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Retrieval and scientific interpretation of ecotoxicological information

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Report Compiled for
Growing Manufacturers CC

Derogation Risk Assessment Report for Muti-Igundane a Grain Bait Rodenticide Containing Coumatetralyl, a CMR Substance of Concern (Reproductive Toxicity Hazard)

Product trade name:
Muti-Igundane (L5718)

INFOTOX Report No 010-2025 Rev 3.0

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28 April 2025

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28 April 2025

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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 Growing Manufacturers CC. We do hereby declare that we are financially and otherwise independent of Growing Manufacturers CC.

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

Willem Christiaan Abraham van Niekerk

28 April 2025

Executive Summary

This document is a risk assessment report supporting an application for derogation for the restricted use of Muti-Igundane, a grain bait formulation anticoagulant rodenticide with the active ingredient coumatetralyl. The general public has access to Muti-Igundane, which is supplied to general goods shops.

Muti-Igundane is identified as a substance of concern due to classification as a reproductive toxicity hazard category 1B according to the Globally Harmonized System of Classification and Labelling of Chemicals ("GHS"). The classification is due to the active ingredient coumatetralyl, which is classified in GHS reproductive toxicity category 1B (H360D), indicating a hazard to the development of the unborn child ("D").

Product name, registered suppliers and Act 36 of 1947 registration number:

Product	Act 36 of 1947 registration numbers	Registered manufacturer/supplier/distributer
Muti-Igundane, a grain bait formulation rodenticide	L5718	Growing Manufacturers CC

The product is to be applied in small quantities (20 to 50 gram) in a covered bait station; the use of bait boxes is strongly recommended.

The 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 Danish CA Assessment Report on Coumatetralyl, Product-type PT 14 (Rodenticides) with the view of satisfying regulatory requirements for placing biocidal products on the market, submitted 20 February 2009.
- The German Competent Authorities ("CAs") functioning as the Evaluating Competent Authority of the European Community ("EC") to carry out the assessment report evaluating coumatetralyl as a biocidal product, Product type 14 (rodenticide) with the view of satisfying regulatory requirements for placing biocidal products on the market, submitted by the German CA on 13 February 2018.
- Coumatetralyl is currently not registered for use as a rodenticide in the US; therefore, documents potentially compiled by the US Environmental Protection Agency ("USEPA") are not available for review.

Human health risk assessment

The scope of the rodenticide human health risk assessment ("HHRA") is determined by the registered product use. Muti-Igundane grain bait formulation is intended and assessed for primary use by non-professionals. It is not supplied to professional pest control operations or businesses. Non-professionals are the general public, meaning any adult person who is not a professional pest control operator ("PCO") and who applies the rodenticide in a dwelling, shop, workshop or elsewhere.

The purpose is to evaluate the risks of reproductive/developmental toxicity effects in persons exposed to coumatetralyl in Muti-Igundane. 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".

The following human exposure scenarios were identified for assessment:

- Primary dermal and inhalation exposure of non-professionals (domestic users) handling, applying, refilling and disposing of left-over or unused Muti-Igundane grain bait.
- Secondary human exposures are assessed as:
    - Accidental dermal contact of adult non-professionals with the product in the use phase, or with product residues on dead or dying rodents.
    - Accidental exposure of infants/toddlers eating “a small handful” of grain bait.

Adult Muti-Igundane grain bait users applying the product as recommended on the label are not at risk of effects on the development of the foetus in case of pregnant females, and also not at risk of health effects in males, or females who are not pregnant.

The above finding is true whether gloves are worn or not, but cannot be viewed as suggesting that gloves need not be worn while applying or cleaning up the product, or while handling dead rodents. Wearing gloves is recommended on the product label, and should be adhered to by all users. Recommending the use of gloves is a protective measure for all bait users, and also protects against diseases carried and spread by rodents.

Secondary exposure of adults in accidental dermal contact with the grain bait does not result in unacceptable exposure and a risk to health is not indicated. An unacceptable risk is shown for infants/toddlers accidentally eating grain bait. However, accidental ingestion by children can be avoided by following “strongly recommended” label instructions to use bait boxes, and to keep the bait 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.

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 coumatetralyl 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, although risks to predatory birds might be low. However, mitigation measures such as limiting access by non-target organisms and frequent inspections to search for and correctly 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 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:

- An anti-coagulant poison for control of rats and mice.
- Muti-Igundane grain bait is for the use of non-professionals, that is, the general public, who may use the product in homes, shops and other areas.

Mitigation measures

Mitigation measures presented in Section 9 of this report should be implemented in full, with particular emphasis on the following:

- 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.
- Precautions, e.g., keeping the product away from children, pets and directions for use on the product label must be followed.
- It is noted that the Muti-Igundane product label already “strongly recommends” to use of bait boxes or other suitable containers, and this must be retained on the label. It is not suggested that bait box use must be mandatory to the South African consumer, where a need for access to low-cost rodenticides is foreseen, specifically in low-income groups. Mandatory use of bait boxes implies an additional cost premium, which might cause rodenticide use to be unaffordable to those needing it most.
- The product must not be used as permanent baits for the prevention of rodent infestation.
- Search for and remove dead rodents at frequent intervals during treatment.
- Remove the remaining product at the end of treatment period.
- When placing bait points close to water drainage systems, ensure that bait contact with water is avoided.
- Protect bait from the atmospheric conditions. Place the baiting points in areas not liable to flooding.
- Gloves should be used when handling the grain bait, and when handling dead rodents.

Support for the restricted use application

Acceptable levels of exposure and risk are shown when the product is used according to label instructions. When the above mitigatory measures are applied, accidental poisoning of bystanders, children, pets and non-target animals can be effectively limited. Therefore, the application for derogation of Muti-Igundane is supported, provided that recommended mitigation measures are effectively implemented.

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List of Abbreviations

AAPCC	American Association of Poison Control Centers
AEL	Acceptable exposure level
AVK	Anti-vitamin K
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
FGARS	First generation anticoagulant rodenticides
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
HEEG	Human Exposure Expert Group
HHRA	Human health risk assessment
IDS	USA Incident Data System
IPCS	International Programme on Chemical Safety
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
NOAELs	No-observed-adverse-effect levels
NRC	US National Research Council
OECD	Organisation for Economic Co-operation and Development
PCOs	Pest control operators
PNECs	Predicted no-effect concentrations
POD	Point of departure
PPE	Personal protective equipment
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
SDSs	Safety data sheets
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 Product identification

This document is a risk assessment report supporting an application for derogation for the restricted use of the registered solid rodenticide product Muti-Igundane, containing the anticoagulant active coumatetralyl, which has been identified as a reproductive toxicity hazard.

Report prepared for:		
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Assessed product	Muti-Igundane	
Act 36 of 1947 registration number	L5718	

1.2 Regulatory context

In a document circulated to "All Regulatory Holders" on 18 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 Muti-Igundane rodenticide grain bait formulation 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 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

[1] Registration, Evaluation, Authorisation and Restriction of Chemicals.
[2] http://www.ecetoc.org/tools/targeted-risk-assessment-tra/.

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.

