HET COLLEGE VOOR DE TOELATING VAN GEWASBESCHERMINGSMIDDELEN EN BIOCIDEN

1 WIJZIGING TOELATING AMBTSHALVE

Ambtshalve wijziging van de toelating als bedoeld in artikel 48 van verordening 528/2012/EU alsmede artikel 6:19 Algemene wet bestuursrecht op basis van de werkzame stof chloorfacinon

Rozol Pat'

BESLUIT HET COLLEGE als volgt:

1.1 Wijziging toelating

Het middel Rozol Pat' is laatstelijk bij besluit d.d. 22 maart 2013 toegelaten tot 30 juni 2016. De toelating van het middel Rozol Pat' wordt gewijzigd en is met ingang van datum dezes toegelaten voor de in bijlage I genoemde toepassingen. Voor de gronden van dit besluit wordt verwezen naar bijlage II bij dit besluit.

1.2 Samenstelling, vorm en verpakking

De toelating geldt uitsluitend voor het middel in de samenstelling, vorm en de verpakking als waarvoor de toelating is verleend. Het middel wordt aangeboden en geëtiketteerd voor professioneel gebruik.

1.3 Gebruik

Dit middel is uitsluitend bestemd voor professioneel gebruik en mag enkel in ruimten worden toegepast.

1.4 Classificatie en etikettering

Mede gelet op artikel 69 van verordening 528/2012/EU en artikel 50, eerste lid, sub d, Wet gewasbeschermingsmiddelen en biociden,

1. De aanduidingen die op de verpakking moeten worden vermeld, worden hierbij vastgesteld als volgt:

aard van het preparaat: Lokmiddel (klaar voor gebruik)

werkzame stof:	*gehalte:*
chloorfacinon	0,0050 %

letterlijk en zonder enige aanvulling:

andere zeer giftige, giftige, bijtende of schadelijke stof(fen): -

gevaarsymbool: *aanduiding:*

Waarschuwingszinnen: -

Veiligheidsaanbevelingen:

S02 -Buiten bereik van kinderen bewaren.

Specifieke vermeldingen: -

2. Behalve de onder 1. bedoelde en de overige bij wet voorgeschreven aanduidingen en vermeldingen moeten op de verpakking voorkomen:

   a. letterlijk en zonder enige aanvulling:
   het wettelijk gebruiksvoorschrift
   De tekst van het wettelijk gebruiksvoorschrift is opgenomen in Bijlage I, onder A.

   b. hetzij letterlijk, hetzij naar zakelijke inhoud:
   de gebruiksaanwijzing
   De tekst van de gebruiksaanwijzing is opgenomen in Bijlage I, onder B.
   De tekst mag worden aangevuld met technische aanwijzingen voor een goede bestrijding mits deze niet met die tekst in strijd zijn.

2 DETAILS VAN DE TOELATING EN DE WIJZIGING

2.1 Wijziging toelating

Artikel 48 verordening 528/2012/EG bepaalt dat lidstaten te allen tijde een toelating opnieuw kunnen bekijken indien er aanwijzingen bestaan, dat niet langer wordt voldaan aan een van de in artikel 19 van de Verordening genoemde eisen.

De wijziging van de toelating van Rozol Pat' houdt in dat het middel wordt toegelaten als middel ter bestrijding van zwarte ratten en huismuizen door professionele gebruikers. Het gebruik door niet-professionelen en het gebruik van Rozol Pat' als middel ter bestrijding van bruine ratten wordt niet toegelaten.

2.2 Korte Historie
Het middel Rozol Pat' is in april 2013 toegelaten als middel ter bestrijding van zwarte en bruine ratten (professioneel gebruik) en huismuizen (professioneel en niet-professioneel gebruik) in ruimten.
Dit besluit is gepubliceerd op 02 april 2013.

In juni 2013 werd het Ctgb bekend met het rapport van de Wageningen UR Livestock Research van medio april '*Onderzoek naar de resistentie van de bruine rat in Nederland – 2012'* dat een duidelijk wetenschappelijk signaal afgeeft over resistentiegevaar bij ratten. Het Ctgb heeft nader onderzoek verricht en er is hierover regelmatig contact geweest met de toelatingshouder. Voornoemd rapport van de WUR is met hem gedeeld.

WUR Livestock Research 'Onderzoek naar de resistentie van de bruine rat in Nederland – 2012'
Zoals reeds gememoreerd is medio april 2013 de volgende studie gepubliceerd door Wageningen UR Livestock Research:
'*Onderzoek naar de resistentie van de bruine rat in Nederland – 2012'*
Hierin worden de resultaten van onderzoek naar het voorkomen van genetische mutaties bij bruine ratten in Nederland beschreven.

Dit onderzoek toont aan dat hoewel het percentage resistente ratten over heel Nederland mee lijkt te vallen (25%), het vermoeden bestaat dat in bepaalde regio's dit percentage veel hoger ligt. Resistente bij bruine ratten met de zgn 'Duitse mutatie' (CysCys) werden niet alleen aangetroffen in die regio's waarvan al langer bekend is dat er resistentie kan optreden (Twente, Achterhoek), maar ook in de regio Rotterdam en de Noord-Oostpolder. Ratten met de 'Franse mutatie' (Phe-Phe) werden op meerdere locaties in het land aangetroffen: in de Gelderse Vallei, Zuid-Oost Brabant en Noord-Limburg. Daarnaast lijken heterozygoot resistente dieren met zowel de Duitse (tyr-cys) als de Franse (tyr-phe) mutaties zich verder door Nederland te verspreiden.

In mei 2013 is er een draft rapport gepresenteerd in de Europese Competent Authority-meeting (CA-51) waarin een uitgebreid overzicht gegeven wordt over ontwikkeling van resistentie in rodents tegen Vitamin K anticoagulants (VKA's). Dit concept rapport geeft een duidelijke indicatie over de zorgen over cross resistentie tussen eerste en tweede generatie anticoagulantia in knaagdieren, met name de bruine rat. Over de situatie in zwarte rat en muizen is minder informatie beschikbaar.

De nieuwe informatie is uitvoerig bediscussieerd met de toelatinghouder in juli en augustus 2013. Liphatech heeft d.d. 29-8-2013 een reactie gestuurd van een onafhankelijke Franse expert in dit expertiseveld: de heer professor Etienne Benoit.

Het College heeft dit rapport tevens bestudeerd en voorgelegd aan een van de medeauteurs van het WUR rapport uit april. Het Ctgb komt tot de conclusie dat niet wordt voldaan aan de toelatingseisen en dat het besluit van 22 maart 2013 dient te worden gewijzigd.
Voor de onderbouwing wordt verwezen naar paragraaf 2.5.4.3 van bijlage II (het Product Assessment Report) van dit besluit.

In artikel 6:19 Algemene wet bestuursrecht (Awb) heeft Liphatech op 6 mei 2013 bezwaar gemaakt tegen het besluit van 22 maart 2013.
Op grond van artikel 6:19 Awb wordt dit bezwaar van rechtswege geacht mede te zijn gericht tegen dit nieuwe besluit.

Degene wiens belang rechtstreeks bij dit besluit is betrokken kan gelet op artikel 4 van Bijlage 2 bij de Algemene wet bestuursrecht en artikel 7:1, eerste lid, van de Algemene wet bestuursrecht, binnen zes weken na de dag waarop dit besluit bekend is gemaakt een bezwaarschrift indienen bij: het College voor de toelating van gewasbeschermingsmiddelen en biociden (Ctgb), Postbus 217, 6700 AE WAGENINGEN. Het Ctgb heeft niet de mogelijkheid van het elektronisch indienen van een bezwaarschrift opengesteld.

Wageningen, 6 december 2013

HET COLLEGE VOOR DE TOELATING VAN GEWASBESCHERMINGSMIDDELEN EN BIOCIDEN,

ir. J.F. de Leeuw
voorzitter

Dit middel is uitsluitend bestemd voor professioneel gebruik

HET COLLEGE VOOR DE TOELATING VAN GEWASBESCHERMINGSMIDDELEN EN BIOCIDEN

BIJLAGE I bij het besluit d.d. 6 december 2013 tot wijziging van de toelating van het middel Rozol Pat', toelatingnummer 13974 N

A.
WETTELIJK GEBRUIKSVOORSCHRIFT

Toegestaan is uitsluitend het gebruik als middel ter bestrijding van zwarte ratten en huismuizen in ruimten, met dien verstande, dat het middel moet worden uitgelegd in speciaal hiervoor bestemde lokaasdoosjes. Plaats het lokaas buiten bereik van kinderen, vogels en (huis)dieren. Verwijderd houden van eet- en drinkwaren en van diervoeder.

De dosering en resistentie management zoals aangegeven in de gebruiksaanwijzing moet worden aangehouden.

Het middel is uitsluitend bestemd voor professioneel gebruik.

B.
GEBRUIKSAANWIJZING

Toepassingen:

Rozol Pat' is een kant-en-klaar lokaas in pastaformulering tegen zwarte ratten en huismuizen. Het zakje waarin Rozol Pat' zich bevindt niet openen – de knaagdieren eten hier doorheen.

Plaats het lokaas in lokaasdozen buiten bereik van andere dieren (bijvoorbeeld vogels, zoogdieren, huis- of landbouwdieren) en kinderen. Het lokaas zo vast maken dat het niet weggesleept kan worden. De lokaasdozen markeren zodat duidelijk is dat ze rodenticiden bevatten.

De lokaasdozen vervolgens uitzetten op plaatsen waar de zwarte ratten en muizen geregeld komen: in de nabijheid van holingangen, op looppaden (sporen!), in verborgen ruimten zoals verlaagde plafonds en op plaatsen waar de dieren voedsel halen of knagen. De lokaasdozen niet toepassen in de buurt van oppervlaktewater.

Na gebruik handen wassen.

Zoals uit het Wettelijk Gebruiksvoorschrift blijkt, mag het middel niet buiten worden toegepast.

Het middel dient gedurende een aantal dagen in voldoende mate te worden gegeten door ratten en muizen.

Dosering:

Bestrijding van zwarte ratten:
Plaats de lokaasdozen op een afstand van 4 tot 10 meter van elkaar afhankelijk van de grootte van de rattenplaag. Plaats 100 tot 200g lokaas per plek. (NB: vooral hooggelegen voerplaatsen inrichten).

Bestrijding van muizen:
Plaats de lokaasdozen op een afstand van 1 tot 3 meter van elkaar afhankelijk van de grootte van de muizenplaag. Plaats 30 tot 50g lokaas per plek.

Vervolg bestrijdingsactie:
Controleer de eerste opname na 3 dagen en vervolgens regelmatig op basis van opname (wekelijks of elke 14 dagen). Vervang verdwenen lokaas. Middel dat beschimmeld of verontreinigd is totaal vervangen. Indien bij een lokaaspunt alle lokaas verdwenen is, onmiddellijk lokaas bijvullen en meer lokaaspunten inrichten en/of de controlefrequentie verhogen. Het lokaas verversen tot er in het geheel geen opname meer plaatsvindt.

In de meeste gevallen zal de bestrijding met behulp van dit middel binnen 35 dagen voltooid zijn. Indien na 35 dagen nog activiteit van huismuizen of zwarte ratten wordt waargenomen, moet de mogelijke oorzaak hiervan worden onderzocht en maatregelen worden getroffen.

Wanneer de opname van lokaas is gestopt, de resten van het lokaas verzamelen en veilig verwijderen als gevaarlijk afval (cf. Eural). Dode dieren (de eerste worden na ca. 3 dagen gevonden) eveneens verzamelen en in plastic verpakt in het vuilnisvat deponeren, opdat huisdieren en andere dieren niet door het opeten van de kadavers worden vergiftigd. Katten tijdens een bestrijdingsactie extra goed voeren. Verder de nodige maatregelen (laten) treffen in het belang van rat- en muiswering (ingangen afdichten, mogelijk voer verwijderen, etc.).

Indien in aangebouwde ruimten ook ratten of muizen aanwezig zijn, zullen de resultaten slechts blijvend zijn, wanneer ook daar een bestrijdingsactie wordt uitgevoerd.

Resistentie management:
Het gebruik van dit middel is alleen toegestaan indien het een onderdeel vormt van een integrated pest management systeem (IPM). Het middel mag niet preventief gebruikt worden. Voor de werkzame stof aanwezig in het middel, chloorphacinon, is er een groot risico dat muizen of ratten resistentie ontwikkelen en in delen van Nederland is resistentie tegen ratten en muizen al aanwezig. Zoek informatie (internet, beroepsvereniging) om te controleren of er resistentie tegen chloorfacinon aanwezig is in het gebied waar het middel gebruikt gaat worden. Gebruik dit middel niet in gevallen dat resistentie aanwezig is of waarschijnlijk is, bijvoorbeeld in gevallen dat vorige bestrijdingsacties met chloorfacinon bevattende middelen niet hebben geresulteerd in een duidelijke vermindering van de populatie.

Eerste Hulpmaatregelen:
Houd dit etiket beschikbaar wanneer medisch advies wordt ingewonnen.
In geval van nood contact opnemen met een dokter.
Tegengif: Vitamine K1 (onder medische begeleiding)

HET COLLEGE VOOR DE TOELATING VAN GEWASBESCHERMINGSMIDDELEN EN BIOCIDEN

BIJLAGE II bij het besluit d.d. 6 december 2013 tot wijziging van de toelating van het middel Rozol Pat', toelatingnummer 13974 N

Product Assessment Report

Rozol PAT'

Amendment d.d. 06-12-2013

Internal registration/file no:	20110651
Authorisation/Registration no:	13974N
Granting date/entry into force of authorisation/ registration:	08-03-2013 Amendment of authorisation: 06-12-2013
Expiry date of authorisation/ registration:	30-06-2016
Active ingredient:	Chlorophacinone
Product type:	PT14

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

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1 General information about the product application

1.1 Applicant

Company Name:	Liphatech S.A.S.
Address:	Bonnel BP 3
City:	Pont du Casse
Postal Code:	47480
Country:	France
Telephone:	+33 563 693 570
Fax:	+33 553 479 501
E-mail address:	corg@liphatech.fr

1.1.1 Person authorised for communication on behalf of the applicant

Name:	Gabrielle COR
Function:	Regulatory affairs manager
Address:	Bonnel BP 3
City:	Pont du Casse
Postal Code:	47480
Country:	France
Telephone:	+33 563 693 630
Fax:	+33 553 479 501
E-mail address:	corg@liphatech.fr

1.2 Current authorisation holder[1]

Liphatech S.A.S.

1.3 Proposed authorisation holder

Company Name:	Liphatech S.A.S.
Address:	Bonnel BP 3
City:	Pont du Casse
Postal Code:	47480
Country:	France
Telephone:	+33 563 693 570
Fax:	+33 553 479 501
E-mail address:	corg@liphatech.fr
Letter of appointment for the	Not applicable

[1] Applies only to existing authorisations

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

1.4 Information about the product application

Application received:	04-07-2011
Application reported complete:	29-01-2013
Type of application:	First authorisation
Further information:	The authorisation has been changed on 06-12-2013 due to new scientific information. In the section on efficacy the amendments are explained.

1.5 Information about the biocidal product

1.5.1 General information

Trade name:	Rozol Pat'
Manufacturer's development code number(s), if appropriate:	CLOPA0,0050_01F_F01265_00
Product type:	14
Composition of the product (identity and content of active substance(s) and substances of concern; full composition see confidential annex):	Chlorophacinone 0.0050%
Formulation type:	RB
Ready to use product (yes/no):	Yes
Is the product the very same (identity and content) to another product already authorised under the regime of directive 98/8/EC (yes/no); If yes: authorisation/registration no. and product name: or Has the product the same identity and composition like the product evaluated in connection with the approval for listing of active substance(s) on to Annex I to directive 98/8/EC (yes/no):	No

1.5.2 Information on the intended use(s)

Below is the intended use as applied for by the applicant at the start of the evaluation.
These uses/claims have been adapted during the evaluation.
See SPC for the final authorised use.

Overall use pattern (manner and area of use):	Rozol Pat' is a blue rodenticide paste bait used for the control of rats and mice - in and around buildings (professional and non-professional use) - in open areas and waste dumps (professional use only). The paste is contained in a sachet which is not opened by the operator. Details of use are shown in Table 2.5.3.1
Target organisms:	*Rattus norvegicus* (Norway rat, Brown rat) *Rattus rattus* (Black rat) *Mus musculus* (House mouse)
Category of users:	Professional and non-professional
Directions for use including minimum and maximum application rates, application rates per time unit (e.g. number of treatments per day), typical size of application area:	Rats: **up to 200 g** bait per bait station. Bait points placed at **4 to 10** meter distance of each other. Mice: **up to 100 g** bait per bait station. Bait points placed at **1 to 3** meter distance of each other.
Potential for release into the environment (yes/no):	Yes
Potential for contamination of food/feedingstuff (yes/no)	No
Proposed Label:	Translation of the final Dutch labels, see Annex 9.
Use Restrictions:	Not for use in sewers.

1.5.3 Information on active substance(s)

Active substance chemical name:	chlorophacinone
CAS No:	3691-35-8
EC No:	223-003-0
Purity (minimum, g/kg or g/l):	>97.8%
Inclusion directive:	2009/99/EG, d.d. 4 augustus 2009
Date of inclusion:	1 July 2011
Is the active substance equivalent to the active substance listed in Annex I to 98/8/EC (yes/no):	Yes
CONFIDENTIAL: this information should not be disclosed to third parties	

Manufacturer of active substance(s) used in the biocidal product:	
Company Name:	Liphatech S.A.S. at AlzChem Trostberg GmbH
Address:	Chemie Park Trostberg, Dr Albert Frank strasse 32
City:	Trostberg
Postal Code:	83308
Country:	Germany
Telephone:	+33 5 53 69 36 30
Fax:	+33 5 53 69 81 81
E-mail address:	corg@liphatech.fr

1.5.4 Information on the substance(s) of concern

No substances of concern are present in the active substance/formulation.

1.6 Documentation

1.6.1 Data submitted in relation to product application

New studies concerning the product Rozol Pat' have been submitted with respect to physical-chemical properties, analytical methods and efficacy of the product. The studies are listed in Annex 2.

1.6.2 Access to documentation

The applicant does not need to provide a letter of access as the applicant is also notifier of the dossier on the active substance chlorophacinone placed on Annex I of the Biocides Directive 98/8/EC.

2 Summary of the product assessment

2.1 Identity related issues

Trade name	Rozol Pat'			
Active ingredient	Purity (%w/w)	CAS No.	EC No.	Content (%)
Chlorophacinone	>97.8%	3691-35-8	223-003-0	0.005 (pure active)
Remark: chlorophacinone is present as the racemic mixture of the two enantiomers No substance of concern is found in Rozol Pat'.				

2.2 Classification, labelling and packaging

2.2.1 Harmonised classification and labelling of the biocidal product

Proposal for the classification and labelling of the formulation concerning physical chemical properties

Classification and labeling of the formulation concerning physical chemical properties is not required.

Supported shelf life of the formulation: three years in PP.

Proposal for the classification and labelling of the formulation concerning toxicological properties

Proposed classification based on Directive 1999/45/EC

Human toxicology:

Professional and non-professional users:

Substances, present in the formulation, which should be mentioned on the label by their chemical name (other very toxic, toxic, corrosive or harmful substances):			
-			
Symbol:	-	Indication of danger:	-
R phrases	-	-	
S phrases	S2	Keep out of the reach of children	
Special provisions:	-	-	
DPD-phrases			
Child-resistant fastening obligatory?			no
Tactile warning of danger obligatory?			no

Explanation:	
Hazard symbol:	-
Risk phrases:	-
Safety phrases:	S46 is not indicated according to Annex VI of Directive 67/548/EEC, as the product is not classified as dangerous.
Other:	-

Proposed classification based on Regulation EC 1272/2008

Human toxicology:

Signal word:	-		
Pictogram:	-		
	Hazard class-and-Category	**Code**	**Hazard statement**
Hazard statements:	-	-	-
Precautionary statements:		P102	Keep out of reach of children

Explanation:	
Pictogram:	-
H-statements:	-
P-statements:	The P-statement is chosen based on the specific restrictions for the inclusion of clorophacinone in Annex I of the Directive 98/8/EC.

Proposal for the classification and labelling of the formulation concerning environmental properties

Classification and labelling of the formulation concerning environmental properties is not required.

2.2.2 Packaging of the biocidal product

Professional use

Outer packaging type applied for	Inner packaging type applied for	Packaging sizes evaluated	Packaging sizes authorised in NL*
PP bucket with lid	Paper bag/PP sachet: 10 to 40 g	Up to 20 kg	800g to 20 kg
Cardboard carton with integral plastic (PP/PE) bag	Paper bag/PP sachet: 10 to 40 g	Up to 20 kg	800g to 20 kg
Plastic (PP/PE) container	Paper bag/PP sachet: 10 to 40 g	Up to 1.5 kg	800 g to 1.5 kg
Plastic (PP/PE) pouch	Paper bag/PP sachet: 10 to 40 g	Up to 20 kg	800 g to 1 kg
Carton containing prefilled PP/HDPE/PS bait stations	Paper bag/PP sachet: 10 to 40 g	Up to 10 kg	800g to 10 kg

*Member state specific regulations only allow pack sizes of up to 200 g. for non-professional use and from 800 g. for professional use, concerning authorisation of rodenticides in the Netherlands.

Non-professional use (not accepted in NL)

Outer packaging type applied for	Inner packaging type applied for	Packaging sizes evaluated	Packaging sizes authorised in NL
PP bucket with lid	Paper bag/PP sachet: 10 to 40 g	Up to 5 kg	-
Cardboard carton with integral plastic (PP/PE) bag	Paper bag/PP sachet: 10 to 40 g	Up to 4 kg	-
Plastic (PP/PE) container	Paper bag/PP sachet: 10 to 40 g	Up to 4 kg	-
Plastic (PP/PE) pouch	Paper bag/PP sachet: 10 to 40 g	Up to 4 kg	-
Carton containing prefilled PP/HDPE/PS bait stations	Paper bag/PP sachet: 10 to 40 g	Up to 3 kg	-

-

2.3 Physico/chemical properties and analytical methods

The applicant is owner of the Annex I dossier. The physico/chemical properties for the active substance chlorophacinone are detailed in the Annex I dossier, Doc IIIA, Section 3.

The methods for the active substance chlorophacinone, the impurities and the enantiomeric ratios of the active substance in the technical active substance are detailed in the Annex I dossier, Doc IIIA, Section 4.1.

2.3.1 Physico-chemical properties

The product is not the representative product included in the CA report to support the inclusion of chlorophacinone in annex I of Directive 98/8/EC. The applicant has submitted the following studies.
For some endpoints data of other products has been used. The compositions of these products are comparable to Rozol Pat' and allow for acceptable extrapolation.

