



Health
Canada Santé
Canada

Your health and
safety... our priority.

Votre santé et votre
sécurité... notre priorité.

Proposed Special Review Decision

PSRD2022-02

Special Review of Potassium Dimethyldithiocarbamate and its Associated End- use Products: Proposed Decision for Consultation

Consultation Document

(publié aussi en français)

7 September 2022

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6607 D
Ottawa, Ontario K1A 0K9

Internet: canada.ca/pesticides
pmra.publications-arla@hc-sc.gc.ca
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra.info-arla@hc-sc.gc.ca

Canada 

ISSN: 2561-6366 (online)

Catalogue number: H113-30/2022-2E (print)
H113-30/2022-2E-PDF (PDF version)

© Her Majesty the Queen in Right of Canada, as represented by the Minister of Health Canada, 2022

All rights reserved. No part of this information (publication or product) may be reproduced or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, or stored in a retrieval system, without prior written permission of Health Canada, Ottawa, Ontario K1A 0K9.

Table of Contents

1.0	Introduction.....	1
2.0	Uses of potassium dimethyldithiocarbamate in Canada	1
3.0	Aspects of concern that prompted the special review.....	1
4.0	Evaluation of the aspects of concern that prompted the special review	1
4.1	Toxicology summary	2
4.2	Dietary exposure and risk assessment.....	2
4.3	Occupational and non-occupational risk assessment.....	3
4.3.1	Toxicology reference values	3
4.3.2	Non-occupational exposure and risk assessment.....	3
4.3.3	Occupational exposure and risk assessment	4
4.4	Aggregate risk assessment	7
4.5	Cumulative assessment	7
4.6	Health incident reports	8
5.0	Proposed special review decision for potassium dimethyldithiocarbamate	8
6.0	Next steps.....	9
7.0	Other information.....	9
	List of Abbreviations	10
Appendix I	Registered products containing potassium dimethyldithiocarbamate ¹	11
Appendix II	Toxicology reference values for health risk assessment.....	13
Table 1	Updated toxicology reference values for use in health risk assessment for potassium dimethyldithiocarbamate (based on the reference values selected for the human health risk assessment of ziram as presented in RVD2018-39)	13
Appendix III	Occupational exposure and risk assessment	14
Table 1	Potassium dimethyldithiocarbamate long-term occupational applicator exposure and risk assessment.....	14
Table 2	Potassium dimethyldithiocarbamate occupational applicator cancer exposure and risk assessment	15
Table 3	Long-term exposure and risk assessment (cancer and non-cancer) for workers handling metal working fluids	16
Appendix IV	Proposed label amendments for end-use products containing potassium dimethyldithiocarbamate, for the protection of human health.....	17

1.0 Introduction

The Pest Management Regulatory Agency (PMRA) initiated the special reviews of sodium dimethyldithiocarbamate and potassium dimethyldithiocarbamate in 2018 under subsection 17(1) of the *Pest Control Products Act* based on the toxicology data submitted under section 12 of the *Pest Control Products Act*, following the re-evaluation of sodium and potassium dimethyldithiocarbamate salts (PRVD2011-05 and RVD2012-01).

Registrants of the active ingredient sodium dimethyldithiocarbamate voluntarily discontinued registration of all products containing sodium dimethyldithiocarbamate. Therefore, the special review of sodium dimethyldithiocarbamate was closed in May 2022. Consequently, this regulatory proposal only pertains to potassium dimethyldithiocarbamate.

Pursuant to subsection 18(4) of the *Pest Control Products Act*, Health Canada has evaluated the aspects of concern that prompted the special review of pest control products containing potassium dimethyldithiocarbamate. The aspects of concern for this special review are relevant to human health.

2.0 Uses of potassium dimethyldithiocarbamate in Canada

Potassium dimethyldithiocarbamate is a broad-spectrum biocide registered in Canada for use as a slimicide in industrial fluids and as a material preservative for a variety of substances including metal working fluids and brine solutions. All currently registered pest control products containing potassium dimethyldithiocarbamate (Appendix I) are considered for the special review.

3.0 Aspects of concern that prompted the special review

Based on the review of the data submitted under Section 12 of the *Pest Control Products Act*, Health Canada updated the potassium dimethyldithiocarbamate toxicology reference values for health risk assessments (Appendix II). The following aspects of concerns were identified for the special review under subsection 17(1) of the *Pest Control Products Act*:

- Potential cancer and non-cancer risks from occupational handler and post-application exposure.

4.0 Evaluation of the aspects of concern that prompted the special review

Following the initiation of the special review, Health Canada requested information related to the aspects of concern from provinces and other relevant federal government departments and agencies in accordance with the subsection 18(2) of the *Pest Control Products Act*. No information was received relating to the aspects of concern.

In order to evaluate the aspects of concern for potassium dimethyldithiocarbamate, Health Canada considered currently available relevant scientific information, which includes information considered for the re-evaluation of potassium dimethyldithiocarbamate (PRVD2011-05 and RVD2012-01), information submitted under section 12 of the *Pest Control*

Products Act following the re-evaluation of potassium dimethyldithiocarbamate, and any relevant information obtained since then.

