HET COLLEGE VOOR DE TOELATING VAN GEWASBESCHERMINGSMIDDELEN EN BIOCIDEN

1 TOELATING

Gelet op de aanvraag d.d. 27 augustus 2013 (20131134 TNBWE) van

Zapi S.p.A.
Via Terza Strada 12
35026 CONSELVE
ITALIË

tot verkrijging van een toelatingals bedoeld in artikel 19 van de Verordening (EU) 528/2012, op basis van de werkzame stoffen difenacoum en bromadiolon,

MUSKIL BLOK FLUO-NP professioneel

Mede gelet op artikel 89 lid 2 juncto artikel 91 van de Verordening (EU) 528/2012, juncto artikel 44, eerste lid, Wet gewasbeschermingsmiddelen en biociden zoals deze luidde voor de inwerkingtreding van Verordening (EU) 528/2012

BESLUIT HET COLLEGE als volgt:

1.1 Toelating

1. Het middel MUSKIL BLOK FLUO-NP professioneel is toegelaten voor de in bijlage I genoemde toepassingen onder nummer 14327 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 31 maart 2015.

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.

1.3 Gebruik

Het middel mag slechts worden gebruikt met inachtneming van hetgeen in bijlage I onder A bij dit besluit is voorgeschreven.

1.4 Classificatie en etikettering
Mede gelet op artikel 50 Wet gewasbeschermingsmiddelen en biociden worden voorschriften gegeven.
Dit leidt tot de volgende voorschriften:

aard van het preparaat: Lokmiddel (klaar voor gebruik)

werkzame stof:	*gehalte:*
difenacoum	0,0025 %
bromadiolon	0,0025 %

letterlijk en zonder enige aanvulling:

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

gevaarsymbool:	*aanduiding:*
Xn	Schadelijk

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.

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 MUSKIL BLOK FLUO-NP professioneel (14327 N), een middel op basis van de werkzame stoffen difenacoum en bromadiolon. Het middel wordt aangevraagd als middel ter bestrijding van bruine ratten en huismuizen in afgesloten ruimten.

2.2 Informatie met betrekking tot de stof
Er zijn in Nederland reeds andere middelen op basis van de werkzame stoffen difenacoum en bromadiolon toegelaten.
Beide werkzame stoffen zijn goedgekeurd onder EU Verordening 528/2012.
De werkzame stof bromadiolon is bij Richtlijn 2009/92/EG, dd 31 juli 2009 van de Europese Commissie van de Europese Gemeenschappen opgenomen in de Unielijst van goedgekeurde stoffen volgens Verordening 528/2012/EC.
De werkzame stof difenacoum is bij Richtlijn 2008/81/EG, dd 29 juli 2008 van de Europese Commissie van de Europese Gemeenschappen opgenomen in de Unielijst van goedgekeurde stoffen volgens Verordening 528/2012/EC.

2.3 Karakterisering van het middel
Het betreft een middel op basis van 0.0025% difenacoum en 0.0025% bromadiolon, beide werkzame stoffen zijn anticoagulanten. Diverse precursors van stollingsfactoren ondergaan Vitamine K afhankelijke post-translationele modificaties. Difenacoum en bromadiolon zijn Vitamine K antagonisten die vermoedelijk aangrijpen op het enzym K1 epoxide reductase.

2.4 Voorgeschiedenis
De aanvraag is op 8 augustus 2013 ontvangen; op 27 augustus 2013 zijn de verschuldigde aanvraagkosten ontvangen.

2.5 Eindconclusie
Bij gebruik volgens het Wettelijk Gebruiksvoorschrift/Gebruiksaanwijzing is het middel MUSKIL BLOK FLUO-NP professioneel op basis van de werkzame stoffen difenacoum en bromadiolon voldoende werkzaam en heeft het geen schadelijke uitwerking op de gezondheid van de mens en het milieu.

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

Wageningen, 10 januari 2014

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. 10 januari 2014 tot toelating van het middel MUSKIL BLOK FLUO-NP professioneel, toelatingnummer 14327 N

A.
WETTELIJK GEBRUIKSVOORSCHRIFT

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

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

Het middel is uitsluitend bestemd voor professioneel gebruik.

B.
GEBRUIKSAANWIJZING

Toepassingen:
MUSKIL BLOK FLUO NP professioneel is een kant-en-klaar lokaas in blokvorm van 10 tot 100 gram tegen bruine ratten en huismuizen.

Het lokaas uitzetten op plaatsen waar de ratten en muizen geregeld komen: in de nabijheid van hol ingangen, op looppaden (sporen!) en op plaatsen waar de dieren voedsel halen of knagen. 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. Lokaas niet toepassen in de buurt van waterafvoersystemen waar het middel met water in contact kan komen.

Gebruik bij het uitzetten van het lokaas handschoenen.
Na gebruik handen wassen.