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

	Method	Purity/Specification	Results	Reference
Physical state and nature	Visual	Blue paste: F01265, Batch: F1265, Nominal: 50 mg/kg	Paste	Caruel, H. (2008) IIIB 3.1.1-01 Non-GLP
Colour	Visual	Blue paste: F01265, Batch: F1265, Nominal: 50 mg/kg	Blue	Caruel, H. (2008) IIIB 3.1.2-01 Non-GLP
Odour	Olfactory	Blue paste: F01265, Batch: F1265, Nominal: 50 mg/kg	Cereal odour	Caruel, H. (2008) IIIB 3.1.1-01 Non-GLP
Explosive properties	Expert statement	Blue paste: F01265, Nominal: 50 mg/kg	Not explosive	Curl, M and Wright, E. (2011a) IIIB 3.2-01 Non-GLP
Oxidizing properties	Expert statement	Blue paste: F01265, Nominal: 50 mg/kg	Not oxidising	Curl, M and Wright, E. (2011b) IIIB 3.3-01 Non-GLP
Flash point	n.a.			
Autoflammability	There are no auto-flammable components in the formulation.			
Other indications of flammability	EEC A10 (flammability of solids)	Study conducted with an alternative paste formulation F00060	F00060 paste is not flammable and blue paste F01265 containing chlorophacinone will also not be flammable, based on their	Demangel, B. (2008a) IIIB 3.4-01 GLP

	Method	Purity/Specification	Results	Reference
			comparable compositions.	
Acidity / Alkalinity	CIPAC MT31.2	Study conducted with an alternative paste formulation F00060	F00060 paste has an acidity of 0.08% m/m H_2SO_4. Blue paste F01265 will have a similar acidity.	Demangel, B. (2008b) IIIB 3.5-01 GLP
Relative density / bulk density	Pyknometer method using displacement	Study conducted with an equivalent paste (LR363, Lot 8390)	F00060 paste has a density of 1.1444 g/mL at 25°C and blue paste F01265 will have a similar density.	Zobel, M. (2007) IIIB 3.6-01 GLP
Storage stability – stability and shelf life	Longterm stability study 25°C – 2 years	blue Paste F1265_00. Batch F1265. Nominal 50 mg/kg.	Content of a.s.: Initial: 51.61 mg/kg Final: 47.53 mg/kg The active substance content content showed an acceptable decrease, aspect of test item and packaging and pH did not change significantly after storage at 25°C for 2 years. Test was performed in PP packaging.	Caruel, H. (2011) IIIB 3.7-02 GLP
Effects of temperature	Accelerated stability study 40°C – 8 weeks	Blue paste F01265_00 Batch F1265 Nominal content 50 mg/kg	Content of a.s.: Initial: 50.08 mg/kg Final: 51.55 mg/kg The active substance content remained stable, aspect of test item and packaging and pH of dispersion did not change significantly. Test was performed in PP packaging.	Caruel, H. (2010) IIIB 3.7-01 GLP
Effects of light	The product will not be exposed to direct (sun)light.			
Reactivity towards container material	Longterm stability study 25°C – 2	blue Paste F1265_00. Batch F1265.	Packaging: PP box stable for 2 years.	Caruel, H. (2011) IIIB 3.7-02

	Method	Purity/Specification	Results	Reference
	years	Nominal 50 mg/kg.		GLP
	Accelerated storage stability 54°C - 2 weeks	Chlorophacinone paste. Batch F2914. a.i.: 48.68 mg/Kg	No damage and no alteration in PE and PP sachet or in paper, non-woven film.	Deslux, R. (2012), IIIB 3.7-03
Technical characteristics in dependence of the formulation type	n.a.			
Compability with other products	This ready to use paste preparation is not intended to be used or mixed with other products.			
Surface tension	n.a.			
Viscosity	n.a.			
Particle size distribution	n.a.			

2.3.2 Analytical methods

	Principle of method
Technical active substance as manufactured:	HPLC-UV (CA report chlorophacinone)
Impurities in technical active substance:	Confidential information (CA report chlorophacinone)
active substance in the formulation:	HPLC-UV after extraction. Method is validated for the product. Specificity, linearity, repeatability and recovery rate have been tested.

2.4 Risk assessment for Physico-chemical properties

The product is not oxidising, not explosive, not highly flammable and not expected to be corrosive. Risks regarding physical and chemical properties of the product are not expected.

2.5 Effectiveness against target organisms

2.5.1 Function

Rozol Pat' is a rodenticide (PT14) based on 0.005% w/w chlorophacinone. The product is applied for as a product for both professional and non-professional use.

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

In the application the following target organisms were indicated:
Rozol Pat' paste bait is used to control:
Rattus norvegicus (Norway rat/Brown rat)*
Rattus rattus (Roof rat/Black rat)
Mus musculus (House mouse)

Professional use: the control of rats and mice in and around buildings, in open areas and waste dumps.

Non-professional use: the control of rats and mice in and around buildings*.

Rozol Pat' paste bait is used to protect human food and animal feedstuffs and for general hygiene purposes.

**The uses and claims as applied for by the applicant differ from the authorised use. See SPC for final authorised uses.*

2.5.3 Effects on target organisms

Chlorophacinone is a first-generation anticoagulant rodenticide. It disrupts the normal blood clotting mechanisms resulting in increased bleeding tendency and, eventually, profuse haemorrhage and death. Effectiveness of the active substance depends on exposure (i.e. consumption of the bait by the target organism). For effective and comprehensive control of rats and mice, a bait concentration of 50 mg active /kg bait is proposed.

Rozol Pat' differs from the products described in the CAR of chlorophacinone since the bait is a paste. Therefore, the studies presented in the CAR are not applicable and new laboratory and field studies have been conducted with mice and rats using paste bait formulations containing 50 mg/kg chlorophacinone. The results are described in Section IIIB 5.10.2 and are summarised in table 2.5.3.0 below.

Besides these efficacy studies two studies have been provided showing that the warfarine sensitive strains of *R. norvegicus* and *M. musculus* were suitably sensitive to warfarine (IIIB 5.10.2-8 and IIIB 5.10.2-9). Furthermore, studies have been provided showing that neither the packaging of a block bait in either polyethylene or polypropylene film, nor the addition of the bittering agent denatonium benzoate (0.01% or 0.001%) to a rodenticide green block formula had any effect on the palatability of the bait (IIIB 5.10.2-6 and 7).

Table 2.5.3.0: Efficacy of the active substance from its use in the biocidal product – paste bait formulations

Test substance	Test organism(s)	Test system / concentrations applied / exposure time	Test results: effects, mode of action, resistance*	Reference
Blue paste F01265_00	House Mouse *Mus musculus* (wild strain, sensitive to warfarin)	Laboratory study, using bait aged for 4 months, single free-choice test with a total of 20 mixed sex animals, 4 day exposure. Test Method: EPPO PP1/214(1)	Palatability of the treated bait was greater than the reference diet in the test diet (attractivity value = 0,66) . Efficacy was 85% occurring between 7 and 14 days after initial consumption.	IIIB 5.10.2-03
Blue paste F01265_00	House Mouse *Mus musculus* (wild strain, sensitive to warfarin)	Laboratory study, using bait aged for 3 years, single free-choice test with a total of 23 mixed sex animals, 4 day exposure. Test method: EPPO PP1/214(1)	Palatability of the treated bait was superior to the reference diet (attractivity value = 0,74). Efficacy was 91% occurring between 4 and 15 days after initial consumption.	IIIB 5.10.2-12
Red block F00507 (active: 50mg/kg chlorophacinone)	House Mouse *Mus musculus* (wild strain)	Field study conducted at 2 sites, in and around agricultural buildings with high mice activity. Bait stations contained 40g bait at 16 locations at site 1 and 12 location at site 2. The number of mice estimated on the maximum food intake recorded during treatment was 263 (site 1)	Based on consumption estimates the efficacy under field conditions was 95.5%. (site 1) and 92.6% (site 2). Mortality was observed from 6 to 20 days at site 1 (70 dead mice) and from 4 to 20 days at site 2 (21 dead mice), with the cause of death confirmed as bait consumption with signs of intra-peritoneal bleeding. The block bait tested was effective	IIIB 5.10.2-10

Test substance	Test organism(s)	Test system / concentrations applied / exposure time	Test results: effects, mode of action, resistance*	Reference
		and 108 mice (site 2). Assessments were conducted throughout the duration of the trial at 1- 4 day intervals. During each assessment the food/bait at each station was weighed and replenished, and the amount consumed was calculated. During the treatment, searches were conducted for dead and dying mice in and around the site. The duration of the whole test (incl pre- and post-treatment) was 59-66 days.	under field conditions against mice when in competition against natural food sources and other environmental factors.	
Blue paste F01265_00	House Mouse *Mus musculus* (wild strain)	Field study conducted at 1 site, in and around agricultural buildings with high mice activity. Bait stations contained 40g bait at 24 locations (20 in building, 4 around building), positioned at a distance of 2 to 15 m between stations. The number of mice estimated on the maximum food intake recorded during treatment was 126. Assessments were conducted throughout the duration of the trial at 1- 4 day intervals (one 7 day interval at end of baiting phase). During each assessment the food/bait at each station was weighed and replenished, and the amount consumed was calculated. During the treatment, searches were conducted for dead and dying mice in and around the site. Pre baiting: 22 days. Baiting: 25 days. Post-baiting: 7 days.	Based on consumption estimates the efficacy under field conditions was 98.4%. Mortality was observed during baiting from day 6 on (42 dead mice during baiting, 3 during post-baiting), with the cause of death confirmed as bait consumption with signs of intra-peritoneal bleeding. The paste bait tested was effective under field conditions against mice when in competition against natural food sources and other environmental factors.	IIIB 5.10.2-13
Blue paste F01265_00	Rat *Rattus norvegicus* (wild strain, sensitive to warfarin)	Laboratory study, using bait aged for 17 months, two free-choice tests with a total of 20 mixed sex animals, 4 day exposure. Test Method: EPPO PP1/214(1)	Palatability of the treated bait was equivalent to or similar to the reference diet (attractivity value = 0,45 and 0,42). Efficacy was 96% occurring between 7 and 11 days after initial consumption.	IIIB 5.10.2-02
Blue paste F01265_00	Rat *Rattus norvegicus* (wild strain, sensitive to warfarin)	Laboratory study, using bait aged for 3 years, single free-choice test with a total of 10 mixed sex animals, 4 day exposure. Test Method: EPPO PP1/214(1)	Palatability of the treated bait was equivalent to the reference diet (attractivity value = 0,47). Efficacy was 90% occurring between 7 and 14 days after initial consumption.	IIIB 5.10.2-11
Blue paste F01265_00	Rat *Rattus norvegicus* (wild strain)	Field study conducted at 2 farm sites in France in and around buildings. The number of rats	Based on consumption estimates the efficacy under field conditions was 97,6% Mortality was observed from 4 to 11	IIIB 5.10.2-04

Test substance	Test organism(s)	Test system / concentrations applied / exposure time	Test results: effects, mode of action, resistance*	Reference
		calculated on the maximum food intake recorded before treatment was 59 for site 1 and 40 for site 2. Bait stations (12 on site 1 and 10 on site 2) were positioned where high levels of rodent activity were identified and were positioned 2-15 metres apart. Each bait contained 150 g paste (applied in sachets containing 10 g of blue paste). Assessments were conducted throughout the trial and were done every 1-4 days; baits were weighed and replenished, then the amount consumed was calculated. The duration of the whole test was 64 days for site 1 and 67 days for site 2.	days at site 1 (12 dead rats) and from 5 to 14 days at site 2 (7 dead rats), with the cause of death confirmed as bait consumption with signs of intra-peritoneal bleeding. The paste bait tested was effective under field conditions against rats when in competition against natural food sources and other environmental factors.	
Blue paste F01265_00	Rat *Rattus rattus* (wild strain, sensitive to warfarin)	Laboratory study, using bait aged for 17 months, two free-choice tests with a total of 20 mixed sex animals, 4 day exposure. Test Method: EPPO PP1/214(1)	Palatability of the treated bait was greater than that of the reference diet in each test (attractivity value = 0,66 and 0,63). Efficacy was 90% occurring between 7 and 14 days after initial consumption.	IIIB 5.10.2-01
Blue paste F01265_00	Rat *Rattus rattus* (wild strain)	Field study conducted at 2 farm sites in France in and around buildings. The number of rats calculated on the maximum food intake recorded before treatment was 65 for site 1 and 51 for site 2. Bait stations (12 on each site) were positioned where high levels of rodent activity were identified and were positioned 2-15 metres apart. Each bait contained 150 g paste (applied in sachets containing 10 g of blue paste) . Assessments were conducted throughout the trial and were done every 1-4 days; baits were weighed and replenished, then the amount consumed was calculated. The duration of the whole test was 67 days for site 1 and 57 days for site 2.	Based on consumption estimates the efficacy under field conditions was 98%. Mortality was observed from 4 to 34 days at site 1 (9 dead rats) and from 4 to 18 days at site 2 (8 dead rats), with the cause of death confirmed as bait consumption with signs of intra-peritoneal bleeding. The paste bait tested was effective under field conditions against rats when in competition against natural food sources and other environmental factors.	IIIB 5.10.2-05

* Efficacy laboratory study = mean mortality of male and female animals tested (in %); Efficacy of field study = (Ipre-Ipost)/Ipre*100% (Ipre = mean (stabilized) intake in pre-baiting period, Ipost=mean daily intake in post-baiting period); Palatability (=attractivity of the bait) is expressed as the

attractivity value calculated as A/(A+B) (A = amount of test bait consumed, B = amount of standard bait consumed).

These tests show the efficacy of the Blue paste F01265_00 in laboratory choice tests and field tests against all the target organisms and the efficacy of Red bait block F00507 against *M. musculus* in the field. F00507 is a red bait block containing 50 mg/kg chlorophacinone. Blue paste F01265_00 is identical to Rozol Pat'. Note that during product authorisation, the applicant has amended the study reports with reference IIIB5.10.2-01 to 05; the tested product has been amended from green paste F00871_02 to blue paste F01265_00.

Lab studies:
Efficacy and palatability of the product has been sufficiently demonstrated in laboratory choice tests for *R. norvegicus* and *R. rattus* (90-96% mortality). Although the efficacy of the product was somewhat lower for *M. musculus* in the choice test using bait aged for 4 months (85%, IIIB 5.10.2-03), the efficacy is shown to be sufficient (91% mortality) in the choice test using bait aged for 3 years. It is therefore concluded that efficacy has been sufficiently demonstrated in laboratory mortality and palatability tests for all the target organisms.
The studies also show that the palatability of the product is still sufficient after a storage period of 3 years.

Field studies:
A field study with a block rodenticide containing 50 mg/kg chlorophacinone was provided. This study showed a high efficacy of the block rodenticide against mice in the field. However, a field study with a block rodenticide is not representative for the palatability of a gel in sachets.

Also field studies with Blue paste F01265_00 were provided. Blue paste F01265_00 is identical to Rozol Pat'. The efficacy of the product in these field tests has been sufficiently demonstrated for *R. rattus, R. norvegicus* and *M. musculus* (98% mortality for all target organisms).
Note that for mice the application rate in the field study is lower than the application rate proposed by the applicant (see Table 1.5.2). Moreover, the Competent Authority NL is of the opinion that for both rats and mice a minimum application rate should be stated, based on expert opinion these have been determined at 100g for rats and 30 g for mice.

It can be concluded that Rozol Pat' is effective in controlling *R. rattus, R. norvegicus* and *M. musculus* at a use dosage of 100-200 g bait per bait point for rats (distance of 4-10 m between bait points) and 30-50 g bait per bait point for mice (distance of 1-3 m between bait points).

2.5.3.1 Dose
The active substance is incorporated into a paste bait at a concentration of 50 mg/kg and used by both professional and non-professional users. Each sachet contains 10 to 40 gram of product. A box contains sachets of one weight.

Table 2.5.3.1: Summary of use pattern for chlorophacinone paste bait for professional and amateur users

Species	Recommended Application rate for one bait point/baiting point intervals[#]	Frequency of controls	Checking / Replenishing	Time of treatment and place of application
Non-professional users				
Mice	30 to 50 g of paste in	Dispose the product	At each check, re-apply the bait if	All year

	one or more sachets per bait station. Place 1 station every 1 to 3 m	and check 3 days after first application, then regularly once a week or 15 days	only a part of the bait is consumed. In case all bait is eaten, refill the station and use more bait stations and/or increase the control frequency.	In & around buildings.
Rats: Brown & Black	100 to 200 g of paste in 2 or more sachets per bait station. Place 1 station every 4 to 10 m.	Dispose the product and check 3 days after first application, then regularly once a week or 15 days	At each check, re-apply the bait if only a part of the bait is consumed. In case all bait is eaten, refill the station and use more bait stations and/or increase the control frequency.	
Professional users*				
Mice	High infestation 30 to 50 g of paste in one or more sachets per bait station. Place 1 station every 1 to 1.5 m	Dispose the product and check 3 days after first application, then regularly once a week or 15 days	At each check, re-apply the bait if only a part of the bait is consumed. In case all bait is eaten, refill the station and use more bait stations and/or increase the control frequency.	All year In & around buildings In open areas In waste dumps.
	Low infestation 30 to 50 g of paste in one or more sachets per bait station. Place 1 station every 2 to 3 m	Dispose the product and check 3 days after first application, then regularly once a week or 15 days	At each check, re-apply the bait if only a part of the bait is consumed. In case that all bait is eaten at a bait station, refill the bait station and use more bait stations and/or increase the control frequency.	
Rats: Brown & Black	High infestation 100 to 200 g of paste in 2 or more sachets per bait station. Place 1 station every 4 to 5 m.	Dispose the product and check 3 days after first application, then regularly once a week or 15 days	At each check, re-apply the bait if only a part of the bait is consumed. In case that all bait is eaten at a bait station, refill the bait station and use more bait stations and/or increase the control frequency.	All year In & around buildings In open areas In waste dumps.
	Low infestation 100 to 200 g of paste in 2 or more sachets per bait station. Place 1 station every 8 to 10 m.	Dispose the product and check 3 days after first application, then regularly once a week or 15 days	At each check, re-apply the bait if only a part of the bait is consumed. In case that all bait is eaten, refill the station and use more bait stations and/or increase the control frequency.	

*: Since it is also possible that the professional user will identify a medium infestation the RMS proposes to put only the shortest and longest distance on the label (1 to 3 m for mice, 4 to 10 m for rats) and let the professional user decide what distance is most appropriate.
In case of a black rat infestation, preferably higher bait points should be chosen.

2.5.3.2 Mode of action

Chlorophacinone is a first-generation anticoagulant rodenticide. It disrupts the normal blood clotting mechanisms resulting in increased bleeding tendency and, eventually, profuse haemorrhage and death. As with other anticoagulant rodenticides, the active substance is a vitamin K antagonist. It interferes with the regeneration of prothrombin, disturbing the normal blood clotting mechanisms and causing an increased tendency to haemorrhage. The site of action is the liver, where several of the blood coagulation precursors undergo vitamin K dependent post translation processing before they are converted into the respective pro-coagulant zymogens. The point of action appears to be the inhibition of K1 epoxide reductase. Rodents usually die within three to six days of the first consumption. Clinical symptoms may be observed around one to two days before death.

2.5.3.3 Limitations

The original information provided in the PAR of 22nd March 2013

The product is not recommended for the concomitant use with other specific biocidal products (5.11.3).

For the authorisation of rodenticides for controlling rats, the RMS, the Netherlands, is of the opinion that the general public is not able to use rodenticides against rats in a correct way. Incorrect use can cause resistance in rats which will increase problems of controlling rats in the future. Furthermore, in the Netherlands the control of rats and use of rodenticides against rats is restricted to licensed professional users and rodenticides against rats have never been used by the general public. Therefore the authorisation of rodenticides for controlling rats in the Netherlands is restricted to licensed professional users only due to national policy.

New limitations added to the PAR of 1st November 2013
Due to the widespread occurrence of resistance in brown rats in the Netherlands against first-generation anti-coagulants, including chlorophacinone (see paragraph 2.5.3.4) and the risk of further development of cross-resistance in brown rats against second-generation anti-coagulants the use of this product against brown rats is not authorised in the Netherlands.

Due to the risks of further spread of resistance to first-generation anti-coagulants including chlorophacinone in house mice and the risk of further development of cross-resistance in house mice against second-generation anti-coagulants, the use of Rozol Pat' by non-professionals is not authorised in the Netherlands.
Non-professionals are normally allowed to control house mice in the Netherlands with anticoagulants. House mice and brown rats, however, often occur together and it cannot be excluded that non-profs will apply bait products in regions with resistant brown rat populations. Even when the product is intended for mice it can be expected that brown rats in the neighbourhood will eat from the bait and in this way remain selection pressure for the resistance genes in rats.
It is not feasible to expect from non-profs that they will be able to monitor resistance and apply a resistance management strategy. Moreover, it is not possible to inform non-professionals on the presence of resistance in certain populations and regions. Ctgb has therefore decided to restrict the use of Rozol Pat' to professional use only.
Professional users will be able to monitor resistance and apply resistance management strategies. It is also possible to inform professionals on regional differences in rodent resistance.

2.5.3.4 Resistance

The original information provided in the PAR of 22nd March 2013
There have been cases of resistance to first generation anticoagulants including chlorophacinone in some EU member states. Nevertheless, the resistance is not widespread and chlorophacinone remains effective in most of the rodent control situations.

New information provided on resistance for the adapted PAR of 1st November 2013
Shortly after the authorisation of Rozol Pat' (13974N) on the 22nd March 2013, an appeal was made to the CA NL by a specialist and by a professional user organisation that the authorisation of Rozal Pat' for the Dutch market should be reconsidered as the product is based on chlorophacinone to which widespread resistance in brown rats was present in NL. Also resistance of house mice to chlorophacinone in the Netherlands appeared to be already reported in the 1970s (Bosman, 1978).

In May 2013 also the results of a new study investigating the anticoagulant resistance of the brown rat in the Netherlands became available (WUR, 2013)[1]. In this report samples of rat droppings collected throughout the Netherlands in 2012 were analysed for the presence of resistance genes. Although the number of samples that were included in the study was limited (n=169), it was clear that overall 25% of the brown rats are resistant based on two different mutations Tyr139Cys and Tyr139Phe, in the report referred to as the German resistance gene and the French resistance gene. The resistance rates vary between different regions in the Netherlands. In particular in the region Twente in the eastern part of

the Netherlands all samples were found to be resistant. But resistance is also spread over a considerable part of the country, in particular in the eastern, central and southern region and the city of Rotterdam. Moreover, the resistant rats seem to be spreading over the country. The resistance situation in the population of black rats and house mice was not investigated and is not clear at the moment. The study report mentions that it is not clear how the resistance genes and the rates of homozygosity /heterozygosity affect the resistance against the authorised active substances in the Netherlands.
However, from studies in the UK, Germany and France (RRAG, 2010; Buckle and Prescott, 2012; Prescott et al., 2010; Grandemange et al, 2010) it is known that brown rats carrying the mutations found in the Netherlands are resistant to the first generation anticoagulants among which warfarin, chlorophacinone and coumatetralyl. It was concluded that applying products based on these active substances in a population in which these resistance genes are present will accelerate the selection for homozygous resistance in this population and will make such a populations very difficult to control.
Also cross-resistance with the second generation anticoagulants bromadiolon and difenacoum is described in rat populations with these resistance genes. As a consequence products based on these active substances are found to be less effective in these populations (e.g. Buckle et al., 2013; RRAG, 2010).

In May 2013 also an extensive overview over the resistance development to Vitamin K anticoaglants (VKA's) in rodents in Europe was presented in a draft report that was discussed at the 51st CA-meeting (CA-meeting 51, circabc.europa.eu). This report confirms the concerns on cross resistance between first and second generation anticoagulants in rodents, in particular for the brown rat. For the situation of resistance in black rats and house mice to anticoagulants less information is available, but resistance has been reported in several countries and there is also reason for concern of further development of resistance and cross-resistance to VKA's in these species, but the situation is not as critical as for brown rats. In practice brown rats and black rats do not occur at the same location but both species may coexists with house mice populations. In the Netherlands resistance of house mice to chlorophacinone has been reported in the 1970s (Bosman, 1978)

As a consequence of the new information provided on the spread of resistant brown rats in our country and considering the risk on cross-resistance form first-generation anti-coagulants to second-generation anticoagulants bromadiolon en difenacoum, the CA NL does not consider products based on chlorophacinone suitable for the control of brown rats in the Netherlands. Ctgb therefore has decided to exclude the control of brown rats from the label claim of Rozol Pat' in NL and restrict the use of Rozol Pat' to the control of black rats and mice only in the Netherlands.

