Product Assessment Report

DIFERAT PASTE

<Date>

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Granting date/entry into force of authorisation/ registration: **13 March 2013**

Expiry date of authorisation/ registration:**31 March 2015**

Active ingredient:	Difenacoum
Product type:	PT14: Rodenticides

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

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	DIFERAT PASTE	
Manufacturer's development code		
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 ACTIVA is the manufacturer of the active substance in DIFERAT PASTE, 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

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

- Read attached instructions before use

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 DIFERAT PASTE consists in a “fresh paste” intended for both professional and non-professional use to control rodent pests in and around industrial, commercial and residential buildings, in open areas and waste dumps. It is effective against all rodents in civil and industrial field and it is particularly attractant and palatable to house mice (Mus musculus), brown rats (Rattus norvegicus) and black rats (Rattus rattus).

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 of 20 g each. The treatments last at maximum 6 weeks. The amount of used product per application 40 g per 100 square meters for house mice and 60 - 100 g per 100 square meters for rats, depending on the severity of the infestation. Bait points are placed typically every 5-10m. The product is placed in a bait station or fixed to a structure such that rats and mice can eat them. In situations where bait boxes cannot be used, the bait is covered such that non-target organisms cannot reach them.

Baiting points are inspected at least weekly and replenished when bait has been eaten. Dead rodents are removed for disposal in order to prevent them being eaten by non-target animals and birds.

2.6 DOCUMENTATION

The applicant Kollant S.p.a. 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 Kollant S.p.a. in support of the product DIFERAT PASTE containing difenacoum.

Additional tests/information were required by IT Competent Authority.

3 PHYSICOCHEMICAL PROPERTIES

3.1 IDENTITY AND PHYSICO-CHEMICAL PROPERTIES

DIFERAT PASTE is a ready to use bait in the form of a solid paste furnished in heat sealed food paper bags of 20 g each. Other than the active ingredient, it is composed of food-grade materials forming a bait base. Product is dyed blue to make it unattractive to wildlife and to birds in particular.

DIFERAT PASTE does not contain additives or impurities that would be of toxicological or environmental concern. The full details of the identity of the biocidal product are confidential and can be found in the Document IIIB – Confidential data.

DIFERAT PASTE does not exhibit hazardous physical-chemical properties. It has pH of 6.61 (1% aqueous solution) and a bulk density of 1.28 g/mL. The product doesn't show oxidizing or explosive properties, it isn't flammable and it shows no ignition temperature. A test of storage stability at room temperature for two years (the final report will be available in September 2011) is in progress; however from a test after a storage period of 12 weeks at 35°C it can be concluded that a shelf life of two years can be proposed.

A summary of physical-chemical properties provided by Kollant to support the DIFERAT PASTE authorization can be found in Annex A of this document. Please, consider that the information therein presented by Kollant 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 Kollant in 2012 upon request of the IT-CA.

Additional tests/information were required by IT Competent Authority in order to permit the authorization of the biocidal product DIFERAT PASTE. The requested data/information were submitted by Kollant (see ANNEX E).

No further data are deemed necessary.

3.2 ANALYTICAL METHODS FOR DETECTION AND IDENTIFICATION

Acceptable methods for determination of difenacoum and associated impurity present at quantity >0.1% w/w in the technical grade material as manufactured are available and reported in 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. A method for determination of difenacoum in DIFERAT PASTE has been developed and validated and it is suitable for the specific determination of the difenacoum content in the rodenticide bait.

The methods for the analysis of difenacoum in soil and water 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 Rapporteur Member State Finland.

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

Additional tests/information were required by IT Competent Authority in December 2011 in order to permit the authorization of the biocidal product DIFERAT PASTE. The requested data/information were submitted by Kollant at the latest in March 2012 (see ANNEX E).

No further data are deemed necessary.

3.2.1 FORMULATION ANALYSIS

The content of difenacoum in DIFERAT PASTE formulation samples was determined by high pressure liquid chromatography (HPLC) with a UV-vis detector and quantified using an external standard.

The validation of this method was carried out in terms of linearity, precision and accuracy according to CIPAC Guidelines.

The validity criteria were fulfilled, therefore the method proved to be suitable for the analysis of commercial batches of DIFERAT PASTE.

There are no other components in the formulation which are of toxicological or ecotoxicological relevance (confidential information, see Section B2.2).

Summary of analytical methods for the determination of difenacoum

Sample	Test substance	Analytical method	Fortification range / N° of measurements	Linearity	Specifity	Recovery			LOD ng/mL	LOQ mg/kg	Reference
						Range	Mean	SD			
DIFERAT PASTE	Difenacoum	HPLC-UV	0.00375, 0.005 and 0.00625 % w/w / two measurements at each level	$r^2 > 0.999$	Yes	100 – 108	104	-	-	-	B4.1

4 HUMAN HEALTH RISK ASSESSMENT

4.1 EFFECTS ASSESSMENT

New data

In the biocidal product, DIFERAT PASTE, a paste bait, the active substance (0.005% difenacoum) is adsorbed to the food ingredients, which are then contained within a matrix formed by the paste.

