Product Assessment Report

MURIN DIFE PASTA GIRASOLE

August 2012 (revised on January 2013)

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Authorisation/Registration no:	
Granting date/entry into force of authorisation/ registration:	
Expiry date of authorisation/ registration:	
Active ingredient:	Difenacoum
Product type:	PT14: Rodenticides

Biocidal Product Assessment Report (PAR) related to Product Authorisation under Directive 98/8/EC.

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1 APPLICANT, ACTIVE INGREDIENT MANUFACTURER, PRODUCT FORMULATOR AND AUTHORISATION HOLDER

1.1 APPLICANT

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1.3 MANUFACTURER/FORMULATOR OF PRODUCT

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1.4 AUTHORISATION HOLDER

As in 1.1.

2 GENERAL PRODUCT INFORMATION

2.1 IDENTITY OF THE BIOCIDAL PRODUCT

Trade name	MURIN DIFE PASTA GIRASOLE	
Manufacturer's development code	None	
Ingredients of preparation	**Function**	**Content (%w/w)**
Difenacoum (CAS 56073-07-5)	Active ingredient	0.005
Denatonium Benzoate (CAS 3734-33-6)	Human taste deterrent	0.001
Other Components	Confidential information[a]	Up to 100
[a] please, refer to confidential information in Annex D (Summary of product characteristics)		

2.2 STATEMENT OF TECHNICAL EQUIVALENCE

Activa supported difenacoum inclusion into Annex I of BPD in a Task Force with PelGar. Since the manufacturer of the active substance in MURIN DIFE PASTA GIRASOLE is not different, technical equivalence is not to be addressed.

2.3 PRODUCT TYPE

Rodenticide (PT14)

2.4 CLASSIFICATION AND LABELLING

The current classification and labelling according to Directive 99/45/EC and Regulation (EC) 1272/2008, are provided in the tables below.

Not classified in accordance with the Directive 1999/45/EC.

Symbol(s):	None
Indication(s) of danger:	None
Risk phrases:	None
Safety phrases:	S2: Keep out of reach of children. S13: Keep away from food, drink and animal feeding stuffs. S 20/21: When using, do not eat, drink or smoke S 24: Avoid contact with skin S46: If swallowed, seek medical advice immediately (show the label where possible). S61: Avoid release to the environment. Refer to special instructions/Safety data sheet.

Further, the content of the label should be updated with the additional safety phrases recommended in the Assessment Report (2009):

- Baits must be securely deposited in a way so as to minimize the risk of consumption by other animals or children. Where possible, secure baits so that they cannot be dragged away.
- Search for and remove dead rodents at frequent intervals during treatment (unless used in sewers), at least as often as when baits are checked and/or replenished. Dispose of dead rodents in accordance with local requirements.
- Unless under the supervision of a pest control operator or other competent person, do not use anticoagulant rodenticides as permanent baits.
- Remove all baits after treatment and dispose of them in accordance with local requirements

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

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

2.5 INTENDED USE

The formulation MURIN DIFE PASTA GIRASOLE consists in a “fresh paste” intended for both professional and domestic use to control rodent pests in and around industrial, commercial, civil and residential buildings, in open areas and waste dumps. The formulation is a ready to use bait containing 0.005 % w/w of the anticoagulant active ingredient difenacoum. The product is supplied in heat sealed food paper bags containing from 10 to 20 g of fresh paste or in single dose plastic containers containing from 25 to 150g of fresh paste. The treatments last at maximum 6 weeks. The amount of used product per application ranges from 40 to 200 g per baiting point. Bait points are placed typically every 5-10m. The product is placed in a bait station or fixed to a structure such that rats and mice can eat them. In situations where bait boxes cannot be used, the bait is covered such that non-target organisms cannot reach them. Baiting points are inspected frequently and replenished when bait has been eaten. Dead rodents are removed for disposal as soon as possible in order to prevent them being eaten by non-target animals and birds. When no more bait is eaten and rodent activity stops, the baits are moved into areas with higher rodent activity. The product can also be used as permanent treatment for prevention of infestation, but only under the supervision of a trained pest control operator. In this case, lower doses are needed (60-80 g per baiting point) and inspection and replacement occurs 4-6 times per year.

2.6 DOCUMENTATION

The applicant submitted a Letter of Access from ACTIVA S.r.l. on the active substance difenacoum. ACTIVA S.r.l. was part of the “Activa/Pelgar Difenacoum and

Brodifacoum Task Force", which submitted the Annex II complete dossier to RMS Finland.

A full new product dossier was submitted by in support of the product MURIN DIFE PASTA GIRASOLE containing difenacoum.

3 PHYSICOCHEMICAL PROPERTIES

MURIN DIFE PASTA GIRASOLE consists of solid ready-to-use paste baits with a characteristic odour, containing 0.005% w/w of difenacoum as the active substance. MURIN DIFE PASTA GIRASOLE is mainly composed of food-grade materials forming the bait-base. Baits are dyed dark green to make them unattractive to wildlife and to birds in particular. Baits are furnished in heat sealed food paper bags (10 to 20 g each) or in single dose plastic containers (25 to 150 g each).

Since none of the components are officially classified or self-classified as explosive or oxidising, it can be anticipated that MURIN DIFE PASTA GIRASOLE has neither explosive nor oxidising properties (also confirmed by oxygen balance for individual ingredients and/or structural analysis).

Since none of the components are officially classified or self-classified as flammable/highly flammable, it can be anticipated that MURIN DIFE PASTA GIRASOLE is not highly flammable.

Self-ignition temperature proved to be 360.5°C. None of the components is known to evolve any flammable gases in contact with water/humid air or to be pyrophoric.

The measurement of the pH a 1% w/v aqueous dispersion is not considered relevant, due to either nature and use of MURIN DIFE PASTA GIRASOLE (solid ready-for-use paste baits, not intended for dissolution/emulsion/dispersion in water). Relative density D^{20}_{4} proved to be 1.1139.

As regards the effect of temperature on MURIN DIFE PASTA GIRASOLE, an adequate justification for the adoption of an alternative time/temperature regime (12 weeks at 35°C vs. 2 weeks at 54°C) has been provided. No change in appearance was observed, whereas the a.i. content proved to decrease by 14%.

Since a significant chemical change has occurred, further information is necessary: the fate of difenacoum must be addressed and degradation products must be identified and quantified. This request is not deemed prejudicial to the authorization of MURIN DIFE PASTA GIRASOLE.

Though photodegradation is considered as a minor removal process for the active substance, difenacoum is photodegradable. Anyway, no testing on the effect of light is considered necessary for MURIN DIFE PASTA GIRASOLE, since the exposure of the product to sunlight is negligible if MURIN DIFE PASTA GIRASOLE is correctly stored and used. The effect of humidity on the product has not been addressed. Anyway, no further testing is required since packaging is supposed to prevent the product from contact with external humidity during transport/storage.

After 2-year storage at ambient warehouse temperature, no change in appearance was observed and the a.i. content proved to deviate by +4%. It is generally accepted that the biological performance is not affected by deviations of ± 10%, so results can support a shelf-life claim of 2 years. Following observation after both accelerated storage and storage at ambient warehouse temperature for 6, 12, and 24 months, the container did not present any deformation in either bottom or lateral layers, or loss of sample or evident corrosion phenomena.

Owing to the physical state and nature of MURIN DIFE PASTA GIRASOLE (solid ready-to-use paste bait) and its use pattern, no further testing is deemed necessary for technical characteristics. MURIN DIFE PASTA GIRASOLE is not intended to be used with other products (including other biocidal products), either.

Surface tension, viscosity and particle size distribution are not required for MURIN DIFE PASTA GIRASOLE (solid ready-to-use paste baits).

All results are summarised below. On the basis of the available data, it can be conclude that MURIN DIFE PASTA GIRASOLE does not pose any physical-chemical hazards. Therefore, the need for a risk characterisation for physical-chemical hazards is not envisaged.

A summary of the physical-chemical data originally provided by Vebi to support the MURIN DIFE PASTA GIRASOLE authorization can be found in Annex A of this document. Please, consider that the information therein presented by Vebi does not reflect IT-CA conclusions following evaluation of the physical-chemical data-set. Furthermore, it has been partly superseded by new studies submitted by Vebi in 2012 upon request of the IT-CA.

Summary of physical-chemical and technical properties submitted for MURIN DIFE PASTA GIRASOLE the product authorization phase. Tests were carried out on batches 912014 and 111303 (nominal a.i. content 0.005% w/w).

