HET COLLEGE VOOR DE TOELATING VAN GEWASBESCHERMINGSMIDDELEN EN BIOCIDEN

Dit is een rectificatie van het besluit van 2 november 2012. Het besluit van 2 november 2012 komt te vervallen. De waarschuwingszin S37 wordt toegevoegd voor verpakkingen voor professioneel gebruik.

1 TOELATING

Gelet op de aanvraag d.d. 20 juni 2011 (20110643 TNB) van

LiphaTech S.A.S.
3 Bonnel BP
47480 PONT DU CASSE
FRANKRIJK

tot verkrijging van een toelating als bedoeld in artikel 49, eerste lid, Wet gewasbeschermingsmiddelen en biociden voor de biocide, op basis van de werkzame stof bromadiolon,

MAKI PAT'

gelet op artikel 44, Wet gewasbeschermingsmiddelen en biociden,

BESLUIT HET COLLEGE als volgt:

1.1 Toelating

1. Het middel MAKI PAT' is toegelaten voor de in bijlage I genoemde toepassingen onder nummer 13839 N met ingang van datum dezes. Voor de gronden van dit besluit wordt verwezen naar bijlage II bij dit besluit.
2. De toelating geldt tot 30 juni 2016.

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.

Een middel wordt aangeboden en geëtiketteerd ofwel voor professioneel gebruik, ofwel voor niet-professioneel gebruik.

1.3 Gebruik
Het middel dat uitsluitend bestemd is voor professioneel gebruik mag slechts worden gebruikt met inachtneming van hetgeen in bijlage I Prof onder A bij dit besluit is voorgeschreven.

Het middel dat uitsluitend bestemd is voor niet-professioneel gebruik mag slechts worden gebruikt met inachtneming van hetgeen in bijlage I Niet Prof onder A bij dit besluit is voorgeschreven.

1.4 Classificatie en etikettering
Gelet op artikel 50, eerste lid, sub d, Wet gewasbeschermingsmiddelen en biociden,

1. De aanduidingen, welke ingevolge artikelen 9.2.3.1 en 9.2.3.2 van de Wet milieubeheer en artikelen 14, 15a, 15b, 15c en 15d van de Nadere regels verpakking en aanduiding milieugevaarlijke stoffen en preparaten op de verpakking moeten worden vermeld, worden hierbij vastgesteld als volgt:

   aard van het preparaat: Lokmiddel (klaar voor gebruik)

werkzame stof:	*gehalte:*
Bromadiolon	0.005%

   op verpakkingen die (mede) bestemd zijn voor huishoudelijk gebruik: het kca-logo (het kca-logo is het logo voor klein chemisch afval bestaande uit een afvalbak met een kruis erdoor als opgenomen in bijlage III bij de genoemde Nadere regels)

<u>letterlijk en zonder enige aanvulling:</u>

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

gevaarsymbool:	*aanduiding:*
Xn	Schadelijk

<u>Verpakking voor professioneel gebruik</u>
Waarschuwingszinnen:

R48/20/21/22 -Schadelijk: gevaar voor ernstige schade aan de gezondheid bij langdurige blootstelling bij inademing, aanraking met de huid en opname door de mond.

Veiligheidsaanbevelingen:

S02	-Buiten bereik van kinderen bewaren.
S37	-Draag geschikte handschoenen
S46	-In geval van inslikken onmiddellijk een arts raadplegen en verpakking of etiket tonen.

<u>Verpakking voor niet-professioneel gebruik</u>
Waarschuwingszinnen:

R48/20/21/22 -Schadelijk: gevaar voor ernstige schade aan de gezondheid bij langdurige blootstelling bij inademing, aanraking met de huid en opname door de mond.

Veiligheidsaanbevelingen:

S02	-Buiten bereik van kinderen bewaren.
S13	-Verwijderd houden van eet- en drinkwaren en van diervoeder.
S46	-In geval van inslikken onmiddellijk een arts raadplegen en verpakking of etiket tonen.

Specifieke vermeldingen: -

2. Behalve de onder 1. bedoelde en de overige bij de Wet Milieugevaarlijke Stoffen en Nadere regels verpakking en aanduiding milieugevaarlijke stoffen en preparaten 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 AANVRAAG

Het betreft een aanvraag tot verkrijging van een toelating van het middel MAKI PAT' (13839 N), een middel op basis van de werkzame stof bromadiolon. Het middel wordt aangevraagd voor professionale gebruikers als middel ter bestrijding van zwarte en bruine ratten en huismuizen in ruimten en voor niet-professionele gebruikers als middel ter bestrijding van huismuizen in ruimten.

2.2 Informatie met betrekking tot de stof

Er zijn in Nederland reeds andere middelen op basis van de werkzame stof bromadiolon toegelaten.
De werkzame stof bromadiolon is bij Richtlijn 2009/92/EC, dd 31 juli 2009 van de Europese Commissie van de Europese Gemeenschappen opgenomen in Bijlage I van Richtlijn 98/8/EG.

2.3 Karakterisering van het middel

Bromadiolone is a second-generation single-dose anticoagulant rodenticide. It disrupts the normal blood clotting mechanisms resulting in increased bleeding tendency and, within a relatively short time frame (typically 2-4 days), profuse haemorrhage and death. Effectiveness of the active substance depends on exposure (i.e. consumption of the bait by the target organism).

2.4 Voorgeschiedenis

De aanvraag is op 29 juni 2011 ontvangen; op 4 juli 2011 zijn de verschuldigde aanvraagkosten ontvangen. Bij brief d.d. 29 maart 2012 is de aanvraag in behandeling genomen.

2.5 Eindconclusie

Bij gebruik volgens het Wettelijk Gebruiksvoorschrift/Gebruiksaanwijzing is het middel MAKI PAT' op basis van de werkzame stof bromadiolon voldoende werkzaam en heeft het geen schadelijke uitwerking op de gezondheid van de mens en het milieu (artikel 49, Wet gewasbeschermingsmiddelen en biociden).

Degene wiens belang rechtstreeks bij dit besluit is betrokken kan gelet op artikel 119, eerste lid, Wet gewasbeschermingsmiddelen en biociden 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 september 2013

HET COLLEGE VOOR DE TOELATING
VAN GEWASBESCHERMINGSMIDDELEN
EN BIOCIDEN,

ir. J.F. de Leeuw
voorzitter

HET COLLEGE VOOR DE TOELATING VAN GEWASBESCHERMINGSMIDDELEN EN BIOCIDEN

BIJLAGE I bij het besluit d.d. 6 september 2013 tot toelating van het middel MAKI PAT', toelatingnummer 13839 N

A.
WETTELIJK GEBRUIKSVOORSCHRIFT

Toegestaan is uitsluitend het gebruik als middel ter bestrijding van zwarte en bruine 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 controlefrequentie zoals aangegeven in de gebruiksaanwijzing moet worden aangehouden.

Het middel is uitsluitend bestemd voor professioneel gebruik.

B.
GEBRUIKSAANWIJZING

Toepassingen:

MAKI PAT' is een kant-en-klaar lokaas in pastaformulering tegen zwarte en bruine ratten en huismuizen. Het zakje waarin MAKI 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.

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

De lokaasdozen vervolgens uitzetten op plaatsen waar de 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 waterafvoersystemen waar het middel met water in contact kan komen. Na gebruik handen wassen.

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

Dosering:

Bestrijding van 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: in geval van zwarte ratten 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, bruine ratten en/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.

Het gebruik van dit middel is alleen toegestaan indien het een onderdeel vormt van een integrated pest management systeem (IPM).

Resistentie management:
Voor de werkzame stof aanwezig in het middel, bromadiolon, is er een risico dat muizen of ratten resistentie ontwikkelen. Gebruik dit middel daarom niet in gevallen dat resistentie waarschijnlijk is, bijvoorbeeld in gevallen dat vorige bestrijdingsacties met bromadiolon bevattende middelen niet hebben geresulteerd in een duidelijke vermindering van de populatie. Het middel mag niet permanent gebruikt worden.

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 I bij het besluit d.d. 6 september 2013 tot toelating van het middel MAKI PAT', toelatingnummer 13839 N

A.
WETTELIJK GEBRUIKSVOORSCHRIFT

Toegestaan is uitsluitend het gebruik als middel ter bestrijding van 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 controlefrequentie zoals aangegeven in de gebruiksaanwijzing moet worden aangehouden.

Het middel is uitsluitend bestemd voor niet-professioneel gebruik.

B.
GEBRUIKSAANWIJZING

Toepassingen:

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

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

De lokaasdozen vervolgens uitzetten op plaatsen waar 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. 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 de huismuizen.

Richtlijnen:

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.

Wanneer de opname van lokaas is gestopt, de resten van het lokaas verzamelen en in plastic verpakt aanbieden bij het Klein Chemisch Afval (KCA) depot. 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.).

Als 28 dagen na start van de behandeling de bestrijding van de muizen niet afdoende is dient een professionele plaagdierbestrijder ingeschakeld te worden.
Neem voorzorgsmaatregelen om herbesmetting met muizen te voorkomen.

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

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)

Product Assessment Report

MAKI PAT’

21-09-2012

Internal registration/file no:	20110643
Authorisation/Registration no:	13839N
Granting date/entry into force of authorisation/ registration:	02-11-2012
Expiry date of authorisation/ registration:	30-06-2016
Active ingredient:	Bromadiolone
Product type:	PT14

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

Contents

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:	rollinf@desangosse.com

1.1.1 Person authorised for communication on behalf of the applicant

Name:	Dr. François ROLLIN
Function:	Regulatory manager
Address:	Bonnel BP 3
City:	Pont du Casse
Postal Code:	47480
Country:	France
Telephone:	+33 563 693683
Fax:	+33 553 479 501
E-mail address:	rollinf@desangosse.com

1.2 Current authorisation holder[1]

Not applicable.

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:	rollinf@desangosse.com
Letter of appointment for the applicant to	Not applicable

[1] Applies only to existing authorisations

represent the authorisation holder provided (yes/no):	

1.4 Information about the product application

Application received:	04-07-2011
Application reported complete:	29-03-2012
Type of application:	First authorisation
Further information:	Applicant has indicated to submit an application for mutual recognition in BE, CZ, DE, DK, EL, FR, HU, IT, PL, PT, RO, SI, SK, UK.

1.5 Information about the biocidal product

1.5.1 General information

Trade name:	MAKI PAT'
Manufacturer's development code number(s), if appropriate:	BROPA0,0050_05F_F01153_00
Product type:	14
Composition of the product (identity and content of active substance(s) and substances of concern; full composition see confidential annex):	Bromadiolone 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)

Overall use pattern (manner and area of use):	MAKI PAT' is a red 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**[1] bait per bait station. Bait points placed at **4 to 10** meter distance of each other. Mice: **up to 50 g**[1] 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 Dutch labels, see below this table[2].
Use Restrictions:	Not for use in sewers.

[1]For rodenticides a minimum application rate should be stated in The Netherlands. Based on expert opinion these have been determined at 100g for rats and 30 g for mice.

Translation of the Dutch labels:

Professional use

A.
LEGAL INSTRUCTIONS FOR USE

This product can only be used for the control of black and brown rats and house mice in buildings, provided that the bait should 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:
MAKI PAT' is a ready-to-use paste bait for use against black and brown 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.

As stated in the legal instructions for use, this product should not be used outside.

Do not place the bait stations near water drainage systems where it can come into contact with water. Wash hands after use.

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 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 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.

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.

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.

The use of this product should be combined with the implementation of an integrated pest management system (IPM).

Resistance management:
For the active substance bromadiolone present in the product, there is a risk that mice and rats may develop resistance. This product should therefore not be used in cases in which resistance is likely, for example in cases in which earlier treatment with a bromadiolone containing product did not result in a clear reduction of the population. The product should not be used permanently.

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

Non-professional use:

A.
LEGAL INSTRUCTIONS FOR USE

This product can only be used for the control of house mice in buildings, provided that the bait should 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 non-professional use only.

B.
DIRECTIONS FOR USE

Uses:

MAKI PAT' is a ready-to-use paste bait for use against 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 (do not tear the sachets!). The bait stations should be marked to make clear that they contain rodenticide.

Place the bait stations in places where 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.

As stated in the legal instructions for use, this product should not be used outside.

Do not place the bait stations near water drainage systems where it can come into contact with water. Wash hands after use.

The product should be eaten in sufficient amount by the rats and mice during several days.

Dosing:

Control of mice:
Bait stations will be placed at 1 to 3 meter distance of each other, depending on the size of the infestation. Use 30 - 50 g bait per 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, wrapped in plastic and safely removed as 'Klein Chemisch Afval' (KCA, small chemical waste). 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.).

When the control of house mice appears to be insufficient after 28 days from the start of the treatment, consult a professional pest controller. Take precautionary measures to prevent reinfestation with mice.

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.

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

1.5.3 Information on active substance(s)[2]

Active substance chemical name:	Bromadiolone
CAS No:	28772-56-7
EC No:	249-205-9
Purity (minimum, g/kg or g/l):	≥ 96.9% w/w
Inclusion directive:	Annex I of 98/8/EG for PT14
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
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
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1.5.4 Information on the substance(s) of concern[3]

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

1.6.2 Access to documentation

The applicant LiphaTech S.A.S is owner of the data of the Bromadiolone Assessment report for pt14.

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

2 Summary of the product assessment

2.1 Identity related issues

Trade name	Maki Pat'			
Active ingredient	Purity (%w/w)	CAS No.	EC No.	Content (%)
Bro-madiolone	≥ 96.9% w/w	28772-56-7	249-205-9	0.0050 (pure active)

Remark: Bromadiolone consists of four enantiomers (two racemic dl diastereoisomers present at the specification ≥80% and ≤20%).

No substance of concern is found in Maki 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: two years in PP. Extrapolation to PE is allowed.