Non-professionals are only allowed to control house mice in the Netherlands. House mice and brown rats often occur together and it cannot be excluded that non-profs will apply bait products in regions with resistant brown rats. It is not feasible to expect from non-professionals that they will be able to monitor resistance and apply a resistance management strategy. Moreover, it is not possible to inform non-professionals on the presence of resistance in certain populations/regions. The CA NL has therefore decided to restrict the use of Rozol Pat' to professional use only.

Professional users will be able to monitor resistance and apply resistance management strategies. Ctgb believes that it is also possible to inform professionals on regional differences in resistance. The possibility of other risk mitigation measures such as the French resistance monitoring system, in which the authorisation holders will have to report resistance reported by users every two years to the competent authorities have been discussed. In the Netherlands such a system is not in place and cannot be created on short term for just this product. Moreover, Ctgb strongly doubts whether such a system will be effective in the Dutch situation in which resistance is already present in brown rat populations throughout the country.

In response to the considerations above, the applicant has provided a statement with arguments on the further development of resistance and of cross-resistance to second-generation VKA's by the use of Rozol Pat'. The main argument of the applicant is that use of a first generation VKA, such as Rozol Pat' may be useful to control micro populations of non-resistant rats and even be used to reduce resistance levels in resistant rat populations by removing selection pressure. Also the occurrence and the mechanism of cross resistance is disputed.

In the Netherlands micro populations of non-resistant rats have not been found and are not likely to be present because of the short distances between farms and the high selection pressure by use of VKA's (WUR, 2013). In Denmark, the strategy of using first and second generation VKA's in alternation (warfarin, then coumatetralyl, followed by difenacoum) has resulted in extremely high levels of resistance of rats, even to difenacoum, in most of the country (Lodal, 2001). Another strategy would be a major shift towards the use of newer second generation VKA's (brodifacoum, difethialone), hoping that moving from chlorophacinone or warfarin to one of these AVK's represents a change that cannot result in an adaptation of the rat population. This is the strategy that is currently used in the Netherlands, but we now also see that resistant rats are further spreading throughout the country.
Although lowering AVK selection pressure could potentially result in a return of susceptible animals (as there might be a biological cost associated with resistance) this is still highly hypothetical. In such a situation, second generation AVKs could function as treatment against resistant populations and first generation could be used in those cases where no resistance is suspected, which is rare in the Netherlands. Because of the current state of knowledge, i.e. resistance is found all over the Netherlands and it is not clear where susceptible populations can be found,this strategy is currently not our choice.

The use of Rozol Pat' to control brown rats in the Netherlands is therefore is not authorised by CA NL as it is not sufficiently effective to control brown rats, may lead to bioaccumulation in predators by the occurrence of partly poisoned rats and will also lead, to our opinion, to further development of resistance and cross-resistance to second generation VKA's in brown rat populations. Also the use of Rozol Pat' by non-professionals will not be authorised for the Netherlands by the CA NL.
Rozol Pat' is authorised to be used to control black rats and house mice in buildings by professionals only in the Netherlands.

The situation on resistance in rodents in other EU countries may differ from the Dutch situation. It is therefore up to the different CA's of the EU countries to take their own decision in the authorisation of Rozol Pat' to control brown rats, black rats and house mice by professionals and non-professional in and around buildings, in open areas and waste dumps. Rozol Pat' should not be used in areas where resistance against chlorophacinone is present in rats or mice, to prevent spreading of resistant populations.

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2.5.3.4.1 Resistance management strategy

A management strategy to minimise the likelihood of resistance to the active substance developing in the target species was provided by the applicant. It consists of the following three components:

Firstly, in general ineffective use of chlorophacinone rodenticides is often misdiagnosed as resistance. The success of a control campaign is often dependant on how the control measures are conducted in practice. It is therefore most important to select an appropriate control strategy. An effective control programme needs to consider the following aspects:

- Identification of target organism and selection of an appropriate product.
- Correct positioning of bait stations.
- Attractiveness of bait selected/competition with abundant food sources.
- Baiting for an adequate time.
- Understanding the extent and area of infestation to ensure an adequate amount is used over a sufficient area.
- Immigration from neighbouring populations.

Secondly, to avoid the development of resistance in susceptible rodent populations the following points should be adopted for all control programmes:

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

Thirdly, when resistance to chlorophacinone is suspected or identified, the following should be conducted:

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

Where individual infestations are found to be resistant or contain resistant individuals it is possible that the resistance extends further to neighbouring properties:

- Where there are indications that resistance may be more extensive than a single infestation, apply area or paste control rodent programmes.
- The area under such management should extend at least to the area of known resistance and ideally beyond.
- These programmes must be effectively co-ordinated and should encompass the procedures identified above.

The use of differing bait formulations is an integral part of the resistance avoidance plan and as such, paste bait formulations provide suitable alternate preparations of anticoagulant rodenticide. In NL professionals always need to be certificated as a pest controller. These professionals are educated in the above described resistance management strategies. It can not be expected that non-professionals have any knowledge on resistance management.

2.5.3.5 Humaneness

The use of chlorophacinone as a rodenticide could cause suffering of vertebrate target organisms. The use of anti-coagulant rodenticides is necessary as there are at present no other valuable measures available to control the rodent population in the European Union. Rodent control is needed to prevent disease transmission, contamination of food and feeding stuffs and structural damage.
It is recognised that anticoagulants like chlorophacinone do cause pain in rodents but it is considered that this is not in conflict with the requirements of Art. 5.1 of the BPD “to avoid unnecessary pain and suffering of vertebrates”, as long as effective, but comparable less painful alternative biocidal substances or biocidal products or even non-biocidal alternatives are not available.

2.5.4 Evaluation of the label claim

The applicant has provided a Dutch label (WG/GA). This has been adapted to our standards. For the convenience of the competent authorities authorising this product through mutual recognition, the Dutch labels, translated in English, are added to the PAR in annex 9.

Field of use
Efficacy is claimed for indoor and outdoor use. However, authorisation for this product in NL is only allowed for indoor use for environmental reasons (see 2.8). The Dutch label (WG/GA) has been adapted accordingly.

Target species
The Ca NL has decided not to authorize the use of Rozol Pat' to control brown rats in NL due to the spread of the resistant brown rats in the Netherlands and the cross-resistance among the first-generation anti-coagulants and between the first- and second-generation anti-coagulants. The Dutch label (WG/GA) has been adapted accordingly.

The organisms claimed to be controlled by non-professionals are brown rats, black rats and mice. However, the authorisation to use rodenticides for controlling rats in the Netherlands is restricted to licensed professional users only due to national policy. The Dutch label (WG/GA) has been adapted accordingly

Non-professionals are allowed to control only the house mice in the Netherlands. House mice and brown rats often occur together and it cannot be excluded that non-profs will apply bait products in regions with resistant brown rats, thus continuing selection pressure on resistant brown rats. It is not feasible to expect from non-professionals that they will be able to monitor resistance and apply a resistance management strategy. Moreover, it is not possible to inform non-professionals on the presence of resistance in certain populations/regions. Therefore the use of Rozol Pat' for control of house mice is restricted to professional use only. The Dutch label (WG/GA) has been adapted accordingly

Use instructions
Based on the data of the field studies, the use dosages for mice have been adapted to 30 – 50 g bait per bait point and for rats to 100 – 200 g bait per bait point (see also Table 2.5.3.4).

Resistance management
In the PAR a resistance management strategies is outlined. A short remark on resistance is added to the Dutch label (WG/GA): For the active substance chlorophacinone present in the product, there is a risk that mice and rats may develop resistance and in some parts of the Netherlands resistance is already present. This product should therefore not be used in cases in which resistance is likely, for example in cases in which earlier treatment with a chlorophacinone containing product did not result in a clear reduction of the population. Always contact with the appropriate authorities to check for the latest knowledge on occurrence of resistance.

2.6 Exposure assessment

2.6.1 Description of the intended use(s)

Rozol Pat' is a ready-to-use rodenticide paste bait in sachets based on 0.005% w/w chlorophacinone. The product applied for is for both professional and non-professional use. Professional use is restricted to the control of rats and mice in and around buildings, in open areas and waste dumps. Non-professional use is restricted to the control of rats and mice in and around buildings. Baits should preferably be placed in tamper-resistant bait stations. For rats 100 to 200 g bait should be placed per bait station, which should be positioned at 4 to 10 meter distance of each other. For mice 30 to 50 g bait should be placed per bait station, which should be positioned at 1 to 3 meter distance of each other. After disposal of the product the bait should be checked regularly: first check 3 days after application, then every week or 15 days.

2.6.2 Assessment of exposure to humans and the environment

For the product Rozol Pat' to be used by professionals and non-professionals for the control of rats and mice in and around buildings, in open areas and around waste sites with the purpose of protecting human food and animal feedstuffs, and for general human hygiene no new studies have been provided. The environmental exposure and risk assessment of the biocidal product blue paste F01265 bait containing 50 mg/kg chlorophacinone (Rozol Pat') from the applicant was examined appropriately according to standard requirements. The product was not a reference product in the EU-review program for inclusion of the active substance in Annex I of Directive 98/8/EC. For the environmental exposure and risk assessment of Rozol Pat', the applicant considers the EUBEES 2 scenario for blocks to be appropriate for paste baits.

The applicant has submitted an effect and exposure assessment for Rozol Pat'. The RMS NL has updated this risk assessment for the environmental aspect. For authorisation purposes the risk assessment of Rozol Pat' performed by the applicant is included in this Product Authorisation Report.

Environmental exposure to soil occurs when Rozol Pat' is deployed outdoor. Non-target vertebrates may be exposed to Rozol Pat' either directly by ingestion of exposed paste (primary poisoning) or indirectly by ingestion of the carcasses of target rodents that contain chlorophacinone residues (secondary poisoning). See for more detail section 2.8 below.

2.7 Risk assessment for human health

Rozol Pat' is not a reference product of the CAR for chlorophacinone; however, the risk assessment in the CAR was performed for a related product Product P1 – Red blocks containing 50 mg chlorophacinone/kg. Based on the composition the results of the studies with this product are considered to be applicable for Rozol Pat'.

No new studies with Rozol Pat' have been submitted with respect to toxicological properties of the product.

2.7.1 Hazard potential

2.7.1.1 Toxicology of the active substance

The toxicology of the active substance was examined extensively according to standard requirements. The results of this toxicological assessment can be found in the CAR. The threshold limits and labelling regarding human health risks listed in Annex 4 „Toxicology and metabolism" must be taken into consideration.

2.7.1.2 Toxicology of the substance(s) of concern

The biocidal product does not contain substances of concern.

2.7.1.3 Toxicology of the biocidal product

The toxicology of the biocidal product was examined appropriately according to standard requirements. The product was not a reference product in the EU- review program for inclusion of the active substance in Annex I of Directive 98/8/EC. For the toxicology of

Rozol Pat' the applicant submitted data of the comparable product Product P1 – Red blocks containing 50 mg chlorophacinone/kg, which was evaluated in the CAR. Both products contain the equal amounts of the active substance, and the concentrations of other co-formulants are comparable. Based on this the studies on Product P1 – Red blocks containing 50 mg chlorophacinone/kg are considered to be suitable for the risk assessment of Rozol Pat'. No new information is required.

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

2.7.2 Exposure

The biocidal product Rozol Pat' contains the active substance chlorophacinone (pure: 0.050 g/kg). Rozol Pat' bait is a ready-to use paste bait for the control of black and brown rats and mice in and around buildings, waste dump places and open areas with the purpose of protecting human food and animal feedstuffs, and for general human hygiene. Rozol Pat' is supplied in ready to use sachets (weight: 5-40 g) which are not intended to be opened by the user.
The product is intended for both professional and non-professional use. However, non-professional use against rats is not permitted in the Netherlands by specific national policy.

The potential for exposure to chlorophacinone paste baits is summarised in the table below.

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

Inhalation exposure

Chlorophacinone is not volatile and Rozol Pat' bait is a non-dusty cereal based paste formulation containing the active substance chlorophacinone which is not volatile. Therefore, the risk of inhalation exposure to chlorophacinone for professional or amateur users during use is not considered a relevant exposure path. Similarly, for non-users, the risk of inhalation exposure to residues during or after application via the environment is considered to be negligible.

Dermal exposure

Rozol Pat' is supplied ready for use in sachets which are not intended to be opened by the user. The product is placed in position by hand; however dermal exposure during application can be excluded due to the presence of the packaging. Once in place the product packaging will be damaged by rodents as they feed and the paste bait will be exposed. Dermal exposure to paste is therefore possible during clean-up operations, but this will be limited to the hands and exposure to other parts of the body is negligible. Children could potentially be the group most at risk as they may play inside or around buildings where baits have been placed. However, product labels and good practice advise users to prevent access to bait by children.

Oral exposure

Rozol Pat' bait is not likely to reach the mouth of professional or amateur users. Therefore, the risk during use is considered to negligible. To prevent dermal-oral uptake, the following

sentence is included in the WG/GA (instruction of use) "Wash hand after use". Similarly, for non-users, risk of oral exposure to residues during or after application is considered to be negligible. Children or infants may play close to the floor where baits have been placed indoors. However, product labels and good practice advise users to prevent access to bait by children. Rozol Pat' bait also contains a bittering agent to prevent infants from ingesting bait.

2.7.2.1 Exposure of professional users

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

The exposure assessment to Rozol Pat' has been performed by the applicant by considering three exposure scenarios: bait placement in and around buildings, application around waste dumps and application in open areas.

Rozol Pat' is supplied in sachets ready to use by professional users. A maximum dose of 200 g for rats and 100 g for mice is used per one bait point. As a worst-case, a maximum application of 6 sachets of 40 g per one bait point is considered. As the product is supplied in ready to use sachets, dermal exposure during loading is considered to be negligible. Once in place the product packaging will be damaged by rodents as they feed and red paste bait will be exposed. Dermal exposure to paste is therefore possible during clean-up operations but will be limited to the hands and exposure to other parts of the body is negligible.

According to HEEG opinion (2010) on the number of manipulations in the assessment of rodenticides (anticoagulants) a maximum of 75 manipulations per day per person is assumed (placing of 60 bait stations per day and cleaning of 15 bait stations per day). This corresponds to the maximum handling of 75 x 6 x 40 = 18 kg product/day, or 18 x 0.05 = 900 mg chlorophacinone handled per day. This scenario has been considered by the applicant for bait placement in and around buildings.

Two additional exposure scenario's for professional user have been considered by the applicant: aplication around waste dump (landfill) perimeters for control of rodents and application in open areas for control of rodents. In the first scenario, as a worst case a maximum of 50 bait points treated per day plus remains of 50 bait points collected is considered, which corresponds to 100 x 6 x 40 = 24 kg product/day, or 24 x 0.05 = 1200 mg chlorophacinone handled per day. In the second scenario a maximum of 30 bait points treated per day is assumed, corresponding to 30 x 6 x 40 = 7.2 kg product/day, or 360 mg chlorophacinone handled per day.

The same exposure scenarios (bait placement in and around buildings, application around waste dumps and application in open areas) were considered in the CAR of chlorophacinone; however, as a worst-case approach, the assessment of the product (Product P1 – Red blocks containing 50 mg chlorophacinone/kg) without protective sachets was performed. Therefore dermal exposure during loading was also taken into account in the CAR, leading to overall higher total exposure estimates. The number of manipulations considered in the CAR were 75 treated and 75 collected bait points per day for the applications in and around buildings and around waste dumps, and 75 treated and none collected for the application in open area. Although the numbers of manipulations considered in the CAR represent a more worst-case approach, taking into account the advised maximal number of manipulations according to the HEEG opinion (2010) the numbers of manipulations proposed by the applicant are considered acceptable.

The applicant has submitted two operator exposure studies using wax block bait which is considered to be a suitable surrogate for blue paste bait in a clean-up/disposal scenario. The studies were conducted using Racumin Ready Bait (cracked wheat) containing 0.031% w/w

coumatetralyl and Storm Secure 20G containing 0.0056% w/w flocoumafen. These studies were also assessed in the CAR of chlorophacinone. Following clean-up of 5 wax block residues from a single bait station, the mean residue on hands was 3.41 mg product equivalents/sample. The corresponding residues for cleaning up bait stations containing residues from 6 paste sachets and disposing of the unwanted bait will be (3.41 / 5) x 6 = 4.09 mg product equivalent/sample.

Operator body weight is assumed to be 60 kg. The dermal penetration of chlorophacinone is considered to be 1.7%.

The total systemic exposure to chlorophacinone of professional operators cleaning up Rozol Pat' bait considered 75 manipulations per day according to HEEG (2010) is estimated at 8.70×10^{-7} mg chlorophacinone/kg bw/day without PPE. For two additional scenarios (application around waste dump and application in open area) considered by the applicant the total systemic exposure of 2.89×10^{-6} mg chlorophacinone/kg bw/day and 1.74×10^{-6} mg chlorophacinone/kg bw/day without PPE is estimated.
For professional users the use of gloves can be expected. Gloves are assumed to reduce the exposure of hands by 90%. This results in the total systemic exposure of 8.70×10^{-8}, 2.89×10^{-7} and 1.74×10^{-7} mg chlorophacinone/kg bw/day for three described scenarios, respectively.

2.7.2.2 Exposure of non-professional users and the general public

In Annex 7 "Safety for non-professional operators and the general public", the results of the exposure calculations for the active substance and the substance of concern for the non-professional user and the general public are laid out.

The exposure assessment to Rozol Pat' has been performed by the applicant.

According to HEEG opinion (2010) on the number of manipulations in the assessment of rodenticides (anticoagulants) a maximum of 10 manipulations per day per person (5 loading bait stations per day and 5 cleaning bait stations per day) is proposed for non-professional user. This corresponds to the maximum handling of 10 x 6 x 40 = 2.4 kg product/day, or 2.4 x 0.05 = 120 mg chlorophacinone handled per day.

As the product is supplied in ready to use sachets, dermal exposure during loading is considered to be negligible. Once in place the product packaging will be damaged by rodents as they feed and the red paste bait will be exposed. Dermal exposure to paste is therefore possible during clean-up operations but will be limited to the hands and exposure to other parts of the body is negligible.

The same number of manipulations was considered in the CAR of chlorophacinone for non-professional users. However, as a worst-case approach, the assessment of the product (Product P1 – Red blocks containing 50 mg chlorophacinone/kg) without protective sachets was performed. Therefore dermal exposure during loading was also taken into account in the CAR, leading to overall higher total exposure estimates.

Non-professional users are assumed not to wear protective gloves (or other protective clothing) when handling the products. Operator body weight is assumed to be 60 kg. The dermal penetration of chlorophacinone is considered to be 1.7%.

Exposure assessment was evaluated based on the submitted operator exposure studies. Following clean-up of 5 wax block residues from a single bait station, the mean residue on hands was 3.41 mg product equivalents/sample. The total systemic exposure to chlorophacinone of non-professional operators cleaning up Rozol Pat' bait in and around buildings is estimated at 2.89×10^{-7} mg/kg bw/day**.**

Indirect exposure to ROZOL PAT due to the ingestion of a bait by an infant has been considered. It is assumed that an infant may ingest 10 mg of product treated with repellent,

such as blue paste. Body weight is assumed to be 10 kg for infants. Total indirect systemic exposure to chlorophacinone following the ingestion of ROZOL PAT bait is estimated at 0.00005 mg/kg bw/day for infants. However, Rozol Pat' bait contains bittering agent which would cause any person to immediately expel it from the mouth by reflex action. Furthermore, product labels and good practice advise users to prevent access to bait by children.

2.7.2.3 Exposure to residues in food

The acute or chronic exposure to residues in food resulting from the intended uses is unlikely. Therefore the risk for consumers to residues from food is considered negligible.

2.7.3 Risk Characterisation

With proper use in accordance with regulations harmful effects on the health of users and third parties are not expected. The estimated exposures for the intended use are compared to the respective systemic AEL.

The AELs of 0.000017 mg/kg bw/day for repeated exposure and of 0.000033 mg/kg bw/day for acute exposure have been set in the CAR of chlorophacinone.

2.7.3.1 Risk for Professional Users

The following total systemic exposures to chlorophacinone have been estimated for professional users for three exposure scenarios (application in and around buildings, application around waste dump and application in open areas):

Without PPE: 8.70×10^{-7}, 2.89×10^{-6} and 1.74×10^{-6} mg chlorophacinone/kg bw/day, respectively
With PPE (gloves), considering 90% reduction: 8.70×10^{-8}, 2.89×10^{-7} and 1.74×10^{-7} mg chlorophacinone/kg bw/day

Professional operators are considered to be exposed to the product regularly, therefore the AEL for repeated exposure of 0.000013 mg/kg bw/day is considered. The estimated exposure levels correspond to the following percentages of $AEL_{long\text{-}term}$:

Without PPE: 5.1%, 17.0% and 10.2%, respectively.
With PPE (gloves, 90% reduction): 0.51%, 1.70% and 1.02%, respectively

Based on the risk assessment, it can be concluded that no adverse health effects are expected for the unprotected professional operator, after dermal and respiratory exposure to chlorophacinone as a result of the application of Rozol Pat'.

2.7.3.2 Risk for non-professional users and the general public

The total systemic exposure to chlorophacinone of non-professional operators cleaning up Rozol Pat' bait in and around buildings is estimated at 2.89×10^{-7} mg/kg bw/day. Non-professional users are considered not to be exposed to the product on a regular basis, therefore repeated exposure is considered to be not relevant for them and the AEL for acute exposure of 0.000033 mg/kg bw/day is considered. The estimated exposure level of 2.89×10^{-7} corresponds to 0.88% of AEL_{acute}.

Total indirect systemic exposure to chlorophacinone following the ingestion of Rozol Pat' bait is estimated at 0.00005 mg/kg bw/day for infants. Such exposure is considered to occur only incidently, therefore the AEL for acute exposure of 0.000033 mg/kg bw/day is considered. The estimated exposure corresponds to 151.5% of AEL_{acute}. The risk to infants thus appears to be of concern. According to DOC I of CAR on chlorophacinone the products containing

chlorophacinone are required to carry precautionary phrases on the label to mitigate the risk of secondary human exposure. These include:

- "Baits must be securely deposited in a way so as to minimise the risk of consumption by non-target animals or children. Where possible, secure baits so that they cannot be dragged away".
- "Keep out of reach of children"

If these safety measures are taken into account, the risks of infant exposure due to the ingestion of bait are considered to be mitigated.

Based on the risk assessment, it can be concluded that no adverse health effects are expected from indirect exposure to chlorophacinone as a result of use of Rozol Pat'.

2.7.3.3 Risk for consumers via residues

The acute or chronic exposure to residues in food resulting from the intended uses is unlikely and is considered negligible (see 2.7.2.3).

2.8 Risk assessment for the environment

Production of chlorophacinone and formulation of paste baits at the manufacturing sites takes place in closed systemsProduction and formulation systems have air treatment and all liquid effluent is stored in liquid waste storage tanks and disposed of to specialist dangerous waste processors. Contaminated solid waste is stored in dedicated containers and incinerated in a special incinerator. Consequently environmental exposure *via* manufacture, formulation, distribution and storage is considered negligible.