Endpoint	Result	Method/Guideline	Reference
Appearance	Physical state and nature: solid paste	EPA Guidelines OPPTS 830.6303 (visual observation carried out independently by three inspectors)	IIIB 3.1.1
	Colour: dark green (Short code: GR4 - according to the Sigma-Aldrich Color chart)	EPA Guidelines OPPTS 830.6302 (visual observation carried out independently by three inspectors. The description of the colour has been reported qualitatively)	IIIB 3.1.2
	Odour: characteristic odour	EPA Guidelines OPPTS 830.6304 (olfactory assessment carried out independently by three inspectors)	IIIB 3.1.3
Explosive properties	Since none of the components are officially classified or self-classified as explosive (also confirmed by structural analysis and oxygen balance), it can be anticipated that MURIN DIFE PASTA GIRASOLE does not possess explosive properties	Justification for non-submission of data	IIIB 3.2
Oxidising properties	Since none of the components are officially classified or self-classified as oxidising (also confirmed by structural analysis), it can be anticipated that MURIN DIFE PASTA GIRASOLE does	Justification for non-submission of data	IIIB 3.3

Endpoint	Result	Method/Guideline	Reference
	not possess oxidising properties		
Flash-point and other indications of flammability or spontaneous ignition	Flash-point: not applicable Auto-flammability: self-ignition temperature proved to be 360.5°C Flammability: since none of the components are officially classified or self-classified (see relevant MSDSs) as flammable/ highly flammable, it can be anticipated that MURIN DIFE PASTA GIRASOLE is not highly flammable None of the components is known to evolve any flammable gases in contact with water/humid air or to be pyrophoric, either. No further testing on MURIN DIFE PASTA GIRASOLE is deemed necessary	Justification for non-submission of data EC A.16	IIIB 3.4
Acidity/Alkalinity	The measurement of the pH of a 1% w/v aqueous dispersion is not considered relevant, due to either nature and use of MURIN DIFE PASTA GIRASOLE (ready-for-use paste bait, not intended for dissolution/emulsion/dispersion in water)	CIPAC MT 75.3 (not accepted)	IIIB 3.5
Bulk density	D^{20}_{4}= 1.1139	EC A.3, OECD 109 (Hydrostatic balance method)	IIIB 3.6/02
Storage stability - stability and shelf life	Effect of temperature: No change in appearance was observed, whereas the a.i. content proved to decrease by 14%. Since a significant chemical change has occurred, **further information is necessary: the fate of the a.i. must be addressed and degradation products must be identified and quantified** [1] Effect of humidity: Not addressed. Anyway, packaging is supposed to prevent the product from contact with external humidity during transport/storage Shelf-life: No change in appearance was observed. It is generally accepted that the biological performance is not affected by deviations of ± 10%. Since the a.i. content proved to deviate by +4% after 2-year storage, results can support a	Modified CIPAC MT 46 (12 weeks at 35°C. Justification by the Applicant: "*Testing at 54°C is prevented by the nature of the product, which is a paste formulation composed of ingredients with a low melting point.*") Storage at ambient warehouse temperature after 6, 12, and 24 months. Analytical method CH032/2010 for the determination of the a.i. content; 830.6302, 830.6303 and 830.6304 for appearance	IIIB 3.7

Endpoint	Result	Method/Guideline	Reference
	shelf-life claim of 2 years <u>Reactivity towards container material</u>: the container did not present any deformation in either bottom or lateral layers, or loss of sample or evident corrosion phenomena <u>Effect of light</u>: The a.i. is photodegradable, though photodegradation is a minor removal process for difenacoum. Anyway, no testing is required, since the exposure of MURIN DIFE PASTA GIRASOLE to sunlight is negligible when the product is correctly stored and use	Observation after accelerated storage (12 weeks at 35°C) and after storage at ambient warehouse temperature for 6, 12, and 24 months Justification for non-submission of data	
Technical characteristics	Owing to the physical state and nature of MURIN DIFE PASTA GIRASOLE (solid ready-for-use paste bait) and its use pattern, no further testing is deemed necessary	Justification for non-submission of data	IIIB 3.8
Compatibility with other products	Not required. MURIN DIFE PASTA GIRASOLE is not intended to be used with other products (including other biocidal products)	Justification for non-submission of data	IIIB 3.9
Surface tension	Not required for MURIN DIFE PASTA GIRASOLE, which is a solid ready-for-use paste bait	Justification for non-submission of data	IIIB 3.10
Viscosity	Not required for MURIN DIFE PASTA GIRASOLE, which is a solid ready-for-use paste bait	Justification for non-submission of data	IIIB 3.11
Particle size distribution	Not required for MURIN DIFE PASTA GIRASOLE, which is a solid ready-for-use paste bait	Justification for non-submission of data	IIIB 3.12

3.1 ANALYTICAL METHODS FOR DETECTION AND IDENTIFICATION

Acceptable methods for the determination of difenacoum and the only impurity present at quantity >0.1% w/w in the technical grade material manufactured by Pelgar are available in the Competent Authority Report (CAR) on Difenacoum (PT 14) prepared according to Art. 11(2) of Directive 98/8/EC by the RMS-Finland.
The RMS-Finland required also Activa to submit additional analytical data in the product authorization phase, in order to prove the isomeric composition and the impurity profile of their technical material (manufactured by Tezza s.r.l. using the same manufacturing process as Pelgar). In July 2011, Activa eventually clarified the impurity profile of their technical material and submitted a new five-batch analysis.
Information on purity, isomeric composition and impurities is now available from both Members of the Task Force based on their respective 5-batch analysis, thus allowing

the assessment of the technical equivalence of the two sources. Access to active substance data is granted to Vebi by Activa s.r.l. LoA.

The methods for the analysis of difenacoum residues in soil and water by HPLC-DAD and LC-MS/MS, respectively, have been acceptably validated and regarded to be sufficiently sensitive with respect to the levels of concern. An acceptable analytical method for the determination of residues of difenacoum on food matrices (cucumber, wheat and lemon) is available which enables the analysis down to level of 0.01 mg/kg. A summary of all these methods is reported in the Competent Authority Report (CAR) on Difenacoum (PT 14) prepared according to Art. 11(2) of Directive 98/8/EC by the RMS-Finland. Access to these data is granted to Vebi by Activa s.r.l. LoA.

Additional methods by LC-MS/MS for the analysis of difenacoum in sediment, bovine liver, bovine muscle and oilseed rape seed down to 0.01 mg/kg have been submitted by Activa for the product authorization phase, as required by the RMS-Finland. All these methods meet the requirements provided for by SANCO/825/00 and the Additional Guidance to TNSG on Data Requirements on analytical methods. Access to these data is granted to Vebi by Activa s.r.l. LoA.

As regards co-formulants in MURIN DIFE PASTA GIRASOLE, some are classified as dangerous substances, but exist in such small concentration that none of them lead to the classification of MURIN DIFE PASTA GIRASOLE. No analytical method for the determination of residues in soil/sediment, air, water, body fluids and tissues, food/feedstuffs is deemed necessary for co-formulants.

3.2 FORMULATION ANALYSIS

A method by HPLC with UV detection at 270 nm for the determination of difenacoum in MURIN DIFE PASTA GIRASOLE has been developed and validated according to SANCO/3030/99 rev. 4. Quantitation was performed using an external standard.
Difenacoum was extracted from MURIN DIFE PASTA GIRASOLE using a mixture solution of dichloromethane and methanol (40:60) with a low quantity of formic acid (for a 20 g sample, 100 mL of the mixture solution and 1 mL of formic acid are used). The resulting solution was placed in a sonication bath for 15 minutes and stirred overnight. The extract was centrifuged at 8000 rpm for 10 minutes; after 4 hours, 3 µL of the supernatant were injected for analysis. Since validation criteria were fulfilled, the submitted HPLC/UV method was considered acceptable for the analysis of commercial batches of MURIN DIFE PASTA GIRASOLE.

No analytical methods are required for co-formulants.