The product DIFERAT Paste 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 (LD50>2000 mg/kg bw) and dermal (LD50>2000 mg/kg bw) exposure. Therefore DIFERAT Paste 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. These conclusions are also supported by the available information for difenacoum and on the Safety Data Sheets of the other components of the product.

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. In all cases, according to TNsG, the risk of exposure by inhalation is negligible (10-5 mg/m3). 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

DIFERAT PASTE is intended for use by the general public (domestic use) applying the product ONLY in 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 of Doc.IIB and the results summarised below.

Non professional exposure	
75-percentile "DIFERAT PASTE"	
Default	**Exposure**
Assuming that conventional bait boxes are loaded	5.3×10^{-8} mg/kg bw/day

No dermal contact during placing of baits. Potential exposure only during clean-up.	1.1 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 both when bait boxes are loaded by the user (% AEL = 5) and during the clean-up task (% AEL = 1).

For secondary exposure, no acceptable margin of safety is calculated for infants ingesting 5 g (% AEL=2.27x106) or 10 mg (% AEL=4.55x103) 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, DIFERAT PASTE 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 DIFERAT PASTE according to the label. In the same way, no adverse effects of the product DIFERAT PASTE 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 DIFERAT PASTE in and around buildings.

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 DIFERAT PASTE 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 use of DIFERAT PASTE. No terrestrial studies was conducted for the rodenticidal products. The ecotoxicological effects were 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.

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 DIFERAT PASTE.

In the terrestrial environment, birds and mammals may be at risk for secondary poisoning if they feed on contaminated soil organisms.

The calculation of PECoral, 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

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 in domestic, industrial and commercial sites, including farms and sewage systems to protect commodities, buildings/structures and components from contamination and damage.

6.3 EFFECTS ON TARGET ORGANISMS

The efficacy of DIFERAT PASTE, 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 DIFERAT PASTE in household, civil and industrial fields.

Laboratory choice and efficacy studies with fresh paste bait and with aged paste bait on rats and mice were performed in compliance with the EU Biocidal Products Directive 98/8/EC (BPD) and to the detailed principles set out in the Technical Notes for Guidance in support of annex VI of directive 98/8/EC of the European Parliament and the Council concerning the placing of biocidal products on the market (Common principals and practical procedures for the authorisation and registration of products. Short title: TNsG on Product Evaluation. The studies were conducted on brown rats (Rattus norvegicus), black rats (Rattus rattus) and house mice (Mus musculus). The studies on aged paste bait are in progress and will be submitted as soon as available. The results on fresh paste bait evidenced as DIFERAT PASTE is palatable according to the criteria given in TNsG on Product Evaluation (bait intake more than 20% of the total food consumption in all the studies) and effective (100%) on brown rats (Rattus norvegicus), black rats (Rattus rattus) and house mice (Mus musculus). The results of the field studies evidenced as DIFERAT PASTE showed a good acceptance and provided a complete effectiveness (100%) against the populations present into the trial site.

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.

6.5 BAIT AVERSION

Several elements of behaviour such as neophobia and conditioned or unconditioned aversion to bait can help rodents to avoid ingesting a fatal dose and may explain treatment failures that cannot be accounted for by physiological resistance. Anyway, the results of the field studies evidenced as DIFERAT PASTE showed a good acceptance and provided a complete effectiveness (100%) against the populations present into the trial site.

6.6 EVALUATION OF THE LABEL CLAIMS

New Data

New studies for the product Bonirat Pasta Bait are available as follows:

House mice (Mus musculus):
Mice (Mus musculus) (CD1) purchased from Charles River Laboratories. These animals are an outbred strain and were chosen for testing for their genetic variance, closer to the feral strains than inbred strains. Palatability test was carried out for 4 days. The mice were kept individually in cages (Euro standard type II) under a 12 hours light – 12 hours dark light regime with temperatures of 25°C ±2°C and a relative humidity of 60% ±10%. The intake of contaminated food was 75% of the total food consumption. The mortality was of 100%; the time of death was 9 days (as days after first bait application).

Brown rat (Rattus norvegicus Berk):

Poisoning: 12 days (8 bait stations filled with about 200 g of poisoned pasta baits).

The trial was set up in an agricultural habitat (chicken breeding and eggs packing) in which a Norway rat population was detected. No rodenticide treatments were carried out in this site over the previous six months. The mortality was of 8 dead rats found; the time of death was 9 days (as days after first bait application). In the pre-treatment census the estimated population size was approx. 40 rats, on the base of footprints tracking and the average daily bait takes was 817.3g; the post-treatment census showed no footprints (0 rats).

Black rat (Rattus rattus L.) Roof rat:

Poisoning: 11 days (8 bait stations filled with about 200 g of poisoned pasta baits).

The trial was set up in agricultural habitat (farm with chicken, capon and turkey breeding stables and granary/fodder warehouses) in which a Roof rat infestation was detected. No rodenticide treatments were carried out in this site over the previous six months.The mortality was of 1 dead rat found; the time of death was 6 days (as days after first bait application). In the pre-treatment census the estimated population size was 35-40 rats, on the base of footprints tracking and the average daily bait takes was 159.5g; the post-treatment census showed no footprints (0 rats).

