Proposed Re-evaluation Decision PRVD2011-05

Sodium and Potassium Dimethyldithiocarbamate Salts

(publié aussi en français)

14 February 2011

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. 6604-E2
Ottawa, Ontario
K1A 0K9

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

Canada

ISSN: 1925-0959 (print)
1925-0967 (online)

Catalogue number: H113-27/XXXX (print)
H113-27/XXXX (PDF version)

Table of Contents

Overview

What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the biocides sodium and potassium dimethyldithiocarbamate salts, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration of products containing sodium or potassium dimethyldithiocarbamate for sale and use in Canada.

An evaluation of available scientific information found that products containing sodium and potassium dimethyldithiocarbamate salts do not present unacceptable risks to human health or the environment when used according to label directions. As a condition of the continued registration of the dimethyldithiocarbamate salt uses, new risk-reduction measures are proposed to be included on the labels of affected products. Additional data are being requested as a result of this re-evaluation.

It should be noted that for end-use products containing more than one active ingredient under re-evaluation, registration status might change as a result of the re-evaluation of the remaining affected active ingredient(s).

This proposal affects all end-use products containing sodium or potassium dimethyldithiocarbamate registered in Canada. Once the final re-evaluation decision is made, the registrants will be instructed on how to address the new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for sodium and potassium dimethyldithiocarbamate salts and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of sodium and potassium dimethyldithiocarbamate salts.

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).

[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act.*

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health *and* the environment. Regulatory Directive DIR2001-03, *Pest Management Regulatory Agency Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

Sodium and potassium dimethyldithiocarbamate salts, two of the active ingredients in the current re-evaluation cycle, have been re-evaluated under Re-evaluation Program 1. This program relies as much as possible on foreign reviews, typically United States Environmental Protection Agency (USEPA) Reregistration Eligibility Decision (RED) documents. For products to be re-evaluated under Program 1, the foreign review must meet the following conditions:

- it covers the main science areas, such as human health and the environment, that are necessary for Canadian re-evaluation decisions;
- it addresses the active ingredient and the main formulation types registered in Canada; and
- it is relevant to registered Canadian uses.

Given the outcome of foreign reviews and a review of the chemistry of Canadian products, the PMRA will propose a re-evaluation decision and appropriate risk-reduction measures for Canadian uses of an active ingredient. In this decision, the PMRA takes into account the Canadian use pattern and issues (for example, the federal Toxic Substances Management Policy [TSMP]).

Based on the health and environmental risk assessments published in the 2009 RED, the USEPA concluded that sodium and potassium dimethyldithiocarbamate salts were eligible for reregistration provided risk-reduction measures were adopted. The PMRA compared the American and Canadian use patterns and found the USEPA assessments described in this RED were an adequate basis for the proposed Canadian re-evaluation decision. When necessary, additional risk assessments were conducted by the PMRA.

For more details on the information presented in this overview, please refer to the Science Evaluation section of this consultation document.

What Are Sodium and Potassium Dimethyldithiocarbamate Salts?

Sodium and potassium dimethyldithiocarbamate salts are broad spectrum biocides. They are registered in Canada for use as slimicides in industrial fluids including air washing systems, cooling water systems, petroleum secondary and tertiary recovery water, drilling muds/completion fluids/packer fluids/drilling fluids, pulp and paper mills. They are also used as material preservatives in metal working fluids, and crude oil/diesel/distillate heating oil (during storage). In addition potassium dimethyldithiocarbamate is used for preservation of paper making additives and brine solution (leather industry), while sodium dimethyldithiocarbamate is used for preservation of cotton fabric, paper and paperboard, and paste (starch, alginate and casein).

Health Considerations

Can Approved Uses of Sodium and Potassium Dimethyldithiocarbamate Salts Affect Human Health?

Sodium and potassium dimethyldithiocarbamate salts are unlikely to adversely affect human health when used according to the revised label directions.

People could be exposed to sodium and potassium dimethyldithiocarbamate salts through consumption of food that has come in contact with treated paper products, by wearing/contacting treated leather products; occupational exposure of workers involved in various industrial processes may also occur. The PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

Sodium and potassium dimethyldithiocarbamate salts are unlikely to adversely affect human health provided that risk-reduction measures were implemented. Additional mitigation measures are proposed by the PMRA to further protect the Canadian population.

Environmental Considerations

What Happens When Sodium and Potassium Dimethyldithiocarbamate Salts Are Introduced into the Environment?

Sodium and potassium dimethyldithiocarbamate salts are unlikely to adversely affect the environment due to limited potential for environmental exposure.

Sodium and potassium dimethyldithiocarbamate salts are unlikely to pose an adverse effect to the environment if used according to the revised labels. The PMRA proposes additional label statements regarding environmental hazard and prohibiting effluent discharge into the environment.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human health and the environment. These directions must be followed by law. As a result of the re-evaluation of the dimethyldithiocarbamate salts, the PMRA is proposing further risk-reduction measures for product labels.

Human Health

- Additional hazard label statements
- Additional instructions concerning good hygiene practices in occupational settings
- Additional personal protective equipment (PPE) for workers

- A label statement limiting the use of dimethyldithiocarbamate salts to non-food contact materials and products

Environment

- Improvements to environmental label statements

A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision.

What Additional Scientific Information Is Required?

Data are required as a condition of continued registration under sections 12 and 19 of the *Pest Control Products Act*. The registrants of these active ingredients must provide these data or an acceptable scientific rationale to the PMRA within the time line specified in the section 19 letter or the decision letter. Appendix I lists all data requirements.