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

Proposed classification based on Directive 1999/45/EC

Professional user:

Symbol:	Xn	
Indication of danger:	Harmful	
R-phrases:	R48/20/21/22	Danger of serious damage to health by prolonged oral, dermal and inhalation exposure
S-phrases:	S2	Keep out of the reach of children
	S37	Wear protective gloves
	S46	If swallowed, seek medical advice immediately and show this container or label

Explanation:	
Hazard symbol:	Xn is obligatory with the assigned R-phrase.
Risk phrases:	R48/20/21/22 is assigned based on the calculation using the proposed classification of the Technical Committee on Classification and Labelling for bromadiolone (TC&L, May 2007), which is the current status although

	the discussion at ECHA is not finalised. The R48/20/21/22 classification and specific limit values are also included/supported by data in the CAR of bromadiolone.
Safety phrases:	S13 is not obligatory for professional users with the assigned R-phrase. S37 is assigned based on the risk assessment.
Other:	-

Non-professional user:

Symbol:	Xn	
Indication of danger:	Harmful	
R-phrases:	R48/20/21/22	Danger of serious damage to health by prolonged oral, dermal and inhalation exposure
S-phrases:	S2	Keep out of the reach of children
	S13	Keep away from food, drink and animal feedingstuffs
	S46	If swallowed, seek medical advice immediately and show this container or label

Explanation:	
Hazard symbol:	Xn is obligatory with the assigned R-phrase.
Risk phrases:	R48/20/21/22 is assigned based on the calculation using the proposed classification of the Technical Committee on Classification and Labelling for bromadiolone (TC&L, May 2007), which is the current status although the discussion at ECHA is not finalised. The R48/20/21/22 classification and specific limit values are also included/supported by data in the CAR of bromadiolone.
Safety phrases:	-
Other:	The product is labelled as harmful, therefore tactile warning of danger is obligatory for non-professional users.

<u>Proposed classification based on Regulation EC 1272/2008</u>

Professional user:

Signal word:	Warning		
Pictogram:	GHS08		
	Hazard class-and-Category	**Code**	**Hazard statement**
Hazard statements:	STOT RE Cat. 2	H373	May cause damage to haemolytic system through prolonged or repeated exposure
Precautionary statements:		P102	Keep out of reach of children
		P260	Do not breathe dust
		P280a	Wear protective gloves
		P314	Get medical advice/attention if you feel unwell
		P501	Dispose of contents/container to …

Explanation:	
Pictogram:	GSH08 is obligatory with the assigned H-statement.
H-statements:	H373 is assigned based on the human toxiciolgical data provided in the CAR for bromadiolone and the proposed classification of the Technical Committee on Classification and Labelling for bromadiolone (TC&L, May 2007), which is the current status although the discussion at ECHA is not finalised. Furthermore, bromadiolone is included in the Registry of

	submitted Harmonised Classification and Labelling intentions (see www.echa.eu).
P-statements:	P-statements are chosen according to the Guidance on Labelling and Packaging in accordance with Regulation (EC) No 1272/2008 and the risk assessment.

Non-professional user:

Signal word:	Warning		
Pictogram:	GHS08		
	Hazard class-and-Category	**Code**	**Hazard statement**
Hazard statements:	STOT RE Cat. 2	H373	May cause damage to haemolytic system through prolonged or repeated exposure
Precautionary statements:		P102	Keep out of reach of children
		P260	Do not breathe dust
		P314	Get medical advice/attention if you feel unwell
		P501	Dispose of contents/container to …

Explanation:	
Pictogram:	GSH08 is obligatory with the assigned H-statement.
H-statements:	H373 is assigned based on the human toxiciolgical data provided in the CAR for bromadiolone and the proposed classification of the Technical Committee on Classification and Labelling for bromadiolone (TC&L, May 2007), which is the current status although the discussion at ECHA is not finalised. Furthermore, bromadiolone is included in the Registry of submitted Harmonised Classification and Labelling intentions (see www.echa.eu).
P-statements:	P-statements are chosen according to the Guidance on Labelling and Packaging in accordance with Regulation (EC) No 1272/2008 and the risk assessment.

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

Classification and labeling 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 authorised by RMS**	**Packaging sizes authorised in NL***
PP bucket with lid	Paper bag/PP sachet: 10 to 40 g	Up to 21 kg	800g to 20 kg
Cardboard carton with integral plastic (PP/PE) bag	Paper bag/PP sachet: 10 to 40 g	Up to 25 kg	800g to 20 kg
Plastic (PP/PE)	Paper bag/PP sachet: 10 to 40 g	Up to 1.5 kg	800 g to 1.5 kg

container			
Plastic (PP/PE) pouch	Paper bag/PP sachet: 10 to 40 g	Up to 20 kg	800 g to 20 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

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

Non-professional use

Outer packaging type applied for	Inner packaging type applied for	Packaging sizes authorised by RMS	Packaging sizes authorised in NL*
PP bucket with lid	Paper bag/PP sachet: 10 to 40 g	Up to 4 kg	Up to 200g
Cardboard carton with integral plastic (PP/PE) bag	Paper bag/PP sachet: 10 to 40 g	Up to 3 kg	Up to 200g
Plastic (PP/PE) container	Paper bag/PP sachet: 10 to 40 g	Up to 3 kg	Up to 200g
Plastic (PP/PE) pouch	Paper bag/PP sachet: 10 to 40 g	Up to 3 kg	Up to 200g
Carton containing prefilled PP/HDPE/PS bait stations	Paper bag/PP sachet: 10 to 40 g	Up to 3 kg	Up to 200g

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

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 bromadiolone are detailed in the Annex I dossier, Doc IIIA, Section 3.

The methods for the active substance bromadiolone, 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

Other indications of flammability	EEC A10 (flammability of solids)	Study conducted with alternative formulation F00060. Nominal 50 mg/kg.	Paste formulation F00060 is not flammable and red paste F01153 is expected to have the same property.	Demangel, B. (2008) IIIB 3.4-01 GLP
Acidity / Alkalinity	CIPAC MT75	Red Paste F001153. Batch F1292. Nominal 50 mg/kg.	pH of a 1% dispersion was 6.43	Caruel, H. (2010) IIIB 3.5-01 GLP
Relative density / bulk density	FAO method using displacement	Red paste F001153 Batch F1473 Nominal 50 mg/kg	Density: 1.149 g/mL measured at 25°C.	Caruel, H. (2011) IIIB 3.6-02 GLP
Storage stability – stability and shelf life	GIFAP Monograph No.17	Red Paste F001153. Batch F1292. Nominal 50 mg/kg.	Content of a.s.: Initial: 60.24 mg/kg Final: 54.42 mg/kg The active substance content showed an acceptable decrease, aspect of test item and packaging and pH of 1% dispersion did not change significantly after storage at 25°C for 2 years.	Caruel, H. (2007), IIIB 3.7-01
Effects of temperature	Accelerated storage stability 40°C - 8 weeks According to CIPAC MT 46.1	Red paste F001153 Batch F1292 Nominal 50 mg/kg	Content of a.s.: Initial:60.73 mg/kg Final:58.41 mg/kg The active substance content remained stable, aspect of test item and packaging and pH of 1% dispersion did not change significantly after storage at 40°C for 8 weeks. Test was performed in PP packaging.	Caruel, H. (2009) IIIB 3.7-02 GLP
Effects of light	n.a.			

Reactivity towards container material	GIFAP Monograph No.17	Red Paste F001153. Batch F1292. Nominal 50 mg/kg.	Packaging: PP box stable for 2 years.	Caruel, H. (2007), IIIB 3.7-01
	Accelerated storage stability 54°C - 2 weeks	Bromadiolone paste. Batch F1473. a.i.: 51.86 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
Impurities in technical active substance:	HPLC/UV
active substance in the formulation:	HPLC/UV

2.4 Risk assessment for Physico-chemical properties

No new data/information on physico-chemical properties has been submitted for the product or for the active substance(s) that provides additional data for the risk assessment.

2.5 Effectiveness against target organisms

2.5.1 Function

The product is a rodenticide (PT14) based on 0.005% w/w bromadiolone. The product is for both professional and non-professional use.

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

MAKI PAT' paste bait is used to control:
Rattus norvegicus (Norway rat, Brown rat)
Rattus rattus (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.

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

2.5.3 Effects on target organisms

Bromadiolone is a second-generation single-dose anticoagulant rodenticide. It disrupts the normal blood clotting mechanisms resulting in increased bleeding tendency and, within a relatively short time frame (typically 2-4 days), 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 with MAKI PAT', a bait concentration of 50 mg/kg is proposed.

MAKI PAT' differs from the products described in the CAR of bromadiolone 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 bromadiolone. The results are summarised in table 2.5.3.0 below.

Besides these efficacy studies, two studies have been provided showing that the warfarine resistant strains of R. norvegicus and M. musculus were actually resistant to warfarine (IIIB 5.10.2-09 and 10). Furthermore, studies have been provided showing that neither the packaging of the paste in polyethylene or polypropylene bags, nor the addition of the bittering agent bitrex to the paste had any effect on the palatability of the paste for R. norvegicus (IIIB 5.10.2-07 and 08).

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 *	Reference
Red paste LR0265	Mouse *Mus musculus* (wild strain, sensitive to warfarin)	Laboratory study, using bait aged for 2.5 month, single free-choice test with a total of 24 mixed sex animals, 4 day exposure. Test method: EPPO protocol	Palatability of the treated bait was greater than the reference diet (attractivity value: 0.90). Efficacy was 96% occurring between 7 and 11 days after initial consumption.	IIIB 5.10.2-02
Red paste F01153	Mouse *Mus musculus* (wild strain, resistant to warfarin)	Laboratory study, using bait aged for 4 months, single free-choice test with a total of 24 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 (attractivity value: 0.87). Efficacy was 100% occurring between 7 and 14 days after initial consumption.	IIIB 5.10.2-03
Red paste F001153	Mouse *Mus musculus* (wild strain, resistant to warfarin)	Laboratory study, using bait aged for 32 months, single free-choice test with a total of 10 male and 12 female mice, 4 day exposure Test method: EPPO PP1/214(1)	Palatability of the treated bait was greater than that of the reference diet (attractivity value: 0.79). Efficacy was 100% occurring between 4 and 14 days after initial consumption.	IIIB 5.10.2-14

Test substance	Test organism(s)	Test system / concentrations applied / exposure time	Test results *	Reference
Wheat rodenticide LR0234	Mouse *Mus musculus* (wild strain)	Field study conducted at 2 sites, in and around urban buildings with high mice populations. Bait stations contained 40g bait at 12 locations per site (distances 2-15m between stations). The number of mice estimated on the maximum food intake recorded during treatment was 109 and 76 mice. 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 was 35 days (incl. pre and post baiting period).	Based on consumption estimates the efficacy under field conditions was 100% at each site. At both sites, in the treatment census, the bait began at a high level and then quickly decreased as the bait began to take effect in reducing and controlling the house mice population. At Site 1, 12 dead mice were collected, and 11 mice at Site 2, with the cause of death confirmed as bait consumption with signs of intra-peritoneal bleeding.	IIIB 5.10.2-12
Red paste F01153	Mouse *Mus musculus* (wild strain)	Field study conducted at 1 site, an equestrian centre, in and around buildings with high mice activity. Bait stations contained 20-50g bait at 20 locations. The number of mice estimated on the maximum food intake recorded during treatment was 150-200 animals. Assessments were conducted throughout the duration of the trial, and were undertaken at day 3, 7, 14, 21, 28. During each assessment the food/bait at each station was weighed and replenished, and the consumption in grams was calculated. During the treatment, searches were conducted for dead and dying mice in and around the site. The duration of the whole test was 28 days. The post baiting period was not conducted.	The bait consumption decreased very quickly (max consumption 520 g on day 7); at day 28 consumption of the bait was 0. Approximately 40 dead mice were collected during the treatment (day 7 and 14). Efficacy based on consumption estimates cannot be calculated as there was no post baiting period conducted, but given the strong decrease in consumption to 0 at the end of the trial and the high number of mice found dead, efficacy is sufficiently shown. The paste bait tested was effective under field conditions against mice when in competition against natural food sources and other environmental factors.	IIIB 5.10.2-16
Red paste LR0265	Rat *Rattus norvegicus* (wild strain, sensitive to warfarin)	Laboratory study, using fresh bait, two free-choice tests with a total of 20 mixed sex animals, 4 day exposure. Test method: EPPO protocol	Palatability of the treated bait was equivalent to or similar to that of the reference diet in each test (attractivity values: 0.51 and 0.66). Efficacy was 100% occurring between 7 and 14 days after initial consumption.	IIIB 5.10.2-01

Test substance	Test organism(s)	Test system / concentrations applied / exposure time	Test results *	Reference
Red paste F01153	Rat *Rattus norvegicus* (wild strain, resistant to warfarin)	Laboratory study, using bait aged for 4 months, two 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 equivalent to or similar to that of the reference diet in each test (attractivity values: 0.66 and 0.43). Efficacy was 90% occurring between 4 and 15 days after initial consumption.	IIIB 5.10.2-04
Red paste F01153	Rat *Rattus norvegicus* (wild strain, resistant to warfarin)	Laboratory study, using bait aged for 32 months, single free-choice test with a total of 5 male and 5 female rats, 4 day exposure Test method: EPPO PP1/214(1)	Palatability of the treated bait was equivalent to or similar to that of the reference diet (attractivity value: 0.45). Efficacy was 90% occurring between 7 and 14 days after initial consumption.	IIIB 5.10.2-13
Oat rodenticide LR0216	Rat *Rattus norvegicus* (wild strain)	Field study conducted at 2 sites, in and around agricultural buildings with high rat populations. Bait stations contained 150 or 200g bait at 14 locations (site 1) and 24 locations (site 2), (distances 2-15m between stations). The number of rats estimated on the maximum food intake recorded during treatment was 50 and 84 rats. 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 rats in and around the site. The duration of the whole test was 48-52 days.	Based on consumption estimates the efficacy under field conditions was 100% at each site. At both sites, in the treatment census, the bait began at a high level and then quickly decreased as the bait began to take effect in reducing and controlling the wild brown rats population. At Site 1, 9 dead rats were collected, and 17 rats at site 2, with the cause of death confirmed as bait consumption with signs of intra-peritoneal bleeding.	IIIB 5.10.2-11
Blue paste F00060 (active: 25 mg/kg difethialon)	Rat *Rattus norvegicus* (wild strain)	Field study conducted at 2 sites in France with high rat activity. Bait stations contained 150 g at 18 to 20 locations across the test sites and were positioned 2-15 metres apart. The number of rats calculated on the maximum food intake recorded before treatment was 90 for site 1 and 64 for site 2. 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 approximately 1.5 months for both sites.	Based on consumption estimates the efficacy under field conditions was 97.5% at site 1 and 99.7% at site 2. At Site 1, 23 dead rats were collected and 9 rats at Site 2, with the cause of death confirmed as bait consumption with signs of intra-peritoneal bleeding.	IIIB 5.10.2-15

Test substance	Test organism(s)	Test system / concentrations applied / exposure time	Test results *	Reference
Blue paste F00060 (active: 25 mg/kg difethialon) (Bridging study)	Rat *Rattus norvegicus* (wild strain, warfarin resistant)	Laboratory study, using bait aged for 7 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 that of the reference diet in each test (attractivity values: 0.45 and 0.47). Efficacy was 100% occurring between 3 and 9 days after initial consumption.	IIIB 5.10.2-17
Red paste F01153	Rat *Rattus rattus* (wild strain, sensitive to warfarin)	Laboratory study, using bait aged for 4 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 that of the reference diet in each test (attractivity values: 0.47 and 0.45). Efficacy was 90% occurring between 7 and 14 days after initial consumption.	IIIB 5.10.2-05
Red paste F01153	Rat *Rattus rattus* (wild strain)	Field study conducted at 2 farm sites in France with high rat activity. Bait stations contained 150 g at 10 to 17 locations across the test sites and were positioned 2-15 metres apart. The number of rats calculated on the maximum food intake recorded before treatment was 57 for site 1 and 29 for site 2. Assessments were conducted throughout the trial and were done every 1-4 days (every two days in the high consumption period); baits were weighed and replenished, then the amount consumed was calculated. The duration of the whole test was approximately 2 months for both sites.	Based on consumption estimates the efficacy under field conditions was 100% at each site. At Site 1, 16 dead rats were collected, and 10 rats at Site 2, with the cause of death confirmed as bait consumption with signs of intra-peritoneal bleeding.	IIIB 5.10.2-06

* 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).