Sample	Test substance	Analytical method	Fortification range / N° of measurements	Linearity	Specificity	Recovery			LOQ mg/kg	Ref.
						Range (%)	Mean (%)	%RSD		
MURIN DIFE PASTA GIRASOLE	Difenacoum	HPLC-UV, external std	0.00378 % w/w (n=2) 0.005 % w/w (n=2) 0.0063 % w/w (n=2)	4 determinations at 5 concentration levels over the range 0.0026–0.0077 % w/w y = -75692 + x 831565 r^2 >0.99960	Specific	90.8 – 92. 93.3 – 94. 89.7 – 92. overall 89.7 – 94.	91.6 93.7 91.0 overall 92.1	- - -	-	IIIB 4.1/01

4 HUMAN HEALTH RISK ASSESSMENT

4.1 EFFECTS ASSESSMENT

New data

In the biocidal product, MURIN DIFE PASTA GIRASOLE is a dark green solid ready to use bait in the form of a solid paste, containing 0.005% of the active substance *difenacoum.* Other than the active ingredient, it is composed of food-grade materials forming a bait base, without additives or impurities that would be of toxicological concern.

The product MURIN DIFE PASTA GIRASOLE has been subjected to acute oral and dermal toxicity testing, skin and eye irritation and skin sensitization testing. All the test were conducted according to OECD guidelines and in compliance with GLP principles. The results indicate that the product is not acutely toxic by the oral (LD_{50}>2000 mg/kg bw) and dermal (LD_{50}>2000 mg/kg bw) exposure. Therefore it is not expected to be acutely toxic by either routes of exposure.

In the tested experimental conditions, it is not irritant to the skin neither to the eye of rabbit and it is not a skin sensitizer.

Justification for the non-conduct of certain endpoints

1. The product is formulated as solid paste using mostly food grade materials, which are solid at NTP and of low vapour pressure. The paste is not friable or dusty such that airborne particles can be produced. The paste does not produce respirable particles or vapours. Due to the low vapour pressure of the a.s and the physical state of the product, the amount of potential exposure through inhalation is most likely at very low level. Therefore the applicant considered that a study on acute inhalation toxicity of the product is not required. The RMS agrees with this conclusion.

2. Dermal absorption: an in vitro dermal absorption study is already available within the active substance dossier submitted for Annex I inclusion on a formulation which is representative for the product (a paste bait containing 0.005% of difenacoum). It is therefore concluded that difenacoum dermal absorption is 0.046% of the applied dose, with no need for further studies to be conducted.

3. Related endpoints from Annex IIIB of 98/8/EC: The company states that a) 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, and b) based on intended uses and proper baiting practices of rodenticides, human exposure through residues in livestock is expected to be very limited and feeding and metabolism studies in livestock to permit evaluation of residues in food of animal origin are not required; c) the biocidal product is in a ready to use form and will not undergo industrial processing and/or domestic preparation and so there should be no change to the nature of the product. The RMS Italy accepts these justifications.

4. The active substance difenacoum is not classified as a skin or eye irritant or a skin sensitiser. Nevertheless it shows high acute oral, dermal and inhalation toxicity. For details on toxicological characteristics of the active substance difenacoum see the Combined Assessment Report on difenacoum prepared by RMS Finland. For risk characterization purposes the critical effect is considered related to the maternal

LOAEL of 0.001 mg/kg/day in the teratogenicity study in rabbits is chosen as the basis for the setting of the AOEL.

4.2 EXPOSURE POTENTIAL

4.2.1 Professional use

For professional use, the operator is trained in the correct use of the product, i.e. placement, number of bait boxes required based on the infestation rate area, the amount of product per box and safe handling procedures. The use of PPE, i.e. disposable gloves and a face-mask may be used when loading bait boxes and disposing of remaining bait and carcasses. However, when the product is contained within a bait trap there will be no exposure of the operator to the product. PPE (coverall, boots and gloves) is required as standard when the product is used in sewage systems. During use, professional pest control operators will be exposed during loading of bait boxes and application of the product via the dermal route and to the hands only. Nevertheless, the product is furnished in heat sealed food paper bags or in single dose plastic containers therefore only a limited dermal exposure is expected.

In all cases, according to TNsG, the risk of exposure by inhalation is negligible (10^{-5} mg/m^3). Also measured data from a study conducted to determine exposure during simulated use of rodenticide baits (conducted by CEFIC/EBPF Rodenticides Data Development Group and reported in the CAR on difenacoum under B6.6 (1)) supports this assumption.

The models and calculations are presented in Appendix 1 of Doc.IIB and the results summarised below.

75-percentile			
Professional exposure			
	Application	**Post-application**	**Total exposure**
Without PPE	6.4×10^{-7} mg/kg bw/day	3.3×10^{-8} mg/kg bw/day	6.7×10^{-7} mg/kg bw/day
With PPE	6.4×10^{-8} mg/kg bw/day	3.3×10^{-9} mg/kg bw/day	6.7×10^{-8} mg/kg bw/day

4.2.2 Non professional use

MURIN DIFE PASTA GIRASOLE is intended for use by the general public (domestic use) applying the product ONLY as bait boxes which cannot be refilled. Therefore there will not be any dermal or inhalation exposure to the general public from use of the baits in rodent control. Nevertheless, as worst case, exposure calculations have also been conducted assuming that the bait boxes would have to be loaded by the user. As a worst case scenario, consumers were assumed to load five bait boxes, clean five bait boxes per day and to wear no PPE.

The models and calculations are presented in Appendix 1 in Doc.IIB and the results summarised below.

Non professional exposure	
75-percentile " MURIN DIFE PASTA GIRASOLE"	
Default	**Exposure**
Assuming that conventional bait boxes are loaded	5.3 x 10^{-8} mg/kg bw/day
Potential exposure only during clean-up.	1.1 x 10^{-8} mg/kg bw/day
Total dermal exposure for non-professional users	6.4 x 10^{-8} mg/kg bw/day

4.2.3 **Indirect exposure**

According to TNsG Human Exposure to Biocidal Products (Part 3, pag 55), the chronic scenarios are not relevant and the risk of exposure by inhalation is negligible (10^{-5} mg/m^3).
Moreover, the scenario of children skin contact with exposed baits and dead animals (chronic) is excluded from the risk assessment due to unrealistic assumptions (see Doc II-B, Section 3.2.4 of the Competent Authority Report on Difenacoum).
Within acute scenarios, for infants only the secondary exposure through ingestion of poison baits has been considered, as the worst case, while the dermal contact while handling the bait in connection with ingestion of poison bait it is assumed to be of minor role compared to oral exposure and is excluded from the risk assessment. The "transient mouthing of poison bait" scenario has been assessed considering that either 5 g or 10 mg are ingested per poisoning event.
The calculations are presented in Appendix 1 of Doc II-B and the results summarised below.

Indirect exposure – acute phase reference scenarios	
Infant (10 kg) acute, 5 g per poisoning event	2.5 x 10^{-2} mg/kg bw
Infant (10 kg) acute, 10 mg per poisoning event	5 x 10^{-5} mg/kg bw

However, the bait boxes have been manufactured to prevent incidental poisoning to both non-target animals and man, i.e. children. The boxes are hard plastic and are either locked or sealed shut to prevent access to the bait.

4.3 **RISK CHARACTERISATION**

Primary and acute secondary exposures have been assessed against the same AEL of 0.0000011 mg/kg/day.
For professional users, safe use are predicted whether PPE (gloves) is used (% AEL=6.1) or not (AEL=61).

For non-professional users, a safe use is predicted also not considering the use of PPE (% AEL = 5.8).

For secondary exposure, no acceptable margin of safety is calculated for infants ingesting 5 g (% AEL=2.27x10^6) or 10 mg (% AEL=4.55x10^3) of product.

5 ENVIRONMENTAL RISK ASSESSMENT

5.1 EFFECTS ASSESSMENT

No aquatic, terrestrial or secondary poisoning studies were conducted with the formulation, as they are not required for the rodenticidal products. Moreover, MURIN DIFE PASTA GIRASOLE does not contain substances of concern, therefore the ecotoxicological effects can be derived from the effect studies conducted with the active substance. Also, exposure of the aquatic compartment is not expected after the use of MURIN DIFE PASTA GIRASOLE according to the label. In the same way, no adverse effects of the product MURIN DIFE PASTA GIRASOLE are expected via atmospheric exposure due to low vapour pressure of the active substance and to the mode of use of the product.

5.2 EXPOSURE ASSESSMENT

The main route of potential environmental exposure is from use of the product as a rodenticide.
PEC in surface water, sediment, sewage treatment plants and air considered not relevant, while soil is the main receiving compartment.

