INFOTOX (Pty) Ltd

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Retrieval and scientific interpretation of ecotoxicological information

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Report Compiled for: Regulatory Aspects

Derogation Risk Assessment Report for Solid Rodenticides Containing Brodifacoum, a CMR Substance of Concern (Reproductive Toxicity Hazard)

Product trade names:

Broditop Pasta (L8387)
Di-Rat-Blue (L9836) (grain bait)
Doom Rattex Deadly Wedges (L11294)
Doom Rattex Deadly Pellets (L7725)
Doom Rattex Deadly Powder (L7727)
Doom Rattex Deadly Pellets Chew Through Packs (L7725)
Jaguar Blox (L8259)
Kill-All Grain bait (L8211)
Kill-All Pellets (L7162)
Kill-All Wedges (L7265)
Kombat Rat and Mouse Block (L6425)
Kombat Rat and Mouse Pellet (L6424)
Mortein Rat Kill (L6907)
Pulse pellets (L6190)
Pulse Wax Blocks (L6189)
Rodenthor TM Pasta (L9586)
Rodenthor TM Block (L9396)
Rodex Bait Blocks (L9292)
Rodex Grain Bait (L9291)
Rodex Pasta Bait (9566)
Rodex Rat and Mouse Pellets (L9293)
Rodex Rat R.I.P. (L9709)

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10 April 2025

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Managing Director

10 April 2025

Internal review:

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Expertise and Declaration of Independence

This report was prepared by INFOTOX (Pty) Ltd ("INFOTOX"). Established in 1991, INFOTOX is a professional scientific company, highly focused in the discipline of ecotoxicological risk assessment. Both occupational and environmental human health risks, as well as risks to ecological receptors, are addressed.

Dr Willie van Niekerk, Managing Director of INFOTOX, has BSc, Hons BSc and MSc degrees from the University of Potchefstroom and a PhD from the University of South Africa. He is a Qualified Environmental Professional (QEP), certified by the Institute of Professional Environmental Practice (IPEP) in the USA (No 07960160), and a registered Professional Natural Scientist (Pr Sci Nat, Environmental Science, No 400284/04). Dr Van Niekerk has specialised in chemical toxicology and human health risk assessments, but he has experience in many other areas in the disciplines of analytical and environmental sciences.

Dr Marlene Fourie has BSc and Hons BSc degrees from the University of Stellenbosch and MSc and PhD degrees from the University of Pretoria. Her field of specialisation is reproductive biology/toxicology. Dr Fourie also has an MSc-degree in epidemiology from the University of Pretoria. Following positions as Medical Natural Scientist at the Andrology Unit, Department of Urology, University of Pretoria and the Pretoria Academic Hospital from 1987 to 2001, she joined INFOTOX as a Medical Biological Scientist. Dr Fourie has conducted many health risk assessments and projects relating to the health status of communities. She is a registered Professional Natural Scientist (Pr Sci Nat, Toxicological Science, No 400190/14). Dr Fourie has completed the Globally Harmonised System (GHS) course *Classifying and Labelling Chemicals According to the UN GHS*, presented by the United Nations Institute for Training and Research (UNITAR) in 2017, with previous experience in GHS classification since 2010.

This specialist report was compiled for Regulatory Aspects. We do hereby declare that we are financially and otherwise independent of Regulatory Aspects.

Signed on behalf of INFOTOX (Pty) Ltd, duly authorised in the capacity of Managing Director:

Willem Christiaan Abraham van Niekerk

10 April 2025

Executive Summary

This document is a risk assessment report supporting an application for derogation for the restricted use of certain registered solid rodenticide products, containing the active ingredient brodifacoum, supplied to professional pest control operators ("PCOS") and to the general public.

The solid products are identified as substances of concern due to classification as reproductive hazards category 1A according to the Globally Harmonized System of Classification and Labelling of Chemicals ("GHS"). The classification is due to the active ingredient brodifacoum, which is classified in GHS reproductive toxicity category 1A (H360D), indicating a hazard to the development of the unborn child ("D").

Product names, registered suppliers and Act 36 of 1947 registration numbers:

Product	Act 36 of 1947 registration numbers	Registered manufacturer / supplier / distributer
Broditop Pasta	L8387	Mr. Stefano Migliore
Di-Rat-Blue (grain bait)	L9836	Newton Fertilizers CC
Doom Rattex Deadly Wedges	L11294	Tiger Consumer Brands Ltd
Doom Rattex Deadly Pellets	L7725	Tiger Consumer Brands Ltd
Doom Rattex Deadly Pellets Chew Through Packs	L7725	Tiger Consumer Brands Ltd
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Rodenthor TM Pasta	L9586	Mr. Stefano Migliore
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Rodex Rat & Mouse Pellets	L9293	Innovative Pest Management (Pty) Ltd
Rodex Rat R.I.P.	L9709	Innovative Pest Management (Pty) Ltd

Intended product use:
The general product use description is: Solid anti-coagulant rodenticide product for use in the garden, the home, on the farm, on industrial premises, and other uses for the protection of public health by PCOs as needed. The products are also supplied to domestic users.

The occupational human health risk assessments presented here are based on internationally-accepted human risk assessment principles and methods. The health and ecological risk assessment guidance of the following major international regulatory agencies is followed:

- The United States Environmental Protection Agency ("USEPA"), particularly documents produced by the Office of Chemical Safety and Pollution Prevention during 2020 and 2022.
- The Italian Competent Authorities ("CAs") acing as the Rapporteur Member State of the European Community ("EC") to carry out the assessment report evaluating brodifacoum as a rodenticide, with the view of satisfying regulatory requirements for placing biocidal products on the market, submitted by the Italian CAs 17 September 2009, revised 16 December 2010.
- The French CA Product Assessment Report of a Biocidal Product for Renewal of National Authorisation Applications, submitted 18/12/2017.

Human health risk assessment

The scope of the solid rodenticide human health risk assessment ("HHRA") is determined by the registered product use. The purpose is to evaluate the risks of reproductive/developmental toxicity effects in persons exposed to brodifacoum in the identified products listed above. Since developmental effects are the only health endpoints (aside from mortality) for which dose-response values are available in toxicological studies, there is no other choice but to base acceptable exposure levels of males and children on this health endpoint as well. Therefore, the absence of a systemic risk to health in general, and specifically the absence of a risk to the developing foetus (developmental effects), is implied by a finding of "acceptable exposures or risks".

The following human exposure scenarios were identified for assessment:

- Primary exposure of professional PCOs, non-professionals and domestic users handling, placing, refilling and disposing of unused bait and dead rodents.
- Secondary human exposures are assessed as:
    - Accidental contact of bystanders (adults or children) with the rodenticides while in use.
    - Contact by adults (general public) with dead or dying rodents.
    - Accidental exposure of infants/toddlers transiently mouthing or chewing on bait.

Adult solid bait users, whether professional PCOs, non-professionals or the general public, wearing gloves, are not at risk of a health effect, and specifically not on the development of the foetus in case of pregnant females.

Acceptable risks are also demonstrated for adults not wearing gloves, for some of the solid bait products. However, this can never be used to negate the need for recommending the use of gloves on product labels. Recommending the use of gloves is a protective measure for all bait users, and also protects against diseases carried by rodents.

Inhalation exposure associated with solid bait uses are mostly negligible and not associated with a risk to health, except for unprotected inhalation exposure in the case of PCO use of some products, during some product use phases. This necessitates the recommendation of respirator use (95% protection factor) by PCOs, under some conditions. Details are presented with the mitigation measures recommendations.

Infants/toddlers chewing on solid bait products are at risk of a health effect. Transient mouthing may also result in a risk to health. However, accidental exposure of bystanders, specifically children, can be limited by clear communication of the professional pesticide applicator to such bystanders, and by following label instructions to place the bait station out of reach of children and uninformed persons.

Regardless of the precautionary measures followed, any noted contact of a child with a rodenticide should be brought to the immediate attention of a medical professional, without exception. All product labels must clearly exhibit the contact details of a local/national poison centre.

Environmental (ecological) risk assessment

Secondary exposure in mammals and birds of prey describes the ingestion, by natural predators in the environment, of dead or dying target animals, that is, rats or mice in the case of brodifacoum formulations. The general conclusions of international regulatory assessments based on available toxicity values in predatory birds and non-target predatory mammals is that secondary risks to mammalian and avian predators cannot be excluded. However, mitigation measures such as limiting access by non-target organisms and frequent inspections to search for and dispose of rodent carcasses can limit the risk of secondary poisoning of non-target animals.

Responsible product application and care, with clear instructions on product labels and safety data sheets ("SDSs") to prevent contamination of waterways, should limit aquatic contamination to negligible. Therefore, no risk assessment for secondary poisoning through the aquatic food chain is required, and also no risk assessment for non-mammalian or non-avian terrestrial organisms.

The environmental effects versus societal needs/benefits balance

There is no question that there is a legitimate societal need for cost-effective, relatively inexpensive rodenticides, considering the serious and potentially lethal human diseases, e.g., hantavirus, typhus and the bubonic plague, that are spread by mice and rats. Furthermore, rodent plagues imply a burden of economic costs of property, food and crop damage and spoilage.

Continued access to cost-effective rodenticides can be approached as an issue of environmental justice. The balance of societal need and benefits, versus the overt poisonous nature of the product, is always to be considered regarding any regulatory decisions to limit access to rodenticides. This is particularly important to socio-economically disadvantaged communities. Such communities bear a double burden of more frequent rodent infestations, with concomitant exposure to diseases spread by rodents, possible rat-bite injuries to infants, damage to property and food spoilage and contamination, and limited resources to use other, non-poisonous solutions.

Restricted use applied for

The restricted use applied for is according to the intended product use:

- A highly active anti-coagulant bait for the control of the Norway rat, roof rat, the house mouse and gerbil.
- The restricted use application for use in homes is supported for all solid baits.

Mitigation measures

The following mitigatory label and/or leaflet instructions should be included:

<u>Prior to bait application:</u>

- Where possible, prior to the treatment inform any possible bystanders (e.g. users of the treated area and their surroundings) about the rodent control campaign.
- Consider preventive control measures (e.g. plug holes, remove potential food as far as possible) to improve product intake and reduce the likelihood of reinvasion.

<u>Bait application instructions:</u>

- The use of gloves is highly recommended when handling bait products and dead rodents.
- Solid products other than the powder formulation should not be applied directly in the burrows.
- The use of adequate tamper-resistant bait boxes is highly recommended.
- If the use of bait boxes is not practical, baiting points must be covered and placed in strategic sites to minimise the exposure to non-target animals and to uniformed bystanders.

- Precautions, e.g., keeping the product away from children and pets, and other directions for use on the product label must be followed. Baits must be unattainable to children, pets or other non-target animals in order to minimise the risk of poisoning.
- When placing bait points close to water drainage systems, ensure that bait contact with water is avoided.
- Protect bait from atmospheric conditions (wind and rain). Place the baiting points in areas not liable to flooding.

Precautions during use and disposal (clean-up)

- Bait stations should be visited at least every 2 to 3 days at the beginning of the treatment and at least weekly afterwards, in order to check whether the bait is accepted, bait boxes are intact or that bait stations are still adequately covered, as is practical, and to remove rodent bodies and bait that might have been removed or spilled from the bait station by rodents.
- Search for and remove dead rodents at frequent intervals during treatment.
- While wearing gloves, collect and properly dispose of visible carcasses of target pests or non-target animals. Place carcasses in leakproof plastic bags or other suitable containers and dispose of in the trash or dispose of according to the label disposal instructions.
- Carcasses buried on site must be buried a minimum of 45 cm below the ground surface, preferably deeper.
- All carcasses must be disposed of in a way inaccessible to wildlife, to prevent secondary poisoning of predatory animals.
- Remove the remaining product at the end of treatment period. Clear disposal instructions must be provided on the label.
- Do not use the product as permanent baits for the prevention of rodent infestation or monitoring of rodent activities.

Other precautions

- Any noted contact of a child with a rodenticide bait should be brought to the immediate attention of a medical professional, without exception.

Specific labelling recommendations

- The product information (i.e., label and/or leaflet) shall clearly show that:
  - The product should be used in "*in tamper resistant bait boxes*", or in otherwise "*adequately covered bait stations"*.
  - PCOs shall properly label bait boxes or other bait containers with the following information:
    - "*do not move or open*";
    - "*contains a rodenticide*";
    - product name or Act 36 of 1947 registration number;
    - active substance(s) and
    - "*in case of incident, call a poison centre (insert national phone number)*".
- Wearing gloves while handling bait and dead rodents must be emphasised on all labels.
- PCOs must be advised to use respiratory protection as recommended in this report.

Support for the restricted use application

The balance of societal need and benefits, versus the overt toxic nature of the product, is always to be considered regarding any regulatory decisions to limit access to rodenticides. This is particularly important to socio-economically disadvantaged communities. Such communities bear a double burden of more frequent rodent infestations, with concomitant exposure to diseases spread by rodents, possible rat-bite injuries to infants, damage to property and food spoilage and contamination, and limited resources to use other, non-poisonous solutions. Due to the same cost

concerns, the use of a bait box cannot be made obligatory for domestic or general public users, but recommendations to use bait boxes must be placed on all labels.

The application for derogation of the products assessed in this report is supported, provided that recommended mitigation measures are effectively implemented.

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List of Abbreviations

AEL	Acceptable exposure level
BCFs	Bioconcentration factors
BW	Body weight
CMR	Carcinogenicity, mutagenicity, and reproductive toxicity
EC	European Commission
EC50	The concentration of a compound resulting in a half-maximal response, e.g., immobilisation of invertebrates or inhibition of algal growth
ECB	European Chemicals Bureau
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemical's
ECHA	European Chemicals Agency
ErC50	The aqueous concentration of a test substance resulting in a 50% reduction in growth rate of aquatic organisms
EU	European Union
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
HHRA	Human health risk assessment
IPCS	International Programme on Chemical Safety
KABAM	Aquatic bioaccumulation model
K_{oc}	Partition coefficient organic carbon-water
K_{ow}	Octanol-water partition coefficient
LD50	The dose (mg/kg body weight) of a chemical that is lethal to 50% of exposed experimental animals
LC50	Lethal concentration 50, the concentration required to kill half of a group of aquatic test animals
LOAELs	Lowest-observed-adverse-effect levels
LOC	Level of concern
MOE	Margin of exposure
NOAELs	No-observed-adverse-effect levels
NRC	US National Research Council
OECD	Organisation for Economic Co-operation and Development
OPPT	USEPA Office for Pollution Prevention and Toxics
PCOs	Pest control operators
PNECs	Predicted no-effect concentrations
POD	Point of departure
PPDB	Pesticide Properties Database
PPE	Personal protective equipment
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
SDSs	Safety data sheets
SGARS	Second generation anticoagulant rodenticides
STOT RE	Specific target organ toxicity (repeated exposure)
TNsG	Technical Notes for Guidance
TRA	Targeted Risk Assessment
UF	Uncertainty factors
UFA	Uncertainty in extrapolating animal data to humans

UFH	Variation in susceptibility among the members of the human population
UF_{Sev}	Additional factor for severity of effects.
USEPA	United States Environmental Protection Agency

List of Terms

Acute toxicity	Adverse effects following oral or dermal administration of a single dose of a substance, or multiple doses given within 24 hours, or an inhalation exposure of 4 hours.
Anticoagulants	Chemical substances that decrease the clotting of blood, which, at sufficient blood concentrations, can cause excessive bleeding.
Carcinogenicity	Substance that causes cancer.
Derogation	An exemption from or relaxation of the consideration of this product for removal from the market due to it being considered a CMR product of concern.
Developmental toxicity	Any developmental malformation of the foetus, caused by a toxic substance. that is caused by the toxicity of a chemical or pathogen.
Environmental Fate	Behaviour in or movement of a chemical substance after having been released to the environment. The behaviour in or movements through the environmental compartments of air, soil and water, and the preferred final destiny compartment(s) are described.
Epidemiology	Study of the determinants, occurrence, and distribution of health and disease in a defined population.
Exposure assessment	Identification of environmental pathways, potentially exposed groups, routes of direct and indirect exposure, and estimates of concentrations and duration of exposure.
Genotoxicity	Damage to the cell genes, which may result in mutations.
Mutagenicity	Property of chemical agents to induce genetic mutation.
Neurotoxicity	Ability of a chemical to cause damage or malfunction of the neurological system.
Receptors	People/organisms exposed to the substance of interest.
Registrar	Registrar of the fertilisers, farm feed, agricultural remedies and stock remedies Act, 1947 (Act 36 of 1947) in the Department of Agriculture, Land Reform and Rural Development.
Reproductive toxicity	A substance or agent that can cause adverse effects on the reproductive system, causing the inability to reproduce offspring.
Risk characterisation	Integration of the components described above. The risk characterisation will also provide a review of documented human exposure incidents
Routes of exposure	Inhalation, ingestion, and dermal contact
Surrogate	A chemical with properties, including potential toxicity, that are likely to be similar to another substance of interest for which little information about the properties and/or toxicity are known. “Transferring” the known properties of the surrogate to that of the uncharacterised substance is known as the “bridging principle”, or “read-across” for the purposes of hazard and risk assessment.
Target organ toxicity	The effects on the organ impacted by a hazardous substance
Teratogenic	Causing defects in a developing foetus
Uncertainty review	Identifies the nature and, when possible, the magnitude of the uncertainty and variability inherent in the characterisation of risks

1 Introduction

1.1 Products identification

This document is a risk assessment report supporting an application for derogation for the restricted use of the registered solid rodenticide products listed below.

Report prepared for:		
Name	Regulatory Aspects on behalf of rodenticide manufacturers / retailers	
Contact details	Physical address	63 Glover Avenue, Doringkloof, Centurion, 0157
	Postal address	As physical address
	E-mail address	hannelie@regspecs.co.za

All products in Table 1.1.1 contain the rodenticide active substance brodifacoum, which has been identified as a reproductive toxicity hazard.

Table 1.1.1: Assessed products.

Product	Act 36 of 1947 registration numbers	Registered manufacturer / supplier / distributer
Broditop Pasta	L8387	Mr. Stefano Migliore
Di-Rat-Blue (grain bait)	L9836	Newton Fertilizers CC
Doom Rattex Deadly Pellets	L7725	Tiger Consumer Brands Ltd
Doom Rattex Deadly Pellets Chew Through Packs	L7725	Tiger Consumer Brands Ltd
Doom Rattex Deadly Wedges	L11294	Tiger Consumer Brands Ltd
Doom Rattex Deadly Powder	L7727	Tiger Consumer Brands Ltd
Jaguar Blox	L8259	MC Pharma (Pty) Ltd
Kill-All Grain bait	L8211	Almond Agro Chemicals (Pty) Ltd
Kill-All Pellets	L7162	Almond Agro Chemicals (Pty) Ltd
Kill-All Wedges	L7265	Almond Agro Chemicals (Pty) Ltd
Kombat Rat and Mouse Block	L6425	Kombat (Pty) Ltd
Kombat Rat and Mouse Pellet	L6424	Kombat (Pty) Ltd
Mortein Rat Kill Pellets (Mother registration is Pulse Pellets)	L6907	Reckitt Benckiser South Africa (Pty) Ltd
Pulse pellets	L6190	Lifeguard Sciences (Pty) Ltd
Pulse wax blocks	L6189	Lifeguard Sciences (Pty) Ltd
Rodenthor TM Block	L9396	Mr. Stefano Migliore
Rodenthor TM Pasta	L9586	Mr. Stefano Migliore
Rodex Bait Blocks	L9292	Innovative Pest Management (Pty) Ltd
Rodex Grain Bait	L9291	Innovative Pest Management (Pty) Ltd
Rodex Pasta Bait	L9566	Innovative Pest Management (Pty) Ltd
Rodex Rat & Mouse Pellets	L9293	Innovative Pest Management (Pty) Ltd
Rodex Rat R.I.P	L9709	Innovative Pest Management (Pty) Ltd

1.2 Regulatory context

In a document circulated to "All Regulatory Holders" on 14 April 2022, the Registrar: Act 36 Of 1947, of the Department of Agriculture, Land Reform and Rural Development ("Registrar" and "The Department") refers to an assessment that was carried out at the international level to determine risks to human health due to exposure to active ingredients and their formulations that meet the criteria of carcinogenicity, mutagenicity, and reproductive toxicity ("CMR") categories 1A or 1B according to the Globally Harmonized System of Classification and Labelling of Chemicals ("GHS"). The Department then stated that "*the assessment identified the need to reduce risks to human health associated with such products*".