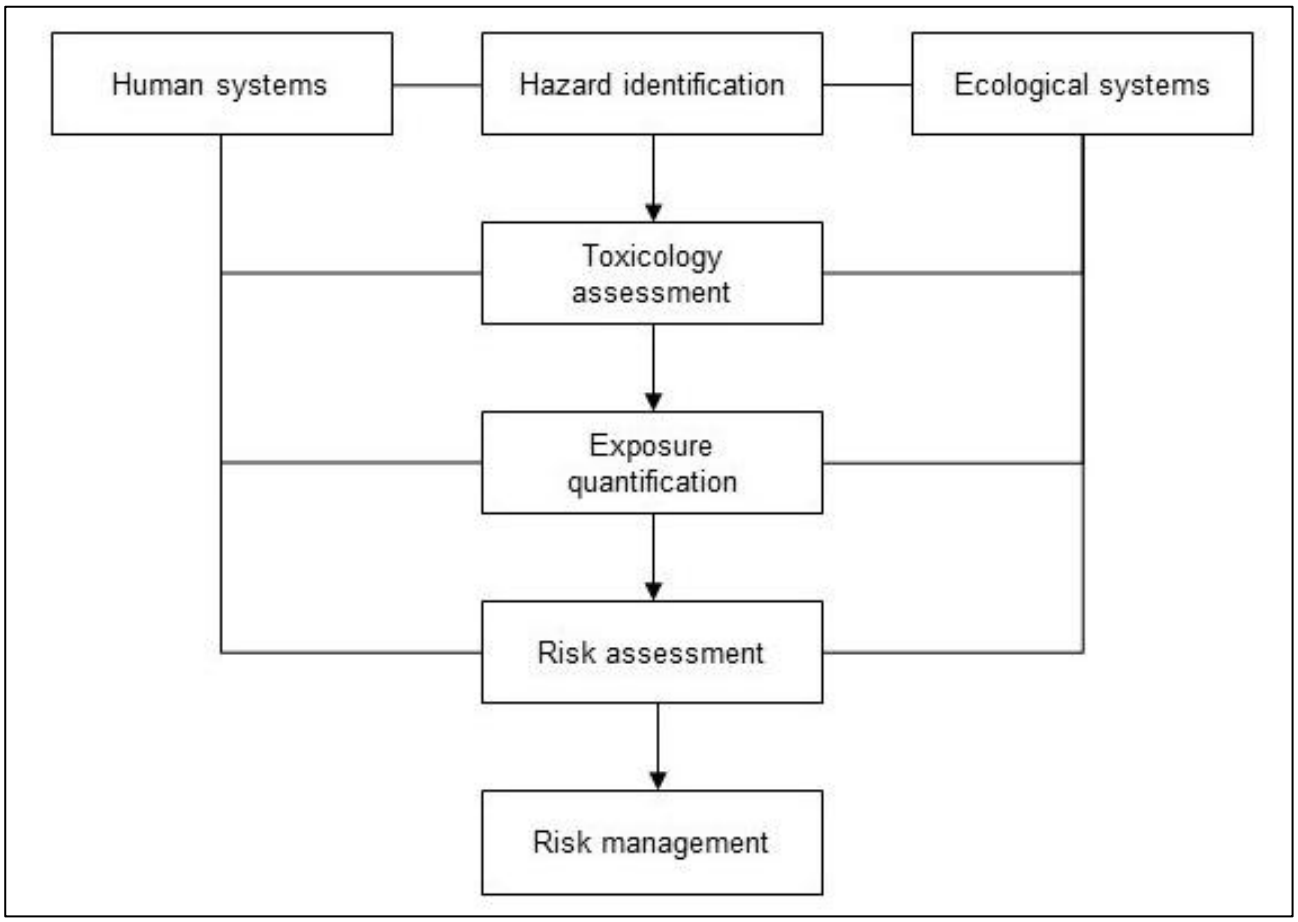

Figure 2.1.1: The holistic health risk assessment paradigm.

It is shown in this INFOTOX report that exposure assessment and health risk quantification are essential steps in managing health risks associated with hazardous chemicals.

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 2.1.1. 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 coumatetralyl. 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") and acceptable exposure level ("AEL") or acceptable operator exposure level ("AOEL") for HHRA purposes, by applying appropriate uncertainty factors and safety factors for infants and children, referring to dose through the routes of exposure. The AEL is the exposure dose that is accepted

as not associated with a risk to human health. 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.

- **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.

  Residential exposure scenarios are assessed, because the rodenticide is for sale in retail outlets catering to the general public:
  - Assuming that non-professionals might not be diligent users of personal protective equipment ("PPE"), exposure while handling rodenticides without gloves or respiratory protection, that is, dermal and inhalation exposure, is assessed.
  - The normal procedure recommended on product labels is to place rodenticides for residential use 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 Coumatetralyl CMR hazard classification

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

Active ingredient identification

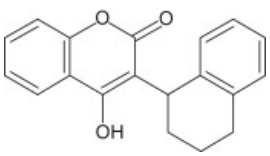 **Coumatetralyl**	**CAS #:** 5836-29-3 **Mol. formula:** $C_{19}H_{16}O_3$ **Molecular weight:** 292.3 g/mol **ISO common name:** 3-(alpha-tetralyl)-4-hydroxycoumarin

Table 3.2.1: CMR GHS classification of coumatetralyl.

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. 1B	H360D	May damage the unborn child	Danger	
Classification according to the European Chemicals Agency ("ECHA" online); harmonised EU classification.				

GHS Category 1B criteria for substance classification:

- Presumed human reproductive toxicant - largely based on evidence from experimental animals
- Animal studies provide clear evidence of an adverse effect on fertility or on foetal development in the absence of other toxic effects. If other toxic effects were present, the adverse effects on reproduction must have been regarded as not secondary to the toxic effects.

The product composition and calculation of the coumatetralyl concentration in Muti-Igundane is presented in Table 3.2.2.

Table 3.2.2: Muti-Igundane formulation and coumatetralyl concentration.

Formulation		Coumatetralyl concentration	
Ingredient	**Weight (kg)**	**kg**	**% w/w**
Wheat seed	567.05	-	-
Racumen Tracking Powder (0.75% coumatetralyl)	28.45	0.75% x 28.45 = 0.213375	0.036
Sunflower oil	4.5	-	-
Total	600	600	-

Hazard classification identifying products as CMR substances of concern:
Coumatetralyl is assigned the H-code H360D; "D" indicating developmental effects (effects on the growing foetus). The hazard classification of Muti-Igundane has been dealt with in the existing product registrations.

The coumatetralyl classification presented in Table 3.2.1 is according to the Summary of Classification and Labelling presented by the European Chemical Agency ("ECHA") (ECHA online). The *Reproductive toxicity hazard, category 1B (H360D)* is associated with a "*Specific Concentration limit*" of *Repr. 1B; H360D: C ≥ 0.003 %* according to the harmonised GHS classification relevant to Annex VI of European Community Regulation (EC) No 1272/2008 (CLP Regulation). The implication of the "*specific concentration limit"* is that the concentration of coumatetralyl in Muti-Igundane grain bait (0.036%, Table 3.2.2) satisfies the reproductive toxicity classification criterium (≥ 0.003 % w/w), according to ECHA guidance and should be classified as a GHS Category 1B Reproductive toxicity hazard.

It is understood that the South African classification regulations actually refer to the GHS as presented in the latest revised edition of the UN “Purple Book”. It is further understood that the Purple Book refers only to the concentration limit of 0.1%. Technically, the concentration of coumatetralyl in Muti-Igundane does not meet the criterium for classification according to the Purple Book. However, the decision to apply for derogation is motivated by the strict classification according the ECHA specific concentration limit.