Non compartment specific exposure relevant to the food chain

Primary poisoning

According to ESD (Larsen, 2003) primary poisoning hazard to mammals and birds (both wild and domestic) can be considered small. In use scenarios where difenacoum is placed in protected bait point, there is the risk for primary poisoning mainly for birds and mammals of equal size or smaller as the target rodents, which may be able to enter the bait stations. Also when target animals carry bait away from e.g. bait stations, non-target animals may be exposed.

Secondary poisoning

Secondary poisoning trough aquatic food chain is not considered due to the non-significant exposure of aquatic organisms to difenacoum after the use of MURIN DIFE PASTA GIRASOLE.

5.3 RISK CHARACTERISATION

The quantitative risk characterization is carried out by comparing the PEC with the PNEC for each environmental compartment and each exposure scenario. For the present assessment, PNEC values referring to the active substance have been used because no ecotoxicity testing has been carried out on the product.

Aquatic compartment

The quantitative risk characterization for the aquatic compartment was not carried out because it is not relevant for the MURIN DIFE PASTA GIRASOLE recommended uses. In fact, residues from indoor use may reach the aquatic environment from disposal by sewerage system or cleaning; but this emission is assumed to be insignificant.

Terrestrial compartment

Exposure of soil organisms to difenacoum by direct contamination of soil may occur following the use of MURIN DIFE PASTA GIRASOLE in and around buildings. No terrestrial study was conducted for the rodenticidal product. The ecotoxicological effects were be derived from the studies conducted with the active substance.

The calculated PEC/PNEC values indicate that there is no concern for the terrestrial compartment for this specific emission scenario.

Biota (non compartment specific effects relevant to the food chain)

$PNEC_{oral}$ for birds and mammals were taken from Doc II-A, Section 4.2.7 of the CAR on Difenacoum, 2009). For the acute exposure situation, no $PNEC_{oral}$ is determined and no quantitative risk characterisation is performed. Instead a qualitative assessment was done by comparing LD50 values to the expected contents of the active substances in birds and mammals.

Primary poisoning

The risk characterisation indicates a very high risk to non-target mammals and birds from direct eating of bait. According to the qualitative assessment, lethal effects are not likely but animals would suffer from sub-lethal effects. Primary poisoning incidents can be minimised by preventing the access of non-target animals to the baits. It is assumed in the ESD that, if the rodenticide baits are used according to the label instructions, the risk for primary poisoning is negligible. However, it is not possible to exclude exposure of all non-target animals, as the baits have to be accessible to target rodents, so they may as well be accessible to non-target mammals and birds of equal or smaller size than the target rodents.

Secondary poisoning

Secondary poisoning trough aquatic food chain was not considered due to the non-significant exposure of aquatic organisms to difenacoum after the use of MURIN DIFE PASTA GIRASOLE.

In the terrestrial environment, birds and mammals may be at risk for secondary poisoning if they feed on contaminated soil organisms. The calculation of PEC_{oral}, predator were conducted for all the different uses and scenarios identified; the obtained PEC/PNEC ratio for birds and mammals exceeds 1 for all the use/scenario combination, indicating a risk of secondary poisoning trough the terrestrial food-chain via earthworm.

Theoretical calculations, experimental results and monitoring data clearly show that difenacoum poses a risk for secondary poisoning. However, the theoretical calculations may overestimate the residues accumulating in the predators. In order to reduce the risk of secondary poisoning, it is very important to follow the use instructions of the rodenticidal baits and carefully take into account the risk mitigation measures provided by Directive of inclusion in Annex I of Difenacoum (EC/2008/81).

As reported in the CAR on Difenacoum 2009, the measures include use of tamper resistant bait boxes, collection of unconsumed baits after termination of the control campaign and collection of dead rodents during and after the control campaign.

6 EFFICACY

6.1 FUNCTION

MG03: Pest control

Product Type 14 - Rodenticide

6.2 ORGANISM(S) TO BE CONTROLLED AND PRODUCTS, ORGANISMS OR OBJECTS TO BE PROTECTED.

Organisms to be controlled are house mice (Mus musculus), brown rats (Rattus norvegicus) and black rats (Rattus rattus). Rodenticides are needed to protect humans and animals from pathogen transmission. Rodenticides are also used on domestic, industrial and commercial sites, including farms and waste dumps to protect commodities, buildings/structures and components thereof from contamination and damage.

6.3 EFFECTS ON TARGET ORGANISMS

The efficacy of MURIN DIFE PASTA GIRASOLE, a paste bait containing 0.005% difenacoum, has been assessed against the label claims, i.e. domestic and professional use (comprising also professional ancillary e.g. farmers, smallholders, food shops, restaurants, etc.) of MURIN DIFE PASTA GIRASOLE in household, civil and industrial fields. In the label it is also claimed that the product does not create alarm or suspicion to the other members of the rodent community.

Laboratory choice and efficacy studies with fresh paste bait and with aged paste bait on rats and mice are in progress and will be submitted as soon as available. For the fresh bait, preliminary results are currently available (Interim draft report, results obtained in compliance with the assay validity criteria and ASTM E565-95) and they evidenced as MURIN DIFE PASTA GIRASOLE is palatable and effective on mouse and rats (92.5% of treated animals died during the post test).

In addition, three field studies were performed on brown rats (Rattus norvegicus), black rats (Rattus rattus) and house mice (Mus musculus).

The results of field studies on black rats (Rattus rattus), house mice (Mus musculus) and brown rats (Rattus norvegicus) evidenced as the product MURIN DIFE PASTA GIRASOLE showed a good acceptance and provided a complete effectiveness (100 %) against the relevant target populations present in the trial sites.

The field study on brown rats (Rattus norvegicus) includes also a comparative assessment of the palatability of tea-bags baits versus bait offered in the single dose plastic containers. The results show that there were only small differences in the bait consumption of MURIN DIFE PASTA GIRASOLE in the presentation of tea-bags (15 grams bait) or single dose plastic containers (100 grams plastic trays): the total consume from the 15 grams baits was 787 grams while 753 grams was the consume from the plastic tray. Therefore both the packages are palatable to brown rat.

6.4 OCCURRENCE OF RESISTANCE

Resistance is exclusively related to the active substance difenacoum and is discussed in Doc II-A, Section 2.4 of the Competent Authority Report (CAR) on Difenacoum (PT 14) prepared according to Art. 11(2) of Directive 98/8/EC by the Rapporteur Member State Finland.

7 MEASURES TO PROTECT MAN, ANIMALS AND THE ENVIRONMENT

7.1 METHODS AND PRECAUTIONS CONCERNING HANDLING, USE, STORAGE, TRANSPORT OR FIRE

Methods and precautions concerning placing on the market
No specific precautions required when handling unopened packs/containers; follow relevant manual handling advice.

Methods and precautions concerning handling and use

Avoid contact with eyes, skin and clothing. Avoid ingestion or inhalation. Wash hands and exposed skin after work. Do not eat, drink or smoke during use.

Personal protection:

- Respiratory protection: Not necessary.
- Hand protection: Suitable gloves. Replace if contaminated.
- Eye protection: Not necessary
- Skin protection: Wear suitable clothing. Replace contaminated clothing.

Methods and precautions concerning storage
Storage in closed containers and in dry and well-ventilated area is recommended. Keep away from children. Keep away from food, drinks or animal feedingstuffs. Protect from light, heat and naked flames.

Methods and precautions concerning transport

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

Methods and precautions concerning fire

Suitable fire-extinguishing media:
Foam and carbon dioxide

Unsuitable fire-extinguishing media:
None in particular

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

Special exposure risks:
Difenacoum may release toxic fumes

7.2 SPECIFIC PRECAUTIONS AND TREATMENT IN CASE OF AN ACCIDENT

Specific treatment in case of an accident, e.g. first-aid measures, antidotes, medical treatment if available

Prevent the access of children and domestic animals. Do not contaminated foodstuffs with the product.

First aid measures:

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

ADVICE FOR DOCTORS*:*

Pharmaceutical-dynamic action: the active substance contained in the product is a competitive antagonist of Vitamin K and reduces the hepatic synthesis of K-dependent factors.
Symptoms: heavy poisoning by ingestion inhibits the vitamin K, causing skin and mucous haemorrhages. The symptomatology of the other systems and apparatus is prevailingly haemorrhagic.
Therapy: in case of ingestion of big quantities, provoke vomiting, perform gastric lavage and monitor the protrombinic activity; if it reduces, give vitamin K.

Controindications: anticoagulants

Emergency measures to protect the environment

Prevent the product from reaching surface waters.