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

Dosering:
Bestrijding van bruine ratten:
Plaats het lokaas in lokaasdozen met intervallen van 5 tot 10 meter van elkaar, afhankelijk van de grootte van de rattenplaag. Gebruik 100 gram lokaas per lokaasdoos.

Bestrijding van muizen:
Plaats het lokaas in lokaasdoosjes met intervallen van 2 tot 5 meter van elkaar, afhankelijk van de grootte van de muizenplaag. Gebruik 30 tot 50 gram lokaas per lokaasdoosje.

Vervolg bestrijdingsactie:
Controleer de eerste opname na 3 dagen en vervolgens regelmatig op basis van opname (wekelijks of elke 14 dagen). Ververs of vul het lokaas daar waar nodig is aan tot er in het

geheel geen opname meer plaats vindt. 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.

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 en/of ratten wordt waargenomen, moet de mogelijk 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 kunnen na ca. 3 dagen gevonden worden) 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 en honden 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 huismuizen aanwezig zijn, zullen de resultaten slechts blijvend zijn, wanneer ook daar een bestrijdingsactie wordt uitgevoerd.

Resistentie management:
Voor de werkzame stoffen in het middel, difenacoum en 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 difenacoum of bromadiolon bevattende middelen niet hebben geresulteerd in een duidelijke vermindering van de populatie.

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

HET COLLEGE VOOR DE TOELATING VAN GEWASBESCHERMINGSMIDDELEN EN BIOCIDEN

BIJLAGE II bij het besluit d.d. 10 januari 2014 tot toelating van het middel MUSKIL BLOK FLUO-NP professioneel, toelatingnummer 14327 N

Product Assessment Report
Mutual Recognition

MUSKIL BLOK FLUO-NP professioneel

3rd of January 2014

Internal registration/file no:	20131134 TNBWE
Authorisation/Registration no:	14327N
Granting date/entry into force of authorisation/ registration:	3rd of January 2014
Expiry date of authorisation/ registration:	31st of March 2015
Active ingredient:	Difenacoum and bromadiolone
Product type:	PT14

Biocidal product assessment report related to product authorisation under EU Regulation 528/2012

Contents

1 General information about the product application

1.1 Applicant

Zapi S.p.A.
Via Terza Strada 12
35026 Conselve
Italy

1.2 Current authorisation holder

Not applicable.

1.3 Proposed authorisation holder

Zapi S.p.A.

1.4 Information about the product application

Application for authorisation based on mutual recognition. The primary assessment has been carried out by reference member state UK.

1.5 Information about the biocidal product

Productname: MUSKIL BLOK FLUO-NP professioneel
Productname in RMS: MUSKIL BLOCK FLUO-NP
PT: 14
Active substance: difenacoum and bromadiolone

2 Summary of the product assessment

2.1 Identity related issues

For the assessment of the identity related issues we refer to Product Assessment Report of the original authorisation.

2.2 Classification, labelling and packaging

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

No classification is required based on the physical and chemical properties of the product based on both 1999/45/EC and Reg (EC) 1272/2008.

Supported shelf life of the formulation: 24 months in PE and PP.

	Packaging authorised/ evaluated by RMS	Packaging applied for in NL	Packaging authorised in NL
Packaging size and type	Labelled plastic bucket with/without inner neutral liner (5, 10, 20, 25, 50, 75, 80 and 100g blocks) – 200g to 15kg	Labelled PP bucket with/without inner PE liner (5, 10, 20, 25, 50, 75, 80 and 100g blocks) - 800g to 15kg	Labelled PP bucket with/without inner PE liner (5, 10, 20, 25, 50, 75, 80 and 100g blocks) – 800g to 15kg
Packaging size and type	Labelled plastic bucket with product in inner bags or in single dose plastic bags (5, 10, 20, 25, 50, 75, 80 and 100g blocks) – 2.5kg to 10kg	Labelled PP bucket with product in inner PE bags or in inner single dose PP bags (5, 10, 20, 25, 50, 75, 80 and 100g blocks) - 2.5kg to 10kg	Labelled PP bucket with product in inner PE bags or in inner single dose PP bags (5, 10, 20, 25, 50, 75, 80 and 100g blocks) - 2.5kg to 10kg
Packaging size and type	Labelled fibre-board carton with inner liner (5, 10, 20, 25, 50, 75, 80 and 100g blocks, loose or in printed plastic bags or in single dose plastic bags) – 1kg to 15kg	Labelled fibre-board carton with inner PE liner (5, 10, 20, 25, 50, 75, 80 and 100g blocks, loose or in printed PE bags or in single dose PP bags) - 1kg to 15kg	Labelled fibre-board carton with inner PE liner (5, 10, 20, 25, 50, 75, 80 and 100g blocks, loose or in printed PE bags or in single dose PP bags) - 1kg to 15kg
Packaging size and type	Printed fibre box with inner neutral bag (5, 10, 20, 25, 50, 75, 80 and 100g blocks) – 200g to 1kg	Printed fibre box with inner PE bag (5, 10, 20, 25, 50, 75, 80 and 100g blocks) - 800g to 1kg	Printed fibre box with inner PE bag (5, 10, 20, 25, 50, 75, 80 and 100g blocks) - 800g to 1kg
Packaging size and type	Printed plastic bag (5, 10, 20, 25, 50, 75, 80 and 100g blocks) – 100g to 1kg	Printed PE bag (5, 10, 20, 25, 50, 75, 80 and 100g blocks) - 800g to 1kg	Printed PE bag (5, 10, 20, 25, 50, 75, 80 and 100g blocks) - 800g to 1kg

