Proposed Special Review Decision PSRD2020-04

Special Reviews of Pymetrozine and Its Associated End-use Products

Consultation Document

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

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

Canada

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1.0 Introduction

Pursuant to subsection 17(2) of the *Pest Control Products Act* (PCPA), Health Canada's Pest Management Regulatory Agency (PMRA) initiated a special review of pymetrozine in 2015 (Canada, 2015) based on the 2014 Norway regulatory decision to prohibit all uses of pymetrozine (Rotterdam Convention 2014). The aspect of concern for the special review under subsection 17(2) is relevant to human health (potential carcionogenicity of pymetrozine).

In addition, pursuant to subsection 17(1) of the *Pest Control Products Act*, Health Canada initiated a special review of pymetrozine in 2017 (Canada, 2017) based on information related to pymetrozine and its transformation products in drinking water. The aspect of concern for the special review under subsection 17(1) of the *Pest Control Products Act* is relevant to human health (potential cancer risk from pymetrozine and its metabolites through drinking water exposure).

Pursuant to subsection 18(4) of the *Pest Control Products Act*, Health Canada has evaluated the aspects of concern that prompted the above two special reviews of pest control products containing pymetrozine.

Scientific assessments and the proposed special review decisions of pymetrozine under subsection 17(2) and subsection 17(1) of the *Pest Control Products Act* are outlined below.

2.0 Uses of Pymetrozine in Canada

Pymetrozine is an insecticide used for the control of aphids in leafy vegetables (Crop Group 4), potatoes, highbush blueberries, tobacco, *Rhodiola rosea*, outdoor ornamentals, greenhouse vegetables (pepper, tomato, cucumber and eggplant) and to control Balsam twig aphid on Christmas trees. It is also registered for the control of aphids and the reduction of whiteflies on ornamental plants in greenhouses.

Pymetrozine end-use products are formulated as water dispersible granules. Application methods include aerial, groundboom, airblast and handheld equipment. All registered pest control products containing pymetrozine (Appendix I) are considered for the two special reviews.

3.0 Aspects of concern that prompted the special reviews

Special review under subsection 17(2) of the *Pest Control Products Act*: Based on the review of the Norway information (Rotterdam Convention, 2014), Health Canada identified the aspect of concern that prompted the special review of pymetrozine under subsection 17(2) of the *Pest Control Products Act* as:

- Human health
  - Potential carcinogenicity of pymetrozine

Special review under subsection 17(1) of the *Pest Control Products Act*: Based on information related to pymetrozine and its metabolites in drinking water, Health Canada identified the aspect of concern that prompted the special review under subsection 17(1) of the *Pest Control Products Act* as:

- Human Health
  - Potential cancer risk from pymetrozine and its metabolites through drinking water exposure

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

Following the initiation of the special reviews, Health Canada requested information related to the aspects of concern from provinces and other relevant federal government departments and agencies in accordance with subsection 18(2) of the *Pest Control Products Act*. In response, no information was received related to the aspects of concern. In addition, Health Canada requested information from the provinces with respect to available water monitoring data of pymetrozine, and information received was considered in the assessment.

In order to evaluate the aspects of concern for pymetrozine, Health Canada considered currently available relevant scientific information, which includes the information submitted by the registrant under subsection 19(1) of the *Pest Control Products Act*, environmental fate information from the European Commission, the Canadian water monitoring data, the Norwegian decision, and existing Health Canada assessments (Canada 2002 and Canada, 2003).

4.1 Evaluation of the aspect of concern under subsection 17(2) of the *Pest Control Products Act*: potential carcinogenicity of pymetrozine

Based on the available information, pymetrozine is not considered to be genotoxic. Long-term studies in both rats and mice provided evidence of treatment-related tumours in the liver at the highest dose level tested in both mice and rats. A slightly increased incidence in benign hepatoma or carcinoma or combined hepatoma and carcinoma was also seen at the second highest dose level in female rats and male mice (Canada, 2002).

Possible genotoxic effects for the metabolite CGA 300407 were mentioned in the Norwegian decision (Rotterdam Convention, 2014). The available information on the pymetrozine metabolite, CGA 300407 (CA 1055 B), showed that CGA 300407 was negative in the bacterial reverse mutation assay and did not induce micronuclei in a mouse bone marrow micronucleus test, although it was uncertain if the test material reached the bone marrow in the second study. It was also negative in an unscheduled deoxyribonucleic acid (DNA) synthesis assay with primary mouse hepatocytes. No evidence of DNA damage was observed in the mouse liver in vitro (Comet assay). However, CGA 300407 was clastogenic in mammalian cytogenetic assays in Chinese hamster ovary cells and in human lymphocytes in the presence and absence of metabolic activation. It also induced DNA damage in the mouse fore-stomach in vivo. Overall, Health Canada concluded that the available information does not provide sufficient evidence to indicate that CGA 300407 is less toxic than parent pymetrozine. In addition, genotoxicity of other metabolites of pymetrozine was considered as part of the dietary assessment (see Section 4.2.2).

In order to determine the approach for characterization of cancer risks for pymetrozine, Health Canada considered all available information, including several mechanistic type studies conducted in rats and/or mice (for example, hepatic cell proliferation, liver and thyroid biochemical and morphology, promotional effects) (Canada, 2002), as well as the newly submitted data on the CGA 300407 metabolite. In light of the uncertainty regarding the mode of action for the observed pymetrozine-induced tumours, Health Canada continues to consider a more conservative quantitative risk assessment methodology utilizing linear extrapolation, as described in PRDD2002-03, to be appropriate for characterization of potential cancer risks in humans. A cancer potency factor (q_1*) of 1.19×10^{-2} $(mg/kg\ bw/day)^{-1}$ calculated on the basis of the total tumour data (combined benign hepatomas and carcinomas) from the mouse oncogenicity study was used to assess cancer risks for the Canadian population.

4.1.1 Potential cancer risk from exposure to pymetrozine

To determine if risk to Canadians from exposure to pymetrozine was acceptable, Health Canada conducted scientifically-based risk assessments relative to the aspect of concern (potential cancer risk).

Exposure to pymetrozine may occur through consuming food and drinking water, working as a mixer/loader/applicator, and/or by entering treated sites to perform postapplication activities. There is also a potential for non-occupational exposure to spray drift during commercial applications. As such, Health Canada assessed potential dietary (Section 4.1.1.1) occupational (Section 4.1.1.2) and non-occupational (Section 4.1.1.3) cancer risks resulting from exposure to pymetrozine.

The cancer risk is determined by calculating the lifetime average daily dose (LADD) from dermal, inhalation and/or oral exposure. The LADD is multiplied by the cancer potency factor (q_1*) to obtain a lifetime cancer risk estimate, which is a measurement of probability. A lifetime cancer risk in the range of 1×10^{-5} in worker populations and in the range of 1×10^{-6} in residential populations is generally acceptable.