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

7.3 PROCEDURES FOR CLEANING APPLICATION EQUIPMENT

No application equipment is needed.

7.4 IDENTITY OF RELEVANT COMBUSTION PRODUCTS IN CASES OF FIRE

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

7.5 PROCEDURES FOR WASTE MANAGEMENT OF THE BIOCIDAL PRODUCT AND ITS PACKAGING

Product: Dispose the product waste in accordance with the local rules. Do not reuse or recycle the unused product.

Empty packaging: empty containers are considered wastes of the same class of the contents and should be disposed of in accordance with the relevant local rules.

Carcasses of dead rodents collected during campaign should be disposed of according to local rules.

7.6 POSSIBILITY OF DESTRUCTION OR DECONTAMINATION FOLLOWING ACCIDENTAL RELEASE

Air:

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

Soil and water:

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

Collect the material thoroughly into suitable containers. Wash the contaminated area with a soapy solution; collect waste waters for treatment.

7.7 UNDESIRABLE OR UNINTENDED SIDE-EFFECTS

The product is palatable to non-target species in sufficient quantity to produce toxic effects. The active substance will have the same toxic effect in non-target species as in target species. See Section B7.8.7.2 for details of effects on non-target species.

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

7.8 POISON CONTROL MEASURES

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

7.9 PACKAGING

The product is a ready-to-use paste bait furnished in two different type:

a) heat sealed food paper bags: 10 – 12.5 – 15 – 20 g
b) single dose plastic containers: 25 – 40 – 80 – 100 – 150 g

Users	Material	Type	Size
Professional	PET bag	a) and b)	1 – 3 – 5 – 10 – 20 – 25 kg
Domestic	PET bag	a) and b)	100 – 150 – 200 – 250 – 300 – 450 – 500 g

8 DECISION

8.1 NECESSARY ISSUES ACCOUNTED FOR IN THE PRODUCT LABEL

The following elements have been taken into account when authorising MURIN DIFE PASTA GIRASOLE:

- The use of appropriate personal protective equipment should be guided in the use instructions.
- Exposure assessment shows that professional and non professional exposure is acceptable.
- The restriction of product to specific areas and manners of use has been considered.
- Product design and use restrictions should be optimised in order to ensure sufficient efficient rodent control while at the same time minimizing the risk for primary poisoning. This includes the use of tamper resistant bait boxes and the need to secure the baits so that rodents cannot remove the bait from the bait box.
- When tamper-resistant bait stations are used, they should be clearly marked to show that they contain rodenticides and that they should not be disturbed.
- Difenacoum baits should not be placed where food, feedingstuffs or drinking water could be contaminated.
- In case no standard safety phrases are required on the product label, adequate safety instructions should be provided in the use instructions.
- Baits must be securely deposited in a way so as to minimise the risk of consumption by other animals or children. Where possible, secure baits so that they cannot be dragged away.
- Search for and remove dead rodents at frequent intervals during treatment (unless used in sewers), at least as often as when baits are checked and/or replenished. Dispose of dead rodents in accordance with local requirements.
- Unless under the supervision of a pest control operator or other competent person, do not use anticoagulant rodenticides as permanent baits.
- Remove all baits after treatment and dispose of them in accordance with local requirements.
- Keep out of the reach of children.
- The population size of the target rodent should be evaluated before a control campaign. The number of baits and the timing of the control campaign should be in proportion to the size of the infestation.
- A complete elimination of rodents in the infested area should be achieved.

- Resistant management strategies should be developed, and difenacoum should not be used in an area where resistance to this substance is suspected.

- The authorisation holder shall report any observed resistance incidents to the Competent Authorities or other appointed bodies involved in resistance management.

- When the product is being used in public areas, the areas treated must be marked during the treatment period and a notice explaining the risk of primary or secondary poisoning by the anticoagulant as well as indicating the first measures to be taken in case of poisoning must be made available alongside the baits.

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

Due to the unacceptable risk calculated for infants ingesting the product, it is considered appropriate to limit aspects of the packaging for non professional use as a further risk mitigation measure. Non-professional baits are to be used in refillable tamper-resistant bait stations and supplied as inner packs or units containing at most enough bait for one bait-point (either rat or mouse) with a maximum pack-size of 500g.

8.2 REQUIREMENT FOR FURTHER INFORMATION

As regards the effect of temperature on MURIN DIFE PASTA GIRASOLE, no change in appearance was observed, whereas the a.i. content proved to decrease by 14%.

Since a significant chemical change has occurred, further information is necessary: the fate of difenacoum must be addressed and degradation products must be identified and quantified. This request is not deemed prejudicial to the authorization of MURIN DIFE PASTA GIRASOLE.

No further data are deemed necessary.

ANNEX A. PHYSICOCHEMICAL PROPERTIES

(Information is as summarised by the company. Please note that no amendments to this table have been made by the IT-CA and this summary is provided for MS information only)

Subsection (Annex Point)	**Results**	**Method**	**Reference**
3.1 Appearance (IIB III.3.1)			
3.1.1 Physical state and nature	Solid paste	EPA Guidelines OPPTS 830.6303	Garofani S. (2010a)
3.1.2 Colour	Dark green	EPA Guidelines OPPTS 8306302	Garofani S. (2010a)
3.1.3 Odour	Characteristic odour	EPA Guidelines OPPTS 8306304	Garofani S. (2010a)
3.2 Explosive properties (IIB III.3.2)	Not explosive. None of the components is classified as explosive under directive 67/548/EC.		
3.3 Oxidising properties (IIB III.3.3)	Not oxidising. None of the components of the product is classified as oxidisers under the directive 67/548/EC.		
3.4 Flash-point and other indications of flammability or spontaneous ignition (IIB III.3.4.)	No ignition temperature, not flammable. Flash-point study is not required since the test article is a solid paste. None of the components of the product is classified as flammable under the directive 67/548/EC. No evidence of flammability in use.		
3.5 Acidity/Alkalinity (IIB III.3.5)	pH = 6.52 (1% aqueous dispersion)	CIPAC MT 75.3	Garofani S. (2010a)
3.6 Relative density/bulk density (IIB III.3.6)	1.10 g/mL	CIPAC MT 33	Garofani S. (2010a)
3.7 Storage stability - stability and shelf life (IIB III.3.7)			
Effect of temperature (2 years at ambient temperature)characteristics	Test ongoing. A storage stability test at room temperature for two years is in		

Subsection (Annex Point)	Results			Method	Reference
	progress and the final report will be available on April 2012.				
Effect of temperature (12 weeks at 35°C)	**Test**	**Initial**	**12 weeks**		
	a.i. content (%w/w)	0.0050 ± 0.0005	0.0043± 0.0005		
	Weight variation (%)	-	-0.82% (mean value)		
	Appearance	Dark green solid with characteristic odour	Dark green solid with characteristic odour		
	pH	6.52	6.34		
	Tap density (g/mL)	1.100	1.104		
Reactivity towards container material	The container did not present any deformation in either bottom or lateral layers, or loss of sample or evident corrosion phenomena.				
Effect of sunlight	Exposure of the product to sunlight is limited if it is correctly stored and used. In fact the use, exposure is limited to the time it takes to place the bait and cover it or to close the bait box. Due to the very short length of time of exposure it is considered that further information is unnecessary.				
3.8 Technical characteristics (IIB III.3.8)					
Wettability/ Suspensibility	Not relevant to solid paste baits which are not mixed with water.				
Wet sieve analysis	Not relevant to solid paste baits which are not mixed with water.				
Emulsifiability	Not relevant to solid paste baits which are not mixed with water.				
Disintegration time	Not relevant to solid paste baits.				
Attrition/friability of granules; integrity of tablets	Not relevant to solid paste baits.				
Persistence of foaming	Not relevant to solid paste baits which are not mixed with water.				
Flowability/Pourability	Not relevant to solid paste baits which are not mixed with water.				
Dustability	Not relevant to solid paste baits.				

