Re-evaluation Decision RVD2024-08

Natamycin and Its Associated End-use Products

Final Decision

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Re-evaluation decision for natamycin 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.

This document presents the final re-evaluation decision[1] for the re-evaluation of natamycin, including the response to comments received, and the required label updates. All products containing natamycin regulated under the *Pest Control Products Act* in Canada are subject to this re-evaluation decision.

Natamycin, also known as pimaricin, is a naturally-occurring antimycotic substance, produced by the soil bacterium *Streptomyces natalensis, Streptomyces lydicus*, and *Streptomyces chattanoogensis*. Natamycin prevents the germination of fungal spores. Natamycin is registered to suppress dry bubble disease in mushroom production facilities. It is also registered for use as a preservative for samples of milk used in analytical testing laboratories.

Currently registered products containing natamycin can be found in the Pesticide Product Information Database and in Appendix I. The Proposed Re-evaluation Decision PRVD2024-02, *Natamycin and its Associated End-use Products*[2] containing the evaluation of natamycin and proposed decision, underwent a 90 day consultation period ending on 4 June 2024. PRVD2024-02 proposed continued registration of natamycin products in Canada, with updates to label directions and precautions to reflect the current labelling standards and to improve clarity (Appendix IV).

Health Canada received comments during the public consultation. Commenters are listed in Appendix II. The comments are summarized in Appendix III along with the responses by Health Canada. The comments did not result in changes to the proposed re-evaluation decision as described in PRVD2024-02. A reference list of information used as the basis for the proposed re-evaluation decision is included in PRVD2024-02.

Re-evaluation decision for natamycin

Health Canada has completed the re-evaluation of natamycin. Under the authority of the *Pest Control Products Act*, Health Canada has completed all required evaluations and consultations and has determined that the registration of products containing natamycin is required to be amended, in accordance with paragraph 21(2)(a) of the *Pest Control Products Act*. An evaluation

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

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

of available scientific information respecting the health and environmental risks and value of natamycin found that all uses of natamycin products meet current standards for protection of human health and the environment and have acceptable value when used according to the amended conditions of registration which includes updates to standard label statements as general label improvement. Label amendments, as summarized below and listed in Appendix IV, 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 amendments, including any revised/updated label statements, as a result of the re-evaluation of natamycin, are summarized below. Refer to Appendix IV for details.

Label improvements to meet current standards:

Human health

- Update to precautionary and first aid statements

Environment

- Updates to storage and disposal statements

Value

To reduce the development of resistance:

- Resistance management statement for mushroom use

Implementation of the re-evaluation decision

Regulatory Directive DIR2018-01, *Policy on Cancellations and Amendments Following Re-evaluation and Special Review* provides information and general timelines regarding the implementation of post-market decisions, (for example, up to 24-month timeline for label amendments). The post-market decision considers potential health and environmental risks regarding the use of the pest control product, and its value, when establishing the implementation timelines.

Amendment timeframe

The implementation timeline of 24 months for the required amendments (label updates) for pest control products containing natamycin is considered acceptable. These required amendments must be implemented within 24 months after the publication date of this decision document.

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 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.

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

Other information

Any person may file a notice of objection[3] regarding this decision on natamycin 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 and Pest Management Section of the Canada.ca website (Public Engagement Portal - Public Engagement Forms - Notice of Objection) or contact PMRA's Pest Management Information Service.

The relevant confidential test data on which the decision is based (as referenced in PRVD2024-02) are available for public inspection, upon application, in PMRA's Reading Room. For more information, please contact the PMRA's Pest Management Information Service.

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

Appendix I Registered products containing natamycin in Canada

Table 1 Products containing natamycin requiring (label) amendments[1]

Registration number	Marketing class[2]	Registrant	Product name	Formulation type	Active ingredient[3] (%)
22612	T	Advanced Instruments Inc.	Pimaricin Technical	Dust or Powder	PIM – 85
28530	C	Advanced Instruments Inc.	Brotab Milk Preservative	Tablet	PIM – 1.62 BND – 42.63
30520	T	DSM Food Specialties B.V.	Natamycin TGAI	Solid	PIM – 91.02
30521	C	DSM Food Specialties B.V.	Zivion M	Suspension	PIM – 10.34

1 As of 17 September 2024, excluding discontinued products or products with a submission for discontinuation.

2 T = Technical Grade Active Ingredient, C = Commercial

3 PIM = Natamycin; BND = Bronopol

Appendix II List of commenters to PRVD2024-02

List of commenters' affiliations for comments submitted in response to PRVD2024-02

Category	Commenter
Public[1]	General public

[1] One comment received three times from the same individual.

Appendix III Comment(s) and response(s)

Health Canada received one written comment during the public consultation of the natamycin proposed re-evaluation decision. Commenter affiliation is listed in Appendix II. Summarized comment and Health Canada's response is provided below.

1.0 Comment related to the health assessment

1.1 Comment

A general comment was received from the public related to the health assessment of natamycin; specifically on the requirement of animal testing.

Health Canada response

Health Canada requires information on the potential toxic effects of pesticides to determine the potential hazards and risk to human health and the environment from pesticide exposure. Toxicity information typically includes, in part, animal testing data generated by pesticide manufacturers. These studies are conducted according to international testing protocols, which include requirements to ensure protection of the welfare of laboratory animals. While animal toxicity testing currently plays a critical role in assessing human health and environmental risks from exposure to pesticides, Health Canada supports the reduction of unnecessary animal testing where scientifically justified. To this end, Health Canada does consider requests from pesticide manufacturers to waive requirements for animal studies or to consider validated non-animal alternatives in hazard assessment when feasible and supported scientifically. Health Canada issued guidance for industry on the waiving of mammalian acute toxicity studies in 2013. Health Canada is also an active participant in various international activities aimed at reducing animal testing while ensuring the protection of human health and the environment. Continued analysis of international trends and approaches is important to ensure continued alignment and harmonization. While non-animal alternatives exist for certain types of tests (for example, in vitro tests for irritation), animal testing continues to provide a more accurate assessment of a variety of other potential effects, and more importantly, at what dose level effects may occur, so that this information can then be used to protect human health and the environment.

