Proposed Re-evaluation Decision PRVD2016-12

Sodium Omadine

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Overview

What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the antimicrobial active ingredient sodium omadine, 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 omadine for sale and use in Canada.

An evaluation of available scientific information found that some uses of products containing sodium omadine do not present unacceptable risks to human health or the environment when used according to the proposed label directions. The use of sodium omadine as a material preservative in latex emulsions (paints, adhesives, caulks, grouts, patching compounds, and sealants) is proposed to be cancelled to address potential risks of concern to human health. As a requirement of the continued registration of remaining sodium omadine uses, new risk-reduction measures are proposed for end-use products registered in Canada including revised label directions. No additional data are being requested at this time.

This proposal affects the end-use product containing sodium omadine registered in Canada. Once the final re-evaluation decision is made, the registrant will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for sodium omadine 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 omadine.

The PMRA will accept written comments on this proposal up to 90 days from the date of publication of this document. Please forward all comments to Publications (please see contact information indicated on the cover page of this document).

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 DIR2012-02, *Re-evaluation Program Cyclical Re-evaluation*, presents the details of the cyclical re-evaluation approach, which is in line with the requirements of the *Pest Control Products Act*.

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

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

What is Sodium Omadine?

Sodium omadine is a broad-spectrum antimicrobial active ingredient, registered in Canada for use in the preservation of aqueous synthetic fibre lubricants (spin finishes); aqueous based metalworking fluids and fluid concentrates. It is also registered for “in-can” and “dry film” preservation of latex emulsions used in adhesives, caulks, patching compounds, sealants, paints and grouts, and for the preservation of gypsum wallboards. At manufacturing facilities, the commercial end-use product containing sodium omadine can be incorporated into materials or solutions to be preserved by open pour or a closed mixing/loading system.

Health Considerations

Can Approved Uses of Sodium Omadine Affect Human Health?

Sodium omadine is unlikely to affect your health when used according to the proposed label directions.

Workers can be exposed to sodium omadine while handling the commercial-class product in industrial settings and/or through contact with treated solutions (for example metalworking fluids) or finished products (for example paint and caulks). There are no domestic-class products containing sodium omadine; however, the general public can be exposed to this active ingredient while handling treated finished products (for example paint and caulks). Dietary exposure to sodium omadine is not expected based on the currently registered use pattern.

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.

Toxicological endpoints for sodium omadine human health assessment have been updated during the re-evaluation. Risk to workers and the general public are not of concern taking into consideration mitigation measures proposed to minimize potential exposure.

Environmental Considerations

What Happens when Sodium Omadine is Introduced into the Environment?

Sodium Omadine is unlikely to affect non-target organisms when used according to the proposed label directions.

Material preservative uses of sodium omadine are unlikely to result in unacceptable risk to the environment. Standard environmental advisory label statements to minimize surface water contamination are proposed.

Proposed 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 sodium omadine, the PMRA is proposing further risk-reduction measures to protect human health:

- Additional personal protective equipment to protect workers in industrial/manufacturing settings
- Cancellation of sodium omadine use for "in-can" preservation of latex emulsions (paints, adhesives, caulks, grouts, patching compounds, and sealants) to protect workers and the general public

In addition, standard environmental hazard and advisory label statements are proposed to be added to the end-use product label.

Next Steps

Before making a final re-evaluation decision on sodium omadine, the PMRA will consider any 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 omadine, also known as sodium pyrithione, is a broad-spectrum antimicrobial active ingredient (a.i.) used as a material preservative.

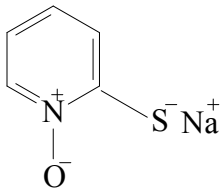
Following the re-evaluation announcement for sodium omadine, the registrant of the technical grade active ingredient in Canada indicated their intention to support all currently registered uses, except for the use of sodium omadine in the preservation of aqueous synthetic fibre lubricants (spin finishes) and for "dry-film" preservation of latex-based emulsions. Currently registered product containing sodium omadine are listed in Appendix I. Only uses being supported by the registrant were considered in the re-evaluation of sodium omadine.

The purpose of this re-evaluation is to review existing information on the active ingredient, sodium omadine, and the currently registered sodium omadine technical and commercial class end-use products, to ensure that risk assessments meet current standards.

