Re-evaluation Decision RVD2023-17

1,3-bis(hydroxymethyl)-5,5-dimethylhydantoin and hydroxymethyl-5,5-dimethylhydantoin and Its Associated End-use Products

Final Decision

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Re-evaluation Decision for 1,3-bis(hydroxymethyl)-5,5-dimethylhydantoin (DMY) and hydroxymethyl-5,5-dimethylhydantoin (MMY) and Associated End-use Products

Under the authority of the *Pest Control Products Act,* all registered pesticides must be re-evaluated by Health Canada's Pest Management Regulatory Agency (PMRA) to ensure that they meet current health and environmental standards and have value. The re-evaluation considers data and information from pesticide manufacturers, published scientific reports and other regulatory agencies, as well as comments received during public consultations. Health Canada applies internationally accepted risk assessment methods as well as current risk management approaches and policies. More details, on the legislative framework, risk assessment and risk management approach, are provided under the section of Evaluation Approach of this document.

1,3-bis(hydroxymethyl)-5,5-dimethylhydantoin (DMY) and hydroxymethyl-5,5-dimethylhydantoin (MMY) are antimicrobial material preservatives used in a wide variety of products such as liquid detergents, soft soaps, room deodorizers and air fresheners, water-based surfactants, polymer emulsions, protective and decorative coatings, water-based gels for household and industrial products, textiles, water-based adhesives, latex for paper and coatings and water-based inks. Currently registered products containing DMY and MMY can be found in the Pesticide Product Information Database and in Appendix I. The Proposed Re-evaluation Decision, PRVD2022-10,[1] *1,3-bis(hydroxymethyl)-5,5-dimethylhydantoin and hydroxymethyl-5,5-dimethylhydantoin and Associated End-use Products*, underwent a 90-day consultation period which ended 28 August 2022. PRVD2022-10 proposed that products containing DMY and MMY are acceptable for continued registration in Canada provided that the additional proposed risk mitigation measures are implemented. The proposed risk mitigation measures to protect human health and the environment include requiring a closed transfer system, as well as updated label statements to reflect current standards for personal protective equipment and for paper and paperboard use, and updating label statements to prohibit effluent discharge.

Health Canada received two comments during the consultation period conducted in accordance with section 28 of the *Pest Control Products Act*. Both comments were in support of the re-evaluation from the registrant of the technical grade active ingredient. The comments did not result in revisions to the risk assessments and did not result in changes to the proposed re-evaluation decision as described in PRVD2022-10. Therefore, this decision is consistent with the proposed re-evaluation decision stated in PRVD2022-10.

A reference list of information used as the basis for the proposed re-evaluation decision is included in PRVD2022-10; no further information was used in the final re-evaluation decision. Therefore, the complete reference list of all information used in this final re-evaluation decision is set out in PRVD2022-10.

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

This document presents the final re-evaluation decision[2] for the re-evaluation of DMY and MMY, including the required amendments (risk mitigation measures) to protect human health and the environment as well as the label amendments required to bring labels to current standards. All products containing DMY and MMY that are registered in Canada are subject to this re-evaluation decision.

Re-evaluation Decision for DMY and MMY

Health Canada has completed the re-evaluation of DMY and MMY. Under the authority of the *Pest Control Products Act*, Health Canada has determined that continued registration of products containing DMY and MMY is acceptable. An evaluation of available scientific information found that the uses of DMY and MMY products meets current standards for protection of human health and the environment and have acceptable value when used according to revised conditions of registration which includes new mitigation measures. Label amendments, as summarized below and listed in Appendix II, are required.

Risk mitigation measures

Registered pesticide product labels include specific directions for use. Directions include risk mitigation measures to protect human health and the environment and must be followed by law. The required label amendments including any revised/updated label statements and/or mitigation measures, as a result of the re-evaluation of DMY and MMY, are summarized below. Refer to Appendix II for details.

Human health

To protect human health, the following risk-reduction measures are required:

- To protect workers using end-use products during the manufacturing process:
    - A closed transfer system for commercial-class liquid (solution) products
- To protect workers, updated label statements are required to reflect current standards for personal protective equipment (PPE)
- To protect consumers, label statements are required to reflect current standards for paper and paperboard use

Environment

To protect the environment, the following risk-reduction measures are required:

- An update to the label statement prohibiting effluent discharge

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

Implementation of the re-evaluation decision

Regulatory Directive DIR2018-01, *Policy on Cancellations and Amendments Following Re-evaluation and Special Review* provides general timelines for implementation of post-market decisions.