4 Environmental fate and behaviour

4.1 Coumatetralyl in air

Coumatetralyl in solution is not considered volatile and is not expected to partition into the atmosphere to a significant extent (Danish CA 2009 and German CA 2018), due to:

- Low vapour pressure less than 1×10^{-3} Pa (20°C).
- Henry’s law constant less than 6.64×10^{-2} $Pa.m^3.mol^{-1}$

Coumatetralyl is expected to rapidly photolyse and photodegrade, with a DT_{50} of approximately 2 to 7 hours, depending on the estimation method (Danish Ca 2009 and German CA 2018).

4.2 Coumatetralyl in water

Coumatetralyl is moderately soluble in water, depending on the pH (Danish CA 2009 and Lewis et al. 2016). Values at 20°C increase with increasing pH:

- At pH 5: 4.78×10^{-3} g/l.
- At pH 7: 4.60×10^{-1} g/l.
- At pH 9: 4.65 g/l.

Coumatetralyl is hydrolytically stable at pH 4 to 9, but is rapidly photodegradable, with a half-life (DT_{50}) of 8.6 hours to 3.6 days, depending on the available light intensity, e.g., summer versus winter (German CA 2018). It is not readily biodegradable in water (Danish CA 2009).

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

- 1.5 “under neutral conditions”, but ranges from -0.1 at pH 9 to 3.4 at pH 5 (German CA 2018).
- 3.46 at pH 7 (Lewis et al. 2016).

According to the German CA (2018) the log K_{ow} is below the bioaccumulative screening criterion of log K_{ow} 4.5. Fish bioconcentration factors for edible parts, viscera and whole fish are listed as 3.32, 20.8 and 11.4 respectively, reflecting a relatively low potential to bioconcentrate.

4.3 Coumatetralyl 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 coumatetralyl is 301.8 litre/kg, the average value from a range of 71 to 735, obtained from screening tests with 5 soil types (Danish CA 2009, cited by the German CA 2018). The Danish CA (2009) concluded that coumatetralyl is moderately leachable in sandy soil, but that no leaching was observed in loamy sand and sandy loam. Lewis et al. (2016) considered coumatetralyl moderately mobile, based on a cited K_{oc} of 453, close to the average value reported by the German CA (2018). The potential for groundwater contamination should thus be moderate to low and the German CA (2018) calculated a soil / water partitioning coefficient, $K_{soil\text{-}water}$, of 9.054 m^3/m^3 from a mean Koc value of 295.99 litre/kg, based on a pool of values reported for different soil types.

Although not readily biodegradable, coumatetralyl is rapidly degraded in soil, with calculated DT_{50} values of 5.9 to 8.7 days at 22°C, corresponding to 13.1 to 19.4 days at 12°C (German CA 2018).

4.4 Summary

The environmental fate concerns regarding coumatetralyl are summarised in Table 4.4.1.

Table 4.4.1: Summary of environmental fate concerns for coumatetralyl.

Concern	Notes	Reference
Volatilisation	Not volatile	Danish CA (2009) and German CA (2018)
Aquatic bioconcentration/ bioaccumulation	Not considered persistent in the aquatic environment. Although stable to hydrolysis, coumatetralyl is highly susceptible to photolysis.	German CA (2018)
Groundwater contamination	Moderate to low potential	German CA (2018)
Sediment contamination	Insufficient information	Danish CA (2009) and German CA (2018)
Persistence in soil	Not persistent, is rapidly degraded in soil.	German CA (2018)
Residues of concern	Major soil metabolite is 13-hydroxycoumatetraly, no specific toxicity data provided.	German CA (2018)

5 Environmental assessment

5.1 Primary vs secondary environmental exposure

Primary exposure of non-target species, that is, direct contact with and ingestion of the rodenticide, is not expected, since the usual rodenticide label instructions are to place the bait out of reach of animals. However, the use of bait boxes is not mandatory, although regularly recommended on labels; therefore, attention is given to primary exposure and risk assessments conducted by the reviewed regulatory authorities (e.g., the Danish and German CAs, referred to below).

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 coumatetralyl formulations.

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.

Coumatetralyl is a first-generation anticoagulant rodenticide ("FGAR"). FGARs are referred to as 'multi-dose anticoagulants', meaning that rodents must consume several consecutive feedings of bait before a lethal dose is accumulated. Once ingested, FGARs also break down quicker than second-generation anticoagulant rodenticides. Therefore, the risk of secondary poisoning is less if rodents poisoned with an FGAR is ingested by predatory non-target animals (APVMA 2023).

5.2 Toxicity to non-target species

Coumatetralyl toxicity to non-target species

As can be expected of a rodenticide ingredient, coumatetralyl is very toxic to mammals; more toxic than to birds (German CA 2018).

An LD50 value of 35 mg/kg bw is reported by the German CA (2018) for the assessment of acute primary exposure (ingestion of the bait) by mammals.

The predicted no-effect concentrations ("PNECs") used in the assessment of primary and secondary poisoning are:

- $PNEC_{oral\text{-}mammals}$ = 1.0 x 10^{-4} mg/kg bw.
- $PNEC_{oral\text{-}mammals}$ = 0.14 mg/kg food (secondary poisoning).

The avian acute toxicity LD50 of coumatetralyl is 2 000 mg/kg bw, interpreted as showing "*only a low acute avian toxicity"*, supported by the fact that mortalities were not observed in the treated groups (Danish CA 2009). The LD50 is used for the assessment of primary acute ingestion in birds (German CA 2018).

The proposed PNECs for the assessment of primary and secondary ingestion are:

- $PNEC_{oral\text{-}birds}$ = 0.0667 mg/kg bw.
- $PNEC_{oral\text{-}birds}$ = 0.667 mg/kg food (secondary poisoning).

Coumatetralyl is toxic to organisms in the aquatic compartment, as demonstrated by acute toxicity study results in fish (LC50 = 53 mg/litre), invertebrates (EC50 > 14 mg/litre) and algae (72h ErC50 > 18 mg/litre) (Danish CA 2009).

Secondary poisoning through the aquatic food chain is not assessed, because responsible product application and care, with clear product label and safety data sheet ("SDS") instructions to prevent contamination of waterways, should limit aquatic contamination to negligible.

The acute toxicity of coumatetralyl to earthworms is considered as low. The coumatetralyl LC50 calculated for exposure of the test species (*Eisenia fetida*) for up to 14 days is 225 mg/kg dw soil (Danish CA 2009), from which a $PNEC_{soil}$ of 0.2 mg/kg soil wet weight was derived (German CA 2018).

5.3 Environmental assessments by international regulatory authorities

Potential aquatic toxicity was not assessed by the German CA (2018), since direct emissions to surface water were assumed negligible, because of the recommended application in bait boxes. This is also applicable to Muti-Igundane, since bait box use is recommended on the product label. Although not completely excluding rainwater run-off of bait residues, this recommendation does limit the risk of aquatic contamination with coumatetralyl.

In the terrestrial compartment, primary exposure of mammalian non-target species cannot be excluded. Because of the lower toxicity to birds, pointed out in Section 5.2, a lower risk to birds is expected.

The German CA (2018) concluded that non-target mammals and birds are at risk of primary poisoning if they get access to a wax block coumatetralyl formulation. If the rodenticide wax block baits are applied in bait boxes, the risk for primary poisoning can be mitigated significantly, but it may not be possible to exclude exposure of all non-target animals. This is also applicable to a grain bait formulation, such as Muti-Igundane.