2.0 The Technical Grade Active Ingredient and Its Properties and Uses

2.1 Identity

Common name		This compound has not been listed by the ISO. The PMRA has previously accepted sodium omadine, sodium 2-pyridinethiol-1-oxide and sodium pyrithione
Function		Material Preservative
Chemical Family		Pyridines
Chemical name		
1	**International Union of Pure and Applied Chemistry (IUPAC)**	Sodium 2-sulfidopyridine-N-oxide
2	**Chemical Abstracts Service (CAS)**	2-Pyridinethiol, 1-oxide, sodium salt (1:1)
CAS Registry Number		3811-73-2
Molecular Formula		C_5H_4NOSNa

Structural Formula	
Molecular Weight	149.15
Purity of the Technical Grade Active Ingredient	Sodium-2-pyridinethiol-1-oxide at 40.5%

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 Toxic Substances Management Policy Track 1 substances, are not expected to be present in the product.

2.2 Physical and Chemical Properties

Property	Result
Vapour pressure at 22°C	14.05 mm Hg
Ultraviolet (UV) / visible spectrum	λ_{max} = 240, 283 and 340 nm
Solubility in water	53% for the corresponding solid, but not applicable for this product since it is a solution in water.
***n*-Octanol/water partition coefficient (K_{ow})**	K_{ow} = 0.00265
Dissociation constant	4.56 ± 0.01

2.3 Description of Registered Sodium Omadine Uses

Currently registered products containing sodium omadine are listed in Appendix I. The commercial product containing 40.5% sodium omadine can be applied to materials and solutions to be preserved via open pour or a closed mixing/loading system. In Canada, sodium omadine is registered for:

- preservation of aqueous synthetic fibre lubricants and metalworking fluids and fluid concentrates (including cutting, cooling and lubrication fluids) at the maximum application rate of the active ingredient (506 ppm);
- "in-can" and "dry film" preservation of latex emulsions used in adhesives, caulks, patching compounds, sealants, paints and grouts at the maximum application rate of the active ingredient (648 ppm);

- preservation of gypsum wallboards at the maximum application rate of the active ingredient (980 ppm).

The uses of sodium omadine for preservation of aqueous synthetic fiber lubricants (spin finishes) and for "dry film" preservation of latex-based emulsions are no longer supported by the registrant and, therefore, must be removed from the end-use product label. The proposed label amendments are listed in Appendix II.

All supported uses of sodium omadine were considered in the re-evaluation of sodium omadine, except for use in the preservation of gypsum wallboards which was granted a full registration in 2013 based on up-to-date assessments.

3.0 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.

When assessing health risks, the PMRA considers two key factors: 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).

3.1 Toxicology Summary

In laboratory animals, sodium omadine was slightly toxic via oral and dermal routes, and moderately toxic via the inhalation route of exposure. The active ingredient was found to be a slight to moderate skin irritant and was assumed to be a severe eye irritant based on physico-chemical characteristics. Sodium omadine did not cause an allergic skin reaction. Slight to moderate evidence of neuromuscular toxicity (a low incidence of loss of limb function) was noticed at high dosages in all acute studies.

Sodium omadine did not cause cancer in animals exposed via oral and dermal routes of administration and is unlikely to damage genetic material. Reproductive effects on mating and fertility were reported in rats orally exposed to sodium omadine. Developmental effects, including malformations and variations in ossification of skeletal elements, were observed at doses that were toxic to the mother dermally or orally exposed to sodium omadine. There was no evidence of developmental effects in rabbits dermally exposed to sodium omadine.

Neuromuscular degeneration, predominantly affecting the hind limbs of animals, was a consistent finding in the toxicological database for sodium omadine. The level of concern for this endpoint for fetal/young animals and humans is reduced for a number of reasons including the fact that rats appear to be more sensitive to neurotoxic effects than primates. No additional data to address neurotoxicity effects observed in toxicity studies in animals is required at this time, however, additional data may be required if a request for expansion of the use pattern is received.

3.2 Toxicological Endpoints for the Human Health Risk Assessment

3.2.1 *Pest Control Products Act* Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects. This factor should take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children and potential pre- and post-natal toxicity. A different factor may be determined to be appropriate based on reliable scientific data.