4.1 Toxicology summary

Health Canada conducted a re-evaluation of potassium and sodium dimethyldithiocarbamate salts with the conclusions published in the Proposed Re-evaluation Decision Document (PRVD2011-05) and in the Re-evaluation Decision Document (RVD2012-01). Health Canada concluded that additional data were required to support the continued registration of these salts, and as such, toxicology data were required under section 12 of the *Pest Control Products Act*. The required data included combined chronic toxicity/oncogenicity studies in the mouse and rat and a multi-generation reproductive toxicity study in the rat.

In response to the data requirements for potassium and sodium dimethyldithiocarbamate salts, the registrant submitted information on the use pattern, a published report of a chronic toxicity study in rats exposed to ziram (a zinc salt of dimethyldithiocarbamate), a report of a carcinogenicity study in mice and rats dosed with ziram, and the results of computer modelling (Derek Nexus) in 2014. In their response, the registrant indicated that the structural and biological activity of ziram was directly analogous to that of potassium and sodium dimethyldithiocarbamate salts and that data on ziram could be considered for the assessment of the potential toxicity of potassium and sodium dimethyldithiocarbamate salts. Health Canada agreed with the registrant that ziram, and the potassium and sodium dimethyldithiocarbamate salts all appear to be structurally related, and used a read-across approach, which allowed for the examination of all of the available toxicity data for ziram, and the potassium and sodium dimethyldithiocarbamate salts. Based on the different parameters examined, it appeared that ziram and the potassium and sodium dimethyldithiocarbamate salts are of similar toxicity. Some gaps and inconsistencies were noted when the different endpoints from the various toxicity studies were compared; however, for the most part, these differences could be attributed to dose selection. Given the similarity between the different salts, Health Canada concluded that the toxicity studies conducted with ziram could be used for the risk assessment of potassium dimethyldithiocarbamate, and thus took a modified approach for the fulfillment of the Section 12 data requirements for potassium dimethyldithiocarbamate based on the available ziram data.

4.2 Dietary exposure and risk assessment

There are no food or food contact uses associated with the preservative uses of potassium dimethyldithiocarbamate. Residues of potassium dimethyldithiocarbamate in potential drinking water sources are not expected as potassium dimethyldithiocarbamate salts are not stable in water (PMRA# 2773561).

4.3 Occupational and non-occupational risk assessment

Occupational and non-occupational (for example, residential) risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

4.3.1 Toxicology reference values

4.3.1.1 Toxicology reference values for occupational and non-occupational exposure to potassium dimethyldithiocarbamate

As a result of the considerations in Section 4.1, the reference values for potassium dimethyldithiocarbamate were revised from those that were presented in RVD2012-01 to those that were established for ziram and presented in RVD2018-39. In using the read-across methodology supported by the registrant, Health Canada established a q_1^* of 1.82×10^{-2} (mg/kg bw/day)⁻¹ for use in the cancer risk assessment for potassium dimethyldithiocarbamate based on ziram data. Extension of the read-across approach for non-cancer endpoints supported the use of the ziram reference values for potassium dimethyldithiocarbamate. As such, the long-term dermal and inhalation reference values for the potassium dimethyldithiocarbamate risk assessment were based on the point of departure from the 2-year dietary rat chronic toxicity study conducted with ziram. Revised toxicology reference values based on those for ziram are presented in Appendix II, Table 1.

Dermal absorption

No dermal absorption (DA) studies were submitted by the registrants for potassium dimethyldithiocarbamate nor were any available in the literature. Due to this, a DA value of 100% was selected for the special review of potassium dimethyldithiocarbamate.

Refinement of this value using physical/chemical properties such as molecular weight and formulation type was explored; however, they do not suggest that potassium dimethyldithiocarbamate has a low DA potential.

4.3.2 Non-occupational exposure and risk assessment

Non-occupational (residential) risk assessment involves estimating risks to the general population, including adults, youth, children, during or after pesticide application.

4.3.2.1 Residential applicator exposure and risk assessment

A residential applicator assessment for potassium dimethyldithiocarbamate was not required since there are no registered domestic-class pesticide products.

4.3.2.2 Residential postapplication exposure and risk assessment

Residential postapplication exposure occurs when an individual is exposed through dermal, inhalation and/or incidental oral (non-dietary ingestion) routes as a result of being in a residential environment where a consumer product containing potassium dimethyldithiocarbamate as a material preservative has been used.

Potassium dimethyldithiocarbamate is registered for use as a material preservative in pulp and paper manufacturing, however, all end-use product labels currently contain a statement which prohibits its use in any paper product or food packaging material that would come into contact with food. Considering this, potential food dietary exposure to potassium dimethyldithiocarbamate is expected to be minimal based on a qualitative assessment.