Subsection (Annex Point)	Results	Method	Reference
3.9 Compatibility with other products (IIB III.3.9)	Not required since the product is a ready-to-use solid paste and it is not intended to be added to or mixed with any other product		
3.10 Surface tension (IIB III.3.9)	Not required since the product is a ready-to-use solid paste		
3.11 Viscosity (IIB III.3.9)	Not required since the product is a ready-to-use solid paste		
3.12 Particle size distribution	Not required since the product is a ready-to-use solid paste		

ANNEX B. HUMAN HEALTH TOXICOLOGY DATA

(Information is as summarised by the company. Please note that no amendments to this table have been made by the IT-CA and this summary is provided for MS information only)

Table B.1. Company summary of Acute Toxicology

Route	Method Guideline	Species, strain, sex, No./Group	Dose levels Duration of exposure	Values LD_{50}/LC_{50}	Reference
Oral	OECD 423 GLP	Rat, SD strain, Females, 6 (3/group)	2000 mg/kg	LD_{50}>5000 mg/kg bw	Mapari, P.V. (2010). Murin Dife Pasta Girasole: Acute Oral Toxicity Study In Rats. INTOX Pvt Ltd., Draft Report No. 10306 (unpublished).
Dermal	OECD 402 GLP	Rat, SD strain, Males and Females, 10 rats (5/sex/group)	2000 mg/kg 24 hours exposure	Test in progress	P. R. Pachpute (2010). Murin Dife Pasta: Acute Dermal Toxicity Study in Rats. INTOX Pvt. Ltd., Protocol No. P/10307/ADR/10 - 20, February 2010 (unpublished).

Table B.2. Company summary of Skin irritation

Species	Method	Average score 24, 48, 72 h		Reversibility (yes/no)	Result	Reference
		Erythema	Oedema			
Rabbit	OECD 404 GLP	-	-	-	-	Pachpute, P. R. (2010). Murin Dife Pasta: acute dermal irritation / corrosion study in rabbits. INTOX Pvt. Ltd., Protocol N° P/10308/ADI/10, 20 February 2010 (unpublished).

Table B.3. Company summary of Eye irritation

Species	Method	Average score 24, 48, 72 h	Reversibility	Result	Reference

		Cornea	Iris	Conjunctiva		(yes/no)		
				Redness	Chemosis			
Rabbit	OECD 405 GLP	-	-	-	-	-	-	Pachpute, P. R. (2010). Murin Dife Pasta: acute eye irritation / corrosion study in rabbits. INTOX Pvt. Ltd., Protocol N° P/10309/ADI/10, 20 February 2010 (unpublished).

Table B.4. Company summary of Sensitisation

Species	Method	Number of animals sensitised/total number of animals	Result	Reference
Guinea pig	OECD 406 GLP	-	-	Pachpute P. R., (2010). Murin Dife Pasta: skin sensitisation study by Guinea-pig maximisation test (GPMT), INTOX Pvt. Ltd., Protocol N° p/10310/SS-GPMT/10, 11 February 2010 (unpublished).

ANNEX C. EFFICACY OF THE ACTIVE SUBSTANCE FROM ITS USE IN THE PRODUCT

(Information is as summarised by the company. Please note that no amendments to this table have been made by the IT-CA and this summary is provided for MS information only)

Test substance	Test organism(s)	Test system / concentrations applied / exposure time	Test conditions	Test results: effects, mode of action, resistance	Reference

<table>
<tr><th>Test substance</th><th>Test organism(s)</th><th>Test system / concentrations applied / exposure time</th><th>Test conditions</th><th>Test results: effects, mode of action, resistance</th><th>Reference</th></tr>
<tr><td colspan="6">boratory studies</td></tr>
<tr><td>MURIN DIFE PASTA GIRASOLE (fresh bait)</td><td>Rats and mice</td><td>Rats: SD
Mice: CD-1
Females and males

Palatability test: 4 days</td><td>Daily volumes of approx. 15 g (rats) and approx. 10 g (mice).

Controls: standard diet
Palatability test: 4 days
Observation period: 14 days</td><td>Male and female rats
Intake of contaminated food (% of the total food consumption): n.a.
Mortality: % = 85; Time of death (days after first bait application) = Post test
Male and female mouse
Intake of contaminated food (% of the total food consumption): n.a.
Mortality: % = 100; Time of death (days after first bait application) = Post test</td><td>B5.10.2/04
Freli V; 17/03/2010. Rodenticide Efficacy Evaluation - according to ASTM565-95 and Palatability Results after experimentation. BIOLAB S.p.A., Study program 2010/74 Ami (Draft Interim Report).</td></tr>
<tr><td>MURIN DIFE PASTA GIRASOLE (aged bait)</td><td>Rats and mice</td><td>Test in progress</td><td>Test in progress</td><td>Male rats
Intake of contaminated food (% of the total food consumption): -
Mortality: % = -; Time of death (days after first bait application) = -
Female rats
Intake of contaminated food (% of the total food consumption): -
Mortality: % = -; Time of death (days after first bait application) = -</td><td>B5.10.2/05</td></tr>
</table>

<table>
<tr><th>Test substance</th><th>Test organism(s)</th><th>Test system / concentrations applied / exposure time</th><th>Test conditions</th><th>Test results: effects, mode of action, resistance</th><th>Reference</th></tr>
<tr><td colspan="6">Field studies</td></tr>
<tr>
<td>MURIN DIFE PASTA GIRASOLE</td>
<td>Norway rat
(Rattus norvegicus B.)</td>
<td>Norway rat

Poisoning: 37 days (14 bait stations filled with about 100 g of poisoned pasta baits)</td>
<td>The trial was set up in an agricultural habitat (farm) which appeared to harbour an established Rattus norvegicus population.
No rodenticide treatments were carried out in this site over the previous four months.
TRIAL SITE:
Country Italy
Region Veneto (North east Italy)
Site description House 1, House 2, Warehouse 1, Warehouse 2, Garage, Goose pen, Chicken pen.

Pre-treatment: 7 days (14 bait stations filled with about 100 g of unpoisoned pasta baits; 10 tracking patches)
Lag period: 13 days
Poisoning: 37 days (14 bait stations filled with about 100 g of poisoned pasta baits; 10 tracking patches)
Lag period: 7 days
Post-treatment: 14 days (14 bait stations filled with about 100 g of unpoisoned pasta baits; 10 tracking patches)</td>
<td>
<table>
<tr><th colspan="2">Norway rats</th></tr>
<tr><td colspan="2">Mortality</td></tr>
<tr><td>Dead rats found</td><td>Time of death</td></tr>
<tr><td>5</td><td>From day 10 to day 23 of poisoning phase</td></tr>
</table>
<table>
<tr><th colspan="3">Norway rats</th></tr>
<tr><td>Estimated population size</td><td>Average daily bait takes</td><td>Tracking patches</td></tr>
<tr><td><u>Pre-treatment census</u>:</td><td>44 g</td><td>Footprints
(Tracking score 1.46)</td></tr>
<tr><td><u>Post-treatment census</u>:</td><td>0</td><td>0</td></tr>
</table>
</td>
<td>B5.10.2/03
Castellini, Stefano; 03/12/2010. Efficacy and comparison evaluation of
MURIN DIFE PASTA GIRASOLE (difenacoum 0,005% a.i. pasta bait)
for the control of Norway rat (Rattus norvegicus B.) in Italy. Testing Facility: Dr. Castellini</td>
</tr>
</table>

<table>
<tr><th>Test substance</th><th>Test organism(s)</th><th>Test system / concentrations applied / exposure time</th><th>Test conditions</th><th>Test results: effects, mode of action, resistance</th><th>Reference</th></tr>
<tr>
<td>MURIN DIFE PASTA GIRASOLE</td>
<td>Roof Rat
(Rattus rattus L.)</td>
<td>Roof rat.

Poisoning: 10 days (8 bait stations filled with about 200 g of poisoned pasta baits).</td>
<td>The trial was set up in an agricultural habitat (farm) which appeared to harbour an established Rattus rattus population.
No rodenticide treatments were carried out in this site over the previous four months.