By extension, as the worker population could include pregnant women, it is necessary to afford the same level of protection to the foetus or nursing offspring that may be exposed via its mother. Consequently, an additional *Pest Control Products Act*-like uncertainty factor may be applied to worker exposure scenarios if available data identify concerns for potential effects on the young, or if appropriate data are not available to adequately address the concerns.

With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, the database for sodium omadine contains the full complement of required studies, including developmental toxicity studies in rats and rabbits and a two-generation reproductive toxicity study in rats.

With respect to identified concerns relevant to the assessment of risk to infants and children, effects on pups were observed in both rat developmental and 2-generation reproduction studies. Under the conditions of the study, there was no evidence of teratogenic effects in rabbits exposed to sodium omadine. The rat developmental NOEL of 3 mg/kg bw/day was set based on rib and limb malformations, and variations in ossification of skeletal elements observed at a LOEL of 7 mg/kg bw/day. However, concern for these endpoints in the rat developmental toxicity study is tempered by the occurrence of significant maternal toxicity (neuromuscular degeneration, mortality, and body weight loss) at the same dose level. In the gavage 2-generation rat reproduction study, the reproductive NOEL of 1.5 mg/kg bw/day was established based on effects on mating and fertility (decreased number of pairs successfully mated, increased time to achieve successful mating, and decreased fertility in F0 generation animals only) observed at a LOEL of 3.5 mg/kg bw/day. An offspring NOEL of 1.5 mg/kg bw/day was established based on slightly decreased number of pups born, reduced female pup weight at weaning, and delayed development (opening of pinna (F1 only) and eyes, delayed development of the startle response observed at a LOEL of 3.5 mg/kg/bw/day.

A systemic maternal NOEL of 0.5 mg/kg bw/day was established based on microscopic evidence of skeletal muscle atrophy in three F2 parental females at 1.5 mg/kg bw/day, impaired hind limb function (one F0 female) or hind limb paralysis (two F1 females), macroscopic (females only) and microscopic evidence of hind limb skeletal wastage (primarily females).

The existing evidence indicates that the young are not more sensitive to sodium omadine than maternal animals. Therefore, in consideration of the above noted effects on the young, the PMRA proposes to reduce the *Pest Control Products Act* factor to 3-fold, recognizing that concerns for serious effects (malformed (bent) ribs and limbs, late resorptions) observed in the rat dermal developmental study are tempered by the occurrence of maternal toxicity (mortality, body and thymus weight, reduced limb function) at the same dose levels. A 3-fold *Pest Control Products Act* factor would apply to exposure scenarios that utilize the endpoint from the rat dermal developmental toxicity study for risk assessment. Further, to address concern for exposure of pregnant female workers, an additional 3-fold uncertainty factor would apply to occupational exposure scenarios that utilize this endpoint for risk assessment. For all other scenarios, the *Pest Control Products Act* factor was reduced to 1-fold.

3.2.2 Toxicological Endpoints for Occupational and Residential Risk Assessment

Dermal exposure
For dermal exposure assessments (short- to long-term on irregular or intermittent basis), the NOEL of 3 mg/kg bw/day from the dermal rat developmental study was considered the most appropriate endpoint. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variations have been applied. For reasons outlined in the *Pest Control Products Act* Hazard Characterization section, an additional 3-fold uncertainty factor has been applied to address concerns for prenatal exposure. This results in a target MOE (or Composite Assessment Factor (CAF)) of 300.

Inhalation exposure
For inhalation exposure assessments (short- to long-term on irregular or intermittent basis), the NOEL of 0.281 mg/kg bw/day from a 90-day inhalation study in rats was considered the most appropriate endpoint. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variations have been applied. This results in a target MOE of 100. The selected endpoint is considered protective of developmental effects.

Non-dietary oral exposure (children, short-term)
For assessment of non-dietary oral exposure of children, the NOEL of 0.5 mg/kg bw/day from a 90-day gavage study in rats was considered the most appropriate endpoint. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variations have been applied. The *Pest Control Products Act* factor was reduced to 1-fold for this scenario as the endpoint discussed in the *Pest Control Products Act* factor section above does not apply to this population. This results in a target MOE of 100.

Toxicological endpoints selected by the PMRA for the human health risk assessment are listed in Appendix III.

3.3 Occupational Exposure and Risk

Workers can be exposed to sodium omadine while handling the commercial-class product in industrial settings (primary handlers) and/or through contact with treated metalworking fluids or latex-based products (secondary handlers).