Potassium dimethyldithiocarbamate is registered for use as a material preservative of the brine solutions during the curing of leather products. Exposure may result when coming into contact with leather products made from hides/skins cured in the potassium dimethyldithiocarbamate treated brine solutions. Based on a submitted study (PMRA# 1956512), no detectable levels of potassium dimethyldithiocarbamate are expected to be found in leather made from potassium dimethyldithiocarbamate treated hides. Therefore, exposure to potassium dimethyldithiocarbamate residues in the final leather products, if applied according to the rates prescribed on the current product labels, is expected to be minimal based on a qualitative assessment.

4.3.3 Occupational exposure and risk assessment

There are potential exposures to workers mixing and loading potassium dimethyldithiocarbamate commercial-class end-use products when treating fluids used in industrial facilities and material preservation scenarios.

4.3.3.1 Occupational primary handler exposure and risk assessment

Exposure to potassium dimethyldithiocarbamate is expected to be intermittent (a few minutes daily or once a week) over an intermediate to long-term duration (that is >30 days to several months).

Based on the use pattern, the major scenarios identified are:

- Manual transfer of liquids (conventional container)
- Closed transfer of liquids (assessed qualitatively)

A closed transfer (injection) system has the characteristics where there is no contact of workers with the active ingredient and thus workers are assumed to have no potential for exposure. Due to this, occupational risk (cancer and non-cancer) for closed transfer (injection) systems were assessed qualitatively and risks were determined to be acceptable.

Potassium dimethyldithiocarbamate end-use product labels have both open and closed transfer requirements but do not specify when one or the other is required, therefore, both types of systems were considered in the risk assessment. Occupational risk (cancer and non-cancer) to

workers from open transfer activities in small scale facilities were assessed quantitatively. It was assumed that large scale facilities would have closed transfer systems already in place and these scenarios were assessed qualitatively.

No appropriate chemical-specific handler exposure data were available for potassium dimethyldithiocarbamate. Therefore, dermal and inhalation exposures for occupational applicators were estimated using the liquid pour (PMRA# 2296582, 2296584) exposure study submitted by the Antimicrobial Exposure Assessment Task Force II (AEATF II). While there are limitations in the use of generic data, these exposure data represent the most reliable information currently available. Inhalation exposures were based on light inhalation rates (17 L/min).

There is limited information available to estimate the amount of potassium dimethyldithiocarbamate handled in one day by workers for the various Canadian industrial facilities or material preservation scenarios. The United States Environmental Protection Agency (USEPA) “Antimicrobial Division Draft Summary of Amounts Handled or Treated for Occupational Handler Scenarios” (PMRA# 3084493¹) contains standard values for the majority of industrial processes. As industrial facilities have a range of production capacities, an amount handled per day (AHPD) value of up to 38 L end-use product/day was utilized to address all small scale facilities that would use an open pour method to mix, load, and apply the antimicrobial. Use information submitted to the PMRA indicated that 9.46–18.8 L end-use product/day is handled in brine solutions/brine curing scenarios (PMRA# 2912486). This value is consistent with the open pour value in PMRA# 3084493¹ for leather tanning scenarios (5 gallons end-use product/day) and was used in the occupational risk assessment.

For the cancer risk assessment, it was assumed workers in industrial facilities or material preservation scenarios would handle potassium dimethyldithiocarbamate every work day of the year, except when on vacation (250 days per year). It was also assumed that a worker in a “Technician and Related Support” career would handle potassium dimethyldithiocarbamate each year over the span of their career of 22.2 years (PMRA# 1945742). This value also addresses the years of exposure for the ‘Operators, Fabricators, and Laborers’ (14.7 years).

The calculated combined MOEs and cancer risks for workers handling potassium dimethyldithiocarbamate showed that risks were not acceptable at single layer personal protection equipment (PPE) (long pants, long-sleeved shirt, chemical-resistant (CR) gloves). Risks could not be mitigated with additional PPE as exposure in the AEATF II study was primarily to the hands and exposure to the remainder of the body was minimal. To mitigate risks, it is proposed that closed transfer systems be used for all commercial-class potassium dimethyldithiocarbamate end-use products. The quantitative cancer and non-cancer long-term occupational handler risk assessment for potassium dimethyldithiocarbamate is presented in Appendix III, Tables 1 and 2.

¹ PMRA# 3084493. USEPA (2018). Summary of Amounts Handled or Treated for Occupational Handler Scenarios. EPA: Washington, DC.

4.3.3.2 Occupational secondary handler exposure and risk assessment

Downstream workers in industrial facilities and material preservation scenarios:

There are potential exposures to workers using potassium dimethyldithiocarbamate in industrial facilities and as a material preservative. Downstream workers are not expected to handle potassium dimethyldithiocarbamate treated fluids, however, limited contact may occur (PMRA# 2912486). Exposure is expected to be low given the occupational hygiene standards in these workplaces that require safe work conditions. Workers are expected to be wearing PPE as required by laws related to worker health and safety, which would limit potential exposure. Additionally, as the vapour pressure of potassium dimethyldithiocarbamate is low (not calculated as the melting point is $> 300^{\circ}\text{C}$; PMRA# 2773561), inhalation exposure of the vapour from volatilization is considered to be minimal. Therefore, the risk assessment for downstream workers in industrial facilities and in material preservation scenarios was considered qualitatively, unless discussed below, and was determined to be acceptable.