4.1.1.1 Dietary exposure and risk assessment

Based on the risk assessment, the cancer dietary (food plus drinking water) risk is not considered acceptable under the current conditions of use. To mitigate potential dietary risks, all outdoor uses of pymetrozine are proposed for cancellation. For details of the cancer dietary risk assessment refer to Section 4.2.5.

4.1.1.2 Occupational exposure and risk assessment

Exposure to pymetrozine may occur through working as a mixer/loader/applicator, and/or by entering treated sites to perform postapplication activities.

4.1.1.2.1 Dermal absorption factor

A dermal absorption factor was determined to be 7% based on an *in vivo* rat study (Canada, 2002).

4.1.1.2.2 Cancer risk assessment for mixer/loaders and applicators

There is a potential for dermal and inhalation exposure of workers mixing/loading and applying pymetrozine. Based on the current use pattern the following exposure scenarios are expected:

- Mixing/loading of water-dispersible granules and application as a spray using groundboom equipment (outdoor ornamentals, potatoes, Crop Group 4 leafy vegetables, tobacco, Christmas trees, *Rhodiola rosea*)
- Mixing/loading of water-dispersible granules and application as a spray using airblast equipment (outdoor ornamentals, Christmas trees, highbush blueberries)
- Mixing/loading of water-dispersible granules and application as a spray using aerial equipment (potatoes)
- Mixing/loading of water-dispersible granules and application as a spray using hand-held equipment (outdoor and greenhouse ornamentals, greenhouse tomatoes, cucumbers, peppers and eggplants)
- Mixing/loading of water-dispersible granules and application as a spray using an automated sprayer in a greenhouse (greenhouse ornamentals and greenhouse vegetables)

Chemical-specific handler exposure data were not available for pymetrozine, therefore, dermal and inhalation exposures were estimated using unit exposure data from the Agricultural Handlers Exposure Task Force (AHETF) and the Pesticide Handlers Database (PHED).

For workers mixing/loading and applying (M/L/A) using automated sprayers in greenhouses, only the mixing/loading scenario was assessed as no applicator exposure is anticipated for this type of application equipment.

Additional assumptions included using maximum application rates, default values for area treated per day, current personal protective equipment (PPE), and an average worker body weight of 80 kg. Dermal exposure was adjusted for a 7% dermal absorption factor. To calculate a lifetime average daily dose (LADD), daily exposure was amortized over an individual's lifetime assuming an exposure frequency of 30 days per year, a career duration of 40 years, and a life expectancy of 78 years.

The cancer risk assessment for mixer/loaders and applicators is summarized in Appendix II, Tables 2.1 and 2.2. The estimated lifetime cancer risks for all assessed scenarios are below 1×10^{-5} (when workers are wearing a long-sleeved shirt, long pants and chemical-resistant gloves) and are considered acceptable. A label statement is proposed to indicate that the PPE required for workers involved in mixing/loading and application consists of a long-sleeved shirt, long pants and chemical-resistant gloves.

4.1.1.2.3 Cancer risk assessment for postapplication workers

For workers entering treated fields and greenhouses to conduct postapplication activities, dermal exposure is considered to be the primary route of exposure. Considering the low volatility of pymetrozine and assuming that at least 12 hours have passed before re-entry, inhalation exposure to pymetrozine is not expected to be of concern for postapplication workers re-entering treated sites (outdoor and indoor).

For workers re-entering a treated site, restricted-entry intervals (REIs) are calculated to determine the minimum length of time required before workers can enter after application. The REI is the duration of time that must elapse in order to allow residues to decline to a level where non-cancer and cancer risks are considered to be acceptable for postapplication worker activities.

Exposure to workers entering treated sites was estimated using activity-specific transfer coefficients (TCs) and dislodgeable foliar residue (DFR) values. The DFR refers to the amount of residue that can be dislodged or transferred from a surface, such as leaves of a plant. The TC is a measure of the relationship between exposure and DFRs for individuals engaged in a specific activity, and is calculated from data generated in field exposure studies. The TCs are specific to a given crop and activity combination and reflect standard agricultural work clothing worn by adult workers. The activity-specific TC from the Agricultural Re-Entry Task Force (ARTF) was used.

For cancer assessment, lifetime average daily dose (LADD) estimates were calculated assuming 30-day time-weighted average (TWA) DFR values, crop-specific TC values, an 8-hour work day, an average worker body weight of 80 kg, a dermal absorption factor of 7%, 30 days of exposure per year (unless otherwise stated), 40 year career duration, and a lifetime of 78 years. A maximum spray volume of 2000 L water/ha was assumed for the greenhouse risk assessments. In addition, a spray volume of 1000 L/ha was considered for the greenhouse cut flower assessment for refinement purposes. To obtain cancer risk estimates, the estimated LADD was multiplied by the q_1*.

Outdoor uses

The postapplication cancer risk assessment for outdoor uses of pymetrozine is summarized in Appendix III, Table 3.1. The cancer risks to workers entering treated fields on day 0 (day of application) are considered acceptable for all outdoor uses except outdoor ornamentals grown for cut flowers. The cancer risk is not considered to be acceptable for workers involved in hand-harvesting, disbudding and hand-pruning of outdoor ornamentals grown for cut flowers. An REI of 1 day would be necessary to mitigate the postapplication exposure risk. However, as the outdoor uses are proposed for cancellation based on dietary risks of concern (see Section 4.2.5), the REI of one day is not included as part of the proposed risk management measures (Section 6.0).

Greenhouse uses

The postapplication cancer risk assessment for greenhouse uses of pymetrozine is summarized in Appendix III, Tables 3.2 and 3.3.

Cancer risk to greenhouse workers involved in postapplication activities in greenhouse vegetables and ornamentals are acceptable, except for workers involved in hand-harvesting, disbudding and hand-pruning of greenhouse ornamentals grown for cut flowers. Therefore, the following mitigation measures are proposed for greenhouse ornamentals grown for cut flowers:

> A limit of 1000 L spray solution/ha and, a reduction of the maximum application rate from 10 g a.i./100 L to 8.5 g a.i./100 L

For greenhouse vegetables, the current product label only specifies a minimum spray volume of 1000 L water/ha, however a maximum spray volume is not specified. Therefore, a maximum spray volume of 2000 L/ha is proposed to be added for greenhouse vegetables for clarity.

The proposed label amendments are summarized in Appendix VII.

4.1.1.3 Non-occupational exposure and risk assessment

There are no registered domestic-class products containing pymetrozine; therefore, domestic handler exposure is not anticipated. However, the current commercial end-use product labels do not limit application to only commercial settings. For clarity, a label statement prohibiting the use of pymetrozine in residential settings is required. But, as the outdoor uses are proposed for cancellation (based on dietary risk - Section 4.2.5), the label statement prohibiting the use of pymetrozine in residential settings is not included as part of the proposed risk management measures (Section 6.0).

There is a potential for exposure to pymetrozine residues during agricultural applications of pymetrozine (bystander) and from contact with treated ornamentals (retail plants).