Avian and mammalian predators feeding on contaminated soil organisms such as earthworms were found not to be at risk of secondary poisoning if the assessed wax block baits are deployed. Risks of secondary poisoning via the aquatic food chain was not assessed, because aquatic food chain contamination was likely to be insignificant (German CA 2018), which is also true for Muti-Igundane.

Regarding secondary exposure of mammals, the German CA (2018) concluded that the death of mammals and birds that had consumed poisoned rodents cannot be excluded. The risk in mammals is higher than in birds, and risks to predatory birds might be low.

5.4 Environmental assessment by the South African GRIFFON Poison Information Centre

Dr Gerhard Verdoorn has corresponded with Growing Manufacturers regarding the secondary poisoning risks of Muti-Igundane, expressing the opinion that the risk of secondary poisoning for owls is "*extremely low*". The letter is attached as Annexure 1.

6 Human health and toxicological review

6.1 Pertinent human health effects

Coumatetralyl is an FGAR, as explained previously, a first-generation repeated-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. 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).

According to the 2022 Annual Report of the American Association of Poison Control Centers ("AAPCC"), more than 3 000 anticoagulant rodenticide ingestion incidents were reported in the

United States; approximately half of these in children younger than 6 (cited by Isackson and Irizarry 2024). Similar data are not available for South Africa, but the US data show that incident numbers can be significant.

Detailed recent data are not easily accessible, but the Office of Chemical Safety and Pollution Prevention of the USEPA (2022a) has performed an updated analysis of exposure incidents reported to both the USA Incident Data System ("IDS") and the AAPCC. Reviewing AAPCC data, a 46% decline in child rodenticide exposures was found from 2011 to 2017. In the IDS, FGAR incidents had increased by 81% from 2009 to 2018, but in the AAPCC, FGAR incidents had decreased over time from 337 incidents in 2004 to 187 incidents in 2017 (55% decrease). The increase in FGAR incidents was noted only in the IDS, and incident counts were low, namely 52 in the IDS in 2018.

Considering occupational exposure incidents, 21 were reported to the NIOSH SENSOR-Pesticides database from 2011 to 2015, 9 to the Californian database from 2012 to 2016, and 2 in the IDS (2015 to 2019). Overall, the USEPA (2022a) 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).

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. The severity statistics and the nature of the observed health effects demonstrate that proper training of pesticide applicators and the use of personal protective equipment are effective management tools limiting occupational exposure risks.

Similarly updated European incident data were not provided by the German CA (2018), but the Danish CA (2009) reported the following medical data derived from accidents with rodenticides registered in the "Medical Department" (no further identification provided) for a production period of more than 20 years up to the year 2002. Germany was the source of 35 complaints/adverse incidents with products containing coumatetralyl, of which 17 were requests for information: 7 attempted suicides, and 2 alleged wilful poisoning attempts.

Accidental ingestion of a maximum of 40 g of product was reported in 8 cases, without any symptoms. Two further symptomatic accidental cases were reported: oral absorption of two teaspoons of "Racumin Plus" by an adult showed a slight coagulation inhibition and a child having ingested an unknown amount required vitamin K1 therapy. No sequelae were observed in these cases. Unfortunately, the coumatetralyl content of the product was not specified (Danish CA 2009).

Contact with eyes or skin had occurred in another 7 cases, either by accident or by lack of personal protective equipment (e.g., distributing a coumatetralyl grain bait formulation with bare hands). Symptoms were reported in 5 cases: 3 of short-term nausea, 1 of swelling and itching of the hands after washing, and 1 case of eye irritation. The irritation effect was regarded as definitely due to the product, the skin reaction as possibly caused by coumatetralyl powder contact, and the nausea as most probably a secondary reaction to the fear of being poisoned (Danish CA 2009).

According to current knowledge, coumatetralyl has no endocrine disrupting properties (Danish CA 2009 and German CA 2018).

6.2 Routes of absorption

Oral absorption
The Danish CA (2009) and the German CA (2018) adopted a coumatetralyl oral absorption factor of 75% for the risk assessment of a paste bait, and this is applied to other solid bait formulations as well.

Dermal absorption
The German CA (2018) reported the following values:
- 100% as a default value.
- 1.14% determined from in vivo and in vitro studies on a 0.375 mg coumatetralyl/g paste (0.038%) formulation. The value is also used for absorption from the Muti-Igundane grain bait assessed in this report.

Inhalation
Coumatetralyl in solid preparations has a very low volatilisation potential. Due to its physico-chemical properties (low vapour pressure of less than 0.001 Pa at 20°C and low Henry's law constant of less than 0.0664 $Pa.m^3.mol^{-1}$) (Section 4.1), coumatetralyl 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, a default absorption value of 100% is assumed (German CA 2018).

6.3 Toxicological studies

Metabolism (in mammals) is rapid and the main metabolite of coumatetralyl is 13-hydroxy-coumatetralyl, accounting for up to 27% of the applied dose. There is no evidence indicating that the metabolite is more toxic than the parent compound (Danish CA 2009).

The Danish CA (2009) had calculated and reported the following LD50 values for coumatetralyl:
- Rat LD50 oral, in fasted animals:
  - Male rats: 30 mg/kg bw
  - Female rats: 15 mg/kg bw
- Rat LD50 dermal:
  - Male rats: 100 < LD50< 500 mg/kg bw
  - Female rats: 258 mg/kg bw
- Rat LC50 inhalation:
  - Male rats: approximately 0.063 $mg.litre^{-1}(4\ hours)^{-1}$
  - Female rats: approximately 0.039 $mg.litre^{-1}(4\ hours)^{-1}$

Short-term (28-days) teratogenicity was studied with rats and rabbits. The NOAELs from these studies are:
- Rat NOAELs:
  - 0.14 mg/kg-day for embryo- and/or fetotoxicity.
  - 0.035 mg/kg-day for maternal toxicity (LOAEL = 0.070 mg/kg-day).
- Rabbit NOAELs:
  - 0.025 mg/kg-day for embryo- and/or fetotoxicity (LOAEL = 0.05 mg/kg-day).
  - 0.0125 mg/kg-day for maternal toxicity (LOAEL = 0.025 mg/kg-day).

The Danish CA (2009) cited an unpublished repeated dose (subchronic 16-week feeding) study in the rat. The critical effect of coumatetralyl, as observed in other toxicological studies, is on blood

coagulation. Reported observations are haemorrhage and prolonged blood clotting time. The oral NOAELs are:

- 0.0068 mg/kg-day (females).
- 0.0083 mg/kg-day (males).

Reproductive and developmental toxicity

The decision by the European authorities to classify coumatetralyl as a developmental hazard (H360D) needs some background discussion. The following information from unpublished studies are obtained from the Danish CA (2009).

A multigeneration study was not required, based on the high risk of death by haemorrhage from the natural events of reproduction and parturition, nullifying the study objective in any case, and based on the absence of potential long-term exposure of the public population. Teratogenicity studies were conducted in the rat and rabbit, and no effects on the developing foetus were seen in either species.