Next Steps

Before making a final re-evaluation decision on sodium and potassium dimethyldithiocarbamate salts, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision[2] that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

[2] "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Science Evaluation

1.0 Introduction

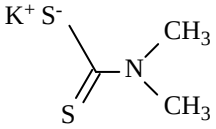
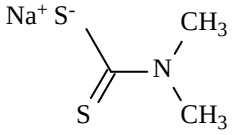
Sodium and potassium dimethyldithiocarbamate salts are broad spectrum biocides that are registered in Canada as for use as slimicides and material preservatives.

All uses of sodium and potassium dimethyldithiocarbamate salts are supported by the Canadian registrants with the exception of sodium dimethyldithiocarbamate use in preservation of alginate paste and, as a surface treatment in paper/paperboard and cotton fabric. These uses were voluntarily discontinued by the registrant of the end-use product Vancide 51 Industrial Preservative (Registration Number 13928).

The PMRA used recent assessments of sodium and potassium dimethyldithiocarbamate salts from the United States Environmental Protection Agency (USEPA) and conducted additional assessment when necessary. The USEPA Reregistration Eligibility Decision (RED) document for Sodium and Potassium Dimethyldithiocarbamate Salts dated June 2009, as well as other information on the regulatory status of the dimethyldithiocarbamate salts in the United States can be found at www.regulations.gov (Docket ID # EPA-HQ-OPP-2009-0321).

2.0 The Technical Grade Active Ingredients, Their Properties and Uses

2.1 Identity of the Technical Grade Active Ingredients

Common name		Potassium dimethyldithiocarbamate	Sodium dimethyldithiocarbamate
Chemical Family		Carbamate	Carbamate
Chemical name			
1	**International Union of Pure and Applied Chemistry (IUPAC)**	Potassium *N*, *N*-dimethyldithiocarbamate	Sodium *N*, *N* - dimethyldithiocarbamate
2	**Chemical Abstracts Service (CAS)**	Carbamic acid, *N*, *N*-dimethyldithio-, monopotassium salt	Carbamic acid, *N*, *N*, - dimethyldithio-, sodium salt
CAS Registry Number		128-03-0	128-04-1
Molecular Formula		$C_3H_6NS_2K$	$C_3H_6NS_2Na$
Structural Formula			
Molecular Weight		159.29	143.21

Based on the manufacturing process used, impurities of human health or environmental concern as identified in the Canada Gazette, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including TSMP Track 1 substances, are not expected to be present in the products.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredients

Property	Potassium Dimethyldithiocarbamate	Sodium Dimethyldithiocarbamate
Vapour pressure at 25°C	Not required as the melting point is > 300 °C.	4.17E-09 mm Hg
Solubility in water	Miscible.	Miscible.
n-Octanol/Water partition coefficient (Kow) at 25ºC	Not available.	<1.0

2.3 Comparison of Use Patterns in Canada and the United States

Sodium and potassium dimethyldithiocarbamate salts are biocides registered in Canada for use as:

- Slimicides in industrial fluids including air washing systems, cooling water systems, petroleum secondary and tertiary recovery water, drilling muds/completion fluids/packer fluids/drilling fluids, pulp and paper mills;
- Material preservatives in metal working fluids, and crude oil/diesel/distillate heating oil (during storage).

In addition potassium dimethyldithiocarbamate is used for preservation of paper making additives and brine solution (leather industry), while sodium dimethyldithiocarbamate is used for preservation of cotton fabric, paper and paperboard, and paste (starch, alginate and casein).

Currently registered in Canada, there are 1 technical and 31 commercial end-use products containing potassium dimethyldithiocarbamate, and 1 technical, 1 manufacturing concentrate and 10 commercial end-use products containing sodium dimethyldithiocarbamate. Products containing sodium and potassium dimethyldithiocarbamate salts are formulated as a solution and can be applied by commercial workers via an open pour or a closed system (metering pump).

In the US, at the time of the RED, sodium and potassium dimethyldithiocarbamate salts were registered as material preservatives for fuels, metal working fluids, paints, coatings, adhesives, cloth and paper/paperboard and, as antifoulants/slimicides in a variety of liquids including industrial/commercial cooling water, air washer water, sugar mill/pulp process water, marine heat exchanger, gas/oil recovery fluid, industrial wastewater treatment systems, industrial water purification systems, reverse osmosis water systems and pasteurizing cooling water.

The American and Canadian uses were compared and it was determined that Canadian uses are encompassed by the American use pattern, with the exception for potassium dimethyldithiocarbamate use for preservation of the brine solution. However, based on the comparison of formulation types, application rates and methods, it was concluded that the USEPA RED for the sodium and potassium dimethyldithiocarbamate salts provide sufficient information for the re-evaluation of all Canadian uses as slimicides or material preservatives (including the use in the brine solution). Additional risk assessments were conducted by the PMRA to ensure the safety of the Canadian population.

All current uses, except the uses in alginate paste and as surface treatment of cotton fabric and paper/paper board, are being supported by the Canadian registrants and were, therefore, considered in the re-evaluation of sodium and potassium dimethyldithiocarbamate salts. The uses of sodium dimethyldithiocarbamate in alginate paste and, as a surface treatment in paper/paperboard and cotton fabric will be removed from the label of the end-use product Vancide 51 Industrial Preservative (Registration Number 13928). Appendix II lists all dimethyldithiocarbamate salt products that are registered as of October 4, 2010, under the authority of the *Pest Control Products Act*.