For bystanders, potential exposure to spray drift is expected to be significantly lower than the inhalation exposure of an applicator, for whom the potential cancer inhalation risks are considered to be acceptable under current conditions of use (see Section 4.1.1.2.2). In addition, current labels have statements to mitigate spray drift to residential areas. On this basis, the potential risk to bystanders is considered to be acceptable under the current conditions of use. No further risk mitigation measures are proposed.

For individuals exposed to pymetrozine residues on retail plants, potential exposure is expected to occur on an intermittent short-term basis and to be significantly lower than exposure of greenhouse workers. The cancer risks for postapplication greenhouse workers is considered to be acceptable with the proposed mitigation measures (Section 4.1.1.2.3). On this basis, the potential cancer risks from exposure to pymetrozine residues on retail plants is also considered acceptable with the proposed mitigation measures (Section 6.0).

4.1.1.4 Aggregate exposure and risk assessment

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

There are no residential uses registered, thus there is no direct exposure expected.

All outdoor uses of pymetrozine are proposed for cancellation to mitigate the cancer dietary risk (Section 6.0). Bystander exposure is not expected from greenhouse uses. Aggregate risk from food and water is considered acceptable for greenhouse uses.

For individuals handling treated retail plants, only greenhouse uses were considered in the aggregate risk assessment. Given the intermittent nature of exposure, potential exposure to pymetrozine residues on retail plants is not expected to make a significant contribution to overall exposure. On this basis, the aggregate cancer risks for individuals coming in contact with treated retail plants is considered to be acceptable provided that all outdoor uses are cancelled (Section 6.0).

4.1.1.5 Cumulative exposure and risk assessment

The *Pest Control Products Act* requires that Health Canada consider the cumulative exposure to pesticides with a common mechanism of toxicity according to SPN2018-02, *Cumulative Health Risk Assessment Framework*. Pymetrozine is a 1,2,4-triazine. Health Canada will be conducting a cumulative health risk assessment for the triazine group of pesticides in the future.

Overall conclusion for the special review of pymetrozine under subsection 17(2) of the *Pest Control Products Act*:

Based on the available information, the assessment of the aspect of concern (potential carcionogenicity of pymetrozine) indicated that:

- The cancer dietary (food plus drinking water) risk is not considered acceptable under current conditions of use. Therefore, the following risk mitigation measures are proposed:
  - Cancellation of all outdoor uses of pymetrozine.
  - A revised label statement prohibiting effluent or runoff from greenhouses containing pymetrozine to enter into aquatic systems is proposed for labels with greenhouse uses as per current standard label practice.
- The cancer risk to mixers/loaders/applicators (greenhouse and outdoor use) is considered to be acceptable when workers are wearing PPE consisting of a long-sleeved shirt, long pants and chemical-resistant gloves. A label statement is proposed to indicate that the PPE required for workers involved in mixing/loading and application consists of a long-sleeved shirt, long pants and chemical-resistant gloves.
- The cancer risk to postapplication workers is considered to be acceptable for all outdoor uses under the current conditions of use except outdoor ornamentals grown for cut flowers. An REI of 1 day would be necessary to mitigate the postapplication exposure risk for outdoor ornamentals grown for cut flowers (workers involved in hand-harvesting,

disbudding and hand-pruning). However, as the outdoor uses are proposed for cancellation (based on dietary risks) the required REI is not included as part of the proposed risk management measures.

- The cancer risk to postapplication workers is considered to be acceptable under the current conditions of use for all greenhouse uses except for ornamentals grown for cut flowers. However, with the following proposed risk mitigation measures, potential postapplication risk to workers of greenhouse ornamentals grown for cut flowers would also be acceptable:
  - A limit of 1000 L spray solution/ha, and a reduction of the maximum application rate from 10 g a.i./100 L to 8.5 g a.i./100 L.

In addition, specify the maximum spray volume of 2000 L/ha for greenhouse vegetables for clarity.

4.2 Evaluation of the aspect of concern under subsection 17(1) of the *Pest Control Products Act*: potential cancer risk from pymetrozine and its metabolites through drinking water exposure

Potential carcinogenicity of pymetrozine and its metabolites is described under Section 4.1.

4.2.1 Environmental fate and behaviour of pymetrozine and its transformation products in the environment

Pymetrozine is stable to hydrolysis at pH 7 but undergoes hydrolysis under acidic conditions resulting in two major transformation products, CGA 215525 and CGA 300407.

In soil, phototransformation of pymetrozine is not expected to be a major route of transformation (half-lives ranged between 1.9 and 6.2 days). Aerobic biotransformation of pymetrozine exhibited a biphasic pattern with DT_{50} values between 5 to 527 days. Major transformation products were CGA 359009, CGA 363431, CGA 180777 and CGA 294849. Although CGA 363430, CGA 300407 and CGA 255548 residues were observed to exceed 10% of the parent, they were considered to be transitional in nature as quantities of these residues rapidly decreased.

In water, phototransformation of pymetrozine is a major route of transformation with a half-life of 2.1 days. Major aqueous phototransformation products were CGA 215525 and CGA 249257. CGA 359009 was the only major transformation product seen in aerobic aqueous biotransformation studies. Aerobic aqueous biotransformation followed a biphasic pattern (DT_{50} values: 7.6 to 527 days). Major transformation products found in anaerobic aqueous biotransformation studies were CGA 249257, GS 23199 and CGA 180777. The DT_{50} under anaerobic aqueous conditions was 74 to 109 days.

Pymetrozine is moderately mobile to immobile in soil, while its transformation products are moderately to very highly mobile in soil (Appendix IV, Table 4.1).

4.2.2 Definition of the residue in drinking water

The residue definition in drinking water includes the parent (pymetrozine) and the following major transformation products, identified in environmental fate studies: CGA 215525, CGA 359009, CGA 249257, CGA 294849, CGA 363431 and GS 23199.

Although CGA 180777 (also known as niacin, a form of vitamin B12) was identified as a major transformation product in environmental fate studies (see Section 4.2.1 above), it was not included in the residue definition for drinking water as it is an essential nutrient, is ubiquitous in the environment and is not of toxicological concern.

The potential toxicity of the metabolites of pymetrozine and their impact on the residue definition were examined. It was concluded that there was insufficient evidence, based on the available information, to suggest that any of the metabolites (other than CGA 128632) were less toxic than pymetrozine and that they should be excluded from the residue definition on the basis of toxicity considerations.

4.2.3 Drinking water modelling

Level 2 Estimated Environmental Concentrations (EECs) for the combined residue of pymetrozine and six transformation products - CGA 215525, CGA 359009, CGA 249257, CGA 294849, CGA 363431, and GS 23199 expressed as parent equivalents - in potential sources of drinking water were calculated using the Pesticides in Water Calculator (PWC V 1.52) model. Modelling for surface water included a small reservoir adjacent to an agricultural field, and used scenarios representing different crops and regions across Canada. Modelling for groundwater used scenarios representing different regions of Canada. The reported EECs were the highest from across these scenarios. All scenarios were run for 50 years. The results are presented in Appendix V, Table 5.1. Environmental fate data used in the modelling are summarized in Appendix V, Tables 5.2 and 5.3.