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.

3.3.1 Primary Handler Exposure and Risk Assessment

Sodium omadine can be incorporated into materials or solutions to be preserved during the manufacturing process via open pour or a closed mixing/transfer systems. Exposure of workers handling commercial products containing sodium omadine is expected to be intermittent over a short-/intermediate- to long-term duration, predominately via the dermal route.

The risk assessment for chemical workers applying the liquid product containing sodium omadine was conducted using exposure data from the Chemical Manufacturers Association (CMA) Antimicrobial Exposure Study. Given the limitations of the exposure study (low and variable laboratory and field recoveries); the 90th percentiles of dermal and inhalation exposure doses generated from the input CMA data were used by the PMRA to estimate potential risks to workers handling sodium omadine.

The dermal and inhalation risks for workers handling sodium omadine were assessed using a conservative scenario, that is, open pour of liquid product while assuming different levels of personal protective equipment (PPE). For workers applying sodium omadine product via open pour, short-/intermediate- and long-term target dermal and inhalation MOEs were achieved assuming PPE consisting of chemical-resistant coveralls over a long-sleeved shirt, long pants, and chemical-resistant gloves. The currently used closed mixing/loading system technology in industrial settings is also considered adequate to protect workers without the requirement of additional PPE.

Based on the results of the risk assessment, additional PPE is proposed to mitigate exposure of workers in industrial/manufacturing settings. The use of protective eyewear is required on the current end-use product label.

The proposed label amendments are listed in Appendix II.

3.3.2 Secondary Handler Exposure and Risk

There is potential for exposure of workers to sodium omadine in occupational settings resulting from contact with treated metalworking fluids or latex-based products (for example paints, sealants, and grouts).

3.3.2.1 Metalworkers

For workers coming in contact with metalworking fluids, short- to long-term duration inhalation and dermal exposures are expected.

In the lieu of chemical-specific exposure data, dermal and inhalation exposure estimates for metalworkers were calculated using the modeling approach previously described by the PMRA in the Proposed Registration Decision for 2-methyl-4-isothiazolin-3-one (PRD2011-02).

The daily dermal exposure estimate was calculated assuming that metalworker's hands and forearms will be submerged continuously for 10 hours in the treated metal working fluid. The short- to long-term target dermal MOE was achieved under current conditions of use.

The inhalation exposure estimate was calculated assuming default values for the air concentration of active ingredient, a typical inhalation rate, and a typical exposure time. The short- to long-term inhalation MOE was achieved under current conditions of use.

Since the risk assessment did not identify risks of concern for metalworkers under current conditions of use, no additional mitigation measures are proposed by the PMRA.

3.3.2.2 Professional Painters

For workers handling/applying latex-based products (for example paint, sealants, and grouts), short- to long-term dermal and inhalation exposures are expected.

Exposure estimates for workers handling/applying treated latex-based products were derived using exposure data from the Canadian Pesticide Handlers Exposure Database (PHED). There are limitations with PHED as it does not contain exposure scenarios that correspond with all of the sodium omadine uses (for example, sealants and grouts). As a result, it was necessary for these scenarios to extrapolate from the most representative PHED scenario, which is paint application. In the absence of use information for products such as grouts and sealants, it was assumed that exposure resulting from paintbrush applications would be equal to or greater than exposure from applying other latex-based products. The PHED paintbrush scenario may be conservative in extrapolating to other uses (such as sealants and grouts); therefore, the assessment is not expected to underestimate exposure, but may be conservative.

Daily exposure estimates for professional painters were calculated using PHED unit exposure values for workers wearing a single layer of clothing and no gloves while applying paint. Additional assumptions included the maximum (648 ppm) or typical (98-410 ppm) application rates and default volumes of paint applied per day.

For professional painters using paintbrush and airless sprayer, short- to long-term dermal target MOEs were not achieved at all assessed application rates (MOE 19-259, target MOE=300). The short- to long-term inhalation target MOE is achieved under current conditions of use.

Taking into consideration the results of the risk assessment for painters, seriousness of the dermal endpoint, and the lack of feasible mitigation measures for professional painters, the PMRA proposes to cancel the use of sodium omadine for "in-can" preservation of latex emulsion-based paints, adhesives, grouts, sealants, and patching compounds. The proposed label amendments are listed in Appendix II.