Consideration in the following text is confined to environmental releases following the use of Rozol Pat' containing 50 mg chlorophacinone/kg in the scenario in and around buildings, in open areas and around waste sites. Rozol Pat' is a ready-to-use product and further dilution prior is not foreseen.

The risk characterisation for the environment is based on proprietary product information, authoritative guidance documents describing good application practice (Crop Life International, Rodenticide Resistance Action Committee, Technical Monograph; UK Health and Safety Executive, 1999; UK Health and Safety Executive, 2003), on the EUBEES 2 'Emission scenario document for biocides used as rodenticides' (Larsen, 2003), hereafter referred to as EUBEES 2, and on the Technical Guidance Document (TGD; ECB 2003).

The risk characterisation and the underlying assumptions presented here are also confirmed in the Assessment Report for chlorophacinone (Product Type 14).

Application of Rozol Pat' containing 50 mg/kg chlorophacinone is confined to rodent control in the scenario in and around buildings, in open areas and around waste sites.

No studies were submitted with the product authorisation application for the active substance or for the product that were not already evaluated during the Annex I active review stage or studies. Detailed data on the fate and distribution of chlorophacinone in the environment and the effect of the active substance on environmental organisms can be consulted in Doc IIA of the revised final draft Assessment Report (December 2008) for chlorophacinone (PT14). The PNEC derivation is also described in detail in the Assessment Report for Chlorophacinone (Product Type 14) and included in the table below.

Summary of the PNECs derived for chlorophacinone in the different compartments

Compartment	Organism	Endpoint	AF	PNEC
Aquatic	Fish (*O. mykiss*)	LC50 (96 h) = 0.45 mg a.s/l	1,000	0.00045 mg a.s/l
STP	Microorganisms from an activated sludge	NOEC > 344 mg/l water solubility limit	10	34.4 mg/l
Sediment	Sediment-dwelling organisms	Covered by the aquatic compartment		
Soil	Earthworm (*E. foetida*)	LC50 > 340 mg a.s/kg dry soil*	1,000	0.30 mg a.s/kg wwt soil**
Terrestrial	Birds (*C. virginianus*)	5-d LD50 = 17.3 mg/kg bw LC50 = 95 mg a.s/kg food	3,000	0.0058 mg/kg bw 0.03 mg a.s/kg food
Terrestrial	Mammals (*Rattus norvegicus*)	NO(A)EL =0.005 mg a.s/kg bw NOEC = 0.1 mg a.s/kg food	90	0.000056 mg/kg bw 0.0011 mg a.s/kg food***

* based on nominal concentrations and for a standard soil of 3.4% o.m. content.

** No test on plants has been requested according to TM's decision.

*** For species with a food ingestion ratio of about 0.15 (ingestion up to 15% of their body weight as food per day)., (see complementary document prepared by the RMS Suárez E. *et al.*, 2008. Assessing the environmental risk for primary and secondary poisoning in birds and mammals of the rodenticide chlorophacinone. INIA-MARM report. July 2008).

2.8.1 Exposure Assessment

An environmental exposure assessment has been conducted based on the fate and distribution properties of the active substance, chlorophacinone, as determined from laboratory studies. The predicted environmental concentration (PEC) of chlorophacinone has been estimated, where appropriate, in various environmental compartments (surface water, groundwater, sediment, air and soil) following realistic worst case and, where appropriate, normal case usage scenarios.
The following PEC values are based on proprietary product information[2] and on the EUBEES 2 'Emission scenario document for biocides used as rodenticides' (Larsen, 2003)

These PEC values and the underlying assumptions are also confirmed in the revised final draft Assessment Report for chlorophacinone (Product Type 14).

2.8.1.1 Fate and distribution in the environment

The environmental fate and behaviour of the active substance chlorophacinone is summarised in the Assessment Report for chlorophacinone (Product Type 14).

2.8.1.2 PEC in surface water, ground water and sediment

The PEC of chlorophacinone in surface water, groundwater and sediment is considered for uses in and around buildings, in open areas and around waste sites. Contamination of surface water or sediment with chlorophacinone from the placing of Rozol Pat' in these areas is highly unlikely. Negligible exposure of surface water under these circumstances is also stated in the EUBEES 2 emission scenario document. In the Netherlands, however, it is well known that rats live near surface waters and that therefore also rodenticide campaigns may occur near these surface waters. Agreed scenarios to calculate the exposure in surface water

[2] Larsen, J. (2003). Emission scenario document for biocides used as rodenticides. Supplement to the methodology for risk evaluation for biocides, CA-Jun03-Doc.8.2-PT14. Report prepared in the context of the EU project entitled "Gathering, review and development of environmental emission scenarios for biocides" (EUBEES 2).

from leaching of rodenticides are lacking, therefore risk mitigation measures derived from CLP characteristics of the active substance are set in place.

Furthermore, due to the likely low soil concentrations the restricted use patterns and the strong adsorption of the active substance to soil, it is considered that chlorophacinone will not move to groundwater in significant quantities.

2.8.1.3 PEC in air

For chlorophacinone, the estimated half-life for the hydroxyl reaction in air is 14.3 hours, the vapour pressure as determined by OECD 104 is $4.76 \cdot 10^{-4}$ Pa (22.8°C) and the Henry's law constant is 0.013725 $Pa.m^3.mol^{-1}$ (based on a water solubility of 13.0 mg a.s/l). Therefore chlorophacinone is not expected to volatilise to air in significant quantities following use in any of the usage scenarios (i.e. in and around buildings, open areas and waste dumps) and the potential concentration of chlorophacinone in air is considered to be negligible.

2.8.1.4 PEC in soil

The PECs of chlorophacinone in soil arising from the various usage scenarios are considered, as follows:

In and around buildings

The PEC of chlorophacinone in soil is considered for uses in and around buildings as follows:

Exposure of the terrestrial compartment (soil) will occur when Rozol Pat' is deployed outdoors. EUBEES 2 considers a scenario that entails outdoor baiting with bait blocks around a farm building. In this situation, exposure is assumed to arise through a combination of transfer (direct release) and deposition *via* urine and faeces (disperse release) onto soil. The EUBEES 2 scenario for blocks is considered to be appropriate for paste baits.

Direct release is estimated to amount to 1.0% of the total bait deployment during the entire campaign, concentrated within 10 cm of the individual secured bait points. However, since Rozol Pat' is applied in packaging, the release is anticipated to be lower and a direct release of 0.1% is assumed to be more realistic. Similarly, EUBEES 2 considers that 90% of the total amount of rodenticide consumed by the target rodents over the duration of the outdoor baiting campaign enters soil *via* urine and faeces.

The maximum application rate for Rozol Pat' containing 50 mg chlorophacinone/kg entails the deployment of 240 g bait in each of ten secured bait points spaced 5 m apart against a 55 m length of external wall. EUBEES 2 assumes that direct release is concentrated in a 10 cm strip in front of and to both sides of each bait point (0.09 m^2). Based on penetration to a depth of 10 cm and a bulk soil density of 1700 kg/m^3, the mass of soil affected by the direct release around each secured bait point is 15.3 kg. To estimate the concentration of chlorophacinone in soil arising from disperse release, it is assumed that most of the activity of the target rodents is confined to a strip of ground running along the length of the baited wall and extending to 10 m in front of it (presenting an area of 550 m^2). Based on the depth and soil density values, the mass of soil receiving disperse inputs is 93,500 kg.

EUBEES 2 considers two levels of baiting. In the first, described as the "realistic worst-case", the campaign lasts 21 days and secured bait points (initially filled on day 1 and repeatedly and completely emptied by the target rodents) are refilled on days 3, 7, 14 and 21. In the other, "typical" scenario, bait consumption progressively declines as the campaign proceeds, such that the replenishments made on days 3, 7, 14 and 21 represent 100%, 25-50%, 10% and 0%, respectively, of the quantity initially deployed on day 1. It should be noted that the "typical" scenario is more representative of the consumption pattern for a potent anticoagulant rodenticide such as chlorophacinone, as demonstrated by field studies.

In both scenarios, the direct and disperse chlorophacinone releases ($Elocal_{soil}$, mg) to the relevant soil surfaces may be calculated according to:

$Elocal_{soil} = Q_{prod} \times Fc_{prod} \times N_{sites} \times N_{refill} \times F_{release,\ soil}$,

where:

Q_{prod} = weight of Rozol Pat' (240 g) per secured bait point;
Fc_{prod} = concentration of chlorophacinone in the paste bait (0.050 mg/g);
N_{sites} = number of secured bait points (10);
N_{refill} = number of refills during the campaign (5 in "realistic worst-case" and 1.5 in "typical" scenario)
$F_{release,\ soil}$ = fraction released to soil (0.001 for direct release and 0.9 for disperse release).

Concentrations of chlorophacinone in soil following baiting around buildings with Rozol Pat'

Baiting scenario (EUBEES 2)	**Direct release (mg/0.09 m^2)**	**Disperse release (mg/550 m^2)**	**PECsoil (mg chlorophacinone/kg ww)[a]**	
			mean[b]	**max[c]**
Realistic worst-case	0.60	540.0	0.0058	0.0097
Typical	0.18	162.0	0.0017	0.0029

[a] based on uniform distribution to 10 cm depth and wet soil bulk density of 1.7 g/cm^3;
[b] disperse release applied to total area (550 m^2);
[c] direct + disperse release within 10 cm in front of and to sides of each bait point.

Clocal concentrations (PECsoil, mg chlorophacinone/kg wet soil) have been calculated as indicated below. The mass of soil affected by the direct release around each secured bait point is 15.3 kg; the soil affected by indirect release around 10 bait stations is 93,500 kg.

Realistic worst-case (values for typical case shown in brackets):

Direct release: $Clocal,\ direct = \frac{E\ local,\ soil,\ direct}{15.3 \times 10}$ = 0.0039 mg/kg (0.0012 mg/kg ww);

Indirect release: $Clocal,\ indirect = \frac{E\ local,\ soil,\ indirect}{93{,}500}$ = 0.0058 mg/kg (0.0017 mg/kg ww);

Maximum concentration in soil: Clocal, direct + Clocal, indirect = 0.0097 mg/kg (0.0029 mg/kg ww).

Open areas
Paste baits are applied in open areas by inserting them inside the openings of the tunnels of the target rodents and, according to the scenario presented in EUBEES 2, two such treatments would typically be applied in the space of six days. Bait deployment comprising 6 × 40 g pastes per application per tunnel entrance is considered in this assessment as a worst-case compared to the 100 g bait application suggested in EUBEES 2. Based on a tunnel of 8 cm diameter, worst-case soil exposure is assumed to occur to a depth of 10 cm from the contact half (*i.e.* the burrow floor) of a 30 cm tunnel section in which the bait is placed. This section of tunnel floor is assumed to receive an input corresponding to 5% of the product during application and a further 20% as the bait is consumed.

Concentrations of chlorophacinone in soil following baiting in open areas with paste bait

Baiting scenario (EUBEES 2)	**Chlorophacinone applied (mg)[a]**	**Total direct deposition (mg)[b]**	**PECsoil (mg chlorophacinone/kg ww)[c]**
Worst-case	24.0	6.0	0.415

[a] based on 2 × (6 × 40 g) pastes containing 50 mg chlorophacinone/kg;
[b] based on inputs during application and consumption giving a combined deposition of 25%;
[c] based on uniform distribution in a semi-cylinder of soil of 4 cm and 14 cm inner and outer radius, respectively, 30 cm length (volume: 8,500 cm^3) and a wet soil bulk density of 1.7 g/cm^3.

The predicted concentration of 0.415 mg chlorophacinone/kg soil represents the worst-case in the immediate vicinity of each bait application. However, since paste baits are supplied in sachets, the extent of release of chlorophacinone into the floor of the tunnel is likely to be considerably less than the 25% suggested in EUBEES 2. Moreover, as the target rodents will eat and translocate portions of edible baits, and since much of the active substance will subsequently be excreted over a wide area outside the tunnel network, soil concentrations elsewhere will be considerably lower.

Waste dumps
Paste baits are deployed around the perimeter of waste-dumps and land-fill sites to control populations of rats. EUBEES 2 suggests a worst-case scenario in the event of an infestation outbreak that entails 40 kg of paste protected and distributed over an area of 1 ha, with a total of seven such applications per year. In this situation, soil exposure is assumed to arise through a combination of deposition via urine and faeces plus the rodenticide contained in the carcasses of poisoned target rodents. The EUBEES 2 scenario for blocks is considered to be appropriate for paste baits. In general, ninety percent of the total amount of rodenticide consumed by the target rodents over the duration of each baiting campaign is assumed to enter soil over the 1 ha surface.

According to the worst-case scenario, the total chlorophacinone release ($Elocal_{soil}$, mg) to the soil surface may be calculated according to:

$$Elocal_{soil} = Q_{prod} \times Fc_{prod} \times N_{app} \times F_{release,\ soil},$$

Where:

Q_{prod} = the total weight of paste (40 kg)
Fc_{prod} = the concentration of chlorophacinone in the paste product (50 mg/kg)
N_{app} = the number of applications (7)
$F_{release,\ soil}$ = the fraction released to soil (0.9).

Worst-case concentration of chlorophacinone in soil following baiting around waste dumps/landfills with bait pastes

Baiting scenario	Release to soil (mg chlorophacinone/ha)	PECsoil (mg chlorophacinone/kg ww)[a]
Worst-case (EUBEES 2)[b]	12600	0.0074

[a] based on uniform distribution to 10 cm depth and wet soil bulk density of 1.7 g/cm^3;
[b] based on seven applications of chlorophacinone in pastes/year.

2.8.1.5 Non compartment specific exposure relevant to the food chain (secondary poisoning)

The exposure of chlorophacinone directly to non-target birds and mammals and indirectly via target rodent carcasses (secondary poisoning) is quantified in section 2.8.2. These exposure routes to non-target vertebrates are not considered to have consequences for widespread contamination of environmental compartments.

2.8.2 Risk Assessment

The risk characterisation and the underlying assumptions presented here are also confirmed in the Assessment Report for chlorophacinone (Product Type 14).

2.8.2.1 Aquatic compartment (incl. sediment)

Contamination of surface water or sediment with chlorophacinone following the use of Rozol Pat' in and around buildings, open areas and around waste dumps is highly unlikely. Negligible exposure of surface water is also stated in the EUBEES 2 emission scenario document. Furthermore, due to the likely low concentrations in soil the restricted usage patterns and the strong adsorption of the active substance to soil, it is considered that chlorophacinone will not move to groundwater in significant quantities. Therefore, chlorophacinone concentrations in surface waters have not been calculated and, since exposure is expected to be negligible, PEC/PNEC quotients are not presented. The use of Rozol Pat' represents a very low risk to aquatic and sediment-dwelling biota and no further assessment of risk is necessary.

In the Netherlands, however, it is well known that rats live near surface waters and that therefore also rodenticide campaigns may occur near these surface waters. Agreed scenarios to calculate the exposure in surface water from leaching of rodenticides are lacking, therefore risk mitigation measures derived from CLP characteristics of the active substance are set in place.

2.8.2.2 Atmosphere

For chlorophacinone, the estimated half-life for the hydroxyl reaction in air is 14.3 hours, the vapour pressure as determined by OECD 104 is $4.76 \cdot 10^{-4}$ Pa (22.8°C) and the Henry's law constant is 0.013725 $Pa.m^3.mol^{-1}$ (based on a water solubility of 13.0 mg a.s/l). Therefore chlorophacinone is not expected to volatilise to air in significant quantities following use in any of the usage scenarios (i.e. in and around buildings, open areas and waste dumps) and the potential concentration of chlorophacinone in air is considered to be negligible.

2.8.2.3 Terrestrial compartment

Soil exposure occurs both through a combination of direct and indirect releases from the use of Rozol Pat' in the scenario "in and around buildings", in open areas and around waste sites.

In and around buildings

Exposure of the terrestrial compartment (soil) will occur when Rozol Pat' is deployed outdoors.

EUBEES 2 considers a scenario that entails outdoor baiting with paste bait around a farm building. In this situation, exposure is assumed to arise through a combination of transfer (direct release) and deposition *via* urine and faeces (disperse release) onto soil. The EUBEES 2 scenario for blocks is considered to be appropriate for paste baits. Direct release is estimated to amount to 1.0% of the total bait deployment during the entire campaign, concentrated within 10 cm of the individual secured bait points. However, since Rozol Pat' is applied in packaging, the release is anticipated to be lower and a direct release of 0.1% is assumed to be more realistic. Similarly, EUBEES 2 considers that 90% of the total amount of rodenticide consumed by the target rodents over the duration of the outdoor baiting campaign enters soil *via* urine and faeces.

The maximum application rate for Rozol Pat' containing 50 mg chlorophacinone/kg entails the deployment of 240 g bait in each of ten secured bait points.

EUBEES 2 considers two levels of baiting. In the first, described as the "realistic worst-case", the campaign lasts 21 days and secured bait points (initially filled on day 1 and repeatedly

and completely emptied by the target rodents) are refilled on days 3, 7, 14 and 21. In the other, "typical" scenario, bait consumption progressively declines as the campaign proceeds, such that the replenishments made on days 3, 7, 14 and 21 represent 100%, 25-50%, 10% and 0%, respectively, of the quantity initially deployed on day 1. It should be noted that the "typical" scenario is more representative of the consumption pattern for a potent anticoagulant rodenticide such as chlorophacinone.

The risks to the terrestrial environment posed by contamination of soil by chlorophacinone following "realistic worst-case" and "typical" outdoor use of Rozol Pat' are assessed by calculating ratios of PEC/PNEC, as indicated below. As stated above, the "typical" pattern is the one more likely to apply to an efficient anticoagulant rodenticide such as chlorophacinone.

PECsoil/PNECsoil for soil-dwelling invertebrates exposed to chlorophacinone following outdoor use of bait pastes around buildings

Baiting scenario (EUBEES 2)	**maximum PECsoil (mg chlorophacinone/kg ww)**	**PNECsoil (mg chlorophacinone/kg ww)**	**PEC/PNEC ratio**
Realistic worst-case	0.0097	0.30	0.03
Typical	0.0029	0.30	0.01

The PEC/PNEC ratios are less than 1.0, indicating that the exposure to chlorophacinone that arises following the use of Rozol Pat' in and around buildings presents no unacceptable risks to soil-dwelling invertebrates.

Open areas
Rozol Pat' is applied in open areas by inserting them inside the openings of the tunnels of the target rodents and, according to the scenario presented in EUBEES 2, two such treatments would typically be applied in the space of six days. Bait deployment comprising 6 × 40 g pastes per application per tunnel entrance is considered in this assessment as the closest practical approximation to the 100 g bait application suggested in EUBEES 2. Based on a tunnel of 8 cm diameter, worst-case soil exposure is assumed to occur to a depth of 10 cm from the contact half (*i.e*. the burrow floor) of a 30 cm tunnel section in which the bait is placed. This section of tunnel floor is assumed to receive an input corresponding to 5% of the product during application and a further 20% as the bait is consumed.

The predicted concentration of 0.415 mg chlorophacinone/kg ww soil represents the worst-case in the immediate vicinity of each bait application.

PECsoil/PNECsoil for soil-dwelling invertebrates exposed to chlorophacinone following use of paste bait in rodent tunnels in open areas

Baiting scenario (EUBEES 2)	**PECsoil (mg chlorophacinone/kg ww)**	**PNECsoil (mg chlorophacinone/kg ww)**	**PEC/PNEC ratio**
Worst-case	0.415	0.30	1.4

The PEC/PNEC ratios calculated indicate a marginal risk based on the PEC that represents a localised "hotspot" of contamination near the entrance of each baited tunnel.

Waste dumps
Paste baits are deployed around the perimeter of waste-dumps and land-fill sites to control populations of rats. EUBEES 2 suggests a worst-case scenario in the event of an infestation outbreak that entails 40 kg of paste protected inside bait boxes distributed over an area of 1 ha, with a total of seven such applications per year. In this situation, soil exposure is

assumed to arise through a combination of deposition via urine and faeces plus the rodenticide contained in the carcasses of poisoned target rodents. The EUBEES 2 scenario for blocks is considered to be appropriate for paste baits. In general, ninety percent of the total amount of rodenticide consumed by the target rodents over the duration of each baiting campaign is assumed to enter soil over the 1 ha surface.

The risks to earthworms posed by contamination of soil by chlorophacinone following the "worst-case" use of pastes at waste dumps and landfill sites are assessed by calculating ratios of PEC/PNEC, as indicated below.

PECsoil/PNECsoil for soil-dwelling invertebrates exposed to chlorophacinone following use of paste bait at waste dumps and landfill sites

Baiting scenario	PECsoil (mg chlorophacinone /kg ww)	PNECsoil (mg chlorophacinone/kg ww)	PEC/PNEC ratio
Worst-case (EUBEES 2)	0.0074	0.30	0.025

The PEC/PNEC ratio is less than 1.0 under the worst case suggested by EUBEES 2. The exposure to chlorophacinone that arises from the use of Rozol Pat' at waste dumps and landfill sites therefore presents no unacceptable risks to soil organisms.

2.8.2.4 Non compartment specific effects relevant to the food chain (primary and secondary poisoning)

Non-target vertebrates (birds and mammals) may be exposed to Rozol Pat' containing chlorophacinone either directly by ingestion of exposed paste (primary poisoning) or indirectly by ingestion of the carcasses of target rodents that contain chlorophacinone residues (secondary poisoning).

Based on toxicity data chlorophacinone is very toxic and presents a hazard to birds and non-target mammals.

The Emission Scenario Document for Biocides used as Rodenticides (EUBEES 2) presents exposure scenarios and assessments which give a basis for evaluating the primary and secondary poisoning risk to non-target animals. It is proposed to introduce tiered approaches for assessing the risks through both primary and secondary poisoning and to derive different PECs for each step.

Exposure scenarios for quantification of primary and secondary poisoning according to EUBEES 2

	Primary poisoning	Secondary poisoning
Tier 1	Risk is quantified as the ratio between the concentration in the food for the non-target organism (PECoral) and the predicted no-effect-concentration for oral intake for the non-target organism (PNECoral)	Risk is quantified as the ratio between the concentration in the rodent immediately after a last meal on day 5 (EC5) and the predicted no-effect-concentration for oral intake for the non-target organism (PNECoral)
Tier 2	Risk is quantified as the ratio between the estimated daily intake of a compound (ETE) and the predicted no-effect-concentration for oral intake for the non-target organism	Risk is quantified as the ratio between the estimated concentration in predatory mammals or birds and the no-observed-adverse-effect levels

	(PNECoral). For the long-term exposure the estimated concentration of the active substance in the animal can be calculated and compared with the NOAEL.	(NOAEL) for the organism.

Object of a quantitative risk assessment will be:
• Primary poisoning, Tier 1
• Primary poisoning, Tier 2 for 5 day exposure
• Secondary poisoning; Tier 1 for long-term exposure
• Secondary poisoning; Tier 2 for long-term exposure

Object of a qualitative risk assessment will be:
• Primary poisoning, Tier 2 for 1 day exposure
• Secondary poisoning; Tier 1 for short-term exposure

The primary and secondary poisoning assessment has further on been conducted in accordance with the newly developed guidance document on the PNECoral derivation for the primary and secondary poisoning assessment of anticoagulant rodenticides, which has been adopted by the Competent Authorities and published on JRC IHCP's biocides website. It describes a quantitative risk assessment for the long-term exposure situation regarding primary and secondary poisoning with anticoagulant rodenticides and what PNECoral to be used for this assessment. As at the moment no guidance is available on how to derive a PNECoral for an acute exposure situation, only a qualitative risk assessment for the acute primary and secondary poisoning situations is carried out.