Although the developmental studies with coumatetralyl in rat and rabbit failed to indicate developmental toxicity, the compound is structurally and mechanistically analogue to the human developmental toxicant warfarin, which is also an anticoagulant anti-vitamin K ("AVK") substance. EU experts unanimously agreed that AVK rodenticides should collectively be regarded as teratogens (Danish CA 2009) and this stance had not changed at the time of the German CA (2018) assessment.

Neurotoxicity, genotoxicity and carcinogenicity

Neurotoxic effects were not observed in any of the unpublished acute or subchronic laboratory animal tests (Danish CA 2009) and were not reported in the German CA (2018).

In vitro genotoxicity tests were negative, and thus coumatetralyl is unlikely to be genotoxic (Danish CA 2009). It was considered unlikely that coumatetralyl is carcinogenic, based on the lack of mutagenic/genotoxic effects and the absence of any other effects that may lead to non-genotoxic carcinogenesis. Furthermore, carcinogenic effects have not been reported in humans on long-term warfarin administration of (a coumarin compound as is coumatetralyl). Lastly, according to current epidemiological models, the manifestation of carcinogenic effects is dependent on repeated long-term exposure, which is not relevant to rodenticide use patterns.

7 Approaches to rodenticide health risk management

7.1 USEPA human health risk management strategy

Coumatetralyl is not a registered rodenticide in the USA, but 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, quantitative risk assessments are not required or conducted. 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

The Danish CA (2009) and the German CA (2018) based the human health risk assessments on the 2007 version of the EU Technical Notes for Guidance ("TNsG"), originally described in ECB (2004). 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). The TNsG provides indicative exposure values for a range of generic exposure scenarios discussed in the TNsG, amongst these for 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 where 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. Examples of possible coverings are pieces of corrugated iron, or planks, or other sturdy materials.

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, e.g., 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 (as defined for industrial users). In South Africa, the term PCO is applicable and PCOs are required to be registered in South Africa. PCOs are not relevant to the health risk assessments presented in this report.

- 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 than applicable to PCOs.

Muti-Igundane is intended for use by non-professionals. Exposure and risks to users are assessed in that context.

Rodenticide use phases

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

- Application,
- Use, and
- Disposal phases.

The TNsG (ECB 2007) phase descriptions are:

Application phase and application practices

The TNsG (ECB 2007) 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 where the rodenticides are 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 grain bait formulations assessed in this report.

The TNsG (ECB 2007) assumes that grain baits may be used indoors and outdoors, and can be placed in larger, unenclosed surfaces. The application of grain bait is described as:

- 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. More elaborate enclosed bait boxes, which have holes for the rodents to enter, are available.
- The application of grain bait is described as the loading of bait boxes or bait stations with grain bait decanted, spooned or transferred from larger containers. Spooning might be applicable to Muti-Igundane, but grains might also simply be sprinkled from the sachet in which it is provided.
- Grains may also be placed directly into rodent burrows/holes with a spoon or small shovel. In this case, the burrows/holes should preferably be covered to prevent access by children and non-target animals such as pets and birds.

The use of bait boxes, or other special containers, are "strongly recommended" on the Muti-Igundane product label. Bait stations, including bait boxes (box-like bait stations) for solid rodenticide products are described as follows by the TNsG:

- 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.

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.
- Bait box use is "strongly" recommended on the product label, but it is assumed that this is not always adhered to for products registered in South Africa.
- 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 (toddlers and infants) by transient mouthing of contaminated hands.

Disposal (clean-up) phase:
- Final inspection of rat holes and bait points.
- Removal/cleaning of 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.

7.2.2 Solid rodenticide exposure: terminology and variables

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"*. 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 unused or spilled bait, dragged away from the bait station by rodents.

Exposure variables

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 quantities 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 summarises exposure data gathered largely in the Nordic countries. The quantities 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.

TNsG application phase, “use” phase and disposal (clean-up) phase exposure variables are presented in this section. 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, as presented in the TNsG (ECB 2007). Secondary exposure assumptions for accidental contact by adults and children are presented in the exposure and/or risk assessment described in Section 8.

Application phase exposure variables:
Directions for use of Muti-Igundane are to place 20 to 50 grams of bait in covered bait stations, which is in agreement with the ECB (2007) values for domestic users in Table 7.2.2.1. The Muti-Igundane sachet netto grain bait mass is 125 g.

Exposure variables for calculations regarding a non-professional applying Muti-Igundane are as suggested by the TNsG (ECB 2007) in Table 7.2.2.1.

Table 7.2.2.1: TNsG-based exposure variables for grain bait application.

Formulation	Grain bait per application	Handling duration	Event frequency (per day)		Days per year	
			Normal	Worst case	Normal	Worst case
Non-professional applicator/domestic or general public users						
TNsG: Impregnated grain	25 to 50 g (TNsG)	<5 min	1	2	1	20
Muti-Igundane	According to TNsG					

Disposal phase exposure variables:
- Users are assumed to remove/clean the bait box, which may result in handling of product not consumed by the target rodents.
- Disposal activities include cleaning up and disposal of rodenticide dragged away from the bait station by rodents. Disposal 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 might not be extensive.
- Brooming may give rise to dust containing the active substance, which might be inhaled.
- The TNsG (ECB 2007) default assumption is that 15% of the applied grain remains to be disposed (Table 7.2.2.2).

Table 7.2.2.2: TNsG-based exposure variables during the clean-up (disposal) phase.

Formulation	Grain bait remaining for clean-up	Handling duration	Event frequency (per day)	
			Normal	Worst case
Non-professional				
Muti-Igundane	15% of 50 g = 7.5 g	5 min	1	1

7.2.3 Toxicity values

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.

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".

The German CA (2018) conducted human health risk calculations using the systemic Acceptable Exposure Levels ("AELs") for coumatetralyl set in the Assessment Report by the Danish CA (2009) (Table 7.2.3.1). The AEL is the exposure dose that is accepted as not associated with a risk to human health. Since coumatetralyl is not volatile, significant levels in air are unlikely, except in cases of product suspension in air. It follows that the most relevant modes of exposure for operators and consumers are by dermal contact and by inhalation, if product residues are suspended in air during clean-up.

The subchronic exposure AEL presented in Table 7.2.3.1 is provided for the sake of completeness, but the subchronic exposure scenario is not assessed by the Danish CA (2009) or the German CA (2018), since it is not considered applicable to the rodenticide use scenarios.

Table 7.2.3.1: Summary of coumatetralyl AELs.

*Point of departure (POD)	Uncertainty Factors	AEL	**Study and toxicological effects
Acute exposure			
NOAEL administered = 0.0125 mg/kg-day	UF_A= 10 UF_H= 10 UF_{Sev} = 3 Total UF= 300	3.1 x 10^{-5} mg/kg-day	A correction factor for limited oral absorption of 0.75 was applied to the administered NOAEL. See section 6.3 for the rabbit teratogenicity study information.
Subchronic exposure (medium term)			
NOAEL administered = 0.0083 mg/kg-day	UF_A= 10 UF_H= 10 UF_{Sev} = 3 Total UF= 300	1.7 x 10^{-5} mg/kg-day	A correction factor for limited oral absorption of 0.75 was applied to the administered NOAEL. See section 6.3 for the rat repeated dose (subchronic) study information.
Chronic exposure			
Not assessed, because repeated long-term exposure of consumers is not foreseen (German CA 2018). The potential for accumulation in the body is not high, based on results from radioactivity studies in rats, summarised by the Danish CA (2009). The site of accumulation is the liver, but the rate of excretion from the liver is not known. Seven days after a single treatment, approximately 50% of the administered radioactivity remained in the body. After repeated dosing, the retained radioactivity decreased to 18%. Further detailed information from the unpublished study is not provided.			
** Source: Danish CA (2009). *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.			