2.2.2 Proposal for the classification and labelling of the formulation concerning health

Substances, present in the formulation, which should be mentioned on the label by their chemical name (other very toxic, toxic, corrosive or harmful substances):
-

Symbol:	Xn	Indication of danger:	Harmful
R phrases	R48/20/21/22	Harmful: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed	
S phrases	S2	Keep out of the reach of children	
	S37	Wear suitable gloves	
	S46	If swallowed, seek medical advice immediately and show this container or label.	
Special provisions:	-	-	
DPD-phrases			
Child-resistant fastening obligatory?			Not applicable
Tactile warning of danger obligatory?			Not applicable

Explanation:	
Hazard symbol:	-
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 difethialone (TC&L, May 2007), which is the current status although the discussion at ECHA is not finalised.
Safety phrases:	S2, S13 and S20 are not obligatory for professional users with the assigned R-phrase.
Other:	-

2.2.3 Proposal for the classification and labelling of the formulation concerning the environment

No classification is required based on the physical and chemical properties of the product based on both 1999/45/EC and Reg (EC) 1272/2008.

2.3 Physico/chemical properties and analytical methods

For the assessment of the physical and chemical properties we refer to Product Assessment Report of the original authorisation.

2.4 Risk assessment for Physico-chemical properties

For the risk assessment for physico-chemical properties we refer to Product Assessment Report of the original authorisation.

2.5 Effectiveness against target organisms

For the assessment of the effectiveness against target organisms we refer to Product Assessment Report of the original authorisation. The conclusions of the RMS are acceptable.

The label claim
The applicant has provided a Dutch label (WG/GA). This has been adapted to our standards.

Professional/non-professional use
In the PAR efficacy was demonstrated for professional and non-professional use. However, authorisation for this product in NL was only requested for professional use.

Indoor use

According to the PAR/SPC this product is intended for use in and around buildings and in sewers. However, authorisation for this product in NL was requested and authorised for indoor use only.

2.6 Exposure assessment

2.6.1 Description of the intended use(s)

For the description of the intended use(s) we refer to Product Assessment Report of the original authorisation.

2.6.2 Assessment of exposure to humans and the environment

2.6.2.1 Humans

For the assessment of the exposure to humans we refer to Product Assessment Report of the original authorisation.

The formulation MUSKIL BLOK FLUO-NP professioneel is a wax block bait containing 0.0025% bromadiolone and 0.0025% difenacoum as active substances and is intended for the use against rats and mice inside buildings (PT14). The intended doses are 100 g bait for the use against rats and 50 g bait for the use against mice. The formulation is supplied as blocks of 5, 10, 20, 25, 50, 75, 80 and 100 g. MUSKIL BLOK FLUO-NP professioneel is intended for professional use only. The Product Assessment Report (PAR) was prepared by the RMS UK.

Bromadiolone is an existing active substance, included in the Union List of Approved Substances under Regulation 528/2012/EC. The classification and labelling of bromadiolone in the PAR is identical to classification and labelling of brodifacoum in the final CAR of bromadiolone (2011, RMS Sweden). For brodifacoum also specific concentration limits were set in May 2007 by the Technical Committee on Classification and Labelling of Dangerous Substances. These specific concentration limits were also considered by the RMS UK.

Difenacoum is an existing active substance, included in the Union List of Approved Substances under Regulation 528/2012/EC. The classification and labelling of difenacoumin the PAR is identical to classification and labelling of difenacoum in the final CAR of bromadiolone (2009, RMS Finland). However, for difenacoum also specific concentration limits were set in May 2007 by the Technical Committee on Classification and Labelling of Dangerous Substances, which are also included in the Competent Authority Assessment Report of difenacoum, but which were not considered by the RMS UK.

The applicant has submitted acute oral and acute dermal toxicity, skin and eye irritation and skin sensitization studies with MUSKIL BLOK FLUO-NP professioneel, which were found acceptable by the RMS UK. Based on the results of these studies, the formulation MUSKIL BLOK FLUO-NP professioneel does not need to be classified for acute oral (LD50 > 2000 mg/kg bw) and acute dermal toxicity (LD50 > 2000 mg/kg bw). The formulation MUSKIL BLOK FLUO-NP is considered to be not irritating to skin and eyes and not sensitizing to skin. The evaluation of the RMS is accepted by the Ctgb.