House mouse (Mus musculus L.):

Poisoning: 10 days (8 bait stations filled with about 200 g of poisoned pasta baits)

The trial was set up in an agricultural habitat (farm with cow breeding stable and fodder warehouse) which appeared to harbour an established Mus musculus population. No rodenticide treatments were carried out in this site over the previous six months. The mortality was of 1 dead rat found; the time of death was 6 days (as days after first bait application). In the pre-treatment census the estimated population

size was 35-40 mice, and the average daily bait takes was 121.5g; the post-treatment census showed no footprints (0 rats). No dead mice found.

Brown rat (Rattus norvegicus):

Rats (Rattus norvegicus) (CD) purchased from Charles River Laboratories. These animals are an outbred strain and were chosen for testing for their genetic variance, closer to the feral strains than inbred strains. For male rats the intake of contaminated food was 40.74% of the total food consumption. The mortality was of 100%; the time of death was 9 days (as days after first bait application). For female rats the intake of contaminated food was 66.73% of the total food consumption. The mortality was of 100%; the time of death was 9 days.

Black rat (Rattus rattus):

Rats (Rattus rattus) were obtained from the EUREKA GmbH roof rat breeding facility at the TU Kaiserslautern. The first two pairs of this breeding line came from the breeding stock of Dr. Schmolz at the German Federal Environmental Agency (UBA) in Berlin. For male rats the intake of contaminated food was 80.20% of the total food consumption. The mortality was of 100%; the time of death was 14 days (as days after first bait application). For female rats the intake of contaminated food was 59.18% of the total food consumption. The mortality was of 100%; the time of death was 14 days.

A summary of these studies can be found in Annex C of this document.

6.7 UNACCEPTABLE EFFECTS OF THE BIOCIDAL PRODUCT

Evaluation of humaneness

There is no specific data requirement connected with a substance or product that may cause unnecessary suffering to target vertebrates. No data specific for products containing difenacoum has been submitted or evaluated with respect to suffering of the target organism. Anticoagulants work by causing fatal haemorrhages. The symptoms after a lethal intake of difenacoum can be seen 1-2 days before death occurs. Death normally occurs 3-5 days after the first consumption. This indicates that death does not occur immediately and consequently the question arises if the symptoms are connected with the animal feeling pain and whether it is suffering. A data overview (Anticoagulant rodenticide humaneness, data overview 1992), for 8 different anticoagulants gives little evidence of any significant differences between different rodenticides in terms of time of death, post mortem findings and mode of fatal haemorrhage. Data shows that in most cases symptoms indicate that the animals slowly weaken through several haemorrhages in different organs. The behaviour of the animals indicates that they might feel pain and in most cases do suffer before death occurs.

The use of anticoagulant rodenticides is necessary as there are at present no other valuable measures available to control the rodent population in the EU. Rodent control is needed to prevent disease transmission, contamination of food and feeding stuffs and structural damage. It is recognised that such substances do cause pain inrodents but it is considered that this is not in conflict of Art. 5.1 of the BPD “to avoid unnecessary pain and suffering of vertebrates”, as long as effective, but comparably less painful alternative biocidal substances or products, or even non-biocidal alternatives are not available.

7 MEASURES TO PROTECT MAN, ANIMALS AND THE ENVIRONMENT

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

7.1.1 METHODS AND PRECAUTIONS CONCERNING HANDLING AND USE

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

7.1.2 METHODS AND PRECAUTIONS CONCERNING STORAGE

- Store in a cool, dry, well-ventilated area.
- Store in the closed original container.
- Keep/store out of reach of children and companion animals
- Keep/store away from food, drink and animal feedstuffs.
- Protect from light, heat and naked flames.

7.1.3 METHODS AND PRECAUTIONS CONCERNING TRANSPORT

Not classified as dangerous for transport. Normal precautions for stable and non-reactive products should be adopted.

7.1.4 METHODS AND PRECAUTIONS CONCERNING FIRE

Suitable fire-extinguishing media:
Foam and Carbon dioxide (CO_2).

Extinguishing media which must not be used for safety reasons:
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.

Specific exposure risks:
Difenacoum may release toxic fumes.:

Dispose of residues to certified waste disposal operator for incineration and licensed waste disposal site.

7.1.5 SPECIFIC PRECAUTIONS AND TREATMENT IN CASE OF AN ACCIDENT

General advice: In the case of accident or if you feel unwell, seek medical advice immediately (show the label where possible and report the authorisation number).

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

First aid measures:

- Inhalation: Unlikely to present an inhalation hazard.
- Skin contact: Flush skin immediately and thoroughly with soap and water. Seek medical advice.
- Eye contact: Flush immediately and thoroughly with soap and water. Seek medical advice.
- Ingestion: Seek medical advice immediately and show the container or label.

