEC_{sediment}$ (0.043 mg/kg_{wwt}) is derived through the Equilibrium Partitioning Method. However, due to the absence of measured data for the determination of a $PEC_{sediment}$ and according to the GBPR a quantitative risk characterization cannot be carried out. Therefore the risk for the sediment compartment will be covered by the risk for the aquatic compartment.

According to the GBPR and considering the log Kow > 5, the PEC/PNEC ratio for the aquatic compartment is increased by a factor of 10 to take into account the possible additional uptake via sediment ingestion.

2.8.2.1.3 STP micro-organisms

The toxicity to microorganisms in a sewage treatment plant (STP) was estimated by a respiration inhibition test (OECD 209) submitted by Activa / PelGar brodifacoum and difenacoum Task Force. No effect of brodifacoum on aerobic biological sewage treatment processes was expected. Due to the lack of measured values of test substance concentration, the EC_{10} was conservatively set greater than brodifacoum water solubility (0.058 mg a.s/L).

Table 2.8.2-2 Toxicity to STP microorganisms

Guideline/Test method	Species / Inoculums	Endpoint / Type of test	Duration	Results [mg a.s/L] EC_{10}	EC_{20}	EC_{50}	EC_{80}	Reference
OECD 209	Activated sludge	Respiration Inhibition	3h	> 0.058*				Activa / PelGar Brodifacoum and Difenacoum Task Force CAR a.s. Doc III-A 7.1.4

* corresponding to the water solubility at pH=7 and T=20°C

Justification of $PNEC_{micororganisms}$

According to GBPR when an EC_{10} from a respiration inhibition test is used, an assessment factor of 10 must be applied.

PNEC STP microorganisms > 0.0058 mg a.s/L

Additional endpoints:

According to the combined AR of brodifacoum, a lower PNEC value for sewage treatment microorganisms is provided by Syngeta Limited: **PNEC STP microorganisms > 0.0038 mg a.s/L**. Therefore, as the data set are considered equivalent, the worst case PNEC from the combined AR must be used in the risk assessment.

2.8.2.2 Atmosphere

Brodifacoum has a low volatility and is not intended to be sprayed or fumigated. It is formulated into a non-volatile solid consequently its occurrence in air is highly unlikely. Moreover, significant phototransformation in air due to hydroxyl radicals would be expected. Brodifacoum 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 effect of brodifacoum, in soil concentration ranging up to 994 mg/kg dry weight, were found on earthworms in a test conducted according to the guideline OECD 207. LC_{50} was determined to be > 994 mg/kg dry weight, corresponding to a LC_{50} >879.6 mg/kg in wet weight.

Table 2.8.2-3 Toxicity to soil organisms

Guideline / Test method	Species	Endpoint / Type of test	Exposure design	duration	Results (mg a.s/kg wwt soil) NOEC	LC_{50}	Reference
OECD 207	*Eisenia foetida*	LC_{50}	soil exposure	14days	879.6	>879.6	Activa / PelGar Brodifacoum and Difenacoum Task Force CAR a.s. Doc IIIA 7.5.1.2

Justification of $PNEC_{soil}$

Since LC_{50} was determined to be >879 mg/kg wet weight, when corrected for soil humidity, an assessment factor of 1000 was used in accordance with GBPR (2003).

$PNEC_{soil}$ > 0.88 mg/kg wet weight

2.8.2.4 Non compartment specific effect relevant to the food chain

The exposure of brodifacoum directly to non-target birds and mammals (primary poisoning) and indirectly via target rodent carcasses (secondary poisoning) is considered in 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 NOEC/NO(A)EL	LD_{50}	Reference
OPPTS 850.2100	Japanese quail	LD_{50}/ acute oral Single dose followed by 14 days oservation	-	LD_{50} = 19 mg a.s/kg bw	Activa / PelGar Brodifacoum and Difenacoum Task Force CAR a.s. Doc IIIA 7.5.3.1.1
OECD 416	Rat Wistar	High dose F1: haemorrhagic diathesies 2-generation	NO(A)EL Parental (females) = 0.001 mg/kg bw/day)	-	Morris, 1995

2.8.2.4.1 Primary poisoning & 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.

For mammals the acute toxicity to rat: a LD_{50} value =< 5 mg a.s. /kg bw is provided.
Additional endpoints:

According to the combined AR of brodifacoum, a lower **LD_{50}** value of **0.4 mg a.s. /kg bw (**recalculated into **LC_{50} = 8 mg/kg food**, using the conversion factor bw/dfi of 20 from table 22 in the GBPR II is the lowest value for the acute toxicity.**)** is provided by another notifier. Therefore, as the data set are

considered equivalent, the worst case LD_{50} value from the combined AR is used in the qualitative assessment for comparisons with estimated daily uptakes of brodifacoum (ETE, mg a.s. /kg bw).

For birds the acute toxicity to Japanese quail: **LD_{50} = 19 mg a.s. /kg bw** is provided.

Additional endpoints:
According to the combined AR of brodifacoum, a lower LD_{50} value of **0.31 mg a.s. /kg bw** is provided by another notifier. Therefore, as the data set are considered equivalent, the worst case LD_{50} value from the combined AR is used in the qualitative assessment for comparisons with estimated daily uptakes of brodifacoum (ETE, mg a.s. /kg bw).

Studies on dietary toxicity were submitted by another notifier in the combined AR and provided a **LC_{50} = 0.72 mg/kg food**. No data about the dietary toxicity to birds was submitted by Activa / PelGar Brodifacoum and Difenacoum Task Force in the combined AR.

Long-term quantitative assessment
For **mammals**, in a two-generation fertility study with rats, a NOAEL of 0.001 mg/kg bw/day was estimated. According to the GBPR, the NOAEL is transformed into a NOEC using a conversion factor of 20, and the AF_{oral} of 90 is applied to this NOEC, which results in a

$PNEC_{oral}$ (mammal) = 0.001/90 = 1.1E-05 mg/kg bw/day
equivalent to

$PNEC_{oral}$ (mammal) = 0.001*20/90 = 2.22E-04 mg/kg food

For **birds** the NOEC for brodifacoum is based on the results of the chronic toxicity study with difenacoum (on Japanese Quail), chosen as reference chemical for second generation anticoagulants (NOEC > 0.1 mg difenacoum /kg diet). An extrapolation factor of 8.05 was applied to correct for differences in toxicity based on the acute test results for difenacoum (LD_{50} = 66 mg/kg, male and females) and brodifacoum (LD_{50} = 19 mg/kg bw), both related to Japanese quail. brodifacoum results show high toxicity to birds, with NOEC = 0.012 mg brodifacoum/kg diet (obtained as NOEC > 0.1 mg difenacoum /kg diet / 8.05) and NOEL = 0.0012 mg brodifacoum/kg bw/d.

According to GBPR, an assessment factor of 30 is applied to derive the PNEC:

$PNEC_{oral}$ for birds (dose) = 0.0012/30 = 4E-05 mg/ kg bw/ day
equivalent to

$PNEC_{oral}$ for birds (conc. In food) = 0.012/30 = 43E-04 mg/kg food

Additional endpoints: according to the combined AR of brodifacoum, a lower **$PNEC_{oral}$ for birds** is provided by another notifier. The long-term toxicity was extrapolated by read across to reproduction toxicity of difenacoum to Japanese Quail (NOEC > 0.1 mg Difenacoum /kg diet), selected as representative compound of the second generation anticoagulants. A factor of 26 was applied to take into account differences in toxicity between the two compounds. A NOEC = 0.0038 mg brodifacoum /kg diet and a NOEL = 3.85E-04 mg brodifacoum/kg bw/d are derived.

According to GBPR, an assessment factor of 30 is applied to derive the PNEC:

$PNEC_{oral}$ for birds (dose) = 1.3E-05 mg/ kg bw/ day
equivalent to

$PNEC_{oral}$ for birds (conc. In food) = 1.3E-04 mg/kg food

Therefore, as the data set are considered equivalent, the worst case PNEC from the combined AR is used in the risk assessment.

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2.8.2.5 Summary of PNECs of the active substance brodifacoum

Table 2.8.2-5 Summary of the brodifacoum (a.s.) PNECs used for risk assessment

Compartment		Test Value	AF	PNEC	Source
Aquatic	PNECwater	72h E_rC_{50} = 0.04 mg a.s./L	1000	0.04 µg a.s./L	Combined AR
	$PNEC_{STP}$	EC_{10} > 0.0038 mg a.s. /L	100	> 0.0038 mg a.s/L	combined AR
Terrestrial	$PNEC_{soil}$	14-d LC_{50} > 879.6 mg a.s. /kg ww soil	1000	> 0.88 mg/kg wet weight	Combined AR
Primary and secondary poisoning	$PNEC_{oral}$ for birds	NOEC = 0.0038 mg/kg food NOEL = 3.85E-04 mg/kg bw/day	30	1.3E-04 mg/kg food 1.3E-05 mg/ kg bw/ day	Combined AR
	$PNEC_{oral}$ for mammals	NO(A)EL=0.001mg a.s/kg bw/day NOEC= (0.001*20)=0.02 mg a.s/kg food	90	1.1E-05 mg/kg bw/day 2.22E-04 mg/kg food	Combined AR

According to the combined AR, the lowest PNEC values (from Syngenta limited or Activa / PelGar brodifacoum and difenacoum Task Force) are used in the risk assessment.

2.8.2.6 PBT and ED Assessment

Persistence
According to results given in the combined AR, brodifacoum is not readily, inherently or anaerobically biodegradable. In addition, brodifacoum is hydrolytically stable, but undergoes rapid photolysis in water. These results indicate, according to screening criteria, that brodifacoum can be considered as potentially persistent (P) and very persistent (vP).

Bioaccumulation
Based on log Kow = 6.12 and BCFfish = 35 645 $L.Kg^{-1}$ (according to Equation 75; GBPR), brodifacoum potentially fulfils the B criterion and vB criterion.

Toxicity
Brodifacoum is proposed to be classified as Repr. Cat 1 or 2, R61. brodifacoum is also proposed to be classified as T+;R26/27/28, R43, R48/23/24/25, R61, N;R50/53. According to the GBPR, brodifacoum fulfils the T criterion.

Brodifacoum is considered as a potential PBT, according to the GBPR on Risk Assessment (2003).

2.8.3 Effects on environmental organisms for biocidal product

It is important to note that the applicant did not provide ecotoxicological data about the biocidal product FANGA B+. So the whole effect assessment for the product is based on the data obtained from the active substance brodifacoum (Combined Assessment Report According to Directive 98/8EC, Active substance in Biocidal Products, Brodifacoum CAS 56073-10-0, Product Type 14 (Rodenticides), RMS Italy, Revision 2: November 2010).

Denatonium benzoate is used in the biocidal product as bittering agent. This substance is classified as “Toxicto aquatic organisms, may cause long-term adverse effects in the aquatic environment” in the frame of the Directive 91/414/EEC. Nevertheless at the concentration used in FANGA B+, the substance does not contribute to the classification of the biocidal product.

The 2,6−di−tert.−butyl−p−crésol as ”BHT” is used in the biocidal product as antioxydant. This substance is classified as Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic

environment" according to the product Data Sheet. Nevertheless in the concentration used in the product FANGA B+, the substance does not contribute to the classification of the biocidal product.