3.0 Impact on Human Health and the Environment

In its 2009 RED, the USEPA concluded that the end-use products formulated with sodium and potassium dimethyldithiocarbamate salts met the safety standard under the American *Food Quality Protection Act* and would not pose unreasonable risks or adverse effects to humans and the environment if used according to the revised product labels.

3.1 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels at which no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species.

In Canada, exposure to sodium and potassium dimethyldithiocarbamate salts may occur through consumption of food that has come in contact with treated paper products, through wearing/contacting treated leather products, and through occupational exposure. When assessing health risks, the PMRA considers two key factors: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers).

Sodium dimethyldithiocarbamate is acutely moderately toxic via the dermal route, has very low toxicity via the inhalation route and is slightly toxic via the oral route of exposure. It is corrosive to the eye and mildly to slightly irritating to the skin but it is not a dermal sensitizer. Potassium dimethyldithiocarbamate is acutely slightly toxic via oral and dermal routes of exposure. It is a moderate to slight eye irritant and a slight skin irritant and a dermal sensitizer. An acute inhalation study for potassium dimethyldithiocarbamate was not available.

Based on the acute toxicity and irritancy results, the following mitigation measures are proposed by the PMRA to further protect workers exposed to products containing:

- Sodium dimethyldithiocarbamate – protective eyewear, a long-sleeved shirt, long pants and chemical resistant gloves during handling the product, clean-up and repair activities; hazard label statement (eye and skin irritation potential).
- Potassium dimethyldithiocarbamate – Personal Protective Equipment (PPE) as above; hazard label statement (sensitization and eye irritation potential).

Based on positive mutagenicity results observed in a bacterial reverse mutation test and in an *in-vitro* mammalian cell gene mutation test, the USEPA requested additional chronic/oncogenicity and 2-generation reproduction studies as confirmatory data in order to support uses associated with long-term/high volume exposure (in this case, the metal working fluid use).

A data gap was identified by the PMRA in the toxicology database for dimethyldithiocarbamate salts, therefore, the PMRA proposes to request the following studies to support the Canadian dimethyldithiocarbamate salts uses (Section 12):

DACO 4.4.4 Combined Chronic/Oncogenicity (rat and mouse)
DACO 4.5.1 Multigeneration Reproduction (rat)

The USEPA's toxicological endpoints for assessing risk to human health are summarized in Appendix III.

3.1.1 Contaminants and Degradates/Metabolites of Toxicological Concern

Ethylene thiourea
Sodium and potassium dimethyldithiocarbamate salts are chemically similar to ethylenebisdithiocarbamates, a group of non-systemic fungicides including mancozeb, maneb, zineb and nabam, which can degrade into ethylene thiourea (ETU), a potentially hazardous chemical. However, based on results from the hydrolysis study, as well as monitoring data showing no detection of ETU in the presence of sodium or potassium dimethyldithiocarbamate alone, the USEPA concluded that ETU was not a degradation product of concern for dimethyldithiocarbamate salts.

Carbon disulfide and dimethylamine
Sodium and potassium dimethyldithiocarbamate salts are not stable in aqueous conditions and are prone to degradation to form dimethylamine (DMA) and carbon disulfide (CS_2). The rate of degradation increases as pH decreases. Both CS_2 and DMA are highly volatile, with a vapour pressure of 4.7×10^7 mPa and 2.02×10^8 mPa, respectively. Inhalation was found to be the major route of exposure to both degradates. Exposure of workers to CS_2 and DMA is discussed further in Section 3.1.2.2.

3.1.2 Occupational Exposure and Risk Assessment

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used 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.

Workers can be exposed to dimethyldithiocarbamate salts while handling the end-use products and through post-application exposure to the treated fluids or materials.

3.1.2.1 Handler Exposure and Risk

Based on the current use pattern, it was determined that there is a potential for short- to long-term dermal and inhalation exposure of workers to sodium and potassium dimethyldithiocarbamate salts while adding the products to industrial process fluids or material via an open liquid pour or a closed system (metering pump).

Taking into consideration the maximum application rates and the volume/amount of treated fluids or materials, the USEPA determined that the following scenarios are associated with the highest exposure of workers adding sodium and potassium dimethyldithiocarbamate salts by an open liquid pour for:

- Material preservative uses - the paint scenario
- Slimicide uses – the air washer/cooling water system and oil drilling fluids and muds scenarios

For the representative open liquid pour scenarios, short- to long term dermal and inhalation exposure of workers (wearing baseline PPE and gloves) were assessed using unit exposure values from the Chemical Manufacturers Association (CMA) antimicrobial exposure study. Short- to long-term dermal and inhalation MOEs were above the target MOE of 1000 for all representative scenarios, indicating no risk of concern.

For workers applying the chemicals via a closed system (metering pump), the risk of exposure to sodium and potassium dimethyldithiocarbamate salts is considered to be low.

Based on PPE worn by workers in the CMA study used in the above assessments and the acute toxicity properties of sodium and potassium dimethyldithiocarbamate salts, the PPE consisting of a long-sleeved shirt, long pants, gloves and protective eyewear is proposed by the PMRA for all workers during handling activities, clean-up and repair. Additional instructions concerning good hygiene practices are also proposed to be included on all end-use product labels.

In addition, as application rates and directions for use are not listed on the label of the end-use product Busan 85 Liquid Microbicide Concentrate (Registration Number 18619), the PMRA requires the registrant to amend the label to include detailed directions for use instructions for all the uses that are eligible for continued registration.