Health considerations

When conducting human health risk assessments, risks from exposure to a pesticide are estimated by comparing potential exposures with the most relevant endpoint from toxicology studies, with standard protection factors incorporated to further protect human health, including the most sensitive population. These factors provide an inherent level of protection from exposures that could result in adverse effects to human health. Furthermore, Health Canada applies additional protection factors if warranted by the hazard profile of the pesticide or by the quality and completeness of the underlying data. When risks of concern are identified in the human health exposure scenarios, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce potential risks would be required in order to support continued registration of the product/use.

Potential and relative health risks are thus considered acceptable during the general 2-year implementation period unless there is evidence from incident reports or other sources of real-world post-market surveillance data suggesting that there are adverse health effects occurring as a result of the use of the product(s) according to the currently approved label/use conditions. Other considerations may include how widely the product is used, the populations potentially exposed to the product and/or other factors.

Taking into consideration these factors, the 2-year implementation timeline for label amendments for DMY/MMY is considered appropriate from a human health perspective.

Environmental considerations

The registered uses of DMY and MMY are considered to be indoor uses and the potential for environmental exposure is considered to be low. Therefore, the risks to the environment are considered to be acceptable under the current conditions of use.

Based on the above, Health Canada has determined that the potential risks to human health and the environment from the use of DMY and MMY under the current conditions of use are considered acceptable during the 24-month time period required to implement the required mitigation measures.

Refer to Appendix I for details on specific products impacted by this decision.

Next steps

To comply with this decision, the required amendments (mitigation measures and label updates) must be implemented on all product labels no later than 24 months after the publication date of this decision document. Accordingly, both registrants and retailers will have up to 24 months from the publication date of this decision document to transition to selling the product with the newly amended labels. Similarly, users will also have the same 24-month period from the date of this decision document to transition to using the newly amended labels, which will be available on the Public Registry.

Other information

Any person may file a notice of objection[3] regarding this decision on DMY and MMY and its associated end-use products within 60 days from the date of publication of this Re-evaluation Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides section of the Canada.ca website (Request a Reconsideration of Decision) or contact PMRA's Pest Management Information Service.

The relevant confidential test data on which the decision is based (as referenced in PRVD2022-10) are available for public inspection, upon application, in PMRA's Reading Room. For more information, please contact PMRA's Pest Management Information Service.

[3] As per subsection 35(1) of the *Pest Control Products Act.*

Evaluation Approach

Legislative framework

The Minister of Health's primary objective under the *Pest Control Products Act* (the Act) subsection 4(1) is to prevent unacceptable risks to individuals and the environment from the use of pest control products.

As noted in the preamble of the Act, it is in the national interest that the attainment of the objectives of the federal regulatory system continue to be pursued through a scientifically-based national registration system that addresses risks to human health, the environment and value both before and after registration and applies to the regulation of pest control products throughout Canada; and that pest control products with acceptable risk and value be registered for use only if it is shown that their use would be efficacious and if conditions of registration can be established to prevent unacceptable risks to human health and the environment.

For the purposes of the Act, the health or environmental risks of a pest control product are acceptable if there is reasonable certainty that no harm to human health, future generations or the environment will result from exposure to or use of the product, taking into account its conditions of registration as per subsection 2(2) of the *Pest Control Products Act*.

Risk for the human health and environment, and value are defined under the Act subsection 2(1) as follows:

> **Health risk**, in respect of a pest control product, means the possibility of harm to human health resulting from exposure to or use of the product, taking into account its conditions or proposed conditions of registration.
>
> **Environmental risk**, in respect of a pest control product, means the possibility of harm to the environment, including its biological diversity, resulting from exposure to or use of the product, taking into account its conditions or proposed conditions of registration
>
> **Value**, in respect of a pest control product, means the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact.

When evaluating the health and environmental risks of a pesticide and determining whether those risks are acceptable, subsection 19(2) of the *Pest Control Products Act* requires Health Canada to apply a scientifically-based approach. The science-based approach to assessing pesticides considers both the toxicity and the level of exposure of a pesticide in order to fully characterize risk.

Risk and value assessment framework

Health Canada uses a comprehensive body of modern scientific methods and evidence to determine the nature as well as the magnitude of potential risks posed by pesticides. This approach allows for the protection of human health and the environment through the application of appropriate and effective risk management strategies, consistent with the purpose described in the preambular text set out above.