Regarding the qualitative assessment only a description of the toxicity of the substance compared to the possible single uptake is presented instead of carrying out a quantitative risk assessment. It is important to stress that this qualitative assessment is a simple comparison of the acute exposure situation with single dose LD50 values. It is not intended to be used for risk characterisation; no PNECoral shall be derived and hence no PEC/PNEC ratio can be established. This comparison gives only a first indication of the acute toxicity of the substance. Regarding the long-term exposure situation a quantitative risk assessment of the primary and secondary poisoning situation is carried out. However, it is not possible to quantify primary or secondary exposure accurately, given highly variable factors such as the specific locality of a rodent control campaign, whether there are non-target scavengers or predators present, whether predators will catch many rodents and whether such rodents will contain high levels of chlorophacinone. Because of many uncertainties the following assessments of risk should be considered as a worst case.

Chlorophacinone is presented in a matrix of cereal flour bound together with hydrogenated vegetable fat. Presentation of chlorophacinone in this processed matrix has the benefit of reducing the appeal of the bait to non-target organisms that would otherwise readily consume loose chlorophacinone-treated cereal grains (Marsh, 1985). Marsh noted that modification of cereal grains by rolling and milling reduces their acceptance by birds that would readily consume them in their natural state.

Rozol Pat' is individually packaged in sachets and is deployed with the wrapping intact. This reduces the appeal to non-target vertebrates that rely predominantly on visual rather than olfactory recognition of potential food items. It is known that visual stimuli are particularly important to birds in the selection of novel foods and sachets containing paste are likely not to be visually appealing to birds as food, based on their shape, texture and colour (WHO, 1995). Inclusion of a blue dye in chlorophacinone paste bait is likely to reduce its appeal as a potential food item still further.

Gemmeke (2000)[3] noted that pigeons, Japanese quails, various crows, jackdaws, magpies and pheasants presented with a choice of natural and dyed seeds of various crop species all preferred the untreated option, and that seeds artificially coloured green, grey, black, pink, blue, violet and brown-violet were either untouched or only eaten in small (*ca*. 10%) amounts. Similarly, Moran (1999)[4] found that pigeons and partridges preferred undyed grains of their favoured seeds (whole-grain wheat and sorghum, respectively), but that pigeons showed no colour discrimination when only the seeds of a species normally avoided were available. Although species, sex and even individual preferences will modulate the response of birds to colour, there is evidence from the literature that colours in the middle of the visible colour spectrum range are generally better deterrents than other colours. For example, Marsh (1985)[5], (citing Kalmbach (1943)[6], Kalmbach and Welch (1946)[7], Caithness and Williams (1971)[8], Pank, (1976)[9] and Brunner and Coman (1983)[10]) reported that green and yellow were particularly effective colours for discouraging intake of rodenticidal baits and suggested that the deterrent effect of the colorant may in some cases be a visual cue coupled with taste-conditioned aversion. However, EUBEES 2 states clearly that it is impossible to quantify the effect of the coloured bait and that colour preferences vary between species and may change depending on the context (e.g. depending on the hunger of the animals). Birds are therefore not considered to be at low risk of primary poisoning, although the worst case scenarios described below may over-estimate uptake for birds. However, this can not be quantified and will not be considered in the primary poisoning risk assessment. As paste in sachets seems to have a very low likelihood to be ingested by birds the default value for the avoidance factor of 1 from EUBEES 2 is lowered to 0.5 for this product type.

Primary poisoning of mammals is included in this assessment since non-target mammals are less reliant solely on visual stimuli in identifying potential food and may ingest paste bait.

A secondary poisoning risk assessment was carried out for birds and mammals for the use scenario “in and around buildings”.

PNECoral derivation for primary and secondary poisoning

In EUBEES 2 no guidance is given on how to derive the PNECoral values. The PNECoral derivation described in the TGD for the secondary poisoning assessment considers the oral intake of a chemical via fish or worms and a long-term exposure situation. No guidance is given regarding primary poisoning. In EUBEES 2 it is mentioned that both an acute and a long-term risk assessment should be conduced for anticoagulant rodenticides, because although the mode of action is generally chronic, some anticoagulant rodenticides (including rodenticides containing chlorophacinone) have substantial acute toxicity. But comparing an acute poisoning incident, which represents a single uptake of the anticoagulant rodenticide by a non-target mammal or a bird, to a PNECoral which has been derived in accordance with the TGD, considerably overestimates the risk due to the choice of long-term studies as a basis for deriving the PNECoral. The TGD does not give

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[3] Gemmeke, H. (2000). Fraßabschreckende Wirkung von gefärbtem Saatgut auf Vögel. http://www.bba.de/oekoland/oeko3/voegel.htm

[4] Moran, S. (1999). Rejection of dyed field rodent baits by feral pigeons and chukar partridges. *Phytoparasitica* **27** (1): 9-17

[5] Marsh, R.E. (1985) Techniques used in rodent control to safeguard nontarget wildlife.

[6] Kalmbach, E.R. 1943. Birds, rodents and colored lethal baits. Transactions of the North American Wildlife Conference, 8: 408-416.

[7] Kalmbach, E.R. and Welch, J.F. (1946). Colored rodent baits and their value in safeguarding birds. *J. Wildlife Management*, 10: 353-360.

[8] Caithness, T.A. and Williams, G.R. (1971). Protecting birds from poisoned baits. New Zealand Department of Internal Affairs, Wildlife Publication No. 129.

[9] Pank, S. (1976). Effects of seed and background colours on seed acceptance by birds. *J. Wildlife Management*, **40**: 769-774.

[10] Brunner, H. and Coman, B.J. (1983). The ingestion of artificially coloured grain by birds, and its relevance to vertebrate pest control. *Australian Wildlife Research* **10**: 303-310.

guidance on how to derive acute PNECoral in addition to the long-term PNECoral. Nothing is stated on the choice of studies, endpoints and assessment factors.

Therefore the acute primary and secondary poisoning risk assessment for the food chains rodenticide (bait) → rodenticide-eating mammal or bird (primary poisoning) and the food chain rodenticide (bait) → rodent → rodent-eating mammal or bird (secondary poisoning) is only assessed in a qualitative, and not in a quantitative way. It is important to stress that this qualitative assessment is not intended to be used for the risk characterisation of primary and secondary poisoning of rodenticides and shall not be used for a comparative assessment. This comparison should only give a first indication of the acute toxicity of the substance. Regarding the long-term exposure situation a quantitative risk assessment is carried out. The risk characterisation for the primary and secondary poisoning risk assessment is based on the long-term exposure situation as described in EUBEES and on PNECoral values which are derived according to the TGD. The PNECsoral used for primary and for secondary poisoning are the same, as is anticipated that chlorophacinone taken up via chlorophacinone containing products is as toxic and equal available to non-target animals as chlorophacinone taken up via poisoned rodents.

PNECoral related to the concentration in the food
For primary and secondary poisoning at Tier 1 the PNECoral is related to the food concentration [mg/kg food] and values for PNEC oral were derived according to the TGD.

Birds:
Based on the 5-days short-term dietary LC50 study performed by several authors, in Bobwhite quail (*Colinus virginianus*), the 5-days LC50 of chlorophacinone is 95 mg a.s/kg food.

According to the Risk Assessment TGD the oral assessment factor (AForal) for extrapolation of bird toxicity data in a 5-day dietary assay is 3,000. PNECoral (bird) = 95/3000 = 30 µg/kg food.

Birds in a 90-day reproduction study with no GLP (Ri=3) resulted in a NOEC of 0.1 mg/kg food with AF_{oral} of 30 would result in $PNEC_{birds}$ of 1/30 = 0.03 mg a.s/kg food based on mortality. This result is considered as additional information which supports the PNEC calculated with the former AF of 3,000 (short-term dietary studies) for birds. This information is confirmed by the extrapolation from the difenacoum data.

PNECoral (bird) = 30 µg/kg food.

Mammals:
Results (NOAEL) from the repeated dose toxicity studies are used for PNECoral derivation. In principle the lowest NOAEL should be used to derive a PNECoral, predator. Rat was the most sensitive species to chlorophacinone. It seems justified to use this value for the PNECoral derivation for mammals, even though it is the target organism, as the effect mechanism of chlorophacinone is not target specific but general for warm blood organisms

Rat: NOAEL (77-112 days, repeated dose) = 5 µg/kg bw; Conversion factor 20; Assessment factor 90.

PNECoral (mammal) = 1.1 µg/kg food

For dogs there is a non-valid single dose study available with a LD50 much lower than 2 mg/kg bw as all animals died in this study. The study results suggest that dogs might be orally more sensitive than rats, as higher mortality is observed at similar or lower doses than in the rat studies. However, a higher sensitivity of dogs cannot be definitively concluded as dogs were fed with a vitamin K deficient diet, which might influence the

potency of the administered chemical. In any case, there is no evidence that the rat is more sensitive that other mammal species.

The PNEC for dogs is therefore set equal to the PNECoral (mammal) = 1.1 µg/kg food

PNECoral – Related to dose
At Tier 2 of the primary and the secondary poisoning assessment the PECoral is related to the dose [mg/kg bodyweight] and therefore PNECoral has also to be expressed on the basis of the dose. For converting the PNECoral values from a concentration in food [mg/kg food] to a dose related PNECoral [mg/kg body weight], and vice versa, the following equation can be used, if necessary:

Daily dose [mg/kg bw day] = conc. in food [mg/kg] * daily food consumption [g/bird day]/body weight [g]

Birds:
Based on the 5-days short-term dietary LD50 study, performed by several authors, in Bobwhite quail (*Colinus virginianus*), the 5-days LD50 of chlorophacinone is 17.3 mg a.s/kg bw.

According to the Risk Assessment TGD the oral assessment factor (AForal) for extrapolation of bird toxicity data in a 5-day dietary assay is 3,000. This information is confirmed by the extrapolating the data from difenacoum.

PNECoral (bird) = 5.8 µg/kg bw.

Mammals:
Results (NOAEL) from the repeated dose toxicity studies are used for PNECoral derivation. In principle the lowest NOAEL should be used to derive a PNECoral, predator. Rat was the most sensitive species to chlorophacinone. It seems justified to use this value for the PNECoral derivation for mammals, even though it is the target organism, as the effect mechanism of chlorophacinone is not target specific but general for warm blood organisms.

Rat: NOAEL (77-112 days, repeated dose) = 5 µg/kg bw; Assessment factor 90

PNECoral (mammal) = 0.056 µg/kg bw

For dogs the same PNEC was used considering the insufficient data available.

Primary poisoning

In and around buildings

Non-target birds and mammals may encounter paste bait containing chlorophacinone if they are small enough to be able to reach the bait, or because the bait is inadequately safeguarded or a secured bait point has become damaged, or by finding pieces of paste which have been removed by target rodents. However, good practice requires that control sites are checked regularly during baiting campaigns and that damaged points have to be repaired or replaced and that spilt bait is removed.
A primary poisoning assessment for mammals and birds has been carried out. Regarding birds, the avoidance factor for the paste formulation has been lowered as paste in sachets is unlikely to be consumed by birds. Dyed bait blocks and pellets might not appeal to birds as a source of food as well. However, as indicated in the EUBEES 2 document colour preferences vary between species and may change depending on the context. Therefore, as a worst case approach, primary poisoning is considered.

Tier 1 risk assessment
Quantities of paste bait (40 g size) are placed at secured bait points in and around buildings. Based on the maximum number used (6) and the concentration of active substance (50 mg/kg), the following table indicates various amounts of chlorophacinone that may be taken from a bait point. These provide chlorophacinone ingestion estimates for a first tier, estimate of exposure to non-target mammals.

Quantities of chlorophacinone in paste bait potentially accessible to non-target vertebrates following deployment at secured bait points in and around buildings

Maximum paste size and maximum number per bait point	Maximum weight of chlorophacinone per bait point (mg)	Proportion of bait point contents accessible (%)	Chlorophacinone potentially ingested by non-target vertebrates (mg) ≡ PECoral
40 g × 6 (rat control)	12.0	100	12.0
		50	6.0
		40	4.8
		30	3.6
		20	2.4
		10	1.2

As an absolute worst case the risk at this tier is quantified as the ratio between the concentration of chlorophacinone in food and the PNECoral. It is assumed that non-target animals have direct access to an unlimited amount of formulated product. Chlorophacinone concentration in the bait is 50 mg/kg and hence the PECoral is 50 mg/kg food. The PNECoral for birds is 30 µg/kg food, the PNECoral (mammal and dog) is 1.1 µg/kg food. The PEC/PNEC values are rounded values. There are many uncertainties related to the calculation of PEC/PNEC values. Moreover, the PEC/PNEC values are very high. Therefore, not the exact numbers have been presented but rounded figures (e.g. 45,000 instead of 45,455).

Mammals: PEC/PNEC ≈ 45,000
Dogs: PEC/PNEC ≈ 45,000
Birds: PEC/PNEC ≈ 1,700

This conservative approach clearly highlights a high risk to birds and non-target mammals if chlorophacinone containing products are freely consumed. This risk characterisation has been carried out with the PNECoral values representative for a long-term exposure situation.

Tier 2 risk assessment: Acute effects

At Tier 2 a refinement of the Tier 1 is made by assessing the amount of food ingested by non target animals by the equation:

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

- where ETE is the estimated theoretical exposure to the active substance, FIR is the non-target mammal food intake [g/d] (fresh weight), BW is bodyweight [g], C is the concentration of active substance in the fresh diet 50 mg/kg (paste), AV is the avoidance factor (default 1.0 = no avoidance; AV = 0.5 for birds when product is paste), PT is the fraction of diet obtained in the treated area (default 1.0) and PD is the fraction of food type in the diet (default 1.0).

This is a worst case scenario as it assumes that the entire food of the non-target animals (except for birds) is the bait (PD = 1) and that AV and PT are both 1. The concentration of

chlorophacinone in the products is 50 mg/kg. In a second step for mammals AV is 0.9, PT is 0.8 and PD is 1 to represent a more realistic worst case situation. For birds AV is set to 0.5 at both steps as the product is a paste in a sachet as this product is less likely to be consumed by birds than bait blocks. The ETE is estimated for one day without taking excretion into account. Data on bodyweight is taken from EUBEES 2, if not otherwise stated.

ETE (1 day) for non-target mammals and birds ingesting paste bait containing chlorophacinone without excretion

Non-target mammal	Typical bodyweight (g)	Daily mean food intake (g dry weight/day)[3]	ETE after one meal [mg/kg bw] Step 1[1]	ETE after one meal [mg/kg bw] Step 2[1]
Dog	10,000[a]	456	2.28	1.82
Cat	3,000 [2]	170	2.83	2.27
Pig	25,000	969 (600) [5]	1.20 [6]	0.96
General non target mammal	5,700 [4]	287	2.52	2.01
Tree sparrow	22	7.6	8.64	6.91
Chaffinch	21.4	6.42	7.50	6.00
Woodpigeon	490	53.1	2.71	2.17
Pheasant	953	103	2.69	2.16

[1] Step 1: AV, PT and PD = 1; Step 2: AV = 0.9, PT = 0.8 and PD = 1 (both steps for birds AV = 0.5),
[2] Mean bodyweight from chlorophacinone dossier.
[3] From EUBEES 2, Section 3.2.1., logFIR = 0.822 logBW - 0.629.
[4] From EUBEES 2, Table 3.5 (weight of a fox is anticipated)
[5] EUBEES 2 give an upper limit of 600 g for daily meal.
[6] based on FIR calculated with 600 g

Comparison of ETE (1 day) for non-target mammals and birds, without excretion, with LD50 values

Non-target mammal	ETE [mg/kg bw] Step 1	ETE [mg/kg bw] Step 2	LD50 mammals/birds [mg/kg bw]
Dog	2.28	1.82	<< 2 (dog)
Cat	2.83	2.27	3.15 (male rat)[1]
Pig	1.20 [6]	0.96	3.15 (male rat)[1]
General non target mammal[2]	2.52	2.01	3.15 (male rat)[1]
Tree sparrow	8.64	6.91	257 (quail)[3]
Chaffinch	7.50	6.00	257 (quail)[3]
Woodpigeon	2.71	2.17	257 (quail)[3]
Pheasant	2.69	2.16	257 (quail)[3]

[1] single dosage 21 days post exposure period (no valid LD50 for cat / pig available)
[2] Body weight of a fox was chosen
[3] single dosage 30 days post exposure

Taking into account excretion in non-target animals, assuming a default elimination factor of 0.3 according to EUBEES 2, the following values for ETE at step 1 and 2 can be calculated.

Comparison of ETE (1 day) for non-target mammals and birds, consideration excretion, with LD50 values

Non-target mammal	ETE [mg/kg bw] Step 1	ETE [mg/kg bw] Step 2	LD50 mammals/birds [mg/kg bw]
Dog	1.60	1.28	<< 2 (dog)
Cat	1.98	1.59	3.15 (male rat)[1]
Pig	0.84	0.67	3.15 (male rat)[1]
General non target mammal[2]	1.76	1.41	3.15 (male rat)[1]
Tree sparrow	6.05	4.84	257 (adult quail)[3]
Chaffinch	5.25	4.20	257 (adult quail)[3]
Woodpigeon	1.90	1.52	257 (adult quail)[3]
Pheasant	1.89	1.51	257 (adult quail)[3]

[1] single dosage 21 days post exposure period (no valid LD50 for cat / pig available)
[2] Body weight of a fox was chosen
[3] single dosage 30 days post exposure

As no acute PNECoral could be derived the exposure concentrations are only compared in a qualitative way with acute LD50 values. It is clear from the above two tables that for birds values for ETE are after one meal do not exceed the lowest single dosage LD50 for birds of 257 mg/kg bw. For mammals except for dogs (step 1) ETE is below the single dose LD50 value of << 2 mg/kg bw. However, this qualitative assessment is a simple comparison of the acute exposure situation with single dose LD50 values and the conclusion should not be that the substance is not acutely toxic or "unproblematic" with regard to the acute primary poisoning situation of mammals. A comparison has been made with a single dose LD50 without applying an assessment factor. This comparison is not intended to be used for risk characterisation as no PNECoral has been derived and hence no PEC/PNEC ratio can be established.

Tier 2 risk assessment - long-term effects

EUBEES 2 suggests a long-term scenario for 5 days of exposure and considering elimination (excretion). The principle in the calculations is for the first 5 days that the animal eats the same daily amount and eliminates 30 % of its content of residues (default value). Therefore, the concentration of residues on day 5 is calculated stepwise:

EC=ETE*(1-EL), where EL is the fraction eliminated

EC1 = ETE
EC2 = ETE * (1 - 0.3)
EC3 = (EC2 + ETE) * (1 - 0.3)
EC4 = (EC3 + ETE) * (1 - 0.3)
EC5 = (EC4 + ETE) * (1 - 0.3)

Elimination factors are only available for rats. They indicate an elimination of approximately 26 % per day during the first 3 days after dosing. For simplification an elimination factor of 0.3 is used for the entire time, in accordance with EUBEES 2, and this elimination rate is used for all animals. However, this is only a preliminary approach as the elimination rates in other animals but rats might be different. This approach may under- or overestimate the concentration in the non target animals. In a first step, AV, PT and PD all are 1.

In a second approach AV and PT can be reduced (AV = 0.9 for mammals and 0.5 for birds, PT = 0.8 and PD = 1) to represent a more realistic worst case. Results of the long term PEC/PNECoral ratios for non-target animals exposed to paste containing 50 mg chlorophacinone /kg in the scenario “in and around buildings” are presented in the Table below. The ETE was calculated including an elimination factor of 0.3 per day from body

residues. The expected concentration of chlorophacinone in the animals after 5 days after excretion is calculated. There are many uncertainties related to the calculation of PEC/PNEC values. Moreover, the PEC/PNEC values presented in the table below are very high for mammals (up to 238,000) and for birds (up to 4,100).

Long term PEC/PNECoral for non-target mammals and birds

Non-target mammal	EC_5 Step 1[1] [mg/kg bw]	EC_5 Step 2[2] [mg/kg bw]	PNECoral [µg/kg bw]	PEC/PNEC Step 1[1]	PEC/PNEC Step 2[2]
Dog	6.3	5.06	0.056	113,000	90,000
Cat	13.3	10.7	0.056	238,000	191,000
Pig	3.33	2.66	0.056	60,000	47,500
Non target mammal[3]	11.8	9.47	0.056	211,000	169,000
Tree sparrow	23.95	19.16	5.8	4,100	3,300
Chaffinch	20.80	16.64	5.8	3,600	2,900
Woodpigeon	7.51	6.01	5.8	1,300	1,040
Pheasant	7.47	5.98	5.8	1,300	1,030

[1] AV, PT and PD = 1; AV of 0.5 for birds
[2] AV = 0.9, PT = 0.8 and PD = 1; AV of 0.5 for birds
[3] Body weight of a fox was chosen

Conclusion primary poisoning
When comparing the concentration of chlorophacinone in food with the PNECoral a high risk can be identified. Regarding the short-term exposure at Tier 2, ETE values after 1 day for birds and for non-target mammals do not exceed the LD50 value for birds and mammals both without and with excretion. Concerns exist as to the risk for dogs feeding on bait. The toxicity test used for the comparison, however, was done with dogs feeding on a vitamin K deficient diet, possibly causing oversensitivity to anticoagulants.

ETE values after 5 days intake of chlorophacinone (long-term exposure) are higher than those after a single day of exposure. Even though excretion from the non-target animal is anticipated accumulation of chlorophacinone in the non-target animals outweigh loss of chlorophacinone in non-target animals due to excretion. For the long-term assessment all PEC/PNECoral ratios are far above one. Mammals are at considerably at greater risk than birds with respect to primary poisoning according to the EUBEES 2 default scenarios. In general small animals have a higher risk than large ones.

The worst-case PEC/PNEC ratio for birds at step 1 is about 4,120 (sparrow) and about 238,000 for mammals (cat).

The worst-case PEC/PNEC ratio for birds at step 2 is about 3,300 (sparrow) and about 191,000 for mammals (cat).

Worst case assumptions have been made. It was assumed that the non-target animals have fed entirely, respectively mostly, on chlorophacinone containing products (PT was 1 and 0.8, respectively) and that no avoidance (AV = 1) respectively little avoidance (AV = 0.9) for mammals. For birds the avoidance factor for paste was set to 0.5. Consumption of these quantities of chlorophacinone containing products is clearly a worst case and the risk in reality might probably not be as high as presented in these scenarios.

Based on the maximum recommended baiting regime that entails deployment of 240 g paste per secured bait point, the daily food intakes of 456, 170 and 600 g for dogs, cats and pigs correspond to the contents of 1.9, 0.71 and 2.5 bait points, respectively. However, as the PEC/PNEC ratio for dogs is above 10,000 the PEC/PNECoral value below 1 for dogs would only be achieved for a single meal if the daily intake of paste by dogs was less

than 0.01 % of its daily food requirement (<0.05 g bait per day for dogs). This is much less than the weight of one sachet (40 g) of which 6 are placed in one bait point. As the EC5 is higher than the EC1 (ETE after 1 day) these values would be lower for the long-term assessment.