Appendix IV Label amendments for products containing natamycin

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

1. Technical grade active ingredient:

1.1 Replace the term “guarantee” with “active ingredient”.

1.2 Based on a classification of minimally-irritating to the eyes, currently registered technical grade active ingredient products containing natamycin no longer require the following label statements:

On primary display panel the following signal words:

“DANGER - EYE IRRITANT”

On the Secondary display panel under **PRECAUTION**:

“Severely irritating to the eye; DO NOT get in eyes”

1.3 All registered natamycin product labels must include standard first aid statements as per the new PMRA Guidance Document, *First Aid Labelling Statements* (Canada, 2022).

1.4 The following statement must be included in a section entitled **DISPOSAL**:

“Canadian manufacturers should dispose of unwanted active ingredients and containers in accordance with municipal and provincial/territorial regulations. For additional details and clean-up of spills, contact the manufacturer and the provincial/territorial regulatory agency.”

2. For all commercial class products:

2.1 Replace the term “guarantee” with “active ingredient”.

2.2 Product labels must include standard first aid statements as per the new PMRA Guidance Document, *First Aid Labelling Statements* (Canada, 2022).

2.3 The following statement must be included in a section entitled **STORAGE**:

“Store this product away from food or feed”

3. For commercial class end-use product registered for use as a preservative for milk samples (tablet formulation):

3.1 Under the **PRECAUTIONS** section, precautionary label statements should be updated to meet current standards:

"Workers are required to wear a long-sleeved shirt, long pants, chemical-resistant gloves, protective eyewear (goggles or face shield), shoes and socks during mixing, loading, clean-up and repair when handling the product."

4. For commercial class end-use product registered for use in mushroom facilities (suspension formulation):

4.1 Under the **PRECAUTIONS** section, precautionary label statements should be updated to meet current standards:

"Workers are required to wear a long-sleeved shirt, long pants, waterproof gloves, shoes and socks during mixing, loading, application, clean-up and repair. For postapplication activities including data gathering, harvesting, and handling of used compost and casing, workers must wear a long-sleeved shirt, long pants, waterproof gloves, socks and shoes."

4.2 Add the following statement to a section entitled **DIRECTIONS FOR USE**:

"DO NOT allow releases, effluent or runoff from mushroom houses containing this product to enter lakes, streams, ponds or other waters."

4.3 Add the following statement to a section entitled **DISPOSAL**:

For recyclable containers:

"DO NOT reuse this container for any purpose. This is a recyclable container, and is to be disposed of at a container collection site. Contact your local distributor/dealer or municipality for the location of the nearest collection site. Before taking the container to the collection site:

1. Triple- or pressure-rinse the empty container. Add the rinsings to the spray mixture in the tank.

2. Make the empty, rinsed container unsuitable for further use.

If there is no container collection site in your area, dispose of the container in accordance with provincial/territorial requirements."

For returnable containers:

> "DO NOT reuse this container for any purpose. For disposal, this empty container may be returned to the point of purchase (distributor/dealer)."

For containers that can be refilled for the user by the distributor/dealer:

> "For disposal, this container may be returned to the point of purchase (distributor/dealer). It must be refilled by the distributor/dealer with the same product. DO NOT reuse this container for any other purpose."

Disposal of unused, unwanted product:

> "For information on disposal of unused, unwanted product, contact the manufacturer or the provincial/territorial regulatory agency. Contact the manufacturer and the provincial/territorial regulatory agency in case of a spill, and for clean-up of spills."

4.4 Add Site of Action Grouping and Identification Symbol on the front panel

GROUP	48	FUNGICIDE

4.5 The following statement must be included in a section entitled **RESISTANCE MANAGEMENT RECOMMENDATIONS**

> "For resistance management, [Product Name] contains a Group 48 fungicide. Any fungal population may contain individuals naturally resistant to [Product Name] and other Group 48 fungicides. A gradual or total loss of pest control may occur over time if these fungicides are used repeatedly in the same location. Other resistance mechanisms that are not linked to site of action but specific for individual chemicals, such as enhanced metabolism, may also exist. Appropriate resistance-management strategies should be followed.

To delay fungicide resistance:

- Where possible, rotate the use of [Product Name] or other Group 48 fungicides with different groups that control the same pathogens.
- Use tank mixtures with fungicide from a different group that is effective on the target pathogen when such use is permitted.
- Fungicide use should be based on an integrated disease management program that includes scouting, historical information related to pesticide use and crop rotation and considers host plant resistance, impact of environmental conditions on disease development, disease thresholds, as well as cultural, biological and other chemical control practices.
- Where possible, make use of predictive disease models to effectively time fungicide applications.
- Monitor treated fungal populations for resistance development. Notify [Registrant Name] if reduced sensitivity of the pathogen to [Product Name] is suspected.

If disease continues to progress after treatment with this product, do not increase the use rate. Discontinue use of this product, and switch to another fungicide with a different site of action, if available.

- Contact your local extension specialist or certified crop advisors for any additional pesticide resistance-management and/or IPM recommendations for specific crops and pathogens.

For further information and to report suspected resistance, contact (company representatives) at (toll free number) or at (Internet site).”