Category 1A covers substances that are known to be CMR, mainly according to human evidence. Category 1B covers substances presumed to be CMR based on data from animal studies. The Registrar stated his intention to "*prohibit the use of ingredients and their formulations that meets* (sic) *the criteria of CMR categories 1A or 1B of the GHS as from 01 June 2024*".

However, in exceptional circumstances, the Registrar may grant registration of an implicated agricultural remedy when it can be demonstrated that: *"a) The risk to humans, animals or the environment from exposure to the active substance in an agricultural remedy, under realistic worst-case conditions of use, is negligible*" (and other conditions not relevant to this INFOTOX report).

In February 2024, the Registrar issued a Guideline for the Application for a Derogation for an Agricultural Remedy Identified as a Substance of Concern. This INFOTOX report deals with the assessment of risk to humans, animals and the environment, associated with the use of the rodenticide products indicated in Section 1. Specific attention is given to the risk of reproductive toxicity effects in occupational workers.

2 Background to human health risk assessment

2.1 The health risk assessment paradigm

A significant factor in the Organisation for Economic Co-operation and Development (OECD 2021) guidance document on key considerations for the identification and selection of safer chemical alternatives deals with the likelihood of exposure (human and ecological). OECD recommended that routes of exposure to a hazardous chemical that are unlikely, based on measured exposure data or physical-chemical properties of the substance of concern, should be excluded from the assessment. More correctly, the statement should refer to pathways of exposure (air, soil, water, and sediment), and routes of exposure (inhalation, ingestion, and dermal contact).

This recommendation of the OECD (2021) takes the assessment a step further from the hazard data of chemicals represented in the GHS, to the level where the potential for exposure of humans and ecological receptors is assessed, and through accounting for the toxicology of a substance or formulation, the level of risk is determined. This is aligned with the observations and recommendations of Karamertzanis et al. (2019).

Karamertzanis et al. (2019) evaluated the impact on classifications of carcinogenicity, mutagenicity, reproductive and specific target organ toxicity after repeated exposure in the first ten years of implementation of the REACH[1] regulation. The authors highlighted that classification for

[1] Registration, Evaluation, Authorisation and Restriction of Chemicals.

carcinogenicity, mutagenicity, reproductive toxicity, and specific target organ toxicity (repeated exposure) ("STOT RE") triggers several obligations for manufacturers, importers, and professional users.

Karamertzanis et al. (2019) then stated: "*In addition to such consequences under other legislations* (sic)*, registrants are required to carry out exposure assessment and risk characterisation for substances that are classified and, hence, classification under REACH is a trigger for risk assessment for human health."*

OECD (2021) referred to the European Centre for Ecotoxicology and Toxicology of Chemical's ("ECETOC")[2] Targeted Risk Assessment ("TRA") tool for calculating the risk of exposure from chemicals to workers, consumers, and the environment. This illustrates the logic of basing the final decision about the safety of a chemical or formulation on health risk assessment, rather than only on hazard identification, as represented in the GHS.

The original paradigm for regulatory human health risk assessment ("HHRA") in the USA was developed by the US National Research Council (NRC 1983). This model has been adopted and refined by the US Environmental Protection Agency ("USEPA") and other international agencies as published under the International Programme on Chemical Safety (IPCS 1999; IPCS 2010), and is widely used for quantitative human health risk assessments. Figure 2.1.1 illustrates the health risk assessment paradigm in a simple diagram.

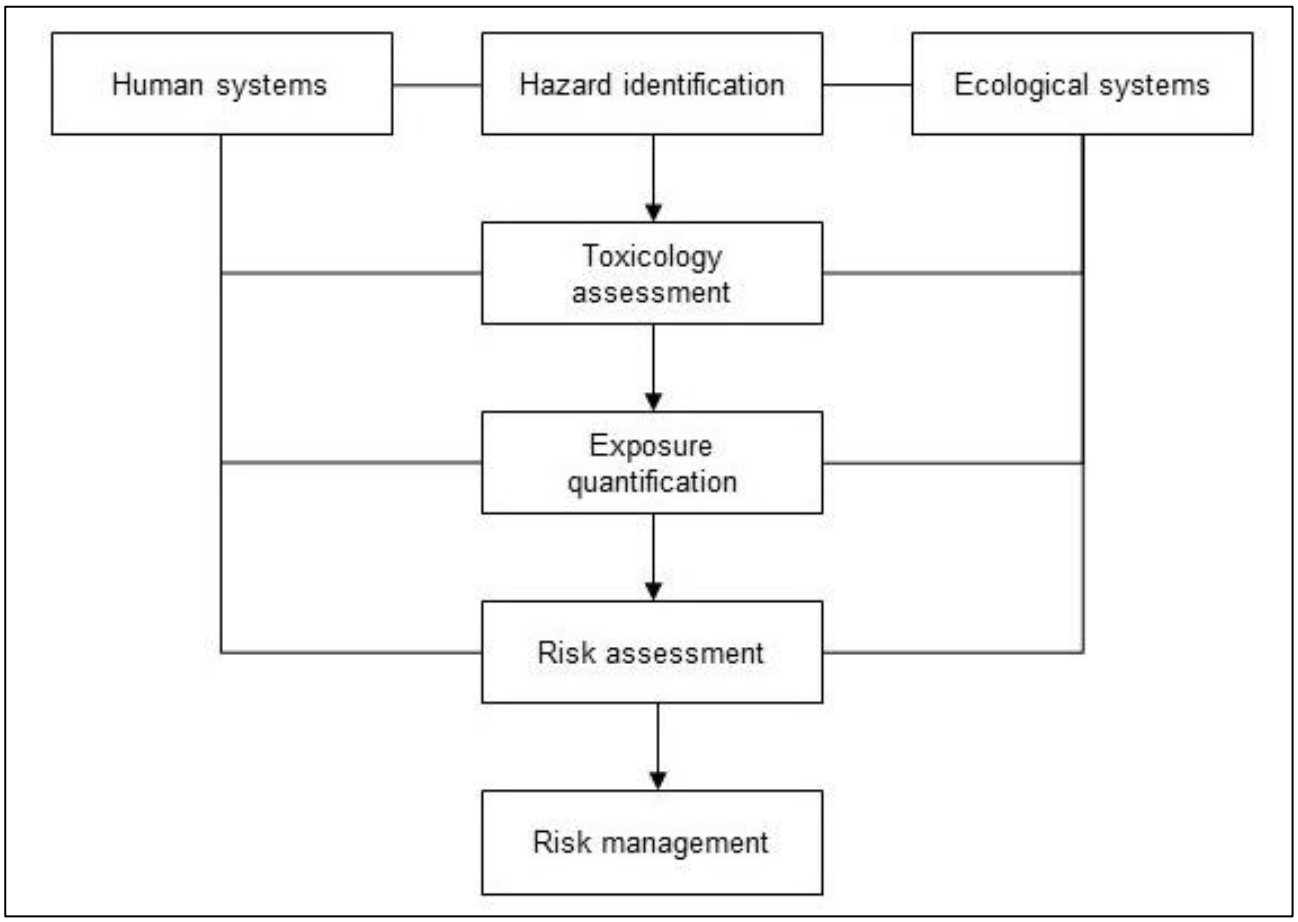

Figure 2.1.1: The holistic health risk assessment paradigm.

[2] http://www.ecetoc.org/tools/targeted-risk-assessment-tra/.

2.2 Human health risk assessment methodology

The human health risk assessment ("HHRA") paradigm divides human health risk assessment into several logical steps, as illustrated in Figure 2.2.1. All of these are not fully applicable to the toxicological risk assessment for the purpose of derogation of rodenticides:

- **Hazard assessment** is the identification of the chemical constituent of concern and the hazard it poses, in this case reproductive/developmental toxicity hazards of brodifacoum. This is discussed in Section 3.

- **Dose-response assessment** (toxicological assessment) addresses the relationship between levels of uptake and the manifestation of adverse effects (reproductive/developmental toxicity).

    - Toxicological information from available reproductive/developmental studies and applied standard risk assessment methodologies are used to derive a point of departure ("POD") or acceptable exposure level ("AEL"), and level of concern ("LOC") for the HHRA purposes, by applying appropriate uncertainty factors and safety factors for infants and children, referring to dose through the routes of exposure. The derived toxicological values will be protective specifically against potential reproductive/developmental effects of the product. This ensures compliance with the Guideline for the Application for a Derogation for an Agricultural Remedy Identified as a Substance of Concern, issued by the registrar: Act 36 of 1947, in February 2024. Health risks may also be assessed following the margin of exposure ("MOE") approach. The MOE approach is basically a comparison of the calculated exposure dose and the toxicity limit value for a specific health effect, referred to as the health effect endpoint.

    - The calculated MOE is compared to the level of concern ("LOC"), also referred to as a benchmark MOE. The LOC is the margin of exposure between the calculated exposure and the POD that indicates a risk of health effects associated with the calculated exposure. Each POD is associated with a specific numerical LOC value. Therefore, if a calculated MOE is higher in value than the LOC associated with the POD used for the MOE calculation, a risk to health under the assessed exposure conditions is highly unlikely and excluded for all practical purposes. However, if the calculated MOE is lower than the associated LOC, a risk to health cannot be excluded.

- **Exposure assessment considers** the identification of environmental pathways, potentially exposed groups, routes of direct and indirect exposure, and estimates of concentrations and duration of exposure. A conceptual model of application practices and exposure pathways and routes applicable to the identified receptors was constructed to guide the exposure assessment for the health risk assessment.

  The HHRA focuses on the following <u>occupational user exposure</u> scenarios:
    - The oral, dermal and inhalation routes of exposure of pest control operators ("PCOs").

  <u>Residential user exposure</u> scenarios are assessed, because the rodenticides are for sale in retail outlets catering to the general public:
    - Assuming that non-professionals might not be diligent users of personal protective equipment ("PPE"), the exposure of domestic users (non-professionals) handling rodenticides without gloves, that is, dermal exposure, is assessed.

- The normal procedure recommended on product labels is to place rodenticides for residential exposure out of reach of children, and away from food products or places where food may be stored or prepared. E.g., label instructions are: "*Set bait stations where these will be inaccessible to children and domestic animals*".
- Nonetheless, accidental mouthing or ingestion of bait by infants/toddlers are assessed.

- **Risk characterisation** involves the integration of the components described above. The risk characterisation also provides a review of documented human exposure incidents, if available.

- **Uncertainty review** identifies the nature and, when possible, the magnitude of the uncertainty and variability inherent in the characterisation of risks.

3 Hazard identification

3.1 The need for GHS classification

Internationally, there is a demand for safer chemicals and technologies, and it is appropriate to utilise information in the GHS as a starting point. This INFOTOX report relates specifically to active ingredients and their formulations that meet the criteria of CMR categories 1A or 1B in the GHS. Information in the GHS represents hazard data, not information on risk.

3.2 Brodifacoum CMR hazard classification

The GHS hazard classification identifying the product as a CMR hazardous substance of concern, is: Reproductive toxicity category 1A (H360D); "D" indicating a hazard of developmental effects (effects on the growing foetus) (Table 3.2.1).

Active ingredient identification

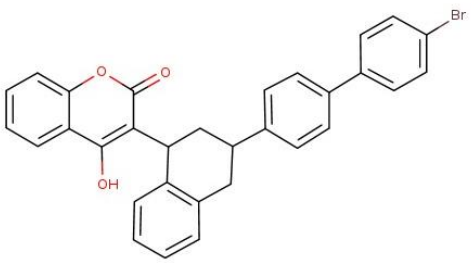 **Brodifacoum**	**CAS #:** 56073-10-0 **Mol. formula:** $C_{31}H_{23}BrO_3$ **Molecular weight:** 523.4 g/mol

Table 3.2.1: CMR GHS classification of brodifacoum.

Hazard class and category code	Hazard statement code	Hazard statement	Signal word	Pictogram
Carcinogenic	Not classified	Not applicable	Not applicable	Not applicable
Mutagenic	Not classified	Not applicable	Not applicable	Not applicable
Reproductive Toxicity Cat. 1A	H360D	May damage the unborn child	Danger	
Classification according to the European Chemicals Agency ("ECHA" online); harmonised EU classification.				

GHS Category 1A criteria for substance classification:

- Known human reproductive toxicant - largely based on evidence from humans
- Known to have produced an adverse effect on development in humans; or
- Evidence from animal studies, possibly supplemented with other information, provides a strong presumption that the substance has the capacity to interfere with reproduction in humans.

Table 3.2.2 presents the brodifacoum concentrations of the rodenticide products included in this assessment report. All products are mixtures of more than one chemical substance. None of the other constituent substances have been classified as CMR hazards. The complete compositions are not provided here, in order to protect proprietary information, but have been made available to the Registrar of Act 36 of 1947, in confidence, at the time of the application for registration.

The listed products are assigned the H-code H360D because the concentrations of brodifacoum are sufficient to justify the reproductive toxicity classification (≥ 0.003 % w/w, Table 3.2.2), according to guidance of the European Chemical Agency ("ECHA") (ECHA online) on the GHS classification of chemical mixtures containing brodifacoum.

Table 3.2.2: Concentrations of brodifacoum in the solid rodenticide products.

Formulation components	Active ingredient content	
	g/kg	Weight %
Wedge/block formulation		
Jaguar Blox	0.05	0.005
Kombat Rat and Mouse Block	0.05	0.005
Pulse Wax Blocks	0.05	0.005
Rodenthor TM Block	0.05	0.005
Rodex Bait Blocks	0.01	0.001
Rodex Rat R.I.P. (Blocks)	0.01	0.001
Doom Rattex Deadly Wedges	0.05	0.005
Kill-All Wedges	0.05	0.005
Pellet bait		
Doom Rattex Deadly Pellets	0.05	0.005
Doom Rattex Deadly Pellets Chew Through Packs	0.05	0.005
Kill-All Pellets	0.05	0.005
Kombat Rat and Mouse Pellet	0.05	0.005
Mortein Rat Kill	0.05	0.005
Pulse pellets	0.05	0.005
Rodex Rat and Mouse Pellets	0.01	0.001
Grain bait		
Di-Rat-Blue	0.008	0.0008
Kill-All Grain Bait	0.02	0.002
Rodex Grain Bait	0.01	0.001

Formulation components	Active ingredient content	
	g/kg	Weight %
Paste bait		
Broditop Pasta	0.05	0.005
Rodenthor® Pasta Bait	0.05	0.005
Rodex Pasta Bait	0.05	0.005
Powder formulation		
Doom Rattex Deadly Powder	0.03	0.003

4 Environmental fate and behaviour

4.1 Brodifacoum in air

Brodifacoum in solution is not expected to partition into the atmosphere to a significant extent (French CA 2017), due to:

- Vapour pressure far less than 1 x 10^{-6} Pa.
- Henry's law constant (calculated on the basis of water solubility of 0.24 mg/litre at pH 7) far less than 2.18 x 10^{-3} $Pa.m^3.mol^{-1}$

Brodifacoum is expected to rapidly photolyse and photodegrade (DT_{50} = 0.217 days) (French CA 2017).

4.2 Brodifacoum in water

Brodifacoum is essentially insoluble in water at pH 5, but increasing the pH increases solubility (French CA 2017). The University of Hertfordshire Pesticide Properties DataBase ("PPDB", Lewis et al. 2016) lists a solubility of 0.0038 mg/litre at 20°C, interpreted as "low" solubility in water.

The aqueous hydrolysis DT_{50} at 20°C and pH 7 is 30 days, interpreted as indicating moderate persistence (Lewis et al., 2016) and likely stability (USEPA 2020a) of brodifacoum in environmental water bodies.

The log of the octanol/water partition coefficient (log K_{ow}) at pH 7 and 20°C is listed as:

- 4.92 (French CA 2017), and
- 6.12 (Lewis et al. 2016).

The log K_{ow} values indicate a relatively high propensity to accumulate in lipid-like environments as opposed to a watery environment, that is, brodifacoum is lipophilic and hydrophobic. Brodifacoum will thus be able to penetrate cell walls with relative ease and is likely to accumulate in the fatty deposits of exposed organisms.

Bioconcentration factors ("BCFs") in fish, found in the literature are 6 000 litre/kg (PPDB, Lewis et al. 2016) and 2 450 (unitless) (USEPA 2020a), both reflecting the potential to bioconcentrate.

4.3 Brodifacoum in soil

The organic carbon partition coefficient ("K_{oc}") in soil indicates the mobility of a chemical in soil, that is, the propensity of a chemical substance to bind to the organic matter present in soil. A high Koc value is associated with a strong bond to the soil particles, and thus less mobility (less likely to move, or leach, through soil). A lower Koc value indicates chemical mobility, and faster leaching rates through soil. A higher Koc can thus also indicate potential accumulation of a chemical in soil over time, under conditions of continuous addition to soil.

The K_{oc} of brodifacoum is 9 155 litre/kg in the pH range 7.1 to 7.6, quoted by the French CA (2017) and the USEPA (2020a), presumably both from Lewis et al. (2016), interpreted as indicating that brodifacoum can be considered immobile in soil. The potential for groundwater contamination should thus be low.

4.4 Summary

The USEPA (2020(a)) has summarised the environmental fate concerns for brodifacoum as presented in Table 4.4.1.

Table 4.4.1: USEPA summary of environmental fate concerns for brodifacoum.

Concern	Yes	No	Notes
Aquatic bioconcentration/ bioaccumulation	Possible; relatively high log Kow and fish BCF (see Section 4.2)		Assessed using a K_{ow}-based aquatic bioaccumulation model ("KABAM") for chemicals with a log K_{ow} > 3.1
Groundwater contamination		X	Low mobility in soil: K_{oc} = 9 155 litre/kg (see Section 4.3)
Sediment contamination		X	-
Persistence in the environment	Moderately persistent		-
Residues of concern	Brodifacoum		Potential for metabolites formation in aquatic environment is negligible, due to: • strong and rapid adsorption of brodifacoum to sediments • slow transformation of brodifacoum in water (Italian CA 2010)
Secondary exposure of non-target animals/birds/fish etc.	X		-
Volatilisation		X	Not volatile (see Section 4.1)

5 Environmental assessment

Brodifacoum toxicity to non-target species

As can be expected of a rodenticide ingredient, brodifacoum is very toxic to mammals. The Italian CA (2010) proposes the following predicted no-effect concentrations ("PNECs"):

- $PNEC_{oral\text{-}mammals}$ = 2.22 x 10^{-4} mg/kg food, corresponding to
- $PNEC_{oral\text{-}mammals}$ = 1.1 x 10^{-5} mg/kg bw.

The avian acute toxicity of brodifacoum varies markedly between different species (Italian CA 2010). Brodifacoum is acutely toxic to the mallard duck with an LD50 value of 0.31 mg/kg bw, while it is judged as moderately toxic in the Japanese quail, with an LD50 value of 19 mg/kg bw.

Based on 5-day dietary toxicity studies with Laughing Gulls, the Italian CA (2018) has also concluded that brodifacoum is very toxic to birds upon short term exposure; the lowest endpoint being an LC50 of less than 0.72 mg/kg food. The "food" in these tests were masticated rodent tissue with brodifacoum, where 60 per cent mortality occurred at the lowest dose level of 0.72 mg/kg food by day 18 of the post exposure observation period.

Brodifacoum is very toxic to organisms in the aquatic compartment. This is demonstrated by toxicity study results in fish (LC50 = 0.04 mg/litre), invertebrates (EC50 = 0.25mg/litre) and algae (72h ErC50 = 0.04 mg/litre), with fish and algae being the most sensitive groups (Italian CA 2017).

The earthworm toxicity of brodifacoum is considered as low, since exposure to brodifacoum up to 994 mg/kg dw in artificial soil did not show any effects on the test species (*Eisenia fetida*) (Italian CA 2010).

Primary exposure

Primary exposure of non-target species, that is, direct contact with the rodenticide, is not expected for the solid formulations of brodifacoum-containing rodenticides, since the usual rodenticide label instructions are to place the bait in areas of infestation, out of reach of children and animals. Therefore, primary exposure is not assessed.

Secondary exposure

Cleaning of bait stations might result in the release of brodifacoum into municipal drains, ending up in sewage treatment plants, but the Italian CA (2017) presented a study showing no effects on activated sludge from a sewage treatment plant treating predominantly domestic sewage. The degree of confidence in the result is relatively high, since the test was carried out at nominal concentration "much higher" than the water solubility of brodifacoum.