3.4 Non-occupational Exposure

3.4.1 Residential Exposure and Risk

The registered end-use product containing sodium omadine is not available for use by homeowners. However, treated latex-based products may be used by consumers and have the potential for postapplication residential exposure. Sodium omadine-treated finished products that may routinely be used in the residential setting include paint, adhesives, grouts, sealants and patching compounds.

For homeowners handling/applying treated latex-based products exposure is expected to be of a short-term duration. Dermal and inhalation exposure estimates for homeowners were calculated using surrogate PHED data for individuals wearing a short-sleeved shirt, short pants, and no gloves while painting with a paintbrush or an airless sprayer. In the absence of use information for products such as grouts, sealants, adhesives, and patching compounds, it was assumed that exposure resulting from applications of paint using a paintbrush would be equal to or greater than exposure from applying these products. Additional assumptions included the maximum (648 ppm) and typical (98 and 410 ppm) application rates and default volumes of paint applied daily.

For homeowners using a paintbrush, short-term dermal and inhalation target MOEs were achieved assuming the application rate of 98 ppm. Dermal risks of concern have been identified at higher application rates. For homeowners using an airless sprayer, dermal risks of concern have been identified at all assessed application rates (MOE 29-190, target dermal MOE=300). Inhalation risks for these individuals were not of concern.

The potential non-dietary risk for children from ingestion of paint chips is not of concern.

To protect the general population, the PMRA proposes to cancel the use of sodium omadine for "in-can" preservation of latex emulsion-based paints, adhesives, grouts, sealants, and patching compounds. The proposed label amendments are listed in Appendix II.

3.4.2 Residue Limits in Food Commodities

In Canada, sodium omadine is not registered for food or feed use. There are no Canadian Maximum Residue Limits (MRLs) established for imported commodities for sodium omadine.

3.4.3 Dietary Exposure and Risk

Exposure from food is not anticipated based on the currently registered use pattern. The current commercial product label does not have a statement prohibiting the use of sodium omadine in food contact materials. Considering the proposed cancellation of the use of sodium omadine as a preservative in latex-based adhesives, such statement is not required. Exposure from drinking water is not anticipated considering that direct applications to food/fed crops are not expected and industrial uses are unlikely to result in a significant environmental exposure. On this basis, a quantitative dietary exposure assessment for sodium omadine was not required.

3.4.4 Aggregate Exposure and Risk

Aggregate risk combines the different routes of exposure to sodium omadine in residential settings. Short- and intermediate-term aggregate risk assessments are comprised of contributions from food, drinking water and non-occupational exposure (dermal, inhalation).

Based on the registered use pattern and taking into consideration the proposed mitigation measures, dietary and residential exposures to sodium omadine are not expected. On this basis, the aggregate exposure and risk assessment was not required.

3.4.5 Cumulative Exposure and Risk

The *Pest Control Products Act* requires that the PMRA consider the cumulative exposure to pesticides with a common mechanism of toxicity. For the current re-evaluation, the PMRA did not identify a common mechanism of toxicity for sodium omadine and other pest control products. Therefore, there is no requirement for a cumulative assessment at this time.

4.0 Environment

Sodium omadine was found to be resistant to hydrolysis as well as photolysis based on the submitted absorption spectra. No data are available regarding the microbial degradation of sodium omadine in soil, water or sediment. Bioaccumulation is considered unlikely based on the reported *n*-octanol-water partition coefficient factor (K_{ow}) of 0.00265. The active ingredient is highly toxic to fish based on the 96h LC_{50} of 7.6-9.6 mg a.i./L for bluegill sunfish and 6.6-8.0 µg a.i./L for rainbow trout. Standard environmental toxicity label statements are proposed to be added to the product label.

Material preservative uses of sodium omadine are unlikely to result in unacceptable risk to the environment, as environmental exposure is expected to be limited. Based on current PMRA practices, standard advisory label statements to minimize surface water contamination are proposed to be included on the end-use product label. The proposed label amendments are listed in Appendix II.