The proposed label amendments are listed in Appendix IV.

3.1.2.2 Post-application Exposure and Risk

Post-application exposure to dimethyldithiocarbamate salts
The post-application occupational risk assessment considers exposures of workers to sodium and potassium dimethyldithiocarbamate salts in industrial fluids, metal working fluids, brine solution and in the finished products (for example, paper).

The potential post-application exposure of workers and risk from sodium and potassium dimethyldithiocarbamate salts is negligible in the industrial settings. The potential for post-application worker exposure to sodium and potassium dimethyldithiocarbamate salts in paper, paperboard is expected to be minimal considering that the actives are added during the manufacturing process and are expected to be bound to the material. Consequently, no mitigation measures are proposed by the PMRA.

The USEPA determined that there is a potential for post-application worker exposure to sodium and potassium dimethyldithiocarbamate salts in the treated metal working fluids. However, short- to long term dermal and inhalation MOEs above the target MOE of 1000 indicated no risk of concern.

Post-application dermal and inhalation exposure of workers removing hides to potassium dimethyldithiocarbamate from the treated brine solution should be minimal taking into consideration the low vapour pressure value of potassium dimethyldithiocarbamate. Dermal exposure to potassium dimethyldithiocarbamate is expected to be minimal considering the low application rate.

Post-application exposure to degradates of toxicological concern
The PMRA determined that there are two potential post-application scenarios which may result in workers exposure to degradates of toxicological concern, DMA and CS_2:

- workers inhaling brine solution vapours while removing hides from the treated brine solution by hand
- workers inhaling metal working fluid aerosols while operating a machine

The PMRA is unable to assess human health risks from exposure to DMA and CS_2 at this time due to the lack of appropriate exposure data. Therefore, the PMRA requires under Section 19 of the *Pest Control Products Act* the following data to complete the re-evaluation of dimethyldithiocarbamate salts:

DACO 5.14 Existing air monitoring data for carbon disulfide (CS_2) and dimethylamine (DMA) or an acceptable scientific rationale demonstrating that occupational exposure limits set by the provincial regulations are met (potassium dimethyldithiocarbamate use in the brine solution; potassium dimethyldithiocarbamate and sodium dimethyldithiocarbamate uses in metal working fluids)

For workers removing hides from the treated brine solution, in addition to baseline PPE required for all workers, the PMRA proposes long chemical resistant gloves, an impermeable apron, and rubber safety boots to mitigate potential skin irritation effects of potassium dimethyldithiocarbamate.

The proposed label amendments are listed in Appendix IV.

3.1.3 Non-Occupational Exposure and Risk Assessment

The currently registered Canadian uses of sodium and potassium dimethyldithiocarbamate salts are limited to industrial settings and therefore, residential handler exposure is not expected.

Individuals in residential settings may be exposed to sodium or potassium dimethydithiocarbamate residues in food as a result of indirect food contact with treated paper or by wearing or coming in contact with leather products made from hides cured in the treated brine solution.

3.1.3.1 Residential Post-application Exposures and Risk

The PMRA determined that exposure of individuals to potassium dimethyldithiocarbamate residues in leather products is expected to be negligible based on the study provided by the registrant showing no detectable levels of the active ingredient in leather made from treated hides.

3.1.3.2 Exposure from Food and Drinking Water

Acute dietary risk is estimated by determining how much of a pesticide residue may be ingested with the daily diet and comparing this potential exposure to an acute reference dose, which is the dose at which an individual could be exposed over the course of one day and expect no adverse health effects. The acute reference dose is referred to as the ARD in Canada, and, in the RED, it is expressed as the acute population adjusted dose (aPAD). The ARD or aPAD is based on a relevant endpoint from toxicology studies and on safety factors protective of the most sensitive population subgroup (see Appendix III).

Chronic dietary risk is estimated by determining how much of a pesticide residue may be ingested with the daily diet and comparing this potential exposure to an acceptable daily intake, which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. The acceptable daily intake is referred to as the ADI in Canada, and, in the RED, it is expressed as the chronic population adjusted dose (cPAD). The ADI or cPAD is based on a relevant endpoint from toxicology studies and on safety factors protective of the most sensitive population subgroup (see Appendix III).

Dietary exposure resulting from indirect food contact with paper was assessed by the USEPA. The dietary exposure estimates for paper uses did not exceed the USEPA's level of concern for the acute or chronic exposure durations. For the most sensitive population subgroup (children), the acute exposures were reported to occupy 0.54% to 1.5% of the aPAD, and the chronic exposures were reported to occupy 35% to 100% of the cPAD. Although, children's chronic exposure from the paper coating uses was estimated to occupy 100% of the cPAD, the estimated exposure doses were expected to be overestimated since the calculations were based on the conservative assumption of a 100% migration of the residues from treated paper to food. On this basis, the USEPA concluded that the risks associated with dietary exposure were not of concern.

For a pesticide that is used as a material preservative in the production of materials that are intended for food contact (for example, paper, paperboard), a no-objection status issued by Health Canada is required to ensure the safety of the product. For end-use products which did not obtain a no-objection status, a label statement limiting the use of the pesticide as a material preservative to non-food contact materials and products is proposed by the PMRA.

The proposed label amendments are listed in Appendix IV.

The USEPA concluded that sodium and potassium dimethyldithiocarbamate salts are not stable in soil or water. Considering application of dimethyldithiocarbamate salts as a material preservative or slimicide in industrial settings, it was concluded that drinking water contamination is unlikely.