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

2.8.3.1 Aquatic compartment (including water, sediment and STP)

2.8.3.1.1 Aquatic organisms

Refers to section Aquatic compartment (including water, sediment and STP)

2.8.3.1.2 Sediment dwelling organisms

Refers to section Aquatic compartment (including water, sediment and STP)

2.8.3.1.3 STP micro-organisms

Refers to section Aquatic compartment (including water, sediment and STP)

2.8.3.2 Atmosphere

Refers to section Atmosphere

2.8.3.3 Terrestrial compartment

Refers to section Terrestrial compartment

2.8.3.4 Non compartment specific effect relevant to the food chain

Refers to section
Erreur ! Source du renvoi introuvable.

2.8.3.5 Summary of PNECs

Refers to section Summary of PNECs of the active substance brodifacoum

2.8.4 Environmental exposure assessment

As the product contains no substances of concern except brodifacoum, it is considered that risks posed to environment following the use of FANGA B+ can adequately be assessed based on the evaluation conducted for the active substance. Therefore the exposure assessment is carried out with the data obtained from the active substance brodifacoum only.

The product FANGA B+ is a rodenticide bait containing 0.001% brodifacoum (0.01 g/kg). The product is in the form ofa paste (individually packaged in sachet). Baits are placed in secured bait box for professional and non-professional users. The product is used as 40 g for mouse and 200 g for rat / bait point. The secured bait points are refilled 4 times over 28 days. Dead rodents and unconsumed baits are removed each week.

FANGA B+ is used in the following areas:

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

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

2.8.4.1 Aquatic compartment (surface water, sediment, STP)

Exposure of the aquatic compartment *via* the STP after the treatment with rodenticides is only relevant for sewers. Contamination of surface water, STP or sediment with brodifacoum from the placing of bait in and around buildings, in open areas or in waste dumps is considered negligible according to the ESD PT14.

2.8.4.2 Atmospheric compartment

Due to its physico-chemical properties (low vapour pressure of 2.6 x 10^{-22} Pa at 20°C and low Henry's law constant of 2.35 x 10^{-18} $Pa.m^3.mol^{-1}$), brodifacoum is not expected to be present in the atmosphere in significant quantities. The exposure of air is therefore considered negligible for the application of FANGA B+ biocidal product.

2.8.4.3 Terrestrial compartment (soil and groundwater)

2.8.4.3.1 In and around buildings

The exposure assessment has been carried out according to the ESD (Larsen, 2003) for rodenticides (ESD PT14)[15] and the GBPR IV Part B[16]. The ESD PT14 indicates that the only primary compartment to be exposed during a use in and around buildings is the terrestrial compartment. Emission calculations to soil and groundwater were conducted with the default parameters of the ESD PT14 as well as the specific information on the product provided by the applicant:

- A brodifacoum concentration of 0.001% (w/w),
- The protection of baits in bait stations,
- Maximal dose rates: 200 g for rats and 40 g for mice,
- Minimal distance between two bait points: 4 m for rats and 1 m for mice (default value)/ 5 m for rats and 1 m for mice (specific parameter),
- Number of refilling times: 5 (default value) / 4 (specific parameter).

Exposure of the terrestrial compartment (soil) will occur when brodifacoum bait is deployed outdoors. ESD (Larsen, 2003) considers a scenario that entails outdoor baiting with bait blocks around a farm building. In this situation, exposure is assumed to arise through a combination of transfer (direct release) and deposition *via* urine and faeces (disperse release) onto soil. The active substance metabolism is taken into account; ESD (Larsen, 2003) considers that, in general, 90% of the total amount of rodenticide consumed by the target rodents over the duration of the outdoor baiting campaign enters soil via urine and faeces.
In both scenarios, the direct and disperse brodifacoum releases ($Elocal_{soil}$, mg) to the relevant soil surfaces may be calculated according to the input values presented in the table below. The different PEC values are calculated using the GBPR equations. The degradation in soil was not considered in the calculations.

Table 2.8.4-1:PEC brodifacoum in soil and groundwater for uses in and around buildings

		ESD Default parameters: realistic worst-case		**Refined and specific parameters: typical scenario**		
Symbol	**Variable/parameters**	**Rat**	**Mouse**	**Rat**	**Mouse**	**Unit**
INPUTS						
$Q_{prod:}$	Amount of product used in control operation for each bait box	200	40	200	40	[g]
$Fc_{product}$:	Concentration of active substance in product	0.01	0.01	0.01	0.01	[$g.kg^{-1}$]
Nsites:	Number of application sites	10	10	10	10	[-]
N_{refil}:	Number of refilling times	5	5	4	4	[-]
$F_{release\text{-}D,\ soil}$:	Fraction of product released directly to	0.01	0.01	0.01	0.01	[-]

[15]EUBEES 2 - Emission scenario document for biocides used as rodenticides (Larsen, 2003)
[16]Guidance on the Biocidal Products Regulation, Volume IV Environment - Part B Risk Assessment (active substances), Version 1.0, April 2015

	soil					
$F_{release\text{-}ID,\ soil}$:	Fraction released indirectly to soil	0.9	0.9	0.9	0.9	[-]
K_{oc}	Organic carbon adorption coefficient	9 155	9 155	9 155	9 155	[L.kg-1]
Distance	Distance between 2 bait points	4	1	5	1	[m]
$AREA_{exposed\text{-}D}$:	Area directly exposed to rodenticide originating from one bait box	0.09	0.09	0.09	0.09	[m^2]
$AREA_{exposed\text{-}ID}$:	Area indirectly exposed to rodenticide	440	110	510	110	[m^2]
$DEPTH_{soil}$:	Depth of exposed soil	0.1	0.1	0.1	0.1	[m]
RHO_{soil}:	Density of exposed soil	1700	1700	1700	1700	[$kg.m^{-3}$]
OUTPUTS						
$Elocal_{soil\text{-}campaign,\ direct}$:	*Direct emission to soil from a campaign*	1.00E-03	2.00E-04	8.00E-04	1.60E-04	[$g.camp^{-1}$]
$Elocal_{soil\text{-}campaign,\ indirect}$:	*Indirect emission to soil from a campaign*	8.91E-02	1.78E-02	7.13E-02	1.43E-02	[$g.camp^{-1}$]
$Elocal_{soil\text{-}campaign}$:	*Total emission to soil from a campaign*	9.01E-02	1.80E-02	7.21E-02	1.44E-02	[$g.camp^{-1}$]
$Clocal_{soil\text{-}D}$	*Local concentration in soil due to direct release ($AREA_{exposed\text{-}D}$) after a campaign:*	6.54E-03	1.31E-03	5.23E-03	1.05E-03	[$mg.kg^{-1}_{wwt}$]
$Clocal_{soil\text{-}ID}$	*Concentration in soil due to indirect (disperse=$AREA_{exposed\text{-}ID}$) release after a campaign:*	1.19E-03	9.53E-04	7.62E-04	7.62E-04	[$mg.kg^{-1}_{wwt}$]
$Clocal_{soil}$	***Worst case total concentration in soil* = $Clocal_{soil\text{-}D}$ + $Clocal_{soil\text{-}ID}$= *PECsoil***	**7.73E-03**	**2.26E-03**	**5.99E-03**	**1.81E-03**	**[$mg.kg^{-1}_{wwt}$]**
$Clocal_{soil\ mean\ concentration}$	***Mean concentration in soil. The total amount of product release (=$Elocal_{soil\text{-}campaign}$) is divided by the whole area exposed(=$AREA_{exposed\text{-}ID}$)***	**1.20E-03**	**9.64E-04**	**7.71E-04**	**7.71E-04**	**[$mg.kg^{-1}_{wwt}$]**
Kp_{soil}	*Partition coefficient solid-water in soil*	1.83E+02	1.83E+02	1.83E+02	1.83E+02	[$L.kg^{-1}$]
$K_{soil\ water}$	*Soil-water partitioning coefficient*	2.75E+02	2.75E+02	2.75E+02	2.75E+02	[$m^{3}.m^{-3}$]

PEClocal $_{soil, porew}$	***Worst case concentration in groundwater (based on the total concentration in soil)***	**4.78E-05**	**1.40E-05**	**3.71E-05**	**1.12E-05**	**[mg.L^{-1}]**
PEClocal $_{soil, porew}$	***Mean concentration in groundwater (based on mean concentration in soil)***	**7.45E-06**	**5.96E-06**	**4.77E-06**	**4.77E-06**	**[mg.L^{-1}]**

High-tier assessment for groundwater

For the scenario "in and around buildings", the calculated values for the groundwater compartment indicated a potential risk to groundwater. A higher-tier assessment of the potential for groundwater contamination has also been carried out using the simulation model FOCUS-PEARL 4.4.4. Simulations were performed for all nine FOCUS scenarios.

It is necessary to calculate an effective brodifacoum application rate on a per-hectare basis.

The corresponding application rate of brodifacoum to land can be calculated using the following equation :

$$Appl_{rate} = Q_{prod} \times Fc_{product} \times N_{refil} \times N_{sites} \times AREA_{total} / AREA_{exposed}$$

Where:

Symbol	Value	Unit	Source
Q_{prod}	0.2*	[kg]	Input
$Fc_{product}$	1E-05	[kg.kg^{-1}]	Input
N_{sites}	10**	[-]	Input
N_{refil}:	5	[-]	Input
$AREA_{exposed}$	440	[m^2]	Input
$AREA_{total}$	10 000	[m^2]	Input
$Appl_{rate}$	2.27E-03	[kg.ha^{-1}.yr^{-1}]	Output

.* Amount of product used in control operation for each bait box

.** ESD Default parameters: realistic worst-case

One application of brodifacoum were modelled each year during the simulation period (20 years), each at a rate of 2.27 g $_{a.s.}$ha^{-1}. In accordance with FOCUS guidelines, applications were simulated to the soil surface. Canopy interception was set to 0% in the simulations.

Relevant input variables in PEARL

Parameter	Unit	Value
Substance parameters		
Molecular weight	g.mol^{-1}	523.42
Water solubility (20 °C)	mg.L^{-1}	0.058
Molar enthalpy of dissolution	kJ.mol^{-1}	27
Saturated vapour pressure (20 °C)	Pa	2.6E-22
Molar enthalpy of vaporisation	kJ.mol^{-1}	95
Diffusion coefficient in water (20 °C)	m².d^{-1}	4.3E-05
Diffusion coefficient in air (20 °C)	m².d^{-1}	0.43
Half-life (20°C, pF2)	d	157
Arrhenius activation energy	kJ.mol^{-1}	65.4
K_{om}** value	mL.g^{-1}	5310.32

Freundlich exponent 1/n	-	0.951
Method of subroutine description	-	pH independent
Tab Scenario		
Location		All 9 EU scenarios
Crop Calendar		GRASS
Irrigation		FOCUS standard irrigation scheme
Tillage		No tillage
Repeat interval for application events (years)		1
Deposition		No deposition
Absolute Application		
Application type		To the soil surface
Date		01-May
Dosage (kg/ha)		2.27E-03

Overview of results of FOCUS runs

RESULT_TEXT	Brodifacoum	LOCATION
Concentration closest to the 80th percentile (ug/L)	0.000000	CHATEAUDUN
Concentration closest to the 80th percentile (ug/L)	0.000000	HAMBURG
Concentration closest to the 80th percentile (ug/L)	0.000000	JOKIOINEN
Concentration closest to the 80th percentile (ug/L)	0.000000	KREMSMUENSTER
Concentration closest to the 80th percentile (ug/L)	0.000000	OKEHAMPTON
Concentration closest to the 80th percentile (ug/L)	0.000000	PIACENZA
Concentration closest to the 80th percentile (ug/L)	0.000000	PORTO
Concentration closest to the 80th percentile (ug/L)	0.000000	SEVILLA
Concentration closest to the 80th percentile (ug/L)	0.000000	THIVA

Calculated PEC_{GW} for brodifacoum, represented by the 80th percentile annual average leachate concentration at a soil depth of 1 m, were <0.0001 $\mu g.L^{-1}$ for all scenarios. All PEC_{GW} values for brodifacoum and its metabolites were therefore several orders of magnitude below the trigger value of 0.03 $\mu g.L^{-1}$, indicating safe use for brodifacoum.