5.0 Value

Sodium omadine is a broad-spectrum antimicrobial active ingredient used as a material preservative to inhibit the growth of bacteria and fungi in a number of industrial and consumer aqueous-based products such as metalworking fluids and latex emulsions. It is the only active ingredient currently registered to prevent mould and mildew growth in gypsum wallboard that is installed in areas of high humidity. Several active ingredients or combinations of active ingredients are registered for the preservation of metal-working fluids and latex emulsions; however, many of them are considered potential skin sensitizers. Sodium omadine provides an additional option for formulators who are concerned by the use of potential skin sensitizers in the manufacture of their products.

6.0 Pest Control Product Policy Considerations

6.1 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, in other words, persistent (in air, soil, water and/or sediment), bioaccumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

During the re-evaluation process, sodium omadine was 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. In order for sodium omadine to meet Track 1 criteria, the criteria for both bioaccumulation and persistence (in one media) must be met. The PMRA has reached the following conclusion:

- Persistence: No data are available regarding the persistence of sodium omadine in soil, water, or sediment.
- Bioaccumulation: The log octanol-water partition coefficient factor of -2.57 for sodium omadine was reported. Given that TSMP Track 1 criterion is ≥5.0, it is concluded that sodium omadine does not meet the criterion for bioaccumulation.
- Sodium omadine does not meet all Track 1 criteria and therefore is not considered a Track 1 substance.

6.2 Formulants and Contaminants of Health or Environmental Concern

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

During the re-evaluation of sodium omadine, contaminants in the technical are compared against the *List of Pest Control Product Formulants and Contaminants of Health or Environmental*

Concern maintained in the *Canada Gazette*.[3] 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 omadine does not contain any contaminants of health or environmental concern identified in the *Canada Gazette.*

7.0 Incident Reports

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

As of 30 October 2015, no incident reports had been submitted for sodium omadine.

8.0 Organisation for Economic Co-operation and Development Status

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups 34 member countries and provides governments with a setting in which to discuss, develop and perfect economic and social policies.

As part of the re-evaluation of an active ingredient, the PMRA takes into consideration recent developments and new information on the status of an active ingredient in other jurisdictions, including OECD member countries. In particular, decisions by an OECD member to prohibit all uses of an active ingredient for health or environmental reasons are considered for relevance to the Canadian situation.

Sodium omadine is currently acceptable for use in other OECD countries, including the United States and Europe. No decision by an OECD member country to prohibit all uses of sodium omadine for health or environmental reasons has been identified.

9.0 Proposed Re-evaluation Decision

The PMRA is proposing that most uses of products containing sodium omadine are acceptable for continued registration with additional risk-reduction measures to protect human health.

The proposed mitigation measures are presented in Appendix II. No additional data are being requested at this time.

[3] *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

10.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2012-02, *Re-evaluation Program Cyclical Re-evaluation*, can be found on the Pesticides and Pest Management portion of Health Canada's website at www.hc-sc.gc.ca. 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.

The United States Environmental Protection Agency Registration Review documents for sodium omadine (Docket ID 2011-0611) are available at http://www.regulations.gov.

List of Abbreviations

bw	body weight
CAS	Chemical Abstracts Service
cm^2	centimetre(s) squared
DACO	data code
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_{ow}	*n*-octanol–water partition coefficient
LOEL	Lowest Observed Effect Level
mg	milligram(s)
mL	millilitre
mm Hg	millimetre mercury
MOE	Margin Of Exposure
MRL	Maximum Residue Limit
nm	nanometre
NOEL	No Observed Effect Level
PMRA	Pest Management Regulatory Agency
PRVD	Proposed Re-evaluation Decision
RVD	Re-evaluation Decision
TSMP	Toxic Substances Management Policy
UV	ultraviolet

Appendix I Registered Products Containing Sodium Omadine as of 30 October 2015

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (w/w)
29714	Technical	ARCH CHEMICALS, INC.	SODIUM OMADINE 40% TECHNICAL	solution	40.5%
24098	Commercial	ARCH CHEMICALS, INC.	SODIUM OMADINE 40% AQUEOUS SOLUTION INDUSTRIAL FUNGICIDE & BACTERICIDE	solution	40.5%

Appendix II Label Amendments for the End-Use Product Containing Sodium Omadine

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 following label statements.