Lab studies:
Efficacy against *R. norvegicus* and *M. musculus* has been sufficiently demonstrated in test with the product (Red paste F01153) and a similar product (Red paste LR0265). Since *R. norvegicus* and *M. musculus* wild strains are tested with Red paste LR0265 and *R. norvegicus* and *M. musculus* warfarin-resistant strains were tested with Red paste F01153 and both gave good results, it can be concluded that there is no significant difference in palatability between the two bait formulations.
Efficacy of the product in lab tests has been sufficiently demonstrated for *R. rattus* (90% efficacy).
Therefore it can be concluded that efficacy has been sufficiently demonstrated in laboratory mortality and palatability tests for all target organisms, both wild strain and warfarine resistant strains. The studies show that the palatability of the product is still sufficient after a storage period of 32 months.

Field studies:

Efficacy of the product in field tests has been sufficiently demonstrated for *R. rattus* (100% efficacy).
For *M. musculus,* efficacy of Red paste F01153 in the field could not be calculated due to the missing post baiting period. However, given the strong decrease in consumption to 0 at the end of the trial and the high number of mice found dead (comparable or even higher numbers than in the field study on wheat rodenticide LR0234, which included a post baiting period), efficacy in the field is sufficiently shown for *M. musculus*.
For *R. norvegicus* two field test with another product have been provided: blue paste F00060 with active difethialon (25mg/kg), but similar bait (paste in sachets) and oat rodenticide LR0216 with similar active bromadiolone (50mg/kg), but different bait (grain). The results of the field study with F00060 show that *R. norvegicus* can open and have access to this type of bait (gel in sachets) and are sufficiently attracted to this bait under field conditions. Furthermore, this product has a high efficacy (97.5%-99.7%) with the active substance difethialon. Results of the field study with LR0216 show that this product with the active bromadiolone has a high efficacy (100%). Both products have a comparable high efficacy in the field (97.5-100%) based on consumption before and after baiting and comparable percentages of rats are found dead (26/134; 32/154). However, mean daily consumption of the pasta bait (502 and 497g) was somewhat lower than that of the oat bait (548 and 816g). Laboratory studies (free-choice tests) with pasta products, one with difethialon (IIIB 5.10.2-17) and one with bromadiolone (IIIB 5.10.2-1), can be used as bridging study. These laboratory studies show a mean consumption rate of 45.18g/kg body weight (difethialon) and 31.6 g/kg body weight (bromadiolone) and 100% mortality. Since a lower amount of bait with bromadiolone already gives the same mortality as a slightly higher amount of bait with difethialon, we assume that the field studies are representative for the efficacy of MAKI PAT'.

It is therefore concluded that efficacy has been sufficiently demonstrated for all target organisms in the field. Note that efficacy in sewers has not been demonstrated.

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 red 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 one or more sachets per bait station. Place 1 station every 1 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 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.	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. Dispose 1 station every 1 to 1.5 m	Dispose the product, check 3 days after first application, then regularly every 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. Dispose 1 station every 2 to 3 m	Dispose the product, check 3 days after first application, then every 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. Dispose 1 station every 4 to 5 m.	Dispose the product, check 3 days after first application, then regularly as consumption persist then every 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. Dispose 1 station every 8 to 10 m.	Dispose the product, check 3 days after first application, then every 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.	

2.5.3.2 Mode of action

Bromadiolone is a second-generation single-dose anticoagulant rodenticide. It disrupts the normal blood clotting mechanisms resulting in increased bleeding tendency and, within a relatively short time frame (typically 2-4 days), 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 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.

Efficacy in sewers has not been demonstrated. Furthermore, the Dutch CA is of the opinion considering the risk of primary and secondary poising determined in the PAR, the use

needs to be restricted to indoor use only for authorization in the Netherlands (see section 2.8).
The area of use is therefore restricted for professionals to in and around buildings, and waste dumps and for non-professionals to in and around buildings.

2.5.3.4 Resistance

Bromadiolone paste is efficacious against warfarin resistant (first generation anticoagulant) rodents (rats and mice).
Some suspected cases of resistance to bromadiolone have been reported in some areas in the UK. Therefore, a management strategy should be outlined to minimise the likelihood of resistance to the active substance developing in the target species.

2.5.3.4 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 anticoagulant rodenticides is often misdiagnosed as resistance. The success of a control campaign is often dependent 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 anticoagulant 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 anticoagulant rodenticides as permanent baits routinely. Use permanent baits only where there is a clear and identified risk of immigration or introduction or where protection is afforded to high risk areas.
- Monitoring of rodent activity should be undertaken using visual survey, through the use of non-toxic placebo monitors or by other effective means.
- Record details of treatment.
- Where rodent activity persists due to problems other than resistance, use alternate baits or baiting strategy, extend the baiting programme or apply alternate control techniques to eliminate the residual infestation (acute or sub-acute rodenticides, gassing or trapping).
- Ensure that complete elimination of the infestation is achieved.
- As appropriate during the rodenticide treatment apply effective Integrated Pest Management measures (remove alternate food sources, remove water sources, remove harbourage and proof susceptible areas against rodent access).

Thirdly, when resistance to anticoagulants 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 resistance management strategies. It can not be expected that non-professionals have any knowledge on resistance. Therefore, it is stated on the Dutch label that a professional pest controller should be consulted when the control of the rodents is not sufficient.

2.5.3.5 Humaneness

The use of bromadiolone 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 bromadiolone 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

In the PAR a resistance management strategies is outlined. A short remark on resistance is added to the Dutch label (WG/GA), this differs for professional and non-professional use since non-professionals are not expected to have knowledge on resistance.
For professional use:

For the active substance in this product, bromodialone, there is a risk of development of resistance. Therefore, this product should not be used in cases where resistance against bomodialone is presumed, for instance in cases where the last treatment with bromodialone containing products did not results in a reduction of the population.

For non-professional use (mice only 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.

For the convenience of the competent authorities authorising this product through mutual recognition the Dutch labels, translated in English, are added to the PAR (see 1.5.2).

2.6 Exposure assessment

2.6.1 Description of the intended use(s)

MAKI PAT' is a ready-to-use rodenticide paste bait in sachets based on 0.005% w/w bromadiolone. The product 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.

2.6.2 Assessment of exposure to humans and the environment

For the product MAKI PAT' no new operator exposure studies have been submitted by the applicant. The applicant has submitted the human exposure assessment which was based on two operator exposure studies using wax block bait which were also assessed in the CAR of bromadiolone and used for risk assessment. These 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. Wax blocks were considered to be a suitable surrogate for the paste bait in protective sachets. The submitted exposure assessment was assessed and updated if necessary by the RMS NL.

The environmental exposure and risk assessment of the biocidal product red paste F01153 containing 50 mg/kg bromadiolone (MAKI PAT') from the applicant was examined appropriately according to standard requirements. No new studies have been provided concerning environmental exposure. 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 MAKI 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 MAKI PAT'. The RMS NL has updated this risk assessment for the environmental aspect. For authorisation purposes the risk assessment of MAKI PAT' performed by the applicant is included in this Product Authorisation Report.
Environmental exposure to soil occurs when MAKI PAT' is deployed outdoors. Non-target vertebrates may be exposed to MAKI PAT' either directly by ingestion of exposed paste (primary poisoning) or indirectly by ingestion of the carcasses of target rodents that contain bromadiolone residues (secondary poisoning). See for more detail section 2.8 below.

2.7 Risk assessment for human health

MAKI PAT' is a ready-to-use paste bait used for the control of rats and mice.

MAKI PAT' is not a reference product of the CAR for bromadiolone; however, the risk assessment in the CAR was performed for two products, Super Caid AS Appat and Super Caid Bloc, respectively. Based on the composition of these two products which have been evaluated in the CAR and the composition of MAKI PAT' , the results of the evaluation with these products are considered to be applicable for MAKI PAT' .

GLP-compliant studies have been submitted by the applicant with the product MAKI PAT' to address acute oral and dermal toxicity, skin and eye irritation and skin sensitization (see 2.7.1.3 for results). The applicant also provided a GLP-compliant acute inhalation toxicity study with Bromadiolone (1%) powder, containing 1% bromadiolone and 99% wheat starch, which is considered to be a suitable surrogate for inhalation toxicity of bromadiolone grain formulations. The LC50 was < 0.523 mg/L air, indicating that the product is toxic by inhalation and should be classified as T, R23. However, as bromadialone is not volatile (vapour pressure 2.13 x 10^{-8} Pa at 25°C) and the product is applied in the form of paste, inhalation is considered to be not a relevant exposure route. Therefore no classification is warranted for acute inhalation toxicity. In addition GLP-compliant dermal penetration studies have been provided which are evaluated in the CAR .

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

GLP-compliant studies have been submitted by the applicant with the product MAKI PAT' to address acute oral and dermal toxicity, skin and eye irritation and skin sensitization.

a) Acute oral toxicity

Following gavage application of a single limit dose of 2000 mg/kg bw MAKI PAT' to the group of 6 female rats no mortalities occurred. The median lethal oral dose, $LD_{50,}$ was >2000 mg/kg bw. Based on this MAKI PAT' does not need to be classified for oral toxicity.

b) Acute dermal toxicity

Following dermal administration of a limit dose of 2000 mg/kg bw MAKI PAT' to the group of 5 male and 5 female rats there were no mortalities. The median lethal dermal dose LD_{50} was > 2000 mg/kg bw. Based on this MAKI PAT' does not need to be classified for dermal toxicity.

c) Skin irritation

In the skin irritation study with three female rabbits only weak erythema (average score at 24, 48 and 72 hours 0.11) was observed following 4 hours semi-occlusive application. Based on this MAKI PAT' is considered not irritating to skin.

d) Eye irritation

Instillation of MAKI PAT' to the eyes of three rabbits resulted in no corneal changes and no iridial reaction. Conjunctival redness and swelling, no more than slight in severity, transient in duration, were apparent at the first observation and redness persisted to 24 hours. No

other reactions were observed. Based on this MAKI PAT' is considered to be not irritating to eyes.

e) Skin sensitization

MAKI PAT' gave no evidence for inducing delayed contact hypersensitivity in a Buehler test conducted in twenty guinea pigs. None of the test animals showed any dermal irritation during the induction phase and no reactions were evident in the control or test group following challenge. Based on this MAKI PAT' is considered to be not a skin sensitizer.

The applicant also provided a GLP-compliant acute inhalation toxicity study with Bromadiolone (1%) powder, containing 1% bromadiolone and 99% wheat starch, which is considered to be a suitable surrogate for inhalation toxicity of bromadiolone grain formulations. The LC50 was < 0.523 mg/L air, indicating that the product is toxic by inhalation and should be classified as T, R23. However, as bromadiolone is not volatile (vapour pressure 2.13 x 10^{-8} Pa at 25°C) and the product is applied in the form of paste, inhalation is considered to be not a relevant exposure route, and the product will not be classified for acute inhalation toxicity.

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 MAKI PAT' contains the active substance bromadialone (pure: 0.050 g/kg). MAKI PAT' is a ready-to-use paste bait used 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. MAKI PAT' is supplied ready for use in sachets (weight: 10-40 g) which are intended to be used directly (not to be opened by the user).

The product is intended for both professional and non-professional use. It should be noted, however, that non-professional use against rats is not permitted in the Netherlands by national specific policy, but will be assessed in this risk assessment..

The potential for exposure to bromadiolone 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

Bromadiolone is not volatile and MAKI PAT' bait is a non-dusty cereal based paste formulation. Therefore, the risk of inhalation exposure to bromadiolone 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

MAKI PAT' is supplied ready for use in polypropylene/paper 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 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. 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

MAKI 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". For non-users, risk of oral exposure to residues during or after application is considered to be negligible if the instruction of use is followed. 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. MAKI PAT' bait also contains a bittering agent to prevent infants 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 MAKI 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.

MAKI PAT' is supplied in sachets ready to use by professional users. A maximum dose of 200 g for rats and 50 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 by the applicant. As the product is supplied in ready to use polypropylene/paper protective sachets, which will not be opened by the user, dermal exposure during loading is considered to be negligible, as protective packaging will prevent any contact of the user with the product. 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.