Metal working fluids (cutting fluids):

Potassium dimethyldithiocarbamate end-use products are used to preserve metal working fluids. Workers using the treated metal working fluids are expected to be exposed to potassium dimethyldithiocarbamate via dermal contact of the fluids and through inhalation of the mist/aerosol.

An inhalation assessment was conducted following the USEPA Chemical Engineering Branch model which measures oil mist concentrations for metal working operations and measures inhalation exposure to the mists and aerosols. A dermal risk assessment was conducted using the 2-hand immersion model (PMRA# 3354881).

Using the maximum registered rate of 1000 ppm, both cancer and non-cancer risks were identified. To mitigate risk, a lower registered rate of 80 ppm will be proposed as the maximum rate for use in metal working fluids (cutting fluids). At this rate, risks (cancer and non-cancer) are determined to be acceptable. The postapplication risk assessment for metal working fluids (cutting fluids) is presented in Appendix III, Table 3.

Brine solutions/brine curing:

Potassium dimethyldithiocarbamate is registered for use as a material preservative of the brine solutions during the curing of leather products. No model currently exists for assessing risk to downstream workers in the leather industry.

Dermal exposure is considered to be extensive, and to the entire body, for workers handling the treated brine solutions as well as treated leather. Due to this, and the lack of data to assess potential exposures, the use of potassium dimethyldithiocarbamate in brine solutions/brine curing is proposed to be removed from potassium dimethyldithiocarbamate product labels.

4.4 Aggregate risk assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal and inhalation).

In an aggregate risk assessment, the combined potential risk associated with food, drinking water and various residential exposure pathways is assessed. A major consideration is the likelihood of co-occurrence of exposures from the use of products containing potassium dimethyldithiocarbamate as a preservative. Additionally, only exposures from routes that share common toxicological endpoints can be aggregated.

There are no registered potassium dimethyldithiocarbamate food uses, nor is it used in products designed for food packaging materials or in areas where food is stored, handled or processed. Residues of potassium dimethyldithiocarbamate in potential drinking water is not expected as potassium dimethyldithiocarbamate salts are not stable in water (PMRA# 2773561). Incidental oral and dermal exposure to potassium dimethyldithiocarbamate from its use as a material preservative during the leather manufacturing process is not expected as exposure to potassium dimethyldithiocarbamate residues is expected to be minimal.

Therefore, aggregate exposure and risks were considered to be acceptable based on a qualitative assessment.

4.5 Cumulative assessment

The *Pest Control Products Act* requires that Health Canada consider the cumulative exposure to pest control products with a common mechanism of toxicity. Accordingly, an assessment of potential common mechanism of toxicity with other pesticides was undertaken for potassium dimethyldithiocarbamate. Potassium dimethyldithiocarbamate is a member of the dimethyldithiocarbamate class of pesticides along with sodium dimethyldithiocarbamate, ziram, ferbam, and thiram. Since all agricultural uses of ferbam and ziram were cancelled along with the material preservative uses of ziram and sodium dimethyldithiocarbamate, the only uses for consideration in a cumulative risk assessment are the seed treatment use of thiram and the material preservative use of potassium dimethyldithiocarbamate.

Ziram, which was used to characterize the toxicity of potassium dimethyldithiocarbamate, is structurally related to thiram. Both ziram and thiram inhibit the enzyme acetaldehyde dehydrogenase, and induce some similar toxic effects in mammals, including evidence of neurotoxicity. It is unknown whether a common mode of action underlies these similar toxic effects. However, the anticipated dietary and residential exposure to potassium dimethyldithiocarbamate from the material preservative uses are considered to be minimal, and thus would contribute very little to the cumulative risk from potential co-exposure to thiram and potassium dimethyldithiocarbamate. Therefore, cumulative risk is acceptable.

4.6 Health incident reports

As of 18 February 2022, no incident reports involving potassium dimethyldithiocarbamate salts related to the aspects of concern had been reported to the PMRA.

5.0 Proposed special review decision for potassium dimethyldithiocarbamate

Under the authority of the *Pest Control Products Act* and based on an evaluation of available relevant scientific information related to the aspects of concern for human health, Health Canada is proposing continued registration of potassium dimethyldithiocarbamate and associated end-use products registered for sale and use in Canada with the risk mitigation measures below.

Risk mitigation measures

Human health

As a result of the special review of potassium dimethyldithiocarbamate salts, the PMRA is proposing further risk-reduction measures on product labels. Additional revisions to the potassium dimethyldithiocarbamate labels are proposed to meet the current labelling standards and for consistency. This includes updating the PPE label statement. Refer to Appendix IV for all proposed label amendments.