4.2.4 Drinking water monitoring

A search for Canadian monitoring data (from the years 2000 to present) on pymetrozine in groundwater and surface water was undertaken as part of the special review. Limited Canadian data are available (surface water, Alberta only). American databases and reports were also searched for pymetrozine water monitoring data. The American databases searched included the California's Department of Pesticide Regulation (CDPR) database and the Water Quality Portal, which encompasses data from the United States Geological Survey's National Water Quality Assessment program (NAWQA), and the United States Environmental Protection Agency's STORET data warehouse. Annual Reports from the United States Department of Agriculture's Pesticide Data Program were also included in the search.

No monitoring data were available for pymetrozine in groundwater from Canada. American monitoring data for pymetrozine in groundwater were rare (1 detection out of 845 samples), with the maximum concentration of pymetrozine detected in groundwater being 0.016 µg/L.

Detection of pymetrozine in Canadian and American surface water were rare (1 detection out of 2490 samples or 0.04% of samples), with the maximum concentration of pymetrozine being 0.0032 µg/L. Very little Canadian data is available and sampling is limited to Alberta. Therefore, EECs from water modeling were used in the drinking water risk assessment.

4.2.5 Dietary exposure assessment

The dietary exposure assessment was conducted using the Dietary Exposure Evaluation Model - Food Commodity Intake Database™ (DEEM-FCID™, Version 4.02, 05-10-c) program which incorporates food consumption data from the National Health and Nutritional Examination Survey, What We Eat in America (NHANES/ WWEIA) dietary survey for the years 2005-2010 available through CDC's National Center for Health Statistics (NCHS).

The refined chronic cancer risk assessment was conducted using median residues from Canadian and/or American field trials, experimental processing factors and/or anticipated residues for processed commodities, and percent crop treated data. Levels in potential sources of drinking water were estimated based on Level 2 modelling for the combined residue of pymetrozine and six metabolites – CGA 215525, CGA 359009, CGA 249257, CGA 294849, CGA 363431 and GS 23199 expressed as parent equivalents. EECs in surface water (yearly EECs ranging from 1.7 to 4.2 µg a.i./L) and in groundwater (yearly EEC = 45 µg a.i./L) were calculated using the Pesticide Water Calculator model (PWC, version 1.52) based on the modelled outdoor uses (for details refer to Section 4.2.3).

The cancer risk is determined by multiplying the lifetime average daily dose (LADD) by the cancer potency factor (q_1*) to obtain a lifetime cancer risk estimate, which is a measurement of probability. A lifetime cancer risk that is equal to or below 1×10^{-6} (one-in-a-million) usually indicates acceptable risk for the general population.

The lifetime cancer risk from exposure to pymetrozine in food and drinking water (EEC value = 45 µg a.i./L, Level 2, ground water) was estimated to be 1×10^{-5} for the general population, which is above 1×10^{-6}. A critical commodity contribution analysis indicates that drinking water is the largest contributor to the cancer risk (95.72% of total exposure; cancer risk of 1×10^{-5}). The lifetime cancer risk from exposure to pymetrozine in food only was estimated to be 5×10^{-7} for the general population, which is considered acceptable (Appendix VI, Table 6.1).

Based on the risk assessment, the cancer dietary (food plus drinking water) risk is not considered acceptable under current conditions of use. To mitigate potential dietary risks, all outdoor uses of pymetrozine are proposed for cancellation.

The modelled residues of pymetrozine and its metabolites in drinking water are based on the outdoor use scenarios. While effluent from greenhouses may be a potential route of contamination of surface drinking water sources, the current end-use product labels include use directions prohibiting the discharge of effluent, waste and drainage water containing pymetrozine into aquatic systems. The potential for indirect contamination of surface drinking water is expected to be minimal following applications of pymetrozine in greenhouses. Based on the above, the potential cancer dietary risk resulting from greenhouse applications of pymetrozine is considered to be acceptable.

A label statement prohibiting the discharge of greenhouse effluent into aquatic systems is proposed to be added for the ENDEAVOR® 50WG Insecticide product label (Reg. No. 27273) as per current standard label practice. The proposed label amendments are summarized in Appendix VII.

Overall conclusion for the special review of pymetrozine under subsection 17(1) of the *Pest Control Products Act*:

Based on the available information, the assessment of the aspect of concern (potential cancer risk from pymetrozine and its metabolites through drinking water exposure) indicated that:

- The cancer dietary (food plus drinking water) risk is not considered acceptable under current conditions of use. Therefore, the following risk mitigation measures are proposed:
  - Cancellation of all outdoor uses of pymetrozine.
  - A revised label statement prohibiting effluent or runoff from greenhouses containing pymetrozine to enter into aquatic systems is proposed for with greenhouse uses as per current standard label practice.

5.0 Incident reports

As of 23 June 2020, there were no Canadian incident reports relating to the aspects of concern identified above. Four scientific studies involving pymetrozine have been reported to the Incident Reporting Program and were considered for this special review.

6.0 Proposed special review decision for pymetrozine

Special review under subsection 17(1) of the *Pest Control Products Act*

Evaluation of available scientific information related to the aspect of concern (potential cancer risk from pymetrozine and its metabolites through drinking water exposure) found that the potential dietary cancer risk of pymetrozine is considered to be acceptable with the following proposed risk mitigation measures:

- Cancel all outdoor uses of pymetrozine:
  - leafy vegetables (Crop Group 4)
  - potatoes
  - highbush blueberries
  - tobacco
  - *Rhodiola rosea*
  - outdoor ornamentals
  - Christmas trees
- A revised label statement prohibiting effluent or runoff from greenhouses containing pymetrozine to enter into aquatic systems as per the current label standards.

Special review under subsection 17(2) of the *Pest Control Products Act*

Evaluation of available scientific information related to the aspect of concern (potential carcinogenicity of pymetrozine) found that:

- The potential cancer risk (dietary) is considered to be acceptable with the following proposed risk mitigation measures:
  - Cancel all outdoor uses of pymetrozine:
    - leafy vegetables (Crop Group 4)
    - potatoes
    - highbush blueberries
    - tobacco
    - *Rhodiola rosea*
    - outdoor ornamentals
    - Christmas trees
  - A revised label statement prohibiting effluent or runoff from greenhouses containing pymetrozine to enter into aquatic systems as per the current label standards.
- The potential cancer risk of pymetrozine (occupational) is considered to be acceptable with the following proposed risk mitigation measures:
  - PPE requirement of a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes during mixing, loading, application, clean-up and repair.
  - For greenhouse ornamentals grown for cut flowers to minimize exposure to postapplication workers: A limit of 1000 L spray solution per hectare; and a reduction of the maximum application rate from 10 g a.i./100 L to 8.5 g a.i./100 L.
  - For greenhouse vegetables: To improve clarity, a maximum spray volume of 2000 L/ha is proposed.

As the outdoor uses are proposed for cancellation, the following risk mitigation measures are not included as part of the proposed risk management measures at this time:

- revised REI for outdoor ornamentals grown for cut flowers
- label statement indicating prohibition of use in residential areas.