Responsible product application and care, with clear product label and SDS instructions to prevent contamination of waterways, should limit aquatic contamination to negligible. Therefore, no risk assessment for secondary poisoning through the aquatic food chain is required, and also no risk assessment for non-mammalian or non-avian terrestrial organisms.

Secondary exposure in mammals and birds of prey describes the ingestion, by natural predators in the environment, of dead or dying target animals, that is, rats or mice in the case of solid brodifacoum formulations. However, the French CA (2017) has pointed out that a secondary poisoning hazard can only be ruled out completely when the rodenticide is used in fully enclosed spaces so that rodents cannot move to outdoor areas or to (parts of) buildings where predators may have access.

The assessment of secondary exposure where predators have access to dead or dying rodents is not trivial. One approach to the study of secondary exposures of predators requires field studies conducting detail experimental examinations, e.g., of the stomach content of predators. The experimental data are then incorporated into complex probabilistic risk assessments. However, these complex assessments do not guarantee sufficient evidence to support definitive conclusions, since important uncertainties and data gaps tend to remain, as found in a study example evaluated by the USEPA (USEPA 2005).

The general conclusions of assessments based on available toxicity values in predatory birds and non-target predatory mammals is that secondary risks to mammalian and avian predators cannot be excluded (Italian CA 2010, French CA 2017 and USEPA 2005).

6 Human health and toxicological review

6.1 Pertinent human health effects

Brodifacoum is a second-generation single-dose anticoagulant rodenticide. It disrupts the normal blood clotting mechanisms by inhibiting vitamin K. The result of biochemical interference is an increased bleeding tendency and, eventually, haemorrhage and death (Italian CA 2010). The chemical "backbone" involved in the toxic effect is 4-hydroxycoumarin, which is common to some of the most common rodenticides, such as brodifacoum, bromadiolone, coumatetralyl, coumafuryl, and difenacoum (Murphy and Lugo 2015).

The USEPA (2020b) studied incident records of rodenticide exposures (not necessarily ingestion, and not necessarily resulting in death). The total number of rodenticide incidents slightly decreased from 198 incidents in 2009 to 146 incidents reported in 2018, and incidents specifically with second generation anticoagulant rodenticides ("SGARS"), such as brodifacoum, had decreased by 79 per cent from 164 incidents in 2009 to 34 incidents in 2018. Similar data are not available for South Africa, but the USEPA data show that incident numbers can be described as moderate.

Overall, the USEPA found a low frequency of 21 occupational incidents from 2011 to 2015, for all types of anticoagulant rodenticides, of which 15 cases involved zinc phosphide. Of the 21 occupational cases, 1 case was high in severity, 5 cases were moderate in severity, and 15 cases were low in severity. Ten cases sought care in an ER or hospital; and 11 cases contacted poison control for treatment and guidance (all 11 cases that contacted poison control were low in severity). This demonstrates that proper training of pesticide applicators and the use of personal protective equipment are effective management tools limiting occupational exposure risks.

The health effect most frequently reported by the occupational cases was nausea, followed by altered taste (metallic or chemical taste), vomiting, upper respiratory pain/irritation, and shortness of breath. These symptoms are relevant to acute (single) exposure incidents.

6.2 Routes of absorption

Oral absorption

The French CA (2017) reported an estimated brodifacoum oral absorption factor of more than 75 per cent, but concluded that "almost complete" (100%) oral absorption can be accepted.

Dermal absorption

The French CA (2017) reported the following values:

- Pellets and grains:
  - 5% as a worst-case estimate, because of the experimental procedure and because the exposure period exceeded the usual time of 8 hours applicable to professional handling.
  - 0.647% as a valid rate, generalised from a study on difenacoum.
- Wax blocks: 0.047%, generalised from a study on difenacoum.
- Wearing gloves is assumed to reduce the exposure of hands by 90% (French CA 2017).

Inhalation

Brodifacoum in solid preparations has a very low volatilisation potential. Due to its physico-chemical properties (low vapour pressure of 2.6×10^{-22} Pa at 20°C and low Henry's law constant of 2.35×10^{-18} $Pa.m^3.mol^{-1}$), brodifacoum is not expected to be present in the atmosphere in significant quantities when applied in solid form. The potential for inhalation exposure is thus low, but if

inhalation exposure should take place, e.g., to dusts, toxicity is expected to be similar to oral exposure (French CA 2017).

6.3 Toxicological studies

Metabolism (in mammals) is limited and the toxicologically relevant chemical species is brodifacoum (French CA 2017).

Acute toxicity data presented by the French CA (2017) are the LD_{50} of "about" 0.4 mg/kg in the male rat and mouse, and a skin (dermal) LD50 of 7.48 mg/kg in rat females; "even lower", but not specified, in males. These values were reported from unpublished studies, and the original studies are not available for further scrutiny. Acute inhalation studies were waived for ethical and animal welfare reasons, considering the low vapour pressure of brodifacoum.

The French CA (2017) reported unpublished repeated dose (subchronic 90-day) oral studies in the rat and dog, showing clinical signs, haematological and post mortem data consistent with the known pharmacological action of impairment of the clotting cascade, resulting in increased prevalence of haemorrhage, leading to death. There were no indications of other secondary toxicities, also not histopathological changes. The lowest subchronic repeated-dose no-observed-effect-level ("NOEL") in the above study was 0.001 mg/kg-day, based on biochemical signs of decreased blood clotting potential, and haemorrhagic changes seen at necropsy.
In conclusion, the subchronic oral toxicity NOEL is in the range of 0.04 to 0.001 mg/kg-day. Based on results from the acute dermal and inhalation toxicity studies, route-to-route extrapolation of the results of the subchronic oral toxicity studies are justified, assuming serious damages associated with prolonged exposure through dermal and inhalation routes as well (French CA 2017).

Reproductive and developmental toxicity
The decision by the European authorities to classify brodifacoum as a developmental hazard (H360D) needs some background discussion. The following information from unpublished studies are obtained from the French CA (2017).

Reproductive and developmental toxicity studies on brodifacoum did not reveal any specific effects in two prenatal toxicity studies in the rat and rabbit, respectively, evaluated as "adequate" by the French CA (2017). General toxicity effects were observed, explainable by brodifacoum's anticoagulant properties. The lowest NOAELs for rabbits and rats in these studies were 0.002 and 0.001 mg/kg-day, respectively.

Maternal haemorrhages were observed at dose levels higher than 0.01 mg/kg in rats, but no effects on conceptuses up to the highest dose level of 0.04 mg/kg. Interference with coagulation was evident on a biochemical level in rabbit dams treated at 0.004 mg/kg, but there was no evidence of developmental toxicity effects. The highest dose of 0.005 mg/kg caused a high proportion of maternal deaths in rabbits, but no significant effects in the offspring.

The French CA also reported results of a two-generation study on rats. Developmental toxicity was not observed in the absence of general toxicity, but haemorrhagic effects on the parental generation were confirmed, as well as a parental NOAEL of 0.001 mg/kg.

In spite of these findings, and because the OECD Guideline 414 used at that time might have had limitations in the detection of developmental effects of coumarin-related compounds, a provisional decision had been made to apply the reproductive toxicity hazard classification to all anticoagulant active substances on the basis of analogy to warfarin (specifics not cited by the French CA).

Neurotoxicity, genotoxicity and carcinogenicity

Neurotoxic effects were not observed in any of the unpublished acute or subchronic laboratory animal tests available to the French CA (2017).

Brodifacoum displayed no mutagenic activity in a standard battery of genotoxicity tests. Long-term carcinogenicity studies were not considered technically feasible and concern about possible non-genotoxic carcinogenic effects are not justified from the available repeated-dose or a two-generation study on rats. Brodifacoum is also devoid of chemical structures known to be associated with possible carcinogenicity. Thus, there is no evidence indicating a possible classification of carcinogenicity.

7 Approaches to rodenticide health risk management

7.1 USEPA human health risk management strategy

The USEPA (2020b) accepted that anticoagulant pesticides are extremely acutely toxic by all routes of exposure. Therefore, the USEPA did not aim to derive toxicity values, such as reference concentrations or acceptable daily intakes, as a basis for an overall human health risk assessment and risk management strategy for brodifacoum or the other anticoagulants. The USEPA waived further human health data requirements, and did not require any additional toxicological data, since it was concluded that additional data would not inform or impact the overall risk management strategy.

The USEPA overall risk management strategy is to limit potential non-target exposures. This strategy is followed because the available hazard and toxicity profile for the rodenticides informed the pivotal conclusion that *any* potential exposure may result in adverse effects and potential risks of concern; therefore, a quantitative risk assessment was not conducted or required as a necessity

Rather, the USEPA determined that labelled uses of these products should be modified, as needed, to assure that occupational and non-occupational dermal and inhalation exposures are limited as far as possible. The occupational mitigation measures most recommended are the use of suitable PPE.

7.2 The European Union approach to human health risk management

7.2.1 Rodenticide users and use phases

Exposure to brodifacoum in rodenticides was calculated by the French CA (2017) according to the recommendations in the Technical Notes for Guidance (“TNsG”) on Human Exposure to Biocidal Products, compiled by the European Chemicals Bureau (“ECB”) of the European Commission (“EC”) (ECB 2007). The TNsG provides indicative exposure values for a range of generic exposure scenarios discussed in the TNsG, amongst these European Union (“EU”) Product Type 14: Rodenticides.

The TNsG assumes a general rule that rodenticides are formulated, sold (packaged) and applied (placed) in such a way that humans and non-target animals should not be exposed. Bait stations in which the rodenticide is to be placed should protect people and non-target animals from exposure,

and the use of bait boxes is usually recommend. In case bait boxes are not practical, the bait station must be covered in order to prevent access by non-target animals and unaware bystanders.

Rodenticide users

The TNsG (ECB 2007) distinguishes two main types of users, namely:

- Users in contact with the biocidal product as a consequence of their professional life. In this assessment of products registered in South Africa, "professional" users are viewed as occupationally exposed PCOs:
  - Industrial users: involved in manufacturing, handling and/or packaging of actives or products in industry. These are not applicable to the health risk assessments presented in this report.
  - Professional users: those using end-products outside industry. In South Africa, the term PCO is applicable and PCOs are required to be registered in South Africa. PCOs are relevant to the health risk assessments presented in this report.
  - Professional users are sometimes assessed according to sub-categories of "trained" and "untrained" professionals. An example of an "untrained" professional would be a person managing orchards or plantations where rodenticides are used to protect young saplings from rodents stripping the bark. In the case of untrained professional users, at least a basic knowledge of the associated hazards, PPE use and the interpretation and implementation of safety instructions on product labels and SDSs is assumed.

- Non-professional users (consumers): "*member of the general public who may primarily be exposed to biocides by using a consumer product"* (ECB 2007). In the case of the rodenticides assessed in this report, the "*consumer product*" referred to is a rodenticide product accessible to lay persons, sold in shops where the product is accessible to the general public.
  - According to the TnsG the consumer is "*unlikely to take informed measures to control exposure and to follow exactly the instructions for using the biocidal product*".
  - The non-professional use pattern is expected to involve a lower frequency and/or duration of use.

Exposure terminology

Primary and secondary exposure scenarios are distinguished in the TNsG (ECB 2007):

- Primary exposure "*occurs to the individual who actively uses the biocidal products, i.e. the user*". The user may be a professional at work or a non-professional, that is, a consumer (see previous definitions of professionals and non-professionals).
- Secondary exposure "*may occur after the actual use or application of the biocidal product"*. The TNsG further differentiates between professional user secondary exposure as:
  - *Intentional secondary* exposure, that is, any secondary exposure incurred during a worker's regular employment duties, e.g., a carpenter exposed to wood dust impregnated with a biocide.
  - *Incidental secondary* exposure scenarios not necessarily incurred during employment but resulting from the professional use of a biocide, e.g., home laundering of contaminated work clothes.
  - The ECB (2007) concluded that, in most instances, secondary exposure scenarios are best assessed using the methodology for non-professional users (consumers).

Intentional secondary exposure, as defined above, is not applicable to rodenticides, because the rodenticides are not applied to consumer products, or to surfaces to which persons (occupational or the general public) might subsequently be exposed.

While reviewing the human health risk assessments of EU competent authorities, it was apparent that the term “secondary exposure” was generally applied to bystanders in accidental contact with rodenticides, principally during the use- and disposal phases (see definitions below). Such accidental contact should, in any case, also account for the incidental secondary dermal exposure to contaminated clothing being laundered, because of the conservative (high-end) accidental exposure values that are used (see the exposure values descriptions provided below). The term “secondary exposure” is applied accordingly in this solid rodenticide human health risk assessment report, meaning accidental contact of adult or child bystanders with the product.

Secondary exposure also includes inappropriate contact with dead rodents or left-over bait, e.g., a bystander cleaning up dead rodents or left-over or spilled bait, dragged away from the bait station by rodents. Secondary exposure of bystanders is assessed and the risks are reported numerically, or relative to the primary exposures and risks of PCOs.

Rodenticide use phases

The TNsG (ECB 2007) distinguishes the following phases, based on handler use patterns:

- Application,
- Use, and
- Disposal phases.

In the case of solid rodenticides, the product “as supplied” is applied during the application and use phase. The use exposure variables are thus similar. A smaller mass of rodenticide might be applied during the use phase, but, for ease of presentation in this report, exposure and risks during the application and use phases are assumed similar. Risks indicated for the “application phase” are thus also valid for the “use phase”, although it might, in an unknown proportion of cases, slightly overestimate exposure during the “use phase”. This is of little practical importance, because the rodenticide label instructions do not prescribe the application of different masses during the use phase.

Some disposal phase activities, such as cleaning up and disposing of spilled bait and dead rodents, might also be applicable during the use phase, but are not considered separately in the “use” phase. The conservative disposal phase exposure variables are viewed as sufficiently representative of exposure during clean-up and disposal activities in the use phase.

The TNsG (ECB 2007) phase descriptions are:

Application phase:

- Transfer of bait from the product packaging to the bait station. The place where the bait is dispensed (“placed”) is referred to as the bait station.
- Several bait station constructs are possible, such as merely hiding the rodenticide under a cover, to prevent or at least diminish contact after placing, or placing the rodenticide in a pipe, long enough to prevent bait contact by scavenger or predatory non-target animals, or application of the solid bait in a secure, tamper-proof bait box.
- The most prominent handler exposure scenarios, based on formulation use patterns, are:
    - Placing of bait boxes.
    - Loading of bait boxes or bait stations with grain bait, bait pellets or wax blocks/rounds/wedges from larger containers.
    - Securing large paraffin blocks at bait stations in sewers.
    - Applying bait by hand.

Use phase (after application):

- This is the baiting period, when the biocidal product is available for consumption by the target organism.
- Rodenticides are usually confined to areas with a minimum of human access. The TNsG assumes that bait-boxes in private and industrial areas are “locked off” to prevent contact, but this assumption is not applied in the risk assessment of products registered in South Africa, and is not relevant to the application of powder formulations.
- As stated before, it is assumed that activities and exposure during this phase is not much different from the application and disposal phases. Primary user exposure is thus not specifically assessed during the use phase, because exposures during the application and disposal phase are applicable to these activities during the use phase.
- The largest number of bystanders are exposed in this phase, e.g., unaware workers, adults and children in the vicinity, usually accidentally or by curiosity. Bystander exposure includes possible contact of the general public, or unaware workers, with dead rodents or spilled bait, assessed mainly as part of the disposal (clean-up) phase.
- Human exposure could be by accidental touching (dermal contact) and, in the case of children, by transient mouthing or chewing of bait.

Disposal (clean-up) phase:

- Final inspection of rat holes, bait points, drain and sewerage, as professionals decide when to stop the local campaign, and are assumed to remove/clean the bait stations, which may result in exposure.
- Normally, the same person applies the rodenticide, disposes of empty packaging, collects residues and dead rodents, and empties containers for disposal.
- Bystander exposure includes possible contact of the general public, or unaware workers, with dead rodents or spilled bait.

7.2.2 Solid rodenticide application practices and exposure variables

Occupational exposure to brodifacoum in rodenticides was calculated by the French CA (2017) according to the TNsG recommendations, using “indicative exposure values” for a range of generic exposure scenarios discussed in the TNsG, amongst these for the European Union (“EU”) Product Type 14: Rodenticides.

The TNsG assumes a general rule that rodenticides are formulated, sold (packaged) and applied (placed) in such a way that humans and non-target animals should not be exposed. Bait stations in which the rodenticide is to be placed should protect people and non-target animals from exposure. Nevertheless, the TNsG considers primary exposure to the rodenticide applicator. This is relevant to the solid formulations assessed in this report.

The TNsG (ECB 2007) describes the use of bait stations, including bait boxes (box-like bait stations) for solid rodenticide products as follows:

- These boxes/stations, especially when tamper-proof, are used to prevent human contact with the rodenticide.
- Several application methods are available, such as merely hiding the rodenticide under a cover, to prevent or at least diminish contact after placing, or placing the rodenticide in a pipe, long enough to prevent contact with the bait. More elaborate enclosed bait boxes, which have holes for the rodents to enter, are available.
- Boxes/stations should be placed in such a way that bystanders, such as children, and non-target animals, cannot reach the bait. However, contamination of the bait boxes’ surroundings with

rodenticide from spillage caused by the rodents, or due to the rodents' contaminated urine, faeces and carcasses, is possible.

Wax bait wedges, rounds or blocks

- Wax bait wedges, rounds or blocks are usually placed in bait boxes.

Pellets, impregnated grain and maize:

- May be used indoors and outdoors, and can be placed in larger, unenclosed surfaces.
- May be placed directly into rodent burrows/holes with a spoon or small shovel. In this case, the burrows/holes may be covered to prevent access by children and non-target animals such as pets and birds.
- The surroundings may be contaminated with the rodenticide from spillage by rodents and with contaminated urine, faeces and carcasses.

Paste baits are not specifically described, but application practices are assumed similar to that for wax blocks and treated products, with some variations described in more detail in Section 8.4.1.

Contact powders

- Contact powders (tracking powders) may be used indoors and outdoors.
- Rodents pick up the powder on their feet; the powder is subsequently consumed during grooming.
- The concentration of rodenticide in contact powders is usually much larger than in other edible solid baits.
- The treated areas should be covered, to prevent bystander and non-target animal exposure.

Exposure variables

The TNsG summarises exposure data gathered largely in the Nordic countries. TNsG application phase, "use" phase and disposal (clean-up) phase exposure variables are presented in this section. The amounts and frequencies of exposure provided in the tables are according to the formulated products for which data were collected in the Nordic countries and might not be directly applicable to the South African products. Substantiated product- and scenario-specific data are preferred, e.g., from South African suppliers, but the TNsG exposure data may be used when actual measured data are not available.

The TNsG primary exposure data compiled for the application phase are summarised in Table 7.2.2.1, and that for the use phase (after the initial application, while in use) in Table 7.2.2.2. Secondary exposure assumptions for accidental contact by adults and children are presented as applicable to specific product formulations, in the relevant exposure and/or risk assessment described in Section 8.

Table 7.2.2.1: TNsG-based primary exposure variables for solid rodenticide application.

Formulation	Amount per application	Handling duration	Event frequency (per day)		Days per year	
			Normal	Worst case	Normal	Worst case
Professional applicator						
Wax blocks	250 g	5 min	4	8	55	220
Pellets, impregnated grain	150 to 400 g	5 min	4	16	55	220
Powder	250 g	10 min	2	4	55	110
Bait station placing	40 g	As above	2 x bait stations, 4 times per year			

Formulation	Amount per application	Handling duration	Event frequency (per day)		Days per year	
			Normal	Worst case	Normal	Worst case
Non-professional applicator: not applicable (not for residential/domestic use)						
Wax blocks	20 to 40 g	<5 min	1	1	1	20
Pellets, impregnated grain	25 to 50 g	<5 min	1	2	1	20
Bait station placing	40 g	As above	2 x bait stations, 4 times per year			

Post-application use phase:
The duration and frequency variables are based on professionals and non-professionals, the latter assumed similar to the general public user, attending the feeding stations and replacing/adding new baits.

Table 7.2.2.2: TNsG-based primary exposure variables during the post-application use phase.