ADVICE FOR DOCTORS:

- Pharmaceutical-dynamic action: the active substance contained in the product is a competitive antagonist of Vitamin K and reduces the hepatic synthesis of K-dependent factors.
- Symptoms: heavy poisoning by ingestion inhibits the vitamin K, causing skin and mucous 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

Environmental precautions

- 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.

7.1.6 PROCEDURES FOR CLEANING APPLICATION EQUIPMENT

No application equipment is required.

7.1.7 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.

7.1.8 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 recycling 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 safely.

7.1.9 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 or the product to the atmosphere is negligible.

Water (including drinking water):

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

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

Soil:

Avoid soil contamination. If the product gets into soil, it should be removed mechanically and disposed of 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.

7.1.10 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 induce vomiting and seek for veterinary showing the container or label.

7.1.11 POISON CONTROL MEASURES

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

7.1.12 PACKAGING

The packaging details for the biocidal product, DIFERAT PASTE, as presented by the applicant, are outlined below for professional and non professional users.

Applicant proposed packaging

Users	Material	Size
Professional	PET bag	1 – 2 – 5 – 10 – 20 – 25 kg
Domestic	PET bag	40 – 100–140 – 200 – 300 – 400 –500 g / 1 kg

Considering 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.

The packaging details, for the non professional use of the biocidal product DIFERAT PASTE, considered appropriate are outlined below.

Packaging restrictions for non professional use

Bait type	Material	Size
Baits 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)	PET bag	40 – 100–140 – 200 – 300 – 400 –500 g

8 DECISION

8.1 NECESSARY ISSUES ACCOUNTED FOR IN THE PRODUCT LABEL

The following elements have been taken into account when authorising DIFERAT PASTE:

- 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.
- The size of the package placed on the public market should be limited to 500g.
- 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.

8.2 REQUIREMENT FOR FURTHER INFORMATION

Additional tests/information were required by IT Competent Authority in December 2011 in order to permit the authorization of the biocidal product DIFERAT PASTE. The requested data/information were submitted by Kollant at the latest in March 2012.

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)

Endpoint	Result	Method/Guideline	Reference
Physical state and nature	Solid paste	EPA Guidelines OPPTS 830.6303	Garofani S. (2010a) B3.1.1
Colour	Blue	EPA Guidelines OPPTS 8306302	Garofani S. (2010a) B3.1.2
Odour	Characteristic odour	EPA Guidelines OPPTS 8306304	Garofani S. (2010a) B3.1.3
Explosive properties	No evidence of explosive properties based on the components	A statement	
Oxidising properties	No evidence of oxidizing properties based on the components	A statement	
Flash-point and other indications of flammability or spontaneous ignition	The test article is a solid pasta therefore a flash-point study is not required. No evidence of flammability in use. None of the components of the product are classified as flammable under the directive 67/548/EC.	A statement	
Acidity/Alkalinity	6.61	CIPAC MT 75.3	Garofani S. (2010a) B3.5
Bulk density	1.10 g/mL	CIPAC MT 333	Garofani S. (2010a) B3.6
Storage stability - stability and shelf life	A test of storage stability at room temperature for two years is in progress and the final report will be available in September 2011. However from the data after a storage period of 12 weeks at 35°C it can be concluded that the shelf life is at least two years.	CIPAC MT 46	Garofani S. (2010b) B3.7/01 Garofani S. (2010c) B3.7/02
Technical characteristics	Wettability, suspensibility, wet sieve analysis, emulsifiability, persistent foaming, flowability were not tested since the product is not intended to be mixed with water. Disintegration time, attrition and dustability attitudes were not tested since it is not required for a paste bait.	None	None
Compatibility with other products	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	None	None
Surface tension	Not required since the product is not intended to be mixed with water.	None	None
Viscosity	Not required since the product is not intended to be mixed with water.	None	None
Particle size distribution	Not required since the product is a paste bait.	None	None

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, Wistar strain, Females, 12 (3/group)	2000 mg/kg 300 mg/kg	LD_{50} 5000 mg/kg bw	Shinde, K. (2009). Acute oral toxicity study of Diferat in rats. Jai Research Foundation, Study N° 9012, September 22, 2009 (unpublished).
Dermal	OECD 402 GLP	Rat, Wistar strain, Males and Females, 10 rats (5/sex/group)	2000 mg/kg 24 hours exposure	LD_{50}>2000 mg/kg bw	Shinde, K. (2009). Acute dermal toxicity study of Diferat in rats. Jai Research Foundation, Study N° 9013, September 22, 2009 (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	0.00	0.00	-	Non irritant	Shinde, K. (2009) Acute dermal irritation study of Diferat in rabbits. Jai Research Foundation, Study N° 9014, September 22, 2009 (unpublished).