Based on the assessment of the aspects of concern under subsection 17(1) and subsection 17(2) of the *Pest Control Products Act*, Health Canada's Pest Management Regulatory Agency, under the authority of the *Pest Control Products Act*, is proposing to confirm the current registration of pymetrozine products for sale and use in Canada with the proposed risk mitigation measures (Appendix VII) pursuant to subsection 21(1) of the *Pest Control Products Act*.

These proposed special review decisions are a consultation document.[1] Health Canada 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*.

7.0 Next steps

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

List of abbreviations

a.i.	active ingredient
ARTF	Agricultural Re-Entry Task Force
bw	body weight
d	day(s)
DEEM-FCID	Dietary Exposure Evaluation Model - Food Commodity Intake Database
DFR	dislodgeable foliar residue
DNA	deoxyribonucleic acid
DT_{50}	half-life
EEC	Estimated Environmental Concentration
g	gram(s)
ha	Hectare
kg	kilogram(s)
K_{oc}	soil-water organic carbon coefficient
K_d	distribution coefficient (between soil and water)
L	litre(s)
LADD	lifetime average daily dose
PMRA	Pest Management Regulatory Agency
PHED	Pesticide Handlers Database
PPE	personal protective equipment
PWC	Pesticide Water Calculator
q_1*	cancer potency factor
REI	Re-entry interval
TC	transfer coefficient
TWA	time-weighted average
µg	Microgram

Appendix I Registered pymetrozine products in Canada

Table 1.1 Products subject to proposed label amendments[a]

Registration number	Marketing class	Registrant	Product name	Formulation type	Guarantee
27272	Technical	Syngenta Canada Inc.	Pymetrozine Technical	Solid	98.3%
27273	Commercial	Syngenta Canada Inc.	Endeavor 50WG Insecticide	Water-dispersible granules	50%
27274	Commercial	Syngenta Canada Inc.	Fulfill 50WG Insecticide	Water-dispersible granules	50%

[a] As of 12 May 2020.

Appendix II Mixer/loader/applicator exposure and risk assessment

Table 2.1 Cancer exposure and risk estimates for workers mixing/loading and applying Pymetrozine using groundboom, airblast and aerial application equipment

Crop		Maximum AR[a] (kg a.i./ha)	ATPD[b] (ha)	LADD[c] (mg/kg bw/day)	Cancer risk[d]
Mixing loading of dry flowable (AHETF) and application using open cab groundboom equipment (AHETF); PPE: a long sleeved shirt, long pants and chemical-resistant gloves					
Outdoor ornamentals		0.500	27.5	2.26×10^{-4}	3×10^{-6}
Potatoes		0.097	240	3.80×10^{-4}	5×10^{-6}
Tobacco, Crop Group 4 (leafy vegetables)		0.097	12	1.90×10^{-5}	2×10^{-7}
Rhodiola rosea		0.060		1.18×10^{-5}	1×10^{-7}
Mixing loading of dry flowable (AHETF) and application using open cab airblast equipment (AHETF); PPE: a long sleeved shirt, long pants and chemical-resistant gloves					
Highbush blueberries, Christmas trees		0.097	7	1.07×10^{-4}	1×10^{-6}
Outdoor ornamentals		0.500		5.54×10^{-4}	7×10^{-6}
Mixing loading of dry flowable (AHETF) and application using aerial equipment (AHETF); PPE: a long sleeved shirt, long pants and chemical-resistant gloves					
Potatoes	Mixer/loader	0.097	318	4.48×10^{-4}	5×10^{-6}
	Applicator			3.18×10^{-6}	4×10^{-8}

AR = application rate; ATPD = area treated per day; LADD = lifetime adjusted daily dose; PPE = personal protective equipment; AHETF = agricultural handler exposure task force

[a] Maximum AR (kg a.i./ha) – as per current product labels

[b] ATPD (ha) - default PMRA values

[c] LADD (mg/kg bw/day) = [(dermal unit exposure (mg/kg a.i.) × 7% DAF + inhalation unit exposure (mg/kg a.i.)) × AR (kg a.i./ha) × ATPD (ha)/average worker body weight of 80 kg] × frequency of exposure (50 days/year) × lifetime exposure (40 years/78 years).

[d] Cancer risk = LADD × q_1* of 1.19×10^{-2} $(mg/kg\ bw/day)^{-1}$; occupational cancer risk threshold of 1×10^{-5}

Table 2.2 Cancer risk assessment for workers mixing/loading and applying Pymetrozine using hand-held equipment

Application equipment	Maximum AR[a] (kg a.i./L)	Volume handled per day[b] (L)	LADD[c] (mg/kg bw/day)	Cancer risk[d]
Mixing/loading of dry flowable (AHETF) and application using hand-held equipment (PHED); PPE: a long-sleeved shirt, long pants and chemical resistant gloves.				
Manually-pressurized handwand	0.0001	150	1.10×10^{-6}	1×10^{-8}
Mechanically-pressurized handgun	0.0001	3800	1.14×10^{-4}	1×10^{-6}
Backpack sprayer	0.0001	150	3.72×10^{-6}	4×10^{-8}

AR = application rate; ATPD = area treated per day; LADD = lifetime adjusted daily dose

[a] Maximum Application Rate (kg a.i./L) – based on the following label restrictions: outdoor ornamentals 10 g a.i./100 L and 5000 L/ha; greenhouse ornamentals (including cut flowers) 10 g a.i./ 100 L; greenhouse peppers, tomatoes, cucumbers and eggplants 100 g a.i./1000 L/ha.

[b] Volume handled per day (L) – default PMRA values

[c] LADD (mg/kg bw/day) = [(dermal unit exposure (mg/kg a.i.) × 7% DAF + inhalation unit exposure (mg/kg a.i.)) × AR (kg a.i./ha) × ATPD (ha)/average worker body weight of 80 kg] × frequency of exposure (50 days/year) × lifetime exposure (40 years/78 years).