Formulation	Amount per application	Handling duration	Event frequency (per day)		Days per year	
			Normal	Worst case	Normal	Worst case
Professional						
Wax blocks	250 g	<5 min	1/7	1	110	220
Pellets, impregnated grain	150 to 400 g	<5 min	1 to 2	16	110	220
Powder	250 g	<5 min	1	1	24	110
Non-professional						
Wax blocks	20 to 40 g	<5 min	1	1	1	20
Pellets, impregnated grain	25 to 50 g	<5 min	1	1	1	20
Powder	250 g	<5 min	1	1	1	20

Disposal phase:
- Professionals and non-professionals are assumed to remove/clean the bait box, which may result in handling of surplus formulated product.
- Disposal activities include cleaning up and disposal of rodenticide dragged away from the bait station by rodents.
- Frequency of exposure may be taken as once a day, once a year.
- Should include handling of carcasses, which may have residues of the active substances on the skin or having bled on the floor. However, it appears that dead rats and mice often are swept up with a broom, together with other refuse (ECB 2007), implying that dermal contact will be minimal.
- Brooming may give rise to dust containing the active substance.

7.2.3 Toxicity values and human health risk calculations

Regulatory authorities derive limit values protecting the health of humans; that is, exposure levels or dose values that are not expected to result in adverse effects on health of the general population, including sensitive individuals and children.

The USEPA (2020b) did not derive toxicity values, such as reference concentrations or acceptable daily intakes, as a basis for an overall human health risk assessment and risk management strategy for brodifacoum or the other anticoagulants, since it was accepted that anticoagulant pesticides are

extremely acutely toxic by all routes of exposure. Therefore, the USEPA waived further human health data requirements, and did not require any additional toxicological data from commercial applicants seeking registration of rodenticide products for sale in the USA, since it was concluded that additional data would not inform or impact the overall risk management strategy.

The French CA (2017) conducted human health risk calculations using the systemic Acceptable Exposure Levels ("AELs") for brodifacoum set in the Assessment Report by the Italian CA (2010) (Table 7.2.3.1). The AEL is the exposure dose that is accepted as not associated with a risk to human health.

Table 7.2.3.1: Summary of brodifacoum AELs.

*Point of departure (POD)	Uncertainty Factors	AEL	*Study and toxicological effects
Acute exposure			
NOAEL = 0.001 mg/kg-day	UF_A= 10 UF_H= 10 UF_{Sev} = 3 Total UF= 300	3.3 x 10^{-6} mg/kg-day	Confidential data from unpublished teratogenicity (developmental toxicity) oral exposure study in the rat (Italian CA 2010). Maternal haemorrhage at dose levels > 0.01 mg/kg-day, but no effects on conceptuses up to highest dose level of 0.02 mg/kg-day.
Subchronic exposure (medium term)			
NOAEL = 0.002 mg/kg-day	UF_A= 3 UF_H= 10 Total UF= 30	6.67 x 10^{-6} mg/kg-day	Confidential data from unpublished developmental toxicity oral exposure study in the rabbit (Italian CA 2010). Biochemical signs of anti-coagulant effects at 0.004 mg/kg-day in dams, but no developmental toxicity effects up to highest dose of 0.04 mg/kg-day.
Chronic exposure			
NOAEL = 0.001 mg/kg-day	UF_A= 10 UF_H= 10 UF_{Sev} = 3 Total UF= 300	3.3 x 10^{-6} mg/kg-day	Confidential data from unpublished two-generation oral exposure study in the rat (Italian CA 2010). Parental toxicity with haemorrhage at 0.004 mg/kg-day in dams, but no reproductive or developmental effects in the absence of general toxicity.
** Source: Italian CA (2010). *Point of Departure (POD): Data point derived from dose-response data, used to extrapolate risks associated with lower environmentally relevant human exposures. NOAEL: no-observed-adverse-effect level. LOAEL: lowest-observed-adverse-effect level. UF: uncertainty factor. UFA: extrapolation from animal to human (interspecies). UFH: potential variation in sensitivity among members of the human population (intraspecies). UF_{Sev}: additional factor for severity of effects.			

The French CA (2017) HHRA was conducted by calculating the rodenticide operator's systemic dose of brodifacoum. For this purpose, dermal absorption was assumed as presented in Section 6.2 (5% for pellets and grains; 0.047% for wax blocks; assuming 90% reduction of dermal exposure when using gloves) and a default body weight of 60 kg. The systemic dose is expressed as a percentage of the AEL, and the risk of a health effect is deemed unacceptable if the systemic dose is approximately 100 per cent, or more, of the AEL.

In short, the systemic dose is calculated with Equation 7.2.3.1.

Systemic dose (mg/kg-day) = Systemic exposure (mg/day) / body weight (kg) Equation 7.2.3.1

Systemic exposure is calculated with Equation 7.2.3.2:

Systemic exposure = Exposure per event x events per day Equation 7.2.3.2

Where:

Systemic exposure	Systemic exposure per work day (mg/day).
Exposure per event	e.g., 0.007 mg/event, calculated in Section 7.2.2 for a pest controller using gloves while cleaning up in the disposal phase.
Events per day	Number of events per day; that is, estimated or default number of clean-up events per day.

8 Human health risk assessment of solid rodenticides containing brodifacoum

8.1 Wax blocks/wedges

8.1.1 The Italian CA assessment

Table 3.2.2 presents the percentage by mass of brodifacoum in each solid formulation product, showing that the highest brodifacoum content in the blocks/wax products is 0.05 g/kg (0.005 weight %).

The Italian CA (2010) reviewed health risk assessments for professional users (occupational scenario) and for non-professional users (residential/farm/domestic scenario), based on the use of a wax block formulation presented by an applicant for registration, with a brodifacoum content of 0.005 weight %. The results of the health risk assessments reviewed by the Italian CA (2010) are thus directly applicable to the majority of wax block/wedge formulations in this report, and are a likely over-estimation of the risks associated with the Rodex products (Rodex Bait Blocks and Rodex Rat R.I.P. blocks), which have a brodifacoum content of 0.001 weight % (Table 3.2.2).

The exposure assessment was carried out for ready-for-use brodifacoum wax blocks in a bait box, but the conservative assessment parameters included activities such as filling of bait boxes.

The assessment parameters were as follows:

- Default exposure values were from the Technical Notes for Guidance (TNsG) on Human exposure to Biocidal Product Type 14: Rodenticides, except for “worst-case” adjustments given below.
- Exposure values were also derived from operator exposure studies where exposure of non-professional operators carrying out a range of tasks (decanting of loose grain baits, filling of bait boxes and cleaning up and disposal of bait) was measured using two end-use products, wax and loose grain bait.
- Calculations were adjusted to worst-case assumptions of daily usage e.g. daily number of manipulations/handlings (including application and post application tasks) and product-specific information on amount of bait to be used per bait point.
- The 90th percentile (highly conservative) of professional applicators’ daily bait handling frequency was used, numbering per operator per day:
    - 60 manipulations for application
    - 15 for handling baits during clean-up.

- Non-professionals (equivalent to the general public):
  - Are assumed not to use wax blocks on a daily basis.
  - The skin is the main exposure route and non-professional users are assumed not to wear protective gloves.
- Indirect (secondary) exposure as a result of use was assessed according to the scenarios listed in the TNsG:
  - Adult incidental dermal contact with blocks/wedges.
  - Infant ingestion by transient mouthing (ingesting 10 mg of wax block).
  - Infant ingestion by chewing on bait.
  - Infant ingestion is a conservative assumption, because the taste deterrent (bittering agent) included in the formulation will deter the child from extensive mouthing.
- A default body weight of 60 kg for an adult, which is lower than the default of 70 kg often used (e.g., by the USEPA (2011)). The lower body weight results in a conservative (higher) dose estimate, and thus a higher risk estimate.
- Dermal absorption default value of 3% was used for the values presented in Table 8.1.1.1. This is higher than the recommended value of 0.047% for wax blocks (French CA 2017) and would result in an over-estimation of absorption by the dermal route.
- The skin is the main exposure route. Inhalation exposure is only applicable to manufacturing, not to users (professional or not). Oral exposure of pest control operatives is not expected, since good hygiene measures are routinely given on SDSs, e.g., washing before eating or smoking.

The outcomes of the registrant's dermal exposure calculations for professional users are presented in a range, since exposure was calculated based on an exposure study and on TNsG default values, respectively:

- Loading of bait boxes: 2.7×10^{-6} to 1.25×10^{-6} mg/kg-day.
- Application of blocks in sewer: 3.1×10^{-6} to 1.25×10^{-6} mg/kg-day.
- Disposal of bait boxes: 1.92×10^{-7} to 1.25×10^{-6} mg/kg-day.

The outcomes of the registrant's total exposure calculations for non-professional users (not wearing PPE) are:

- Systemic dose for disposal of bait boxes: 3.15×10^{-6} mg/kg-day.

The outcomes of the registrant's dermal exposure calculations for exposed persons not wearing PPE, for acute (short-term) indirect (secondary exposures) are:

- Acute dermal exposure: 2.5×10^{-5} mg/kg-day of an adult in incidental contact with bait blocks.
- Acute oral exposure of an infant ingesting pellets:
  - 5×10^{-5} mg/kg-day when ingesting 0.01 g pellets.
  - 2.5×10^{-2} mg/kg-day when ingesting 5 g pellets.

The scenarios reviewed by the Italian CA (2010) for dermal exposure are summarised in Table 8.1.1.

The Italian CA (2010) review conclusions are:

- Exposures are acceptable for the professional and non-professional users, in the scenarios indicated in Table 8.1.1.
- Regarding the unacceptable exposure result of the "adults handling dead rodents" (without gloves), using a more appropriate dermal absorption value of 0.047%, instead of the overestimation of 3%, exposures and risks would be acceptable.
- Accidental intake of 5 gram of wax block bait poses a risk to infants.

Table 8.1.1: Summary of dermal exposure in assessed wax block/wedge scenarios.

Note to table: risk results presented in this table are based on the overestimated dermal absorption of 3%, as calculated in the registrant assessment reviewed by the Italian CA (2010).

Scenario description	Gloves worn	Exposure assessment	% AEL / MOE	Exposure acceptable?
Professional users (occupational exposure): application and post application – direct exposure				
Products used on a single occasion (compared to AEL_{acute})	Yes	Calculated based on TNsG	0.94%	Yes
	Yes	Operator exposure studies	*0.14 – **2.33%	Yes
Products used on a repetitive or daily basis (compared to $AEL_{chronic}$)	Yes	Calculated based on TNsG	41.7%	Yes
	Yes	Operator exposure studies	*6.4 – **103%	Yes
Non-professional users (residential/farm/domestic scenario): application-, post application and indirect exposure as a result of use				
Disposal of bait boxes, exposure dose compared to acute NOAEL	No	Measured and based on TNsG	MOE = 634	Yes
Adults handling dead rodents, exposure dose compared to acute NOAEL	No	Calculated based on TNsG	MOE = 80	No
Infant ingesting 5 g of wax block	Not applicable	Calculated based on TNsG	MOE = 10	No
Infant transient mouthing (ingesting 10 mg of wax block)	Not applicable	Calculated based on TNsG	MOE = 5 000	Yes

Gloves: Wearing gloves is assumed to reduce the exposure of hands by 90%.
% AEL: exposure dose as a % of the AEL (AELs presented in Table 7.2.3.1).
MOE LOC = 100 (according to the applicant). Exposure is not acceptable if MOE < LOC.
Exposure assessment: Calculated using TNsG values or based on operator exposure studies.
* Measured during disposal of bait boxes.
** Measured during application of blocks in sewers.

8.1.2 Assessment of wax blocks/wedges included in this report

As stated in Section 7.1.1, the results of the Italian CA (2010) review of the registrant's wax block risk assessment are directly applicable to the wax block/wedge formulations in this report. The registrant's wax block formulation contained 0.005 weight per cent of brodifacoum, as did all of the formulations assessed in this report, except for the Rodex products that contain less brodifacoum (0.001 weight %, Table 3.2.2). The exposure and risk results of the Rodex products would thus be lower than the results reviewed by the Italian CA.

The Italian CA (2010) conclusion is that exposures in the expected handling scenarios are acceptable for the professional and non-professional (general public) users. Therefore, it is reasonable to conclude that the brodifacoum exposures of professional and non-professional users of the South African wax block/wedge products assessed in this report (Table 1.1.1) would likewise be acceptable, since the brodifacoum contents of the assessed products are comparable.

With regard to indirect (secondary exposure) to wax blocks in use, a health risk is unlikely for adults in contact with dead rodents (without wearing gloves or protective clothing). A risk to infants transiently mouthing wax blocks/wedges is not foreseen. Chewing on wax blocks would be associated with a risk to health of infants, but is not likely to occur commonly, because the taste deterrent (bittering agent) included in the formulation will cause the child to spit out any chewings.

8.2 Pellet bait

8.2.1 The Italian CA assessment

Table 3.2.2 presents the percentage by mass of brodifacoum in each solid formulation product, showing that the highest brodifacoum content in the pellet bait products is 0.05 g/kg (0.005 weight %).

The Italian CA (2010) reviewed health risk assessments for professional users (occupational scenario) and for non-professional users (residential/farm/domestic scenario), based on the use of a pellet formulation presented by an applicant for registration, with a brodifacoum content of 0.005 weight %. The results of the health risk assessments reviewed by the Italian CA (2010) are thus directly applicable to the majority of pellet formulations in this report. The results represent an over-estimation of the risks associated with the Rodex (Rodex Rat and Mouse Pellets) product, which has a brodifacoum content 0.001 weight % (Table 3.2.2).

The exposure assessment was carried out for a ready-to-use cereal-based brodifacoum pellet formulation. The product exposure assessment was carried out for pellets in a bait box, but the frequency-of-handling exposure data were from results of a European survey (CEFIC Study), which included decanting, loading/placement and clean/up of bait (Italian CA 2010).

The assessment parameters were as follows:

- Exposure was calculated based on data determined in the CEFIC study.
- Exposure was calculated for professional applicators engaged in decanting, loading/placement and clean/up.
- Calculations were adjusted to worst-case assumptions of daily usage e.g. daily number of manipulations/handlings (including application and post application tasks) and product-specific information on amount of bait to be used per bait point.
- The 90th percentile (highly conservative) of professional applicators' daily bait handling frequency from the CEFIC study was used, numbering per operator per day:
    - 80 manipulations for application.
- For amateur (domestic/non-professional) use:
    - 2 exposure events per day for loading/placing of baits.
    - 2 exposure events per day for the clean-up phase (i.e., 2 stations).
- Indirect (secondary) exposure as a result of use was assessed according to the scenarios listed in the TNsG:
    - Dermal contact with dead rodents: assumed adult contact with 1g of the pellets on the exterior of dead rodents. Acute exposures are estimated.
    - Ingestion of pellets by an infant: assumed 0.01 g (transient mouthing) and 5 g (chewing) of pellets on a single occasion.
    - Infant ingestion is a conservative assumption, because the taste deterrent (bittering agent) included in the formulation will cause the child to spit out the pellets, thus likely no ingestion.
- A default body weight of 60 kg for an adult, which is lower than the default of 70 kg often used (e.g., by the USEPA (2011)). The lower body weight results in a conservative (higher) dose estimate, and thus a higher risk estimate.
- Dermal absorption default value of 5% was used for the values presented in Table 8.2.1.1. This absorption factor is considered worst-case.

- The skin is the main exposure route. Inhalation exposure is considered negligible (confirmed by the calculation results presented below). Oral exposure of pest control operatives is not expected, since good hygiene measures are routinely given on SDSs, e.g., washing before eating or smoking.

The outcomes of the registrant's total exposure calculations for professional users are:
- Total inhalation exposure: 8.87 x 10^{-8} mg/kg-day.
- Total dermal exposure: 5.26 x 10^{-7} mg/kg-day.
- Total exposure (sum of dermal and inhalation): 6.16 x 10^{-7} mg/kg-day.

The outcomes of the registrant's total exposure calculations for non-professional users (general public, assumed not wearing PPE) are:
- Total inhalation exposure: 8.87 x 10^{-8} mg/kg-day.
- Total dermal exposure: 8.80 x 10^{-8} mg/kg-day.
- Total exposure (sum of dermal and inhalation): 1.77 x 10^{-7} mg/kg-day.

The outcomes of the registrant's dermal exposure calculations for acute (short-term) accidental indirect (secondary exposures) (not wearing PPE) are:
- Acute dermal exposure: 4.17 x 10^{-5} mg/kg-day of an adult handling dead rodents.
- Acute oral exposure of an infant ingesting pellets:
  - 5 x 10^{-5} mg/kg-day when ingesting 0.01 g pellets.
  - 2.5 x 10^{-2} mg/kg-day when ingesting 5 g pellets.

A summary of the risk assessment for brodifacoum pellets, reviewed by the Italian CA (2010), is presented in Table 8.2.1.1.

The Italian CA (2010) review conclusions are:
- Professional users of the product have estimated exposures below the AEL when PPE (protective clothing and gloves) are worn.
- The estimated brodifacoum exposure from the routine preparation, placement and clean-up of bait points is below the AEL for professional users, and the MOEs for non-professional users indicate that estimated exposures are "*considerably below levels associated with potential health effects*".
- Exposures are acceptable for the professional and non-professional users, in the scenarios indicated in Table 8.2.1.1.
- For indirect (secondary exposure):
  - A risk is foreseeable for adults in contact with dead rodents (without wearing gloves or protective clothing).
  - A risk is foreseeable for infants ingesting 0.01 and 5 g of pellets.

Table 8.2.1.1: Summary of dermal exposure in assessed pellet bait scenarios.

Scenario description	Gloves worn	Exposure assessment	% AEL / MOE	Exposure acceptable?
Professional users (occupational exposure): application and post application – direct exposure				
Products used on a single occasion (compared to AEL_{acute})	Yes	Calculated based on CEFIC exposure data	18.5%	Yes
Products used on a repetitive or daily basis (compared to $AEL_{chronic}$)	Yes		18.5%	Yes
			MOE = 1 623	Yes

Scenario description	Gloves worn	Exposure assessment	% AEL / MOE	Exposure acceptable?
Non-professional users (residential/farm/domestic scenario): application-, post application and indirect exposure as a result of use				
Load, place baits and clean up – single day (compared to $NOAEL_{acute}$)	No	Calculated based on CEFIC exposure data	MOE = 5 625	Yes
Load, place baits and clean up – repeated activities (compared to $NOAEL_{chronic}$)	No		MOE = 5 625	Yes
Adults in contact with dead rodents	No	Calculated based on TNsG	MOE = 24	No
Infants ingesting pellets: • 0.01 g ingestion • 5 g ingestion	Not applicable	Calculated based on TNsG	MOES: • 20 • 0.04	No
Gloves: Wearing gloves is assumed to reduce the exposure of hands by 90%. **% AEL:** exposure dose as a % of the AEL (AELs presented in Table 7.2.3.1). **MOE** LOC = 300. Exposure is not acceptable if MOE < LOC. **Exposure assessment:** Calculated based on operator exposure studies.				

8.2.2 Assessment of pellet baits included in this report

The Italian CA (2010) review (Section 8.2.1) of the registrant's brodifacoum pellet bait risk assessment is directly applicable to the pellet formulations in this report. The registrant's pellet formulation contained 0.005 weight % of brodifacoum, as did all of the formulations assessed in this report, except for the Rodex product that contain less brodifacoum (Table 3.2.2: 0.001 weight %). The exposure and risk results of the Rodex product would thus be lower than the results reviewed by the Italian CA.

The Italian CA (2010) conclusion is that exposures in the expected handling scenarios are acceptable for the professional and non-professional users. Therefore, it is reasonable to conclude that the brodifacoum exposures of professional and non-professional users of the South African pellet bait products assessed in this report (Table 1.1.1) would be acceptable, since the brodifacoum contents of the assessed products are comparable.

With regard to indirect (secondary exposure) to pellets in use, a health risk is likely for adults in contact with dead rodents (without wearing gloves or protective clothing). A risk is also likely for infants transiently mouthing or chewing on pellets. However, it must be noted that chewing on pellets is not likely to occur commonly, because the taste deterrent (bittering agent) included in the formulation will cause the child to spit out the pellets.

8.3 Grain bait

8.3.1 Exposure assessment

The assessed products

Table 3.2.2 presents the percentage by mass of brodifacoum in each solid formulation product, showing that the highest brodifacoum content in the grain bait products is 0.02 g/kg (0.002 weight %).

The French CA (2017) reviewed health risk assessments for professional users (occupational scenario) and for non-professional users (residential/farm/domestic scenario), based on the use of a grain bait formulation presented by an applicant for registration, with a brodifacoum content of

0.005 weight %. The formulation assessed by the French CA thus serves as a conservative over-estimation of the South African grain bait products assessed in this report, that all have a lower content of brodifacoum (Table 3.2.2).