For dermal absorption, the applicant has submitted two *in vitro* human skin dermal absorption studies with two paste bait formulations, one containing 0.005% bromadiolone and another containing 0.005% difenacoum. The RMS UK has accepted the reasoning of the applicant that the data obtained for paste formulation can be considered representative for wax blocks. Exposure duration was 24 hours in both studies. In both studies the stratum

corneum was removed by tape stripping, with strips 1-5 and 6-10 pooled. For bromadiolone, two experiments were performed, with 1149 and 1082 ng/cm^2 bromadiolone applied to skin. The mean recovery was 93.4% and 96.4%, respectively. The amount of bromadiolone in the receptor fluid, stratum corneum and unexposed skin was below the limit of lower quantification (0.5 ng/mL). Also in the majority of epidermis/dermis samples the amount of bromadiolone was below the LLOQ. In such cases the LLOQ values were used in the dermal absorption calculations as a worst case. The contents of bromadiolone in the receptor fluid, the skin below the stratum corneum, unexposed skin, strips 1-5 and strips 6-10 of stratum corneum were 0.18% and 0.2%, 0.16% and 0.09%, 0.04% and 0.05%, 0.04% and 0.05% and 0.04 and 0.05% in experiments 1 and 2, respectively.

For difenacoum, also two experiments were performed, with 298 and 254 ng/cm^2 difenacoum applied to skin. The recovery was 105% and 100%, respectively. Difenacoum was not detected in the receptor fluid or unexposed skin of either experiment at the end of the 24 hours, therefore the values based on the Limit of Detection (LOD 0.05 ng/mL) were used in the dermal absorption calculations as the worst case. Also no substance (< LOD) or minimal amounts (below the LLOQ of 0.1 ng/mL) were found in most extracts of epidermis/dermis and lower stratum corneum layers. In these samples also the LOD or LLOQ were used as a worst-case. The receptor fluid, the skin below the stratum corneum, unexposed skin, strips 1-5 and 6-10 of stratum corneum contained 0.07% and 0.08%, 0.06% and 0.09%, 0.02% and 0.02%, 0.07% and 0.05% and 0.03% and 0.06% difenacoum residues, respectively, in experiments 1 and 2.

The RMS UK has in both cases considered that including the residues in the stratum corneum in the total value would result in the overestimation of dermal absorption and has performed the calculations by considering the absorption in the receptor fluid, skin below the stratum corneum and unexposed skin only. This resulted in dermal absorption values of 0.38% and 0.34% in experiments 1 and 2 for bromadiolone and 0.15% and 0.19% for experiments 1 and 2 for difenacoum, respectively. The calculations were performed with the value of 0.38% for bromadiolone and 0.2% for difenacoum. The Ctgb accepts this reasoning.

For bromadiolone the following AEL values were derived in the CAR: $AEL_{long\text{-}term,\ medium\ term}$ = 1.2 x 10^{-6} mg/kg bw/day and AEL_{acute} of 2.3 x 10^{-6} mg/kg bw/day. For difenacoum the following AEL value is derived in the CAR: 1.1 x 10^{-6} mg/kg bw/day. The same values have been used by the RMS in the risk assessment.

The exposure estimates were derived based on the study of Chambers and Snowdon (2004)[1] in which exposure of the operators during the loading of 5 wax blocks of 20 g into bait boxes and cleaning of bait boxes was calculated. The loading of 60 bait boxes per day and cleaning of 15 bait boxes per day was considered by the RMS Ireland in agreement with the HEEG Opinion on the harmonization of the number of manipulations in the assessment of rodenticides (2010) agreed at TM III 2010. This is considered acceptable by the Ctgb.

Exposure assessment

Use in buildings

The indicative exposure values in the study of Chambers and Snowdon (2004)[2] were 5.6 mg biocidal product on hands for the loading of one block and 5.7 mg biocidal product on hands for the cleaning of one bait station. Considering the maximal dose of 100 g for rats and the smallest block size of 5 g, the RMS UK has considered the loading of 20 blocks into one bait box. Based on this the following exposure estimates are derived:

[1] Chambers JG, Snowdon PJ. Study to determine potential exposure to operators during simulated use of anticoagulant rodenticide baits. Synergy Laboratories Limited, study number SYN/1302, 8 March 2004.