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 bromadiolone 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 bromadiolone 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 bromadialone 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 bromadiolone; however, as a worst-case approach, the assessment of the products (Super Caid AS Appat

and Super Caid Bloc) 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. However, a total number of cleaning manipulations was either identical or lower in the CAR (15 for the application in and around buildings and waste dumps, and none for the application in open areas); thus, the approach proposed by the applicant represents a more worst-case scenario.

The applicant has submitted two operator exposure studies using wax block bait which is considered to be a suitable surrogate for red 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 bromadiolone and used for risk assessment. 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 bromadialone is considered to be 1.6%. The same dermal absorption value is used in the CAR of bromadiolone.

The total systemic exposure to bromadiolone of professional operators cleaning up MAKI PAT' bait considered 75 manipulations per day according to HEEG (2010) is estimated at 8.18×10^{-7} mg bromadiolone/kg bw/day without PPE. For two additional scenarios (application around waste dump and application in open area) considered by the registrant the total systemic exposure of 2.73×10^{-6} mg bromadiolone/kg bw/day and 1.64×10^{-6} mg bromadiolone/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 8.18×10^{-8}, 2.73×10^{-7} and 1.64×10^{-7} mg bromadiolone/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 MAKI 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 bromadialone handled per day.

As the product is supplied in ready to use polypropylene/paper protective sachets, dermal exposure during loading is considered to be negligible, as protective packaging will prevent any contact of the user with the product. 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 bromadiolone for non-professional users. However, as a worst-case approach, the assessment of the products (Super Caid AS Appat and Super Caid Bloc) 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 bromadialone is considered to be 1.6%.

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 bromadiolone of non-professional operators cleaning up MAKI PAT' bait in and around buildings is estimated at 2.7×10^{-7} mg/kg bw/day.

Indirect exposure to MAKI 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 red paste. Body weight is assumed to be 10 kg for infants. Total indirect systemic exposure to bromadiolone following the ingestion of MAKI PAT' bait is estimated at 0.00005 mg/kg bw/day for infants. However, MAKI 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.

In the combined Assessment Report of bromadiolone prepared for TM III 2010, the derivation of an acceptable level of exposure value for single use (AEL_{acute}) is based on the teratogenicity study in rabbits, considering the LOAEL of 2 µg/kg bw and a safety factor of 600 (10 for interspecies and 10 for intraspecies variability, 2 for using LOAEL instead of NOAEL and an extra factor of 3 for severity of effects). Applying a correction of 70% oral absorption results in an AEL_{acute} of 0.0023 µg/kg bw. To derive an AEL_{medium}, for repeated exposure, the subchronic study in rabbit is used. The NOAEL in this study is 0.5 µg/kg bw based on the prolonged prothrombin time seen at 1 µg/kg bw. With a safety factor of 300 and with correction of 70% oral absorption, this leads to an AEL_{medium} of 0.0012 µg/kg bw. To set an $AEL_{chronic}$ the same NOAEL as for AEL_{medium} is used, as no chronic studies have been performed. The extra safety factor of 3 will apart from severity of effects also cover for the differences in exposure time.

2.7.3.1 Risk for Professional Users

The following total systemic exposures to bromadiolone 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: 8.18×10^{-7}, 2.73×10^{-6} and 1.64×10^{-6} mg bromadiolone/kg bw/day, respectively
With PPE (gloves), considering 90% reduction: 8.18×10^{-8}, 2.73×10^{-7} and 1.64×10^{-7} mg bromadiolone/kg bw/day.

As professional users are expected to come in contact with MAKI PAT' on a regular basis, the resulting estimated exposure values are compared with the $AEL_{chronic}$ of 0.0012 µg/kg bw. The resulting exposure estimates correspond to the following percentages of $AEL_{chronic}$:

Without PPE: 68.2%, 227.5% and 136.7%, respectively
With PPE (gloves, 90% reduction): 6.8%, 22.8% and 13.7%, respectively

Based on the risk assessment, it can be concluded that no adverse health effects are expected for the protected (gloves) professional operator after dermal and respiratory exposure to bromadiolone as a result of the application of MAKI PAT' .

2.7.3.2 Risk for non-professional users and the general public

The total systemic exposure of 2.73 x 10^{-7} mg bromadiolone/kg bw/day is estimated for non-professional users of MAKI PAT' . As non-professional users are not expected to apply MAKI PAT' on daily basis, the comparison with the $AEL_{chronic}$ is not considered appropriate. Therefore the resulting exposure estimate is compared with the AEL_{acute} of 0.0023 µg/kg bw. The resulting estimated exposure corresponds to 11.9% of AEL_{acute}.

Based on the risk assessment, it can be concluded that no adverse health effects are expected for the unprotected non-professional operator, including the general public, after dermal and respiratory exposure to bromadiolone as a result of the application of MAKI PAT' .

Total indirect systemic exposure to bromadiolone following the ingestion of MAKI PAT' bait is estimated at 0.00005 mg/kg bw/day for infants. As a possible ingestion will be an incidental occurrence, the resulting exposure is compared with the AEL_{acute} of 0.0023 µg/kg bw. The estimated exposure corresponds to 2174% of AEL_{acute}. The risk to infants thus appears to be of concern. According to DOC I of CAR on bromadiolone the products containing bromadiolone are required to carry precautionary phrases on the label to mitigate the risk of secondary human exposure. These include:

- "Prevent access to bait by children, birds and non-target animals (particularly dogs, cats, pigs and poultry)"
- "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"

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 bromadiolone as a result of use of MAKI PAT' .
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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

Bromadiolone is manufactured in the EU at AlzChem Trostberg GmbH (Germany). The plant is ISO compliant and Government Approved (a certificate is available). The premix of active substance used to prepare products is manufactured by Liphatech S.A.S plant at Pont du Casse (France). The plant is ISO compliant and Government Approved (a certificate is available). Production of bromadiolone and formulation of paste baits at these

sites takes place in closed systems. Production 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 MAKI PAT' containing 50 mg bromadiolone/kg in the scenario in and around buildings, in open areas and around waste sites. MAKI PAT' is a ready-to-use product (paste) and further dilution prior to deployment 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 bromadiolone (Product Type 14).
Application of MAKI PAT' containing 50 mg/kg bromadiolone 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 bromadiolone in the environment and the effect of the active substance on environmental organisms can be consulted in Doc IIA of the final Assessment Report of LiphaTech (March 2008) for bromadiolone (PT14). The PNEC derivation is also described in detail in the Assessment Report for bromadiolone (Product Type 14), section 2.8.2.4 and a summary is included in the table below.

Summary of the PNECs derived for bromadiolone in the different compartments

Compartment	Organism	Endpoint	AF	PNEC
Aquatic	Green algae (*S.subspicatus*)	EbC_{50} = 0.17 mg/L	1000 * 10	0.000017 mg/L
STP	Microorganisms from an activated sludge	EC_{50} = 31.6 mg/L	100	0.316 mg/L
Sediment	Sediment-dwelling organisms	Covered by the aquatic compartment		
Soil	Earthworm (Eisenia f*oetida*)	LC_{50} > 8.4 mg/kg ww	1000	0.0084 mg/kg ww
Terrestrial	Birds (Japanese quail)	NOEC = 0.1 mg/kg food NOEL = 0.01138 mg/kg bw/d	30	0.0033 mg/kg food 0.00038 mg/kg bw/d
Terrestrial	Mammals (rat) Mammals (dog)	NOAEL (difethialone) = 2 µg/kg bw/d NOAEL =8 µg/kg bw/d	90 30	0.00044 mg/kg food[1] 0.000022 mg/kg bw/d 0.011 mg/kg food[1] 0.00027 mg/kg bw/d

1 calculated using a conversion factor bw/dfi = 4 (EUBEES mean value for owls).

2.8.1 Exposure Assessment

An environmental exposure assessment has been conducted based on the fate and distribution properties of the active substance, bromadiolone, as determined from laboratory studies. The predicted environmental concentration (PEC) of bromadiolone 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 and on the EUBEES 2 'Emission scenario document for biocides used as rodenticides' (Larsen, 2003)[4]. These PEC values and the underlying assumptions are also confirmed in the final Assessment Report for bromadiolone of LiphaTech (Product Type 14).

2.8.1.1 Fate and distribution in the environment

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

2.8.1.2 PEC in surface water, ground water and sediment

The PEC of bromadiolone 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 bromadiolone from the placing of MAKI 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 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 bromadiolone will not move to groundwater in significant quantities.

2.8.1.3 PEC in air

The vapour pressure of bromadiolone at ambient temperature is 2.13 × 10-8 Pa (OECD 104). Furthermore, the Henry's law constant for bromadiolone is 8.99 × 10-7 Pa.m3.mol-1 (based on a water solubility of 12.5 mg/L). Bromadiolone is therefore not considered volatile and 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).
In addition, the photochemical oxidative degradation half-life of bromadiolone in air has been estimated using the Atmospheric Oxidation Program v1.90 (AOPWIN), which is based on the structural activity relationship (QSAR) methods developed by Atkinson (1985 to 1996). The half-lives for the hydroxyl and ozone reactions in air are estimated to be 2.1 and 2.0 hours respectively, indicating that, if present in air, bromadiolone would not be expected to persist.

Bromadiolone is not expected to volatilise to or persist in air in significant quantities; consequently, the potential concentration of bromadiolone in air is considered to be negligible.

2.8.1.4 PEC in soil

The PECs of bromadiolone in soil arising from the various usage scenarios (in and around buildings, open areas and waste dumps) are considered, as follows:

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[4] 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).

In and around buildings

The PEC of bromadiolone in soil is considered for uses in and around buildings as follows: Exposure of the terrestrial compartment (soil) will occur when MAKI 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 MAKI 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. In the case of bromadiolone, however, this is reduced to 22% in view of the extensive metabolism seen in a study with rats (see Doc. III-A, Section 6.2-01 of the Assessment Report for bromadiolone). This study is summarised below:

Groups of male rats were dosed orally with ^{14}C-bromadiolone on a single occasion at a level of 5.0 mg/kg bw. Three areas were investigated, mass balance, biliary excretion and protein binding. Samples of urine, faeces and bile (from cannulated rats) were collected up to sacrifice at 48 hours after dosing. Blood was collected at 1, 2 and 4 hours after dosing. Extracts were prepared from faeces and gastro-intestinal tract samples. At 1, 2 and 4 hours after dosing radioactivity was extensively (>98.8%) bound to plasma proteins. No change in the degree of binding was observed up to 4 hours. The only tissue sample examined was the gastro-intestinal tract; radioactivity in the G.I tract at 48 hours accounted for 18.0% of the administered dose. Distribution in other tissues or loss in expired carbon dioxide was not measured in the study, hence no exact oral absorption value could be set. Faecal excretion accounted for 53.3% of the radioactive dose after 48 hours while only 0.86% of dose was present in the urine in the first 48 hours following dosing. Radioactivity in the bile duct of cannulated rats accounted for 46.5% of the dose after 48 hours, with urine and faeces from these animals containing 19.4% of the dose. Bromadiolone was rapidly absorbed by rats. Absorbed radioactivity was excreted relatively slowly and almost entirely via the bile and faeces. Urinary excretion represented a minor route of elimination. Analysis of faecal and gastro-intestinal tract extracts showed a single major metabolite, up to 10 minor components and polar radioactivity remaining at the origin of the TLC plate plus unchanged bromadiolone. The unchanged parent, bromadiolone, accounted for ca 22% of the dose in faeces and a further ca 6% of the dose in the G.I. tract. The single major metabolite accounted for ca 15% of the dose in the faeces and ca 4% of the dose in the G.I. tract. Polar radioactivity accounted for > 80% of the sample radioactivity in bile. Treatment of bile with β-glucuronidase reduced the polar fraction to 45% of the sample radioactivity, with unchanged bromadiolone and the single major metabolite amongst the components released. MS analysis suggested the single metabolite was a hydroxylated anologue of bromadiolone; hydroxylation was proposed on the benzylic carbon atom. This is consistent with other similar molecules in the AVK class. None of the metabolites of this class of compounds has been shown to be more, or as, toxic as the unchanged parent.

The maximum application rate for MAKI PAT' containing 50 mg bromadiolone/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/m3, the mass of soil affected by the direct release around each secured bait point is 15.3 kg. To estimate the concentration of bromadiolone 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 m2). Based on the depth and soil density values used above, 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 bromadiolone, as demonstrated by field studies.

In both scenarios, the direct and disperse bromadiolone 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 MAKI PAT' (240 g) per secured bait point;
Fc_{prod} = concentration of bromadiolone 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 0.22 for disperse release).

Concentrations of bromadiolone in soil following baiting around buildings with MAKI PAT'

Baiting scenario (EUBEES 2)	Direct release (mg/0.09 m^2)	Disperse release (mg/550 m^2)	PECsoil (mg bromadiolone/kg ww)[a]	
			mean[b]	max[c]
Realistic worst-case	0.60	132.0	0.0014	0.0053
Typical	0.18	39.6	0.0004	0.0016
a based on uniform distribution to 10 cm depth and wet soil bulk density of 1.7 g/cm3; b disperse release applied to total area (550 m2); c direct + disperse release within 10 cm in front of and to sides of each bait point.				

Clocal concentrations (PECsoil, mg bromadiolone/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 = $\frac{E\ local,\ soil,\ indirect}{93{,}500}$ = 0.0014 mg/kg (0.0004 mg/kg ww);

Maximum concentration in soil: Clocal, direct + Clocal, indirect = 0.0053 mg/kg (0.0016 mg/kg).

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 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 bromadiolone in soil following baiting in open areas with paste bait

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

a based on 2 × (6 × 40 g) pastes containing 50 mg bromadiolone/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 cm3) and a wet soil bulk density of 1.7 g/cm3.

The predicted concentration of 0.415 mg bromadiolone/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 bromadiolone 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 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, but this value is reduced to 22% in this case, based on the extensive metabolism of bromadiolone by rats.

According to the worst-case scenario, the total bromadiolone 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 bromadiolone in the paste product (50 mg/kg)
N_{app} = the number of applications (7)
$F_{release,\ soil}$ = the fraction released to soil (0.22).

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

Baiting scenario	Release to soil (mg bromadiolone/ha)	PECsoil (mg bromadiolone/kg)[a]
Worst-case (EUBEES 2)[b]	3080	0.0018
a based on uniform distribution to 10 cm depth and wet soil bulk density of 1.7 g/cm3; b based on seven applications of bromadiolone in pastes/year.		