The French CA reviewed the grain bait as a ready-to-use product applied in the indoor environment (public and private buildings, farms). Although the assessed brodifacoum-treated cereal grains are always supplied in sachets, which are manually applied in secured bait stations (assumed to be bait boxes), the CA also assessed the use of loose grains, which is applicable to the South African products. The South African products are not supplied in sachets, but application in bait stations or under cover (e.g., inside pieces of drainage pipe or under sections of slate, board, or corrugated iron suitably weighted) is recommended, in order to keep the bait out of reach of children and non-target animals.

The French CA (2017) summarised the potential for human exposure to brodifacoum grain baits as presented in Table 8.3.1.1.

Table 8.3.1.1: Main paths of human exposure

Exposure path	Professional use	General public	Via the environment
Inhalation	Potentially significant	Negligible	Negligible
Dermal	Potentially significant	Potentially significant	Negligible
Oral	Negligible	Potentially significant	Negligible

The French CA (2017) proceeded to conduct a human health risk assessment using the exposure estimations from the CEFIC study, which examined the inhalation and dermal exposures associated with all grain bait use activities, including decanting material from a large container to a pail, filling and placing bait points, and clean-up and disposal of bait points. The CEFIC study selected grain bait containing coumatetralyl as a worst-case representative product of all cereal-based rodenticide baits, and applied results to the brodifacoum grain bait assessment.

Additionally, guidance from the Human Exposure Expert Group ("HEEG") of ECHA was used by the French CA (2017). The HEEG provides guidelines towards a harmonised approach to biocide exposure assessment for industry and competent authorities including the number of manipulations in the assessment of anticoagulant rodenticides applicable to professional pesticide applicators.

The French CA assessed the product for non-professional users, but only during the clean-up phase, since the assessed product was meant for professional use only. Since the products registered in South Africa are not restricted to professional users only, exposures and risks of non-professionals (domestic users in homes, workers on farms or in businesses) are also assessed, during all rodenticide use phases, as applicable to professional users.

The input values used for the exposure and risk calculations presented for loose grain baits are summarised in Table 8.3.1.2. The sources of the variables and the assumptions for variable values are provided with the exposure calculations in the following sections.

The amounts of grain bait recommended according to the labels of registered South African grain baits are summarised in Table 8.3.1.3.

Table 8.3.1.2: Summary of default variables for the grain bait exposure assessments.

Variable	Value	Units
Generic variables		
*Body mass	60	kg
Inhalation rate	1.25	m^3/hour
Dermal absorption rate of brodifacoum	0.647	%
Inhalation absorption rate of brodifacoum	100	%
Brodifacoum active substance in grain bait (French CA product)	0.005	% (w/w)
Maximum brodifacoum active substance in South African grain baits (Table 3.2.2)	0.002	% (w/w)
Grain bait handling - professionals		
Bait loading into bait points, number of activities	63	loadings/day
Mass of bait loaded per bait point, maximum according to grain bait labels (Table 8.3.1.3)	75 (rats)	g/bait point
Calculated total mass of grain decanted per day (75 g/bait point x 63 bait point loadings)	4.73 rounded to 5	kg/day
Time needed for decanting – for inhalation calculations	1	min/kg decanted
Grain bait handling – non-professionals		
Bait loading into bait points, number of activities	5	loadings/day
Mass of bait loaded per bait point, maximum according to grain bait labels (Table 8.3.1.3)	75 (rats)	g/bait point
Calculated total mass of grain decanted per day (75 g/bait point x 5 bait point loadings)	0.38	kg/day
Time needed for decanting – for inhalation calculations	1	min/kg decanted
***Body mass** of 60 kg is used to facilitate direct comparison with French CA calculations.		

Table 8.3.1.3: Bait point and daily grain bait mass decanted of South African products.

Formulation	Bait point mass (g grains per point)	Total kg grain	
		Professionals	Non-professionals
Di-Rat-Blue	Maximum of 75 g, for rats	4.73	0.38
Kill-All Grain Bait	Maximum of 75 g, for rats	4.73	0.38
Rodex Grain Bait	Maximum of 75 g, for rats	4.73	0.38
Professionals: 63 Bait point placings per day, according to the HEEG guidelines used by the French CA (2017). **Non-professionals:** 5 Bait point placings per day, according to the HEEG guidelines used by the French CA (2017).			

Decanting phase for loose grains (professionals)

Dermal dose

Based on CEFIC and HEEG guidance, the amount of product (grain dust/residue) on fingers/hands, while not wearing gloves, is:

- 53.3 mg during the decanting of 3 kg of grain bait, and
- 219.66 mg during the decanting of 12.6 kg of grain bait (French CA 2017).

The French CA (2017) calculated the exposure doses during decanting of a grain bait, taking into account:

- Active substance in product: 0.005% (w/w).
- Dermal absorption: 0.647%.
- Body weight: 60 kg.

The resulting dermal systemic exposure dose of brodifacoum during decanting of 12.6 kg of grain bait per day, calculated by the French CA, is:
- 219.66 mg product x 0.005% brodifacoum x 0.647% absorption / 60 kg =
- 1.18×10^{-6} mg/kg bw-day.

Considering the agreed number of 63 grain bait loadings per day for professional users (French CA 2017), and the highest recommended mass of 75 g bait placed per baiting point (for Rodex Grain Bait in Table 8.3.1.3), the calculated highest total mass of bait to be decanted by a South African professional would be:
- 63 x 75 g = 4.73 kg per day, rounded to 5 kg per day.

Thus, the maximum grain residue on fingers/hands of a professional pest controller decanting a registered South African grain bait product would be:
- (53.3 mg)/(3 kg) x 11.5 kg = 204.3 mg per day.

Based on the above numbers, the equivalent maximum dermal dose by a South African professional decanting 11.5 kg of grain bait per day, with a maximum brodifacoum content of 0.002% (Table 3.2.2) would be:
- 204.3 mg product x 0.002% brodifacoum x 0.647% absorption / 60 kg =
- 4.4×10^{-7} mg/kg bw-day.

Inhalation dose

The French CA (2017) calculated professional users' inhalation exposure during decanting of grain bait, based on:
- A measured air concentration of 2.22 mg/m^3 of grain bait dust/residue when 3 kg of product is decanted.
- The equivalent air concentration is 9.62 mg/m^3 of grain bait dust/residue when 13 kg of product is decanted.
- The equivalent air concentration during decanting of 11.5 kg South African product is:
  - (2.22 mg/m^3)/(3 kg) x 11.5 kg = 8.5 mg/m^3

The French CA (2017) used the following exposure parameters to calculate the potential inhalation dose of brodifacoum:
- Active substance in product: 0.005% (w/w).
- Inhalation rate of 1.25 m^3/hour.
- Inhalation exposure period of 13 minutes to decant 13 kg of biocidal product.
- Inhalation absorption of 100%.
- Body weight of 60 kg.

The resulting inhalation dose of brodifacoum during decanting of 13 kg of grain bait per day (period of decanting = 13 kg x 1 minute/kg = 13 minutes) was calculated by the French CA:
- 9.62 mg/m^3 product x 0.005% brodifacoum x 100% absorption x 1.25 m^3/60 min x 13 min/60 kg
- = 2.17×10^{-6} mg/kg bw-day.

The equivalent brodifacoum inhalation dose by a South African professional decanting 11.5 kg of grain bait per day (period of decanting = 11.5 minutes), with a maximum brodifacoum content of 0.002% (Table 3.2.2) would be:

- 8.5 mg/m^3 product x 0.002% brodifacoum x 100% absorption x 1.25 m^3/60 min x 11.5 min/60 kg
- = 6.80 x 10^{-7} mg/kg bw-day.

Loading phase for loose grains (professionals)

Based on the CEFIC and HEEG guidance, the amount of product (grain dust/residue) on fingers/hands (without gloves) was 2.04 mg per loading (French CA 2017). For the assessment of 63 loadings per day (HEEG default), the amount of biocidal product on hands/fingers is:

- 63 x 2.04 = 128.52 mg/day.

The corresponding systemic dose of brodifacoum during the loading phase is:

- 128.5 mg product/day x 0.005% brodifacoum x 0.647% absorption / 60 kg =
- 6.93 x 10^{-7} mg/kg bw-day (French CA 2017).

Based on the above product loading, the equivalent dermal dose by a South African professional conducting the default of 63 grain bait loadings per day, with a maximum brodifacoum content of 0.002% (Table 3.2.2) would be:

- 125.8 mg product x 0.002% brodifacoum x 0.647% absorption / 60 kg =
- 2.77 x 10^{-7} mg/kg bw-day.

Inhalation exposure was not assessed during the loading phase (French CA 2017), likely because grain dust/residue air concentrations are considered negligible in the loading phase.

Cleaning phase for loose grains (professionals)

Based on the CEFIC and HEEG guidance, the amount of product (grain dust/residue) on fingers/hands (without gloves) was 3.79 mg per cleaning event (French CA 2017). For the assessment of 16 cleanings per day (HEEG default), the amount of biocidal product on hands/fingers is: 16 x 3.79 = 60.64 mg/day.

The corresponding systemic dose of brodifacoum during the cleaning phase is:

- 60.64 mg product/day x 0.005% brodifacoum x 0.647% absorption / 60 kg =
- 3.27 x 10^{-7} mg/kg bw-day (French CA 2017).

Based on the above product loading, the equivalent dermal dose by a South African professional conducting the default of 16 cleanings per day, with a maximum brodifacoum content of 0.002% (Table 3.2.2) would be:

- 60.64 mg product x 0.002% brodifacoum x 0.647% absorption / 60 kg =
- 1.31 x 10^{-7} mg/kg bw-day.

Inhalation exposure was not assessed during the cleaning phase (French CA 2017), likely because air concentrations are considered negligible in the cleaning phase.

Total exposure for loose grains (professionals)

The French CA (2017) calculated the total systemic dermal exposure during one day to control rats (higher mass of product per bait point) as:

- 2.20 x 10^{-6} mg/kg-day without PPE (gloves).
- 1.10 x 10^{-7} mg/kg-day with gloves (5% of the systemic dose without gloves).

The total systemic exposure resulting from inhalation was calculated by the French CA (2017) as:

- 2.17 x 10^{-6} mg/kg-day without PPE and 2.17 x 10^{-7} mg/kg-day with respiratory protection equipment, evidently assuming 90% protection.

The French CA (2017) calculated the combined total exposure (dermal + inhalation), with and without PPE, as presented in Table 8.3.1.4.

The combined total exposure doses of professional operators using the registered South African grain bait products, based on the maximum brodifacoum content of 0.002% (Table 3.2.2), are also presented in Table 8.3.1.4, calculated based on similar PPE premises as the French CA.

Table 8.3.1.4: Professional users: combined brodifacoum exposure dose when handling grain bait.

Exposure assessment	**French CA**				**SA products**			
Maximum brodifacoum content	**0.005%**				**0.002%**			
Route of exposure	**Dermal**		**Inhalation**		**Dermal**		**Inhalation**	
PPE (gloves or respiratory equipment)	**No**	***Gloves**	**No**	****Resp.**	**No**	**Gloves**	**No**	**Resp.**
Activity	**mg/kg-day**							
Decanting grain bait	1.18 x 10^{-6}	-	2.17 x 10^{-6}	-	4.4 x 10^{-7}	-	6.80 x 10^{-7}	-
kg grain bait per day	12.6 kg				11.5 kg			
Loading grain bait	6.93 x 10^{-7}	-	Negligible	-	2.77 x 10^{-7}	-	Negligible	-
Cleaning phase	3.27 x 10^{-7}	-	Negligible	-	1.31 x 10^{-7}	-	Negligible	-
Subtotal during one day at work	2.20 x 10^{-6}	1.10 x 10^{-7}	2.17 x 10^{-6}	2.17 x 10^{-7}	8.49 x 10^{-7}	4.24 x 10^{-8}	6.80 x 10^{-7}	6.80 x 10^{-8}
Grand total: no PPE	4.37 x 10^{-6}				1.53 x 10^{-6}			
Grand total: respiratory PPE during decanting only, no gloves in any phase	2.42 x 10^{-6}				9.17 x 10^{-7}			
Grand total: all PPE	3.27 x 10^{-7}				1.10 x 10^{-7}			

***Gloves**: assumed to afford 95% protection
****Respiratory equipment**: assumed to afford 90% protection
-: not calculated

The calculations are explained here:

Summing the dermal doses for a professional using a rodenticide registered in South Africa with the highest brodifacoum content (0.002% w/w), results in a total systemic dermal exposure (without gloves) of:

- 4.4 x 10^{-7} mg/kg-day (decanting) + 2.77 x 10^{-7} mg/kg-day (loading) + 1.31 x 10^{-7} mg/kg-day (cleaning)
- = 8.5 x 10^{-7} mg/kg-day without gloves, and
- 4.2 x 10^{-8} mg/kg-day with gloves (assuming 95% protection)

The inhalation dose for a professional using a rodenticide registered in South Africa with the highest brodifacoum content (0.002% w/w) is 6.80 x 10^{-7} mg/kg bw-day (decanting) without PPE and, assuming 90% protection with respiratory protection equipment, 6.80 x 10^{-8} mg/kg-day.

The French CA (2017) calculated:

- With respiratory protection during decanting and no gloves during decanting, loading and cleaning:
  - 2.17×10^{-7} mg/kg-day (inhalation) + 2.20×10^{-6} mg/kg-day (total dermal)
  - $= 2.42 \times 10^{-6}$ mg/kg-day.
- With respiratory equipment during decanting and PPE (gloves) during all stages of the control campaign:
  - 2.17×10^{-7} mg/kg-day (inhalation) + 1.10×10^{-7} mg/kg-day (total dermal with gloves)
  - $= 3.27 \times 10^{-7}$ mg/kg bw/day for the control of rats (and mice).

For rodenticides registered in South Africa, based on the same premises as the French CA (2017):

- With respiratory protection during decanting and no gloves during decanting, loading and cleaning:
  - 6.80×10^{-8} mg/kg-day (inhalation) + 8.49×10^{-7} mg/kg-day (total dermal)
  - $= 9.17 \times 10^{-7}$ mg/kg-day.
- With respiratory equipment during decanting and PPE (gloves) during all stages of the control campaign:
  - 6.80×10^{-8} mg/kg-day (inhalation) + 4.24×10^{-8} mg/kg-day (total dermal with gloves)
  - $= 1.10 \times 10^{-7}$ mg/kg bw/day for the control of rats (and mice).

Decanting phase for loose grains (non-professionals)

Dermal dose

The French CA did not calculate exposure during decanting or placing of grain bait products by non-professionals, because all products for that market are supplied in ready-to-use sachets; thus, exposure is excluded. However, exposure during the cleaning phase was calculated, given that rats would tear the packaging to reach the grain bait.

This is not the case for the South African products; therefore, calculations for non-professional users are conducted here, based on the example calculations for professionals, but with exposure variable adjustments as needed.

Considering the agreed number of 5 grain bait loadings per day for non-professional users (French CA 2017), and the highest recommended mass of 75 g bait placed per baiting point (for Rodex Grain Bait in Table 8.3.1.3), the calculated highest total mass of bait to be decanted by a South African non-professional would be:

- 5 x 75 g = 0.38 kg per day (Table 8.3.1.3).

Based on CEFIC and HEEG guidance, the amount of product (grain dust/residue) on fingers/hands, while not wearing gloves, is:

- 53.3 mg during the decanting of 3 kg of grain bait (French CA 2017), and thus
- 16.0 mg during the decanting of a maximum of 0.9 kg of grain bait from a South African product.

The exposure doses of non-professionals, during decanting of a South African grain bait product, are calculated based on:

- Maximum active substance in product: 0.002% (w/w).
- Dermal absorption: 0.647%.
- Body weight: 60 kg.

The maximum grain residue on fingers/hands of a non-professional decanting 0.9 kg of a registered South African grain bait product would be:

- (53.3 mg)/(3 kg) x 0.9 kg = 16.0 mg per day.

Based on the above numbers, the equivalent maximum dermal dose by a non-professional decanting 0.9 kg of grain bait per day, with a maximum brodifacoum content of 0.002% (Table 3.2.2) would be:

- 16.0 mg product x 0.002% brodifacoum x 0.647% absorption / 60 kg =
- 3.4×10^{-8} mg/kg bw-day.

Inhalation dose

The French CA (2017) calculated professional users' inhalation exposure during decanting of grain bait, based on:

- A measured air concentration of 2.22 mg/m^3 of grain bait dust/residue when 3 kg of product is decanted.
- The equivalent air concentration during decanting of 0.9 kg South African product is:
  - (2.22 mg/m^3)/(3 kg) x 0.9 kg = 0.7 mg/m^3

The French CA (2017) used the following exposure parameters to calculate the potential inhalation dose of brodifacoum:

- Active substance in product: 0.005% (w/w).
- Inhalation rate of 1.25 m^3/hour.
- Inhalation exposure period of 1 minute to decant 1 kg of biocidal product.
- Inhalation absorption of 100%.
- Body weight of 60 kg.

The resulting inhalation dose of brodifacoum during decanting of 0.9 kg of grain bait per day (period of decanting = 0.9 kg x 1 minute/kg = 1 minute, rounded) calculated for a South African product with a maximum brodifacoum content of 0.002% (Table 3.2.2) would be:

- 0.7 mg/m^3 product x 0.002% brodifacoum x 100% absorption x 1.25 m^3/60 min x 1 min/60 kg
- = 4.16×10^{-9} mg/kg bw-day.

Loading phase for loose grains (non-professionals)

Based on the CEFIC and HEEG guidance, the amount of product (grain dust/residue) on fingers/hands (without gloves) was 2.04 mg per loading (French CA 2017). For the assessment of 5 loadings per day (HEEG default), the amount of biocidal product on hands/fingers is:

- 5 x 2.04 = 10.2 mg/day.

The corresponding systemic dose of brodifacoum during the loading phase is:

- 128.5 mg product/day x 0.005% brodifacoum x 0.647% absorption / 60 kg =
- 6.93×10^{-7} mg/kg bw-day (French CA 2017).

Based on the above product loading, the equivalent dermal dose by a South African professional conducting the default of 63 grain bait loadings per day, with a maximum brodifacoum content of 0.002% (Table 3.2.2) would be:

- 10.2 mg product x 0.002% brodifacoum x 0.647% absorption / 60 kg =
- 2.20×10^{-8} mg/kg bw-day.

Inhalation exposure was not assessed during the loading phase (French CA 2017).

Cleaning phase for loose grains (non-professionals)

Based on the CEFIC and HEEG guidance, the amount of product (grain dust/residue) on fingers/hands (without gloves) was 4.52 mg per cleaning event for non-professionals (French CA 2017).

For the assessment of 5 cleanings per day (HEEG default), the calculated amount of biocidal product on hands/fingers is: 5 x 4.52 = 22.6 mg/day.

The corresponding systemic dose of brodifacoum during the cleaning phase is:

- 22.6 mg product/day x 0.005% brodifacoum x 0.647% absorption / 60 kg
- = 1.22 x 10^{-7} mg/kg bw-day (French CA 2017).

Based on the above product loading, the equivalent dermal dose by a South African non-professional conducting the default of 5 cleanings per day, with a maximum brodifacoum content of 0.002% (Table 3.2.2) would be:

- 22.6 mg product x 0.002% brodifacoum x 0.647% absorption / 60 kg
- = 4.87 x 10^{-8} mg/kg bw-day.

Inhalation exposure was not assessed during the cleaning phase (French CA 2017).

Total exposure for loose grains (non-professionals)

The combined total exposure doses of professional operators using the registered South African grain bait products, based on the maximum brodifacoum content of 0.002% (Table 3.2.2), are presented in Table 8.3.1.5, calculated based on PPE premises as indicated. It was considered unlikely that non-professionals would be wearing respiratory protection, but gloves may be mandated without inconvenience to non-professional users, and were included in the calculations.

Table 8.3.1.5: Non-professional users: combined brodifacoum exposure dose when handling grain bait.