Based on the recommended baiting regime that entails deployment of a maximum of 240 g paste per secured bait point, the daily food intakes of 7.6, 6.42, 53.1 and 102.7 g for *P. montanus*, *F. coelebs*, *C. palumbus* and *P. colchicus* (values from table 3.1 EUBEES 2) correspond to the contents of at least 0.03, 0.027, 0.22 and 0.43 full bait boxes, respectively. It is unlikely that such amounts of bait would be available to the larger birds whereas smaller species may be able to reach bait inside the bait boxes by entering through the access hole, simply on the basis of their size. However, PEC/PNEC ratios for bigger birds are above 1,000 and for smaller birds above 2,800. Values below 1 for the different bird species would only be achieved if the daily intake of bait blocks/pellets/paste by birds were below 0.1 % of their daily food requirement. That means that for example a chaffinch (*F. coelebs*) had to eat less than 7 mg bait in order not to be at risk.

Gemmeke (2000) noted that pigeons, Japanese quails, various crows, jackdaws, magpies and pheasants presented with a choice of natural and dyed seeds of various crop species all preferred the untreated option, and that seeds artificially coloured green, grey, black, pink, blue, violet and brown-violet were either untouched or only eaten in small (ca. 10%) amounts. According to Harrison et al. (1988), wild birds presented with a selection of foods resembling wheat-based rodenticide baits were generally indifferent to whole, non-coloured wax blocks and consumption amounted to less than 5% of the quantity offered. Considering these figures it becomes clear that birds have a very high risk of primary poisoning even if paste is only a very low share of their daily food intake.

Comparing the quantities of chlorophacinone potentially accessible to non-target vertebrates at one bait point directly with the food based PNECoral of 30 µg/kg food birds are at high risk even if they eat only 1 % of the bait at one bait point.
A potential risk of primary poisoning could clearly be identified both for non-target mammals and for birds. Relatively high assessment factors applied to long-term test results for the derivation of PNECoral and the high toxicity of chlorophacinone to mammals and birds led to a high risk. It is evident that this risk can occur if these animals have free access to products containing chlorophacinone, which is the case for baiting around buildings but probably not for baiting within buildings.

Possible measures to reduce the risk of primary poisoning to non-target animals
Chlorophacinone is both highly and non-selectively toxic to vertebrates and the attempt to refine the primary and secondary assessments to demonstrate acceptable risks to birds and non-target mammals with the tools currently available will prove fruitless.

Information regarding risk reduction measures is presented in chapter 2.8.3 “Possible measures to reduce the risk of primary and secondary poisoning to non-target animals”.

Secondary poisoning

In accordance with the EUBEES 2, the following assessment of secondary poisoning takes into account the levels of chlorophacinone residues in target rodents, based on its concentration in the bait, feeding (chlorophacinone intake) and excretion (chlorophacinone elimination) rates of target rodents, as well as the period over which the bait is eaten before the effects of poisoning inhibit further feeding. These combined factors form the basis of exposure to predators and scavengers upon which to assess risk.

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

mammals therefore exists, even (though to a lesser extent) on occasions when the deployment of paste bait containing chlorophacinone is confined to the interiors of buildings.

However, the extent of possible exposure of predators and scavengers to live prey and carcasses containing rodenticide residues is uncertain. EUBEES 2 cites two published reports of cage and enclosure studies in which the authors observed behavioural changes in poisoned rodents that would appear to increase their susceptibility to predation during daytime and also the likelihood that fatal haemorrhage would occur while the rodents were away from shelter, leaving their carcasses exposed to scavengers. On the other hand, these predictions are contradicted by reports of observations made before, during and after anticoagulant baiting programmes conducted in and around farm buildings, where carcasses found by systematic searches were predominantly either indoors or concealed beneath cover (*e.g.* under haystacks)[11]. Bodies representing only 4% of an estimated initial rat population were found away from cover in one study and (in the absence of evidence of further activity) the majority of the remaining, unrecovered population was assumed to have died underground in a system of burrows.

In accordance with EUBEES 2 guidance, the following assessment of secondary poisoning takes into account the levels of chlorophacinone residues in target rodents, based on its concentration in paste bait, feeding (chlorophacinone intake) and excretion (chlorophacinone elimination) rates of target rodents, as well as the period over which the bait is eaten before the effects of poisoning inhibit further feeding. These combined factors form the basis of exposure to predators and scavengers upon which to assess risk.

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

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

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

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

The default rate of elimination of residues from the bodies of target rodents is 30% per day (faecal route only). The elimination of residues has been measured from a pair of male rats fed with approximately 5.0 mg chlorophacinone/kg bw. Severe haemorrhaging occurred and the test rats eventually died. No significant metabolites of chlorophacinone were identified and so the faecal radioactivity may be assumed to be parent chlorophacinone only. The default daily elimination rate of 30% for anticoagulant rodenticides prescribed by EUBEES 2 is in general accordance with the mean values measured for chlorophacinone, which averaged 33.5% over the first three days and ranged from 37.6% for day 1 to 52.8% for day 2.

[11] Harrison, E.G., Porter, A.J. and Forbes, S. (1988). Development of methods to assess the hazards of a rodenticide to non-target vertebrates. Proceedings of the British Crop Protection Symposium.
Fenn, M.G.P., Tew, T.E. and MacDonald, D.W. (1987). Rat movements and control on an Oxfordshire farm. *J. Zoology, London*. **213**, 745-749.

Elimination of chlorophacinone residues (^{14}C-equivalents) from male rats

Sampling time (days)	Radioactivity excreted (mean % of applied, estimated dose approximately 5.0 mg/kg bw[1])			
	Urine	Faeces	Volatiles	Total
1	0.383	37.19	0.025	37.6
2	0.241	52.54	0.013	52.8
3	0.082	10.08	0.004	10.2
4	0.052	1.8	0.006	1.9
Cumulative 3 day total	0.706	99.81	0.042	100.6
Cumulative 4 day total	0.758	101.61	0.048	102.4

[1] Based on individual doses of 1.43 and 1.28 mg ^{14}C-chlorophacinone per animal, individual bw not stated, range 200 to 250 g.

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

Residues of chlorophacinone in target rodents from the ingestion of paste bait at different times during a control campaign, calculated according to EUBEES 2 (Frodent = 1)

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

[1] TIER 1 short-term (Frodent = 1)

[2] TIER 1 long-term (Frodent = 0.5)

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

However, comparison with semi-field data shows these calculated values to be greatly overestimated. Two studies were conducted to determine the effects of secondary exposure to chlorophacinone on *Pica pica* and *Mustela putorius furo*. In each case a different population of rats was first fed on a diet that comprised exclusively bait pellets containing 50 mg chlorophacinone/kg. Bait consumption as a proportion of food intake by the rats was therefore 100%. The primary feeding phase continued for 5 days, after which

all survivors were euthanised and stored frozen together with carcasses of rats that had succumbed earlier. Four rat carcasses were randomly selected in each study, individually homogenised and analysed to determine residues of chlorophacinone, whilst the remaining carcasses were used as the exposure vehicle for the magpies and ferrets. Measured whole-rat concentrations of chlorophacinone at a time coinciding – according to EUBEES 2 - with the occurrence of peak levels following the last meal on day 5, ranged from 0.2107 to 0.9272 mg/kg bw (mean: 0.467 mg/kg bw) in the first study and from 0.175 to 0.805 mg/kg bw (mean: 0.453 mg/kg bw) in the second. The highest measured concentration corresponds to just 6.7% of the value of 13.866 mg/kg bw predicted for the same time point according to EUBEES 2. In the table below and in the following assessments, the various concentrations of chlorophacinone in target rodents on day 5 and day 7 have therefore been lowered *pro rata* to reflect real, measured residues.

Residues of chlorophacinone in target rodents from the ingestion of paste bait at different times during a control campaign, based on the maximum residue level measured in rats (Frodent is 1)

Time	Residues of chlorophacinone in target rodent (mg/kg bw)		
	20% bait consumption	**50% bait consumption**	**100% bait consumption**
Day 5 after last meal[1]	0.185	0.464	0.927
Day 7 (mean time to death)[2]	0.093	0.232	0.464
[1] Based on 0.9272 mg/kg bw measured after 100% bait consumption for 5 days; [2] Based on excretion of 30% per day and a reduction of approximately 50% between days 5 and 7.			

Tier 1 risk assessment for short-term secondary poisoning
The figures presented in the table above are rather qualitatively compared to the lowest LC50 value for birds. For mammals no such qualitative comparison has been carried out because no short-term LC50 values are available. The LC50 for birds is 95 mg/kg food (Bobwhite quail). This LC50 for birds is higher than the 5 days residue values in target rodents for all bait consumptions (20, 50 and 100 %). Also after one single meal the residue values for 50 and 100 % bait consumption are below the LC50 value for birds. This highlights the low acute toxicity of chlorophacinone to birds.

Tier 1 risk assessment for long-term secondary poisoning
For a more long-term exposure it is assumed that the rodents have fed entirely on rodenticide (PD = 1) and that the non-target animals consume 50 % of their daily intake on poisoned rats (Frodent = 0.5).

Residues of chlorophacinone in target rodents from the ingestion of paste bait at different times during a control campaign, based on the maximum residue level measured in rats (Frodent = 0.5)

Time	Residues of chlorophacinone in target rodent (mg/kg bw)		
	20% bait consumption	**50% bait consumption**	**100% bait consumption**
Day 5 after last meal[1]	0.093	0.232	0.463
Day 7 (mean time to death)[2]	0.046	0.116	0.232
[1] Based on 0.9272 mg/kg bw measured after 100% bait consumption for 5 days; [2] Based on excretion of 30% per day and a reduction of approximately 50% between days 5 and 7.			

As discussed previously, there are many uncertainties related to the calculation of PEC/PNEC values. Moreover, the PEC/PNEC values presented in the tables below are very high.

Tier 1 estimate of PECoral/PNECoral for predatory or scavenging birds ingesting target rodents (on day 5 and day 7 of a control campaign) containing chlorophacinone obtained from areas in and around buildings, Frodent = 0.5

Avian predator/scavenger PECoral/PNECoral - day 5 (maximum rodent residue levels)			**Avian predator/scavenger PECoral/PNECoral - day 7**		
bait = 20% of rodents' food intake/day	**bait = 50% of rodents' food intake/day**	**bait = 100% of rodents' food intake/day**	**bait = 20% of rodents' food intake/day**	**bait = 50% of rodents' food intake/day**	**bait = 100% of rodents' food intake/day**
3.1	7.7	15.5	1.5	3.9	7.7
PNECoral = 0.030 mg/kg food					

Tier 1 estimate of PECoral/PNECoral for predatory or scavenging mammals ingesting target rodents (on day 5 and day 7 of a control campaign) containing chlorophacinone obtained from areas in and around buildings, Frodent = 0.5

Mammalian predator/scavenger PECoral/PNECoral - day 5 (maximum rodent residue levels)			**Mamalian predator/scavenger PECoral/PNECoral - day 7**		
bait = 20% of rodents' food intake/day	**bait = 50% of rodents' food intake/day**	**bait = 100% of rodents' food intake/day**	**bait = 20% of rodents' food intake/day**	**bait = 50% of rodents' food intake/day**	**bait = 100% of rodents' food intake/day**
84	211	421	42	105	211
PNECoral = 0.0011 mg/kg food					

The above PECoral/PNECoral quotients ranging from 1.5 to 15.5 for birds and from 42 to 421 for mammals assume that rodents containing chlorophacinone residues are wholly ingested by predatory or scavenging birds which feed on target rodents. The Tier 1 PECoral/PNEC oral quotients presented above are all above 1. However, it is not certain that the sensitivity of predatory bird species is adequately represented by the PNECoral of 30 µg/kg food derived from a study conducted with bobwhite quail. In addition, there is also evidence that secondary poisoning by anticoagulant rodenticides has been implicated in the deaths of raptorial birds in the wild, albeit not necessarily arising from the uses of chlorophacinone paste bait considered in this assessment, or from uses compliant with current recommended good practice. In view of these uncertainties a refined Tier 2 assessment is set out below, based on representative avian species.

Tier 2 risk assessment for secondary poisoning

In a manner similar to the second tier primary poisoning calculations the concentrations in the relevant predatory mammals and birds can be calculated. In the following table the expected values for uptake of chlorophacinone by a mammal predator or a bird of prey are presented after a single day of exposure and the expected concentration in the non-target animals are presented. It is assumed that rodents fed 100 % on rodenticide (PD = 1) and that predators fed 50 % on poisoned rodents (Frodent = 0.5). The residue of chlorophacinone at day 5 after the last meal is 0.927 mg/kg food. As Frodent in this scenario is 0.5 instead of 1 the residue of chlorophacinone at day 5 after the last meal is 0.464 mg/kg food. The bodyweights and food intake data of raptorial species are drawn from EUBEES 2.

The refined, tier 2 estimate of risk considers exposure of relevant species of avian and mammalian predators, based on their bodyweights and food intakes (table below). The following three tables assume that 50% of the diet of each bird and mammal species on a single day consists of rodents containing chlorophacinone. In each case, chlorophacinone paste baits have contributed either 100%, 50% or 20% of the daily food intake of the rodents eaten by the birds.

Estimated intakes and concentrations of chlorophacinone (CPN) predatory and scavenging birds and mammals ingesting target rodents, assuming poisoned rodents comprise 50% of a bird's diet and that paste bait contributed 100% of the target rodents' daily food intake

Non-target avian or mammalian predator	Mean body weight (g)	Daily food intake (g/day)	Normal susceptible rodents caught on day 5, just after their last meal[a]		Normal susceptible rodents caught on day 7, two days after their last meal[b]	
			CPN consumed (mg)	CPN in predator (mg/kg bw)	CPN consumed (mg)	CPN in predator (mg/kg bw)
Birds						
Tyto alba	294	72.9	0.034	0.115	0.017	0.058
Falco tinnunculus	209	78.7	0.036	0.175	0.019	0.091
Athene noctua	164	46.4	0.022	0.131	0.011	0.067
Strix aluco	426	97.1	0.045	0.106	0.023	0.054
Mammals						
Vulpes vulpes	5,700	520.2	0.241	0.042	0.121	0.021
Mustela putorius	689	130.9	0.061	0.088	0.030	0.044
Mustela erminea	205	55.7	0.026	0.126	0.013	0.063
Mustela nivalis	63	24.7	0.011	0.182	0.006	0.091
Dogs	10,000	456	0.211	0.021	0.106	0.011

[a] Based on a rodent containing 0.927 mg chlorophacinone/kg (100% of their diet is paste bait).
[b] Based on a rodent containing 0.473 mg chlorophacinone/kg (100% of their diet is paste bait).

Estimated intakes and concentrations of chlorophacinone (CPN) in predatory and scavenging birds and mammals ingesting target rodents, assuming poisoned rodents comprise 50% of a bird's diet and that paste bait contributed 50% of the target rodents' daily food intake

Non-target avian or mammalian predator	Mean body weight (g)	Daily food intake (g/day)	Normal susceptible rodents caught on day 5, just after their last meal[a]		Normal susceptible rodents caught on day 7, two days after their last meal[b]	
			CPN consumed (mg)	CPN in predator (mg/kg bw)	CPN consumed (mg)	CPN in predator (mg/kg bw)
Birds						
Tyto alba	294	72.9	0.017	0.057	0.009	0.031
Falco tinnunculus	209	78.7	0.018	0.087	0.009	0.043
Athene noctua	164	46.4	0.011	0.066	0.005	0.030
Strix aluco	426	97.1	0.023	0.053	0.012	0.028

Mammals						
Vulpes vulpes	5,700	520.2	0.121	0.021	0.060	0.011
Mustela putorius	689	130.9	0.030	0.044	0.015	0.022
Mustela erminea	205	55.7	0.013	0.063	0.006	0.031
Mustela nivalis	63	24.7	0.006	0.091	0.003	0.045
Dogs	10,000	456	0.106	0.011	0.053	0.005

[a] Based on a rodent containing 0.464 mg chlorophacinone/kg (50% of their diet is bait block).
[b] Based on a rodent containing 0.237 mg chlorophacinone/kg (50% of their diet is bait block).

Estimated intakes and concentrations of chlorophacinone (CPN) in predatory and scavenging birds and mammals ingesting target rodents, assuming poisoned rodents comprise 50% of a bird's diet and that paste bait contributed 20% of the target rodents' daily food intake

Non-target avian or mammal predator	**Mean body weight (g)**	**Daily food intake (g/day)**	**Normal susceptible rodents caught on day 5, just after their last meal[a]**		**Normal susceptible rodents caught on day 7, two days after their last meal[b]**	
			CPN consumed (mg)	**CPN in predator (mg/kg bw)**	**CPN consumed (mg)**	**CPN in predator (mg/kg bw)**
Birds						
Tyto alba	294	72.9	0.007	0.023	0.003	0.010
Falco tinnunculus	209	78.7	0.007	0.035	0.004	0.019
Athene noctua	164	46.4	0.004	0.026	0.002	0.012
Strix aluco	426	97.1	0.009	0.021	0.005	0.012
Mammals						
Vulpes vulpes	5,700	520.2	0.048	0.008	0.024	0.004
Mustela putorius	689	130.9	0.012	0.018	0.006	0.009
Mustela erminea	205	55.7	0.005	0.025	0.003	0.013
Mustela nivalis	63	24.7	0.002	0.036	0.001	0.018
Dogs	10,000	456	0.042	0.004	0.021	0.002

[a] Based on a rodent containing 0.186 mg chlorophacinone/kg (20% of their diet is bait block).
[b] Based on a rodent containing 0.095 mg chlorophacinone/kg (20% of their diet is bait block).

It has to be stated that the values in the three tables above represent only a single day of exposure. Poisoned rodents are likely to be available for at least several days during a rodenticide treatment, and a predator could therefore be exposed over several days. In principle, exposure should be estimated over several days because of the chronic mode of action of anticoagulant rodenticides (a low dose over several days may be more toxic than a higher dose on one day). Therefore the values in these tables do not necessarily represent a realistic worst case situation.
As discussed previously, there are many uncertainties related to the calculation of PEC/PNEC values.

Tier 2 estimates of PECoral/PNECoral for predatory and scavenging birds and mammals ingesting target rodents (as 50% of their diet) containing chlorophacinone obtained from areas in and around buildings

Non-target avian predator/ scavenger	PECoral/PNECoral (rodent ingesting paste bait at 20% of daily requirement)		PECoral/PNECoral (rodent ingesting paste bait at 50% of daily requirement)		PECoral/PNECoral (rodent ingesting paste bait at 100% of daily requirement)	
	Rodent caught on day 5	Rodent caught on day 7	Rodent caught on day 5	Rodent caught on day 7	Rodent caught on day 5	Rodent caught on day 7
Birds						
Tyto alba	4.0	2.0	9.9	5.0	19.8	9.9
Falco tinnunculus	6.0	3.0	15.0	7.5	30.1	15.0
Athene noctua	4.5	2.3	11.3	5.7	22.6	11.3
Strix aluco	3.6	1.8	9.1	4.6	18.2	9.1
Mammals						
Vulpes vulpes	151	76	378	189	755	378
Mustela putorius	314	157	786	393	1572	786
Mustela erminea	450	225	1124	562	2249	1124
Mustela nivalis	649	325	1623	811	3245	1623
Dogs	75	38	189	94	377	189
Birds PNECoral = 0.0058 mg/kg bw. Mammals PNECoral = 0.000056 mg/kg bw.						

Based on the assumption that 50% of a predatory bird's diet consists of rodents that contain the maximum estimated quantity of chlorophacinone residues, the risk assessment indicates uncertainty in some instances: *i.e*. the PECoral/PNECoral exceeds 1.0, in all cases even if a rodent has eaten only 20% for 5 days followed by non eating period of 2 days.

Summary secondary poisoning

There is clearly a high risk of secondary poisoning of non-target mammals and birds. The risk is slightly higher for mammals than for birds and small animals have a higher risk than large animals.

Regarding the short-term exposure at Tier 1, the concentrations of chlorophacinone in the target rodents, assuming 50 % bait consumption, are higher than the lowest LC50 value for birds.

For the long-term situation at Tier 1 and 2 all PEC/PNEC ratios are clearly above 1.

The worst-case PEC/PNEC ratios at Tier 1 are about 15.5 for birds and 421 for mammals. The worst-case PEC/PNEC ratio for birds at Tier 2 is about 30 (kestrel) and 3200 for mammals (weasel).

For Tier 1 of the long-term scenario it was assumed that the rodents have fed entirely on rodenticide and that the non-target animals consume 50 % of their daily intake on poisoned rats. These assumptions led to a high risk, but even if the rodents have fed only 20 % of their daily intakes by rodenticide and non-target animals consume 50 % of their daily intake on poisoned rats the risk quotients are still over 1 for birds (3.1) and high (84) for other non-target mammals).

At Tier 2 an approach based on the body burden of chlorophacinone in the non-target animals was conducted. At this tier values only for a single day of exposure were

calculated. PEC/PNEC ratios for all species are clearly above 1 even though these values do not necessarily represent a worst case because ingestion of poisoned rat over a few days was not considered.

The apparent risks indicated above may, on the other hand, be overestimated because it takes not into account behavioural factors. For example, many birds of prey will not take dead rodents and this may therefore reduce exposure to species such as owls, although some species prey principally on dead animals. Smaller owls such as *Athene noctua* will take only smaller rodents and not large rats, as assumed above in the risk calculations, and so their exposure will be reduced. Many rodents will be caught by predators at times when they do not contain the relatively high levels of chlorophacinone. However, as shown above, even if the rodents have fed only 20 % of their daily intakes by rodenticide, non-target animals are still at high risk. The majority of the chlorophacinone residues are concentrated in the liver and to a lesser extent in the fat tissues. This may reduce exposure to some, but not all birds, which selectively pick at flesh and discard offal during feeding. For example, Tkladec and Rychnovsky (1990), cited by Luttik et al. (1999), observed that kestrels and weasels do not eat the guts of prey, thus avoiding the tissues containing the highest concentrations of rodenticide residues. On the other hand the PEC/PNEC ratios do not include the possibility of recurrent exposure. Many predatory birds are territorial and may therefore actively hunt in areas where they have experienced good success, even feeding young birds with contaminated prey.

In the context of a scenario that involves baiting in and around houses several of the predators considered above would be relatively exotic in many situations. Species more likely to be encountered are mixed-diet scavengers of the crow family and gulls (e.g. *Pica pica*, *Corvus corone corone* and *Larus ridibundus*) that feed opportunistically on carrion[12] and which are likely to consume the bodies of target rodents whenever they are accessible. A significant difference between these scavengers and the predators considered previously is that whereas the raptors tend to be solitary in habit, corvids and gulls are generally gregarious and several birds may consequently pick at the same carcass. Hence, the available carrion may contribute to a smaller extend to the food intake of an individual bird.

As is the case with birds, the risk to non-target mammals may also be overestimated because they do not take behavioural factors into account. Based on five studies of the abundance of different animals among the gut contents of *E. erminia*, rodent species contributed a mean of 26% of the diet (Gurney et al. 1997) and many of these would not be considered to be target rodents in an indoor baiting scenario. This will effectively reduce the risk; however, only for indoor and not for outdoor baiting. In another study, 32% of the diet of *M. putorius* consisted of rodents. The abundance of rodents in the diet of *M. nivalis* is relatively higher than for other mustelid species, but is still less than 100%. Although mustelids are at greatest risk from secondary poisoning, the fact that their diet is not entirely composed of rodents, and that the rodents that are eaten are not exclusively those encountered in and around buildings, reduces the apparent risk. However, as shown above, even if the rodents have fed only 20 % of their daily intakes by rodenticide non-target animals are still at high risk.