Table B.3. Company summary of Eye irritation

Species	Method	Average score 24, 48, 72 h				Reversibility (yes/no)	Result	Reference
		Cornea	Iris	Conjunctiva				
				Redness	Chemosis			
Rabbit	OECD 405 GLP	0.00	0.00	0.00	0.00	-	Non irritant	Shinde, K. (2009) Acute dermal irritation study of Diferat in rabbits. Jai Research Foundation, Study N° 9015, September 22, 2009 (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	0/20	Non sensitiser	Shinde,K., (2009). Skin sensitisation study of Diferat in Guinea pigs (Guinea Pig Maximization Test). Jai Research Foundation, Study N° 9016, September 22, 2009 (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)

<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">aboratory studies</td></tr>
<tr><td>DIFERAT PASTE</td><td>Brown rat (Rattus norvegicus)</td><td>Rats (Rattus norvegicus) (CD) purchased from Charles River Laboratories. These animals are an outbred strain and were chosen for testing for their genetic variance, closer to the feral strains than inbred strains.

Palatability test: 4 days</td><td>The rats were kept individually in cages (Euro standard type II) under a 12 hours light – 12 hours dark light regime with temperatures of 25°C ±2°C and a relative humidity of 60% ±10%.

Acclimation: 4 days
Pre-test diet take assessment with commercial rat diet (Altromin Pellets 1324): 6 days
Palatability test: 4 days
Commercial rat diet (Altromin Pellets 1324) and observation period : 14 days</td><td>Male rats<table><tr><td rowspan="2">Intake of contaminated food (% of the total food consumption)</td><td colspan="2">Mortality</td></tr><tr><td>%</td><td>Time of death (days after first bait application)</td></tr><tr><td>40.74%</td><td>100%</td><td>9</td></tr></table>Female rats<table><tr><td rowspan="2">Intake of contaminated food (% of the total food consumption)</td><td colspan="2">Mortality</td></tr><tr><td>%</td><td>Time of death (days after first bait application)</td></tr><tr><td>66.73%</td><td>100%</td><td>9</td></tr></table></td><td>B5.10.2/01
Pfeiffer, Hans Jörg, and Karg, Gerhard, 2009. Bait choice feeding trials with rats using a paste formulation containing difenacoum. Study ID: Diferat fresh bait (r1). Eureka GmbH, 2009-08-12</td></tr>
<tr><td>DIFERAT PASTE</td><td>Black rat (Rattus rattus)</td><td>Rats (Rattus rattus) were obtained from the EUREKA GmbH roof rat breeding facility at the TU Kaiserslautern. The first two pairs of this breeding line came from the breeding stock of Dr. Schmolz at the German Federal Environmental Agency (UBA) in Berlin.

Palatability test: 4 days</td><td>The rats were kept individually in cages (Euro standard type III) under a 12 hours light – 12 hours dark light regime with temperatures of 25°C ±2°C and a relative humidity of 60% ±10%.

Pre-test diet take assessment with commercial rat diet (Altromin Pellets 1324): 7 days
Palatability test: 4 days
Commercial rat diet (Altromin Pellets 1324) and observation period : 14 days</td><td>Male rats<table><tr><td rowspan="2">Intake of contaminated food (% of the total food consumption)</td><td colspan="2">Mortality</td></tr><tr><td>%</td><td>Time of death (days after first bait application)</td></tr><tr><td>80.20%</td><td>100%</td><td>14</td></tr></table>Female rats<table><tr><td rowspan="2">Intake of contaminated food (% of the total food consumption)</td><td colspan="2">Mortality</td></tr><tr><td>%</td><td>Time of death (days after first bait application)</td></tr><tr><td>59.18%</td><td>100%</td><td>14</td></tr></table></td><td>B5.10.2/02
Pfeiffer, Hans Jörg, and Karg, Gerhard, 2009. Bait choice feeding trials with roof rats using a paste formulation containing difenacoum. Study ID: Diferat fresh bait (rr1). Eureka GmbH, 2009-08-12</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">Laboratory studies</td></tr>
<tr><td>DIFERAT PASTE</td><td>House mice
(Mus musculus)</td><td>Mice (Mus musculus) (CD1) purchased from Charles River Laboratories. These animals are an outbred strain and were chosen for testing for their genetic variance, closer to the feral strains than inbred strains.

Palatability test: 4 days</td><td>The mice were kept individually in cages (Euro standard type II) under a 12 hours light – 12 hours dark light regime with temperatures of 25°C ±2°C and a relative humidity of 60% ±10%.

Acclimation: 4 days
Commercial rat and mouse diet (Altromin Pellets 1324): 6 days
Palatability test: 4 days
Observation period (commercial rat diet -Altromin Pellets 1324): 14 days</td><td>
<table>
<tr><td colspan="3">Male mice</td></tr>
<tr><td rowspan="2">Intake of contaminated food
(% of the total food consumption)</td><td colspan="2">Mortality</td></tr>
<tr><td>%</td><td>Time of death
(days after first bait application)</td></tr>
<tr><td>75.74%</td><td>100%</td><td>9</td></tr>
</table>
<table>
<tr><td colspan="3">Female mice</td></tr>
<tr><td rowspan="2">Intake of contaminated food
(% of the total food consumption)</td><td colspan="2">Mortality</td></tr>
<tr><td>%</td><td>Time of death
(days after first bait application)</td></tr>
<tr><td>81.86%</td><td>100%</td><td>8</td></tr>
</table>
</td><td>B5.10.2/03
Pfeiffer, Hans Jörg, and Karg, Gerhard, 2009. Bait choice feeding trials with mice using a paste formulation containing difenacoum. Study ID: Diferat fresh bait (m1). Eureka GmbH, 2009-08-12</td></tr>
<tr><td>DIFERAT PASTE
(aged paste bait)</td><td>Brown rat
(Rattus norvegicus)