Exposure assessment	**SA products**		
Maximum brodifacoum content	**0.002%**		
Route of exposure	**Dermal**		**Inhalation**
PPE (gloves or respiratory equipment)	**No**	**Gloves**	**No**
Activity	**mg/kg-day**		
Decanting grain bait	3.45 x 10^{-8}	-	4.16 x 10^{-9}
kg grain bait per day	1.0 kg		
Loading grain bait	2.20 x 10^{-8}	-	Negligible
Cleaning phase	4.87 x 10^{-8}	-	Negligible
Subtotal during one day using bait	1.05 x 10^{-7}	5.26 x 10^{-9}	4.16 x 10^{-9}
Grand total: no PPE	1.09 x 10^{-7}		
Grand total: gloves in all phases, but no respiratory protection	9.42 x 10^{-9}		
Note: The French CA (2017) calculated exposure of non-professionals only for the cleaning phase, the dermal exposure was 1.22 x 10^{-7} mg/kg-day, without gloves, based on 0.005% brodifacoum. ***Gloves**: assumed to afford 95% protection **-**: not calculated			

8.3.2 Grain products risk assessment

The risk assessment calculations are conducted by comparing the calculated brodifacoum exposure doses (Section 8.3.1) to the acute AEL for brodifacoum (Table 7.2.3.1) of 3.3×10^{-6} mg/kg-day. The risk assessment is summarised in Table 8.3.2.1 (professionals) and in Table 8.3.2.2 (non-professionals). Exposure doses less than 100 per cent of the AEL are considered acceptable.

Risk assessment conclusion – loose grain bait products in South Africa

Acceptable risks are shown for professionals using loose grain baits supplied in South Africa and assessed in this report. As expected, risks are even lower when gloves and respiratory protection are used.

Assuming that non-professionals might not be diligent users of PPE, the assessment was done without PPE use by non-professionals. No unacceptable risks were found.

With regard to indirect (secondary exposure) to loose grains in use, a health risk related to adults in contact with dead rodents, due to grain residues on fur is considered of low relevance by the French CA. Rather, gloves are recommended when handling dead rodents, in order to prevent contact with rodent-borne diseases; therefore, exposure due to this scenario is considered negligible (French CA 2017).

Secondary acute oral exposure by a child (infant) ingesting bait, was handled by reverse calculation by the French CA (2017). It was calculated that ingestion of more than 0.88 mg of product per day by an infant is needed to exceed the AEL, based on:

- An acute AEL of 3.3×10^{-6} mg brodifacoum/kg-day.
- Infant body weight of 10 kg.
- Oral absorption of 75%.
- Brodifacoum content of 0.005%.

The equivalent required ingestion by an infant, of a product registered in South Africa (maximum of 0.002% brodifacoum), would be 0.88 mg x (0.005%)/(0.002%) = 2.2 mg, which is less than one grain of wheat. Although a risk to infants cannot be excluded, no more than transient mouthing of grains is expected, because the taste deterrent (bittering agent) included in the formulation will cause the child to spit out the grain. Nonetheless, any noted contact of a child with grain bait, or with any other type of rodenticide, should be brought to the immediate attention of a medical professional, without exception.

Table 8.3.2.1: Professionals' grain bait brodifacoum health risks.

Activity	Without PPE						With PPE (Gloves during all activities; respiratory equipment during decanting)					
	Exposure dose (mg/kg-day)			Risk = (Dose/AEL) % AEL_{acute} = 3.3 x 10^{-6} mg/kg-day			Exposure dose (mg/kg-day)			Risk = (Dose/AEL) % AEL_{acute} = 3.3 x 10^{-6} mg/kg-day		
Route of exposure	**Dermal**	**Inhalation**	**Total**	**Dermal**	**Inhalation**	**Total**	**Dermal**	**Inhalation**	**Total**	**Dermal**	**Inhalation**	**Total**
Decanting grain bait	4.41 x 10^{-7}	6.80 x 10^{-7}	1.12 x 10^{-6}	13%	21%	34%	2.20 x 10^{-8}	6.80 x 10^{-8}	9.00 x 10^{-8}	0.7%	2.1%	2.7%
Loading grain bait	2.77 x 10^{-7}	Negligible	2.77 x 10^{-7}	8%	Negligible	8%	1.39 x 10^{-8}	Negligible	1.39 x 10^{-8}	0.4%	Negligible	0.4%
Cleaning phase	1.31 x 10^{-7}	Negligible	1.31 x 10^{-7}	4%	Negligible	4%	6.54 x 10^{-9}	Negligible	6.54 x 10^{-9}	0.2%	Negligible	0.2%
Total	8.49 x 10^{-7}	6.80 x 10^{-7}	1.53 x 10^{-6}	26%	21%	46%	4.24 x 10^{-8}	6.80 x 10^{-8}	1.10 x 10^{-7}	1.3%	2.1%	3.4%

Table 8.3.2.2: Non-professionals' grain bait brodifacoum health risks without PPE use.

Route of exposure All exposure without PPE	Exposure dose (mg/kg-day)			Risk = (Dose/AEL) % AEL_{acute} (mg/kg-day) = 3.3 x 10^{-6}		
	Dermal	**Inhalation**	**Sum**	**Dermal**	**Inhalation**	**Sum**
Decanting grain bait	3.45 x 10^{-8}	4.16 x 10^{-9}	3.86 x 10^{-8}	1.05	0.13	1.17
Loading grain bait	2.20 x 10^{-8}	Negligible	2.20 x 10^{-8}	0.67	Negligible	0.67
Cleaning phase	4.87 x 10^{-8}	Negligible	4.87 x 10^{-8}	1.48	Negligible	1.48
Total	1.05 x 10^{-7}	4.16 x 10^{-9}	1.09 x 10^{-7}	3.19	0.13	3.31

8.4 Paste bait

8.4.1 Exposure assessment

The assessed products and scenarios

Table 3.2.2 presents the percentage by mass of brodifacoum in each solid formulation product, showing that the highest brodifacoum content in the paste (pasta) bait products is 0.05 g/kg (0.005 weight %).

Neither the Italian CA (2010), nor the French CA (2017), or the USEPA (2020b) reviewed health risk assessments for paste bait formulations. The German CA (2018) assessed a paste formulation containing coumatetralyl. As mentioned in Section 7.3.1, CEFIC had viewed a bait formulation with coumatetralyl as a worst-case representative of other similar bait forms (cereal-based baits in that case). Therefore, it is appropriate to use the German CA (2018) coumatetralyl paste bait assessment as a template for the assessment of the registered South African paste bait products assessed in this report.

The German CA reviewed the paste bait as a ready-to-use bait supplied and used as a of 10 g sachet with a "highly viscous, dough-like log in a paper sachet", used in and around buildings. The registered South African products are also supplied in a ready-to-use sachet, usually referred to as a "T"-bag. The pasta content and number of South African product bags to be deployed per bait station are summarised in Table 8.4.1.1. The German CA (2018) treated the pasta formulation supplied in a sachet as intended for use by non-professionals. Thus, exposure of professional pest controllers was considered not applicable and associated risks were not assessed. Use by professionals only is not specified on the product labels of paste baits registered in South Africa; therefore, application by non-professionals is applicable to the South African products.

The German CA (2018) summarised the potential for human exposure to pasta baits as presented in Table 8.4.1.2, grouped by routes of exposure. The summary list of scenarios assessed by the German CA, following from the identified relevant routes of exposure, is shown in Table 8.4.1.3. These will also be assessed for the registered South African products.

Table 8.4.1.1: South African products "T"-bag paste content, numbers of bags applied per bait point and label-recommended PPE use.

Product	Brodifacoum weight % (Table 3.2.2)	"T"-bag pasta content (g per bag)	Number of bags presented per bait point	Gloves recommended during application (on label)
Rodex Paste Bait L9566	0.005	15	10 (Rats) 2 (Mice)	Yes
Rodenthor® Pasta Bait FATAL ATTRACTION (BRODITOP PASTA) L8387	0.005	10	10 (Rats) 2 (Mice)	No

Table 8.4.1.2: Main paths of human exposure.

Exposure path	Professional use	General public	Via food
Inhalation	Not applicable	Not relevant	Not applicable
Dermal	Not applicable	Not relevant	Not applicable
Oral	Not applicable	Not relevant	No

Table 8.4.1.3: List of scenarios for paste rodenticide products, assessed by the German CA.

Scenario	Primary or secondary exposure and scenario description	Exposed group
Application and disposal – bait station	Primary exposure - biocidal product in sachets is placed in bait stations by an adult; max. 20 sachets per bait point, 5 bait points	Non-professional
Application and disposal – skewered on a wire	Primary exposure - biocidal product in sachets is speared on a wire by an adult; max. 20 sachets per bait point, 5 bait points	Non-professional
Mouthing	Secondary exposure - swallowing/ingestion of baits by toddlers: a) Swallowing of one bite b) Transient mouthing of a bait (e.g. with repellent)	General public

Non-professional exposure

The German CA (2018) based the primary exposure scenarios on an exposure study already submitted for coumatetralyl, but re-evaluated taking into consideration the Biocides Human Health Exposure Methodology (ECHA 2015) and the 2007 version of the TNsG on Human Exposure (ECB 2007). See description of the TNsG in Section 7.2.1.

Application and disposal – bait station

The German CA (2018) described the scenario as follows:

- The biocidal product is directly applied by the non-professional user, who places the bait sachets at the baiting points.
- For disposal the non-professional user collects the sachets, which might be partly eaten and damaged.
- Product mass: 10 g paste/sachet.
- Indicative exposure value for the application of sachets: 0.4917 mg paste per placed sachet.
- Indicative exposure value for the disposal of sachets: 0.1138 mg paste per disposed sachet.
- Note: the indicative exposure is the 75th percentile of paste exposure to the skin of subjects handling sachets with 10g paste/sachet, determined in an experimental exposure study.
- Number of sachets placed: 100.
- This is equivalent to 10 sachets (instructions on registered products for rat infestation) placed at an assumed 10 baiting points, viewed as a likely maximum for registered South African paste bait rodenticides.

The other default values for the registered South African products are:

- The assumed adult body weight is 60 kg, as for the assessment of all other rodenticide products in this report.
- The dermal absorption rate of brodifacoum from a “viscous, dough-like” paste formulation is not specifically available, but assumed to be the “worst-case estimate” of 5% for pellets and grains (Section 6.2).
- The brodifacoum content of the registered paste bait products is as presented in Table 8.4.1.1.
- PPE use is not included in the calculations, because use by non-professionals is assessed, and it is assumed that that non-professionals might not be diligent users of PPE.

Systemic exposure of a non-professional for the scenario of application in a bait station, with subsequent disposal of left-over of torn sachets, is calculated according to the German CA (2018):

- $Exposure_{dermal}$ = [(indicative $exposure_{application}$ + indicative $exposure_{disposal}$) x number of sachets x brodifacoum content x dermal absorption] / body weight adult
- = [(0.4917 mg + 0.1138 mg) x 100 x 0.005% x 5%] / 60 kg
- = 2.52 x 10^{-6} mg/kg-bw

Therefore, the maximum systemic exposures of a non-professional applying and cleaning up registered South African paste formulations listed in Table 8.4.1.1, according to the assessed scenario, is:

- 2.52×10^{-6} mg/kg-bw

Application and disposal – sachets skewered on a wire

The German CA (2018) described the scenario as follows:

- This scenario represents a dermal contact worst case for all paste applications, where the biocidal product has to be fixed (e.g. to avoid that they are dragged away by rodents).
- The biocidal product is applied by the non-professional user, who secures the bait sachets after spearing them on a wire.
- For disposal the non-professional user retrieves the wire and collects the sachets, which might be partly eaten and damaged.
- Product mass: 10 g paste/sachet.
- Indicative exposure value for the application of sachets: 2.5233 mg paste per placed sachet.
- Indicative exposure value for the disposal of sachets: 1.2892 mg paste per disposed sachet.
- Number of sachets placed: 100.
- This is equivalent to 20 sachets (maximum number per baiting point, according to German applicant) placed at an assumed 5 baiting points.
- This is viewed as a likely maximum for registered South African paste bait rodenticides.

The other default values for the registered South African products are as for the bait point scenario, except for the brodifacoum content, which is according to Table 8.4.1.1.

Systemic exposure of a non-professional for the scenario of application in a bait station, with subsequent disposal of left-over of torn sachets, is calculated according to the German CA (2018):

- $\text{Exposure}_{\text{dermal}}$ = [(indicative $\text{exposure}_{\text{application}}$ + indicative $\text{exposure}_{\text{disposal}}$) x number of sachets x brodifacoum content x dermal absorption] / body weight adult
- = [(2.5233 mg + 1.2892 mg) x 100 x 0.005% x 5%] / 60 kg
- = 1.59×10^{-5} mg/kg-bw

Therefore, the maximum systemic exposures of a non-professional applying and cleaning up registered South African paste formulations listed in Table 8.4.1.1, according to the assessed scenario, is:

- 1.59×10^{-5} mg/kg-bw

Secondary exposure: mouthing by infants/toddlers

- The German CA (2018) views the ingestion and mouthing of rodenticide bait by an infant/toddler as "*an exceptional scenario, which may occur accidentally*".
- Based on the TNsG (ECB 2007) consumption of up to 5 g is assumed if no bait boxes are used and no bittering agent is added.
- The risk of oral exposure is minimised by addition of a bittering agent (as for paste products registered in South African) and by an appropriate covering of baits (e.g. by use of a bait station), which is recommended for the registered South African products.
- The minimised accidentally ingested amount is expected to be 10 mg per mouthing event, since it is likely that that the bittered bait will be spit out and not swallowed.
- Inhalation exposure is considered not relevant due to the physical-chemical properties of brodifacoum (see Section 6.2) and considering the specific use conditions (paste formulation to be placed out of reach of children and uniformed persons).

- The German CA (2018) accepts that the potential dermal exposure of toddlers/infants is covered by the oral exposure assessment.
- The default body weight of and infant/toddler is 10 kg.

The other default values for the registered South African products are:
- The oral absorption rate of brodifacoum from a "viscous, dough-like" paste formulation is not specifically available, but assumed to be 75% (Section 6.2).
- The brodifacoum content of the registered paste bait products is as presented in Table 3.2.2.
- A bittering agent is included in the products registered in South Africa; therefore, transient mouthing with ingestion of 10 mg per mouthing event is assumed.

Systemic exposure of an infant/toddler for the scenario of accidental ingestion by transient mouthing is calculated according to the German CA (2018) method:
- $Exposure_{oral}$ = Ingested amount x brodifacoum content x oral absorption / body weight
- = (10 mg x 0.005% x 75%] / 10 kg
- = 3.75×10^{-5} mg/kg-bw

Professional exposure

Based on informal queries to local rodenticide suppliers, it appears that pasta baits are not frequently used by professional pest control operators ("PCOs"). Therefore, it is assumed that the bait use of PCOs is similar to that of non-professionals (100 sachets placed on one day) and that risks of professionals would be as for non-professionals.

8.4.2 Paste products risk assessment

The risk assessment calculations are conducted by comparing the calculated brodifacoum exposure doses (Section 7.4.1) to the acute AEL for brodifacoum (Table 7.2.3.1) of 3.3×10^{-6} mg/kg-day. The risk assessment for non-professionals is summarised in Table 8.4.2.1. Exposure doses less than 100 per cent of the AEL are considered acceptable.

Exposure and risk calculations are based on PPE use premises as indicated. It was considered unlikely that non-professionals would be wearing respiratory protection, but gloves may be mandated without inconvenience to non-professional users, and were included in the calculations. It is acceptable to assume that the dermal exposure dose with gloves will be 5 per cent of that without gloves (French CA 2017).

Acceptable risks are shown for non-professionals applying and disposing of sachets placed in a bait station, for all products assessed. Unacceptable risks are shown for pastes containing 0.005% brodifacoum when non-professionals skewer sachets on a wire, without the use of gloves. As expected, risks are lower when gloves are used, in which case the activity of applying and cleaning up bait skewered on a wire is acceptable (Table 8.4.2.1).

The risk assessment for non-professionals demonstrates that use of gloves if skewering paste sachets should be mandatory, and clear instructions to this effect should be provided on product labels. Wearing gloves also protects against possible secondary exposure while handling dead rodents.

For secondary exposure, an unacceptable risk is identified for children accidentally mouthing baits with 0.005% brodifacoum. According to the German (2018) assessment of a paste bait containing coumatetralyl, specific risk mitigation measures are required to prevent exposure to children, and

these are also applicable to paste products containing brodifacoum and registered in South Africa. The mitigation measures for paste baits are not different from other bait forms and are discussed in the Discussion Section (Section 9). Any noted contact of a child with paste bait, or with any other type of rodenticide, should be brought to the immediate attention of a medical professional, without exception.

Table 8.4.2.1: Brodifacoum paste bait health risks of non-professionals and infants/toddlers.

Route of exposure	Exposure dose (mg/kg-day)		Risk = (Dose/AEL) % AEL_{acute} (mg/kg-day) = 3.3×10^{-6}		
	Dermal (all adult)	Oral (infant/toddler)	Dermal	Oral	Acceptable Yes/No
Primary exposure, without PPE					
Application and disposal – bait station	2.52×10^{-6}	-	76%	-	Yes
Application and disposal – sachets skewered on a wire	1.59×10^{-5}	-	481%	-	No
Primary exposure, with gloves. Gloves are assumed to afford 95% dermal protection.					
Application and disposal – bait station	1.26×10^{-7}	-	4%	-	Yes
Application and disposal – sachets skewered on a wire	7.94×10^{-7}	-	24%	-	Yes
Secondary exposure					
Accidental mouthing by infants/toddlers	-	3.75×10^{-5}	-	1 136%	No

With regard to indirect (secondary exposure) to paste baits in use, a health risk related to adults in contact with dead rodents, due to paste residues on fur is considered of low relevance, following the conclusions of the French CA (2017) regarding grain baits. Rather, gloves are recommended when handling dead rodents, in order to prevent contact with rodent-borne diseases; therefore, exposure to paste bait residues on rodent fur is considered negligible.

Considering that professional PCOs should wear gloves at all times during the control operation, the extrapolated risks to professional PCOs would also be acceptable.

8.5 Powder formulation

8.5.1 Exposure assessment

It is important to note that the Doom Rattex Deadly Powder assessed here is primarily a bait and not a tracking powder. The ECB (2007) describes the use of contact powders (tracking powders) indoors and outdoors as follows: "*rodents pick up the powder on their feet which is then consumed during grooming*". However, the Rattex Powder product is actually a bait, with a granular (like mealie-meal) consistency, rather than like a talcum powder. The powder is meant to be consumed by rats rather than adhering to the limbs/body with subsequent ingestion during grooming.

Primary exposure of users occurs during the intended use of the powder formulation, described as follows on the product label: "*kills most rats and mice – including Norway rat, roof rat and house mice – after a single feed. Use it to control rodent infestations in homes, farms, stores, warehouses and grain storage areas.*"

The powder is available to the general public, or at retail outlets such as supermarkets, hardware stores, etc. Therefore, the primary exposure risk assessment is concerned with PCOs and non-professionals (amateurs and domestic users.)

Secondary exposure of adults and children in accidental contact with the product during the in-use phase is assessed, although label instructions are to "*Locate Doom Rattex Deadly Powder in places inaccessible to children*". Label instructions for "*Rats and mice in the roof"* is to "*Throw an open sachet of Doom Rattex Deadly Powder through trap door into roof space*". This implies that spilled powder in the roof space might be available for dermal contact by service providers subsequently entering the roof space, e.g., electricians, plumbers or other maintenance workers. Although not necessarily a frequent occurrence, a scenario of rodents dragging the sachets away from the deployed places, to where children and adults might come in contact with spilled powder, cannot be excluded. Therefore, accidental exposure of children is assessed.

Primary exposure

Primary exposure of PCOs (professionals) is assessed during the application phase and the disposal (clean-up) phase. Inhalation and dermal exposure are of main interest during the application phase. With outdoor use, exposure to the product is not applicable during the clean-up phase, because the powder is usually left in the rat burrows. With indoor use, removal by sweeping with a broom of brush may disperse dust into air, resulting in inhalation and even dermal exposure.

The routes of exposure to be included in the risk assessment are approached as described below, based on TNsG data and product-specific use scenarios.

Inhalation of powder is assessed by the ECB (2007) for the application of contact powder with a dust blower, with an estimate of 5% inhalation exposure of the applied amount. This method is not an option on the Doom Rattex label, but small volumes of inhalable dust generation is possible. Inhalation of fine powder particles is thus assessed, particularly because the product is available to the general public, who might not be as aware as PCOs of the need to prevent dust generation and inhalation.