[d] Cancer risk = LADD × q_1* of 1.19×10^{-2} $(mg/kg\ bw/day)^{-1}$; occupational cancer risk threshold 1×10^{-5}

Appendix III Postapplication exposure and risk assessment

Table 3.1 Lifetime cancer risks to workers from postapplication exposure to Pymetrozine from outdoor uses

Crop	Re-entry activity	30-day TWA DFR[a] (µg a.i./cm^2)	TC[f] (cm^2/hr)	LADD[g] (mg/kg bw/day)	Cancer risk[h]	Cancer REI (days)
Blueberry, highbush	Irrigation (hand-set)	0.0770[b]	1750	3.98×10^{-5}	5×10^{-7}	0
	Hand-weeding, bird control, scouting, hand pruning, frost control		640	1.45×10^{-5}	2×10^{-7}	
Rhodiola rosea	Hand weeding	0.1342[c]	4400	1.74×10^{-4}	2×10^{-6}	0
	Irrigation (hand-set)		1750	6.93×10^{-5}	8×10^{-7}	
	Scouting		1300	5.15×10^{-5}	6×10^{-7}	
Christmas Trees	Irrigation (hand-set)	0.1503[d]	1750	7.76×10^{-5}	9×10^{-7}	0
	Harvesting		1400	6.21×10^{-5}	7×10^{-7}	
	Pruning (hand), scouting, shaping		580	2.57×10^{-5}	3×10^{-7}	
	Hand weeding, grading, tagging		100	4.43×10^{-6}	5×10^{-8}	
Potatoes	Irrigation (hand-set)		1750	7.76×10^{-5}	9×10^{-7}	0
	Roguing		1100	4.88×10^{-5}	6×10^{-7}	
	Scouting		210	9.31×10^{-6}	1×10^{-7}	
Tobacco	Irrigation (hand-set)		1750	7.76×10^{-5}	9×10^{-7}	0
	Harvesting, canopy management		800	3.55×10^{-5}	4×10^{-7}	
	Scouting, hand weeding		90	3.99×10^{-6}	5×10^{-8}	
CG 4 Leafy Vegetables	Irrigation (hand-set)		1750	7.76×10^{-5}	9×10^{-7}	0
	Hand harvesting		1100	4.88×10^{-5}	6×10^{-7}	
	Scouting (except boy choy & nappa)		210	9.31×10^{-6}	1×10^{-7}	
	Hand weeding, thinning		70	3.10×10^{-6}	5×10^{-8}	
Outdoor ornamentals (except cut flowers)	irrigation (hand-set)	1.1182[e]	1750	5.77×10^{-4}	7×10^{-6}	0
	all activities except irrigation (hand set)		230	7.59×10^{-5}	9×10^{-7}	
Outdoor ornamentals grown for cut flowers	**Hand harvesting, disbudding, hand pruning**		4000	1.32×10^{-3}	$\mathbf{2 \times 10^{-5}}$	**1**
	irrigation (hand-set)		1750	5.77×10^{-4}	7×10^{-6}	0
	all activities except hand harvesting, disbudding, hand pruning or irrigation (hand-set)		230	7.59×10^{-5}	9×10^{-7}	0

DFR = Dislodgeable Foliar Residue; TWA time weighed average; TC = Transfer Coefficient; LADD = lifetime adjusted daily dose

[a] 30-day TWA DFR estimated assuming 25% residue deposition following application with 10% dissipation per day over 30 days.
[b] Where the 30-day TWA DFR is based on two applications, 120 days apart, at a rate of 96.5 g a.i./ha (in other words, 1 application pre-bloom and 1 application postharvest) for highbush blueberries.
[c] Where the 30-day TWA DFR is based on three applications, 7 days apart, at a rate of 60 g a.i./ha for *Rhodiola rosea*
[d] Where the 30-day TWA DFR is based on two applications, 7 days apart, at a rate of 96.5 g a.i./ha for potatoes, leafy vegetables, tobacco, and Christmas trees.
[e] Where the 30-day TWA DFR is based on three applications, 7 days apart, at a rate of 500 g a.i./ha for outdoor ornamentals, assuming 0.1 g a.i./L and a maximum spray volume of 5000 L/ha.
[f] TC - from the Agricultural Re-Entry Task Force (ARTF)
[g] LADD (mg/kg bw/day) = [30-day TWA DFR (µg a.i./cm^2) × 0.001 (µg/mg) × 7% dermal absorption × TC (cm^2/hr) × 8 (hrs/day)] / average worker body weight (80 kg) × frequency of exposure (30 days/year) × lifetime exposure (40 yrs./78 yrs.)
[h] Cancer risk = LADD × q_1* of 1.19×10^{-2} (mg/kg bw/day)$^{-1}$, occupational cancer threshold 1×10^{-5}

Table 3.2 Lifetime cancer risks to workers from postapplication exposure to Pymetrozine from greenhouse vegetable uses

Crop	Application rate	Re-entry Activity	30-day TWA DFR[a] (µg a.i./cm^2)	TC[b] (cm^2/hr)	LADD[c] (mg/kg bw/day)	Cancer risk[d]	Cancer REI
Greenhouse Vegetables (tomatoes, cucumbers, peppers, eggplant)	2 × 100 g a.i./ha RTI of 7 days	All activites	0.3442	1,400	1.19×10^{-3}	1×10^{-5}	0

DFR = Dislodgeable Foliar Residue; TWA time weighed average; TC = Transfer Coefficient; LADD = lifetime adjusted daily dose; REI = Restricted Entry Interval

[a] 30-day TWA DFR estimated assuming 25% residue deposition following application with 2% dissipation per day over 30 days based on two applications, 7 days apart, at the registered maximum label rate of 100 g a.i./ha. The current product label specifies a minimum spray volume of 1000 L water/ha, however a maximum spray volume is not specified. A maximum spray volume of 2000 L water/ha was assumed for the risk assessment (PRDD2002-03) and must be specified on the label for clarity.
[b] TC - from the Agricultural Re-Entry Task Force (ARTF)
[c] LADD (mg/kg bw/day) = [30-day TWA DFR (µg a.i./cm^2) × 0.001 (µg/mg) × 7% dermal absorption × TC (cm^2/hr) × 8 (hrs/day)] / average worker body weight (80 kg) × frequency of exposure (250 days/year) × lifetime exposure (40 years/78 years). Where the exposure frequency of 250 working days per year is based on 52 weeks in a year × 5 working days in a week = 260 working days minus 10 vacation days and assuming the worst case scenario of 1 crop cycle per year and that application of pymetrozine occurs on day 0 and day 8.
[d] Cancer risk = LADD × q_1* of 1.19×10^{-2} (mg/kg bw/day)$^{-1}$, occupational cancer threshold 1×10^{-5}

Table 3.3 Lifetime cancer risks to workers from postapplication exposure to Pymetrozine from greenhouse ornamental uses

Crop	Application rate[a]		Number of application per crop cycle	30-day TWA DFR[b] ($\mu g/cm^2$)	Activity	TC[c] (cm^2/hr)	Frequency of exposure (days/year)	LADD[d] (mg/kg bw/day)	Cancer risk[e]	REI
	g a.i. /100L	g a.i. /ha								
Ornamentals, except cut flowers, greenhouse	**Spray volume = 2000 L/ha**									
	10	200	2 RTI 7 days	0.6885	all activities except irrigation (hand set)	230	250	3.90×10^{-4}	5×10^{-6}	0
Ornamentals grown for cut flowers	10	200	2 RTI 7 days	0.6885	container moving, pinching, weeding hand, scouting, plant support/stalking, transplanting	230	250	3.90×10^{-4}	5×10^{-6}	0
	Spray volume = 1000 L/ha									
	10	100	2 RTI 7 days	0.3442	disbudding, hand pruning and hand harvesting cut flowers	4000	100[f]	1.36×10^{-3}	**2×10^{-5}**	4
			1	0.1894				7.50×10^{-4}	9×10^{-6}	0
	8.5	85	2 RTI 7 days	0.2926				1.16×10^{-3}	1×10^{-5}	0
	5	50	2 RTI 7 days	0.1721				6.80×10^{-4}	8×10^{-6}	0

DFR = Dislodgeable Foliar Residue; TWA = time weighed average; TC = Transfer Coefficient; LADD = lifetime adjusted daily dose; REI = Restricted-Entry Interval

[a] Application rate (g a.i./100 L) as per current product label, application rate in g a.i./ha estimated assuming currently registered rates of 5–10 g a.i./100 L and a spray volume of 2000 or 1000 L/ha

[b] 30-day TWA DFR estimated assuming 25% residue deposition following application at the specified rate with 2% dissipation per day over 30 days.