I) The following uses of sodium omadine are no longer supported by the registrant, and must be removed from the end-use product label:

> aqueous synthetic fibre lubricants (spin finishes)
>
> "dry film" preservation of latex emulsions used in paints, adhesives, caulks, grouts, patching compounds, and sealants

II) The following use of sodium omadine is proposed to be removed from the end-use product label:

"in-can" preservation of latex emulsions used in paints, adhesives, caulks, grouts, patching compounds, and sealants

III) The following statement is proposed to be included in a section entitled **PRECAUTIONS**:

> Wear chemical-resistant coveralls over a long-sleeved shirt and long pants, goggles or a face shield, and chemical-resistant gloves during mixing/loading/application via open pour, clean up, maintenance, and repair. Chemical-resistant coveralls are not required for workers applying the product via a closed mixing/loading system.

IV) The following statements are proposed to be included in a section entitled **DIRECTIONS FOR USE**.

> DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.
>
> DO NOT discharge effluents containing this product into sewer systems, lakes, streams, ponds, estuaries, oceans, and other waters unless the effluent has been detoxified to suitable means.

V) The following statements are proposed to be included in a section entitled **ENVIRONMENTAL HAZARDS**:

TOXIC to aquatic organisms. It is not to be used in circumstances that would cause or allow it to enter lakes, streams, ponds, estuaries, oceans or other waters in contravention of federal or provincial regulatory requirements. The requirements of applicable laws should be determined before using the product.

Appendix III Toxicological Endpoints for Human Health Risk Assessment

Exposure Scenario	Dose (mg/kg bw/day)	Study	CAF/Target MOE
Non-dietary oral exposure (children, short-term)	NOEL=0.5	90-day gavage study in rats; LOEL=2 mg/kg bw/day based on an increased incidence of piloerection, hind limb skeletal muscle atrophy and reduced hind limb tactile response	100[1]
Short- to long term dermal exposure	NOEL=3	Dermal developmental study in rats; LOEL=7 mg/kg bw/day based on rib and limb malformations, and variations in ossification of skeletal elements	300[2]
Short- to long-term inhalation exposure	NOEL=0.281[3] (0.0011 mg/L)	90-day inhalation study in rats; LOEL=0.0061 mg/L based on hind limb dysfunction during week 13, depressed body weight during week 11 to 13, depressed hemoglobin levels at week 6 and histopathological evidence of skeletal muscle atrophy	100[4]

NOEL, no observed effect level; LOEL, Lowest Observed Effect Level; CAF, Composite Assessment Factor; MOE, Margin of Exposure

1 Target MOE of 100 = 10-fold interspecies extrapolation × 10-fold intraspecies variations × 1-fold *Pest Control Products Act* factor, the *Pest Control Products Act* factor was reduced to 1-fold as the endpoint discussed in the *Pest Control Products Act* factor section above does not apply to this population

2 CAF/Target MOE of 300 = 10-fold interspecies extrapolation × 10-fold intraspecies variations × 3-fold *Pest Control Products Act* factor

3 Inhalation NOEL of 0.281 mg/kg bw/day = NOEL (0.0011 mg/L) × A (100%, default) × CF (conversion factor for SD rats of 42.62 L/hr./day) × D (duration of exposure 6 hrs./day) × AF (animal factor; default=1)

4 Target MOE of 100 = 10-fold interspecies extrapolation × 10-fold intraspecies variations

References

A. Studies Considered in the Chemistry Assessment

List of Studies/Information Submitted by Applicant/Registrant (Unpublished)

PMRA Document Number	Reference
1511712	Technical Chemistry File OMA-ARU-3 Sodium Omadine, DACO: 2.99
1793925	The Stability of Sodium Pyrithione with Metals, DACO: 2.14.13
1762642	2009, Sodium Omadine 40% Technical Starting Materials, Process, Formation of Impurities, DACO: 2.11.2, 2.11.3, 2.11.4
1946856	Preliminary Analysis of Sodium Omadine 40% Aqueous Solution, DACO: 2.13.1
2299788	Physical/chemical Properties of Sodium Pyrithione, DACO: 2.14.11, 2.14.4, 2.14.5, 2.14.7

B. Studies Considered in the Human Health Risk Assessment

List of Studies/Information Submitted by Applicant/Registrant (Unpublished)