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

The exposure of bromadiolone 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 bromadiolone (Product Type 14).

2.8.2.1 Aquatic compartment (incl. sediment)

Contamination of surface water or sediment with bromadiolone following the use of MAKI 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 bromadiolone will not move to groundwater in significant quantities. Therefore, bromadiolone 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 MAKI 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 and at the label it should be indicated: Do not place the bait stations near water drainage systems where it can come into contact with water.

2.8.2.2 Atmosphere

Bromadiolone exhibits a negligible vapour pressure of 2.13×10^{-8} Pa at ambient temperature. The use pattern and means by which bromadiolone is deployed in paste bait, coupled with its low volatility, ensure that exposure to non-target biota via the atmosphere is highly unlikely.

2.8.2.3 Terrestrial compartment

Soil exposure occurs both through a combination of direct and indirect releases from the use of MAKI 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 MAKI PAT' is deployed outdoors.

EUBEES 2 considers a scenario that entails outdoor baiting with rodenticide 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. 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. Since MAKI PAT' is individually wrapped in sachets, the release is anticipated to be lower and a direct release of 0.1% is considered 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. In the case of bromadiolone, however, this is reduced to 22% in view of the extensive metabolism seen in a study with rats.

The maximum application rate for MAKI PAT' 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 bait stations (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 an anticoagulant rodenticide such as bromadiolone.

Concentrations of bromadiolone in soil following baiting around buildings with MAKI PAT'

Baiting scenario (EUBEES 2)	**Direct release (mg/0.09 m^2)**	**Disperse release (mg/550 m^2)**	**PECsoil (mg bromadiolone/kg ww)[a]**	
			mean[b]	**max[c]**
Realistic worst-case	0.60	132.0	0.0014	0.0053
Typical	0.18	39.6	0.0004	0.0016
a based on uniform distribution to 10 cm depth and wet soil bulk density of 1.7 g/cm3; b disperse release applied to total area (550 m2); c direct + disperse release within 10 cm in front of and to sides of each bait point.				

The risks to the terrestrial environment posed by contamination of soil by bromadiolone following "realistic worst-case" and "typical" outdoor use of MAKI 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 bromadiolone.

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

Baiting scenario (EUBEES 2)	**maximum PECsoil (mg bromadiolone/kg ww)**	**PNECsoil (mg bromadiolone/kg ww)**	**PEC/PNEC ratio**
Realistic worst-case	0.0053	0.0084	0.6
Typical	0.0016	0.0084	0.2

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

Open areas

MAKI 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.

Concentrations of bromadiolone in soil following baiting in open areas with bait pastes.

Baiting scenario (EUBEES 2)	**Bromadiolone applied (mg)[a]**	**Total direct deposition (mg)[b]**	**PECsoil (mg bromadiolone/kg ww)[c]**
Worst-case	24.0	6.0	0.415
a based on 2 × (6 × 40 g) pastes containing 50 mg bromadiolone/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 bromadiolone/kg soil represents the worst-case in the immediate vicinity of each bait application.

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

Baiting scenario (EUBEES 2)	**PECsoil (mg bromadiolone/kg ww)**	**PNECsoil (mg bromadiolone/kg ww)**	**PEC/PNEC ratio**
Worst-case	0.415	0.0084	49.4

The PEC/PNEC ratios calculated indicate a potential 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, but this value is reduced to 22% in this case, based on the extensive metabolism of bromadiolone by rats. According to the worst-case scenario, the total bromadiolone release (Elocalsoil, 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 bromadiolone in the paste product (50 mg/kg)

N_{app} = the number of applications (7)

$F_{release,\ soil}$ = the fraction released to soil (0.22).

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

Baiting scenario	Release to soil (mg bromadiolone/ha)	PECsoil (mg bromadiolone/kg)[a]
Worst-case (EUBEES 2)[b]	3080	0.0018
[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 bromadiolone in pastes/year.		

The risks to earthworms posed by contamination of soil by bromadiolone 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 bromadiolone following use of paste bait at waste dumps and landfill sites

Baiting scenario	PECsoil (mg bromadiolone/kg ww)	PNECsoil (mg bromadiolone/kg ww)	PEC/PNEC ratio
Worst-case (EUBEES 2)	0.0018	0.0084	0.2

The PEC/PNEC ratio is less than 1.0 under the worst case suggested by EUBEES 2. The exposure to bromadiolone that arises from the use of MAKI PAT' at waste dumps and landfill sites therefore presents no unacceptable risks to soil-dwelling 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 MAKI PAT' containing bromadiolone either directly by ingestion of exposed paste (primary poisoning) or indirectly by ingestion of the carcasses of target rodents that contain bromadiolone residues (secondary poisoning).
Based on toxicity data bromadiolone 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 (PNECoral). For the long-term exposure the estimated concentration of the active substance in the animal can be calculated and compared with the NOAEL.	Risk is quantified as the ratio between the estimated concentration in predatory mammals or birds and the no-observed-adverse-effect levels (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 bromadiolone. Because of many uncertainties the following assessments of risk should be considered as a worst case.

Bromadiolone is presented in a matrix of cereal flour bound together with hydrogenated vegetable fat. Presentation of bromadiolone in this processed matrix has the benefit of reducing the appeal of the bait to non-target organisms that would otherwise readily consume loose bromadiolone-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.

MAKI 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 red dye in bromadiolone paste bait is likely to reduce its appeal as a potential food item still further.

Gemmeke (2000)[5] 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)[6] 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)[7], (citing Kalmbach (1943)[8], Kalmbach and Welch (1946)[9], Caithness and Williams (1971)[10], Pank, (1976)[11] and Brunner and Coman (1983)[12]) 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.

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

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

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

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

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

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

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

[12] 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.

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”.

PNEC oral 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 bromadiolone) 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, with 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 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 bromadialone taken up via bromadialone containing products is as toxic and equal available to non-target animals as bromadialone 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:
The PNECoral for birds was derived from an avian reproduction study with Japanese quail on the related substance difenacoum. The study was done over 20 weeks and the highest administered diet concentration of difenacoum, 0.1 mg/kg diet, did not result in any substance-related effects, thus resulting in a NOEC of 0.1 mg/kg diet. As agreed at TMII-07 in Brussels in May-07 the long-term PNEC for bromadiolone for birds is derived from this study. No extra assessment factor due to read across is added with the argument that difenacoum is more toxic than bromadiolone, both for aquatic organisms (acute) and birds (acute and short-term).

According to the Risk Assessment TGD the oral assessment factor (AForal) for extrapolation of bird toxicity data from a chronic study is 30 resulting in a PNECoral (bird) of 3.3 µg/kg food.

Mammals:

Rats

The most sensitive subchronic study for rats is a 90 days study (of the analogue difethialone) which resulted in a NOAEL of 2 µg/kg bw/d. With a conversion factor of 20 for conversion of the NOAEL which is based on bodyweight to a NOEC which is based on daily food intak,e a NOEC of 40 µg/kg food is calculated.
According to the Risk Assessment TGD the oral assessment factor (AForal) for extrapolation of mammalian toxicity data from a 90 d subchronic study is 90 resulting in a PNECoral (rat) of 0.44 µg/kg food.

Dogs

The most sensitive subchronic study for dogs is a 90 days study which resulted in a NOAEL of 8 µg/kg bw/d. With a conversion factor of 40 for conversion of the NOAEL which is based on bodyweight to a NOEC which is based on daily food intake, a NOEC of 40 µg/kg food is calculated.
According to the Risk Assessment TGD the oral assessment factor (AForal) for extrapolation of mammalian toxicity data from a 90 d subchronic study is 30 resulting in a PNECoral (dog) of 11 µg/kg food. It must be noted that the assessment factor for long-term effects on dogs is set to 30, which accounts for laboratory to field and subchronic to chronic extrapolation, since the PNEC value for dog is used only for the long-term risk assessment of primary poisoning of this species.

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:

The PNECoral for birds was derived from an avian reproduction study with Japanese quail on the related substance difenacoum. The study was done over 20 weeks and the NOEL was 0.01138 mg/kg bw/d.
According to the Risk Assessment TGD the oral assessment factor (AForal) for extrapolation of bird toxicity data from a chronic study is 30 resulting in a PNECoral (bird) of 0.38 µg/kg bw/d.

Mammals:

Rats

The most sensitive subchronic study for rats is a 90 days study (of the analogue difethialone) which resulted in a NOAEL of 2 µg/kg bw/d.
According to the Risk Assessment TGD the oral assessment factor (AForal) for extrapolation of mammalian toxicity data from a 90 d subchronic study is 90 resulting in a PNECoral (rat) of 0.022 µg/kg bw/d.

Dogs

The most sensitive subchronic study for dogs is a 90 days study which resulted in a NOAEL of 8 µg/kg bw/d.
According to the Risk Assessment TGD the oral assessment factor (AForal) for extrapolation of mammalian toxicity data from a 90 d subchronic study is 30 resulting in a PNECoral (dog) of 0.27 µg/kg food. It must be noted that the assessment factor for long-term effects on dogs is set to 30, which accounts for laboratory to field and subchronic to chronic extrapolation, since the PNEC value for dog is used only for the long-term risk assessment of primary poisoning of this species.

Primary poisoning

In and around buildings
Non-target birds and mammals may encounter paste bait containing bromadiolone 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 spilled 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 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 bromadiolone that may be taken from a bait point. These provide bromadiolone ingestion estimates for a first tier, estimate of exposure to non-target mammals.

Quantities of bromadiolone 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 bromadiolone per bait point (mg)	Proportion of bait point contents accessible (%)	Bromadiolone 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 bromadiolone in food and the PNECoral. It is assumed that non-target animals have direct access to an unlimited amount of formulated product. Bromadiolone concentration in the bait is 50 mg/kg and hence the PECoral is 50 mg/kg food. The PNECoral for birds is 3.3 µg/kg food, the PNECoral for rats is 0.44 µg/kg food and the PNECoral for dog is 11 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. 15,000 instead of 15,152).

Birds: PEC/PNEC ≈ 15,000
Rats: PEC/PNEC ≈ 110,000
Dogs: PEC/PNEC ≈ 4,500

This conservative approach clearly highlights a high risk to birds and non-target mammals if bromadiolone 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 bromadiolone/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 mammal bodyweight [g], C is the concentration of active substance in the fresh diet 50 mg/kg (paste bait), 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 bromadiolone 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 bromadiolone 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 difethialone 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	8.1 (dog)
Cat	2.83	2.27	Min 0.56 (rat)[1]
Pig	1.20	0.96	Min 0.56 (rat)[1]
General non	2.52	2.01	Min 0.56 (rat)[1]

Non-target mammal	ETE [mg/kg bw] Step 1	ETE [mg/kg bw] Step 2	LD50 mammals/birds [mg/kg bw]
target mammal[2]			
Tree sparrow	8.64	6.91	138 (quail)
Chaffinch	7.50	6.00	138 (quail)
Woodpigeon	2.71	2.17	138 (quail)
Pheasant	2.69	2.16	138 (quail)
[1] single dosage 21 days post exposure period (no valid LD50 for cat / pig available) [2] Body weight of a fox was chosen			

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	8.1 (dog)
Cat	1.98	1.59	Min 0.56 (rat)[1]
Pig	0.84	0.67	Min 0.56 (rat) [1]
General non target mammal[2]	1.76	1.41	Min 0.56 (rat) [1]
Tree sparrow	6.05	4.84	138 (quail)
Chaffinch	5.25	4.20	138 (quail)
Woodpigeon	1.90	1.52	138 (quail)
Pheasant	1.89	1.51	138 (quail)
[1] single dosage 21 days post exposure period. LD50 is estimated between 0.56-0.84 mg/kg bw (no valid LD50 for cat / pig available) [2] Body weight of a fox was chosen			

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 138 mg/kg bw. For mammals ETE is above the single dose LD50 values. 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 birds and 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 bromadiolone /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 bromadiolone 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 605,000) and for birds (up to 63,000).

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 [mg/kg bw]	PEC/PNEC Step 1[1]	PEC/PNEC Step 2[2]
Dog	6.3	5.06	0.00027	23,000	19,000
Cat	13.3	10.7	0.000022	605,000	484,000
Pig	3.33	2.66	0.000022	551,000	121,000
Non target mammal[3]	11.8	9.47	0.000022	536,000	430,000
Tree sparrow	23.95	19.16	0.00038	63,000	50,000
Chaffinch	20.80	16.64	0.00038	55,000	44,000
Woodpigeon	7.51	6.01	0.00038	20,000	16,000
Pheasant	7.47	5.98	0.00038	20,000	16,000

[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 bromadiolone 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 do not exceed the LD50 value for birds both without and with excretion. Concerns excist to the risk for mammals (except dogs) feeding on bait.

ETE values after 5 days intake of bromadiolone (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 bromadiolone in the non-target animals outweigh loss of bromadiolone in non-target animals due to excretion. For the long-term assessment all PEC/PNECoral ratios are far above one. In general small animals have a higher risk than large ones.

The worst-case PEC/PNEC ratio for birds at step 1 is about 63,000 (tree sparrow) and about 605,000 for mammals (cat).

The worst-case PEC/PNEC ratio for birds at step 2 is about 50,000 (tree sparrow) and about 484,000 for mammals (cat).

Worst case assumptions have been made. It was assumed that the non-target animals have fed entirely, respectively mostly, on bromadiolone 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 bromadiolone 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 20,000 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 0.005 % 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.

The values for birds are slightly less severe. 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 16,000 and for smaller birds above 44,000. 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 0.1 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 bromadiolone potentially accessible to non-target vertebrates at one bait point directly with the food based PNECoral of 0.38 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 bromadiolone 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 bromadione, 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
Bromadiolone 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 bromadiolone residues in target rodents, based on its concentration in the bait, feeding (bromadiolone intake) and excretion (bromadiolone 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 containing bromadiolone 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)[13]. 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 bromadiolone residues in target rodents, based on its concentration in paste, feeding (bromadiolone intake) and excretion (bromadiolone 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 bromadiolone 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.

[13] 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).