2.8.4.3.2 Open areas

FANGA B+ is applied in open areas inside or near the openings of the tunnels of the target rodents. According to the ESD (Larsen, 2003), the use near the openings of the tunnels is covered by the assessment of the scenario “in and around buildings” with bait box. Thus this section “Open areas” only assesses the use inside the tunnels during which, according to the scenario presented in ESD (Larsen, 2003), two treatments would typically be applied in the interval of six days. Bait deployment comprises 200 g of product against rats and 40 g against mice per application and per tunnel entrance. Based on a tunnel of 8 cm diameter, worst-case soil exposure is assumed to occur to a depth of 10 cm from the contact half (*i.e*. the burrow floor) of a 30 cm tunnel section in which the bait is placed. This section of tunnel floor is assumed to receive an input corresponding to 5% of the product during application and a further 20% as the bait is consumed. This scenario is worst case as the product FANGA B+ is intended to be applied in secured bait boxes only.

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

Table 2.8.4-2PEC of brodifacoum in soil and groundwater for uses in open area

			Rat treatment	Mice treatment	unit
INPUTS	Qprod:	Amount of product used in control operation	200	40	[g.burrow^{-1}]
	$Fc_{product}$:	Fraction of active substance in product	0.01	0.01	[g a.i. kg^{-1}]
	N_{app}:	Number of application sites	1	1	[-]
	N_{refil}:	Number of refilling times	2	2	[-]
	$F_{release, soil, appl}$:	Fraction of product released to soil during application	0.05	0.05	[-]
	$F_{release, soil, use}$:	Fraction of product released to soil during use	0.2	0.2	[-]
	$Vsoil_{exposed}$:	Soil volume exposed to rodenticide	0.0085	0.0085	[m^3]
	RHO_{soil}:	Density of wet exposed soil	1700	1700	[kg.m^{-3}]
	Koc	Organic carbon adorption coefficient	9155	9155	[L.kg^{-1}]
OUTPUTS	$Elocal_{soil\text{-}campaign}$	*Local emission of active substance to soil during a campaign*	1.00E-03	2.00E-04	[g.camp]
	$Clocal_{soil}$	*Local concentration in soil after a campaign*	6.92E-02	1.38E-02	[mg.kg$^{-1}_{wwt}$]

2.8.4.3.3 Waste dumps

The default exposure scenario suggests in the event of an infestation outbreak a treatment with 40 kg of baits distributed over an area of 1 ha, with a total of seven applications per year. In this situation, soil exposure is assumed to arise through a combination of deposition via urine and faeces combined with rodenticide contained in the carcasses of poisoned target rodents. In general, ninety percent of the total amount of rodenticide consumed by the target rodents over the duration of each baiting campaign is assumed to enter soil over the 1 ha surface.

FANGA B+ is intended to be used in bait boxes containing 200 g of biocidal product (0.001%) with 5 m spacing. So to predict the concentration of brodifacoum in soil and groundwater for the uses in waste dump, the intended doses are calculated for the 1 ha surface as below:

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

Q_{prod} = ((100 m /5 m) + 1) x (100 m / 5 m) x 0.2 $kg_{product}$

Q_{prod} = 84 kg/ha

The ESD (Larsen, 2003) considers that, in general, 90% of the total amount of rodenticide consumed by the target rodents over the duration of the outdoor baiting campaign enters soil via urine and faeces.

Table 2.8.4-3 PEC of brodifacoum in soil and groundwater for uses in waste dump

			Anticoagulant-Rat- ESD default values	**Dose for rat intended by the applicant**	**Unit**
INPUT	**Q_{prod}**	Amount of product used in control operation / ha	40	84	[kg.ha^{-1}]
	$Fc_{product}$	Fraction of active substance in product	0.01	0.01	[g a.i.kg^{-1}]

	N_{app}	Number of applications	7	7	[-]
	$F_{release, soil}$	Fraction of product released to soil	0.9	0.9	[-]
	$AREA_{exposed}$	Area exposed to rodenticide	10 000	10 000	[m^2]
	$DEPTH_{soil}$	Depth of exposed soil	0.1	0.1	[m]
	RHO_{soil}	Density of wet exposed soil	1700	1700	[$kg.m^{-3}$]
	Koc	Organic carbon adsorption coefficient	9 155	9 155	[$L.kg^{-1}$]
OUTPUT	**$Elocal_{soil-campaign}$**	*Local emission of active substance to soil from a campaign*	2.5	5.3	[$g.camp^{-1}$]
	$Clocal_{soil}$	*Local concentration in soil after a campaign*	1.48E-03	3.11E-03	[$mg.kg^{-1}_{wwt}$]
	Kp_{soil}	*Partition coefficient solid-water in soil*	1.83E+02	1.83E+02	[$L.kg^{-1}$]
	$K_{soil\ water}$	*Soil-water partitioning coefficient*	2.75E+02	2.75E+02	[$m^3.m^{-3}$]
	PEClocal $_{soil, porew}$	*Concentration in groundwater*	9.17E-06	1.93E-05	[$mg.L^{-1}$]

2.8.4.4 Non-compartmental-specific exposure relevant to the food chain (secondary poisoning)

2.8.4.4.1 Primary poisoning

Non-target birds and mammals may encounter bait containing brodifacoum if they are small enough to be able to reach the bait, or because the bait is inadequately safeguarded or a secured bait point has become damaged, or by finding pieces of bait which have been removed by target rodents. The quantities of brodifacoum potentially accessible to non-target mammals can be calculated based on the size and number of bait at each secured bait point and an estimate of the amount of bait removed from them. The primary poisoning risk assessment is presented in this dossier according to the scenario “in and around building” covering the other uses.

Primary poisoning - Tier1 assessment

The Tier 1 assessment assumes that the whole day’s food requirement is satisfied by consumption of bait and therefore the concentration in food will be the same as the concentration of the active substance in the bait: 10 $mg.kg^{-1}$ (0.001% w/w of brodifacoum in FANGA B+). Hence, **the worst case Tier 1 PEC_{oral} is 10 $mg.kg^{-1}$**.

For birds, a separate, graded assessment of long-term risks of primary poisoning by bait has been done. It is based on different intakes of brodifacoum-treated bait in relation to untreated food, depending on to which extent brodifacoum bait is accessible to birds.

Table 2.8.4-4PECoral for non-target, birds exposed to brodifacoum in bait removed from secured bait points in and around buildings

Proportion of bait point contents accessible, expressed as fraction of ingested food (%)	Bromadiolone conc. potentially ingested by non-target vertebrates (mg/kg) ≡ PECoral
100	10
50	5
40	4

30	3
20	2
10	1
5	0.5
2	0.2
1	0.1

Primary poisoning - Tier 2 assessment, acute exposure

According to ESD (Larsen, 2003), a Tier 2 assessment can be done estimating a daily uptake of a compound (ETE, $mg.kg^{-1}_{bw}.d^{-1}$) by non-target animals according to the equation 19 of ESD:

$ETE = (FIR/BW) * C * AV * PT * PD\ (mg_{brodifacoum}/kg_{bw}/day)$

With:

ETE is the estimated daily uptake of the active substance ($mg.kg^{-1}_{bw}.d^{-1}$),
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 (-),
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 2.8.4-5Expected concentrations of brodifacoum in non-target animals in the worst case (Step 1) and realistic worst case (Step 2) for acute situations.

Non-target mammal	BW (g)[a]	FIR ($g_{dry\ weight}.day^{-1}$)	C ($mg.kg^{-1}$)	ETE = concentration of brodifacoum after one meal ($mg.kg^{-1}_{bw}.d^{-1}$)	
				Step 1	Step 2
Dog	10 000	456[b]	10	0.46	0.33
Pig	80 000	600[a]	10	0.08	0.05
Pig, young	25 000	600[a]	10	0.24	0.17
Tree sparrow	22	7.6[a]	10	3.45	2.49
Chaffinch	21.4	6.42[a]	10	3.00	2.16
Wood pigeon	490	53.1[a]	10	1.08	0.78
Pheasant	953	102.7[a]	10	1.08	0.78

[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 exposure

The long-term risks of brodifacoum are determined by the expected concentrations (EC) in the animal after metabolism and elimination, which is regarded as PEC. The EC are 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 (Larsen, 2003).

$EC = ETE*(1-El)$

According to the ESD (Larsen, 2003), 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 brodifacoum in non-target animals in primary poisoning scenarios after one meal followed by 24 hour elimination period.

Table 2.8.4-6Expected concentrations of brodifacoum in non-target animals in realistic worst case (Step 2) for long-term situation.

Non-target animal	PEC: EC, concentration of brodifacoum after one day elimination (mg/kg)
Dog	0.23
Pig	0.04
Pig, young	0.12
Tree sparrow	1.74
Chaffinch	1.51
Wood pigeon	0.55
Pheasant	0.54

2.8.4.4.2 Secondary poisoning

Secondary poisoning via the aquatic food chain

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

Secondary poisoning via the terrestrial food chain

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

The calculation is done according to equation 80 and 82 (GBPR, 2015):

$$\mathbf{PEC\ oral_{,predator} = C_{earthworm}}$$

$$\mathbf{C_{earthworm} = (BCF_{earthworm} * C_{porewater}) + Clocal_{soil\ mean\ concentration} * F_{gut} * CONV_{soil}) / (1 + F_{gut} * CONV_{soil})}$$

With (example for rat treatment application for the in and around - typical scenario):

$BCF_{earthworm}$ = 15 820 $L.kg_{wet\ earthworm}^{-1}$,
$C_{porewater}$ = 4.77E-06 $mg.L^{-1}$ (based on mean concentration in soil – typical case)
$C\ local_{soil\ mean\ concentration}$= 7.71 E-04 $mg.kg^{-1}_{wwt}$,
F_{gut}= 0.1 $Kg_{dwt}.kg_{wwt}^{-1}$,
$CONV_{soil}$ = 1.13 $Kg_{wwt}.kg\ d_{wt}^{-1}$,

According to the GBPR, the most appropriate scenario is that 50% of the diet comes from a local area and 50% comes from the regional area, thus when the PEClocal, soil is used in calculation, the PECoral,predator to be used in risk assessment is $C_{earthworm}$ x 0.5.