The following mitigation measures are proposed to reduce potential exposure to workers using potassium dimethyldithiocarbamate in industrial facilities or in material preservation scenarios:

- The use of a closed loading and transfer system
- For metal working fluid (cutting fluid) uses, a maximum rate of 80 ppm
- Cancellation of the brine curing/brine solutions uses

Additional Scientific Information

- No additional scientific data are required at this time.

This proposed special review decision is a consultation document.² The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information on the cover page of this document).

² “Consultation statement” as required by subsection 28(2) of the *Pest Control Products Act*.

6.0 Next steps

Before making a special review decision on potassium dimethyldithiocarbamate, the PMRA will consider all comments received from the public in response to this consultation document. A science-based approach will be applied in making a final decision on potassium dimethyldithiocarbamate. The PMRA will then publish a special review decision document, which will include the decision, the reasons for it, a summary of the comments received on the proposed decision, and the PMRA's response to these comments.

7.0 Other information

The relevant confidential test data on which the proposed decision is based (see References Section of this document) are available for public inspection, upon application, in Health Canada's Reading Room. For more information, please contact Health Canada's [Pest Management Information Service](#).

List of abbreviations

µg	microgram
°C	degrees Celsius
ADD	absorbed daily dose
AEATF II	Antimicrobial Exposure Assessment Task Force II
AHPD	amount handled per day
a.i.	active ingredient
bw	body weight
cm ²	centimeters squared
CR	chemical-resistant
DA	dermal absorption
DACO	data code
ED	exposure duration
FQ	frequency of events
FT	film thickness of metal fluid on hands
hr(s)	hour(s)
IR	inhalation rate
KDD	Potassium dimethyldithiocarbamate
kg	kilogram(s)
L	litre(s)
LADD	lifetime absorbed daily dose
m ³	meters cubed
mg	milligram(s)
min	minute
MOE	margin of exposure
NOAEL	no observed adverse effect level
PEL	permissible exposure limit
PMRA	Pest Management Regulatory Agency
PPE	personal protection equipment
ppm	parts per million
PRVD	Proposed Re-evaluation Decision
q ₁ *	cancer potency factor
RVD	Re-evaluation Decision
SA	Surface area of both hands and forearms
UE	unit exposure
USEPA	United States Environmental Protection Agency

Appendix I Registered products containing potassium dimethyldithiocarbamate

Table 1 Registered products containing potassium dimethyldithiocarbamate¹

Registration number	Marketing class	Registrant	Product name	Guarantee
18606	Technical	Buckman Laboratories of Canada Ltd.	Dimet Broad Spectrum Microbicide	50%
18619	Commercial	Buckman Laboratories of Canada Ltd.	Busan 85 Liquid Microbicide Concentrate	50%
20927	Commercial	Buckman Laboratories of Canada Ltd.	KDD-50 Liquid Microbicide	50%
20928	Commercial	Buckman Laboratories of Canada Ltd.	KDD-25 Liquid Microbicide	25%
20929	Commercial	Buckman Laboratories of Canada Ltd.	KDD-20 Liquid Microbicide	20%
20930	Commercial	Buckman Laboratories of Canada Ltd.	KDD-10 Liquid Microbicide	10%
24006	Commercial	Buckman Laboratories of Canada Ltd.	Bulab 6013 Liquid Microbicide	50%
26282	Commercial	1217826 Ontario Inc.	Biosolv-CBT Liquid Microbicide	10%
25235	Commercial	1221122 Ontario Ltd. DBA Keytech Water Management	Biotech III Industrial Microbiocide	10%
20274	Commercial	Aquarian Chemicals Inc.	Aquarian C403 Liquid Microbicide	20%
25211	Commercial	Chemco Products Inc.	Eclipse 608 Microbicide	20%
21691	Commercial	ControlChem Canada Ltd.	Control Chem 2622 Liquid Microbicide	10%
31066	Commercial	Dubois Chemicals Canada, Inc.	Ipacide LWT 826	25%
31255	Commercial	Dubois Chemicals Canada, Inc.	Ipacide LWT 816L	10%
31201	Commercial	Enercon Water Treatment Ltd.	EC-635 Liquid Microbicide	20%
24229	Commercial	Jacklyn Industries Inc.	WC 8303 Liquid Microbicide	20%
24230	Commercial	Jacklyn Industries Inc.	WC 8304 Liquid Microbicide	10%
34063	Commercial	Jutzi Water Technologies Inc.	Formula MB 3030	10%
34064	Commercial	Jutzi Water Technologies Inc.	Formula MB 3035	50%

Registration number	Marketing class	Registrant	Product name	Guarantee
22278	Commercial	Kimik'O Inc.	BD 120 Liquid Microbiocide	20%
22279	Commercial	Kimik'O Inc.	BD 110 Liquid Microbiocide	10%
19433	Commercial	Klenzoid Canada Inc.	Klenzoid FW 129W Liquid Microbiocide	20%
33950	Commercial	Nalco Canada ULC	Nalcon 60585	20%
30852	Commercial	PMC Water Systems Services Inc.	C-3110 Liquid Microbiocide	10%
22865	Commercial	Produits Chimiques Magnus Ltee	Magnatrol 450A	10%
32879	Commercial	Vanchem Performance Chemicals	Algex SL	25%
22457	Commercial	Water Energy Technologies	Wetcide 4210 Liquid Microbiocide	10%
22458	Commercial	Water Energy Technologies	Wetcide 4220 Liquid Microbiocide	20%

¹ as of 31 May 2022, excluding discontinued products or products with a submission for discontinuation. All products are formulated as solutions.