The ETE values for rodents (mice and rats) are based on three theoretical levels of ingestion of paste 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 bromadiolone in paste equal to 50 mg/kg. The ETE values are therefore 5.0, 2.5, 1.00 mg bromadiolone/kg bw for levels of bait consumption equivalent to 100%, 50% and 20% of daily food intake, respectively.

According to EUBEES 2, 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 rats dosed with 5.0 mg bromadiolone/kg bw and sacrificed after 48 hours. A single significant metabolite and several minor breakdown products of bromadiolone were identified, and parent bromadiolone contributed only 22% of the faecal radioactivity. According to WHO (1995)[14], the effects of anticoagulant rodenticides in rats are mediated by the intact parent molecule rather than their metabolites. The default daily elimination rate of 30% for anticoagulant rodenticides prescribed by EUBEES 2 is in general accordance with the mean values measured for bromadiolone, which averaged 32.7% over the first three days and ranged from 12.0% for day 1 to 53.3% for day 2.

Elimination of bromadiolone residues from rats dosed with 5 mg/kg bw

Sampling time (days)	**Radioactivity excreted (% of applied)**	
	Urine	**Faeces**
1	0.59	12.0
2	0.86	53.3

The residue levels are also based on an assumption that ingestion of bromadiolone in paste 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 bromadiolone 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 bromadiolone 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] Used for TIER 1 short-term (Frodent = 1) [2] Used for TIER 1 long-term (Frodent = 0.5)			

[14] WHO (1995). International Programme on Chemical Safety. Anticoagulant Rodenticides (Environmental Health Criteria 175). World Health Organisation, Geneva.

Calculated residue patterns suggest that levels increase following each daily intake until day 5, after which the rodents are assumed to eat no more paste bait, but to continue to excrete residues at approximately 30% per day, resulting in a reduction of residues by approximately 50% between the last intake on day 5 and death on day 7.

However, comparison with semi-field data shows these calculated values to be overestimated. In a study of the effects of secondary exposure to bromadiolone on *Bubo virginianus*, a population of 20 male and 20 female rats was first fed on a diet that comprised exclusively bait pellets containing 50 mg bromadiolone/kg. Bait availability was limited to 15 g/rat/day and was withdrawn and substituted by uncontaminated feed after three days. All rats were euthanised on the morning of the fifth day. Five male rat carcasses were randomly selected and individually homogenised, then analysed to determine whole-body residues of bromadiolone, whilst the remaining carcasses were used as the exposure vehicle for the owls. Measured cumulative bait consumption by male rats during the three-day exposure period was equivalent to bromadiolone intakes ranging from 4.9 to 15.5 mg/kg, with a mean of 11.02 mg/kg bw, or 3.67 mg bromadiolone/kg bw/day. The data tabulated below show the levels of bromadiolone residues predicted according to EUBEES 2, based on the mean daily intake regime described above.

Residues of bromadiolone in rats, predicted according to EUBEES 2, based on a mean measured bait intake equivalent to 3.67 mg bromadiolone/kg bw/day and 30% daily elimination.

Time	**Residues of bromadiolone in rats (mg/kg bw)**
Day 1, after first meal (bait)	3.67
Day 2, before new meal	2.57
Day 2, after second meal (bait)	6.24
Day 3, before new meal	4.37
Day 3, after third meal (bait)	8.04
Day 4, before new meal (uncontaminated feed)	5.63
Day 5, at termination	3.94

The predicted mean bromadiolone residue in male rat carcases at termination on day 5 is 3.94 mg/kg bw. By contrast, the measured concentrations of bromadiolone in five whole male rats ranged from 0.35 to 1.55 mg/kg bw (mean: 0.9 mg/kg bw). The mean measured residue concentration at termination on day 5 corresponds to just 23% of the value predicted for the same timepoint according to EUBEES 2. In the table below and in the following assessments, the various concentrations of bromadiolone in target rodents on day 5 and day 7 have therefore been lowered *pro rata* to reflect real, measured residues.

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

Time	**Residues of bromadiolone in target rodent (mg/kg bw)**		
	20% bait consumption	**50% bait consumption**	**100% bait consumption**
Day 5 after last meal[1]	0.638	1.595	3.189
Day 7 (mean time to death)[2]	0.319	0.797	1.595

[1] Based on values calculated according to EUBEES 2 and corrected by × 23%;
[2] Based on values calculated according to EUBEES 2 and corrected by × 23%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 62 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 bromadiolone 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 bromadiolone 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 bromadiolone in target rodent (mg/kg bw)**		
	20% bait consumption	**50% bait consumption**	**100% bait consumption**
Day 5 after last meal[1]	0.319	0.798	1.595
Day 7 (mean time to death)[2]	0.159	0.399	0.797
[1] Based on values calculated according to EUBEES 2 and corrected by × 23%; [2] Based on values calculated according to EUBEES 2 and corrected by × 23% 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 bromadiolone 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**
96.7	242	483	48	121	242
PNECoral = 0.0033 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 bromadiolone 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**
725	1810	3620	362	906	1880
PNECoral = 0.00044 mg/kg food					

The above PECoral/PNECoral quotients ranging from 48 to 483 for birds and from 362 to 3620 for mammals assume that rodents containing bromadiolone 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 0.0033 mg/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 bromadiolone 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 bromadiolone 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 bromadiolone at day 5 after the last meal is 3.189 mg/kg food. As Frodent in this scenario is 0.5 instead of 1 the residue of bromadiolone at day 5 after the last meal is 1.595 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 bromadiolone. In each case, bromadiolone bait has contributed either 100%, 50% or 20% of the daily food intake of the rodents eaten by the birds.

Estimated intakes and concentrations of bromadiolone (BDN) in predatory and scavenging birds and mammals ingesting target rodents, assuming poisoned rodents comprise 50% of a bird's diet and that 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]	
			BDN consumed (mg)	BDN in predator (mg/kg bw)	BDN consumed (mg)	BDN in predator (mg/kg bw)
Birds						
Tyto alba	294	72.9	0.116	0.395	0.057	0.194
Athene noctua	164	46.4	0.074	0.451	0.036	0.220
Strix aluco	426	97.1	0.155	0.364	0.076	0.178
Falco tinnunculus	209	78.7	0.125	0.598	0.062	0.297
Mammals						
Vulpes vulpes	5,700	520.2	0.829	0.145	0.407	0.071
Mustela putorius	689	130.9	0.209	0.303	0.102	0.148
Mustela erminea	205	55.7	0.089	0.434	0.044	0.215
Mustela nivalis	63	24.7	0.039	0.619	0.019	0.302
Dogs	10,000	456	0.727	0.073	0.364	0.036

[a] Based on a rodent containing 3.189 mg bromadiolone/kg (100% of their diet is paste bait).
[b] Based on a rodent containing 1.563 mg bromadiolone/kg (100% of their diet is paste bait).

Estimated intakes and concentrations of bromadiolone (BDN) in predatory and scavenging birds and mammals ingesting target rodents, assuming poisoned rodents comprise 50% of a bird's diet and that 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]	
			BDN consumed (mg)	BDN in predator (mg/kg bw)	BDN consumed (mg)	BDN in predator (mg/kg bw)
Birds						
Tyto alba	294	72.9	0.058	0.197	0.028	0.095
Athene noctua	164	46.4	0.037	0.226	0.018	0.110
Strix aluco	426	97.1	0.077	0.181	0.038	0.089
Falco tinnunculus	209	78.7	0.063	0.301	0.031	0.148
Mammals						
Vulpes vulpes	5,700	520.2	0.415	0.073	0.203	0.036
Mustela putorius	689	130.9	0.104	0.151	0.051	0.074
Mustela erminea	205	55.7	0.044	0.215	0.022	0.107
Mustela nivalis	63	24.7	0.020	0.317	0.010	0.159
Dog	10,000	456	0.364	0.036	0.182	0.018

[a] Based on a rodent containing 1.595 mg bromadiolone/kg (50% of their diet is paste bait).
[b] Based on a rodent containing 0.797 mg bromadiolone/kg (50% of their diet is paste bait).

Estimated intakes and concentrations of bromadiolone (BDN) in predatory and scavenging birds and mammals ingesting target rodents, assuming poisoned rodents comprise 50% of a predator/scavenger's diet and that bait contributed 20% 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]	
			BDN consumed (mg)	BDN in predator (mg/kg bw)	BDN consumed (mg)	BDN in predator (mg/kg bw)
Birds						
Tyto alba	294	72.9	0.023	0.078	0.012	0.041
Athene noctua	164	46.4	0.015	0.091	0.008	0.045
Strix aluco	426	97.1	0.031	0.073	0.015	0.036
Falco tinnunculus	209	78.7	0.025	0.120	0.013	0.062
Mammals						
Vulpes vulpes	5,700	520.2	0.166	0.029	0.085	0.015
Mustela putorius	689	130.9	0.042	0.061	0.021	0.030
Mustela erminea	205	55.7	0.018	0.088	0.009	0.044
Mustela nivalis	63	24.7	0.008	0.127	0.004	0.063
Dog	10,000	456	0.145	0.015	0.073	0.007

a Based on a rodent containing 0.638 mg bromadiolone/kg (20% of their diet is paste bait).
b Based on a rodent containing 0.319 mg bromadiolone/kg (20% of their diet is paste bait).

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 bromadiolone obtained from areas in and around buildings

Non-target avian predator	PECoral/PNECoral (rodent ingesting bait at 20% of daily requirement)		PECoral/PNECoral (rodent ingesting bait at 50% of daily requirement)		PECoral/PNECoral (rodent ingesting 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	416.3	208.2	1040.8	520.4	2080.9	1040.8
Athene noctua	475.0	237.5	1187.5	593.8	2374.4	1187.5
Strix aluco	382.7	191.4	956.7	478.4	1912.9	956.7
Falco tinnunculus	632.2	316.1	1580.5	790.3	3160.1	1580.5
Mammals						
Vulpes vulpes	1323.3	661.7	3308.3	1654.2	6614.5	3308.3
Mustela putorius	2754.8	1377.4	6887.0	3443.5	13769.6	6887.0
Mustela erminea	3939.8	1969.9	9849.4	4924.7	19692.6	9849.4
Mustela nivalis	5684.9	2842.5	14212.3	7106.2	28415.7	14212.3
Dog	661.2	330.6	1653.0	826.5	3305.0	1653.0
Birds PNECoral = 0.00019 mg/kg bw. Mammals PNECoral = 0.000022 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 bromadiolone residues, the risk assessment indicates uncertainty: *i.e.* the PECoral/PNECoral exceeds 1.0, in all cases even if a rodent has eaten only 20% for 5 days followed by a 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 bromadiolone in the target rodents, assuming 50 % bait consumption, are lower than the 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 483 for birds and 3620 for mammals. The worst-case PEC/PNEC ratio for birds at Tier 2 is about 3160 (kestrel) and 28400 for mammals (weasel).

For Tier 1 of the long-term scenario it was assumed that the rodents have fed entirely on rodenticides 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 rodenticides and non-target animals consume 50 % of their daily intake on poisoned rats the risk quotients are still far above 1 for birds (at least 191) and for other non-target mammals (at least 331).

At Tier 2 an approach based on the body burden of bromadiolone 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 they take no account of 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 A. 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 bromadiolone. 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 bromadiolone 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[15] and 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 MAKI PAT' is assumed to be similar in open areas when compared to 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.

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

[15] 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.

made above for various amounts of MAKI 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 bromadiolone 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 bromadiolone 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 MAKI 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 bromadiolone 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

Bromadiolone 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 bromadiolone.

The more direct the delivery of paste containing bromadiolone 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 bromadiolone 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 bromadiolone 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 Maki Pat' needs to be restricted to indoor use only for authorization in the Netherlands. The main concern of the environmental experts of Ctgb is that the product is based on an active substance with e.g. PBT and vPvB properties, causing risks for secondary poisoning of the non-target vertebrates. 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 bromadiolone, 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, birds and non-target animals (particularly dogs, cats, pigs and poultry)
- 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 bromadiolone which shall be duly taken into consideration for a clear labelling of MAKI 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 bromadiolone 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 MAKI PAT'.

MAKI 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).

Based on the assessment, it is concluded by the Dutch CA that Maki Pat' can be safely used by professional users for the control of black and brown rats and house mice in buildings, and by non-professionals for the control of mice in buildings.

The following classification is proposed based on Directive 1999/45/EC:

Professional user:

Symbol:	Xn	
Indication of danger:	Harmful	
R-phrases:	R48/20/21/22	Danger of serious damage to health by prolonged oral, dermal and inhalation exposure
S-phrases:	S2	Keep out of the reach of children
	S37	Wear protective gloves
	S46	If swallowed, seek medical advice immediately and show this container or label

Non-professional user:

Symbol:	Xn	
Indication of danger:	Harmful	
R-phrases:	R48/20/21/22	Danger of serious damage to health by prolonged oral, dermal and inhalation exposure
S-phrases:	S2	Keep out of the reach of children
	S13	Keep away from food, drink and animal feedingstuffs
	S46	If swallowed, seek medical advice immediately and show this container or label

3.1 National paragraph

In the Netherlands the use of rodenticides against rats is restricted to licensed professional users. The Dutch CA is of the opinion that the general public might use rodenticides against rats in an incorrect way, which can cause resistance in rats. Resistance development will increase problems of controlling rats in the future. For this reason, it is the Dutch CA's national policy to restrict the authorisation of rodenticides for controlling rats to licensed professional users only.