Black rat (Rattus rattus)

House mice
(Mus musculus)</td><td>Test in progress</td><td>Test in progress</td><td>
<table>
<tr><td colspan="3">Male rat/mice</td></tr>
<tr><td rowspan="2">Intake of contaminated food
(% of the total food consumption)</td><td colspan="2">Mortality</td></tr>
<tr><td>%</td><td>Time of death
(days after first bait application)</td></tr>
<tr><td>-</td><td>-</td><td>-</td></tr>
</table>
<table>
<tr><td colspan="3">Female rat/mice</td></tr>
<tr><td rowspan="2">Intake of contaminated food
(% of the total food consumption)</td><td colspan="2">Mortality</td></tr>
<tr><td>%</td><td>Time of death
(days after first bait application)</td></tr>
<tr><td>-</td><td>-</td><td>-</td></tr>
</table>
</td><td>B5.10.2/07</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>DIFERAT PASTE</td><td>Brown rat
(Rattus norvegicus Berk)</td><td>Norway, or brown rat.

Poisoning: 12 days (8 bait stations filled with about 200 g of poisoned pasta baits)</td><td>The trial was set up in an agricultural habitat (chicken breeding and eggs packing) in which a Norway rat population was detected. 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 chicken breeding stables.

Pre-treatment: 6 days (8 bait stations filled with about 200 g of unpoisoned pasta baits; 7 tracking patches)
Lag period: 4 days
Poisoning: 12 days (8 bait stations filled with about 200 g of poisoned pasta baits; 7 tracking patches)
Lag period: 3 days
Post-treatment: 7 days (8 bait stations filled with about 200 g of unpoisoned pasta baits; 7 tracking patches)</td><td>
<table>
<tr><th colspan="2">Brown rats</th></tr>
<tr><td colspan="2">Mortality</td></tr>
<tr><td>Dead rats found</td><td>Time of death</td></tr>
<tr><td>8</td><td>From day 3 of poisoning phase</td></tr>
</table>
<table>
<tr><th colspan="3">Brown 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>:
Approx. 40 rats</td><td>817.3 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>
</td><td>B5.10.2/04
Rovetto, Ivo; 11/18/2009. Efficacy evaluation of DIFERAT (difenacoum 0,005% a.i. pasta bait) against Norway rat (Rattus norvegicus Berk.) in Italy. Sagea Centro di Saggio S.r.l., Trial code: 1012.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>DIFERAT PASTE</td>
<td>Black rat
(Rattus rattus L.)</td>
<td>Roof rat.

Poisoning: 11 days (8 bait stations filled with about 200 g of poisoned pasta baits)</td>
<td>The trial was set up in agricultural habitat (farm with chicken, capon and turkey breeding stables and granary/fodder warehouses) in which a Roof rat infestation was detected. 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 chicken, capon and turkey breeding stables and fodder warehouse.

Pre-treatment: 6 days (8 bait stations filled with about 200 g of unpoisoned pasta baits; 5 tracking patches)
Lag period: 4 days
Poisoning: 11 days (8 bait stations filled with about 200 g of poisoned pasta baits; 5 tracking patches)
Lag period: 3 days
Post-treatment: 7 days (8 bait stations filled with about 200 g of unpoisoned pasta baits; 5 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>:
35-40 rats</td><td>159.5 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">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>1</td><td>On day 6 of poisoning phase</td></tr>
</table>
</td>
<td>B5.10.2/05
Rovetto, Ivo; 11/18/2009. Efficacy evaluation of DIFERAT (difenacoum 0,005% a.i. pasta bait) against Roof rat (Rattus rattus L.) in Italy. Sagea Centro di Saggio S.r.l., Trial code: 1011.BCD.SAG09</td>
</tr>
</table>

<table>
<tr>
<td>DIFERAT PASTE</td>
<td>House mouse
(Mus musculus L.)</td>
<td>House mouse

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 with cow breeding stable and fodder warehouse) 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 Farm house and agricultural buildings lodging cow breeding stable and fodder warehouse..

Pre-treatment: 6 days (8 bait stations filled with about 200 g of unpoisoned pasta baits; 6 tracking patches)
Lag period: 4 days
Poisoning: 10 days (8 bait stations filled with about 200 g of poisoned pasta baits; 6 tracking patches)
Lag period: 3 days
Post-treatment: 7 days (8 bait stations filled with about 200 g of unpoisoned pasta baits; 6 tracking patches)</td>
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<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>:
35-40 mice</td><td>121.5 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>
</td>
<td></td>
<td>B5.10.2/06
Rovetto, Ivo; 11/18/2009. Efficacy evaluation of DIFERAT (difenacoum 0,005% a.i. pasta bait) against House mouse (Mus musculus L.) in Italy. Sagea Centro di Saggio S.r.l., Trial code: 1013.BCD.SAG09</td>
</tr>
</table>

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<td>Roof rat.