This conclusion is considered relevant to the Canadian situation and no further mitigation measures are proposed by the PMRA. No Canadian water monitoring data are available.

3.1.3.3 Aggregate Risk Assessment

Aggregate risk combines the different routes of exposure to sodium or potassium dimethyldithiocarbamate. Acute and chronic aggregate risk assessments are comprised of contributions from food and drinking water exposures. Short- and intermediate-term aggregate risk assessments are comprised of contributions from food, drinking water and non-occupational exposure (dermal, inhalation).

Exposures to sodium and potassium dimethyldithiocarbamate salts from drinking water and residential sources are not expected based on the Canadian use pattern. Consequently, an aggregate risk assessment was not required by the PMRA

3.1.4 Cumulative Effects

The USEPA has not determined whether sodium and potassium dimethyldithiocarbamate salts have a common mechanism of toxicity with other substances or whether it shares a toxic metabolite produced by other substances. Therefore, it was assumed that sodium and potassium dimethyldithiocarbamate salts do not share a common mechanism of toxicity with other substances and a cumulative risk assessment was not required. Consequently, a cumulative risk assessment was not required by the PMRA.

3.2 Environment

3.2.1 Environmental Risk Assessment

The acute toxicity studies with sodium dimethyldithiocarbamate salts showed that the dimethyldithiocarbamate salts are moderately to highly toxic to freshwater fish and highly to very highly toxic to freshwater invertebrates.

Environmental exposure to sodium and potassium dimethyldithiocarbamate salts used for industrial process fluids and material preservatives is considered to be minimal when the products are applied according to label directions and precautions. On this basis, no additional mitigation measures are required at this time; however, improvements to the environmental label statements regarding environmental hazard and effluent discharge are proposed by the PMRA.

The proposed label amendments are listed in Appendix IV.

3.3 Pest Control Product Policy Considerations

3.3.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances (those that meet all four criteria outlined in the policy, namely, CEPA-toxic or equivalent, predominantly anthropogenic, persistent and bio-accumulative).

During the re-evaluation process, dimethyldithiocarbamate salts were assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy,* and evaluated against the Track 1 criteria for persistence and bioaccumulation. In order for dimethyldithiocarbamate salts or their transformation products to meet Track 1 criteria, the criteria for both bioaccumulation and persistence (in one media) must be met.

Based on structural and chemical similarities, the USEPA determined that the environmental fate studies conducted with sodium dimethyldithiocarbamate can be used to fulfill data requirements for potassium dimethyldithiocarbamate.

Sodium dimethyldithiocarbamate does not meet the Track 1 criterion for persistence, as its half-life value in water (less than 67 days) is below the cut-off value of 182 days. Sodium dimethyldithiocarbamate does not meet the Track 1 criterion for bioaccumulation, as its octanol-water partition coefficient (log K_{ow} of -2.41) is below the Track 1 criterion of 5.

On this basis, the PMRA concluded that both sodium and potassium dimethyldithiocarbamate salts do not meet Track 1 criteria and therefore, are not candidates for Track 1 classification.

3.3.2 Contaminants and Formulants of Health or Environmental Concern

During the re-evaluation of sodium and potassium dimethyldithiocarbamate salts, contaminants in the technical were compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*. The list is used as described in the PMRA Notice of Intent NOI2005-01 and is based on existing policies and regulations including: DIR99-03; and DIR2006-02, and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusion:

- Technical grade sodium and potassium dimethyldithiocarbamate salts do not contain any contaminants of health or environmental concern identified in the *Canada Gazette.*

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02.

4.0 Incident reports

Starting 26 April 2007, registrants are required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame.

There were no incident reports submitted for sodium or potassium dimethyldithiocarbamate salts as of October 4, 2010.

5.0 Organization for Economic Co-operation and Development Status of Sodium and Potassium Dimethyldithiocarbamate Salts

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups 33 member countries and provides governments with a setting in which to discuss, develop and perfect economic and social policies. They compare experiences, share information and analyses, seek answers to common problems, and work to co-ordinate domestic and international policies to allow for consistency in practices across nations.

Based on available information, sodium and potassium dimethyldithiocarbamate salts have not been prohibited for use in any of the OECD member states.

As described earlier in this document, the United States, also an OECD member, assessed the registration of all uses of sodium and potassium dimethyldithiocarbamate salts in 2009 and concluded using dimethyldithiocarbamate salts as pesticides does not result in unreasonable adverse effects to human health or the environment provided the risk-reduction measures recommended in the RED document were implemented.

The Canadian re-evaluation of sodium and potassium dimethyldithiocarbamate salts is largely based on the 2009 USEPA assessments and included additional assessments when necessary. Based on these risk assessments, the PMRA concluded that additional mitigation measures are required to further protect human health and the environment.

6.0 Proposed Re-evaluation Decision

The PMRA is proposing continued registration of products containing sodium and potassium dimethyldithiocarbamate salts for sale and use in Canada with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and the environment:

- Additional hazard label statements
- Additional instructions concerning good hygiene practices in occupational settings
- Additional personal protective equipment (PPE) for workers
- A label statement limiting the use of dimethyldithiocarbamate salts to non-food contact materials and products
- Improvements to environmental label statements

The labels of Canadian end-use product must be revised to include the label statements listed in Appendix IV. A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision.

Data are required as a condition of continued registration under Section 12 and 19 of the *Pest Control Products Act*. The registrants of these active ingredients must provide these data or an acceptable scientific rationale to the PMRA within the time line specified in the Section 19 letter and in the decision letter. Appendix I lists all data requirements.