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. **Residue behaviour**

Annex 1: Summary of product characteristics

(a) Product trade name: Maki 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[16]**	**w/w (%)**	**Minimum purity (% w/w)**	**Same source as for Annex I inclusion**
bromadiolone	3-[3-(4'-Bromo[1,1'-biphenyl]-4-yl)-3-hydroxy-1-phenylpropyl]-4-hydroxy-2H-1-benzopyran-2-one	28772-56-7	249-205-9	0.050	g/kg	0.005	≥96.9	yes

Co-formulants					Contents				
Common name	**IUPAC name**	**Function**	**CAS number**	**EC number**	**Concentration**	**Unit**	**w/w (%)**	**Classification**	**Substance of concern**
Red food dye	Disodium-8-acetamido-1-hydroxy-2-phenylazonaphthalenne-3,6-disulphonate	Dye	3734-67-6	223-098-9	0.221	g/kg	0,0221	none	no
Denatonium benzoate	N-(2-(2,6-dimethylphenyl)amino)-2-2oxoethyl)-N,N-diethylbenze	Bittering agent	3734-33-6	223-09-52	0.05	g/kg	0,0050	Xn R20/22, R38, R41, R52/53	no

	methanaminium benzoate								
Propylene glycol	propane-1,2-diol	Solvent	57-55-6	200-338-0	10.129	g/kg	1,0129	none	no
Butyl hydroxyl toluene	2,6-bis(1,1-dimethylethyl)-4-methylphenol	Preservative	128-37-0	204-881-4	0.2	g/kg	0,02	none	no
EDTA	calcium disodium 2-[2-[bis(carboxylatomethyl)amino]ethyl-(carboxylatomethyl)amino]acetate	Preservative	62-33-9	200-529-9	0.1	g/kg	0,01	none	no
Hydrogenated vegetal fat	-	Binder	68919-53-9	-	220	g/kg	22	none	no
Wheat flour	-	Holder	130498-22-5	-	19.7	g/kg	1,97	none	no
Oat flour	-	Holder	130498-22-5	-	744.35	g/kg	74,435	none	no
PEG 300	Poly(oxy-1,2-ethanediyl),α-hydro-ω-hydroxy-ethane-1,2-diol, ethoxylated	Solvent	25322-68-3	500-038-2	5.2	g/kg	0,52	none	no
				Sum	**1000**		**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.

Other preservative, other dye, other binding agent

(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))[17]

Name of the active substance: bromadiolone

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 83
Fax: +33 5 53 47 95 01
E-Mail: rollinf@desangosse.com

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))[17]

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 83
Fax: +33 5 53 47 95 01
E-Mail: rollinf@desangosse.com

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: Xn, harmful

(h) Risk and Safety Phrases:

Professionals:	R48/20/21/22 S2 S37 S46
Non-Professionals:	R48/20/21/22 S2 S13 S46

(i) Product classification according to GHS: GHS08

(j) Hazard statement according to GHS: STOT RE Cat. 2, Code H373.

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)
(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[1]
(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
(r)	Application method[18]:	Covered application, preferably in tamper-resistant bait stations

[1]The Dutch CA is of the opinion that the use of Maki Pat' needs to be restricted to indoor use only for authorization in the Netherlands, see paragraph 2.8.3.

Directions for use:

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

(t) Conditions of use:
Rats: 100 to 200 g bait per bait station. Bait points placed at 4 to 10 meter distance of each other.
Mice: 30 to 50 g bait per bait station. Bait points placed at 1 to 3 meter distance of each other.

(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
MAKI PAT' is a rodenticide containing bromadiolone (0.005%) as an active substance. Bromadiolone is a second-generation single-dose anticoagulant rodenticide. It disrupts the normal blood clotting mechanisms resulting in increased bleeding tendency and, eventually, profuse haemorrhage and death. Antidote vitamin K1 (under medical supervision).
Clinical symptoms: nose bleed, bleeding gums, 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.

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 two year in the original PP packaging, which is supported by ambient temperature storage stability data

(y) Additional information:
In the PAR a resistance management strategies is outlined. A short remark on resistance should be added to the Label. In the Dutch label (WG/GA, see 1.5.2) this differs for professional and non-professional use since non-professionals are not expected to have knowledge on resistance.
For professional use:
For the active substance in this product, bromodiolone, there is a risk of development of resistance. Therefore, this product should not be used in cases where resistance against bomodiolone is presumed, for instance in cases where the last treatment with bromodiolone containing products did not results in a reduction of the population.
For non-professional use (mice only 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> submitted in support of the evaluation of the biocidal product

Section No	Reference No	Author	Year	Title	Owner of data	Data protection claimed	
						Yes	No
IIIB 3.1.1-01		Caruel, H.	2006a	Bromadiolone Red Paste 50 mg/kg BROPA0,0050_05F_LR0265_00 Appearance, Colour, Odour Centre R&D De Sangosse, Pont du Casse, France. Study code: BRO0609D. Non-GLP, Unpublished.	LiphaTech	Yes	
IIIB 3.1.2-01		Caruel, H.	2006a	Bromadiolone Red Paste 50 mg/kg BROPA0,0050_05F_LR0265_00 Appearance, Colour, Odour Centre R&D De Sangosse, Pont du Casse, France. Study code: BRO0609D. Non-GLP, Unpublished.	LiphaTech	Yes	
IIIB 3.1.3-01		Caruel, H.	2006a	Bromadiolone Red Paste 50 mg/kg BROPA0,0050_05F_LR0265_00 Appearance, Colour, Odour Centre R&D De Sangosse, Pont du Casse, France. Study code: BRO0609D. Non-GLP, Unpublished.	LiphaTech	Yes	

Section No	Reference No	Author	Year	Title	Owner of data	Data protection claimed	
IIIB 3.2-01		Curl, M and Wright, E.	2009a	Expert Statement on the Explosive Properties of Blue Paste Formulation. TSGE, Knaresborough, UK. Study No: DFNF00060-12-1-6-Exp. Non-GLP, Unpublished.	LiphaTech	Yes	
IIIB 3.3-01		Curl, M and Wright, E.	2009b	Expert Statement on the oxidising Properties of Blue Paste Formulation. TSGE, Knaresborough, UK. Study No: DFNF00060-12-1-6-Oxp. Non-GLP, Unpublished.	LiphaTech	Yes	
IIIB 3.4-01		Demangel, B.	2008	Flammability of Solids on Difethialone Paste – F00060_01, Defitraces, Brindas, France Study number 08-912021-002 GLP, Unpublished.	LiphaTech	Yes	
IIIB 3.5-01		Caruel, H.	2010	Bromadiolone Red Paste 50 mg/kg Storage stability (25°C – 2 years). BROPA0,0050_05F_F01153_00. Centre R&D De Sangosse, Pont du Casse, France. Study code: BRO0811D GLP, Unpublished.	LiphaTech	Yes	
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	Yes	
IIIB 3.6-02		Caruel, H.	2011	Bromadiolone Red Paste 50 mg/kg Mesure of relative density. BROPA0,0050_05F_F01153_00. Centre R&D De Sangosse, Pont du Casse, France. Study code: BRO1110F GLP, Unpublished.	LiphaTech	Yes	

Section No	Reference No	Author	Year	Title	Owner of data	Data protection claimed	
IIIB 3.7-01		Caruel, H.	2010	Bromadiolone Red Paste 50 mg/kg Storage stability (25°C – 2 years). BROPA0,0050_05F_F01153_00. Centre R&D De Sangosse, Pont du Casse, France. Study code: BRO0811D GLP, Unpublished.	LiphaTech	Yes	
IIIB 3.7-02		Caruel, H.	2009	Bromadiolone Red Paste 50 mg/kg Accelerated Storage stability (40°C – 8 weeks). BROPA0,0050_05F_F01153_00. Centre R&D De Sangosse, Pont du Casse, France. Study code: BRO0809D GLP, Unpublished.	LiphaTech	Yes	
IIIB 3.7-03		Deslux, R.	2012	Bromadiolone bait compatibility packaging study Centre R&D De Sangosse, Pont du Casse, France.Study code: BRO1203B. GLP, Unpublished	LiphaTech	Yes	
IIIB 4.1-01		Caruel, H.	2006b	Bromadiolone Paste 50 mg/kg Analytical Method Validation Centre R&D De Sangosse, Pont du Casse, France. Study code: BRO0601J. GLP, Unpublished.	LiphaTech	Yes	
IIIB 4.1-02		Caruel, H.	2006c	Bromadiolone Red Paste 50 mg/kg Specificity of Analytical Method Validation BROPA0,0050_05F_F00391_00 Centre R&D De Sangosse, Pont du Casse, France. Study code: BRO0610A. GLP, Unpublished.	LiphaTech	Yes	

Section No	Reference No	Author	Year	Title	Owner of data	Data protection claimed	
IIIB 4.1-03		Deslux, R.	2011	Specificity of Analytical Method Validation - BROPA0,0050_05F_F01153_00 Centre R&D De Sangosse, Pont du Casse, France. Study code: BRO1111A. GLP, Unpublished.	LiphaTech	Yes	
IIIB6.1-1		Richeaux, F.	2006	Assessment of acute oral toxicity in rats - Acute Toxic Class Method. Bromadiolone pate rouge 50 mg/kg. Phycher Bio-Developpement, Cestas Cedex, France, Laboratory Report No TA0423-PH-06/317. Report date 20 September 2006 (unpublished).	LiphaTech	☒	☐
IIIB6.1-2		Richeaux, F.	2006	Assessment of dermal toxicity in rats. Bromadiolone pate rouge 50 mg/kg. Phycher Bio-Developpement, Cestas Cedex, France, Laboratory Report No TAD-PH-06/317. Report date 20 September 2006 (unpublished).	LiphaTech	☒	☐
IIIB6.1-3		Duchosal, F. and Biedermann, K.	1994	Technical test and 4-hour acute inhalation toxicity study (Limit test) with Bromadiolone (1% powder) in rats. RCC, Research and Consulting Company, Itingen, Switzerland. Laboratory report no. 362518. Report date 11 April 1994 (unpublished).	LiphaTech	☒	☐
IIIB6.2-1		Richeaux, F.	2006	Assessment of acute dermal irritation. Bromadiolone pate rouge 50 mg/kg. Phycher Bio-Developpement, Cestas Cedex, France, Laboratory Report No IC-OCDE-PH-06/317. Report date 20 September 2006 (unpublished)	LiphaTech	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Data protection claimed	
IIIB6.2-2		Richeaux, F.	2006	Assessment of acute eye irritation. Bromadiolone pate rouge 50 mg/kg. Phycher Bio-Developpement, Cestas Cedex, France, Laboratory Report No IO-OCDE-PH-06/317. Report date 20 September 2006 (unpublished).	LiphaTech	☒	☐
IIIB6.3-1		Richeaux, F.	2006	Assessment of sensitising properties on albino guinea pig by repeated applications. Beuhler test with 9 applications. Bromadiolone pate rouge 50 mg/kg. Phycher Bio-Developpement, Cestas Cedex, France, Laboratory Report No SMB-9-PH-06/317. Report date 20 September 2006 (unpublished)	LiphaTech	☒	☐
IIIB6.4-1		Hassler, S.	2004	Percutaneous Penetration of ^{14}C-Bromadialone formulated as Red Impregnated Oat and Green Blocks through human split thickness skin membrane (*in vitro*). RCC Ltd. Laboratory report number 849290. Report date March 2004 (unpublished).	LiphaTech	☒	☐
IIIB6.4-2		Toner, F.	2007	The *in vitro* percutaneous absorption of radiolabelled Difethialone through human skin. Charles River Laboratories, Tranent, Scotland. Laboratory report number 28076 (Test facility study number 780005). Report date 7 September 2007 (unpublished).	LiphaTech	☒	☐
IIIB 5.10.2-01		Berny, P.	2006a	Study on the Efficacy and Palatability of a Red Paste at 50 mg/kg of Bromadiolone in the Rat, *Rattus Norvegicus*, Wild Strain, Sensitive to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/0604/BDN/Paste/Rn/S/T0. Non-GLP, Unpublished.	LiphaTech	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Data protection claimed	
IIIB 5.10.2-02		Berny, P.	2006b	Study on the Efficacy and Palatability of a Paste at 50 mg/kg of Bromadiolone in the House Mouse, *Mus Musculus*, Wild Strain, Sensitive to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/0601/BDN/Paste/Mm/S/T0. Non-GLP, Unpublished.	LiphaTech	☒	☐
IIIB 5.10.2-03		Berny, P.	2009a	Study on the Efficacy and Palatability of a Paste at 50 mg/kg of Bromadiolone in the House Mouse, *Mus Musculus*, Wild Strain, Resistant to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/0907/BDN/Paste/Mm/R. Non-GLP, Unpublished.	LiphaTech	☒	☐
IIIB 5.10.2-04		Berny, P.	2009b	Study on the Efficacy and Palatability of a Red Paste at 50 mg/kg of Bromadiolone in the Rat, *Rattus Norvegicus*, Wild Strain, Resistant to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/0908/BDN/Paste/Rn/R. Non-GLP, Unpublished.	LiphaTech	☒	☐
IIIB 5.10.2-05		Berny, P.	2009c	Study on the Efficacy and Palatability of a Red Paste at 50 mg/kg of Bromadiolone in the Rat, *Rattus Rattus*, Wild Strain, Sensitive to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/0909/BDN/Paste/Rr/S. Non-GLP, Unpublished.	LiphaTech	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Data protection claimed	
IIIB 5.10.2-06		Berny, P.	2010	Evaluation of the Efficacy of Paste Rodenticide Containing 50 mg/kg Bromadiolone for the Control of Black Rat Infestations in and Around Agricultural Buildings. ENVL, Marcy L'Etoile, France. Study code: FSR-0907. Non-GLP, Unpublished.	LiphaTech	☒	☐
IIIB 5.10.2-07		Berny, P.	2005a	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	☒	☐
IIIB 5.10.2-08		Berny, P.	2005b	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	☒	☐
IIIB 5.10.2-09		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	☒	☐
IIIB 5.10.2-10		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	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Data protection claimed	
IIIB 5.10.2-11		Berny, P.	2010b	Evaluation of the efficacy of a oat rodenticide containing 50 mg/kg Bromadiolone for the control of brown rat infestations in and around the urban building. Laboratoire de Toxicologie, ENVL, Marcy L'Etoile, France. Study codeFSR-0906. Non-GLP, Unpublished.	LiphaTech	☒	☐
IIIB 5.10.2-12		Berny, P.	2010c	Evaluation of the efficacy of a wheat rodenticide containing 50 mg/kg Bromadiolone for the control of house mice infestations in and around the urban building. Laboratoire de Toxicologie, ENVL, Marcy L'Etoile, France. Study codeFSR-0908. Non-GLP, Unpublished.	LiphaTech	☒	☐
IIIB 5.10.2-13		Berny, P.	2011	Study on the Efficacy and Palatability of Paste at 50 mg/kg of Bromadiolone in the Rat, *Rattus Norvegicus*, Wild Strain, resistant to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/1115/BDN/Paste/Rn/R Non-GLP, Unpublished.	LiphaTech	☒	☐
IIIB 5.10.2-14		Berny, P.	2011b	Study on the Efficacy and Palatability of a Paste at 50 mg/kg of Bromadiolone in the House Mouse, *Mus Musculus*, Wild Strain, resistant to Warfarin. ENVL, Marcy L'Etoile, France. Study code: RE/1117/BDN/Paste/Mm/R. Non-GLP, Unpublished.	LiphaTech	☒	☐

Section No	Reference No	Author	Year	Title	Owner of data	Data protection claimed	
IIIB 5.10.2-15		Berny, P.	2009d	Evaluation of the Efficacy of a Paste Rodenticide Containing 25 mg/kg Difethialone for the Control of Brown Rat Infestations in and Around Agricultural Buildings. Laboratoire de Toxicologie, ENVL Report Number FSR-0902 Non-GLP, Unpublished.	LiphaTech	☒	☐
IIIB 5.10.2-16		Bourret A.	2012	Treatment of mice infestation with a paste rodenticide containing 50 mg/kg bromadiolone in a equestrian center. Study code 1201/Equestrian center treatment/BDN/Paste/Mm. Non-GLP, Unpublished.	LiphaTech	☒	☐
IIIB 5.10.2-17		Berny P.	2009a	Study on the efficacy and palatability of paste at 25 mg/kg of difethialone in the rat, Rattus norvegicus, wild strain, resistant to warfarin. Study code: RE/0810/DFN/Paste/Rn/R Non-GLP, Unpublished.	LiphaTech	☒	☐

Annex 3: Analytical methods residues – active substance

Bromadiolone

The analytical methods for residues are taken from the CA report to support the inclusion of bromadiolone in annex I of Directive 98/8/EC.