7.2.4 Exposure and risk calculations

Dose calculations are done with equations recommended by the TNsG (ECB 2007) and according to the harmonised exposure assessment approach for anticoagulant rodenticides, proposed by the Human Exposure Expert Group ("HEEG") of the EC Joint Research Centre Institute for Health and Consumer Protection was used (HEEG 2012). The HEEG provides guidelines towards a harmonised approach to biocide exposure assessment for industry and competent authorities

including the assessment of anticoagulant rodenticides applicable to professional pesticide applicators. The approaches and equations can also be used for the general public, that is, domestic (residential) exposure assessment.

Dermal and inhalation absorption is assumed as presented in Section 6.2 (1.14% and 100%, respectively).

Dermal exposure

The HEEG (2012) recommends the assessment of exposure during decanting of grains from the product packaging. For the assessment of 1 to 4 decanting events, a value of 93.0 mg product available for potential hand exposure is recommended for every 3 kg grain bait (0.000093 kg / 3 kg), which is equal to 0.0031% of the decanted product. This is applicable to decanting of Muti-Igundane grain bait, for which 2 decanting events are assumed for general public users (Table 7.2.2.1). The value of 0.0031% of decanted product available for dermal contact is used in the exposure and risk calculations presented in Section 8.2.

The HEEG (2012) views decanting as an additional activity prior to application of the grain bait in a bait box, or applying the bait at a bait station, which is done by scooping smaller quantities of bait from the container into which grain bait was decanted. In the case of Muti-Igundane grain bait, it is expected that grain will be decanted, spooned or transferred from the product sachet (Figure 7.2.4.1) directly, because the sachet contains a relatively small amount of 125 g of bait. Therefore, the second application event is not relevant to Muti-Igundane grain bait and exposure is calculated only for the "decanting" event.

The TNsG (ECB 2007) default penetration factor of 10% (90% protection) is used to calculate dermal exposure when gloves are used.

Note to figure: the coumatetralyl concentration on this packaging was incorrect at the time the photo was taken, but will be corrected by the supplier.

Figure 7.2.4.1: Muti-Ingudane product packaging as sold to public consumers.

For the assessment of clean-up/disposal, the HEEG (2012) recommends a value of 4.52 mg (0.00452 g) product available for potential hand exposure per event, if a loaded bait box containing grain bait is emptied into a bucket. The estimate per event is valid for 1 to 4 cleaning events per day.

The HEEG (2012) default grain bait value for loading a bait box is 200 g, but an estimate of the left-over grain per bait box is not recommended. Assuming that 15% of the applied bait remains for clean-up (TNsG, ECB 2007), it is calculated that 30 g (15% of 200 g) remains for clean-up in the HEEG example.

The percentage of product available for hand exposure during clean-up, based on the HEEG example, is calculated as 0.00452 g/30 g, which is equal to 0.015% of the remaining product. This is applicable to cleaning-up of Muti-Igundane grain bait, for which 1 clean-up event is assumed for general public users (Table 7.2.2.2). The value of 0.015% of applied product available for dermal contact is used in the exposure and risk calculations presented in Section 8.2.

Inhalation exposure

The HEEG (2012) recommends an air concentration of 9.62 mg product/m^3 air, when 3 kg of bait is decanted, which is used in the exposure and risk calculations presented in Section 8.2. The equivalent air concentration is 0.160 mg product/m^3 air for a residential user decanting 50 g of grains (decanted amounts from Table 7.2.2.1).

The HEEG (2012) assumes that inhalation exposure during clean-up of grain bait is negligible. The assumed clean-up action is emptying of a bait box, which is relevant to Muti-Igundane in indoors application scenarios. If applied outside, or in a covered bait station, the grain is usually left where it is, and a clean-up event is not relevant. However, in the case of general public users, application may be indoors without a bait box, and clean-up by brooming, which might generate coumatetralyl residue dusts. The TNsG (ECB 2007) approach is used for a brooming scenario, calculating the air concentration as presented in Table 7.2.4.1.

Table 7.2.4.1: Indoor grain bait dust air concentrations during clean-up by sweeping with a broom (general public).

Scenario and exposure variable description	Clean-up
Muti-Igundane grains remaining to be disposed	7.5 g (Table 7.2.2.2)
Dispersion in air: 1% of remaining mass released as airborne particles (TNsG, ECB 2007)	1.0% of 7.5 g = 0.075 g/event
Air concentration of grain dust dispersed in a 50 m^3 room (TNsG room default)	0.075 g / 50 m^3 = 0.0015 g/m^3 (1.5 mg/m^3)
Event duration (TNsG default, Table 7.2.2.2)	5 minutes
Inhalation rate (adult) (TNsG default)	1.25 m^3/hour = 0.0208 m^3/min
Volume air inhaled/event	5 min x 0.0208 m^3/min = 0.104 m^3
Mass of grain dust inhaled/event	1.5 mg/m^3 x 0.104 m^3 = 0.156 mg/event

Systemic exposure dose

In short, based on the TNsG (ECB 2007), the systemic dose of coumatetralyl is calculated with Equation 7.2.4.1.

Systemic dose (mg/kg-day)
= Systemic coumatetralyl exposure (mg/day) / body weight (kg) Equation 7.2.4.1

Systemic coumatetralyl exposure is calculated with simplified Equation 7.2.4.2:

Systemic exposure = Coumatetralyl absorbed per event x events per day Equation 7.2.4.2

Where:

Systemic exposure	Systemic exposure per day (mg/day).
Exposure per event	Calculated as explained in Section 8 for the different exposure scenarios.
Events per day	Number of events per day; that is, estimated or default number of application- or clean-up events per day.

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. Detailed calculations are presented in Section 8.

8 Human health risk assessment of Muti-Igundane grain bait

8.1 Exposure scenarios

The grain bait 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 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 "*Place or cover bait in such a way that it is inaccessible to children, pets or birds*". Label instructions for "*Rats in the roof"* is to "*Place open pack above the ceiling*". Although not necessarily a frequent occurrence, a scenario of rodents dragging the sachets away from the deployed places, to where unaware bystanders (children and adults) might come in contact with spilled grain bait, cannot be excluded. Therefore, accidental exposure of children is also assessed.

8.2 Primary exposure doses and risk calculations

Exposure routes

Primary exposure of the general public (non-professionals) is assessed during the application phase and the disposal (clean-up) phase. Dermal exposure is of main interest during the application phase, but inhalation is also assessed. With outdoor use, exposure to the product is not applicable during the clean-up phase, because the grain bait is usually left in the rat burrows. With indoor use, removal by sweeping with a broom may disperse dust into air, causing exposure by inhalation.

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 with soap and water immediately after use or accidental skin contact*" and precautions include "*Do not eat, drink or smoke whilst applying or before washing hands and face"*. Therefore, oral exposure is not considered an important route of primary exposure, and is not included in the assessment.

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.

Primary non-professional exposure: general public/domestic exposure

The results of the exposure calculations are presented in Table 8.2.1. TNsG (ECB 2007) example calculations were followed, with coumatetralyl-specific values as applicable:

- PPE use is not included in the calculations, because it is assumed that non-professionals might not be diligent users of PPE.
- The scenario of handling of dead rodents is considered unrealistic by some international regulatory agencies, or included with dermal product residue contact during clean-up, which is assumed for Muti-Igundane.
- Oral exposure of adult users is considered negligible.