TRIAL SITE:
Country Italy
Region Piedmont (North-western Italy)
Site description Farm-house hayloft, Agricultural buildings lodging chicken breeding stables, mill and fodder warehouses

Pre-treatment: 5 days (8 bait stations filled with about 200 g of unpoisoned census baits, in cereal grains formulation; 8 tracking patches)
Lag period: 3 days
Poisoning: 10 days (8 bait stations filled with about 200 g of poisoned pasta baits; 8 tracking patches)
Lag period: 3 days
Post-treatment: 5 days (8 bait stations filled with about 200 g of unpoisoned census baits, in cereal grains formulation; 8 tracking patches)</td>
<td>
<table>
<tr><th colspan="3">Roof rats</th></tr>
<tr><td>Estimated population size</td><td>Average daily bait takes</td><td>Tracking patches</td></tr>
<tr><td><u>Pre-treatment census</u>:
40-45 rats</td><td>794 g</td><td>Footprints</td></tr>
<tr><td><u>Post-treatment census</u>:
0 rats.</td><td>0</td><td>No footprints</td></tr>
</table>

<table>
<tr><th colspan="2">Roof rats</th></tr>
<tr><td colspan="2">Mortality</td></tr>
<tr><td>Dead rats found</td><td>Time of death</td></tr>
<tr><td>3</td><td>From day 5 (1 rat found dead) to day 7 (2 rats found dead) of poisoning phase</td></tr>
</table>
</td>
<td>B5.10.2/01
Rovetto, Ivo; 02/12/2010. Efficacy evaluation of MURIN DIFE PASTA CON MANDORLE (difenacoum 0,005% a.i. pasta bait) against Roof Rat (Rattus rattus L.) in Italy. Sagea Centro di Saggio S.r.l., Trial code: 1019.BCD.SAG09</td>
</tr>
</table>

<table>
<tr><th>Test substance</th><th>Test organism(s)</th><th>Test system / concentrations applied / exposure time</th><th>Test conditions</th><th>Test results: effects, mode of action, resistance</th><th>Reference</th></tr>
<tr>
<td>MURIN DIFE PASTA GIRASOLE</td>
<td>House mouse
(Mus musculus L.)</td>
<td>House mouse

Poisoning: 11,5 days (8 bait stations filled with about 200 g of poisoned pasta baits)</td>
<td>The trial was set up in an agricultural habitat (farm with cow breeding stables and fodder warehouses) which appeared to harbour an established Mus musculus population.
No rodenticide treatments were carried out in this site over the previous six months.
TRIAL SITE:
Country Italy
Region Piedmont (North-western Italy)
Site description Agricultural buildings lodging cow breeding stables and fodder warehouse.

Pre-treatment: 4,5 days (8 bait stations filled with about 200 g of unpoisoned census baits, in cereal grains formulation; 8 tracking patches)
Lag period: 2,5 days
Poisoning: 11,5 days (8 bait stations filled with about 200 g of poisoned pasta baits; 8 tracking patches)
Lag period: 2,5 days
Post-treatment: 4 days (8 bait stations filled with about 200 g of unpoisoned census baits, in cereal grains formulation; 8 tracking patches)</td>
<td>
<table>
<tr><th colspan="3">House mouse</th></tr>
<tr><td>Estimated population size</td><td>Average daily bait takes</td><td>Tracking patches</td></tr>
<tr><td><u>Pre-treatment census</u>:
between 12 and 18 mice</td><td>70.5 g</td><td>Footprints</td></tr>
<tr><td><u>Post-treatment census</u>:
0 rats.</td><td>0</td><td>No footprints</td></tr>
</table>
<table>
<tr><th colspan="2">House mouse</th></tr>
<tr><td colspan="2">Mortality</td></tr>
<tr><td>Dead rats found</td><td>Time of death</td></tr>
<tr><td>3</td><td>From day 3 (1 mice found dead) to day 6 (1 mice found dead on day 4 and one on day 6) of poisoning phase</td></tr>
</table>
</td>
<td>B5.10.2/02
Rovetto, Ivo; 02/12/2010. Efficacy evaluation of MURIN DIFE PASTA CON MANDORLE (difenacoum 0,005% a.i. pasta bait) against House mouse (Mus musculus L.) in Italy. Sagea Centro di Saggio S.r.l., Trial code: 1020.BCD.SAG09</td>
</tr>
</table>

ANNEX D. SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

(a) Product trade name: MURIN DIFE PASTA GIRASOLE

Applicant : VEBI Istituto Biochimico S.r.l.
Address: Via Desman 43 City: Borgoricco (PD)
Postal Code: 35010 Country: Italy

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

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

Active substance(s)				Contents				
Common name	**IUPAC name**	**CAS number**	**EC number**	**Concentration**	**Unit**	**w/w (%)**	**Minimum purity (% w/w)**	**Same source as for Annex I inclusion**
Difenacoum	3-(3-biphenyl-4-yl-1,2,3,4-tetrahydro-1-napthyl)-4-hydroxycoumarin	56073-07-5	259-978-4	0.05	g/kg	0.005	> 99.5	Yes

Co-formulants					Contents				
Common name	**IUPAC name**	**Function**	**CAS number**	**EC number**	**Concentration**	**Unit**	**w/w (%)**	**Classification**	**Substance of concern**
Denatonium Benzoate	*N*-benzyl-2-[(2,6-dimethylphenyl)amino]-*N*,*N*-diethyl-2-oxoethanaminium benzoate	Human taste deterrent	3734-33-6	223-095-2	0.01	g/kg	0.001	Xn R20/22, R38 R41, R52/53	No
Triethanol amine	2,2',2"-nitrilotriethanol	Emulsifying agent	102-71-6	203-049-8	3.00	g/kg	0.300	Unclassified	No
Polyethylene glycol 200, PEG-4	Not available	Palatable solvent	25322-68-3	500-038-2	1.50	g/kg	0.150	Unclassified	No
Propylene glycol	Propylene glycol or propane-1,2-diol	Palatable solvent	57-55-6	200-338-0	18.50	g/kg	1.850	Unclassified	No
Flour type 00	Not available	Excipient	Not available	Not	471.14	g/kg	47.114	Unclassified	No

Co-formulants					Contents				
Common name	**IUPAC name**	**Function**	**CAS number**	**EC number**	**Concentration**	**Unit**	**w/w (%)**	**Classification**	**Substance of concern**
				available					
Starch of potato	Not available	Excipient	9005-25-8	232-679-6	35.00	g/kg	3.500	Unclassified	
Sugar	β-D-fructofuranosyl α-D-glucopyranoside [β-D-Frucf-(2↔1)- α-D-Glcp]	Excipient	57-50-1	200-334-9	70.00	g/kg	7.000	Unclassified	No
Milk powder	Not available	Excipient	Not available	Not available	7.00	g/kg	0.700	Unclassified	No
Precotto S	Not available	Excipient	Not available	Not available	85.00	g/kg	8.500	Unclassified	No
Fats	Not available	Excipient	Not available	Not available	250.00	g/kg	25.000	Unclassified	No
Vegetable oil	Not available	Excipient	Not available	Not available	16.50	g/kg	1.650	Unclassified	No
BHA	*tert*-butyl-4-methoxyphenol	Antioxidant	25013-16-5	246-563-8	0.25	g/kg	0.025	Xn, Xi, N R22 R40 R41 R43 R50/53 R51 R63	No
BHT	2,6-di-*tert*-butyl-4-methylphenol	Antioxidant	128-37-0	204-881-4	0.25	g/kg	0.025	Xn R22 R36/38	No
Sorbic acid	(2*E*,4*E*)-hexa-2,4-dienoic acid	Preservatives	110-44-1	203-768-7	1.00	g/kg	0.100	Xi R36/37/38	No
Bronopol	2-bromo-2-nitropropane-1,3-diol	Preservatives	52-51-7	200-143-0	0.50	g/kg	0.050	Xn, N R21/22 R37/38 R41 R50	No

Co-formulants					Contents				
Common name	**IUPAC name**	**Function**	**CAS number**	**EC number**	**Concentration**	**Unit**	**w/w (%)**	**Classification**	**Substance of concern**
VERDE MENTA 2B E102 E131 E132	Not available	Colorant	Mixture of three substances: Name: E102 CAS: 1934-21-0 Name: E131 CAS: 3536-49-0 Name: E132 CAS: 860-22-0	- 222-573-8 212-728-8	0.30	g/kg	0.030	Unclassified	No
Water	Di hydrogen oxide	Excipient	7732-18-5	-	4.50	g/kg	0.450	Unclassified	No
Aroma butter	Not available	Aroma	Not available	Not available	0.50	g/kg	0.050	Unclassified	No
Shelled sunflower seeds	Not available	Excipient	Not available	Not available	35.00	g/kg	3.500	Unclassified	No

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

☐ **yes** ☒ **no** ☐ **unknown**

If not, briefly describe the difference.