Analytical methods for residues

Soil (principle of method and LOQ) (Annex IIA, point 4.2)	Soil is extracted by shaking twice with aqueous acetonitrile. Clean up is by passage through a C-8 column solid phase extraction cartridge. Determination is by reverse-phase HPLC/MS-MS (two ion transitions monitored 525.1>250.1 and 527.1>250.1). An Inertsil ODS-EP column is used with acetonitrile/water/acetic acid (70/30/0.1, v/v/v) mobile phase. The LOQ 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 bubbled through a tube containing 2-methoxyehanol collecting liquid. Determination is by reverse-phase HPLC/UV at a wavelength of 280 nm. A Nucleosil C-18 column is used with acetonitrile/0.0425% phosphoric acid (gradient) mobile phase. The LOQ is 0.5 μg/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)	Acetonitrile is added to the water and the sample is washed with hexane. Clean up is by passage through a C-8 column solid phase extraction cartridge. Determination is by reverse HPLC with fluorescence detection (excitation wavelength 310 nm, emission wavelength 390 nm). A Prodigy ODS-2 column is used with phosphate buffer/ acetonitrile/methanol (gradient) mobile phase. The LOQ is 0.05 μg/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-MS/MS with a Phenomenex Luna phenyl-hexyl column and ammonium acetate/methanol (gradient) mobile

	phase (two ion transitions monitored 525>250 and 527>250). The LOQ is 0.05 mg/L (defined as the lowest concentration at which acceptable recovery has been demonstrated). Liver Liver is ground with anhydrous sodium sulphate and extracted by shaking with a mixture of dichlormethane and acetone (1+1, v/v). Clean-up of the filtered extract is by GPC. Determination is by HPLC-MS/MS with a Phenomenex Luna phenyl-hexyl column and ammonium acetate/methanol (gradient) mobile phase (two ion transitions monitored 527>250 and 525>250). The LOQ 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)	Methods for food and feeding stuffs have been provided to be used in case of suspected contamination and/or for monitoring purposes if needed: Cucumber The sample is homogenised with ethyl acetate and sodium sulphate. The homogenised sample is filtered through sodium sulphate and the filtrate is evaporated to dryness under nitrogen. The residue is redissolved in acetone and 2-butylamine is added and the dissolved sample is cleaned up on a SPE cartridge using 2% v/v ethanolic formic acid for elution. The eluate is evaporated to dryness under nitrogen, redissolved in methanol containing the internal standard (coumatetralyl) and filtered. The filtrate is analysed using LC-MS/MS (primary transition 525 →250, qualifier 527 →250; only primary used for validation). Wheat The sample is grinded and homogenised with water and ethyl acetate. The supernatant is filtered and the filtrate is concentrated to <1 ml. The residue is cleaned-up using GPC (cyclohexane/ethyl acetate 50:50 v/v) and the eluate is evaporated to dryness under nitrogen. It is then redissolved in methanol containing the internal standard (coumatetralyl) and filtered. The filtrate is analysed using LC-MS/MS (primary transition 527 →250, qualifier 525 →250; only primary used for validation). Oil seed rape, lemon and meat Samples are extracted by blending then shaking 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 with Thermo Hypersil-Keystone,

	Fluophase PFP column with mobile phase: 95:5 v/v water/acetonitrile + 5 mM ammonium formate + 0.1% formic acid and 95:5 v/v acetonitrile/water + 5 mM ammonium formate + 0.1% formic acid (primary transition: 527.2→250.3 and confirmatory transition: 527.2→81.1).
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	See the entry above.

Annex 4: Toxicology and metabolism –active substance

Bromadiolone

Threshold Limits and other Values for Human Health Risk Assessment

Date: xx.xx.xxxx

Summary			
	Value	Study	SF
AEL long-term	0.0012 µg/ kg bw/day	Rabbit, 90-day study	300 (and correction for 70% oral absorption)
AEL medium-term	0.0012 µg/ kg bw/day	Rabbit, 90-day study	300 (and correction for 70% oral absorption)
AEL acute	0.0023 µg/ kg bw/day	Rabbit, teratogenicity study	600 (and correction for 70% oral absorption)

Inhalative absorption	No data
Oral absorption	70%
Dermal absorption	1.6%

Classification	
with regard to toxicological data (according to the criteria in Dir. 67/548/EEC)*	T+; R26/27/28, T; R48/23/24/25, Repr.Cat. 1; R61 S45, S53
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 for human health***	$C \geq 0.5\%$	T+; R61-26/27/28 –T;R48/23/24/25
	$0.25\% \leq C < 0.5\%$	T+; R26/27/28 – T; R48/23/24/25
	$0.025\% \leq C < 0.25\%$	T; R23/24/25 – T; R48/23/24/25
	$0.0025\% \leq C < 0.025\%$	Xn; R20/21/22 – R48/20/21/22

* The following information with regard to classification and labelling of bromadiolone is entered in the CAR: "Regarding human health effects a provisional classification with R61 was decided in November 2006 by the TC C&L, but without a final decision on the category to be used (Repr.Cat 1 or Repr.Cat 2). The proposed classification for bromadiolone for acute and repeated dose toxicity was agreed upon. However, the classification for human health effects is still under discussion.".

** Bromadiolone 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 bromadiolone, and proposed classification according to Directive 67/548/EEC.
*** The specific concentration limits for bromadiolone have been agreed at the Technical Meeting of Technical Committee on Classification and Labelling in Arona, 15-16 May 2007

Annex 5: Toxicology – biocidal product

Maki Pat'

General information

Formulation Type	Paste bait
Active substance(s) (incl. content)	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 (Buehler test)

* With regards to acute toxicity following inhalation exposure, a study has been provided by the registrant with bromadiolone (1% powder) (1% bromadiolone and 99% wheat starch). The calculated LC50 was < 0.523 mg/L air. However, the product is in the form of a ready for use paste bait, and the content of active substance is 0.005%. Inhalation is not a route of exposure for bromadiolone when using the product, and therefore the product is not classified for inhlation toxicity.

Classification and labelling proposed for the preparation with regard to toxicological properties (Annex IIIB, point 9)	
Directive 1999/45/EC	For professional users: Xn, R48/20/21/22 S2, S37, S46 For non-professional users: Xn, R48/20/21/22 S2, 13, 46
Regulation 1272/2008/EC	**For professional users:** Pictograms: GHS08 Signal word: Warning STOT RE Cat. 2, H373 P102, P260, P280a, P314, P501 **For non-professional users:** Pictograms: GHS08 Signal word: Warning STOT RE Cat. 2, H373 P102, P260, P314, P501

Annex 6: Safety for professional operators

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Exposure assessment

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

Primary exposure of professionals

Product and intended use	Exposure scenario	PPE	Inhalational uptake Exposure (mg/m^3)	Dermal uptake Exposure (mg/m^2)
MAKI 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 red paste on gloves during disposal:	4.09 mg x 15 = 61.35 mg
Total amount of red paste on gloves:	61.35 mg
Concentration of bromadiolone:	50 mg/kg
Amount of bromadiolone on gloves:	$50 \times 61.35 \div 10^6$ mg = 3.07×10^{-3} mg/day
Reduction in exposure from gloves:	90%
Amount of bromadiolone on skin:	$3.07 \times 10^{-3} \times (10 \div 100)$ mg = 3.07×10^{-4} mg/day
Dermal absorption of bromadiolone:	1.6%
Systemic exposure of bromadiolone:	4.91×10^{-6} mg/day
Operator body weight:	60 kg
Dermal exposure of bromadiolone during disposal:	**8.18×10^{-8} mg/kg bw/day**

Product and intended use	Exposure scenario	PPE	Inhalational uptake Exposure (mg/m^3)	Dermal uptake Exposure (mg/m^2)
MAKI 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 red paste on gloves during disposal:	4.09 mg x 50 = 204.5 mg
Concentration of bromadiolone:	50 mg/kg
Amount of bromadiolone on gloves:	50 x 204.5 ÷10^6 mg = 0.0102 mg/day
Reduction in exposure from gloves:	90%
Amount of bromadiolone on skin:	0.010 x (10 ÷ 100) mg = 1.02 x 10^{-3} mg/day
Dermal absorption of bromadiolone:	1.6%
Systemic exposure of bromadiolone:	1.64 x 10^{-5} mg/day
Operator body weight:	60 kg
Dermal exposure of bromadiolone during disposal:	**2.73 x 10^{-7} mg/kg bw/day**

Product and intended use	Exposure scenario	PPE	Inhalational uptake Exposure (mg/m^3)	Dermal uptake Exposure (mg/m^2)
MAKI 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 red paste on gloves during disposal:	4.09 mg x 30 = 122.7 mg
Concentration of bromadiolone:	50 mg/kg
Amount of bromadiolone on gloves:	50 x 122.7 ÷10^6 mg = 6.135 x 10^{-3} mg/day
Reduction in exposure from gloves:	90%

Amount of bromadiolone on skin:	6.135 x 10^{-3} x (10 ÷ 100) mg = 6.135 x 10^{-4} mg/day
Dermal absorption of bromadiolone:	1.6%
Systemic exposure of bromadiolone:	9.82 x 10^{-6} mg/day
Operator body weight:	60 kg
Dermal exposure of bromadiolone during disposal:	**1.64 x 10^{-7} mg/kg bw/day**

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	Bromadiolone	28772-56-7	4.91 x 10^{-5}	8.18 x 10^{-7}	4.91 x 10^{-6}	8.18 x 10^{-8}	-
Application around waste sites for the control of rodents	Bromadiolone	28772-56-7	1.64 x 10^{-4}	2.73 x 10^{-6}	1.64 x 10^{-5}	2.73 x 10^{-7}	-
Application in open areas	Bromadiolone	28772-56-7	9.82 x 10^{-5}	1.64 x 10^{-6}	9.82 x 10^{-6}	1.64 x 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	Bromadiolone	28772-56-7	1.2 x 10-6	No data	1.6%	-	-	8.18 x 10-7	68.2 %	68.2%
Application around waste sites for the control of rodents	Bromadiolone	28772-56-7	1.2 x 10-6	No data	1.6%	-	-	2.73 x 10-6	227.5 %	227.5 %
Application in open areas	Bromadiolone	28772-56-7	1.2 x 10-6	No data	1.6%	-	-	1.64 x 10-6	136.7 %	136.7 %

With PPE (gloves, 90% exposure reduction):

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	Bromadiolone	28772-56-7	1.2 x 10-6	No data	1.6%	-	-	8.18 x 10-8	6.8%	6.8%
Application around waste sites for the control of rodents	Bromadiolone	28772-56-7	1.2 x 10-6	No data	1.6%	-	-	2.73 x 10-7	22.8 %	22.8%
Application in open areas	Bromadiolone	28772-56-7	1.2 x 10-6	No data	1.6%	-	-	1.64 x 10-7	13. 7%	13. 7%

Conclusion:

Based on the risk assessment, no adverse effects from exposure to bromadiolone due to the use of MAKI PAT' are expected for protected (gloves) professional users.

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

Maki Pat'

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

Bromadiolone

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

Exposure scenarios for intended uses (Annex IIIB, point 6.6)	
Primary exposure	Non-professional 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)
MAKI 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 red paste on hands during disposal:	4.09 mg x 5 = 20.45 mg
Total amount of red paste on hands:	20.45 mg
Concentration of bromadiolone:	50 mg/kg
Amount of bromadiolone on hands:	$50 \times 20.45 \div 10^6$ mg = 1.02×10^{-3} mg/day
Amount of bromadiolone on skin:	1.02×10^{-3} mg/day

Dermal absorption of bromadiolone:	1.6%
Systemic exposure of bromadiolone:	1.64 x 10^{-5} mg/day
Operator body weight:	60 kg
Dermal exposure of bromadiolone during disposal:	**2.73 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)**
MAKI 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 bromadiolone :	50 mg/kg
Amount of bromadiolone ingested :	10 x 50 ÷ 10^6 mg = 0.00050 mg
Systemic exposure of bromadiolone :	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	Bromadiolone	28772-56-7	1.64 x 10^{-5}	2.73 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	Bromadiolone	28772-56-7	0.00050	0.000050

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	
Non-professional users, application in and around buildings	Bromadiolone	28772-56-7	2.3 x 10-6	No data	1.6%	-	-	2.73 x 10-7	11.9 %	11.7 %

Exposure scenario	Component	CAS	AEL [mg/kg/d]	Oral exposure [mg/kg/d]		RCR total
				Act. Expo	RCR	
Secondary exposure, infants ingesting a bait	Bromadiolone	28772-56-7	2.3 x 10-6	0.000050	2174%	2174%

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