Poisoning: 11 days (8 bait stations filled with about 200 g of poisoned pasta baits)</td>
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Lag period: 4 days
Poisoning: 11 days (8 bait stations filled with about 200 g of poisoned pasta baits; 5 tracking patches)
Lag period: 3 days
Post-treatment: 7 days (8 bait stations filled with about 200 g of unpoisoned pasta baits; 5 tracking patches).</td>
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<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>
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<td>B5.10.2/05
Rovetto, Ivo; 11/18/2009. Efficacy evaluation of DIFERAT (difenacoum 0,005% a.i. pasta bait) against Roof rat (Rattus rattus L.) in Italy. Sagea Centro di Saggio S.r.l., Trial code: 1011.BCD.SAG09</td>
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TRIAL SITE:
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Region Piedmont (North-western Italy)
Site description Farm house and agricultural buildings lodging cow breeding stable and fodder warehouse..

Pre-treatment: 6 days (8 bait stations filled with about 200 g of unpoisoned pasta baits; 6 tracking patches)
Lag period: 4 days
Poisoning: 10 days (8 bait stations filled with about 200 g of poisoned pasta baits; 6 tracking patches)
Lag period: 3 days
Post-treatment: 7 days (8 bait stations filled with about 200 g of unpoisoned pasta baits; 6 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>:
35-40 mice</td><td>121.5 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>
</td>
<td>B5.10.2/06
Rovetto, Ivo; 11/18/2009. Efficacy evaluation of DIFERAT (difenacoum 0,005% a.i. pasta bait) against House mouse (Mus musculus L.) in Italy. Sagea Centro di Saggio S.r.l., Trial code: 1013.BCD.SAG09</td>
</tr>
</table>

Annex D. Summary of Product Characteristics (SPC)

(a) Product trade name: DIFERAT PASTE

Applicant : Kollant S.p.a.
Address: Via Trieste, 49/53
City: Padova **Postal Code**: 35121 **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
Polyethylene glycol 200 (PEG 4)	Polyethylene glycol	Palatable solvent	25322-68-3	500-038-2	1.50	g/kg	0.150	Unclassified	No
Propylene glycol	1,2-propandiol	Palatable solvent	57-55-6	200-338-0	18.50	g/kg	1.850	Unclassified	No
Copper Phthalocyanine Blue	Not relevant	Colorant	147-14-8	205-685-1	0.50	g/kg	0.050	Unclassified	No
Sugar powder	Sucrose, pure	Bait	57-50-1	200-334-9	25.00	g/kg	2.500	Unclassified	No
Aroma Milk	Not available	Bait	There is no CAS no for	There is no EC No for	1.50	g/kg	0.150	Unclassified	No

Powder			milk powder since it is a complex mixture of individual compounds	milk powder since it is a complex mixture of individual compounds.					
Methylparaben	Methyl 4-hydroxy-2-methylbenzoate	Preservatives	99-76-3	202-785-7	1.00	g/kg	0.100	Xi R36/37/38, R40	No
Sugar	Sucrose	Bait	57-50-1	200-334-9	10.00	g/kg	1.000	Unclassified	No
Talcum CM3	Not available		There is no CAS No. since it is a complex mixture of many individual compounds.	There is no EC No. since it is a complex mixture of many individual compounds.	30.00	g/kg	3.000	Unclassified	No
Vegetable Oil	Not available		8001-22-7	232-274-4	210.00	g/kg	21.00	Unclassified	No
Mixture of Wheat Flours	Not available	Bait	There is no CAS no for mix of cereals since it is a complex mixture of many individual compounds	There is no EC No for mix of cereals since it is a complex mixture of many individual compounds.	726.94	g/kg	72.694	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.

Formulation and quantitative/qualitative composition of the other ingredients are the differences between DIFERAT PASTE and the representative products assessed for the purpose of the Annex I inclusion.

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

☐ **yes** ☒ **no**

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

☐ **yes** ☐ **no**

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

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

Name of the active substance: Difenacoum

Manufacturer

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

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

(d) Formulator(s) of the biocidal product (name(s) and address(es) including location of plant(s))**Errore. Il segnalibro non è definito.**

Formulator

Company Name:	L.I.F.A. S.r.l.				
Address:	Via C. Colombo, 7/7A				
City:	Vigonovo (VE)	Postal Code:	30030	Country:	Italy
Telephone:	+39 049 9983080	Fax:	+39 049 9983005	E-Mail:	giorgio.finotello@lifa.it

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

Physical state and nature of the biocidal product:

(e) Type of formulation: Bait (solid paste bait)

(f) Ready-to-use product: ☐no ☒ yes

Classification and labelling statements of the biocidal product:

(g) Product classification: Not classified

(h) Risk and Safety Phrases:

S2; Keep 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.
S46; If swallowed, seek medical advice immediately (show label where possible).
S61; Avoid release to the environment. Refer to special instructions/Safety data sheet.