Table 8.2.1: General public coumatetralyl exposure: grain bait decanting and clean-up.

Scenario and exposure variable description	Dermal exposure	Inhalation exposure
Generic values		
Mass of grains per bait point	50 g (Table 7.2.2.1)	
Concentration of coumatetralyl in product (Table 3.2.2)	0.036%	0.036%
Body weight (kg)	60	60
Inhalation rate (m^3/hr)	-	1.25
Absorption rate of coumatetralyl (Section 6.2)	1.14%	100%
Decanting, spooning and loading of bait box/station		
Manipulations per day (maximum estimate from Table 7.2.2.1)	2 events	2 events
Mass of grain decanted per event	50 g/event	50 g/event
Exposure time per event (maximum estimate from Table 7.2.2.1)	-	5 minutes = 0.083 hours
Air concentration of product while decanting (see Section 7.2.4)	-	0.160 mg/m^3
Inhalation rate of an adult (ECB 2007)	-	1.25 m^3 air/hour
Mass of product inhaled per event	-	0.083 x 0.160 x 1.25 = 0.017 mg/event
% of product on hands/forearms during decanting event (see Section 7.2.4)	0.0031%	-
Mass of product on hands/forearms (mg per event)	0.0031% x 50 g x 1 000 = 1.55 mg	-
Mass of absorbed coumatetralyl (mg per event)	1.55 x 0.036% x 1.14% = 6.36 x 10^{-6}	0.017 x 0.036% x 100% = 6.00 x 10^{-6}
Coumatetralyl absorbed/day (mg/day)	6.36 x 10^{-6} x 2 events = 1.27 x 10^{-5}	6.00 x 10^{-6} x 2 events = 1.20 x 10^{-5}
Coumatetralyl dose (mg/kg-day) (without PPE)	1.27 x 10^{-5} / 60 = 1.06 x 10^{-7}	1.20 x 10^{-5}/ 60 = 1.00 x 10^{-7}
Coumatetralyl dose (mg/kg-day) (wearing gloves)	1.06 x 10^{-8}	-
Sum of coumatetralyl exposure during decanting and loading of bait box/station		
Coumatetralyl dose (mg/kg-day) (without PPE)	1.06 x 10^{-7} + 1.00 x 10^{-7} = 2.06 x 10^{-7}	
Clean-up		
Manipulations per day (Table 7.2.2.2)	1 event	1 event

Scenario and exposure variable description	Dermal exposure	Inhalation exposure
Mass of grains remaining for clean-up (g) (Table 7.2.2.2)	7.5	7.5
Exposure time per event (maximum estimate from Table 7.2.2.1)	-	5 minutes = 0.083 hours
Air concentration of grain dust while cleaning up (Table 7.2.4.1) (mg/m^3)	-	1.5 mg/m^3
Mass of grain dust inhaled/event (Table 7.2.4.1)	-	= 0.156 mg/event
% of product on hands/forearms during clean-up event (see Section 7.2.4)	0.015%	-
Mass of grain dust on hands/forearms (mg)	0.015% x 7.5 g x 1 000 = 1.13 mg	-
Mass of absorbed coumatetralyl (mg per event)	1.13 x 0.036% x 1.14% = 4.62×10^{-6}	0.156 mg/event x 0.036% x 100% = 5.63×10^{-5}
Coumatetralyl absorbed/day (mg/day)	4.62×10^{-6} x 1 event = 4.62×10^{-6}	5.36×10^{-5} x 1 event = 5.36×10^{-5}
Coumatetralyl dose (mg/kg-day) (without PPE)	7.7×10^{-8}	9.38×10^{-7}
Sum of coumatetralyl exposure during clean-up		
Coumatetralyl dose (mg/kg-day) (without PPE)	$7.7 \times 10^{-8} + 9.38 \times 10^{-7} = 1.01 \times 10^{-6}$	
Coumatetralyl dermal exposure/event = 0.036% (coumatetralyl w/w) x (product exposure / manipulation) x dermal absorption factor. Coumatetralyl inhalation exposure/event = 0.036% (coumatetralyl w/w) x product air concentration (mg product/m^3) x activity minutes per day x inhalation rate x inhalation absorption factor. Dose = coumatetralyl absorbed/day (mg/day) / body weight (60 kg).		

Primary exposure health risks

The risk calculations are conducted by comparing the calculated coumatetralyl exposure doses to the acute AEL (Table 7.2.3.1) of 3.1×10^{-5} mg/kg-day. Exposure doses less than 100% of the AEL are considered acceptable. Risks are summarised in Table 8.2.3. Risks are calculated separately for decanting (application) and clean-up, because it is unlikely that these activities will occur on the same day.

Table 8.2.3: General public user coumatetralyl primary exposure health risks.

Scenario	Dose (mg/kg-day) (Table 8.2.1)	Risk (%)	Acceptable Yes/No
Decanting, spooning and loading of bait box/station Without gloves/respiratory PPE	2.06×10^{-7}	0.7%	Yes
Decanting, spooning and loading of bait box/station Without gloves/respiratory PPE	1.01×10^{-6}	3.3%	Yes
Risk = (Dose/AEL) %. AEL_{acute} (mg/kg-day) = 3.1×10^{-5} (Table 7.2.3.1). PPE: Personal protective equipment.			

8.3 Secondary exposure dose and risk calculations

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

- Accidental dermal contact by adults and children/infants. 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. Infants and toddlers are thus more vulnerable than older children are the most sensitive receptors.
- Exposure of adults may resemble the scenario of dermal contact, calculated using the values applicable to the general public. Potential inhalation during secondary exposure is thus considered negligible.
- The most likely resemblance of accidental contact is to the clean-up scenario, when lesser amounts of product are available for contact, and when the contact frequency is assumed to be only one contact event (see Table 7.2.2.2).
- Accidental ingestion of grain bait by a child is assessed assuming ingestion of 5 g of grains (ECB 2007).
- Doses of infants/toddlers are calculated with the USEPA (2011) default body weight of 11 kg for children aged 1 to <2.

Dermal doses of infants/children are not calculated if ingestion of bait is assessed, since oral absorption doses are calculated assuming 75% coumatetralyl absorption, while dermal absorption is 1.14% (Section 6.2). Therefore, it is reasonable to expect that oral doses would exceed dermal doses by orders of magnitude, and that risks associated with oral exposure would be a fair indication of oral and dermal exposure.

Given an absorption rate of 75% by ingestion, the amount of coumatetralyl absorbed by ingestion of 5 g of grain bait is:
- 5 g bait x 0.036% coumatetralyl x 75% absorption by ingestion.
- = 1.35 mg/event.

Given a toddler/infant body weight of 11 kg (USEPA 2011), and one ingestion event per day, the absorbed coumatetralyl dose is:
- (1.35 mg/day) / 11 kg.
- = 0.123 mg/kg-day.

Assuming that accidental contact of an adult with grain bait is equal to the dermal dose absorbed by a general public user during clean-up, the dermal dose is assumed to be 7.7×10^{-8} (Table 8.2.2).