It should be noted that for end-use products containing more than one active ingredient under re-evaluation, registration status might change as a result of the re-evaluation of the remaining affected active ingredients.

7.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2001-03, *Pest Management Regulatory Agency Re-evaluation Program,* and DACO tables can be found on the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra.infoserv@hc-sc.gc.ca.

The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxiques-toxics/.

The USEPA RED document for dimethyldithiocarbamate salts is available at www.regulations.gov (Docket ID EPA-HQ-OPP-2009-0321).

List of Abbreviations

0C	degree(s) Celsius
µg	microgram
ADI	acceptable daily intake
aPAD	acute population adjusted dose
ARD	acute reference dose
CAS	Chemical Abstracts Service
CEPA	*Canadian Environmental Protection Act*
CMA	Chemical Manufacturers Association
cPAD	chronic population adjusted dose
CS_2	carbon disulfide
DACO	data code
DMA	dimethylamine
ETU	ethylene thiourea
FQPA	*Food Quality Protection Act*
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
Kow	*n*-octanol–water partition coefficient
LOAEL	lowest observed adverse effect level
mg	milligram(s)
mm Hg	millimetre mercury
mPa	milliPascal(s)
MOE	margin of exposure
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
pH	-log10 hydrogen ion concentration
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
PRVD	Proposed Re-evaluation Decision
RED	Reregistration Eligibility Decision
SF	safety factor
TSMP	Toxic Substances Management Policy
UF	uncertainty factor
USEPA	United States Environmental Protection Agency

Appendix I Additional Data Requirements

The following data are required as a condition of continued registration under section 12 of the *Pest Control Products Act*. The registrants are required to provide these data or an acceptable scientific rationale within the timeline specified in the decision letter that will be sent to the registrant by the PMRA.

To support the continued registration of the technical grade sodium and potassium dimethyldithiocarbamate salts the following data are required:

DACO 4.4.4 Combined Chronic/Oncogenicity study (rat and mouse)
DACO 4.5.1 Multigeneration Reproduction (rat)

These studies must be conducted with the Canadian technical grade active ingredient or a product with equivalent formulation and guarantee and be conducted according to the appropriate USEPA Office of Prevention, Pesticides and Toxic Substances or Organisation for Economic Co-operation and Development guidelines.

Data to clarify current levels of degradates of toxicological concern in the air are required. These data are required under section 19 of the *Pest Control Products Act*. The affected registrants must provide these data or an acceptable scientific rationale to the PMRA within the timeline specified in the section 19 letter.

DACO 5.14 Existing air monitoring data for CS_2 and DMA or an acceptable scientific rationale demonstrating that exposure limits are met (potassium dimethyldithiocarbamate use in the brine solution and in metal working fluids; and sodium dimethyldithiocarbamate uses in metal working fluids)

Appendix II Registered Products Containing Dimethyldithiocarbamate Salt as of October 4, 2010.

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (%)
Potassium Dimethyldithiocarbamate					
18606	T	Buckman Laboratories of Canada Ltd.	Dimet Broad Spectrum Microbicide	Solution	50
18619	C	Buckman Laboratories of Canada Ltd.	Busan 85 Liquid Microbicide Concentrate	Solution	50
19039	C	NCH Canada Inc.	Sana Cool II	Solution	10
19433	C	Klenzoid Co. Ltd.	Klenzoid Fw 129W Liquid Microbiocide	Solution	20
20274	C	Aquarian Chemicals Inc.	Aquarian C403 Liquid Microbicide	Solution	20
20927	C	Buckman Laboratories of Canada Ltd.	Kdd-50 Liquid Microbicide	Solution	50
20928	C	Buckman Laboratories of Canada Ltd.	Kdd-25 Liquid Microbicide	Solution	25
20929	C	Buckman Laboratories of Canada Ltd.	Kdd-20 Liquid Microbicide	Solution	20
20930	C	Buckman Laboratories of Canada Ltd.	Kdd-10 Liquid Microbicide	Solution	10
21125	C	NCH Canada Inc.	Cool Saver	Solution	10
21691	C	Controlchem Canada Ltd.	Control Chem 2622 Liquid Microbicide	Solution	10
21695	C	NCH Canada Inc.	Aqua-San Liquid Microbiocide	Solution	10
22278	C	Les Enterprises Ataki Enterprises Inc.	BD 120 Liquid Microbiocide	Solution	20
22279	C	Les Enterprises Ataki Enterprises Inc.	BD 110 Liquid Microbiocide	Solution	10
22418	C	Quebec-O-Chimie Inc.	Unica 210	Solution	10
22457	C	Water Energy Technologies	Wetcide 4210 Liquid Microbicide	Solution	10
22458	C	Water Energy Technologies	Wetcide 4220 Liquid Microbicide	Solution	20
22865	C	Produits Chimiques Magnus Ltee	Magnatrol 450A	Solution	10
22937	C	Henkel Canada Corporation	P3 Biocide 2427	Solution	50
24006	C	Buckman Laboratories of Canada Ltd.	Bulab 6013 Liquid Microbicide	Solution	50