Open areas

Primary poisoning

The primary poisoning risks to birds and mammals from ingestion of Rozol Pat' is assumed to be similar in open areas as compared with the risk for birds and mammals in and around buildings non-target animals may enter treated areas even if openings are covered and may consume bait.

[12] Handbook of the Birds of Europe, the Middle East and North Africa. The Birds of the Western Palearctic (Cramp, S. and Perrins, C.M.: Eds.) Vols. III and VIII. Oxford University Press.

It is not possible to quantify the amount of bait that may be exposed for ingestion by non-target birds and mammals. The levels of risk are adequately covered by the assessments made above for various amounts of red paste bait directly ingested following use in and around buildings.

Secondary poisoning
The secondary poisoning risks to birds and mammals following the use of paste bait containing chlorophacinone in open areas are adequately quantified for uses in and around buildings.

Waste dumps

Primary poisoning
The primary poisoning risks to birds and mammals from ingestion of paste containing chlorophacinone are assumed to be similar to those indicated above for uses in and around buildings. Although the paste bait on waste dumps will initially be deployed in sachets, it is possible that pieces of bait will be dropped following uptake by target rodents, in places where they may become accessible to non-target birds and mammals.

The levels of risk are considered to be adequately represented by the assessments made above for various amounts of Rozol Pat' directly ingested following use in and around buildings.

Secondary poisoning
The secondary poisoning risks to birds and mammals following the use of paste bait containing chlorophacinone in waste dumps are adequately quantified for uses in and around buildings.

2.8.3 Possible measures to reduce the risk of primary and secondary poisoning to non-target animals

Chlorophacinone is both highly and non-selectively toxic to vertebrates and, as previously stated, attempts to refine the primary and secondary assessments to demonstrate acceptable risks to birds and mammals with the tools currently available are proven fruitless. Whilst the approved procedure for estimating theoretical exposure of chemicals and plant protection products allows account to be taken of such factors as avoidance of contaminated food items, there is no approved mechanism for adjusting risk assessments quantitatively to take into account practices and intervention specifically intended to minimise the potential for primary and secondary poisoning of non-target vertebrates.

Careful management of anticoagulant rodenticides is understood by the manufacturing industry and by pest-control professionals to be essential to eliminate or reduce to a minimum the opportunity for exposure of non-target species whilst maximising necessary impact on the target rodents. These measures are described in good practice guidance documents, in training courses and on the labels of the products themselves. They are listed below, among a number of other important mitigating factors that need to be taken into account in the risk assessment for paste bait containing chlorophacinone.

The more direct the delivery of paste containing chlorophacinone to the target animals and the faster their consumption, the shorter the eradication campaign and ultimately the smaller the opportunity for non-target species to discover and ingest the bait. The secured bait points selected for deployment of bait in and around buildings are therefore placed where they are most likely to be encountered exclusively by the target organisms (e.g. on habitual rat-runs), thus maximising exposure of the target rodents and minimising unintended exposure of other non-target vertebrates.

According to recommended practice, baiting campaigns with anticoagulant rodenticides continue until uptake monitoring indicates that eradication of the target rodent population has been achieved, at which point all remaining bait is retrieved and destroyed or securely

disposed off. Elimination of residual bait in this way has two benefits: Firstly it removes the potential for unintended exposure of non-target animals in the absence of competition from rats and mice, thus reducing the risk of primary poisoning, and secondly it reduces the likelihood of resistance (i.e. immunity to a particular active substance) developing among the target rodents. In order to minimise the likelihood of target rodents developing resistance to second-generation anticoagulant rodenticides long-term deployment of bait as a preventative control measure is not recommended.

Resistance has the obvious consequence that rodenticide deployment will fail to elicit the desired response among the target rodent population. If not promptly recognised, it may also lead to extended baiting programmes that result in extended opportunities for accidental primary poisoning of non-target animals. It may also result in a population of rodents that continue to feed on bait and maintain maximal levels of rodenticide in their tissues, thus exposing predators to a heightened risk of secondary poisoning. However, guidance documents warn against this possibility and indicate the need to monitor bait uptake in case it exceeds the expected pattern and to cease ineffectual baiting as soon as resistance is suspected.

Knowledge of the site in which the control campaign is to be conducted also entails taking into account the presence of or possible access by non-target animals and selecting appropriate baits and degrees of bait point protection that minimise the potential for unintended exposure to occur. However, only professionals are supposed to retrieve remaining bait and destroy it in a safe way. Non-professionals are not expected to follow this practice.

Good practice guidance reinforced by product labelling, demands also that site inspections have to be made regularly during baiting campaigns. One of the objectives of these inspections is to search for carcasses of target rodents that must then be collected and disposed off in a manner (e.g. incineration or burial at sufficient depth) that ensures they remain inaccessible to scavengers. This significantly reduces the levels of exposure and the risk of secondary poisoning. Good practice also requires that residents and/or workers in and around the baited area are alerted to the hazards posed by baits and carcasses containing rodenticide, so that they may also take appropriate measures to prevent non-target animals being exposed to and/or consuming poisoned rodents.

Products containing chlorophacinone are placed at secured bait points. The type of secured bait point suitable for a given situation is determined on a case-by-case basis, taking into account such factors as shielding from sunlight and moisture necessary to maintain bait integrity and the level of security required to prevent access to and/or interference by non-target animals, children etc. Where adequate protection is provided by parts of buildings (e.g. cellars, lofts), a secured bait point may simply comprise a tray shielded by an object such as a roofing tile. Bait points that incorporate a degree of physical obstruction to restrict access – termed bait stations - are used in more sensitive environments where there are non-target animals that may otherwise be unintentionally exposed. In particularly sensitive locations the bait is contained in bait boxes; high-security bait stations comprising weather-proof, tamper-proof, rigid casings. Good practice requires as well that these points are regularly checked for damage during inspection visits and repaired or replaced, as appropriate, to prevent access to bait by non-target animals. This might reduce the risk of primary poisoning. The use of dyed bait might further reduce the risk of primary poisoning of birds.

Good practice should require that bait boxes, containing bait in a chamber not directly accessible from the access hole, be used in locations where preliminary site assessment has identified a potential for avian exposure. This reduces both the visibility of the bait and the ability of larger birds to access it simply by putting their head and neck through the entrance hole. For these birds the availability of bait is thus effectively reduced to those pieces of paste translocated and dropped by the target rodents, and good practice requires that these be retrieved on regular inspection visits.

To conclude, the true primary and secondary poisoning risks posed to non-target animals and birds by chlorophacinone containing products might be lower than those indicated in the quantitative assessment of risk as a result of the many mitigating factors listed above. The most significant reductions in exposure and risk are achieved by restricting its use to treatment campaigns of limited duration, limiting access of non-target animals to the bait and removing unused bait and dead and moribund rodents during a baiting campaign to minimise the opportunity of primary secondary exposure of non-target animals. However, it has to be stated that only professionals are expected to follow these instructions.

Despite the possible risk mitigation measures listed above, the Dutch CA is of the opinion that the use of Rozol Pat' needs to be restricted to indoor use only for authorisation in the Netherlands. To the opinion of Ctgb, the evidence for the effectiveness of the risk mitigation measures listed above is weak and therefore, Ctgb does not allow for outdoor use of this product based on chlorophacinone, also not with these specific risk mitigation measures.

2.9 Measures to protect man, animals and the environment

The information submitted covering the requirements as described in the TNsG on Data Requirements, common core data for the product, section 8, points 8.1 to 8.8 should be assessed and summarised here.

The instructions for use must contain the following indications:

- Prevent access to bait by children and non-target animals
- Keep out of reach of children
- 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
- 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.

Antidote vitamin K1 (under medical supervision).

For the measures to protect animals and the environment we refer to the "elements to be taken into account by Member States when authorising products" from the Assessment Report and inclusion directive 2009/92/EC for chlorophacinone which shall be duly taken into consideration for a clear labelling of Rozol Pat'.

The instructions for use must contain the following indications:

- The size of the package placed on the market should be proportionate to the duration of the treatment and appropriate to the pattern of use of particular user groups.
- Product design and use restrictions should be optimised in order to ensure sufficient and efficient rodent control while at the same time minimizing the risk for primary poisoning. This could include 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. It could also include regular check of the bait points for damage and to repair or replace, as appropriate.
- The restriction of products to specific areas and manners of use and also restrictions of products to professionals or trained professionals only, should be considered.
- Baits must be securely deposited in a way so as to minimise the risk of consumption by non-target 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, at least as often as when baits are checked and/or replenished. Dispose of dead rodents in accordance with local requirements.
- Do not use anticoagulant rodenticides as permanent baits. In most cases treatment with this product should have achieved control within 35 days. Should activity of house mice, brown or black rats continue beyond this time, the likely cause should be determined and measures should be taken.
- Remove all baits after treatment and dispose of them in accordance with local requirements.
- Adequate safety instructions (including use of appropriate personal protective equipment) should be provided in the use instructions.
- 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 infestation.
- A complete elimination of rodents in the infested area should be achieved.
- It is recommended to develop and implement an Integrated Pest Management system (IPM). Relevant IPM issues are:
  - Measures for the prevention and/or suppression of harmful organisms;
  - Adequate methods and tools for monitoring of harmful organisms;
  - Preference of non-chemical methods;
  - Target-specificity and minimisation of impact on non-target organisms, health and the environment;
  - Reduction to use of minimum necessary level;
  - Application of strategies on anti-resistance;
  - Check of success on the basis of records, monitoring and documentation.
- The use instruction of products should contain guidance on resistance management for rodenticides.
- Resistant management strategies should be developed, and chlorophacinone 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.

3 Proposal for decision

The Dutch CA considers that sufficient data have been provided to verify the outcome and conclusions, and permits the authorisation of Rozol Pat'.

Rozol Pat' has been applied for and evaluated as a rodenticide against rats and mice for the following use patterns: in and around buildings (professional and non-professional use), open areas (professional use only) and waste dump perimeters (landfill) (professional use only).

Amendment 6-12-2013
Based on the assessment, it is concluded by the Dutch CA that Rozol Pat' can be safely used by professional users for the control of black rats and house mice in buildings.

ANNEXES CONTAIN CONFIDENTIAL DATA: This information should not be disclosed to third parties

4 Annexes:

1. **Summary of product characteristics**
2. **List of studies reviewed**
3. **Analytical methods residues – active substance**
4. **Toxicology and metabolism –active substance**
5. **Toxicology – biocidal product**
6. **Safety for professional operators**
7. **Safety for non-professional operators and the general public**
8. **Translation of Dutch label**

Annex 1: Summary of product characteristics

(a) Product trade name: Rozol Pat'

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

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**
chlorophacinone	2-[2-(4-chlorophenyl)-2-phenylacetyl]indan-1,3-dione	3691-35-8	223-003-0	0.05	g/L	0.0050	97.8	☒ **yes** ☐ **no**

Co-formulants					Contents				
Common name	**IUPAC name**	**Function**	**CAS number**	**EC number**	**Concentration**	**Unit**	**w/w (%)**	**Classification**	**Substance of concern**
Propylene glycol	propane-1,2-diol	Solvent	57-55-6	200-338-0			0.787	-	☐ **yes** ☒ **no**
Polyethylene glycol 300	Poly(oxy-1,2-ethanediyl),α-hydro-ω-hydroxy-ethane-1,2-diol, ethoxylated	Solvent	25322-68-3	500-038-2			0.223	-	☐ **yes** ☒ **no**
Blue food dye E133	disodium 2-[[4-[ethyl-[(3-sulfonatophenyl)methyl]amino]phenyl]-[4-[ethyl-[(3-sulfonatophenyl)methyl]azaniumylidene]cyclohexa-2, 5-dien-1-ylidene]methyl]benzenesulfonate	Dye	3844-45-9	223-339-8			0.022	-	☐ **yes** ☒ **no**
Denatonium benzoate	phenylmethyl-[2- [(2,6-dimethylphenyl)amino]- 2-oxoethyl]-diethylammonium benzoate	Bittering agent	3734-33-6	223-095-2			0.005	Xn R20/22, R38, R41	☐ **yes** ☒ **no**
Oat flour	-	Holder	-	-			74.93	-	☐ **yes** ☒ **no**

Wheat flour	-	Holder	-	-			1.97	-	☐ yes ☒ no
water	water	Solvent	7732-18-5	231-791-2			0.015	-	☐ yes ☒ no
Butylated hydroxytoluene	2,6-bis(1,1-dimethylethyl)-4-methylphenol	Preservative	128-37-0	204-881-4			0.02	-	☐ yes ☒ no
EDTA	calcium disodium 2-[2-[bis(carboxylatomethyl)amino]ethyl-(carboxylatomethyl)amino]acetate	Preservative	62-33-9	200-529-9			0.01	-	☐ yes ☒ no
Vegetal fat	Fatty acids, soya, Me esters	Binder	68919-53-9	272-898-4			22	-	☐ yes ☒ no
Potassium citrate	tripotassium 2-hydroxypropane-1,2,3-tricarboxylate	Preservative	866-84-2	212-755-5			0.01	-	☐ yes ☒ no

Sum	**0.0**		**100.0**

(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.

Different dye, different binder, different attractant

(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: chlorophacinone

Manufacturer

Company Name: Liphatech S.A.S. at AlzChem Trostberg GmbH

Address: Chemie Park Trostberg,
Dr Albert Frank strasse 32
City: Trostberg
Postal Code: 83308
Country: Germany
Telephone: +33 5 53 69 36 30
Fax: +33 5 53 47 95 01
E-Mail: corg@liphatech.fr

Intra-Community VAT number or, for non EU companies, company registration number:
FR91442688206

Manufacturing site same address.

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

Formulator

Company Name: Liphatech S.A.S.
Address: Production centre,Av Jean Serres, ZA Malère
City: Pont du Casse
Postal Code: 47480
Country: France
Telephone: +33 5 53 69 36 30
Fax: +33 5 53 47 95 01
E-Mail: corg@liphatech.fr

Intra-Community VAT number or, for non EU companies, company registration number:
FR91442688206

Formulation site same address.

Physical state and nature of the biocidal product:

(e) Type of formulation: RB

(f) Ready-to-use product: ☐no ■ yes

Classification and labelling statements of the biocidal product:

(g) Product classification: -

(h) Risk and Safety Phrases:

Professionals: S2

Non-Professionals: S2

In NL the use is restricted to professional users.

(i) Product classification according to GHS: -

(j) Hazard statement according to GHS: P102 Keep out of reach of children

Intended uses and efficacy:

(k)	PT:	PT 14 (Rodenticides)
(l)	Target harmful organisms:	*Rattus norvegicus,* (Norway rat, Brown rat) *Rattus rattus* (Black rat) *Mus musculus* (House mouse) In NL the use is restricted to black rats and house mice
(m)	Development stage of target organisms:	Juveniles and adults
(n)	Function/mode of action:	Anticoagulant, bait product
(o)	Field of use:	In and around buildings, in open areas and waste dumps. In NL field of use is restricted to use in buildings
(p)	Application aim:	It is used to protect human food and animal feedstuffs and for general hygiene purposes.
(q)	User category:	Professional and non-professional. In NL the use against black rats and house mice is restricted to professional use for reasons of resistance management (see 2.5.4 for explanation).
(r)	Application method[13]:	Covered application, preferably in tamper-resistant bait stations

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.

13 Indicate how the product will be applied (e.g. brush, spray, dipping, bait, etc). Where the product is to be used by more than one user category, indicate the application method(s) intended for each user category.

(t) Conditions of use:

Species	Recommended Application rate for one bait point/baiting point intervals[#]	Frequency of controls	Checking / Replenishing	Time of treatment and place of application[1]
Non-professional users				
Mice	30 to 50 g of paste in one or more sachets per bait station. Place 1 station every 1 to 3 m	Dispose the product and check 3-4 days after first application, then regularly once a week or 15 days	At each check, re-apply the bait if only a part of the bait is consumed. In case all bait is eaten, refill the station and use more bait stations and/or increase the control frequency.	All year In & around buildings.
Rats: Brown & Black	100 to 200 g of paste in 2 or more sachets per bait station. Place 1 station every 4 to 10 m.			
Professional users				
Mice	30 to 50 g of paste in one or more sachets per bait station. Dispose 1 station every 1 to 3 m	Dispose the product and check 3-4 days after first application, then regularly once a week or 15 days	At each check, re-apply the bait if only a part of the bait is consumed. In case all bait is eaten, refill the station and use more bait stations and/or increase the control frequency.	All year In & around buildings In open areas In waste dumps.
Rats: Brown & Black	100 to 200 g of paste in 2 or more sachets per bait station. Dispose 1 station every 4 to 10 m.			

[1] In NL field of use is restricted to use in buildings

(u) Instructions for safe use of the product
See paragraph 2.9

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

Rozol Pat' is a rodenticide containing chlorophacinone (0.005%) as an active substance.
Chlorophacinone is a first-generation anticoagulant rodenticide. It disrupts the normal blood clotting mechanisms resulting in increased bleeding tendency and, eventually, profuse haemorrhage and death.
Clinical symptoms: nose bleed, gum bleed, bloody saliva, extravasation, sudden or unusual internal pain.
If in contact with eyes:
Keep the eye open and wash slowly and carefully with water during 15-20 minutes
Remove eventual contact lenses after the first 5 minutes and continue washing
Pay attention to possible symptoms mentioned above.
If inhaled:
The product is a non-dusty bait. Inhaling is not considered a relevant route of exposure
If in contact with skin:
Remove contaminated cloths. Wash before re-use.
Wash the skin immediately with water and soap.
Pay attention to possible symptoms mentioned above.
If swallowed:

Wash your mouth with plenty of water
If swallowed, get medical advise immediately. Show the packaging, label or the safety data sheet.
Do not induce vomiting, unless advised by a medical specialist.
Do not administer anything by mouth, if the person is unconscious.
Antidote vitamin K1 (under medical supervision).

For the directions for use regarding the environmental aspect we refer to sections 2.9 and 3 of the PAR.

(w) Instructions for safe disposal of the product and its packaging
See MSDS.

(x) Conditions of storage and shelf-life of the product under normal conditions of storage
The specified shelf life is three year in the original PP packaging, which is supported by ambient temperature storage stability data.

(y) Additional information:

In the PAR resistance management strategies are outlined. A remark on resistance should be added to the Label. We propose to add a different remark for professional and non-professional use since non-professionals are not expected to have knowledge on resistance (see annex 9). It should be noted that non-professional use is not allowed for in the Netherlands.
For professional use:
For the active substance in this product, chlorophacinone, there is a risk of development of resistance and in some parts of the Netherlands resistance in rats and mice is already present. Therefore, this product should not be used in cases where resistance against chlorophacinone is known or presumed, for instance in cases where the last treatment with chlorophacinone containing products did not results in a reduction of the population. Always contact with the appropriate authorities to check for the latest knowledge on occurrence of resistance.
For non-professional use (not accepted in NL):
If 28 days after the start of the treatment the control of mice is not sufficient, a professional in pest control should be consulted.

Annex 2: List of studies reviewed

List of <u>new data</u>[14] submitted in support of the evaluation of the active substance

No new date is submitted in support of the evaluation of the active substance.

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

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
						Yes	No	Yes	No
IIIB 3.1.1-01		Caruel, H.	2008	Chlorophacinone Blue Paste 50 mg/kg, CLOPA0,0050_01F_F01265_00 Appearance, Colour, Odour. Centre R&D De Sangosse, Pont du Casse, France. Study code: CLO0812C. Non-GLP, Unpublished.	Liphatech	☐	☐	☒	☐
IIIB 3.1.2-01		Caruel, H.	2008	Chlorophacinone Blue Paste 50 mg/kg, CLOPA0,0050_01F_F01265_00 Appearance, Colour, Odour. Centre R&D De Sangosse, Pont du Casse, France. Study code: CLO0812C. Non-GLP, Unpublished.	Liphatech	☐	☐	☒	☐