[c] TC from the Agricultural Re-Entry Task Force (ARTF)

[d] LADD (mg/kg bw/day) = [30-day TWA DFR (μg a.i./cm^2) × 0.001 ($\mu g/mg$) × 7% dermal absorption × TC (cm^2/hr) × 8 (hrs/day)] / average worker body weight (80 kg) × frequency of exposure (days/year) × career duration (40 yrs./78 yrs.).

[e] Cancer risk = LADD × q_1* of 1.19×10^{-2} $(mg/kg\ bw/day)^{-1}$, occupational cancer threshold 1×10^{-5}

[f] For workers disbudding, hand pruning and hand harvesting ornamentals grown for cut flowers, the risk assessment was refined by assuming an exposure duration of an 8-hour workday and a maximum of 100 days per year (800 hours/year). The refinement is not expected to underestimate potential exposure given that the current label includes a restriction of a maximum of 2 applications per crop cycle for a total of 3 application per greenhouse per year and harvested ornamentals will be removed from the greenhouse. The assumption that a worker will be exposed to the same level of pymetrozine residues (30-day TWA DFR) for 8 hours per day for 100 days per year, for 40 years is still assumed to be conservative.

Appendix IV Fate and behaviour of Pymetrozine in the environment

Table 4.1 Fate and behaviour of Pymetrozine in the environment – laboratory studies.

Study type	Value-endpoint	Interpretation	Major transformation products
Hydrolysis	$t_{½}$ at pH 7 = stable	Not an important route of transformation in the environment	CGA 215525* CGA 300407
Phototransformation-soil	DT_{50} = 9 d to stable	Not a major route of transformation in the environment	CGA 359009*
Phototransformation-water	DT_{50} = 1.3–2.5 d	Major route of transformation in surface water	CGA 215525* CGA 249257*
Aerobic soil	DT_{50} = 5–527 d	Non-persistent to persistent in soil	CGA 180777 CGA 359009* CGA 363431* CGA 300407 CGA 294849* CGA 255548 CGA 363430
Aerobic aqueous	DT_{50} = 7.6–527 d	Non-persistent to persistent in aerobic water	CGA 359009*
Anaerobic aqueous	DT_{50} = 74–109 d	Moderately persistent in anaerobic water	CGA 249257* GS 23199* CGA 180777
Adsorption/desorption	Pymetrozine K_{oc} = 264–5233 *K*d = 3–51	Moderate mobility to immobile	-
	CGA 249257**: K_{oc} = 8–30 *K*d = 0.03–0.26	Very high mobility	-
	CGA 294849**: K_{oc} = 15–30 *K*d = 0.4–0.6	Very high mobility	-
	CGA 359009**: K_{oc} = 185–367 *K*d = 0.8–3.4	Moderate to highly mobile	-
	CGA 363431**: K_{oc} = 149–470 *K*d = 2.3–5.4	Moderately mobile	-
	GS 23199**: K_{oc} = 23–39 *K*d = 0.1–0.4	Very highly mobile	-
Soil column leaching	Not detected beyond 12 cm depth	Not expected to leach	-

*major transformation product of pymetrozine

**transformation products included in drinking water modelling

Appendix V Drinking water modelling

The following section includes the drinking water EECs and the input parameters for the drinking water modelling.

Table 5.1 Level 2 Estimated Environmental Concentrations of a combined residue of Pymetrozine, CGA 215525, CGA 359009, CGA 249257, CGA 294849, CGA 363431, and GS 23199 in potential sources of drinking water, as the parent equivalent

Use pattern	Groundwater (µg a.i./L)		Surface water (µg a.i./L)	
	Daily[1]	Yearly[2]	Daily[3]	Yearly[4]
2 applications of 96.5 g a.i./ha at a 7 day interval, by ground sprayer	45	45	9.1	2.6
2 applications of 96.5 g a.i./ha at a 7 day interval, by aerial application equipment	45	45	8.5	4.2
2 applications of 96.5 g a.i./ha at a 120 day interval, by airblast sprayer	45	45	3.4	1.2

1 90th percentile of daily concentrations
2 90th percentile of 365-day moving average concentrations
3 90th percentile of the peak concentrations from each year
4 90th percentile of yearly average concentrations

Table 5.2 Major groundwater and surface water model inputs for pymetrozine

Parameter	Surface Water	Groundwater	Formation fraction
	Residue Definition[a]		
Photolysis half-life[c]	2.1 d (CP); stable (CD)	2.1 d (CP); stable (CD)	0.98
Hydrolysis at pH 7	Stable	stable	NA
*K*d[d]	2.7 (CP); 0.49 (CD)	2.7 (CP); 0.49 (CD)	NA
Soil half-life[b]	276 d (CP); stable (CD)[e]	[f]	0.94
Aerobic aquatic half-life[g]	1000 d (CP); 37 d (CD)	1000 d (CP); 37 d (CD)	1
Sediment half-life[h]	126 d (CP)	126 d (CP)	0.35

a. Residue Definition = combined parent (CP; pymetrozine + GCA363431 + CGA359009) + combined daughter (CD; CGA215525 + CGA294849 + GS23199 + CGA249257)
b. For soil, a single set of parent half-life, daughter half-life, and formation fraction was used for surface water, while 8 sets of those 3 values were used for groundwater – one set from each of the 8 soil experiments.
c. Daughter stable to soil degradation, with a formation fraction of 0.98. Values are from a single study.
d. For the combined parent, data were available for pymetrozine and CGA336431, and the 20th percentile of 3 available adsorption values for CGA336431 was used, as it was the lower of the two. For the combined daughter, the 20th percentile of 3 available adsorption values for CGA294849 was used, corresponding to the lowest sorption across all compounds of the combined daughter
e. The daughter was stable to soil degradation with a formation fraction of 0.94. These were calculated from the 90 percent upper confidence bound on the mean of 5 values. 8 experimental half-lives adjusted to a temperature of 20°C were available but for only 5 soils. Duplicate experiments on individual soils were averaged, and that average value included in calculating the confidence bound. Not all experiments indicated the daughter to be stable, and the formation fraction is the highest from all experiments. The unextracted fraction was included in calculations for the parent.
f. The parent half-life, daughter half-life, and formation fraction of daughter were determined separately for each experiment, and all 8 sets modelled. The 8 sets appear in Table 2.

g. These are the 80th percentile of 3 whole system half-lives adjusted to a temperature of 20°C. The unextracted fraction was included in calculations for the parent.
h. For the Combined Parent, data were available for pymetrozine and CGA336431, and the 20th percentile of 3 available adsorption values for CGA336431 was used, as it was the lower of the two. For the Combined Daughter, the 20th percentile of 3 available adsorption values for CGA294849 was used, corresponding to the lowest sorption across all compounds of the combined daughter.