(i) Product classification according to GHS: Not classified

(j) Hazard statement according to GHS: Not relevant

Intended uses and efficacy:

(k) PT: 14

(l) Target harmful organisms: Brown rat (*Rattus norvegicus*), black rat (*Rattus rattus*) and house mouse (*Mus musculus*)

(m) Development stage of target organisms: All development stages

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

(o) Field of use: In and around buildings; In sewerage (Professional use only)

(p) Application aim: Control of rodent species

(q) User category: Professionals and non-professionals

(r) Application method: Bait Station (professionals and non professionals)

Directions for use

(s) Manner and area of use:

See "intended uses and efficacy" section above for information on target organisms, mode of action, field of use, application aim, user category and application method.

(t) Conditions of use:

Professional Use

The bait product can potentially be used under many different circumstances and can be deployed using various means. Baits are manually placed in the rodent infested area. Methods of deployment for professional users are bait stations (tamper proof boxes), bait points (a makeshift arrangement which uses materials and/or the local environment to restrict access to the bait), loose but inaccessible (an arrangement which uses the local environment only to restrict access to the bait).

Baits can be placed in bait boxes which may be fixed to the ground. The bait in such bait boxes can also be secured in place to minimise removal and dispersal by rodents. The product must never be placed indiscriminately.

Non Professional Use

For use, only commercially available bait stations (prefilled or refillable) are authorised. For both rats and mice, the bait should be supplied in inner packs or units, containing at most enough bait for one point (either rat or mouse). The whole pack should contain a maximum of 0.5 kg of bait. Bait stations are manually placed in the rodent infested area. Ideally bait stations should be fixed to the ground. The product must never be placed indiscriminately.

Baiting Strategy

For mouse infestations use bait points of 40g per 100 square meters. Bait points are placed typically every 5-10 metres. For rat infestations use bait points of 60 - 100g per 100 square meters. Place bait points 10 metres apart, reducing to 5 metres apart in areas of high infestation. Baiting points are inspected at least weekly and replenished when bait has been eaten. Dead rodents are removed for disposal in order to prevent them being eaten by non-target animals and birds.

(u) Instructions for safe use of the product:

Professional use

While handling bait material/animal carcasses, wear rubber gloves. Avoid treatments in the presence of not protected food or feed. Do not use for treatment of cultivated sites. When the product is being used in public areas, the areas treated must be marked during the treatment period. 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. In case of contamination wash hands thoroughly with soap and plenty of water. In case of suspected ingestion consult a poison control center. The product can be hazardous if swallowed. If swallowed induce vomiting, immediately contact a poison center and show the container or the label. The product can be

hazardous if swallowed by non target animals and pets. Reload bait stations weekly, if necessary. Remove dead rodents daily and dispose them in accordance with local rules. The product is not intended for permanent use, treatments should last up to six weeks. At the end of the treatment remove the bait stations and dispose them according local rules. The product should be placed securely to minimize the risk of contact by children or non-target animals Read carefully the safety data sheet.

Non professional use

The product should be placed securely to minimize the risk of contact by children or non-target animals. Avoid treatments in the presence of not protected food or feed. Do not use for treatment of cultivated sites.In case of contamination wash hands thoroughly with soap and plenty of water. Do not reuse the container and dispose it in accordance with the local rules. In case of suspected ingestion consult a poison control center. The product can be hazardous if swallowed. If swallowed induce vomiting, immediately contact a poison center and show the container or the label. The product can be hazardous if swallowed by non target animals and pets. Replace weekly tamper-resistant bait stations. The product is not intended for permanent use, treatments should last up to six weeks. At the end of the treatment remove the bait stations and dispose them according local rules.

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

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

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

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

Keep out of the reach of children. Keep container tightly closed. Keep away from food, drink and animal feed stuffs.

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

Keep in a cool, dry, well ventilated area
Shelf life of up to 2 years.

(y) Additional information:

As additional precautionary measure, the following statement has been added :"Avoid to handle the product by hands and use proper gloves".

Non professionals should use only tamper-resistant bait stations.
Tamper-resistant bait stations should be clearly marked to show that they contain rodenticides and that they should not be disturbed.
DIFERAT PASTE for professional use should not be available to the general public.
Individual packs for non-professional use should not exceed 500 g.

ANNEX E. Additional tests/information required by IT Competent Authority

Endpoint	Result	Method/Guideline	Remarks/Justification	Reference
Flammability	Autoflammability		Statement	
Relative density	1.2372	OECD Guidelines for Testing Chemicals. Test Guideline No. 109, Paris, 1981 Official Journal of the European Communities No. L 383 Part A, 29.12.92: Methods for the Determination of Physico-Chemical Properties: A.3 "Relative Density"		Ticco S.P. (2012) Final Report CH-033/2012 "*DIFERAT: Determination of Relative density*"
Storage stability	Effects of temperature		Statement	
Analytical methods for the residue analysis			Letter of access from Activa S.r.l.	
MSDS	Talc CM3	CE 1272/2008 CE 453/2010		