The total amount of biocidal product on hands, considering the loading of 20 blocks per one bait box, loading of 60 and cleaning of 15 bait boxes per day:
60 x (5.6 x 20) + 15 x 5.7 = 6805.5 mg biocidal product

The calculated systemic exposures are:
Without PPE:
For bromadiolone, corrected for 0.0025% concentration, 0.38% dermal absorption and 60 kg professional user body weight:

6805.5 x 0.0025% x 0.38% / 60 = 1.1×10^{-5} mg/kg bw/day

For difenacoum, corrected for 0.0025% concentration, 0.2% dermal absorption and 60 kg professional user body weight:
6805.5 x 0.0025% x 0.2% / 60 = 5.7×10^{-6} mg/kg bw/day

If these values are compared with the $AELs_{long\text{-}term}$ of 1.2×10^{-6} mg/kg bw/day for bromadiolone and 1.1×10^{-6} mg/kg bw/day for difenacoum, the resulting risk indices are:
For bromadiolone: $1.1 \times 10^{-5} / 1.2 \times 10^{-6} = 9.2$
For difenacoum: $5.7 \times 10^{-6} / 1.1 \times 10^{-6} = 5.2$

Based on this, adverse effects due to exposure to bromadiolone and difenacoum due to the application of MUSKIL BLOK FLUO-NP professioneel cannot be excluded. If the use of personal protective equipment is considered (gloves, resulting in 90% exposure reduction), the following exposure estimates are derived:

For bromadiolone: 1.1×10^{-6} mg/kg bw/day
For difenacoum: 5.7×10^{-7} mg/kg bw/day

If these values are compared with the $AELs_{long\text{-}term}$ of 1.2×10^{-6} mg/kg bw/day for bromadiolone and 1.1×10^{-6} mg/kg bw/day for difenacoum, the resulting risk indices are:
For bromadiolone: $1.1 \times 10^{-6} / 1.2 \times 10^{-6} = 0.92$
For difenacoum: $5.7 \times 10^{-6} / 1.1 \times 10^{-6} = 0.52$

Based on the derived risk indices RMS UK has considered that no adverse effects are expected for protected (gloves) professional user from the application of MUSKIL BLOK FLUO-NP professioneel in buildings, when it is supplied as wax blocks of 5 g and above. However, the RMS UK has not taken into account combined exposure to both substances. Therefore an independent assessment was performed by the Ctgb. Both bromadiolone and difenacoum affect the clotting of the blood and have the same mode of action, therefore their combined effects are considered to be additive by default. Therefore the sum of the risk indices of two substances need to be considered. In the present case, the sum of risk indices is (0.92 + 0.52 =) 1.44. Based on this, adverse effects from combined exposure to bromadiolone and difenacoum cannot be excluded even for protected (gloves) professional user. Based on this the application of 5 g blocks cannot be authorised.

If the use of 10 g blocks is considered instead, the number of wax blocks per one bait point is 10. This leads to the following exposure estimates:

The total amount of biocidal product on hands, considering the loading of 10 blocks per one bait box, loading of 60 and cleaning of 15 bait boxes per day:
60 x (5.6 x 10) + 15 x 5.7 = 3445.5 mg biocidal product

The calculated systemic exposures are:
Without PPE:
For bromadiolone, corrected for 0.0025% concentration, 0.38% dermal absorption and 60 kg professional user body weight:

3445.5 x 0.0025% x 0.38% / 60 = 5.5×10^{-6} mg/kg bw/day

For difenacoum, corrected for 0.0025% concentration, 0.2% dermal absorption and 60 kg professional user body weight:
3445.5 x 0.0025% x 0.2% / 60 = 2.9 x 10^{-6} mg/kg bw/day

If these values are compared with the $AELs_{long\text{-}term}$ of 1.2 x 10^{-6} mg/kg bw/day for bromadiolone and 1.1 x 10^{-6} mg/kg bw/day for difenacoum, the resulting risk indices are:
For bromadiolone: 5.5 x 10^{-6}/1.2 x 10^{-6} = 4.6
For difenacoum: 2.9 x 10^{-6}/1.1 x 10^{-6} = 2.6

If the use of personal protective equipment is considered (gloves, resulting in 90% exposure reduction), the following exposure estimates are derived:

For bromadiolone: 5.5 x 10^{-7} mg/kg bw/day
For difenacoum: 2.9 x 10^{-7} mg/kg bw/day

If these values are compared with the $AELs_{long\text{-}term}$ of 1.2 x 10^{-6} mg/kg bw/day for bromadiolone and 1.1 x 10^{-6} mg/kg bw/day for difenacoum, the resulting risk indices are:
For bromadiolone: 5.5 x 10^{-7}/1.2 x 10^{-6} = 0.46
For difenacoum: 2.9 x 10^{-7}/1.1 x 10^{-6} = 0.26

The sum of risk indices is (0.46 + 0.26 =) 0.72

Based on this, no adverse effects are expected for protected (gloves) professional user from exposure to bromadiolone and difenacoum due to the application fo MUSKIL BLOK FLUO-NP professioneel in buildings, when it is supplied in the blocks of 10 g and above.