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (%)
24229	C	Jacklyn Industries Inc.	WC 8303 Liquid Microbicide	Solution	20
24230	C	Jacklyn Industries Inc.	WC 8304 Liquid Microbicide	Solution	10
25211	C	Buckman Laboratories of Canada Ltd.	Eclipse 608 Microbicide	Solution	20
25235	C	1221122 Ontario Ltd. DBA Keytech Water Management	Biotech III Industrial Microbiocide	Solution	10
25907	C	T. Donovan & Son (1997) Limited	Triple C Chemical Biocide 592 Liquid Microbicide	Solution	10
26226	C	Kem Canada Mfg.	Kemtreet 034	Solution	10
26282	C	Norkem Inc.	Biocide B Liquid Microbicide	Solution	10
27043	C	Produits Chimiques Magnus Ltee	Magnatrol 451A	Solution	20
27047	C	Pts Water Management Inc.	Probio-3 Liquid Microbicide	Solution	10
27064	C	Zep Manufacturing Company of Canada	Zep B-T 7400 Liquid Microbicide	Solution	50
27299	C	Custom Blended Treatments Ltd.	C.B.T. Bio B	Solution	20
27640	C	Qwatro Corporation	QT880	Solution	10
Sodium Dimethyldithiocarbamate					
13928	C	R.T. Vanderbilt Company Inc.	Vancide 51 Industrial Preservative	Solution	27.6
15934	C	Drew Canada, Ashland Canada Corp.	Amerstat 272	Solution	15
18211	C	Akzo Nobel Surface Chemistry LLC	Aquatreat Dnm-30 Industrial Microbiocide	Solution	15
18211.12	C	Emerald Foam Control, LLC	Kcide 800	Solution	15
18211.15	C	Kemira Chemicals, Inc.	Fennosan 131-C	Solution	15
18775	C	Drew Canada, Ashland Canada Corp.	Biosperse 280 Liquid For Control Of Bacteria & Fungi	Solution	15
18961	T	Akzo Nobel Surface Chemistry LLC	Aquatreat Nm Manufacturing Concentrate	Solution	40
18962	M	Akzo Nobel Surface Chemistry LLC	Aquatreat Dnm-360 Manufacturing Concentrate	Solution	17
20127	C	Buckman Laboratories Of Canada Ltd.	Busan 1035 Liquid Microbicide	Solution	15

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (%)
22654	C	Akzo Nobel Surface Chemistry LLC	Aquatreat SDM Industrial Microbicide	Solution	40
23182	C	Dubois Chemicals Canada, Inc.	X-Cell 419 Papermill Slimicide	Solution	15
23501	C	Nalco Canada Company	Nalcon 7614 Pulp & Paper Slimicide	Solution	15

T – technical grade products, C – commercial products, M – manufacturing concentrate product

Appendix III Toxicological Endpoints for Dimethyldithiocarbamate Salt Risk Assessments

Exposure Scenario	Dose Used in Risk Assessment	Study and Toxicological Effects	Target UF/SF or MOE
Dermal All durations (short, intermediate, long-term)	**dermal NOAEL =** 60 mg/kg/day	90-Day Dermal toxicity study; LOAEL = 120 mg/kg/day based on decreased leukocyte and platelet counts.	**MOE =** 1000 (10 fold interspecies extrapolation, 10 fold intraspecies variation, 10 fold database SF)
Inhalation All durations (short, intermediate, long-term)	**oral NOAEL** = 2 mg/kg/day	90-day subchronic oral study; LOAEL = 100 mg/kg/day and NOAEL = 2 mg/kg/day based on decreased erythrocyte counts, increased glucose concentration, and increased alkaline phosphatase activity in females, and exocrine pancreatic atrophy with fibrosis in males.	**MOE =** 1000 (10 fold interspecies extrapolation, 10 fold intraspecies variation, 10 fold database SF)
Acute Dietary (Female 13-50 population)	**oral NOAEL =** 13 mg/kg/day	Rabbit developmental study was selected for females (13 to 50 yrs of age); LOAEL = 38 mg/kg/day based on clinical signs (reddish-colored material in cage trays), and possible increased maternal death and abortions.	**aPAD** = 0.13 mg/kg/day **UF =** 100 (10 fold interspecies extrapolation, 10 fold intraspecies variation, FQPA SF = 1 fold)
Acute Dietary (General population)	**oral NOAEL =** 20 mg/kg	**Co-critical studies:** Acute neurotoxicity study; LOAEL = 790 mg/kg/day based on clinical signs of toxicity, numerous functional observational battery parameter effects, and decreased motor activity. NOAEL = 20 mg/kg /day Sub-chronic neurotoxicity study; LOAEL = 98.75 mg/kg/day based on salivation, oral staining and decreased body weight. NOAEL = 1.98 mg/kg/day	**aPAD** = 0.20 mg/kg/day **UF =** 100 (10 fold interspecies extrapolation, 10 fold intraspecies variation, FQPA SF = 1 fold)
Chronic Dietary (All population)	**oral NOAEL** = 2 mg/kg/day	90-day subchronic oral study. LOAEL = 100 mg/kg/day and NOAEL = 2 mg/kg/day based on decreased erythrocyte counts, increased glucose concentration, and increased alkaline phosphatase activity in females, and exocrine pancreatic atrophy with fibrosis	**cPAD** = 0.002 mg/kg/day **UF =** 1000 (10 fold interspecies extrapolation, 10 fold intraspecies variation, 10 fold database SF, FQPA SF = 1 fold)

UF/SF - uncertainty and/or safety factors for dietary assessments; MOE - margin of exposure for occupational or residential assessments; NOAEL - no observed adverse effect level; LOAEL - lowest observed adverse effect level; FQPA SF - Food Quality Protection Act safety factor; aPAD - acute population adjusted dose; cPAD - chronic population adjusted dose

Appendix IV Label Amendments for Products Containing Dimethyldithiocarbamate Salt

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Information on labels of currently registered products should not be removed unless it contradicts the label statements below.