MINOR DIFFERENCES IN NON-ACTIVE INGREDIENTS

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

☐ **yes** ☒ **no**

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

☐ **yes** ☐ **no**

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

(c) Formulator(s) of the biocidal product (name(s) and address(es) including location of plant(s)

Formulator

Company Name:	VEBI Istituto Biochimico S.r.l.				
Address:	Via Desman 43				
City:	Borgoricco (PD)	Postal Code:	35010	Country:	Italy
Telephone:	+39 049 9337111	Fax:	+39 049 5798263	E-Mail:	info@vebi.it

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

Physical state and nature of the biocidal product:

(d) Type of formulation: Solid formulation; paste

(e) Ready-to-use product: ☐no ☒ yes

Classification and labelling statements of the biocidal product:

(f) Product classification: Not classified

(g) Risk and Safety Phrases:

S(1/2) Keep locked up and out of the reach of children
S13 Keep away from food, drink and animal feed stuffs
S20/21 When using, do not eat, drink or smoke
S24 Avoid contact with skin and eye
S37 Wear suitable gloves (only for professionals)
S46 If swallowed, seek medical advice immediately (show label where possible)
S61 Avoid release to the environment. Refer to special instructions/safety data sheet

(h) Product classification according to GHS: Not classified

(i) Hazard statement according to GHS: Not relevant

Intended uses and efficacy:

(j)	PT: 14
(k)	Target harmful organisms: Brown rat (*Rattus norvegicus*), House rat (*Rattus rattus*) and house mouse (*Mus musculus*).
(l)	Development stage of target organisms: Juveniles; Adults.
(m)	Function/mode of action: Rodenticide/Anticoagulant

(n)	Field of use: In and around buildings; Outdoor use (professional use only).
(o)	Application aim: Stored product protection/food protection; Health protection.
(p)	User category: Professionals; Non-professional/general public
(q)	Application method: Covered application (in bait stations, other covering)

Directions for use

(r) Manner and area of use:

Professional Use

- MURIN DIFE PASTA GIRASOLE for professional use is an anticoagulant rodenticide/Vitamin K antagonists. MURIN DIFE PASTA GIRASOLE for professional use can be used in and around buildings and in open areas .
- MURIN DIFE PASTA GIRASOLE for professional use is intended to control House mouse (*Mus musculus*), Brown rat (*Rattus norvergicus*) and Roof rat, House rat (*Rattus rattus*).
- MURIN DIFE PASTA GIRASOLE for professional use is a ready-to-use pasta bait supplied in plastic bags containing 1-3-5-10-20-25 kg of product.
- MURIN DIFE PASTA GIRASOLE for professional use is furnished in two different type:
    1. heat sealed food paper bags: 10 – 12.5 – 15 – 20 g
    2. single dose plastic containers: 25 – 40 – 80 – 100 – 150 g
- MURIN DIFE PASTA GIRASOLE for professional use is manually placed in the rodent infestation area. Paste baits are manually placed into a suitable container, protected from weather, accidental ingestion by children or non-target animals and environmental dispersion. Ideally baits are placed in bait boxes which may fixed to the ground.

Non Professional Use

- MURIN DIFE PASTA GIRASOLE for non professional use is an anticoagulant rodenticide/Vitamin K antagonists. MURIN DIFE PASTA GIRASOLE for non professional use can be used in and around buildings and in open areas (private gardens only).
- MURIN DIFE PASTA GIRASOLE for non professional use is intended to control House mouse (*Mus musculus*), Brown rat (*Rattus norvergicus*) and Roof rat, House rat (*Rattus rattus*).
- MURIN DIFE PASTA GIRASOLE for non professional use should be used in refillable tamper-resistant bait stations and supplied as inner packs containing at most enough bait for one bait point (either rat or mouse). Individual packs for non-professional should not exceed 500g.
- MURIN DIFE PASTA GIRASOLE for non professional use is manually placed in the rodent infested area. Ideally tamper-resistant bait stations should be fixed to the ground.

(s) Conditions of use:

MURIN DIFE PASTA GIRASOLE is a ready-to-use paste bait furnished in heat sealed food paper bags or in single dose plastic containers which has to be used as such and it is not intended to be diluted in any medium, mixed with other products, sprayed or dusted.

After having observed the infested area, place bait- points close to the rodents holes, along their tracks, in places of major presence. Avoid to touch barehanded the product. Utilize the appropriate gloves.

Place the bait inside appropriate containers, protected from bad weather, ingestion from infants and not target animals, in order to avoid any undesired dispersion of bait in the environment.

Place notice and advise of the treatment. Remove the dead animals and eliminate them according to local rules as soon as possible.

MURIN DIFE PASTA GIRASOLE must not be applied as permanent bait, unless under the supervision of a pest control operator. Organize treatments lasting at maximum 6 weeks. At the end of every treatment, remove the containers and /or the residual baits eliminating them according to local rules.

The concentration of the active substance in the product is 0.005% w/w (50 mg/kg). The weight of each paste bait is from 10 to 20g.

Recommended doses are as follows:

Mus musculus: 20 - 40 g per bait point per $10m^2$ (40 g correspond to a maximum application rate of 2 mg ai / 10 m^2).

Rattus norvegicus and *Rattus rattus*: 60-200 g per $10m^2$ (60 – 200 g of product correspond to a maximum application rate of 10 mg ai / $10m^2$)

The amount of product used per application is up to 40 g per $10m^2$ for *Mus musculus* and to 200 g per $10m^2$ for R*attus norvegicus* and R*attus rattus*).

Bait points are placed typically every 2 to 5 m for mouse infestation and 5 to 10 m for rat infestation. Closer placement is required for heavier infestations, so the re-baiting should be unnecessary during a campaign. The duration of the program is at maximum up to 6 weeks. Permanent, preventive treatments are possible under the supervision of a pest control operator or other competent operator. In case of permanent baiting, a minimum dose shall be applied (60-80 g) and the baiting points are inspected 4-6 times per year.

When single dose plastic containers are used, the upper protective layer must be cut just before placing the plastic container in the bait box. The bait must be placed in appropriate bait stations, protected from atmospheric agents, in order to avoid accidental swallowing of infants, non target species and undesired dispersion of bait in the environment.

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

In presence of rat's infestation, do not move or disturb the baiting points for several days after baits placement. If after 7-10 days no more rodent activity is noted, the baits shall be moved in areas with higher rodent activity.

In presence of mice's infestation, in order to increase the efficacy of treatment, baiting points must be moved every 2-3 days when they are inspected and/or replenished.

If all bait is consumed quickly in a particular area, increase the number of baiting points in that area. Generally, it is more effective to increase the number of baiting points, than increase the amount of bait for each baiting point. The use of an higher amount of bait for each baiting point increases the risk for non target animals.

Dead rodents are removed for disposal as soon as possible according to local rules. At the end of treatment bait stations and residual bait must be disposed of according to local rules.

(t) Instructions for safe use of the product:

Professional use

- While handling bait material and/or dead rodents, wear rubber gloves.
- Always be sure that containers are adequately secured and that baits could not be dragged away by rodents.
- Bait points should be removed, in a typical campaign, 6 weeks after initial placement.
- In case of contamination wash hands thoroughly with soap and plenty of water.
- In case of suspected ingestion consult a poison control center.

- Read carefully the safety data sheet.

Non professional use

- While handling dead rodents, wear rubber gloves.
- Always be sure that containers are adequately secured and that baits could not be dragged away by rodents.
- Bait points should be removed, in a typical campaign, 6 weeks after initial placement.
- In case of contamination wash hands thoroughly with soap and plenty of water.
- In case of suspected ingestion consult a poison control center.

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

MECHANISM OF ACTION: the active ingredient of MURIN DIFE PASTA GIRASOLE is a long lasting anticoagulant chemical and decreases the hepatic synthesis of k-dependent factors.

SYMPTONS: Severe poisoning by ingestion causes Vitamin K inibithion , causing dermal and mucous haemorrhages. Symptoms to occur in other systems is mainly haemorrhagic. TERAPY: if large quantities are ingested, induce vomiting, perform gastric lavage and monitor prothrombin activity, if decreased Vitamin K1 should be administered. Follow the appropriate medical protocol.

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

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

(w) Additional information:

- Non professionals baits should be used only in refillable tamper-resistant bait stations and supplied as inner packs or units containing at most enough bait for one bait point (either rat or mouse).
- Bait stations should be clearly marked to show that they contain rodenticides and that they should not be disturbed.
- Individual packs for non-professional use should not exceed 500g (100–160–200–260-500g of product).
- MURIN DIFE PASTA GIRASOLE for professional use should not be available to the general public.
- As additional precautional measure, for non professional use, the following statement (or equivalent) has been added: “Avoid to handle the product and use proper gloves”.