Use in sewers
The RMS UK has also performed the risk assessment for the use of MUSKIL BLOK FLUO-NP professioneel in sewers. The intended dose level is 200 g for rats. Considering the smallest block size of 5 g, 40 blocks need to be placed to achieve the dose level of 200 g. The cleaning operations in sewers will not be performed, therefore only the exposure during the loading phase needs to be taken into account. Based on this the following exposure estimates are derived:

Considering 60 loading applications per day and 40 blocks per one bait point, the total amount of the biocidal product on hands is:

60 x (5.6 x 40) = 13440 mg biocidal product on hands

The calculated systemic exposures are:
Without PPE:
For bromadiolone, corrected for 0.0025% concentration, 0.38% dermal absorption and 60 kg professional user body weight:

13440 x 0.0025% x 0.38% / 60 = 2.2 x 10^{-5} mg/kg bw/day

For difenacoum, corrected for 0.0025% concentration, 0.2% dermal absorption and 60 kg professional user body weight:
13440 x 0.0025% x 0.2% / 60 = 1.1 x 10^{-5} mg/kg bw/day

If these values are compared with the $AELs_{long\text{-}term}$ of 1.2 x 10^{-6} mg/kg bw/day for bromadiolone and 1.1 x 10^{-6} mg/kg bw/day for difenacoum, the resulting risk indices are:
For bromadiolone: 2.2 x 10^{-5}/1.2 x 10^{-6} = 18.3
For difenacoum: 1.1 x 10^{-5}/1.1 x 10^{-6} = 10

Based on this, adverse effects due to exposure to bromadiolone and difenacoum due to the application of MUSKIL BLOK FLUO-NP professioneel in sewers cannot be excluded. If the

use of personal protective equipment is considered (gloves, resulting in 90% exposure reduction), the following exposure estimates are derived:

For bromadiolone: 2.2×10^{-6} mg/kg bw/day
For difenacoum: 1.1×10^{-6} mg/kg bw/day

If these values are compared with the $AELs_{long\text{-}term}$ of 1.2×10^{-6} mg/kg bw/day for bromadiolone and 1.1×10^{-6} mg/kg bw/day for difenacoum, the resulting risk indices are:
For bromadiolone: $2.2 \times 10^{-6} / 1.2 \times 10^{-6} = 1.8$
For difenacoum: $1.1 \times 10^{-6} / 1.1 \times 10^{-6} = 1.0$

Based on this, adverse effects from exposure to bromadiolone and difenacoum due to the use of MUSKIL BLOK FLUO-NP professioneel supplied as 5 g wax block in sewers cannot be excluded even for protected (gloves) professional users. Therefore the use of 5 g wax blocks cannot be authorised.

If the use of 10 g blocks is considered instead, the number of wax blocks per one bait point is 20. Therefore the calculated exposures are therefore expected to be twice as low due to the twice as low number of contacts with the blocks:

Without PPE:
For bromadiolone: 1.1×10^{-5} mg/kg bw/day
For difenacoum: 5.5×10^{-6} mg/kg bw/day

If these values are compared with the $AELs_{long\text{-}term}$ of 1.2×10^{-6} mg/kg bw/day for bromadiolone and 1.1×10^{-6} mg/kg bw/day for difenacoum, the resulting risk indices are:
For bromadiolone: $1.1 \times 10^{-5} / 1.2 \times 10^{-6} = 9.2$
For difenacoum: $5.5 \times 10^{-6} / 1.1 \times 10^{-6} = 5.0$

If the use of personal protective equipment is considered (gloves, resulting in 90% exposure reduction), the following exposure estimates are derived:

For bromadiolone: 1.1×10^{-6} mg/kg bw/day
For difenacoum: 5.5×10^{-7} mg/kg bw/day

If these values are compared with the $AELs_{long\text{-}term}$ of 1.2×10^{-6} mg/kg bw/day for bromadiolone and 1.1×10^{-6} mg/kg bw/day for difenacoum, the resulting risk indices are:
For bromadiolone: $1.1 \times 10^{-6} / 1.2 \times 10^{-6} = 0.92$
For difenacoum: $5.5 \times 10^{-7} / 1.1 \times 10^{-6} = 0.50$

Based on the derived risk indices RMS UK has considered that no adverse effects are expected for protected (gloves) professional user from the application of MUSKIL BLOK FLUO-NP professioneel in sewers, when it is supplied as wax blocks of 10 g and above. However, the RMS UK has not taken into account combined exposure to both substances. Therefore an independent assessment was performed by the Ctgb. Both bromadiolone and difenacoum affect the clotting of the blood and have the same mode of action, therefore their combined effects are considered to be additive by default. Therefore the sum of the risk indices of two substances need to be considered. In the present case, the sum of risk indices is (0.92 + 0.50 =) 1.42. Based on this, adverse effects from combined exposure to bromadiolone and difenacoum cannot be excluded even for protected (gloves) professional user. Based on this the application of 10 g blocks in sewers cannot be authorised.