The risk calculations are conducted by comparing the calculated coumatetralyl exposure doses to the acute AEL (Table 7.2.3.1) of 3.1×10^{-5} mg/kg-day. Exposure doses less than 100 per cent of the AEL are considered acceptable. Risks are summarised in Table 8.3.1.

Table 8.3.1: Coumatetralyl secondary exposure health risks of adults and children.

Scenario	Dose (mg/kg-day)	Risk	Acceptable Yes/No
Adult accidental dermal exposure	7.7×10^{-8}	0.2%	Yes
Infants/toddlers accidental oral exposure	0.123	> 100%	No
Risk = (Dose/AEL) % **AEL_{acute} (mg/kg-day) = 3.1×10^{-5} (Table 7.2.3.1)**			

8.4 Risk interpretation

Acceptable exposures and risks are indicated if the calculated exposure doses of rodenticide users are less than the acceptable exposure level, the AEL. In Table 8.2.3 this is signified by the risk percentage, which is the dose expressed as a percentage of the AEL. Therefore, the exposure dose is acceptable if the calculated risk percentage is less than 100 per cent.

Although the Muti-Igundane product label recommends the use of gloves, it was assumed that the general public may not be diligent PPE users and risks were calculated based on the absence of gloves. It is also not expected that the general public would have access to respiratory PPE, which was thus excluded from the inhalation risk calculations (Table 8.2.2). The outcome of the human health risk assessment for general public users indicates the absence of a risk to adults applying the grain bait by decanting or scooping it from the sachet in which it is provided. The assessment also indicates the absence of a risk to health of adults cleaning up left-over bait, assuming that remains are swept away with a broom.

Given the acceptable risk results of the general public applying or cleaning up left-over bait without wearing gloves, it is reasonable to accept that the risk of adult bystanders accidentally touching or handling the bait would also not indicate a cause for concern (risks would be acceptable).

Unacceptable risks are identified for infants/toddlers eating 5 grams of the grain bait (a small handful, according to ECB 2007). According to international rodenticide risk assessments for product registration purposes, specific risk mitigation measures are required to prevent exposure to children and these are also applicable to the grain bait. Recommendations are discussed in Section 9.3. In any case, any noted contact of a child with a rodenticide should be brought to the immediate attention of a medical professional, without exception.

9 Discussion

9.1 Human health risks and PPE use

The calculated exposure doses and health risks presented in this report are based on conservative assumptions, and risks are likely to represent the higher ranges of possible exposures.

The lack of an appreciable health risk for general public users not wearing gloves while handling the grain bait cannot be viewed as suggesting that gloves need not be worn while dispensing or cleaning up the product, or while handling dead rodents. Wearing gloves is always to be recommended on product labels, and should be adhered to by all users.

Exposure by inhalation is expected to be low to negligible, and the risk calculations confirmed the absence of a risk to the general public while applying the grain bait, or while cleaning up left-over bait.

Unacceptable risks are identified for infants/toddlers accidentally ingesting “a small handful” of the grain bait. Specific risk mitigation measures are required to prevent exposure to children. Measures are recommended and discussed in Section 9.3. In any case, any noted contact of a child with a rodenticide should be brought to the immediate attention of a medical professional, without exception.

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 (2022b) 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 (2022b) 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 (2022b) "*acknowledges that there are many benefits associated with these active ingredients and supports the continued registration of these active ingredients*".

Nonetheless, 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 9.3.

9.3 Proposed mitigation measures

The following mitigation measures should be recommended:

- 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 and drinking as far as possible) to improve product intake and reduce the likelihood of reinvasion.
- It is noted that the Muti-Igundane product label already "strongly recommends" to use of bait boxes or other suitable containers, and this must be retained on the label. It is not suggested that bait box use must be mandatory to the South African consumer, where a need for access to low-cost rodenticides is foreseen, specifically in low-income groups. Mandatory use of bait boxes implies an additional cost premium, which might cause rodenticide use to be unaffordable to those needing it most (see Section 9.2 for a complete discussion).

- Bait 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 a rodenticide should be brought to the immediate attention of a medical professional, without exception.
- The 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 that the bait stations are intact and to remove rodent bodies.
- To reduce the risk of secondary poisoning of non-target animals, search for and remove dead rodents at frequent intervals during treatment.
- Do not use the product as permanent baits for the prevention of rodent infestation.
- Remove the remaining product at the end of treatment period.
- When placing bait points close to water drainage systems, ensure that bait contact with water is avoided.
- Protect bait from the atmospheric conditions. Place the baiting points in areas not liable to flooding.
- Wearing gloves while handling the grain bait must be emphasised on all labels.
- 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.

10 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, females who are not pregnant, and of children on the health endpoint of developmental effects. 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”.

In support of the application for derogation regarding the restricted use of the registered Muti-Igundane grain bait rodenticide, identified as a substance of concern due to the reproductive toxicant properties of the rodenticide ingredient coumatetralyl, the human health risk assessment results lead to the following conclusions:

- Adult users of Muti-Igundane are not at risk of a health effect or of an effect on the development of the foetus in case of pregnant females. This is valid whether or not gloves are used. However, the finding cannot be viewed as suggesting that gloves need not be worn while applying or cleaning up the product, or while handling dead rodents. Wearing gloves is recommended on the product label, and should be adhered to by all users.

- Infants/toddlers chewing on solid bait products are at risk of a health effect. However, accidental exposure of bystanders, specifically children, can be limited by clear communication of the pesticide applicator to such bystanders, and by following label instructions to keep the bait out of reach of children, and 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 toxicity of the anti-coagulant active ingredient coumatetralyl. 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 supplier of Muti-Igundane rodenticide containing coumatetralyl is according to the intended product use: an anti-coagulant poison for control of rats and mice. The use of bait boxes is strongly recommended on the label.

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

- The balance of societal need and benefits, versus the 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 implemented.

11 References

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12 Annexure 1: Environmental assessment by the South African GRIFFON Poison Information Centre

From: Dr Gerhard H Verdoorn <nesher@tiscali.co.za>
Sent: 09 January 2020 11:56 AM
To: ebrahim@growingmnf.co.za
Subject: Muti-Igundane

Dear Ebrahim

Please forward this e-mail directly to Pick and Pay to put ther minds at rest re the secondary poisoning risks of your product Muti-Igundane;

This rodenticide is registered under the Fertilizers, Farm Feeds, Agricultural Remedies and Stock Remedies Act, 1947 (Act No. 36 of 1947) with registration number L5718 and contains 7.5 grams per kilogram coumatetralyl as active ingredient which the same active ingredient used in the Racumin range of rodenticides of Bayer (Pty) Ltd. Coumatetralyl is a first generation anti-coagulant and a multiple feed rodenticide which means the target animal has to ingest the product on at least three successive days to be terminated by the effects of the active ingredient. It is a mammal toxin with a toxicity of LD50 = 16.5 mg/kg body mass for rats while it is virtually non-toxic for birds. The risk of secondary poisoning for owls that may catch rats and mice that ingested Muti-Igundane is extremely low because of the virtual non-toxicity of coumatetralyl for birds, the multiple feed requirement and because its is one of very few anti-coagulants that metabolises rapidly in the targte animal's intestines.

While we fully understand that coumatetralyl is very toxic for mammals as it should be to be an effective rodenticide, it is of no real risk for owls and other avian predators.

Best wishes.

Gerhard

נשר בן-גבנ

Dr Gerhard H Verdoorn: Director

GRIFFON POISON INFORMATION CENTRE

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