PMRA Document Number	Reference
1226823	1987, Sodium Omadine Oral LD50 in Rats, DACO: 4.2.1,4.6.1
1226824	1987, Sodium Omadine Acute Dermal Toxicity in Rabbits/LD50 in Rabbits, DACO: 4.2.2,4.6.2
1226826	1987, Acute Inhalation Toxicity Evaluation on Na Omadine in Rats, DACO: 4.2.3,4.6.3
1226827	1987, Sodium Omadine Primary Dermal Irritation in Albino Rabbits, DACO: 4.2.5,4.6.5
1226828	1987, Sodium Omadine Guinea Pig Maximization Test, DACO: 4.2.6,4.6.6
1226829	1988, 90-Day Oral (Gavage) Toxicity Study in the Rat (Volume I of II), DACO: 4.3.1,4.7
1226830	1988, 90-Day Oral (Gavage) Toxicity Study in the Rat (Volume II of II), DACO: 4.3.1,4.7
1226831	1988, 90-Day Dermal Toxicity Study in the Rat, DACO: 4.3.4,4.7
1226832	Evaluation of the Skin Irritating and Sensitizing Propensities of Sodium Omadine in Humans, DACO: 4.2.5,4.2.6,4.6.5,4.6.6
1226833	1987, Sodium Omadine: Micronucleus Test, DACO: 4.5.4
1226834	1987, Dermal Developmental Toxicity Study in New Zealand White Rabbits with Sodium Omadine, DACO: 4.5.2
1226835	1987, Rat Hepatocyte Primary Culture/DNA Repair Test, DACO: 4.5.4

1226837 1987, Chinese Hamster Ovary (Cho) Cell/Hypoxanthine-Guanine Phosphoribosyl Transferase (HPRT) Mammalian Cell Forward Gene Mutation Assay, DACO: 4.5.4

1227513 1989, One Year Oral Toxicity Study in Cynomolgus Monkeys, DACO: 4.3.6,4.7

1228564 Evaluation of 30 Day Oral Intubation of Sodium Omadine in Fasted & Nonfasted Rats (6030), DACO: 4.2.1

1229202 1989, Rat Two-Generation Reproduction Toxicity Study, DACO: 4.5.1

1229203 1989, Thirteen Week Subchronic Inhalation Toxicity Study on Na Omadine in Rats, DACO: 4.7

1229204 1989, One Year Oral Toxicity Study in Cynomogus Monkeys, DACO: 4.3.6,4.7

1231771 1980, Dermal Teratology Study in Rats , DACO: 4.5.2

1237879 1991, Sodium Omadine: 80 Week Dermal Carcinogenicity Study in the Mouse Volume I of III, DACO: 4.4.2

1238864 1991, Sodium Omadine 104-Week Oral (Gavage) Combined Carcinogenicity and Toxicity Study in the Rat, Part 3 of 3, DACO: 4.4.1,4.4.2

1239051 1991, Sodium Omadine 104-Week Oral (Gavage) Combined Carcinogenicity and Toxicity Study in the Rat, Part 1 of 3, DACO: 4.4.1,4.4.2

1239052 1991, Sodium Omadine 104-Week Oral (Gavage) Combined Carcinogenicity and Toxicity Study in the Rat, Part 2 of 3, DACO: 4.4.1,4.4.2

1237880 1989, Sodium Omadine Disposition and Metabolism in Rats After Oral and Intravenous Administration, DACO: 6.4

1885342 1989, Sodium Omadine Disposition in Rats after Dermal Administration; DACO: 5.8

2344322 2002, Natrium Pyrion Oral Prenatal Developmental Toxicity Study in Rats, DACO: 4.5.2

1145506 1990, Chemical Manufacturers Association Antimicrobial Exposure Assessment Study (Preventol CMK)

C. Studies Considered in the Environmental Risk Assessment

List of Studies/Information Submitted by Applicant/Registrant (Unpublished)

PMRA Document Number	Reference
1226838	Sodium Omadine: Hydrolysis Study, DACO: 8.2.1
1226840	Acute Aquatic Effects of Sodium Omadine on the Rainbow Trout, Salmo Gairdneri, DACO: 9.5.2.1
1226841	Acute Aquatic Effects of Sodium Omadine on the Bluegill Sunfish, Lepomis Macrochirus, DACO: 9.5.2.2
1226839	Sodium Omadine: An Acute Oral Toxicity Study with the Bobwhite, DACO: 9.6.2.1