If the use of 20 g blocks is considered instead, the number of wax blocks per one bait point is 10. Therefore the calculated exposures are therefore expected to be twice as low due to the twice as low number of contacts with the blocks:

Without PPE:
For bromadiolone: 5.5×10^{-6} mg/kg bw/day

For difenacoum: 2.8 x 10^{-6} mg/kg bw/day

If these values are compared with the $AELs_{long\text{-}term}$ of 1.2 x 10^{-6} mg/kg bw/day for bromadiolone and 1.1 x 10^{-6} mg/kg bw/day for difenacoum, the resulting risk indices are:
For bromadiolone: 5.5 x 10^{-6}/1.2 x 10^{-6} = 4.6
For difenacoum: 2.8 x 10^{-6}/1.1 x 10^{-6} = 2.5

If the use of personal protective equipment is considered (gloves, resulting in 90% exposure reduction), the following exposure estimates are derived:

For bromadiolone: 5.5 x 10^{-7} mg/kg bw/day
For difenacoum: 2.8 x 10^{-7} mg/kg bw/day

If these values are compared with the $AELs_{long\text{-}term}$ of 1.2 x 10^{-6} mg/kg bw/day for bromadiolone and 1.1 x 10^{-6} mg/kg bw/day for difenacoum, the resulting risk indices are:
For bromadiolone: 1.1 x 10^{-6}/1.2 x 10^{-6} = 0.46
For difenacoum: 5.5 x 10^{-7}/1.1 x 10^{-6} = 0.25

The sum of risk indices is (0.46 + 0.25 =) 0.71. Based on this, no adverse effects are expected for protected (gloves) professional user from the application of MUSKIL BLOK FLUO-NP professioneel in sewers, when it is supplied as wax blocks of 20 g and above.

Indirect exposure
The RMS UK has also considered a secondary exposure of children due to incidental swallowing of bait. For “transient mouthing of poison bait” scenario, an ingestion of 10 mg bait is considered by TNsG. This results in internal exposure of (10 x 0.0025% x 100% / 10 kg =) 2.5 x 10^{-5} mg/kg bw bromadiolone and 2.5 x 10^{-5} mg/kg bw/day difenacoum for a 10 kg infant, considering 100% oral absorption of both substances. Compared with the AEL_{acute} of 2.3 x 10^{-6} mg/kg bw/day for bromadiolone and 1.1 x 10^{-6} for difenacoum, this results in the risk indices of 10.9 and 2.8. Based on this, a concern for adverse effects due to secondary exposure of an infant that swallowed the bait exists.

2.6.2.2 Environment

For details on the assessment of the exposure to the environment we refer to Product Assessment Report of the original authorisation.

The intended uses in the application for MUSKIL BLOK FLUO-NP professioneel are professional use against rats and mice in private, public, industrial and agriculture buildings and in sewers.

2.7 Risk assessment for human health

For the risk assessment for human health we refer to Product Assessment Report of the original authorisation.

Based on the risk assessment, no adverse effects are expected for protected (gloves) professional user due to the exposure to bromadiolone and difenacoum as a result of application of MUSKIL BLOK FLUO-NP professioneel in buildings, supplied as wax blocks of 10 g and above, for the control of rats and mice. For wax blocks of 5 g, adverse health effects from combined exposure to bromadiolone and difenacoum cannot be excluded even for protected (gloves) professional user. Based on this the application of 5 g blocks cannot be authorised.

Based on the risk assessment, no adverse effects are expected for protected (gloves) professional user due to the exposure to bromadiolone and difenacoum as a result of application of MUSKIL BLOK FLUO-NP professioneel in sewers, supplied as wax blocks of 20 g and above, for the control of rats and mice. For wax blocks of 5 g, and 10 g adverse

health effects from combined exposure to bromadiolone and difenacoum cannot be excluded even for protected (gloves) professional user. Based on this the application of 5 g and 10 g blocks in sewers cannot be authorised.

Based on the risk assessment adverse effects from secondary exposure to brodifacoum cannot be excluded for an infant incidentally swallowing the bait. Therefore the following precautionary phrases should be added to the product label:

- Keep out of the reach of children (P102 or S2)
- Prevent access to bait by children, domesticated animals and pets, (particularly cats, dogs and pigs).

When these risk management measures are taken into consideration, the risk of secondary exposure for children is considered to be mitigated.

2.8 Risk assessment for the environment

The product contains the active substances bromadiolone (0.0025%) and difenacoum (0.0025%). No substances of concern were identified in the product.

For the risk assessment for the environment we refer to Product Assessment Report of the original authorisation. Please note that the PAR contains specific details for the UK market i.e. packaging restrictions and authorisation requirements. These are adjusted for the situation in the Netherlands. The intended use in the PAR concerns in and outdoor use of the product, as well as application in sewers.