The default values suggested by the TNsG allows for the use of up to 1 kg (250 g/event x 4 events; Table 7.2.2.1) as worst case per day. It is doubtful that this is applicable to Doom Rattex powder, considering that the product package netto mass is 100 g of powder. The average daily use by non-professionals (the general public) is thus estimated at 100 g product, on one event, per day. Allowing for PCO use of multiple packets per day, PCO use is assessed at 200 g per event and 4 events per day (800 g per day).

For application inside a room, the ECB (2007) assumes "*immediate and homogenous"* distribution of the entire mass of dispersed particles in a default room size of 50 m^3, without ventilation. The air concentration of the product is then simply calculated as the airborne mass per air volume (mg/m^3).

Application with a dust blower is not relevant to the Rattex powder formulation; therefore, the TNsG estimate of inhalation exposure to 5% of the applied powder is also not relevant. Instead, it is assumed that the amount dispersed into air would be equal to or less than the percentage dispersed during clean-up of a powder product, which is 1% (ECB 2007). This assumption is unlikely to underestimate the application exposure, since cleaning up, e.g., by collecting left-over powder with a broom or brush, should conceivably generate more dust than applying a powder from a sachet.

Since the Rattex powder formulation has a granular consistency, rather than being finely powdered, the application action would be more like pouring the product from the sachet, rather than shaking

the sachet. Therefore, a further 1% reduction in the amount of powder dispersed in air is assumed. The percentage of dispersed Rattex powder formulation is thus 1% of 1%, that is, 0.01%.

Other default values (ECB 2007) are the adult inhalation rate of 1.25 m^3/hour, that is, 0.021 m^3/min, and a default airborne product exposure period of 10 min/application event (Table 7.2.2.1). The period of 10 minutes is acceptable for the clean-up (disposal) phase, but is likely to overestimate exposure during the application phase, considering that a maximum application of 2 packets of powder is assumed. The exposure periods during the application events are thus estimated at 5 minutes, during which 100 g of powder is applied by a non-professional person, or 200 g is applied by a PCO. It is assumed that a non-professional would apply the powder during only one event per day, but the PCO during 4 events per day, at different locations. Therefore, the PCO exposure during the 4 events is accumulated to determine the total exposure during one day. It is further assumed that the PCO would not use the product on subsequent days, since it is unlikely that a PCO would use a sachet product with such a small mass on multiple days, given that other rodenticide products for PCO use are available in much larger package sizes.

For the clean-up (disposal) phase, the TNsG default assumption is that 50% of the mass of applied powder remains. This default is used to estimate the remains suspended in air during indoor clean-up in a default space of 50 m^3, without ventilation. The airborne inhalable suspended particles are estimated at 1% of the residual amount, assuming 50% residues still present. Duration of exposure may be taken as 5 to 30 minutes during a day (ECB 2007). A default value of 10 minutes is used for the calculations in this report. Since the Rattex powder is granular, rather than a fine product, the mass of suspended particles during clean-up is adjusted to an estimated 1% of the exposure assumed for tracking powder, that is, to 0.01%.

The masses of powder inhaled per day in the different scenarios are presented in Table 8.5.1.1.

Table 8.5.1.1: Calculated indoor air powder concentrations (per event).

Scenario and exposure variable description	Application phase		Clean-up (disposal) phase	
	General public	**PCOs**	**General public**	**PCOs**
Applied powder mass/event	100 g	200 g	-	-
Powder remaining for clean-up (mass/day)	-	-	50 g	100 g
Powder available for suspension (%)	0.01%	0.01%	0.01%	0.01%
Suspension in air: powder airborne (g/event)	0.01% of 100 g = 0.01 g/event	0.01% of 200 g = 0.02 g/event	0.01% of 50 g = 0.005 g/event	0.01% of 100 g = 0.010 g/event
Powder air concentration (dispersion in a 50 m^3 room)	0.0002 g/m^3 (0.2 mg/m^3)	0.0004 g/m^3 (0.4 mg/m^3)	0.0001 g/m^3 (0.1 mg/m^3)	0.0002 g/m^3 (0.2 mg/m^3)
Event duration (TNsG default)	5 minutes	5 minutes	10 minutes	10 minutes
Inhalation rate (adult) (TNsG default)	0.0208 m^3/min	0.0208 m^3/min	0.0208 m^3/min	0.0208 m^3/min
Volume air inhaled/event (m^3/event)	0.104 m^3	0.104 m^3	0.208 m^3	0.208 m^3
Powder inhaled/event (mg/event)	0.021 mg/event	0.042 mg/event	0.021 mg/event	0.042 mg/event

Powder remaining for clean-up (mass/day) = 50% of applied mass
Suspension in air: powder airborne = default % airborne x mass of powder in room
Powder air concentration = airborne powder (g/event) / 50 m^3, e.g., 0.01 g / 50 m^3 = 0.0002 g/m^3 (0.2 mg/m^3)
Inhalation rate (adult) (TNsG default) 1.25 m^3/hour = 0.0208 m^3/min
Volume air inhaled/event = event duration x inhalation rate
Powder inhaled/event = powder air concentration x volume air inhaled/event

Ingestion of bait powder

Oral exposure is possible if hands and face are not washed/cleaned after the application, e.g., via contact to food items or by smoking (ECB 2007). Residues from clothes may also be transferred to objects that may get into contact with the mouth. However, the product label clearly states "*Wash hands with soap and water after handling*." Therefore, oral exposure is not considered an important route of primary exposure, and is not included in the assessment.

Dermal exposure to bait powder

Dermal exposure is possible from direct contact without gloves or insufficient covering of the skin during application of the powder formulation. An estimate of the dermal exposure is suggested at 1% of the applied amount, without protection (ECB 2007).

The example calculations of the TNsG includes the following default values:

- The assumed density of the powder transferred to the skin is 0.38 g/cm^3.
- It is assumed that the powder will form a layer with thickness 0.01 cm on the skin.
- The assumed exposed skin is 2 000 cm^2, being the hands and forearms of an adult.

Using the default values, the TNsG equations (Equations 8.5.1.1, 8.5.1.2 and 8.5.1.3) are used to calculate the amount of brodifacoum on the skin:

$$A_{der} = C_{der} \, x \, V_{appl} \, x \, 1\% \qquad \text{Equation 8.5.1.1}$$

Where:

A_{der} =	Amount of active substance on skin (mg).
C_{der} =	Average concentration of brodifacoum in product on skin (mg/cm^3)
V_{appl} =	Volume of applied product in contact with skin (cm^3).

Where the terms are substituted as follows:

$$C_{der} = \frac{Q_{prod} \times 1\% \times Fc_{prod}}{V_{prod} \times D} \qquad \text{Equation 8.5.1.2}$$

Where:

C_{der} =	Average concentration of brodifacoum in product on skin (mg/cm^3).
Q_{prod} =	Amount of undiluted product used (mg).
1% =	Percentage of product available for contact with skin (TNsG default = 1%)
FC_{prod} =	Weight fraction of brodifacoum in the product [(% w/w)/100)].
V_{prod} =	Volume of undiluted product (cm^3). In the case of a powder rodenticide, the product volume is calculated with an assumed product density of 0.38 g/cm^3 on the skin (ECB 2007). E.g., if 100 g of product is applied per event, the volume applied product = (100 g / 0.38 g/cm^3) in cm^3 units.
D =	Dilution factor (1, unitless – not diluted).

and

$V_{appl} = TH_{der} \, x \, AREA_{der}$ Equation 8.5.1.3

Where:

V_{appl} =	Volume of product in contact with skin (cm^3).
A_{der} =	Thickness of layer of product on skin (default = 0.01 cm).
$AREA_{der}$ =	Surface area of exposed skin (cm^2).

Primary exposure

Calculations of primary dermal exposure of PCOs and the general public during the application phase, using Equations 8.5.1.1 to 8.5.1.3, are presented in Tables 8.5.1.2 and 8.5.1.3. The dermal absorption factor of 0.647% applicable to pellets and grains, which might generate dust contaminated with brodifacoum (Section 6.2) is used for the calculation of the systemic brodifacoum dose due to dermal absorption from the powder in contact with the hands and forearms. In the case of PCOs, it is assumed that 4 application events per day would occur at different locations. Therefore, the PCO exposure during the 4 events is accumulated to determine the total exposure during one day.

Application phase primary inhalation exposure calculations with Equations 7.2.3.1 and 7.2.3.2, using the brodifacoum content (0.003% w/w) and the inhalation absorption factor of 100% (Section 6.2) are presented in Table 8.5.1.4 for PCOs. The systemic dose due to inhalation is calculated with and without the use of respiratory equipment, since it is it is reasonable to expect PCOs to use respiratory protection. The combined dermal and inhalation systemic dose of PCOs is also calculated.

It is unlikely that the general public will use respiratory protection and there is not a direct instruction to wear respirators (or other masks) on the product label. The statement "*[In case of inadequate ventilation] wear respiratory protection"* appears on the product SDS, but not on the product label. Therefore, it cannot be assumed that the general public will use protection, and, in any case, even if it was indicated on the label, it is questionable that the public would have easy access to respiratory protection. The application phase primary inhalation exposure calculations of the general public are presented in Table 8.5.1.5, and it is assumed that respiratory protection is not used. The combined dermal and inhalation systemic dose of the general public is also presented.

Table 8.5.1.2: Calculation of the amount of powder and the brodifacoum concentration on the skin during the powder application phase (per event).

Exposure variable	Units	General public	PCO
Powder application phase (deposit in holes/on runs/in roof space)			
C_{der} (Equation 8.5.1.2) Average concentration of brodifacoum in product on skin			
Amount of undiluted product used (Table 8.5.1.1)	g	100	200
Q_{prod}: Amount of undiluted product used	mg	100 000	200 000
Fraction of product available for dermal contact (= 1%, TNsG default)	unitless	0.01	0.01
FC_{prod}: Weight fraction of brodifacoum in product = [(0.003% w/w (Table 3.2.2)) / 100] = 0.00003	unitless	0.00003	0.00003
Density of product particles on skin (TNsG default)	g/cm^3	0.38	0.38
V_{prod}: Volume of undiluted product (cm^3) applied = (g product / density)	cm^3	100 / 0.38	200 / 0.38

Exposure variable	Units	General public	PCO
D: Dilution factor	unitless	1 (not diluted)	1 (not diluted)
C_{der} = Average concentration of brodifacoum in product on skin	mg/cm^3	(100 000 x 0.01 x 0.00003) / (100 / 0.38) x 1	(200 000 x 0.01 x 0.00003) / (200 / 0.38) x 1
V_{appl} (Equation 8.5.1.3) Volume of product in contact with skin			
TH_{der}: Thickness of layer of product in contact with skin (default = 0.01 cm)	cm	0.01	0.01
$AREA_{der}$: Surface area of exposed skin (TNsG default)	cm^2	2 000	2 000
V_{appl} = Volume of powder in contact with skin	cm^3	0.01 x 2 000	0.01 x 2 000

Table 8.5.1.3: Calculation of the amount of brodifacoum on the skin during the powder application phase.

Amount of brodifacoum on skin (mg), calculated with Equation 8.5.1.1. $A_{der} = C_{der} \times V_{appl}$ (C_{der} and V_{appl} calculated in Table 8.5.1.3)	
General public	**PCO**
A_{der} = (100 000 x 0.01 x 0.00003) / (100 / 0.38) x 1 x 0.01 * 2 000 = 0.00228 mg	A_{der} = (200 000 x 0.01 x 0.00003) / (200 / 0.38) x 1 x 0.01 * 2 000 = 0.00228 mg

Table 8.5.1.4: PCOs application phase inhalation and combined dermal and inhalation exposure per application event.

Scenario and exposure variable description	Dermal exposure	Inhalation exposure
Powder application phase (deposit in holes/on runs/mixing of powder)		
Applied powder mass/day (Table 8.5.1.1)	200 g	200 g
Concentration of brodifacoum in product (Table 3.2.2)	0.003% w/w	0.003% w/w
Amount of powder inhaled/event (see Table 8.5.1.1)	-	0.042 mg/event
Brodifacoum exposure/event	0.00228 mg/event (Table 8.5.1.2)	0.042 mg/event x 0.003% = 0.0001 mg/event
Brodifacoum absorption rate (Section 6.2)	0.647%	100%
Brodifacoum absorbed per event	0.00228 mg/event x 0.647% = 1.48 x 10^{-5} mg/event	0.0001 mg/event x 100% = 0.0001 mg/event
Number of events per day		
Body weight (kg)	60	60
Brodifacoum systemic dose without PPE (mg/kg-bw)	2.46 x 10^{-7} (no gloves)	2.08 x 10^{-6} (no PPE)
Brodifacoum systemic dose with PPE (mg/kg-bw)	2.46 x 10^{-8} (with gloves)	Assumed 95% protection: 1.04 x 10^{-7}
Total systemic dose: dermal + inhalation (mg/kg-bw)	2.33 x 10^{-6} (without PPE)	
	1.29 x 10^{-7} (with gloves and respiratory protection)	

Table 8.5.1.5: General public application phase inhalation and combined dermal and inhalation exposure per event.

Scenario and exposure variable description	Dermal exposure	Inhalation exposure
Powder application phase (deposit in holes/on runs/mixing of powder)		
Applied powder mass/day (Table 8.5.1.1)	100 g	100 g
Concentration of brodifacoum in product (Table 3.2.2)	0.003% w/w	0.003% w/w
Amount of powder inhaled/event (see Table 8.5.1.1)	-	0.021 mg/event
Brodifacoum exposure/event	0.00228 mg/event (Table 8.5.1.2)	0.021 mg/event x 0.003% = 0.0001 mg/event
Brodifacoum absorption rate (Section 6.2)	0.647%	100%
Brodifacoum absorbed per event	0.00228 mg/event x 0.647% = 1.48×10^{-5} mg/event	0.0001 mg/event x 100% = 0.0001 mg/event
Body weight (kg)	60	60
Brodifacoum systemic dose		
Without PPE (mg/kg-bw)	2.46×10^{-7} (no gloves)	1.04×10^{-6} (no PPE)
With PPE (mg/kg-bw)	2.46×10^{-8} (with gloves)	Not applicable: assumed not to use respiratory PPE
Total: dermal + inhalation (mg/kg-bw)	1.29×10^{-6} (without PPE)	
	1.07×10^{-6} (with gloves, no respiratory protection)	

Primary dermal and inhalation exposure of PCOs during clean-up is presented in Table 8.5.1.6, and that of the general public using Doom Rattex in the home in Table 8.5.1.7. As explained previously, dermal exposure is estimated at 1% of the residual amount, assuming 50% residues still present, and inhalation exposure at 0.01%. Duration of exposure is assumed to be 10 minutes for inhalation exposure, and other inhalation exposure variables from Table 8.5.1.1 are used.

The dermal exposure calculations for the clean-up phase are based on the same fraction of product available for dermal contact as during the application phase, that is, 1% (Table 8.5.1.2). All other exposure values for the clean-up phase are as for the application phase (Table 8.5.1.5), except the amount of powder residue, which is 50% of that applied in the application phase. Thus, it is reasonable to conclude that the dermal dose during the clean-up phase (Table 8.5.1.6) will be 50% of the dose during the application phase (Table 8.5.1.5), as summarised in Table 8.5.1.6.

Table 8.5.1.6: PCOs powder clean-up dermal, inhalation and combined exposure per event.

Scenario and exposure variable description	Dermal exposure	Inhalation exposure
Clean-up phase (cleaning using a broom, and disposal)		
Brodifacoum concentration in product (Table 3.2.2)	0.003% w/w	0.003% w/w
Applied powder mass/day (Table 7.2.2.1)	200 g	200 g
Assumed residues still present at clean-up	100 g (50% of the applied mass)	100 g (50% of the applied mass)
Dispersion in air: amount airborne/event	-	0.010 g/event (Table 8.5.1.1)
Mass of powder inhaled in 10-min clean-up phase	-	0.042 mg/event (Table 8.5.1.1)

Scenario and exposure variable description	Dermal exposure	Inhalation exposure
Brodifacoum exposure/event	50% of application phase exposure = 0.00114 mg	0.042 mg/event x 0.003% = 0.00013 mg/event
Brodifacoum absorption rate	0.647%	100%
Brodifacoum absorbed per event	0.00114 mg/event x 0.647% = 7.83×10^{-6} mg/event	0.00013 mg/event x 100% = 0.00013 mg/event
Body weight (kg)	60	60
Brodifacoum systemic dose		
Without PPE (mg/kg-bw)	1.23×10^{-7} (no gloves)	2.08×10^{-6} (no PPE)
With PPE (mg/kg-bw)	1.23×10^{-8} (with gloves)	Assumed 95% protection: $2.08 \times 10^{-6} \times 5/100 = 1.04 \times 10^{-7}$
Total systemic dose: dermal + inhalation (mg/kg-bw)	2.21×10^{-6} (without gloves)	
	1.16×10^{-7} (with PPE)	

Table 8.5.1.7: General public clean-up phase dermal, inhalation and combined exposure per event.

Scenario and exposure variable description	Dermal exposure	Inhalation exposure
Clean-up phase: cleaning using a broom, and disposal		
Brodifacoum concentration (Table 3.2.2)	0.003% w/w	0.003% w/w
Applied powder mass/day (Table 7.2.2.1)	100 g	100 g
Assumed residues still present at clean-up	50 g (50% of the applied mass)	50 g (50% of the applied mass)
Dispersion in air: amount airborne/event	-	0.005 g/event (Table 8.5.1.1)
Mass of powder inhaled in 10-min clean-up	-	0.021 mg/event (Table 8.5.1.1)
Brodifacoum exposure/event	50% of application phase exposure = 0.00114 mg	0.021 mg/event x 0.003% = 0.00006 mg/event
Brodifacoum absorption rate	0.647%	100%
Brodifacoum absorbed per event	0.00114 mg/event x 0.647% = 7.83×10^{-6} mg/event	0.00006 mg/event x 100% = 0.00006 mg/event
Body weight (kg)	60	60
Brodifacoum systemic dose		
No PPE (mg/kg-bw)	1.23×10^{-7} (no gloves)	1.04×10^{-6} (no PPE)
With PPE (mg/kg-bw)	1.23×10^{-8} (with gloves)	Not applicable: assumed no respiratory PPE used
Total: dermal + inhalation (mg/kg-bw)	1.16×10^{-6} (without gloves)	
	1.05×10^{-6} (with gloves, no respiratory protection)	

Total exposure per day

The exposure doses per event, calculated in the above tables, are multiplied by the number of events (per day) to calculate the total dose per day (Table 8.5.1.8). Multiple doses are not calculated for non-professionals, since it is assumed that only one exposure event is applicable per day. Therefore, only data for PCOs are presented in Table 8.5.1.8.

Table 8.5.1.8: Total brodifacoum doses for PCOs, exposed during multiple events per day.

Exposure scenario	Application phase, 4 events per day (mg/kg-day)		Clean-up phase, 4 events per day (mg/kg-day)	
	Without PPE	With PPE	Without PPE	With PPE
Inhalation exposure	8.33×10^{-6}	4.17×10^{-7}	8.33×10^{-6}	4.17×10^{-7}
Dermal exposure	2.46×10^{-7}	9.83×10^{-8}	4.92×10^{-7}	4.92×10^{-8}

Secondary exposure

Indirect (secondary) exposure during the use phase is assessed according to the scenarios listed in the TNsG:

- Accidental contact by persons unaware of the nature of the dust, or curious children/infants.
- Exposure may resemble the scenario of dermal contact, calculated using the values applicable to the general public. Inhalation exposure is thus considered negligible.
- The most likely resemblance is to the clean-up scenario (lesser amounts of powder available for contact).

Dermal exposure of children is assessed for infants/toddlers, since the rates of exposure relative to their body size are higher for younger children compared to older children and adults. Infants and toddlers are thus more vulnerable than older children and adults and thus the most sensitive indicators of likely risks of accidental exposure. Dermal doses of infants/children are calculated with a default body weight of 10 kg, and assuming that the total hand area is available for dermal exposure, equal to the USEPA (2011) default of 0.030 m^2 (300 cm^2) for a toddler aged 1 to 2 years.

According to the calculations presented for the general public in Table 8.5.1.7, the brodifacoum absorption per dermal exposure event of an adult during the clean-up phase is 7.38×10^{-6} mg/event, assuming gloves are not worn, and that the skin area available for dermal exposure is 2 000 cm^2.