Appendix II Toxicology reference values for health risk assessment

Table 1 Updated toxicology reference values for use in health risk assessment for potassium dimethyldithiocarbamate (based on the reference values selected for the human health risk assessment of ziram as presented in RVD2018-39)

Exposure scenario	Study	Point of departure and endpoint	Target MOE ¹
Dermal ² and Inhalation ³ - long-term	2-year chronic dietary toxicity study in rats with ziram	NOAEL = 0.70 mg/kg bw/day Clinical chemistry changes, slight anemia, enlarged thyroid, organ weight changes, hyperkeratosis in the forestomach, follicular hypertrophy of the thyroid, atrophy/ degeneration of the sciatic nerve and calf muscle and retarded closure of the epiphyseal plate of the crus bone	100
Cancer	q ₁ * = 1.82 × 10 ⁻² (mg/kg bw/day) ⁻¹ based on incidences of combined mesenteric lymph node and spleen hemangiomas in a chronic/carcinogenicity study in rats with ziram		

¹ MOE refers to a target margin of exposure for occupational and residential assessments

² Since an oral NOAEL was selected, a dermal absorption factor of 100% was used in route-to-route extrapolation.

³ Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) was used in route-to-route extrapolation.

Appendix III Occupational exposure and risk assessment

Table 1 Potassium dimethyldithiocarbamate long-term occupational applicator exposure and risk assessment

Scenario	AHPD ^a		Dermal Exposure ^b (mg/kg bw/day)	Inhalation Exposure ^c (mg/kg bw/day)	Dermal MOE ^d	Inhalation MOE ^d	Combined MOE ^e
	L end-use product/day	kg a.i./day ^f			Target MOE = 100		
Manual Open Pour; Handler PPE: Single layer (long-sleeved shirt, long pants) + CR gloves							
Air Washing Systems, Cooling Tower Systems, Metal Working Fluids (Cutting Fluids), Pulp and Paper Mill Systems (Small Scale Systems)	38	23.28 ^g	0.6214	0.0015	1	470	1
		3.97 ^h	0.1061	0.0025	7	2800	7
Brine Curing, Brine Solutions	18.8	11.56 ^g	0.3086	0.0007	2	950	2
	9.46	5.82 ^g	0.1553	0.0004	5	1900	4
Crude Oil, Diesel and Distillate heating oils; Drilling Muds, Completion Fluids, Packer Fluids, Drilling Fluids	10.6	6.51 ^g	0.1740	0.0004	4	1700	4
		1.11 ^h	0.0297	7.1×10^{-5}	24	9900	24

PPE = personal protection equipment; CR = chemical-resistant; AHPD = amount handled per day; MOE = margin of exposure; NOAEL = no observed adverse effect level; UE = unit exposure; DA = dermal absorption; BW = body weight

Bolded cells indicate MOEs less than the target MOE and risks are not shown to be acceptable.

^a AHPD values (L end-use product/day) based on PMRA# 3084493 and use information PMRA# 2912486. These were converted into kg active ingredient using the % concentration of potassium dimethyldithiocarbamate and density.

^b Dermal Exposure (mg/kg bw/day) = AHPD (kg a.i./day) × UE (2315.38 µg/kg ai) × DA (100%) × 0.001 (µg to mg)/BW (80 kg).

^c Inhalation Exposure (mg/kg bw/day) = AHPD (kg a.i./day) × UE (5.08 µg/kg ai) × 0.001 (µg to mg)/BW (80 kg).

^d MOE = NOAEL (mg/kg bw/day)/Exposure (mg/kg bw/day). Based on a NOAEL of 0.7 mg/kg bw/day from a 2-year dietary chronic toxicity study in rats. Target MOE is 100.

^e Combined MOE = NOAEL (mg/kg bw/day)/(Dermal + Inhalation Exposure (mg/kg bw/day)). Target MOE is 100.

^f kg a.i./day = AHPD (L EP/day) × Concentration of potassium dimethyldithiocarbamate (%) × Product Density (kg/L)

^g Calculated using maximum concentration of potassium dimethyldithiocarbamate (50%) and maximum density (1.23 kg/L).

^h Calculated using minimum concentration of potassium dimethyldithiocarbamate (10%) and minimum density (1.05 kg/L).