Table 2.8.4-7Expected concentrations of brodifacoum in predator

	PEC oral, $_{predator}$mg/kg $_{wet\ earthworm}^{-1}$	
	ESD Default parameters: realistic worst-case	**Refined and specific parameters: typical scenario**
TIER I: Worst case (based on the total concentration in soil)		
Rat treatment	3.40E-01	2.64E-01
Mice treatment	9.94E-02	7.96E-02
TIER I: Mean (based on the mean concentration in soil)		
Rat treatment	5.30E-02	3.39E-02
Mice treatment	4.24E-02	3.39E-02
TIER II: Mean (based on the mean concentration in soil) + considering degradation in soil		
Rat treatment	5.12E-02	3.28E-02
Mice treatment	4.10E-02	3.28E-02

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', 'open areas' and 'waste dumps', 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 brodifacoum in their food, i.e. the poisoned rodents. This PECoral is then compared to the LC50 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 $_{brodifacoum}$.kg $_{bw}^{-1}$.day^{-1})

This equation gives the concentration of brodifacoum in the rat (PECoral) 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:

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

For the active substance brodifacoum, the default value of 0.3 is used for elimination (El).

Table 2.8.4-8Residues of brodifacoum 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	0.20	0.50	1.00
Day 2 before new meal	0.14	0.35	0.70
Day 5 after the last meal	0.55	1.39	2.77

Day 7 mean time to death	0.27	0.68	1.36

According to the ESD, the concentrations of brodifacoum 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, the PEC in rodents after 5 days are used considering that the consumption of rodenticides makes up 100% of total consumptions (refer to Table above).

Table 2.8.4-9Residues of brodifacoum in target animals at specific point in times and varying bait consumption used in the long term assessment

Birds / Mammals	**PEC_{oral} Brodifacoum conc. in target rodent ($mg.kg^{-1}_{bw}$), ESD default values**
Day 5 after the last meal	2.77

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 after a single day of exposure presented as an illustrative example in the ESD.

The amount of a.i. consumed by the non-target animal is 2.77 $mg.kg^{-1}$ bw for rodents caught on day 5 and 3.31$mg.kg^{-1}$ bw for 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 below.

Table 2.8.4-10 Expected concentrations of brodifacoum in non-target animals (predators/carnivores) due to secondary poisoning after a single day of exposure (concentration of brodifacoum in rodenticide bait 0.001%). 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. (mg)[1]**	**Conc. ($mg.kg^{-1}$)[2]**	**Amount a.i. (mg)[1]**	**Conc. ($mg.kg^{-1}$)[2]**
Barn owl *(Tyto alba)*	295	72.9	0.10	0.34	0.12	0.41
Kestrel *(Falco tinnunculus)*	209	78.7	0.11	0.52	0.13	0.62
Little owl *(Athene noctua)*	164	46.4	0.06	0.39	0.08	0.47
Tawny owl *(Strix aluco)*	426	97.1	0.13	0.32	0.16	0.38
Fox *(Vulpes vulpes)*	5700	520.2	0.72	0.13	0.86	0.15
Polecat *(Mustela putorius)*	689	130.9	0.18	0.26	0.22	0.31
Stoat *(Mustela erminea)*	205	55.7	0.08	0.38	0.09	0.45
Weasel *(Mustela nivlis)*	63	24.7	0.03	0.54	0.04	0.65

[1]Amount a.i. consumed by non-target animal

[2] Conc. in non-target animal

2.8.5 Risk characterisation for the environment

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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 (GBPR, 2003) and "Emission Scenario document for biocides used as rodenticides" (Larsen, 2003, ESD PT14).
The environmental risk characterization has been carried out for brodifacoum.

2.8.5.1 Aquatic compartment (including water, sediment and STP)

2.8.5.1.1 In and around building

Exposure scenario is not considered relevant in the ESD for rodenticides. brodifacoum is not expected to occur to any significant extent following the use of FANGA B+ in and around buildings. Therefore, PEC values for brodifacoum in surface water and sediment are assumed to be negligible and have not been further considered.

2.8.5.1.2 Open areas

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

2.8.5.1.3 Waste dumps

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

2.8.5.2 Atmospheric compartment

Due to its physico-chemical properties (low vapour pressure of 2.6×10^{-22} Pa at 20°C and low Henry's law constant of 2.35×10^{-18} $Pa.m^3.mol^{-1}$), brodifacoum is not expected to be present in the atmosphere in significant quantities. The exposure of air is therefore considered negligible for the application of FANGA B+ biocidal product.

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2.8.5.3 Terrestrial compartment (including soil and groundwater)

Soil exposure occurs both through a combination of direct and indirect releases from the use of FANGA B+ bait in the scenario 'in and around buildings', 'open areas' and 'waste dump'.

2.8.5.3.1 In and around building

Exposure of the terrestrial compartment (soil) will occur when FANGA B+ is deployed outdoors.
Realistic worst case and typical case predicted soil concentrations (PECs) have been calculated for the use scenario in and around buildings, for application in control campaign. The resulting PEC/PNEC ratios for the worst case scenario (addition of direct and indirect exposure) for the soil are summarized in the table below:

Table 2.8.5-1PECsoil/PNECsoil for soil organisms exposed to brodifacoum following outdoor use of bait around buildings

Baiting scenario (ESD PT14)	PECsoil (mg $_{brodifacoum}$.kg $_{wwt}$ $soil^{-1}$)	PNECsoil (mg $_{brodifacoum}$.kg $_{wwt}$ $soil^{-1}$)	PEC/PNEC ratio
Realistic worst case			
Rat treatment	7.73E-03	0.88	8.78E-03
Mice treatment:	2.26E-03		2.57E-03
Typical scenario			
Rat treatment	5.99E-03	0.88	6.81E-03
Mice treatment	1.81E-03		2.05E-03

The PEC/PNEC ratios are below 1 indicating no unacceptable risks to the terrestrial compartment when the product FANGA B+ is used in and around building.

The risk is acceptable in groundwater for the use of FANGA B+ in and around building as presented below:

Table 2.8.5-2PEC groundwater due to use of FANGA B+ in and around building

Baiting scenario (ESD PT14)	PEC groundwater (µg $_{brodifacoum}$.L^{-1})	Threshold value in groundwater (µg.L^{-1})	Risk characterization
Realistic worst case			
Rat treatment	<0.0001	0.03	Acceptable[1]
Mice treatment	<0.0001		
Typical scenario			
Rat treatment	<0.0001	0.03	Acceptable[1]
Mice treatment	<0.0001		

[1] After refinement by Focus model

2.8.5.3.2 Open areas

Exposure of the terrestrial compartment (soil) will occur when FANGA B+ bait is applied in open areas by inserting inside the openings of the tunnels of the target rodents.
Predicted soil concentrations (PECs) have been calculated for the use scenario in open areas, for application in rats/rodents control campaign according to the doses claimed by the applicant. The resulting PEC/PNEC ratios for the soil are summarized in the table below:

Table 2.8.5-3PECsoil/PNECsoil for soil organisms exposed to brodifacoum following use of bait in open area

Baiting scenario (EUBEES 2)	PEC_{soil} (mg /kg wwt)	$PNEC_{soil}$ (mg /kg wwt)	PEC/PNEC
Typical use (rat treatment)	6.92E-02	0.88	0.079
Typical use (mice treatment)	1.38E-02		0.016

The PEC/PNEC ratios are below 1.0 and indicate that there are no unacceptable risks to the terrestrial compartment when the product FANGA B+ is used in the tunnels of open areas. According to the EUBEES 2 scenario, the use near the openings of the tunnels is covered by the assessment of the scenario “in and around buildings” with bait box. As argued above (section above**Erreur ! Source du**

renvoi introuvable.), there is no unacceptable risk for the terrestrial compartment (including groundwater) when the FANGA B+ is used near the openings of the tunnels of the target rodents.

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

2.8.5.3.3 Waste dump

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

Table 2.8.5-4PECsoil/PNECsoil for soil organisms exposed to brodifacoum following use of bait at waste dumps

Baiting scenario (ESD PT14)	PECsoil ($mg_{brodifacoum}.kg_{wwt}\ soil^{-1}$)	PNECsoil ($mg_{brodifacoum}.kg_{wwt}\ soil^{-1}$)	PEC/PNEC ratio
Rat treatment (40 $kg.ha^{-1}$)	1.48E-03	0.88	0.002
Rattreatment (84 $kg.ha^{-1}$)	3.11E-03	0.88	0.004

The PEC/PNEC ratios are below 1 indicating that there no unacceptable risks to the terrestrial compartment when the product FANGA B+ is used in waste dump.

Table 2.8.5-5PEC groundwater due to use of FANGA B+ in waste dump

Baiting scenario (ESD PT14)	PEC groundwater ($\mu g_{brodifacoum}.L^{-1}$)	Threshold value in groundwater ($\mu g.L^{-1}$)	Risk characterization
Rat treatment (40 $kg.ha^{-1}$)	9.17E-03	0.03	Acceptable
Rat treatment (84 $kg.ha^{-1}$)	1.93E-02		Acceptable

The risk for groundwater is acceptable.

2.8.5.4 Non-compartmental specific effects relevant to the food chain

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 (GBPR, 2003) and "Emission Scenario document for biocides used as rodenticides" (Larsen, 2003, ESD PT14).
The environmental risk characterization has been carried out for brodifacoum.

Bait containing brodifacoum contains also 50 mg denatonium benzoate per kg, a powerful bittering agent that is intended to deter accidental ingestion of blocks or gains by humans. It may also deter some non-target mammals.

2.8.5.4.1 Primary poisoning

2.8.5.4.1.1 Tier 1 assessment

The PEC value for Tier 1 assessment is compared to the long-term PNEC for mammals and for birds.

Table 2.8.5-6Tier 1 risk characterization of primary poisoning – Long-Term

	PEC[1] $mg.kg\ food^{-1}$	PNEC[1] $mg.kg\ food^{-1}$	PEC/PNEC
Mammals	10	2.22E-04	**45 000**
Birds	10	1.30E-04	**77 000**

[1]Concentration of brodifacoum in food.

The resulting PEC/PNEC ratio reveals a high risk of long-term primary poisoning for mammals.
For **birds**, a separate, graded assessment of long-term risks of primary poisoning by bait has been done. It is based on different intakes of brodifacoum-treated bait in relation to untreated food, depending on to which extent brodifacoum bait is accessible to birds. The PNEC for birds has been used as a worst case in the calculations.

Table 2.8.5-7PEC_{oral}/$PNEC_{oral}$ for non-target, birds exposed to brodifacoum in bait removed from secured bait points in and around buildings

Fraction of ingested food (%)	**PECoral** mg.kg $food^{-1}$	**PNEC** mg.kg $food^{-1}$	**PEC/PNEC**
100	10	1.30E-04	**76 923**
50	5		**38 462**
40	4		**30 769**
30	3		**23 077**
20	2		**15 385**
10	1		**7 692**
5	0.5		**3 846**
2	0.2		**1 538**
1	0.1		**769**

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

2.8.5.4.1.2 Tier 2 assessment, acute exposure

For the acute situation of primary poisoning only a qualitative risk assessment is carried out in accordance with the decision from TM III-06. In this Tier 2 acute qualitative assessment, the PEC values are compared to the LD_{50} value.