Scaling this absorption to that of a child, with an available skin area of 300 cm^2, the dermal brodifacoum absorption of a child would be:

- 7.38×10^{-6} mg/event x (300 cm^2 / 2 000 cm^2)
- = 1.11×10^{-6} mg/event

Ingestion by infants/toddlers is not included as a likely route by the ECB (2007), but accidental transient hand-to-mouth contact by an infant is assumed for the Doom Rattex assessment. The amount of accidentally ingested powder is assumed to be equal to that covering the area of hands in contact with the surface containing the biocide of interest, and in subsequent contact with the mouth, usually assumed to be an area of 20 cm^2 (USEPA 2005).

According to the calculations presented in Table 8.3.1.7, the mass of brodifacoum available on 2 000 cm^2 of skin of an adult during the clean-up phase is 0.00114 mg/event, assuming gloves are not worn.

Scaling this availability to that of a child, with a hand area of 20 cm^2 in contact with firstly the powder and then the mouth, the mass of brodifacoum available for ingestion by the child would be:

- 0.00114 mg/event x (20 cm^2 / 2 000 cm^2)
- = 1.14×10^{-5} mg/event

Given an absorption rate of 75% by ingestion (Section 6.2), the amount of brodifacoum absorbed by a child by accidental ingestion is:

- 1.14 x 10^{-5} mg/event x 75%
- = 8.55 x 10^{-6} mg/event

Finally, given a default infant body weight of 10 kg, the absorbed systemic doses are calculated:
- Dermal absorption dose: 1.11 x 10^{-6} mg/event / 10 kg = 1.11 x 10^{-7} mg/kg-day.
- Oral absorption dose: 8.55 x 10^{-6} mg/event / 10 kg = 8.55 x 10^{-7} mg/kg-day.

8.5.2 Bait powder risk assessment

Risks are calculated by comparing the calculated total brodifacoum exposure doses (Table 8.5.1.8 to the acute AEL (Table 7.2.3.1) of 3.3 x 10^{-6} mg/kg-day. Exposure doses less than 100 per cent of the AEL are considered acceptable. Risk calculations are summarised in Table 8.5.2.1.

Table 8.5.2.1: Brodifacoum powder health risks of primary and secondary exposure.

Exposure scenario	Without PPE			With PPE		
	Dose (mg/kg-day)	Risk	Acceptable Yes/No	Dose (mg/kg-day)	Risk	Acceptable Yes/No
PCOs primary exposure in the application phase (4 events)						
Inhalation exposure	8.33 x 10^{-6}	253	No	4.17 x 10^{-7}	13	Yes
Dermal exposure	2.46 x 10^{-7}	7	Yes	9.83 x 10^{-8}	3	Yes
Sum of inhalation and dermal exposure	8.58 x 10^{-6}	260	No	5.15 x 10^{-7}	16	Yes
PCOs primary exposure: clean-up phase, indoors only (4 events)						
Inhalation exposure	8.33 x 10^{-6}	253	No	4.17 x 10^{-7}	13	Yes
Dermal exposure	4.92 x 10^{-7}	15	Yes	4.92 x 10^{-8}	1.5	Yes
Sum of inhalation and dermal exposure	8.83 x 10^{-6}	267	No	4.66 x 10^{-7}	14	Yes
General public primary exposure: application phase (1 event)						
Inhalation exposure	1.04 x 10^{-6}	32	Yes	Not applicable	Not applicable	Not applicable
Dermal exposure	2.46 x 10^{-7}	7	Yes	2.46 x 10^{-8}	1	Yes
Sum of inhalation and dermal exposure	1.29 x 10^{-6}	39	Yes	1.07 x 10^{-6}	32	Yes
General public primary exposure: clean-up phase (1 event)						
Inhalation exposure	1.04 x 10^{-6}	32	Yes	Not applicable	Not applicable	Not applicable
Dermal exposure	1.23 x 10^{-7}	4	Yes	1.23 x 10^{-8}	0.4	Yes
Sum of inhalation and dermal exposure	1.16 x 10^{-6}	35	Yes	1.05 x 10^{-6}	32	Yes
Secondary exposure (1 event)						
Infants/toddlers accidental dermal exposure	1.11 x 10^{-7}	3	Yes	Not applicable		
Infants/toddlers accidental oral exposure	8.55 x 10^{-7}	26	Yes	Not applicable		
Risk = (Dose/AEL) % AEL_{acute} (mg/kg-day) = 3.3 x 10^{-6} (Table 7.2.3.1)						

PCOs primary exposure

The risk calculations for PCOs demonstrate that dermal exposure of PCOs not wearing gloves is acceptable, during both the application and clean-up phases. As expected, the risks of PCOs wearing gloves are even lower. This does not imply that gloves need not be worn. As recommended on the label, PCOs should wear gloves at all times while handling the product, while cleaning up residual product at the end of the campaign, and while handling dead rodents.

The calculated inhalation exposure of PCOs not wearing respiratory protection, assuming handling of 800 g bait powder during a work day, is not acceptable during the application or indoor clean-up phases. The calculated risks associated with inhalation exposure, assuming the use of a respirator with factor 20 protection (95% protection) are lower, as expected. Therefore, the SDS instruction to "[*In case of inadequate ventilation] wear respiratory protection*" is appropriate. The product label should recommend respiratory protection if more than 2 sachets are applied indoors, or when cleaning up more than 2 sachets indoors.

There is some uncertainty about the true air concentrations of brodifacoum available for inhalation during indoor- and outdoor application events. The air concentrations were calculated based on the assumption that 0.01% of the applied powder is airborne. This is unlikely to be an underestimation, since it is equal to the assumed airborne percentage when sweeping residual powder with a broom during the clean-up phase.

General public primary exposure

Assuming handling of 100 g bait powder per application event, the risk calculations for the general public demonstrate that dermal exposure is acceptable, during both the application and clean-up phases, whether gloves are worn or not. The calculated inhalation exposure is also acceptable during the application and clean-up phases, assuming that respiratory protection is not worn. This assumption is valid, because it is unlikely that the general public will use or have access to respirators.

General public secondary exposure

In the case of secondary exposure, the risks calculated for children in accidental dermal contact with the powder, and for infants/toddlers transferring powder from hands to mouth, are acceptable (Table 8.5.2.1). Nonetheless, contact of a child with any rodenticide remains unacceptable, and measures, as recommended on the product label, should be taken accordingly.

Accidental dermal exposure of an adult with the powder should not result in unacceptable risks, as these risks are likely to be similar to that of an adult applying the powder without the use of gloves (Table 8.5.2.1).

Dermal exposure of children and adults in contact with residual powder rodenticide on the fur of dead rodents should be similar to or less than that assumed for accidental dermal contact. The associated risks should be similar to that calculated in Table 8.5.2.1, and thus acceptable.

The assumed most important secondary exposure scenario of an adult is that of a cleaner in an industrial-, commercial- or office setting cleaning up powder rodenticide residues by sweeping with a broom. Inhalation exposure during this scenario would be similar to that of an adult from the general public cleaning up in the home with a broom, without respiratory protection (Table 8.5.2.1), and thus acceptable.

9 Discussion

9.1 Summary of risks associated with solid rodenticide formulations

The HHRA results presented in this report, concerning the use of solid rodenticide bait formulations registered in South Africa, and identified by name in Section 1.1, are summarised for professional PCOs, non-professional rodenticide users and non-professionals in contact with dead rodents, and infants/toddlers accidentally in contact with the rodenticides.

Wax blocks/wedges

- Exposures in the expected handling scenarios are acceptable for the professional and non-professional users. Non-professional users were assessed assuming that gloves are not worn.
- Secondary exposure was assessed for adults in contact with dead rodents (without wearing gloves or protective clothing). A health risk is unlikely.
- A risk to infants/toddlers transiently mouthing wax blocks/wedges is not foreseen.
- Infants/toddlers chewing on wax blocks are at risk of a health effect, but is not likely to occur commonly, because the taste deterrent (bittering agent) included in the formulation should cause the child to spit out any chewings.

Pellet bait

- Exposures and risks in the expected handling scenarios are acceptable for the professional and non-professional users. Non-professional users were assessed assuming that gloves are not worn.
- Secondary exposure is likely associated with a health risk for adults in contact with dead rodents, if gloves are not used.
- Infants/toddlers transiently mouthing or chewing on pellets are at risk. However, this is not likely to occur commonly, because the taste deterrent (bittering agent) included in the formulation should cause the child to spit out the pellets.

Grain bait

- Acceptable risks are shown for all expected handling scenarios for PCOs and general public users, regardless of whether gloves are worn or not. However, this finding does not negate recommendations to use of gloves, which should remain on product labels.
- Secondary exposure of adults in contact with dead rodents is considered negligible, provided that gloves are worn.
- A risk to health of infants/toddlers transiently mouthing or chewing on grains cannot be excluded. However, this is not likely to occur commonly, because of the taste deterrent (bittering agent) included in the formulation.
- Inhalation exposure was not assessed by the leading European authorities, likely because air concentrations are considered negligible in the cleaning phase. It is agreed that air concentrations applicable to the products registered in South Africa and assessed in this report would be similarly negligible, and associated health risks not of concern.

Paste bait

- Acceptable risks are shown for professionals and non-professionals applying and disposing of sachets placed in a bait station, for all products assessed.
- Unacceptable risks are shown for pastes containing 0.005% brodifacoum when non-professionals skewer sachets on a wire, without the use of gloves.

- The risk assessment for non-professionals demonstrates that use of gloves if skewering paste sachets should be mandatory, and clear instructions to this effect should be provided on product labels.
- Secondary exposure of adults in contact with dead rodents is considered negligible, but gloves should be worn in any case, to protect against diseases carried by rodents.
- An unacceptable risk is shown to the health of infants/toddlers transiently mouthing bait. It is not clear that a bittering agent is included; therefore, the use of tamper-proof bait boxes should be strongly recommended on the label. In any case, any noted contact of a child with paste bait should be brought to the immediate attention of a medical professional, without exception.

Powder (granular) bait

- Risks associated with primary dermal exposure are acceptable for all expected handling scenarios for PCOs and general public users, regardless of whether gloves are worn or not. However, this finding does not negate the need for recommending the use of gloves on product labels.
- Secondary exposure of adults in contact with dead rodents is acceptable even if gloves are not worn, but labels should recommend the use of gloves when disposing of dead rodents.
- Risks of children in accidental dermal contact with the powder, and for infants/toddlers transferring powder from hands to mouth, are acceptable, mostly because the brodifacoum concentration in the powder is not high. Nonetheless, contact of a child with any rodenticide remains unacceptable, and measures, as recommended on the product label, should be taken accordingly.
- Inhalation exposure of PCOs applying and cleaning up (disposing) of the powder product and its residues is assessed as acceptable, under the following strict conditions:
    - PCO use should be addressed, recommending the use of factor-20 respirators when more than 2 sachets are applied indoors, which is currently not recommended on the label.
- Inhalation risks of general public users are acceptable, even in the absence of respiratory protection.

9.2 The risks versus societal needs/benefits balance

There is no question that there is a legitimate societal need for cost-effective, relatively inexpensive rodenticides, considering the serious and potentially lethal human diseases, e.g., hantavirus, typhus and bubonic plague, that are spread by mice and rats. Furthermore, rodent plagues imply a burden of economic costs of property, food and crop damage and spoilage.

The USEPA (2022) approached this need is an issue of environmental justice*, "the fair treatment and meaningful involvement of all people, regardless of race, color, national origin, or income, in the development, implementation, and enforcement of environmental laws, regulations, and policies*". In particular, care is taken with low-income populations who are particularly vulnerable to mouse and rat infestations that are most common in housing for lower socio-economic populations.

Other control measures, e.g., rodent exclusion, can be recommended as an alternative to the use of poisoned bait, but can be expensive and/or time-consuming, and thus not practical, for low-income households and in multi-family dwellings. Furthermore, the USEPA (2022) points out that "*rodent prevention methods often rely on support from the entire community and may be more difficult in communities with a higher population density or with a lower quality of services (e.g., in areas with poor waste management services)*". In these instances, rodent control measures such as mechanical trapping and use of rodenticides may have a higher benefit to these populations relative to more affluent populations.

The poorest populations may thus experience a greater degree of rodent infestations and consequently may be disproportionately overburdened by exposure to the diseases transmitted by rodents. Clearly, the poor may be most affected by severe restrictions on the use of rodenticides, and particularly of second-generation anticoagulant rodenticides, which are cost-effective and currently fairly accessible in general hardware stores and in large supermarkets. Therefore, economically and socially disadvantaged populations may be disproportionately affected by availability or use restrictions of such rodenticides. Undesirable effects would include cost increases or reduction in rodent control, with subsequent detrimental health effects.

Considering the societal need and benefit of continued access to second-generation anticoagulant rodenticides, it is more advantageous to society to rather adopt these as important tools in an integrated pest management approach to the control of rodent infestations. Therefore, in balance, while identifying risks of concern to the environment, the USEPA (2022) "*acknowledges that there are many benefits associated with these active ingredients and supports the continued registration of these active ingredients*".

However, the USEPA and the EC strongly argues for mitigation measures provided as clear label instructions, to ensure that use in accordance with the label directions "*will not generally cause unreasonable adverse effects on the environment taking into account the economic, social, and environmental costs and benefits of the use of any pesticide*". Mitigation measures proposed by international regulating entities are presented in Section 8.3.

9.3 Proposed mitigation measures

Wearing of gloves

The finding of acceptable health risks, even while not wearing gloves in some scenarios, does not mean that gloves need not be worn, since gloves also protect against potential secondary exposure while handling dead rodents and against diseases carried by rodents. As recommended on most product labels, gloves should be used at all times while handling bait, while cleaning up and while handling dead rodents.

Tamper-proof bait boxes for application

International regulatory agencies tend to recommend bait box use, in particular for domestic users or for application in the domestic scenario. Bait boxes are not recommended or obligated on the labels of the assessed FINALE® pellets and wax blocks formulations, but the user is instructed to "*Place …* the product … *in a covered bait station to prevent access by children and domestic animals"*. "*Bait boxes or other special containers*" are "*strongly recommended"* on the RODILON® wax blocks label. The method of risk calculation recommended in international guidance followed in this report does not include consideration of whether bait boxes are used or not. Therefore, the use of bait boxes will not change the risk assessment.

It is clear that bait boxes add an extra layer of protection for bystanders, pets and non-target animals, but it is not argued that bait boxes should be made mandatory, because this will imply and added cost premium to the user. Considering the argument for the continued availability of lower cost, but effective, rodenticides to especially lower-income consumer groups, a blanket measure to make bait box use compulsory is not appropriate. However, bait box use in domestic settings should be encouraged.

Bait box use by PCOs should also not be made compulsory, because it is not always necessary, e.g., in spaces not accessible by bystanders, pets, or non-target animals. Bait boxes are not always

practical, e.g., in tight spaces such as sewers and roof spaces. Bait boxes are also not always the most effective method of application, e.g., outdoor spaces where it is more effective to place bait not in a bait box, but under cover, such as under a piece of corrugated iron, or in a piece of pipe, around grain storage silos, or near farm animal feed stores or places where agricultural livestock are fed, or in sapling plantations.

Other measures

The following measures include those generally proposed by international regulatory agencies to protect man, animals and the environment:

- Where possible, prior to the treatment inform any possible bystanders (users of the treated area and their surroundings) about the rodent control campaign.
- Consider preventive control measures (e.g. plug holes, remove potential food and drinking as far as possible) to improve product intake and reduce the likelihood of reinvasion.
- Precautions, e.g., keeping the product away from children, pets and directions for use on the product label must be followed. Baits must be unattainable to children, pets or other non-target animals in order to minimise the risk of poisoning.
- Any noted contact of a child with any type of rodenticide should be brought to the immediate attention of a medical professional, without exception.
- Solid products other than the powder formulation should not be applied directly in the burrows. Labels should clearly recommend application in a bait box, or covered bait station, but this should not be made mandatory, as argued above.
- The bait stations should be visited at least every 2 to 3 days at the beginning of the treatment and at least weekly afterwards. The purpose of visits is:
    - To check whether bait stations are intact (bait boxes intact or bait stations still adequately covered).
    - To clean up bait dragged out of the bait box/station by rodents.
    - To search for and remove dead rodents, in order to reduce the risk of secondary human exposure and secondary poisoning of non-target animals.
- Do not use the product as permanent baits for the prevention of rodent infestation or monitoring of rodent activities. It is noted that pulse baiting is generally authorised for rodenticides that contain difethialone.
- Remove the remaining product at the end of treatment period.
- When placing bait points close to or in water drainage systems, ensure that bait contact with water is avoided.
- Outdoor bait must be protected from rain. Place the baiting points in areas not liable to flooding.
- For outdoor use, baiting points must be covered and placed in strategic sites to minimise the exposure to non-target species.
- The product information (i.e., label and/or leaflet) shall clearly show that, if PCOs should deploy bait boxes, these should be properly labelled with the following information:
    - "*do not move or open*";
    - "*contains a rodenticide*";
    - product name or Act 36 of 1947 registration number;
    - active substance(s) and
    - "*in case of incident, call a poison centre* (*insert national phone number*)".
- Carcass removal instructions:
    - While wearing gloves, collect and properly dispose of visible carcasses of target pests or non-target animals.
    - Place carcasses in leakproof plastic bags or other suitable containers and dispose of in the trash or dispose of according to the label disposal instructions.

    - Carcasses buried on site must be buried a minimum of 45 cm below the ground surface, preferably deeper.
- All carcasses must be disposed of in a way inaccessible to wildlife, to prevent secondary poisoning of predatory animals.
- Wearing gloves while handling rodenticides must be recommended on all labels.
- In the case of the powder product:
    - PCO use should be addressed, recommending the use of factor-20 respirators when more than 2 sachets are applied indoors, which is currently not recommended on the label.

10 Conclusions

In support of the application for derogation regarding the restricted use of the registered solid rodenticide products, identified as substances of concern due to the reproductive toxicant properties of the rodenticide ingredient brodifacoum, the human health risk assessment results lead to the following conclusions:

- Since developmental effects are the only health endpoints (aside from mortality) for which dose-response values are available in toxicological studies, there is no other choice but to base acceptable exposure levels of males and children on this health endpoint as well. Therefore, the absence of a risk to health in general, and specifically the absence of a risk to the developing foetus, is implied by a finding of “acceptable exposures or risks”. Vice versa, unacceptable risks indicate unacceptable risks of developmental effects.

- Adult solid bait users, whether professional PCOs, non-professionals or the general public, wearing gloves, are not at risk of a health effect on the development of the foetus in case of pregnant females.

- For some of the solid bait products, acceptable risks are also demonstrated for adults not wearing gloves. However, this can never be used to negate the need for recommending the use of gloves on product labels. Recommending the use of gloves is a protective measure for all bait users, and also protects against diseases carried by rodents.

- Infants/toddlers chewing on solid bait products are at risk of a health effect. Transient mouthing may also result in a risk to health. However, accidental exposure of bystanders, specifically children, can be limited by clear communication of the professional pesticide applicator to such bystanders, and by following label instructions to place the bait station out of reach of children and uninformed persons.

- Regardless of the precautionary measures followed, any noted contact of a child with a rodenticide should be brought to the immediate attention of a medical professional, without exception. All product labels must clearly exhibit the contact details of a local/national poison centre.

- A risk of detrimental environmental effects cannot be excluded in the case of primary bait exposure of non-target animals, or secondary exposure of non-target animals to contaminated dead or dying pray, because of the overt toxicity of the anti-coagulant active ingredient brodifacoum. Therefore, it is of primary importance that all possible mitigation measures recommended in Section 9.3 should be followed to limit environmental effects.

- The restricted use applied for by the suppliers of rodenticides containing brodifacoum is according to the intended product use:
  - A highly active anti-coagulant bait for the control of the Norway rat, roof rat, the house mouse and gerbil.
  - The restricted use application for use in homes is supported for all solid baits.

- When the recommended mitigation measures are applied, accidental exposure of bystanders, children, pets and non-target animals can be effectively limited.

- The balance of societal need and benefits, versus the overt toxic nature of the product, is always to be considered regarding any regulatory decisions to limit access to rodenticides. This is particularly important to socio-economically disadvantaged communities. Such communities bear a double burden of more frequent rodent infestations, with concomitant exposure to diseases spread by rodents, possible rat-bite injuries to infants, damage to property and food spoilage and contamination, and limited resources to use other, non-poisonous solutions.

- The application for derogation of the products assessed in this report is supported, provided that recommended mitigation measures are effectively implemented.

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