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

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
IIIB 3.1.3-01		Caruel, H.	2008	Chlorophacinone Blue Paste 50 mg/kg, CLOPA0,0050_01F_F01265_00 Appearance, Colour, Odour. Centre R&D De Sangosse, Pont du Casse, France. Study code: CLO0812C. Non-GLP, Unpublished.	Liphatech	☐	☐	☒	☐
IIIB 3.2-01		Curl, M and Wright, E.	2011a	Expert Statement on the Explosive Properties of Chlorophacinone Blue Paste 0.005% Bait Formulation. TSGE, Knaresborough, UK. Study No: 12-1-17_F01265_00_Exp, Non-GLP, Unpublished.	Liphatech	☐	☐	☒	☐
IIIB 3.3-01		Curl, M and Wright, E.	2011b	Expert Statement on the Oxidising Properties of Chlorophacinone Blue Paste 0.005% Bait Formulation. TSGE, Knaresborough, UK. Study No: 12-1-17_F01265_00_Oxp, Non-GLP, Unpublished.	Liphatech	☐	☐	☒	☐
IIIB 3.4-01		Demangel, B.	2008a	Flammability of Solids on Difethialone Paste – F00060_01, Defitraces, Brindas, France Study number 08-912021-002 GLP, Unpublished.	Liphatech	☐	☐	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
IIIB 3.5-01		Demangel, B.	2008b	Free Acidity or Alkalinity on Difethialone Paste – F00060_01, Defitraces, Brindas, France Study number 08-912021-003 GLP, Unpublished.	Liphatech	☐	☐	☒	☐
IIIB 3.6-01		Zobel, M.L.	2007	Density Determination of DFN Paste 0601 Liphatech Inc, Milwaukee, WI, USA. Study code: 06083. GLP, Unpublished.	Liphatech	☐	☐	☒	☐
IIIB 3.7-01		Caruel, H.	2009	Chlorophacinone blue paste 50 mg/kg – Accelerated Storage Stability (40°C – 8 weeks), CLOPA0,0050_01F_F01265_00. Centre R&D De Sangosse, Pont du Casse, France. Study code: CLO00903C. GLP, Unpublished.	Liphatech	☐	☐	☒	☐
IIIB 3.7-02		Caruel, H.	2011	Chlorophacinone blue paste 50 mg/kg –Storage Stability (25°C – 2 Years), CLOPA0,0050_01F_F01265_00. Centre R&D De Sangosse, Pont du Casse, France. Study code: CLO00903D. GLP, Unpublished.	Liphatech	☐	☐	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
IIIB 3.7-03		Deslux,R.	2012	Chlorophacinone bait compatibility packaging study (54°C, 14days) Centre R&D De Sangosse, Pont du Casse, France. Study code: CLO1203A. GLP, Unpublished.	Liphatech	☐	☐	☒	☐
IIIB 4.1-01		Caruel, H.	2009	Chlorophacinone Paste 50 mg/kg - Analytical method validation. CLOPA0,0050_01F_F01265_00 Centre R&D De Sangosse, Pont du Casse, France. Study code: CLO0903F. GLP, Unpublished.	Liphatech	☐	☐	☒	☐
5	IIIB 5.10.2-01	Berny, P.	2010a	Study on the Efficacy and Palatability of a Paste at 50 mg/kg of Chlorophacinone in the Rat, Rattus rattus, Wild Strain, sensitive to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/1003/CPN/paste/Rr/S. Non-GLP, Unpublished.	Liphatech	☐	☐	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
5	IIIB 5.10.2-02	Berny, P.	2010b	Study on the Efficacy and Attractivity of a Paste at 50 mg/kg of Chlorophacinone in the Rat, *Rattus Norvegicus*, Wild Strain, sensitive to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/1004/CPN/paste/Rn/S. Non-GLP, Unpublished.	Liphatech	☐	☐	☒	☐
5	IIIB 5.10.2-03	Berny, P.	2010c	Study on the Efficacy and Palatability of a Paste at 50 mg/kg of Chlorophacinone in the House Mouse, Mus Musculus, Wild Strain, sensitive to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/1006/CPN/paste/Mm/S. Non-GLP, Unpublished.	Liphatech	☐	☐	☒	☐
5	IIIB 5.10.2-04	Berny, P.	2010d	Evaluation of the efficacy of a paste rodenticide containing 50 mg/kg chlorophacinone for the control of brown rat infestations in and around agricultural buildings. ENVL, Marcy L'Etoile, France. Study code: Report FSR-1001. Non-GLP, Unpublished.	Liphatech	☐	☐	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
5	IIIB 5.10.2-05	Berny, P.	2010e	Evaluation of the efficacy of a paste rodenticide containing 50 mg/kg chlorophacinone for the control of black rat infestations in and around agricultural buildings. ENVL, Marcy L'Etoile, France. Study code: Report FSR-1002. Non-GLP, Unpublished.	Liphatech	☐	☐	☒	☐
5	IIIB 5.10.2-06	Berny, P.	2005b	Study on the Impact of Denatonium Benzoate Variation Concentration on the Palatability of a Rodenticide Block Formula in the Rat, Rattus Norvegicus, Wild Strain. ENVL, Marcy L'Etoile, France. Study code: RE/0404/BDN/Block/Rn. Non-GLP, Unpublished.	Liphatech	☐	☐	☒	☐
5	IIIB 5.10.2-07	Berny, P.	2005c	Study on the Impact of Packaging on the Attractivity of a Block in the Rat, Rattus Norvegicus, Wild Strain. ENVL, Marcy L'Etoile, France. Study code: RE/0314/Pack/R225/Block/Rn. Non-GLP, Unpublished.	Liphatech	☐	☐	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
5	IIIB 5.10.2-08	Berny, P.	2003	Selection of House Mouse Strains, Mus Musculus According to Their Degree of Resistance to an Anticoagulant of 1st Generation: Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/SOU/0202. Non-GLP, Unpublished.	Liphatech	☐	☐	☒	☐
5	IIIB 5.10.2-09	Berny, P.	2002	Selection of Rat Strains, Rattus Norvegicus According to Their Degree of Resistance to an Anticoagulant of 1st Generation: Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/SOU/0201. Non-GLP, Unpublished.	Liphatech	☐	☐	☒	☐
5	IIIB 5.10.2-10	Berny, P.	2010f	Evaluation of the efficacy of a block rodenticide containing 50 mg/kg chlorophacinone for the control of house mice infestations in and around agricultural buildings. ENVL, Marcy L'Etoile, France. Study code: Report FSR-1003. Non-GLP, Unpublished.	Liphatech	☐	☐	☒	☐
5	IIIB 5.10.2-11	Berny, P.	2011	Study on the Efficacy and Attractivity of a Paste at 50 mg/kg of Chlorophacinone in the Rat, *Rattus Norvegicus*, Wild Strain, sensitive to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/1114/CPN/paste/Rn/S. Non-GLP, Unpublished.	Liphatech	☐	☐	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Letter of Access		Data protection claimed	
5	IIIB 5.10.2-12	Berny, P.	2011b	Study on the Efficacy and Palatability of a Paste at 50 mg/kg of Chlorophacinone in the House Mouse, Mus Musculus, Wild Strain, sensitive to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/1116/CPN/paste/Mm/S. Non-GLP, Unpublished.	Liphatech	☐	☐	☒	☐
5	IIIB 5.10.2-13	Grancher, D.	2012	Evaluation of the efficacy of a paste rodenticide containing containing 50 mg/kg chlorophacinone for the control of Mus musculus infestations in and around agricultural buildings. One trial, 1 site: Rhone; France, 2012. Report number FSR-1201. Non-GLP, Unpublished.	Liphatech	☐	☐	☒	☐

Annex 3: Analytical methods residues – active substance

Chlorophacinone

The analytical methods for residues are taken from the CA report to support the inclusion of chlorophacinone in annex I of Directive 98/8/EC.
Please note that the following further information is demanded: Preliminary results of an analytical method for the determination of chlorophacinone in food and feedingstuffs showed that the method was partially acceptable for some of the matrices; however a fully validated method should be necessary when applying for authorisation of the biocidal product at national level for the first time after Annex I Inclusion.

Analytical methods for residues

Soil (principle of method and LOQ) (Annex IIA, point 4.2)	Soil is extracted by shaking with aqueous methanol. Determination of the filtered and diluted extract is by reverse-phase LC-MS/MS (monitored ions 373.4/201.2 m/z). A Luna C-8 column is used with acetonitrile/water/ammonium acetate (gradient) mobile phase. The limit of determination is 0.01 mg/kg (defined as the lowest concentration at which acceptable recovery has been demonstrated).
Air (principle of method and LOQ) (Annex IIA, point 4.2)	Air is passed through Tenax absorption tubes which are eluted with acetonitrile. Determination is by reverse-phase HPLC, Luna C-8 column with acetonitrile/water/ ammonium acetate (gradient) mobile phase. The limit of determination is 0.03 $\mu g/m^3$ (defined as the lowest concentration at which acceptable recovery has been demonstrated).
Water (principle of method and LOQ) (Annex IIA, point 4.2)	Water is extracted by partition into dichloromethane. The extract is evaporated to dryness and reconstituted in aqueous methanol. Determination is by reverse-phase LC-MS/MS (monitored ions 373.4/201.2 m/z). A Luna C-8 column is used with acetonitrile/water/ ammonium acetate (gradient) mobile phase. The limit of determination is 0.05 $\mu g/L$ (defined as the lowest concentration at which acceptable recovery has been demonstrated).
Body fluids and tissues (principle of method and LOQ) (Annex IIA, point 4.2)	Blood Blood is diluted with methanol. Phosphate buffer, a mixture of ethanol/ethyl acetate and trichloroacetic acid solution is added. The sample is shaken and the organic phase

	removed. The sample is re-extracted with ethanol/ethyl acetate. The combined organic extracts are evaporated to dryness and reconstituted in methanol prior to determination. Determination is by HPLC with a Thermo Hypersil Keystone column and ammonium acetate/methanol (gradient) mobile phase (two ion transitions monitored 373>201 and 375>203). The limit of determination is 0.05 mg/L (defined as the lowest concentration at which acceptable recovery has been demonstrated). Liver Liver is blended with phosphate buffer (pH 5.5) and a mixture of ethanol and ethyl acetate (1+19, v/v). A solution of trichloroacetic acid is added and the sample is blended again. Clean-up of the centrifuged extract is by GPC. Determination is by HPLC with Thermo hypersil keystone column and ammonium acetate/methanol (gradient) mobile phase (two ion transitions monitored 373>201 and 375>203). The limit of determination is 0.05 mg/L (defined as the lowest concentration at which acceptable recovery has been demonstrated).
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	Samples are extracted by blending twice with methanol (meat and lemon) or methanol/water (oil-seed rape). After centrifugation the samples are diluted with methanol/water. Determination is by HPLC/MS-MS LOQ: 0.01 mg/kg

Annex 4: Toxicology and metabolism –active substance

Chlorophacinone

Threshold Limits and other Values for Human Health Risk Assessment

Summary			
	Value	Study	SF
AEL long-term	0.000017 mg/kg bw/day	90 day rat oral toxicity study	300
AEL medium-term	0.000017 mg/kg bw/day	90 day rat oral toxicity study	300
AEL acute	0.000033 mg/kg bw/day	Teratogenicity rabbit study	300

Inhalative absorption	No data
Oral absorption	100%
Dermal absorption	1.7%
Classification	
with regard to toxicological data (according to the criteria in Dir. 67/548/EEC)*	T+ R26/27/28, R48/23/24/25, R61 S1/2, S36/37, S45
with regard to toxicological data (according to the criteria in Reg. 1272/2008)	Pictograms: GHS06, GHS08 Signal word: Danger Acute Toxic Cat. 1, H300; H310; H330; STOT RE Cat. 1, H370; Repr. Cat. 1B, H360

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

* The following information with regard to classification and labelling is included in the CAR:
The classification for human health effects of chlorophacinone is in May 2007 still under discussion. For anticoagulant rodenticides, regarding human health effects, a provisional classification with R61 was decided in November 2006 by the C & L, but without a final decision on the category to be used (Repr. Cat.1 or Repr. Cat. 2). The proposed classification for chlorophacinone for acute and repeated dose toxicity was agreed in May 2007. At that moment, the provisionally classification for reprotoxicity was not confirmed as the TC C&L decided to await further results from studies on anticoagulant rodenticides before finalising the discussion on reprotoxicity. Specific concentration limits for chlorophacinone are proposed, but there are still under consideration.
** Chlorophacinone is included in the Registry of submitted Harmonised Classification and Labelling intentions (see www.echa.eu); however, no final conclusion on the classification has been reached yet. The current classification is the self-classification of the RMS (The Netherlands) based on the human toxicological data provided in the CAR of chlorophacinone, and proposed classification according to Directive 67/548/EEC.

Annex 5: Toxicology – biocidal product

Rozol Pat'	
General information	
Formulation Type	Paste bait
Active substance(s) (incl. content)	Chlorophacinone, 0.005%
Category	PT14

Acute toxicity, irritancy and skin sensitisation of the preparation (Annex IIIB, point 6.1, 6.2, 6.3)	
Rat LD50 oral (OECD 420)	> 2000 mg/kg bw
Rat LD50 dermal (OECD 402)	> 2000 mg/kg bw
Rat LC50 inhalation (OECD 403)	No classification*
Skin irritation (OECD 404)	Not irritating
Eye irritation (OECD 405)	Not irritating
Skin sensitisation (OECD 429; LLNA)	Not sensitizing

* An inhalation study of the product is not required. The product contains a small percentage of active ingredient and is classed as nearly dust free. The active substance is not volatile. The physical nature of the product is such that inhalation of volatiles or dust is highly improbable.

Classification and labelling proposed for the preparation with regard to toxicological properties (Annex IIIB, point 9)	
Directive 1999/45/EC	S2
Regulation 1272/2008/EC	P102

Annex 6: Safety for professional operators

Rozol Pat'

Exposure assessment

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

Product and intended use	Exposure scenario	PPE	Inhalational uptake Exposure (mg/m3)	Dermal uptake Exposure (mg/m2)
Rozol Pat' In and around buildings for the control of rodents	Cleaning the remains of 15 bait points/day 6 sachets per bait point. Loading product is not relevant due to protective packaging	Gloves	Not considered for cleaning since negligible measured residues present during cleaning of bait boxes in pilot exposure study.	Measured as 4.09 mg product/gloves (geometric mean value) when cleaning up a bait box containing 6 sachets and disposing of the unwanted bait. Assume negligible amount of bait is consumed.

Dermal Exposure	
Measured value for amount of product on gloves:	4.09 mg product/bait point during disposal
Amount of blue paste on gloves during disposal:	4.09 mg x 15 = 61.35 mg
Total amount of blue paste on gloves:	61.35 mg
Concentration of chlorophacinone:	50 mg/kg
Amount of chlorophacinone on gloves:	50 x 61.35 ÷106 mg = 3.07 x 10-3 mg/day
Reduction in exposure from gloves:	90%
Amount of chlorophacinone on skin:	3.07 x 10-3 x (10 ÷ 100) mg = 3.07 x 10-4 mg/day
Dermal absorption of chlorophacinone:	1.7%
Systemic exposure of chlorophacinone:	5.22 x 10-6 mg/day
Operator body weight:	60 kg
Dermal exposure of chlorophacinone during disposal:	8.70 x 10-8 mg/kg bw/day

Product and intended use	Exposure scenario	PPE	Inhalational uptake Exposure (mg/m3)	Dermal uptake Exposure (mg/m2)
Rozol Pat' Around waste sites for the control of rodents	Cleaning up 50 bait points/ day. 6 sachets per bait point. Loading product is not relevant due to protective packaging	Gloves	Not considered for cleaning since negligible measured residues present during cleaning of bait boxes in pilot exposure study.	Measured as 4.09 mg product/gloves (geometric mean value) when cleaning up a bait box containing 6 sachets and disposing of the unwanted bait. Assume negligible amount of bait is consumed.

Dermal Exposure	
Measured value for amount of product on gloves:	4.09 mg product/bait point during disposal
Amount of blue paste on gloves during disposal:	4.09 mg x 50 = 204.5 mg
Concentration of chlorophacinone:	50 mg/kg
Amount of chlorophacinone on gloves:	50 x 204.5 ÷106 mg = 0.0102 mg/day
Reduction in exposure from gloves:	90%
Amount of chlorophacinone on skin:	0.010 x (10 ÷ 100) mg = 1.02 x 10-3 mg/day
Dermal absorption of chlorophacinone:	1.7%
Systemic exposure of chlorophacinone:	1.73 x 10-5 mg/day
Operator body weight:	60 kg
Dermal exposure of chlorophacinone during disposal:	2.89 x 10-7 mg/kg bw/day

Product and intended use	**Exposure scenario**	**PPE**	**Inhalational uptake Exposure (mg/m3)**	**Dermal uptake Exposure (mg/m2)**
Rozol Pat' Open areas for control of rodents.	Cleaning up 30 bait points/ day. 6 sachets per bait point. Loading product is not relevant due to protective packaging	Gloves	Not considered for cleaning since negligible measured residues present during cleaning of bait boxes in pilot exposure study.	Measured as 4.09 mg product/gloves (geometric mean value) when cleaning up a bait box containing 6 sachets and disposing of the unwanted bait. Assume negligible amount of bait is consumed.

Dermal Exposure	
Measured value for amount of product on gloves:	4.09 mg product/bait point during disposal
Amount of blue paste on gloves during disposal:	4.09 mg x 30 = 122.7 mg
Concentration of chlorophacinone:	50 mg/kg
Amount of chlorophacinone on gloves:	50 x 122.7 ÷106 mg = 6.135 x 10-3 mg/day
Reduction in exposure from gloves:	90%
Amount of chlorophacinone on skin:	6.135 x 10-3 x (10 ÷ 100) mg = 6.135 x 10-4 mg/day
Dermal absorption of chlorophacinone:	1.7%
Systemic exposure of chlorophacinone:	1.04 x 10-5 mg/day
Operator body weight:	60 kg
Dermal exposure of chlorophacinone during disposal:	1.74 x 10-7 mg/kg bw/day

Primary exposure of professionals

Exposure scenario	**Component**	**CAS**	**Dermal Total [mg/day] (no PPE)**	**Dermal Total [mg/kg/d] (no PPE)**	**Dermal Total [mg/day] (gloves, 90% reduction)**	**Dermal Total [mg/kg/d] (gloves, 90% reduction)**	**Inhalation Exposure [mg/m³]**

Application in and around buildings	Chlorophacinone	3691-35-8	5.22×10^{-5}	8.70×10^{-7}	5.22×10^{-6}	8.70×10^{-8}	-
Application around waste sites for the control of rodents	Chlorophacinone	3691-35-8	1.73×10^{-4}	2.89×10^{-6}	1.73×10^{-5}	2.89×10^{-7}	-
Application in open areas	Chlorophacinone	3691-35-8	1.04×10^{-4}	1.74×10^{-6}	1.04×10^{-5}	1.74×10^{-7}	-

Risk assessment

Exposure scenario	**Component**	**CAS**	**AEL [mg/kg/d]**	**Absorption**		**Inhal ext [mg/m3]**		**Derm ext [mg/kg/d]**		**RCR total**
				inh	**derm**	**Act. Expo**	**RCR**	**Act. Expo**	**RCR**	
Application in and around buildings	Chlorophacinone	28772-56-7	0.000017	No data	1.7 %	**-**	**-**	8.70 x 10-7	5.1%	5.1%
Application around waste sites for the control of rodents	Chlorophacinone	28772-56-7	0.000017	No data	1.7 %	**-**	**-**	2.89 x 10-6	17.0%	17.0%
Application in open areas	Chlorophacinone	28772-56-7	0.000017	No data	1.7 %	**-**	**-**	1.74 x 10-6	10.2%	10.2%

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

Rozol Pat'

Non-professional use is not accepted in The Netherlands.

General information	
Formulation Type	Paste bait
Active substance(s) (incl. content)	Chlorophacinone (0.005%)
Category	PT14
Authorisation number	-

Chlorophacinone

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

Exposure scenarios for intended uses (Annex IIIB, point 6.6)	
Primary exposure	Non-professional users, application in and around buildings for the control of rodents
Secondary exposure, acute	Infant, ingesting a bait
Secondary exposure, chronic	-

Non-professional users:

Product and intended use	Exposure scenario	PPE	Inhalational uptake Exposure (mg/m^3)	Dermal uptake Exposure (mg/m^2)
Rozol Pat' In and around buildings for the control rodents	Cleaning the remains of 5 bait points per day. 6 sachets per bait point. Loading is not relevant due to protective packaging	None	Not considered for cleaning since negligible measured residues present during cleaning of bait boxes in pilot exposure study.	Measured as 4.09 mg product/gloves (geometric mean value) when cleaning up a bait box containing 6 sachets and disposing of the unwanted bait.
Dermal Exposure				
Measured value for amount of product on hands:			4.09 mg product/bait point during disposal	
Amount of blue paste on hands during disposal:			4.09 mg x 5 = 20.45 mg	

Total amount of blue paste on hands:	20.45 mg
Concentration of chlorophacinone:	50 mg/kg
Amount of chlorophacinone on hands:	50 x 20.45 ÷10^6 mg = 1.02 x 10^{-3} mg/day
Amount of chlorophacinone on skin:	1.02 x 10^{-3} mg/day
Dermal absorption of chlorophacinone:	1.7%
Systemic exposure of chlorophacinone:	1.73 x 10^{-5} mg/day
Operator body weight:	60 kg
Dermal exposure of chlorophacinone during disposal:	**2.89 x 10^{-7} mg/kg bw/day**

Indirect exposure: infants ingesting a bait:

Product and intended use	**Exposure scenario**	**Inhalational uptake**	**Dermal uptake**	**Oral uptake**
		Exposure concentration (mg/m^3)	**Exposure concentration (mg/m^2)**	**Exposure concentration (mg/event)**
Rozol Pat' In and around buildings for control of rats and mice	Non-users (adults, children and infants) will not be present during application. Infants may ingest part of the paste.	None.	Not applicable.	Assumed in EU guidance to be equivalent to 10 mg wax (infants) for transient mouthing of poison bait treated with repellent.

1. ORAL EXPOSURE ASSESSMENT FOR INFANTS BASED ON DEFAULT VALUES	
Default value for amount of product ingested :	10 mg
Concentration of chlorophacinone :	50 mg/kg
Amount of chlorophacinone ingested :	10 x 50 ÷ 10^6 mg = 0.00050 mg
Systemic exposure of chlorophacinone :	0.00050 mg/day
Body weight :	10 kg
Systemic exposure :	0.000050 mg/kg bw/day

Non-professional users, application in and around buildings for the control of rodents

Exposure scenario	**Component**	**CAS**	**Dermal Total [mg/day]**	**Dermal Total [mg/kg/d]**	**Inhalation Exposure [mg/m³]**
Application in and around buildings	Chlorophacinone	3691-35-8	1.73 x 10^{-5}	2.89 x 10^{-7}	-

Secondary exposure, infants ingesting a bait

Exposure scenario	Component	CAS	Oral Total [mg/day]	Oral Total [mg/kg/d]
Ingestion of a bait	Chlorophacinone	3691-35-8	0.00050	0.000050

Risk assessment

Non-professional users, application in and around buildings for the control of rodents

Exposure scenario	Component	CAS	AEL [mg/kg/d]	Absorption		Inhal ext [mg/m3]		Derm ext [mg/kg/d]		RCR total
				inh	derm	Act. Expo	RCR	Act. Expo	RCR	
Non-professional users, application in and around buildings	Chlorophacinone	3691-35-8	0.000033	No data	1.7 %	-	-	2.89 x 10-7	0.88%	0.88%

Indirect exposure: infants ingesting a bait:

Exposure scenario	Component	CAS	AEL [mg/kg/d]	Oral exposure [mg/kg/d]		RCR ges
				Act. Expo	RCR	
Secondary exposure, infants ingesting a bait	Chlorophacinone	3691-35-8	0.000033	0.000050	384.6%	151.5%

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

Annex 8: Translation of the Dutch labels

Professional use

A.
LEGAL INSTRUCTIONS FOR USE

This product can only be used for the control of black rats* and house mice in buildings, provided that the bait will be placed inside bait stations specifically designed for this purpose. Place the bait out of reach of children, birds, pets and other non-target animals. Keep away from food, drink and animal feeding stuffs.

The dose and control frequency as stated in the directions for use (B) should be sustained.

This product is intended for professional use only*.

B.
DIRECTIONS FOR USE

Uses:
Rozol Pat' is a ready-to-use paste bait for use against black rats and house mice. The sachets in which the paste is offered should not be opened, the rodents will eat through it. The bait should be placed inside bait stations out of reach of other animals (e.g. birds, mammals, pets or farm animals) and children. The bait should be secured to prevent carry of by the rodents. The bait stations should be marked to make clear that they contain rodenticide.

Place the bait stations in places where rats and mice often dwell: close to holes, on tracks, in concealed spaces such as dropped ceilings, and in places were the rodents find food or gnaw. Do not place the bait stations near surface water.
Wash hands after use.
As stated in the legal instructions for use, this product should not be used outside.
The product should be eaten in sufficient amount by the rats and mice during several days.

Dosing:

Control of rats:
Place the bait stations at 4 to 10 meter distance of each other, depending on the size of the infestation. Use 100 - 200 g bait per bait station.
In case of a black rat infestation, preferably higher bait points should be chosen.

Control of mice:
Place the bait stations at 1 to 3 meter distance of each other, depending on the size of the infestation. Use 30 - 50 g bait per bait station.

Follow up of treatment:
Check the uptake of bait after 3 days and thereupon on a regular basis based on bait uptake (weekly or every 14 days). Replace bait that is mouldy or contaminated completely. In case

that all bait is eaten at a bait station, refill the bait station and use more bait stations and/or increase the control frequency. Replace the bait until consumption of the bait stops.

When the uptake of bait has stopped, the remainder of the bait should be collected and safely removed as hazardous waste (cf. Eural). Dead animals (the first may be found after approximately 3 days) should also be collected, wrapped in plastic and disposed of in the dustbin, to prevent poisoning of other animals after eating the cadavers. Cats should be fed well during the treatment. In addition measures necessary for rat and mouse prevention should be taken (sealing entrances, removing possible food, etc.).

Note that if rats or mice are present in attached buildings, results will only remain when a control action is also performed at these locations.

Resistance management:
For the active substance chlorophacinone present in the product, resistance development against rodents in NL has occurred. There is a risk that mice and rats may develop further resistance. This product should therefore **not be used** in cases and areas in which resistance is known or likely, for example in cases in which earlier treatment with a chlorophacinone containing product did not result in a clear reduction of the population.

In most cases, treatment with this product should have achieved control within 35 days. Should activity of house mice, brown or black rats continue beyond this time, the likely cause should be determined and measures should be taken.

The use of this product should be combined with the implementation of an integrated pest management system (IPM). This product should not be used preventively.

First aid:
Keep this label available when medical advice is sought.
In case of emergency contact a physician.
Antidote: Vitamin K1 (under medical supervision).

[*] In NL the use is restricted to professional use and control of black rats and mice, for reasons of resistance management. See 2.5.4 for explanation.