Table 2 Potassium dimethyldithiocarbamate occupational applicator cancer exposure and risk assessment

Scenario	ADD (mg/kg bw/day) ^a	LADD (mg/kg bw/day) ^b	Cancer risk ^c
Manual Pour; Handler PPE: Single layer (long-sleeved shirt, long pants) + CR gloves			
Air Washing Systems, Cooling Tower Systems, Metal Working Fluids (Cutting Fluids), Pulp and Paper Mill Systems (Small Scale Systems)	0.6229 ^d	0.1214	7.1 × 10⁻⁵
	0.1063 ^e	0.0207	4.E-04
Brine Curing, Brine Solutions	0.3093 ^f	0.0603	1.E-03
	0.1557 ^g	0.0303	6.E-04
Crude Oil, Diesel and Distillate heating oils; Drilling Muds, Completion Fluids, Packer Fluids, Drilling Fluids	0.1744	0.0340	6.E-04
	0.0298	0.0058	1.E-04

ADD = absorbed daily dose; LADD = lifetime absorbed daily dose; CR = chemical-resistant; PPE = personal protective equipment; AHPD = amount handled per day

Bolded cells indicate cancer risk greater than 1.E-05 and risks are not shown to be acceptable.

^a ADD (mg/kg bw/day) = Dermal + Inhalation Exposure (mg/kg bw/day) (See Appendix II, Table 1).

^b LADD (mg/kg bw/day) = ADD (mg/kg bw/day) × Treatment Frequency (250 days/year) × Exposure Duration (22.2 years) / (365 days/year × Life Expectancy (78 years))

^c Cancer risk = LADD × q₁* (1.82 × 10⁻² (mg/kg bw/day)⁻¹)

^d Based on maximum concentration of potassium dimethyldithiocarbamate (50%) and maximum density (1.23 kg/L).

^e Based on minimum concentration of potassium dimethyldithiocarbamate (10%) and minimum density (1.05 kg/L).

^f Based on maximum AHPD value of 18.8 L EP/day.

^g Based on minimum AHPD value of 9.46 L EP/day.

Table 3 Long-term exposure and risk assessment (cancer and non-cancer) for workers handling metal working fluids

Scenario	% a.i.	Dermal exposure ^a (mg/kg bw/day)	Inhalation exposure ^b (mg/kg bw/day)	Combined MOE ^c	ADD ^d (mg/kg bw/day)	LADD ^e (mg/kg bw/day)	Cancer risk ^f
Metal Working Fluids (Cutting Fluids)	0.1	0.0440	0.0006	16	0.0447	0.0087	2.E-04
	0.008	0.0035	0.00005	200	0.0036	0.0007	1.E-05

MOE = margin of exposure; ADD = absorbed daily dose; LADD = lifetime absorbed daily dose; SA = surface area of both hands and forearms; FT = film thickness of metal fluid on hands; FQ = frequency of events; BW = body weight; PEL = permissible exposure limit; IR = inhalation rate; ED = exposure duration

Bolded cells indicate target MOE not met or cancer risk identified.

^a Dermal Exposure (mg/kg bw/day) = SA (2013 cm²) × % a.i. × FT (1.75 mg/cm²) × FQ (1)/BW (80 kg)

^b Inhalation Exposure (mg/kg bw/day) = PEL (5 mg/m³) × IR (1.25 m³/hr) × % ai × ED (8 hr/day)/BW (80 kg)

^c Combined MOE = NOAEL (mg/kg bw/day)/(Dermal + Inhalation Exposure (mg/kg bw/day)). Target MOE is 100.

^d ADD (mg/kg bw/day) = Dermal Exposure (mg/kg bw/day) + Inhalation Exposure (mg/kg bw/day)

^e LADD (mg/kg bw/day) = ADD (mg/kg bw/day) × Treatment Frequency (250 days/year) × Exposure Duration (22.2 years) / (365 days/year × Life Expectancy (78 years))

^f Cancer risk = LADD × q₁* (1.82 × 10⁻² (mg/kg bw/day)⁻¹)

Appendix IV Proposed label amendments for end-use products containing potassium dimethyldithiocarbamate, for the protection of human health

Information on approved labels of currently registered products should not be removed unless it contradicts the label statements provided below.

Label amendments for commercial class end-use products containing potassium dimethyldithiocarbamate

Personal protective equipment

When mixing, loading, and applying solution end-use product formulations, the following statement is proposed, unless more protective statements are already present:

“Wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes when handling the concentrated product or treated process fluids and during clean-up and repair. Remove and wash contaminated clothing before re-use.”

Use directions

When mixing and loading all potassium dimethyldithiocarbamate end-use product formulations, the following statement is proposed:

“For use with closed loading and transfer systems only (i.e. dry coupling).”

“A closed transfer system is defined as a procedure for removing a pesticide from its original container, rinsing the emptied container and transferring the pesticide and rinse solution through connecting hoses pipes, and coupling that are sufficiently tight to prevent exposure of any person to the pesticide or rinse solution. Furthermore, the closed transfer system must be equipped with a dry coupling system that is designed to drip less than 2 mL per coupling.”