Considering the risk of primary and secondary poisoning determined in the PAR and the potential PBT and vPvB properties of bromadiolone and difenacoum, the use needs to be restricted to indoor use only.
In addition, the specific provisions in the EU inclusion directive for both active substances state as one of the risk mitigations that the use is restricted to professionals only. In the Netherlands, this risk mitigation is followed for the use of rodenticides against rats.
Further restrictions are necessary to prevent access of non-target animals to the product and these are stated in section 2.9.

Overall conclusion for the aspect environment: The use of the product is acceptable, when the restrictions for use in the Netherlands are applied, including indoor use and professional use against rats only.

2.9 Measures to protect man, animals and the environment

Measure	In WG/GA	WG/GA (in Dutch)
The resistance status of the target population should be taken into account when considering the choice of rodenticide to be used.	Yes	Voor de werkzame stoffen in het middel, difenacoum en 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 combinaties van difenacoum en bromadiolon bevattende middelen niet hebben geresulteerd in een duidelijke vermindering van de populatie.
Baits must be securely deposited in	Yes	Plaats het lokaas in lokaasdozen

a way so as to minimize the risk of consumption by other animals or children.		buiten bereik van andere dieren (bijvoorbeeld vogels, zoogdieren, huis- of landbouwdieren) en kinderen.
Prevent access to bait by children, birds and non-target animals (particularly dogs, cats, pigs and poultry).	Yes	
Where possible, secure baits so that they cannot be dragged away.	Yes	Het lokaas zo vast maken dat het niet weggesleept kan worden.
Unless under the supervision of a pest control operator or other competent person, do not use anticoagulant rodenticides as permanent baits. In most cases, anticoagulant bait should have achieved control within 35 days. Should activity continue beyond this time, the likely cause should be determined.	Yes	Het middel mag niet permanent gebruikt worden. 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 en/of ratten wordt waargenomen, moet de mogelijk oorzaak hiervan worden onderzocht en maatregelen worden getroffen.
Search for and remove dead rodents at frequent intervals during treatment (unless used in sewers), at least as often as when baits are checked and/or replenished. Daily inspection may be required in some circumstances.	Yes	Dode dieren (de eerste kunnen na ca. 3 dagen gevonden worden) verzamelen en in plastic verpakt in het vuilnisvat deponeren, opdat huisdieren en andere dieren niet door het opeten van de kadavers worden vergiftigd.
Dispose of dead rodents in accordance with local requirements. In the UK poisoned rodents may be disposed of by the waste producer at an incinerator or landfill permitted to accept that type of waste, or collected by a registered waste carrier and taken for disposal at a suitably permitted site. For further information on disposal contact the Environment Agency (http://www.environment-agency.gov.uk) or SEPA (http://www.sepa.org.uk).	Yes	
For products to be used in public areas the following safety precaution shall be carried on the label, packaging or accompanying leaflet:	No	Not applicable, as the public area treatment will be performed by trained professionals.
When the product is being used in public areas, the areas treated must be marked during the treatment period and a notice explaining the risk of primary or secondary poisoning by the anticoagulant as	No	Not applicable, as the public area treatment will be performed by trained professionals.

well as indicating the first measures to be taken in case of poisoning must be made available alongside the baits. 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). UK medical professionals should contact the National Poisons Information Service (www.npis.org) for further advice.	Yes	Tegengif: Vitamine K1 (onder medische begeleiding).
Additional		
-		Na gebruik handen wassen.
-		Het gebruik van dit middel is alleen toegestaan indien het een onderdeel vormt van een integrated pest management systeem (IPM).
-		Wanneer de opname van lokaas is gestopt, de resten van het lokaas verzamelen en veilig verwijderen als gevaarlijk afval (cf. Eural).
-		De lokaasdozen niet toepassen in de buurt van waterafvoersystemen waar het middel met water in contact kan komen.
-		Katten en honden tijdens een bestrijdingsactie extra goed voeren

3 Proposal for decision

The authorisation of MUSKIL BLOK FLUO-NP professioneel is based on mutual recognition of the authorisation of RMS UK. For the evaluation we refer to the product assessment report which has been composed by the RMS conform the Common Principles.

It is expected that the application of MUSKIL BLOK FLUO-NP professioneel according to the use instructions, will be effective and that there will be no harm for the health of humans, for those who use the product, and for the environment.

Proposal for the classification and labelling of the formulation
Based on the profile of the substance, the provided toxicology of the preparation, the characteristics of the co-formulants, the method of application and the risk assessment, the following labelling of the formulation is proposed:

Substances, present in the formulation, which should be mentioned on the label by their chemical name (other very toxic, toxic, corrosive or harmful substances):			
-			
Symbol:	Xn	Indication of danger:	Harmful
R phrases	R48/20/21/22	Harmful: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed	
S phrases	S2	Keep out of the reach of children	
	S37	Wear suitable gloves	

	S46	If swallowed, seek medical advice immediately and show this container or label.
Special provisions: DPD-phrases	-	-
Child-resistant fastening obligatory?		Not applicable
Tactile warning of danger obligatory?		Not applicable