Table 5.3 Transformation parameters for the residues of Pymetrozine in soil used in groundwater modelling

Experiment	Parent Half-life	Daughter Half-life	Formation fraction
1	347	Stable	0.21
2	3300	303	0.80
3	754	54	1.00
4	814	163	0.80
5	549	17	1.00
6	322	12	1.00
7	315	Stable	0.27
8	282	Stable	0.18

Appendix VI Results of the cancer dietary exposure analysis

Table 6.1 Summary of dietary exposure and cancer risk for Pymetrozine

Population subgroup	Cancer food only lifetime risk	Cancer drinking water Only lifetime risk[a]	Cancer food and drinking water lifetime risk[a]
General Population	5×10^{-7}	**1×10^{-5}**	**1×10^{-5}**

[a] A lifetime cancer risk that is above 1×10^{-6} indicates unacceptable risk for the general population.

Appendix VII Proposed label amendments for products containing Pymetrozine

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.

The labels of all end-use products containing pymetrozine in Canada are proposed to be amended as follows to further protect human health.

1) All label directions concerning outdoor uses are proposed to be removed. This includes use on :

   - leafy vegetables (Crop Group 4)
   - potatoes
   - highbush blueberries
   - tobacco
   - *Rhodiola rosea*
   - outdoor ornamentals
   - Christmas trees.

2) The following label statement is proposed to be added to the PRECAUTIONS section:

   "Wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes during mixing, loading, application, clean-up and repair."

3) The following label statements are proposed to be added to end-use products with greenhouse uses:

   Add to "DIRECTIONS FOR USE IN GREENHOUSE ORNAMENTALS:"

   Under the Application Rates column add the following:

   "For greenhouse ornamentals grown for cut flowers apply 10–17 g product/100L of water and DO NOT exceed a spray volume of 1000 L water/ha"

   Add to "APPLICATION DIRECTIONS IN GREENHOUSE CUCUMBER, PEPPERS, TOMATOES AND EGGPLANT:"

   "DO NOT exceed a spray volume of 2000 L water/ha"

Under “ENVIRONMENTAL PRECAUTIONS’

Remove the following wording:

“Do not discharge effluent, waste and drainage water containing this product into water bodies, such as lakes, streams, ponds, rivers, and estuaries.”

And replace with:

“DO NOT allow effluent or runoff from greenhouses containing this product to enter lakes, streams, ponds or other waters.”

References

A. Studies/Information Submitted by the Registrant

Occupational Exposure

PMRA Document Number	Reference
1913109	Agricultural Handler Exposure Scenario Monograph: Open Cab Groundboom Application of Liquid Sprays. Report Number AHE1004.
2172938	Agricultural Handler Exposure Scenario Monograph: Closed Cockpit Aerial Application of Liquid Sprays. Report Number AHE1007
2572743	Agricultural Handler Exposure Scenario Monograph: Open Cab Airblast Application of Liquid Sprays. Report Number AHE1006
2572744	Agricultural Handler Exposure Scenario Monograph: Open Pour Mixing and Loading of Dry Flowable Formulations. Report Number AHE1001-1
2539372	Proposal for Endeavor 50 WG (pymetrozine) on *Rhodiola rosea*. Occupational Exposure Information. DACO 5.2.

Toxicology

PMRA Document Number	Reference
2816248	2017, PYMETROZINE Genotoxicity Assessment of Metabolites, DACO: 4.1
2816249	2017, PYMETROZINE Genotoxicity Assessment of CGA 300407, DACO: 4.1
2816250	1993, Acute Oral Toxicity in the Rat, DACO: 4.2.9
2816251	1993, Acute Dermal Irritation/Corrosion Study in the Rabbit, DACO: 4.2.9
2816252	1993, Acute Eye Irritation/Corrosion Study in the Rabbit, DACO: 4.2.9
2816253	1994, Skin Sensitisation Test in the Guinea Pig Maximisation Test, DACO: 4.2.9
2816254	1994, Salmonella and Escherichia /Mammalian-Microsome Mutagenicity Test, DACO: 4.2.9
2816255	1993, Acute Dermal Toxicity in the Rat, DACO: 4.2.9

PMRA Document Number	Reference
2816256	1994, Acute Inhalation Toxicity in the Rat, DACO: 4.2.9
2816257	1993, Acute Dermal Irritation/Corrosion Study in the Rabbit, DACO: 4.2.9
2816258	1993, Acute Eye Irritation/Corrosion Study in the Rabbit, DACO: 4.2.9
2816259	1993, Skin Sensitisation Test in the Guinea Pig Maximisation Test, DACO: 4.2.9
2816261	1993, Acute Oral Toxicity in the Rat, DACO: 4.2.9
2816262	1993, Acute Dermal Toxicity in the Rat, DACO: 4.2.9
2816263	1993, Salmonella and Escherichia /Liver-Microsome Test, DACO: 4.5.4
2816264	2005, Pymetrozine Intermediate CGA 215525: Bacterial mutation assay in S. typhimurium and E.coli YV7010/Regulatory/Report, DACO: 4.5.4
2816265	1993, Cytogenetic Test on Chinese Hamster Cells in Vitro (EC-Conform), DACO: 4.5.5
2816266	2005, Pymetrozine Intermediate CGA 300407: In vitro cytogenetic assay in human lymphocytes SV1307/Regulatory/Report, DACO: 4.5.5
2816267	2006, Benzaldehyde Mouse Fore-Stomach In Vivo Comet Assay SM1356/Regulatory/Report, DACO: 4.5.7
2816268	2006, CGA 300407: Mouse bone marrow micronucleus test SM1357/Regulatory/Report, DACO: 4.5.7
2816269	2006, Benzaldehyde Mouse Bone Marrow Micronucleus Test SM1365/Regulatory/Report, DACO: 4.5.7
2816270	2006, CGA300407 In Vitro Mouse Hepatocyte Unscheduled DNA Synthesis Assay SV1347/Regulatory/Report, DACO: 4.5.8
2816271	2006, CGA300407 Mouse liver in vitro Comet assay SV1364/Regulatory/Report, DACO: 4.5.8
2816272	2006, CGA300407: Mouse fore-stomach in vivo comet assay SM1346/Regulatory/Report, DACO: 4.5.8
2816273	2010, DEREK for Windows Report CGA128632, DACO: 4.5.8

PMRA Document Number	Reference
2816274	2009, DEREK for Windows Report CGA215525, DACO: 4.5.8
2816275	2010, DEREK for Windows Report CGA266591, DACO: 4.5.8
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B. Additional Information Considered

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