For products with metal working fluid uses, the following statement is proposed:

“**DO NOT** apply in metal working fluids at rates higher than [80 ppm of potassium dimethyldithiocarbamate to be reported in product equivalent value].”

For products having uses in paper/paperboard manufacturing process, the following statement is proposed:

“**DO NOT** use this product in the production of paper or paper coatings that will come in contact with food.”

For products with uses in brine curing/brine solutions, the following statement is proposed:

“Not for use in brine solution/brine curing solutions.”

References

Information considered in the toxicology assessment

Information submitted by the registrant

PMRA document number	Reference
1139742	1987. Teratogenicity Study in Rats of MRD-86-933 (Aquatreat SDM: Approximately 40% Sodium Dimethyldithiocarbamate). DACO 4.5.2.
1139776	1987. Teratogenicity Study in Rabbits of MRD-86-933 (Aquatreat SDM: Approximately 40% Sodium Dimethyldithiocarbamate). DACO 4.5.2.
1159199	1987. Final Report: Teratology Study with Busan® 77 in Rabbits. DACO 4.5.2.
1160404	1985. Final Report: Rat Teratology Study. DACO 4.5.2.
2422459	2014. Waiver Request for Combined Chronic/Oncogenicity and Multigeneration Reproduction Study with Sodium or Potassium Dimethyldithiocarbamate. DACO 0.8.
1900462	1983. NTP Technical Report of the Carcinogenesis Bioassay of Ziram (Cas No. 137-30-4) in F344/N Rats and B6C3F ₁ Mice (Feed Study). National Toxicology Program, National Institute of Health. DACO 4.4.4.
2773654	1989. Epiphyseal Lesions of the Femur and Tibia in Rats Following Oral Chronic Administration of Zinc Dimethyldithiocarbamate (Ziram), Toxicology, 54(1): 45-58. DACO 4.4.5.

Additional information considered

Unpublished information

PMRA document number	Reference
1210422	1996. A Dietary Two-generation Reproduction and Developmental Neurotoxicity Study of Ziram in Rats. DACOs 4.5.1 and 4.5.14.
1210409	1994. Ziram (Technical) Potential Oncogenicity to Mice by Repeated Dietary Administration for 80 Weeks. DACO 4.4.3.
1210432	1994. Combined Chronic Toxicity and Oncogenicity of Ziram (Technical) Administered in the Diet to Rats. DACO 4.4.4.

Published information

PMRA document number	Reference
1900457	1997. Chronic Toxicity Studies with Ziram in F344 Rats and Beagle Dogs, Journal of Pesticide Science, 22: 193-207. DACO 4.4.5.
2773563	2016. Pest Management Regulatory Agency (PMRA), Health Canada, Proposed Re-evaluation Decision Document, PRVD2016-06. Ziram. February 29, 2016.
2946830	2018. Pest Management Regulatory Agency (PMRA), Health Canada, Re-evaluation Decision Document, RVD2018-39. Ziram. December 14, 2018.
2759504, 2759518	2009. United States Environmental Protection Agency, Memorandum: Hazard Assessment for the Reregistration Eligibility Decision (RED) Document of Sodium Dimethyldithiocarbamate and Potassium Dimethyldithiocarbamate, June 2, 2009.
2773561	2011. Pest Management Regulatory Agency (PMRA), Health Canada, Proposed Re-evaluation Decision Document, PRVD2011-05. Sodium and Potassium Dimethyldithiocarbamate Salts. February 14, 2011.
2773562	2012. Pest Management Regulatory Agency (PMRA), Health Canada, Re-evaluation Decision Document, RVD2012-01. Sodium and Potassium Dimethyldithiocarbamate Salts. April 20, 2012.

Information considered in the occupational and non-occupational risk assessment

Studies/information provided by registrant

PMRA document number	Reference
1956512	Examination of Crust Leather for Residuals from a Potential Hide Preservative. DACO 5.14.
2912486	2018. Potassium Dimethyldithiocarbamate Use Directions. August 30, 2018. DACO 5.2.

Studies/information provided by AEATF II Task Force

PMRA document number	Reference
2296582	2012, A Study for Measurement of Potential Dermal and Inhalation Exposure During Manual Pouring of a Liquid Containing an Antimicrobial, DACO: 5.4.
2296584	2013, Supplemental report - A Study for Measurement of Potential Dermal and Inhalation Exposure During Manual Pouring of a Liquid Containing an Antimicrobial, DACO: 5.4.

Published information

PMRA document number	Reference
1945742	Carry, M.L. 1988. Occupational Tenure in 1987: Many Workers have Remained in the Field - Monthly Labour Review. U.S. Bureau of Labour Statistics.
2773561	PMRA, 2011. Proposed Re-evaluation Decision Document Sodium and Potassium Dimethyldithiocarbamate Salts. Proposed Re-evaluation Decision (PRVD2011-05). February 14, 2011.
3354881	USEPA, 2009. Sodium and Potassium Dimethyldithiocarbamate: Revised Occupational and Residential Exposure Assessment for the Registration Eligibility Decision (RED). May 14, 2009.