A submission to request label revisions will be required within 90 days of finalization of the re-evaluation decision.

The labels of the Canadian products must be revised to include the following statements to further protect workers and the environment.

I) For the technical grade product and end-use products containing potassium dimethyldithiocarbamate, the following key signal words must be included on the primary panel of the label:

CAUTION POISON
CAUTION-EYE IRRITANT
POTENTIAL SKIN SENSITIZER

The "CAUTION POISON" signal word should also be accompanied by the skull & crossbones symbol within an upside down triangle.

II) For all end-use products containing potassium dimethyldithiocarbamate, the following statements must be included in the section entitled **PRECAUTIONS**:

Harmful if swallowed.
Potential skin sensitizer.
Causes eye irritation. DO NOT get in eyes.

III) For the technical grade and end-use products containing sodium dimethyldithiocarbamate, the following key signal words must be included on the primary panel of the label:

CAUTION POISON
CAUTION SKIN IRRITANT
DANGER CORROSIVE TO EYES

The "CAUTION POISON" signal word should also be accompanied by the skull and crossbones symbol within an upside down triangle.

IV) For all end-use products containing sodium dimethyldithiocarbamate, the following statements must be included in the section entitled **PRECAUTIONS**:

> Harmful if swallowed.
> CORROSIVE to the eye. DO NOT get in eyes.
> May irritate the skin. Avoid contact with skin.

V) For all end-use products containing sodium or potassium dimethyldithiocarbamate salt, the following statements must be included in the section entitled **PRECAUTIONS:**

> Follow manufacturer's instructions for cleaning/maintaining personal protective equipment (PPE). If no such instructions exist for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.
>
> Users should wash hands before eating, drinking, chewing gum, using tobacco or using the toilet.
>
> Users should remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing.
>
> Users should remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible wash thoroughly.
>
> Wear long-sleeved shirt, long pants, chemical-resistant gloves, protective eyewear (goggles or face shield) when handling the product, clean-up and repair activities.

VI) For potassium dimethyldithiocarbamate use for preservation of the brine solution, the following statement must be included in the section entitled **PRECAUTIONS,** immediately following the PPE requirement described above:

> In addition, wear long chemical-resistant gloves, an impermeable apron and rubber safety boots when removing cured hides/skins from the brine raceway.

VII) For use in paper/paperboard manufacturing processes, the following statement must be included in the section entitled **DIRECTIONS FOR USE** (unless a no-objection status is granted by Health Canada for use of the active as a material preservative in paper):

> DO NOT use to treat paper or paperboard which will contact food.

VIII) For all dimethyldithiocarbamate salt end-use products, the following statement must be included in the section entitled **ENVIRONMENTAL HAZARDS**:

> Toxic to aquatic organisms.

IX) For all dimethyldithiocarbamate salt end-use products, the following statements must be included in the section entitled **DIRECTIONS FOR USE**:

> DO NOT discharge effluent containing this product into sewer systems, lakes, streams, ponds, estuaries, oceans or other waters. DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

X) The following uses must be removed from the label of the end-use product Vancide 51 Industrial Preservative (Registration Number 13928):

> Mould-resistant paper and paperboard
> Preservation of cotton fabric
> Preservative for alginate paste

XI) For the label of the end-use product Busan 85 Liquid Microbicide Concentrate (Registration Number 18619), the **DIRECTIONS FOR USE** section, must be amended to include application rates and application methods for the following uses:

> Pulp and paper mill systems
> Papermaking additives
> Cooling water systems and industrial airwashers
> Petroleum secondary recovery waterflooding
> Water-based drilling muds, packer fluids, completion fluids and other water-based drilling fluids
> Metal working fluids
> Crude oil, diesel and distillate heating oils
> Brine solutions/Brine curing (leather industry)

References

A Studies considered in the Chemistry Assessment

List of Studies/Information Submitted By Registrant (Unpublished)

PMRA Document Number 1737553
Reference: Chemistry KDD-BUK-2. Specifications and Analytical Methodology Required for Registration of the Technical Active Ingredient DIMET. Attachment I - Odour, Boiling Point, Solubility, Vapour Pressure, pH, Stability, Viscosity, Attachment II - Colour, Physical State, Relative Density, Solubility, Attachment III - Storage Stability, Corrosion Characteristics.

PMRA Document Number 1737600
Reference: Chemistry KDD-BUK-2. Confidential Appendix to Part 2. Specifications and Analytical Methodology Required for Registration of the Technical Active Ingredient, DIMET. Attachment I - Product Identity, Manufacturing Process, Discussion of Impurities and Supplement.

PMRA Document Number 1303341
Reference: Alco Chemical Corporation, Part 2 Product Chemistry for Aquatreat NM.

B Studies considered in the Health Risk Assessment

List of Studies/Information Submitted By Registrant (Unpublished)

PMRA Document Number 1956512
Reference: Bailey GD and RH Miller, Jr. 1991. Examination of Crust Leather for Residuals from A Potential Hide Preservative. The Journal of American Leather Chemists Association, 86 (5): 185. Data Numbering Code: 5.14.

PMRA Document Number 1919815
Reference: Flynn F., 2010, Vancide 51 (Reg No 13928) Paste Use, Data Numbering Code: 5.2.

PMRA Document Number 1917185
Reference: Paquin S., 2010, Use Information for Busan 85 Liquid Microbicide Concentrate, Data Numbering Code: 5.2.