Table 2.8.5-8Tier 2 acute qualitative risk assessment of primary poisoning

	PEC_{oral}[1] mg.kg^{-1}_{bw}		**LD_{50} dose** mg.kg^{-1}_{bw} d^{-1}	**PEC_{oral}> LD_{50} (y/n)**	
	Step 1	Step 2		Step 1	Step 2
Tree sparrow	3.45	2.49	0.31	y	y
Chaffinch	3.00	2.16		y	y
Wood pigeon	1.08	0.78		y	y
Pheasant	1.08	0.78		y	y
Dog	0.46	0.33	0.4	y	n
Pig	0.08	0.05		n	n
Pig young	0.24	0.17		n	n

[1] PEC_{oral} = ETE, concentration of brodifacoum after one meal

The qualitative approach for the acute situation confirms the potential risk of primary poisoning to dogs. The level of the risk is not clarified for all other species with this approach, as A PEC below the LD50 does not indicate the absence of unacceptable risk if the required margin of safety is not established

2.8.5.4.1.3 Tier 2 assessment, long-term exposure

The PEC values for the Tier 2 assessment of the long-term exposure are compared to the PNEC values.

Table 2.8.5-9Tier 2 long-term risk assessment: PECoral/PNECoral for non-target animals in realistic worst case (step 2) for long-term situation

Non-target animal	PEC_{oral} [1] $mg.kg^{-1}_{bw}$	PNEC $mg.kg^{-1}_{bw}\ d^{-1}$	PEC/PNEC
Dog	0.23	1.10E-05	**20 909**
Pig	0.04		**3 636**
Pig, young	0.12		**10 909**
Tree sparrow	1.74	1.30E-05	**133 846**
Chaffinch	1.51		**116 154**
Wood pigeon	0.55		**42 308**
Pheasant	0.54		**41 538**

[1] PEC_{oral} = EC, concentration of brodifacoum after one day of elimination

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

2.8.5.4.2 Secondary poisoning

2.8.5.4.2.1 Secondary poisoning via the aquatic food chain

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

2.8.5.4.2.2 Secondary poisoning via the terrestrial food chain

The $PEC_{oral\ predator}$ values are compared to the long-term PNEC for mammals and for birds.

Table 2.8.5-10. risk characterization of secondary poisoning via the terrestrial food chain

	$PECoral_{predator}$ $mg/kg_{wet\ earthworm}^{-1}$		PNEC $_{oral}$ $mg.kg_{food}^{-1}$		PEC/PNEC			
	ESD Default parameters	Typical scenario	Mammals	Birds	ESD Default parameters		Typical scenario	
					Mammals	Birds	Mammals	Birds
TIER I: Worst case (based on the total concentration in soil)								
Rat treatment	3.40E-01	2.64E-01	2.22E-04	1.30E-04	**1 532**	**2 615**	**1 189**	**2 031**
Mice treatment	9.94E-02	7.96E-02			**448**	**765**	**359**	**612**
TIER I: Mean (based on the mean concentration in soil)								
Rat treatment	5.30E-02	3.39E-02	2.22E-04	1.30E-04	**239**	**408**	**153**	**261**
Mice treatment	4.24E-02	3.39E-02			**191**	**326**	**153**	**261**
TIER II (based on time-weight average concentration (180d) in soil)								
Rat treatment	5.12E-02	3.28E-02	2.22E-04	1.30E-04	**231**	**394**	**148**	**252**
Mice treatment	4.10E-02	3.28E-02			**185**	**315**	**148**	**252**

Whatever the scenario, the PEC/PNEC ratio exceeds 1 for both earthworm eating birds and mammals.

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

2.8.5.4.2.3.1 Tier 1 assessment, acute

The PEC_{oral} are compared to the LC_{50} value presented in the section above for a qualitative risk assessment in accordance with the decisions taken at the TMII-06.

Table 2.8.5-11Tier 1 long-term risk assessment of secondary poisoning

Non-target animal	**PECoral** $mg.kg^{-1}_{bw}$			**LC_{50} dose** $mg.kg^{-1}_{food}$	**PEC_{oral}> LC_{50} (y/n)**		
	PD=0.2	PD=0.5	PD=1		PD=0.2	PD=0.5	PD=1
Birds	0.55	1.39	2.77	8	n	n	n
Mammals	2.8	6.9	13.9	0.72	**y**	**y**	**y**

[1] PEC_{oral} = Expected concentration in rodent caught on day 5 after meal
PD = fraction of the food type in the diet

This qualitative risk assessment indicates no risk for birds and indicates risk for mammals at all fractions of food type in the diet and with a PEC in rodent caught on day 5 after meal.

2.8.5.4.2.3.2 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.

Table 2.8.5-12Tier 1 long-term risk assessment of secondary poisoning

Non-target animal	**PECoral** $mg.kg^{-1}_{bw}$	**PNEC** $mg.kg^{-1}_{food}$	**PEC /PNEC**
Birds	2.77	1.30E-04	**21 308**
Mammals	2.77	2.22E-04	**12 477**

PEC_{oral} = Expected concentration in rodent caught on day 5 after meal

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

2.8.5.4.2.3.3 Tier 2 assessment, long-term

Table 2.8.5-13Tier 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)*	0.34	0.41	1.30E-05	**26 154**	**31 538**
Kestrel *(Falco tinnunculus)*	0.52	0.62		**40 000**	**47 692**
Little owl *(Athene noctua)*	0.39	0.47		**30 000**	**36 154**
Tawny owl *(Strix aluco)*	0.32	0.38		**24 615**	**29 231**
Fox *(Vulpes vulpes)*	0.13	0.15	1.10E-05	**11 818**	**13 636**
Polecat *(Mustela putorius)*	0.26	0.31		**23 636**	**28 182**
Stoat *(Mustela erminea)*	0.38	0.45		**34 545**	**40 909**
Weasel *(Mustela nivlis)*	0.54	0.65		**49 091**	**59 091**

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

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

2.8.5.5 Conclusion of the risk assessment for the environment

No studies were conducted with the product FANGA B+ for the environment part; therefore the environmental risk assessment has been carried out with data from the Combined AR of brodifacoum. The environmental risk is considered as limited for the indoor use by non-professionals and for the use in and around building by professionals, in strict compliance with the specific use instructions of rodenticidal baits and the use restrictions to reduce the risk for primary and secondary poisoning.

Nevertheless, the Authority in charge of the efficacy and risk assessment is not able to assess the applicability of the specific use instructions and restrictions for

- the outdoor applications by non-professionals ;
- the use in open area by professionals ;
- the use in waste dump by profession

Risk mitigation measures linked to risk assessment for environment

For professionals

- Use in tamper-resistant bait boxes or in covered bait stations. The bait stations must be placed only in areas not accessible to the general public and non-target animals.
- Tamper-resistant bait boxes should be clearly marked to show that they contain rodenticides and that they should not contain other products than rodenticides.
- Never wash the tamper-resistant bait boxes and covered bait stations with water.
- Place the tamper-resistant bait boxes and covered bait stations in areas non-liable to floodings.
- Collect uneaten bait, bait fragments dragged away from the tamper-resistant bait boxes or covered bait stations and dead rodents, during and after treatment[17].
- Baits must be unattainable to children, pets or other non-target animals in order to minimize the risk of poisoning.
- Dispose of the tamper-resistant bait boxes and covered bait stations, packaging, uneaten baits and dead rodents in accordance with local requirements.
- Remove all bait points after the end of treatment.
- Do not throw the product on the ground, into a water course, into the sink or down the drain and into the environment.

For non-professional

- Use only in tamper-resistant bait boxes.
- Tamper-resistant bait boxes should be clearly marked to show that they contain rodenticides and that they should not contain other products than rodenticides.
- Never wash the tamper-resistant bait boxes with water.
- Place the tamper-resistant bait boxes in areas non-liable to floodings
- Collect uneaten bait, bait fragments dragged away from the tamper-resistant bait boxes and dead rodents, during and after treatment.
- Baits must be unattainable to children, pets or other non-target animals in order to minimize the risk of poisoning.
- Dispose of the tamper-resistant bait boxes, packaging, uneaten baits and dead rodents in accordance with local requirements.
- 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.

Disposal considerations

- Collect uneaten bait, bait fragments dragged away from the tamper-resistant bait boxes or covered bait stations and dead rodents, during and after treatment9.

[17] If the dead rodents, uneaten bait and bait fragments dragged away from the tamper-resistant bait boxes or covered bait stations are not entirely collected, primary and secondary poisoning risks remain unacceptable.

- Dispose of the tamper-resistant bait boxes and covered bait stations, packaging, 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.

Required information linked to risk assessment for environment
None.

2.9 Measures to protect man, animals and the environment
See Summary of Product Characteristics (SPC).

3 Proposal for decision to be adopted by the French CA (Ministry of Ecology)

This section is a proposal from the authority in charge of the risk assessment (Anses) for the decision to be adopted by the competent authority in charge of the decision (French Ministry of Ecology).
In case of inconsistency between the risk assessment and the decision, only the original and signed decision has a legal value. The decision specifies the terms and conditions to the making available on the market and use of the biocidal product.

The source of the active substance used in the biocidal product FANGA B+ is ACTIVA, source not used for annex I inclusion. According to the combined CAR (2010), the technical equivalence between Pelgar source and Activa source has been performed and accepted by Italy in August 2013 by IT. Therefore the source Activa is accepted and can be used for the biocidal product FANGA B+

Conclusions of efficacy and risk assessment

Risk assessment for Physico-chemical properties
FANGA B+ is a ready-to-use pasta bait. The product is not highly flammable, not auto-flammable (up to 400°C), not explosive and does not have oxidizing properties.

No change appeared in the appearance of the biocidal product or the packaging after storage procedures for 14 days at 54°C and 2 years at ambient temperature in polypropylene and metal box packaging. The product is therefore compatible with all claimed packaging.

The active substance content was considered as stable after accelerated storage procedure. A decrease in active substance content was observed after 2 years of storage (- 18.4%). The variation of active ingredient can be due to the heterogeneity of the product. A study to demonstrate that the variations of brodifacoum content in the product after storage 2 years are not due to a degradation of the active substance or a new storage stability study including intermediate results is required in post authorization

Summary of efficacy assessment
The product FANGA B+ has shown a sufficient efficacy and can be used for the control of *Rattus norvegicus, Rattus rattus and Mus musculus,* in and around building.

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

Summary of risks characterisation of the product for human health
Based on the risk assessment of the active substance, the risk for professional and non-professional users resulting from the intended use is acceptable for FANGA B+ for the control of rats and mice.

Risk of secondary poisoning to infants and children is considered as relevant. Therefore, even if FANGA B+ contains a bittering agent which reduces the likelihood of ingestion, the baits should be unattainable for children.

Summary of risks characterisation of the product for consumer
The intended uses description of the product FANGA B+ indicates that these uses are not relevant in terms of residues in food and feed. The product is to be used as rodenticide and does not come in direct or indirect contact with food and feedstuff.

Summary of risks characterisation of the product for the environment
No studies were conducted with the product FANGA B+ for the environment part; therefore the environmental risk assessment has been carried out with data from the Combined AR of brodifacoum. The environmental risk is considered as limited for the indoor use by non-professionals and for the use in and around building by professionals, in strict compliance with the specific use instructions of rodenticidal baits and the use restrictions to reduce the risk for primary and secondary poisoning.

Nevertheless, the Authority in charge of the efficacy and risk assessment is not able to assess the applicability of the specific use instructions and restrictions for

- the outdoor applications by non-professionals ;
- the use in open area by professionals ;
- the use in waste dump by professionals

Risk mitigation measures and conditions of use

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.