Health Canada's approach to risk and value assessment is outlined in A Framework for Risk Assessment and Risk Management of Pest Control Products.[4] A high-level overview is provided below.

i) Assessing Potential Health Risks

With respect to the evaluation and management of potential health risks, Health Canada's risk assessments follow a structured, predictable process that is consistent with international approaches and the Health Canada Decision-Making Framework for Identifying, Assessing, and Managing Health Risks.[5]

The evaluation of potential health risks begins with a consideration of the toxicological profile of a pesticide to establish reference doses at which no adverse effect is expected and against which the expected exposure is assessed. This includes, where appropriate, the use of uncertainty (protection) factors to provide additional protection that accounts for the variation in sensitivity among members of human population and the uncertainty in extrapolating animal test data to humans. Under certain conditions, the *Pest Control Products Act* requires the use of another factor to provide additional protection to pregnant women, infants, and children. Other uncertainty factors, such as a database deficiency factor, are considered in specific cases. More details related to the application of the uncertainty factors are provided in SPN2008-01.[6]

Assessments estimate potential health risks to defined populations[7] under specific exposure conditions. They are conducted in the context of the registered conditions of use, such as the use of a pesticide on a particular field crop using specified application rates, methods and equipment. Potential exposure scenarios consider exposures during and after application of the pesticide in occupational or residential settings, food and drinking water exposure, or exposure when interacting with treated pets. Also considered are the anticipated durations (short-, intermediate- or long-term) and routes of exposure (oral, inhalation, or skin contact). In addition, an assessment of health risks must consider available information on aggregate exposure and cumulative effects.

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4 PMRA Guidance Document, *A Framework for Risk Assessment and Risk Management of Pest Control Products*

5 Health Canada Decision-Making Framework for Identifying, Assessing, and Managing Health Risks - August 1, 2000

6 Science Policy Note: *The Application of Uncertainty Factors and the Pest Control Products Act Factor in the Human Health Risk Assessment of Pesticides*

7 Consideration of Sex and Gender in Pesticide Risk Assessment (https://www.canada.ca/en/health-canada/services/consumer-product-safety/reports-publications/pesticides-pest-management/fact-sheets-other-resources/consideration-sex-gender-pesticide-risk-assessment-infographic.html)

ii) Assessing risks to the environment

With respect to the evaluation of environmental risks, Health Canada's environmental risk assessments follow a structured, tiered approach to determine the likelihood that exposure to a pesticide can cause adverse effects on individual organisms, populations, or ecological systems. This involves screening assessments starting with simple methods, conservative exposure scenarios and sensitive toxicity effects metrics, then moving on, where required, to more refined assessments that can include exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods.

The environmental assessment considers both the exposure (environmental fate, chemistry, and behaviour, along with the application rates and methods) and hazard (toxic effects on organisms) of a pesticide. The exposure assessment examines the movement of the pesticide in soil, water, sediments and air, as well as the potential for uptake by plants or animals and transfer through the food web. The possibility for the pesticide to move into sensitive environmental compartments such as groundwater or lakes and rivers, as well as the potential for atmospheric transport, is also examined. The hazard assessment examines effects on a large number of internationally recognized indicator species of plants and animals (terrestrial organisms include invertebrates such as bees, beneficial arthropods, and earthworms, birds, mammals, plants; aquatic organisms include invertebrates, amphibians, fish, plants and algae), and includes considering effects on biodiversity and the food chain. Acute and chronic effects endpoints are derived from laboratory and field studies that characterize the toxic response and the dose–effect relationship of the pesticide.

The characterization of environmental risk requires the integration of information on environmental exposure and effects to identify which, if any, organisms or environmental compartments may be at risk, as well as any uncertainties in characterizing the risk.

iii) Value assessment

Value assessments consist of two components: an assessment of the performance of a pest control product and its benefits.

During re-evaluation, value is examined under current conditions and in light of alternative pest control methods (both chemical and nonchemical) that may have been developed since the pesticide was first registered. An assessment of the benefits associated with the pesticide may also be conducted to demonstrate its value in the current context, and to identify potential alternatives.

Risk management

The outcomes of the assessments of risks to human health and the environment, and the assessment of value, form the basis for identifying risk management strategies. These include appropriate risk mitigation measures and are a key part of decision-making on whether health and environmental risks are acceptable. The development of risk management strategies take place within the context of the pesticide’s conditions of registration. Conditions can relate to, among other things, the specific use (for example, application rates, timing, frequency and

method of application), personal protective equipment, preharvest intervals, restricted entry intervals, buffer zones, spray drift and runoff mitigation measures, handling, manufacture, storage or distribution of a pesticide. If feasible conditions of use that have acceptable risk and value cannot be identified, the pesticide use will not be eligible for registration.