For professional users

Conditions of use linked to efficacy assessment
- Adapt the number of bait points to the infestation level.
- Inspect and resupply the bait points, 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 is 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, professional users must:
    - use the treatment alternately 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;
    - monitor the level of efficacy (periodic check), and investigate the case of reduced efficacy for possible evidence of resistance;
    - not use the product in areas where resistance is suspected or established.

Risk mitigation measures
- Store away from light.
- Gloves have to be worn to help prevention against rodent-borne disease.
- Do not open the sachets.
- Apply strict hygiene measures: do not eat, drink or smoke during handling of the product and wash hands after use of the product.
- Use in tamper-resistant bait boxes or in covered bait stations.
- Tamper-resistant bait boxes should be clearly marked to show that they contain rodenticides and that they should not contain other products than rodenticides.
- Covered bait 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[9].
- Remove all bait points after the end of treatment.
- Never wash the tamper-resistant bait boxes and covered bait stations with water.
- Place the tamper-resistant bait boxes and covered bait stations in areas non-liable to floodings.

- Dispose of the tamper-resistant bait boxes and covered bait stations, packaging, uneaten baits and dead rodents in accordance with local requirements.
- Do not throw the product on the ground, into a water course, into the sink or down the drain and into the environment.

For non-professional users

Conditions of use linked to efficacy assessment (non-professional users)
- 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.
- Inspect and resupply the bait stations as long as the bait is consumed, 3 days after the first application then weekly, in and around building and in open areas.
- Remove all bait stations after the end of treatment.
- 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.

Risk mitigation measures
- 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.
- Baits must be unattainable to children, pets or other non-target animals in order to minimize the risk of poisoning.
- Collect uneaten bait, bait fragments dragged away from the tamper-resistant bait boxes or covered bait stations and dead rodents, during and after treatment.
- Do not place tamper-resistant bait boxes and covered bait stations on surfaces in contact with food, feed or drinks and beverages.
- Remove all bait points after the end of treatment.
- Dispose of the bait boxes, non-consumed baits and dead rodents in accordance with local requirements.
- Never wash the bait boxes 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 non-consumed baits and dead rodents during and after treatment.
- In order to prevent primary and secondary poisoning for children, for domestic and wild animals, bait points must be securely deposited, and placed in non-accessible areas.
- Use only in tamper-resistant secured bait boxes. Tamper-resistant bait boxes should be clearly marked to show that they contain rodenticides. These bait boxes must not be used for other products than rodenticides.
- Remove all the bait boxes after the treatment

Emergency *(information provided in the product Safety Data Sheet)*

If inhaled: breathe fresh air and keep at rest.

If a contact occurs with skin: Remove contaminated clothes and wash skin with soap and rinse copiously with water. Do not use solvents or thinners.

If a contact occurs with eyes: Wash copiously under a trickle of water (tepid if possible) for several minutes, keeping eyelids open under the trickle of water.

If swallowed, seek medical advice immediately and show this container or label. Do not induce vomiting. Whatever the quantity of the product ingested, do not eat and do not drink. In case of emergency, contact 112.

Note to doctor: the product FANGA B+ contains an anticoagulant-rodenticide, treatment with vitamin K1 could be needed for a long time.

Disposal (professional and non-professional)
- Collect uneaten bait, bait fragments dragged away from the tamper-resistant bait boxes or covered bait stations and dead rodents, during and after treatment[9].
- Remove all bait points after the end of treatment.
- Dispose of the tamper-resistant bait boxes and covered bait stations, packaging, 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.

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.

Information required post-authorisation

Required information linked to assessment of physico-chemical properties
A study to demonstrate that the variations of brodifacoum content in the product after storage 2 years are not due to a degradation of the active substance or a new storage stability study including intermediate results is required in post authorization
Required information linked to efficacy assessment
- The authorisation holder has to monitor the resistance phenomenon of rodent populations toward the active substance brodifacoum, and resistance strategies management must be put in place. Results of the resistance monitoring must be submitted to the Competent Authorities (CA) or other appointed bodies involved in resistance management every 2 years.

4 Appendices

Annex 0a: Practical use 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, [illegible])	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 (...)	Primary packaging : type : bulk, individual wrapping.../ nature: bottle, bucket...	Secondary packaging
FANGA B+ Formulation: Pasta	Brown rat: *Rattus norvegicus*	Professionnal	In and around buildings , open areas, waste	180-200 g/secured bait point	3 to 10 days	4 refilling of bait stations Over 28 days Interval between applications (min) : one week	10 and 20 g sachet	5-10 meters	Manual application of baits in secured bait box (plastic PET/PP/PE/PVC) dimensions 230 mm x	yes	sachet	Bucket (PE) - 5-10-15-18-20 kg Carton box (carton) - 5-10-12-15-20-50 kg
	Brown rat: Rattus norvegicus	Non professional	In and around buildings , open areas	180-200 g/secured bait point	3 to 10 days	4 refilling of bait stations Over 28 days Interval between applications (min) : one week	10 and 20 g sachet	5-10 meters	Pre-filled secured boxes Manual application of baits in secured bait box (plastic PET/PP/PE/PVC) dimensions 230 mm x 135 mm x 85 mm	yes	sachet	Bucket (PE) – 0,1-0,2 -0,3-0,4 -0,5 – 0,6-0,7- 0,8- 0,9-1- 1,2- 1,3-1,4-- 1,5 kg Carton box (carton) – 0,1-0,2 -0,3-0,4 -0,5 – 0,6-0,7-0,8- 0,9- 1- 1,2- 1,3-1,4--1,5 kg Metal box (without lacquer)- 0,1-0,2 -0,3-0,4 -0,5 – 0,6-0,7- 0,8- 0,9- 1-1,2- 1,3-1,4-- 1,5 kg Bait box (plastic PET/PP/PE/PVC

	Black rat: *Rattus rattus*	Non Professionnal	In and around buildings , open areas,	180-200 g/secured bait point	3 to 10 days	4 refilling of bait stations Over 28 days Interval between applications (min) : one week	10 and 20 g sachet	5-10 meters	Pre-filled secured boxes Manual application of baits in secured bait box (plastic PET/PP/PE/PVC) dimensions 230 mm x 135 mm x 85 mm	yes	sachet	Bucket (PE) – 0,1-0,2 -0,3-0,4 -0,5 – 0,6-0,7- 0,8- 0,9-1- 1,2- 1,3-1,4-- 1,5 kg Carton box (carton) – 0,1-0,2 -0,3-0,4 -0,5 – 0,6-0,7-0,8- 0,9- 1- 1,2- 1,3-1,4-- 1,5 kg Metal box (without lacquer) - 0,1-0,2 -0,3-0,4 -0,5 – 0,6-0,7- 0,8- 0,9- 1- 1,2-1,3-1,4-- 1,5 kg Bait box (plastic PET/PP/PE/PVC)
	Black rat: *Rattus rattus*	Professionnal	In and around buildings , open areas,	180-200 g/secured bait point	3 to 10 days	4 refilling of bait stations Over 28 days Interval between applications (min) : one week	10 and 20 g sachet	5-10 meters	Manual application of baits in secured bait box (plastic PET/PP/PE/PVC) dimensions 230	yes	sachets	Bucket (PE) - 5-10-15-18-20 kg Carton box (carton) - 5-10-12-15-20-50 kg
	Mice : *Mus musculus*	Professionnal	In and around buildings ,	30-40 g/secured bait point	3 to 10 days	4 refilling of bait stations Over 28 days Interval between applications (min) : one	10 and 20 g sachet	1-2 meters	Manual application of baits in secured bait box (plastic	yes	sachet	Bucket (PE) - 5-10-15-18-20 kg Carton box (carton) - 5-10-12-15-20-50 kg

	Mice : *Mus musculus*	Non Professionnal	In and around buildings , open areas,	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	Pre-filled secured boxes Manual application of baits in secured bait box (plastic PET/PP/PE/ PVC) dimensions	yes	sachets	Bucket (PE) – 0,1-0,2 -0,3-0,4 -0,5 – 0,6-0,7- 0,8- 0,9- 1- 1,2- 1,3-1,4-- 1,5 kg Carton box (carton) – 0,1-0,2 -0,3-0,4 -0,5 – 0,6-0,7- 0,8- 0,9- 1- 1,2- 1,3-1,4-- 1,5 kg Metal box (without lacquer) - 0,1-0,2 -0,3-0,4 -0,5 – 0,6-0,7- 0,8- 0,9- 1- 1,2- 1,3-1,4-- 1,5 kg

Annex 0b: Proposed uses for authorisation

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

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 validated expressed in g/bait point, for high and low infestation (if appropriate)	Methods of application of the bait (ex: pre-filled secured bait box)	Primary packaging: type: bulk, individual wrapping…	Authori-zation
FANGAB+ Formulation: pasta bait	Mice: *Mus musculus*	Professional	In and around buildings	30 - 40 g /secured bait stations separated by 1-2 meters.	Manual application of baits in tamper-resistant bait boxes or in covered bait stations Bait points should be controlled and resupply as long as the bait is consumed: - 3 days after the first application then weekly for use in and around building	Sachet (paper)	Yes
	Black and Brown *rats (Rattus rattus and attus Norvegicus)*	Professional	In and around buildings	180 - 200 g / /secured bait stations separated 5-10 meters			
	Mice: *Mus musculus*	Non Professional	Indoor only	30 - 40 g /secured bait boxes separated by 1-2 meters.	Manual application of baits in tamper-resistant bait boxes or in covered bait stations Bait points should be controlled and resupply as long as the bait is consumed: - 3days after the first application then weekly for use indoor only.		
	Black and Brown *rats (Rattus rattus and attus Norvegicus)*	Non Professional	Indoor only	180 - 200 g /secured bait boxes separated by 5-10 meters.			

Annex 1: Summary of product characteristics

See separated file.

Annex 2: List of studies reviewed

4.1.1.1.1 List of <u>new data</u>[18] submitted in support of the evaluation of the active substance

None

4.1.1.1.2 List of <u>new data</u> submitted in support of the evaluation of the biocidal product

Section n°/ Reference n°	Author	Year	Title	Data protection Y/N	Owner	Letter of acces Y/N	Essential for the evaluation
B3.2, 3.3, 4.1, 4.2, 4.4, 4.17.1	Demangel B	2012	Physico chemical tests on FANGA PATE PRO. DEFITRACES, Report 11-920010-016 of 22 February 2012, GLP.	Y	TRIPLAN	N	Y
B3.2	Demangel B	2012	Physico-chemical tests and chemical stability before and after an accelerated storage procedure for 14 days at 54 ± 2 °C on FANGA PATE PRO In compliance with CIPAC MT 46.3 (CIPAC Handbook J - 2000). DEFITRACES Report 11-920010-017 of 12 March 2012.	Y	Triplan	N	Y
B3.4	Demangel B	2015	Chemical analyses before and after accelerated storage procedure at 40°C for 8 weeks on BDPA10V1, Report n° 15-920010-005 of 29 April 2015, GLP, unpublished.	Y	Triplan	N	Y
B3.4	De Ryckel B	2012	De Ryckel B. 2012. Physical and chemical properties and storage stability of FANGA B+ FIRST INTERIM REPORT Analysis on the test item as received and after 14	Y	Triplan	N	Y

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

			days at 54°C ± 2°C. Centre Wallon de Recherches Agronomiques, Report 22776 of 6 September 2012, GLP				
B3.4	De Ryckel B	2014	De Ryckel B. 2012. Physical and chemical properties and storage stability of FANGA B+ - Final Report - Analysis on the test item as received after 14 days at 54°C ± 2°C and after 16 months and 2 years at 20°C ± 2°C. Centre Wallon de Recherches Agronomiques, Report 22776 of 29 April 2014, GLP	Y	Triplan	N	Y
B5	Ricau H	2012	Ricau H. 2012. Analytical method validation for the determination of Brodifacoum in the FANGA BLOC SP PRO in compliance with SANCO/3030/99 rev.4 from 11/07/00. DEFITRACES, Amended report n° 11-920010-015 of 04 May 2012, GLP.	Y	Triplan	N	Y
B5	Ricau H	2012	Ricau H. 2012. Analytical method validation for the determination of Brodifacoum in the FANGA BLOC SP PRO in compliance with SANCO/3030/99 rev.4 from 11/07/00. DEFITRACES, Amended report n° 11-920010-019 of 18 May 2012, GLP.	Y	Triplan	N	Y
B5	Ricau H	2015	Validation of the analytical method for the determination of brodifacoum in BDPA10V1, Report n° 15-920010-004 of 02 April 2015, GLP, unpublished.	Y	Triplan	N	Y
B6.7	XXXX	2013	Study on the palatability and the efficacy of a bait containing 0.001%	Y	Triplan	N	Y

			(w/w) Brodifacoum in brown rat (*Rattus norvegicus*). Biolytics, Study n° 12-TOX024-3 of 24 January 2013, not GLP (unpublished).				
B6.7	XXXX	2012	Palatability of « FANGA B+ » (10 ppm Brodifacoum) ready-to-use bait targeting brown rat (*Rattus norvegicus*), black rat (*Rattus rattus*) and house mouse (*Mus musculus*). Walloon Agricultural Research Centre – Department Pesticide Research, Report n° ROD 2012 01 of the 19 January 2012, not GLP, unpublished.	Y	Triplan	N	N
B6.7	XXXX	2013	Study on the palatability and efficacy of a 0.001% Brodifacoum paste bait in house mouse (*Mus musculus*). Biolytics, Study n° 12-TOX024-4 of 24 January 2013, not GLP (unpublished).	Y	Triplan	N	Y
B6.7	XXXX	2014	2014. Efficacy evaluation of FANGA B+ (Brodifacoum 0,001% w/w a.i., oily pasta bait) against Roof rat (Rattus rattus L.) in Italy. SAGEA SR Centro di Saggio, Report n° 2008.BCD.SAG13 of 15 janauary 2014, not GLP, unpublished	Y	Triplan	N	Y
B6.7	XXXX	2013	Guicherd A. 2013. Study on the palatability and efficacy of a 0.001% Brodifacoum paste bait in black rat (*Rattus rattus*). Biolytics, Study n° 13-TOX025 of 20 December 2013, not GLP (unpublished).	Y	Triplan	N	Y
B6.7	XXXX	2013	Evaluation of the efficacy of a paste rodenticide (FANGA B+) containing	Y	Triplan	N	Y

			0.001% Brodifacoum for the control of mouse infestation. One trial , 1 Site: Rhones; France, 2012-201. Biolytics, Study n° 13-TOX019 of 20 November 2013, not GLP (unpublished).				
B6.7	XXXX	2013	Evaluation of the efficacy of a paste rodenticide (FANGA B+) containing 0.001% brodifacoum for the control of brown rat (Rattus norvegicus) infestations, Study n°13TOX020, November 2013.	Y	Triplan	N	Y
B6.7	XXXX	2015	Efficacy evaluation on BDPA10V1 (Brodifacoum 0.001% w/w a.i., pasta bait) against Roof rat (Rattus rattus L.) in Italy, Study n°2001.BCD.SAG15, April 2015	Y	Triplan	N	Y
B8.1	XXXX	2012	FANGA BLOC SP PRO assessment of acute dermal irritation. PHYCHER BIO DEVELOPPEMENT, study n°: IC-OCDE-PH-11/0402 of 5 January 2012, GLP.	Y	Triplan	N	Y
B8.2	XXXX	2012	FANGA BLOC SP PRO assessment of acute eye irritation. PHYCHER BIO DEVELOPPEMENT, study n°: IO-OCDE-PH-11/0402 of the 5 January 2012, GLP.	Y	Triplan	N	Y
B8.3	XXXX	2012	FANGA BLOC SP PRO assessment of the skin sensitization potential in the mouse using the local lymph node assay (LLNA). PHYCHER BIO DEVELOPPEMENT, study n°: LLNA-PH-11/0402, report n°: LLNA-	Y	Triplan	N	Y

			PH-11/0402-R1 of the 16 January 2012, GLP				
B8.5.1	XXXX	2012	FANGA BLOC SP PRO evaluation of acute oral toxicity in rats – acute toxic class method. PHYCHER BIO DEVELOPPEMENT, study n°: TAO423-PH-11/0402 of 5 January 2012, GLP.	Y	Triplan	N	Y
B8.5.3	XXXX	2012	FANGA BLOC SP PRO evaluation of acute dermal toxicity in rats. PHYCHER BIO DEVELOPPEMENT, study n°: TAD-PH-11/0402 of 5 January 2012, GLP.	Y	Triplan	N	Y
B8.6	XXXX	2013	In vitro absorption of difenacoum from wax block and pasta bait through human epidermis report n°JV2011-REG, not GLP, unpublished	Y	ACTIVA	Y	Y

Annex 3: Analytical methods residues – active substance

brodifacoum

Methods suitable for the determination of residues (monitoring methods)

Extract from document IIA of final CAR of brodifacoum.

Table 6: Analytical methods for the determination of brodifacoum residue

Sample	Test substance	Analytical method	Fortification range / Number of measurements	Linearity	Specificity	Recovery rate (%)	Limit of determination			Reference
						Range	Mean	RSD		
Soil	*Brodifacoum*	RP-HPLC/DAD (detection at 264 nm)	0.016÷-0.16 mg/kg in soil, with 4 replicates per level	0.256÷-12.8 µg/ml (0.006÷-0.32 mg/kg in soil), single determinations at 8 concentrations levels. r2 = 0.9999 No matrix-matched calibration	Not highly specific LC/MS method for confirmation (only experimental conditions provided)	88.5÷-95.4 (overall)	92.9 (overall)	2.2 (overall)	LOQ = 0.016 mg/kg in soil (lowest validated concentration level)	**IIIA4.2 (a)**
Drinking water *(natural mineral water Fiuggi)*	*Brodifacoum*	RP-HPLC with MS/MS detection. Molecular ion (SIM): 521 (m/z), daughter ion (SRM): 187 (m/z) Quantification by calibration curve, except for spiking level 0.05 µg/l (quantification with the lowest	0.05 µg/l (n=5) 0.5 µg/l (n=5) 5.0 µg/l (n=5) 50 µg/l (n=5)	0.1÷-0.5 µg/ml (0.05÷-0.25 µg/l in water), 4 determinations at 5 concentration levels r = 0.995 (SIM mode) r = 0.997 (SRM mode)	Highly specific	83.5÷-92.0 77.7÷-94.1 72.3÷-94.6 83.2÷-107.7	87.8 82.5 81.7 97.8	3.8 7.2 9.8 10.6	LOQ = 0.0505 µg/l in drinking and ground water; 0.5 µg/l in surface water (lowest validated concentration level) LOD = 0.025 µg/l in water	**IIIA4.2 (c)**
Ground water *(Well SB1 I.Pi.Ci)*			0.05 µg/l (n=5) 0.5 µg/l (n=5) 5.0 µg/l (n=5) 50 µg/l (n=5)			80.4÷-100.6 82.6÷-94.4 80.1÷-94.6 81.3÷-101.2	90.5 98.7 87.3 92.5	9.3 5.6 7.3 7.0		

Sample	Test substance	Analytical method	Fortification range / Number of measurements	Linearity	Specificity	Recovery rate (%)	Limit of determination			Reference
						Range	Mean	RSD		
Surface water *(sampled at Desenzano, Garda lake)*		standard calibration level)	0.05 µg/l (n=5) 0.5 µg/l (n=5) 5.0 µg/l (n=5) 50 µg/l (n=5)			116÷-124.3 79.5÷-88.0 78.7÷-98.6 104.6÷-117	120.6 84.5 87.3 110.8	2.9 4.5 7.8 3.6		
Blood serum (*from Rabbit, lyophilized powder from clotted whole blood)*	*Brodifacoum*	RP-HPLC with MS/MS detection. Molecular ion (SIM): 523 (m/z), daughter ion (SRM): 187 (m/z) Quantification by calibration curve at 0.06 mg/l , quantification with the lowest standard calibration level at 0.3 mg/l	0.06 mg/l (n=5) 0.3 mg/l (n=6)	0.05-0.40 µg/ml (0.05-0.40 mg/l in blood serum), 4 determinations at 5 concentration levels r = 0.99679 (SIM mode) r = 0.99623 (SRM mode	Highly specific	80.8-96.6 86.2-109.1	92.1 101.7	6.5 8.6	LOQ = 0.06 mg/l (lowest validated concentration level)	**IIIA4.2 (d)(2)**
Cucumber	*Brodifacoum*	LC/MS/MS. Internal standard: Difenacoum Linear	0.01 mg/kg (n=5) 0.1 mg/kg (n=5)	0.03-1.2 µg/ml, 2 determinations at 4 concentration levels. Matrix-	Highly specific	82-103 86-106	91 94	9 9	LOQ = 0.01 mg/kg in all 5 matrices (lowest validated	**IIIA4.3 [also IIIA4.2(d)(1) for Meat only]**

Sample	Test substance	Analytical method	Fortification range / Number of measurements	Linearity	Specificity	Recovery rate (%)	Limit of determination			Reference
						Range	Mean	RSD		
Wheat		calibration curve for all determinations, except for both spiking levels in lemon and for the validation in meat at 0.1 mg/kg (multi-level calibration standards used) Brodifacoum precursor ion 1: 521; product ion 1: 79; precursor ion 2: 523; product ion 2: 81 *Coumatetralyl* precursor ion 1: 291; product ion 1: 143; precursor ion 2: 291;	0.01 mg/kg (n=5) 0.1 mg/kg (n=5)	matched calibration solutions used r2: 0.9095÷-0.9963		88-126 71-90	107 84	13 9	concentration level)	
Meat			0.01 mg/kg (n=5) 0.1 mg/kg (n=5)			62-86 45-87	73 61	13 29		
Oil-seed rape			0.01 mg/kg (n=5) 0.1 mg/kg (n=5)			75-99 110-134	86 119	10 8		
Lemon			0.01 mg/kg (n=5) 0.1 mg/kg (n=5)			74-93 62-89	84 76	10 13		

Sample	**Test substance**	**Analytical method**	**Fortification range / Number of measurements**	**Linearity**	**Specificity**	**Recovery rate (%)**	**Limit of determination**			**Reference**
						Range	Mean	RSD		
		product ion 2: 141 Product ion 1 used for measurements								

Annex 4 : Toxicology and metabolism –active substance

<BRODIFACOUM>

Threshold Limits and other Values for Human Health Risk Assessment

Date: 19/11/2014

Summary			
	Value	Study	SF
AEL long-term	3.3 x 10^{-6} mg/kg bw/d	Reproductive 2-generation study in rats	300
AEL medium-term	6.67 x 10^{-6} mg/kg bw/d	Maternal toxicity from developmental study in rabbits	300
AEL acute	6.67 x 10^{-6} mg/kg bw/d3.3 x 10^{-6}	Maternal toxicity from developmental study in rabbitsReproductive 2-generation study in rats	300
ADI	mg/kg bw/d		
ARfD	Not applicable		