The selected risk management strategy is then implemented as part of the re-evaluation decision. The pesticide registration conditions include legally-binding use directions on the label. Any use in contravention of the label or other specified conditions is illegal under the *Pest Control Products Act*. Implementation of post-market decisions follow the framework articulated in the *Policy on Cancellations and Amendments Following Re-evaluation and Special Review*.[8]

Following a decision, continuous oversight activities such as post-market review, monitoring and surveillance, including incident reporting, all play an essential role to help ensure the continued acceptability of risks and value of registered pesticides.

[8] PMRA Regulatory Directive DIR2018-01, *Policy on Cancellations and Amendments Following Re-evaluation and Special Review*

Appendix I Registered products containing DMY and MMY in Canada

Table 1 Products containing DMY and MMY requiring label amendments[1]

Registration number	Marketing class	Registrant	Product name	Formulation type	Active ingredient (%)
25753	Technical Grade Active Ingredient	Arxada, LLC.	Glycoserve	Solution	DMY – 45 MMY – 10
25756			Dantogard XL – 1000T	Solution	DMY – 93.3 MMY – 6.0
25939	Commercial		Dantogard XL-1000 Preservative	Soluble Powder	DMY – 93.3 MMY – 6.0
25754			Dantogard Preservative	Solution	DMY – 32.3 MMY – 7.2
25755			Glycoserve LAD	Solution	DMY 45 MMY – 10.0
25757			Dantogard Plus Preservative	Soluble Powder	DMY – 88.6 MMY – 5.7 IPB – 5.0
27295		Troy Chemical Corporation	Mergal 395	Solution	DMY – 32 MMY – 7.5

IPB = 3-iodo-2-propynyl butyl carbamate

[1] As of 26 October 2023, excluding discontinued products or products with a submission for discontinuation

Appendix II Label amendments for products containing DMY and MMY

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

1. Label amendments for DMY/MMY technical grade active ingredients

On the primary display panel, include the following signal words: "POTENTIAL SKIN SENSITIZER."
In the PRECAUTIONS section, include the statement: "Potential skin sensitizer."

2. Label amendments for commercial class end-use products containing DMY/MMY

2.1 General label improvements

Liquid (solution) end-use product labels, under PRECAUTIONS:

Replace: "Wear long-sleeved shirt, long pants, and chemical-resistant gloves when handling the concentrate."

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

Soluble powder end-use product labels, under PRECAUTIONS:

Replace:
"If there is potential to generate dust, wear dust filtering respiratory protection"; or
"In addition, dust filtering respirator protection is required during handling if there is a potential for dust generation"

With:
"In addition, wear a NIOSH-approved N95 (minimum) filtering facepiece respirator (dust mask) that is properly fit tested when handling the concentrated powder."

Replace:
"Workers must wear a long-sleeved shirt, long pants, chemical resistant gloves and goggles or a face shield during mixing, loading, cleanup and repair"; or
"Wear long-sleeve shirt, long pants, and chemical-resistant gloves and eye protection when handling the concentrate"

With: "Wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes, and protective eyewear (goggles or a face shield) when handling the concentrated powder or treated process fluids and during clean-up and repair. Remove and wash contaminated clothing before re-use."

2.2 All commercial class liquid (Solutions)

"For use with closed loading and transfer systems only (that is, dry coupling)."

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

2.3 DIRECTIONS FOR USE

For the manufacturing of paper coatings, the following statement is proposed:

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

For end-use products Reg. No. 25754, 25755, 25939, and 27295:

Remove the following statement under the Precautions section:

"**DO NOT** discharge into lakes, streams, rivers or ponds."

For end-use product Reg. No. 25757:

Remove the following statement under the DIRECTIONS section

"**DO NOT** discharge effluents containing this product into sewer systems, lakes, streams, ponds, estuaries, oceans or other waters."

Add the following statement under the DIRECTIONS FOR USE section for all products:

"This registration is granted under the *Pest Control Products Act* and does not exempt the user from any other legislative requirements.

Use of this product and management of any resulting discharge or release of effluents containing this product must also be in accordance with the *Fisheries Act* and with any other applicable federal or provincial legislation.

Consult with provincial regulatory authorities on any authorizations or other requirements for use of this product and management of any resulting discharge or release of effluents containing this product."