Inhalative absorption	100%
Oral absorption	75%
Dermal absorption	0.047%

Classification	
with regard to toxicological data (according to the criteria in Dir. 67/548/EEC)	T+ R27/28 T ;R48/24/25 No specific limit concentrations
with regard to toxicological data (according to the criteria in Reg. 1272/2008)	Acute Tox1 H310 Acute Tox 2 H300 STOT RE Cat 1 H372 No specific limit concentrations

Annex 5 : Toxicology – biocidal product

<FANGA B+ >

Date: 19/11/2014

General information

Formulation Type	paste
Active substance(s) (incl. content)	Brodifacoum (0.001% m/m)

Acute toxicity, irritancy and skin sensitisation of the preparation (Annex IIIB, point 6.1, 6.2, 6.3)	
Rat LD50 oral (OECD 420)	> 2 000 mg/kg bw
Rat LD50 dermal (OECD 402)	> 2 000 mg/kg bw
Rat LC50 inhalation (OECD 403)	No data submitted
Skin irritation (OECD 404)	Non irritant
Eye irritation (OECD 405)	Non irritant
Skin sensitisation (OECD 429; LLNA)	Non sensitizing

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
	None
Toxicological data on non-active substance(s) (not tested with the preparation)	None
	None
Further toxicological information	None

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

Annex 6 : Safety for professional operators

<FANGA B+ >

Date: 19/11/2014

Exposure assessment

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

Primary exposure of professionals – FANGA B+ – Control of rats

	Component	**CAS**	**Actual Dermal Total [mg/kg/d]**	**Inhalation Exposure [mg/m³]**	**Model**
Sachet formulation (paper)					
Professionnalrat (without gloves)	Brodifacoum	56073-10-0	5.3×10^{-7}	negligible	CEFIC study

Risk assessment – Professional

Scenario	**Component**	**CAS**	**AEL [mg/kg/d]**	**Absorption [%]**		**Total syst exposure [mg/kg bw/d]**		Risk
				inh	derm	Expo	%AEL	
Sachet formulation (paper)								
Professionnalrat (without gloves)	Brodifacoum	56073-10-0	3.3×10^{-6}	100	0.047	5.3×10^{-7}	16%	Acceptable

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

<FANGA B+>

Date:19/11/2014

General information	
Formulation Type	paste
Active substance(s) (incl. content)	Brodifacoum (0.001% m/m)

<Active Substance>

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	CEFIC Study and HEEG opinion n°12
Secondary exposure, acute	Reverse scenario
Secondary exposure, chronic	na

Conclusion:
Exposure of non-professionals and the general public to the biocidal product containing 0.001% brodifacoum as active substance is considered acceptable, if the biocidal product is used as intended and all safety advices are followed.

Primary exposure of non professionals – FANGA B+ – Control of rats

	Component	**CAS**	**Actual Dermal Total [mg/kg/d]**	**Inhalation Exposure [mg/m³]**	**Model**
Sachet formulation (paper)					
Non Professionnal	Brodifacoum	56073-10-0	4.6×10^{-8}	negligible	CEFIC study

Risk assessment – Non -professional

Scenario	**Component**	**CAS**	**AEL [mg/kg/d]**	**Absorption [%]**		**Total syst exposure [mg/kg bw/d]**		Risk
				inh	derm	Expo	%AEL	
Sachet formulation (paper)								
Non Professionnal	Brodifacoum	56073-10-0	3.3×10^{-6}	100	0.047	4.6×10^{-8}	0.7%	Acceptable

Annex 8: Residue behaviour

brodifacoum

Date: 20.08.2015

Intended Use: TP14 - Rodenticide against wild mice, brown rats and black rats.

Active substance: brodifacoum
Formulation of biocidal product: bait
Place of treatment: In and around buildings and open areas by professional and non-professional users. In waste dumps and landfills by professional users.

The intended use descriptions of the brodifacoum-containing biocidal products for which authorisation is sought indicate that these uses are not relevant in terms of residues in food and feed. The product is to be used as bait stations in and around buildings and open areas. No further data are required concerning the residue behaviour.

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

Annex 9: 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
FANGA B+ 0.001% Brodifacoum	House mice (*Mus musculus*) Brown rat (*Rattus norvegicus*) Black rats (*Rattus rattus*)	Laboratory study House mice: 10 animals (4 males and 6 females) Brown rat: 10 animals (6 males and 4 females) Black rats: 10 animals (4 males and 6 females) Intoxication duration: 20 days with daily measurement of mortality and food consumption.	Acclimation: 7 days in individual cage. D0-D5: routine food has been given: 40.0 g for rats, 10.0 g for mice. D5-D25: routine food and tested baits have been given in different feeding dishes: 40.0 g of routine food and 40.0 g of tested baits for rats 10.0 g of routine food and 10.0 g of tested baits for mice. Food and bait consumption were measured and mortality was observed during 20 days after the first day of intoxication.	For brown rats: Mean palatability percentage = 14.44%. Mortality percentage = 100% For black rats: Mean palatability percentage = 27.15% Mortality percentage = 90% For house mice: Mean palatability percentage = 13.99% Mortality percentage = 90%. Palatability for brown rats and mice are under the criteria of 20 %	ROD 2012 01 R.I = 3
FANGA B+ 0.001% Brodifacoum	Brown rats (*Rattus norvegicus*)	Laboratory study Method: Technical Notes for Guidance on Product Evaluation, Appendices to chapter 7 Product type 14 « Efficacy evaluation of rodenticidal biocidal products » Brown rats: 5 males and 5 females. Intoxication duration: 4 days with daily measurement of mortality and consumption.	Acclimatization: 4 days in individual cage at room temperature. Day 0: reference food and bait biocidal product have been given: - 50 g per animal of reference food for the assessment of palatability, - 50 g per animal of paste bait for the assessment of efficacy during 4 consecutive days with daily consumption measurements. Mortality was observed during 21 days every 24 hours.	- A palatability equivalent to 43% - A good efficacy with a mortality of 90% in a period from day 4 to day 6	Study n°12-TOX024-03 R.I =1

Test substance	Test organisms	Test system / Concentrations applied / exposure time	Test conditions	Test results: effects, mode of action, resistance	Reference
FANGA B+ 0.001% Brodifacoum	House mice (*Mus musculus*)	Laboratory study Technical Notes for Guidance on Product Evaluation, Appendices to chapter 7 Product type 14 « Efficacy evaluation of rodenticidal biocidal products » House mice: 10 males and 10 females. Intoxication duration: 4 days with daily measurement of mortality and consumption.	Acclimatization: 4 days in separate cages (10 males in a cage and 10 females in a second cage) at room temperature. Day 0: reference food and bait biocidal product have been given during 4 consecutive days with daily consumption measurements. Mortality was observed during 21 days every 24 hours or until the death of all animals.	- A palatability equivalent to 61% - A very good efficacy with a mortality of 100% in a period from day 3 to day 9	Study n° 12-TOX024-4 R.I =1
FANGA B+ 0.001% Brodifacoum	House mice (*Mus musculus*)	Field test Method: Technical Notes for Guidance on Product Evaluation, Appendices to chapter 7 Product type 14 « Efficacy evaluation of rodenticidal biocidal products » The trial was located at a test site where house mouse populations had been identified. This site was located in Claveisolles (Rhône department) near Lyon city .	Pre-treatment census: 15 days (50 g of wheat per station per day). Treatment: 20 g of bait per day in each lockable bait station –total 14 bait stations) during 15 days. Post-baiting: 3 days (50 g of wheat per station per day).	Pre-baiting average consumption = 155 g/day => 30 mice Post-baiting average consumption = 0 g Estimated efficacy = 100 %	Study n° 13-TOX019 R.I =1

Test substance	Test organisms	Test system / Concentrations applied / exposure time	Test conditions	Test results: effects, mode of action, resistance	Reference
FANGA B+ 0.001% Brodifacoum	Black rats (*Rattus rattus*)	Laboratory test Method: Technical Notes for Guidance on Product Evaluation, Appendices to chapter 7 Product type 14 « Efficacy evaluation of rodenticidal biocidal products » Black rats: 5 males and 5 females. Intoxication duration: 4 days with daily measurement of mortality and consumption.	Acclimatization: 4 days in individual cage at room temperature. Day 0: reference food and bait biocidal product have been given: - 50 g per animal of reference food for the assessment of palatability, - 50 g per animal of paste bait for the assessment of efficacy during 4 consecutive days with daily consumption measurements. Mortality was observed during 21 days every 24 hours.	A mean palatability equivalent to 59%. A total efficacy, with 100% of mortality for males between day 6 and day 8 and 100 % of mortality for females in a period between day 3 and day 10	Study n°13-TOX025 R.I =1
FANGA B+ 0.001% Brodifacoum	Black rats (*Rattus rattus*)	Field test EPPO PP 1/114(2) The trial was set up in an agricultural habitat (farm) which appeared to harbour an established *Rattus rattus* population.	Pre-treatment census: 15 days (200 g of a mixture of cereal grain and poultry/pig feed per station per day). Treatment: 200 g of bait per day in each lockable bait station – total 8 bait stations) during 15 days. Post-baiting: 7 days (200 g of a mixture of cereal grain and poultry/pig feed per station per day).	Pre-baiting average consumption = 1239 g/day => 80/90 rats Post-baiting average consumption = 0 g Estimated efficacy = 100 %	Study n°2008.BCD.SAG13 R.I =1

Test substance	Test organisms	Test system / Concentrations applied / exposure time	Test conditions	Test results: effects, mode of action, resistance	Reference
FANGA B+ 0.001% Brodifacoum	Brown rat (*Rattus norvegicus*)	Field test Method: Technical Notes for Guidance on Product Evaluation, Appendices to chapter 7 Product type 14 « Efficacy evaluation of rodenticidal biocidal products » The trial was located at a test site where brown rat populations had been identified. This site was located in Claveisolles (Rhône department) near Lyon city	Pre-treatment census: 12 days (50 g of wheat per station per day). Treatment: 100 g of bait per day in each lockable bait station – total 110 bait stations) during 15 days. Post-baiting: 3 days (50 g of wheat per station per day).	Pre-baiting average consumption = 1600 g/day => 80 rats Post-baiting average consumption = 0 g Estimated efficacy = 100 % 19 dead rats found	Study n° 13TOX020 R.I =1
FANGA B+ (BDPA10V1) 0.001% Brodifacoum	Black rats (Rattus rattus)	Field test EPPO PP 1/114(2)	Pre-treatment census: 15 days (200 g of a mixture of cereal grain and poultry/pig feed per station per day). Treatment: 200 g of bait per day in each lockable bait station – total 8 bait stations) during 18 days. Post-baiting: 7 days (200 g of a mixture of cereal grain and poultry/pig feed per station per day).	Pre-baiting average consumption = 938.3 g/day => 60/65 rats Post-baiting average consumption = 0 g Estimated efficacy = 100 %	Study n° 2001.BCD.SAG15 R.I =1

(*) fill in one table for each MG/PT and/or field of use envisage