Proposed Maximum Residue Limit PMRL2023-34

Fludioxonil

(publié aussi en français)

27 June 2023

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

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ISSN: 1925-0835 (print)
1925-0843 (online)

Catalogue number: H113-24/2023-34E (print version)
H113-24/2023-34E-PDF (PDF version)

1.0 Pesticides in Canada

Pesticides provide both organic and conventional growers in Canada with a variety of options to help minimize damage to their crops and livestock from pests. The reason pesticides are used is to help protect crops from pests such as weeds, fungi, and insects. This allows people in Canada to access high-quality nutritious foods all year long.

All pesticides, for both organic and conventionally grown crops, that are approved for use in Canada are regulated by Health Canada's Pest Management Regulatory Agency (PMRA). Pesticide residues that may be present on food commodities imported into Canada are also regulated. Health Canada reviews all new pesticide applications and also re-evaluates existing pesticides on a regular basis.

Maximum residue limits

A maximum residue limit (MRL) is the highest amount of a specific pesticide residue allowed on a particular food commodity when a pesticide is used according to label directions.

Health Canada is responsible for establishing MRLs on food commodities grown domestically or imported into Canada. Different food commodities can have different MRLs for the same pesticide due to differences in how the pesticide is used for each crop or food commodity. MRLs are set after a robust scientific review and provided that the risks meet Health Canada's requirements for the protection of human health.

An MRL is not a measure of the toxicity of a pesticide. It is a scientifically based calculation that estimates the maximum potential concentration of residues on food commodities. This estimation is based on when label directions are followed. It accounts for the highest potential amount of residue that may remain on a food commodity for a given use. This is done so that the actual residue level is not underestimated. More information about these calculations is in Section 5.0, Calculating the proposed MRL. Often, the residues that remain are much lower under typical use conditions. If the use directions change for a given pesticide, the MRL can also change. However, before any change to an MRL is proposed, the risks must meet Health Canada's requirements for the protection of human health.

MRLs are legal limits that are enforced by the Canadian Food Inspection Agency (CFIA). The latest National Chemical Residue Monitoring Program and Chemistry Food Safety report that uses MRLs to determine compliance rates can be requested on the Food safety testing bulletin and reports page on Canada.ca (https://inspection.canada.ca/food-safety-for-industry/food-chemistry-and-microbiology/food-safety-testing-bulletin-and-reports/eng/1453324778043/1453327843364).

Imported food commodities

For the purposes of setting MRLs on imported food commodities, Health Canada evaluates multiple studies from various scientific disciplines on human health. As directed in section 10(3) of the *Pest Control Products Act*, only health risks are assessed for imported food commodities, and only for potential exposure in the diet. This is because the pesticide is applied in the country

from which the food commodity is imported so potential exposure to the residue from that commodity is only through the diet. For example, no Canadian worker such as a grower will be exposed, or exposure to the Canadian environment is expected.

However, if the pesticide is registered for other uses in Canada, a full health, environment and value assessment would be conducted prior to any registration decision for those uses. This would ensure there are no health or environmental concerns, and that the pesticide use has value.

2.0 Purpose of this consultation

Health Canada is consulting the public and seeking your feedback on a proposed MRL increase to address potential fludioxonil residues on imported sugar beet roots.

Fludioxonil is a fungicide registered in Canada for use on various food commodities. The proposed MRL increase was requested by Syngenta Canada to align Canada's current MRL for fludioxonil on sugar beet roots with that of the United States of America (US). This was done so sugar beet roots or any processed food commodities derived from sugar beet roots that may contain fludioxonil residues can be imported and sold in Canada.

The MRL increase is proposed, because the health risk from eating food commodities treated with fludioxonil meets Health Canada's requirements for the protection of human health. The main health assessment required for this consultation was the dietary risk assessment and it was conducted in accordance with Sections 10 and 11 of the *Pest Control Products Act*.

Proposed Canadian MRL for fludioxonil

This increased MRL will not change the Canadian registered labels for fludioxonil, how the pesticide is used in Canada or increase the amount of pesticide residues in the food grown in Canada.

Table 1 summarizes the proposed MRL change for fludioxonil.

Table 1 Proposed maximum residue limit for fludioxonil

Common name	Residue definition[1]	Current MRL (ppm)[2]	Proposed MRL (ppm)[2]	Food commodity
Fludioxonil	4-(2,2-difluoro-1,3-benzodioxol-4-yl)-1*H*-pyrrole-3-carbonitrile	0.02	4.0	Sugar beet roots

[1] Residue Definition upon which MRLs are based typically includes the pesticide itself and sometimes also includes one or more degradation products referred to as metabolites. A searchable residue definition table is available on the Residue Definitions for Chemicals with Maximum Residue Limits Regulated Under the *Pest Control Products Act* page on Canada.ca (https://www.canada.ca/en/health-canada/services/consumer-product-safety/pesticides-pest-management/public/protecting-your-health-environment/pesticides-food/residue-definitions-chemicals-maximum-residue-limits-regulated-under-pest-control-products-act.html).

[2] ppm = parts per million

Based on the results from the dietary risk assessment, Health Canada is proposing to accept the request to **increase** the MRL for fludioxonil from 0.02 ppm to 4.0 ppm on **imported** sugar beet roots. This is because the increased fludioxonil MRL meets Health Canada's requirements for the protection of human health.

The increase was requested by Syngenta Canada to align Canada's current MRL for fludioxonil on sugar beet roots with the US fludioxonil tolerance. The pesticide product used in the US is a co-formulation, containing the pesticides fludioxonil and azoxystrobin. As such, the application for a proposed MRL for azoxystrobin on sugar beet roots will be consulted on under a separate document.

- The term "**tolerance**" is used in the US to describe the maximum residue limit.
- The request is based on a different application method used on sugar beet roots registered for use in the US, explained below.

  Current Canadian registered use for sugar beets: before planting, application of fludioxonil to sugar beet seeds. This application prevents fungal diseases during the early growth phase of the crop.

  American registered use relevant to this consultation: post-harvest direct spraying of sugar beet roots. Fludioxonil is applied to sugar beets in storage and for transport to prevent fungal diseases in the mature harvested crop.

To view all the products containing fludioxonil registered in Canada:

- Access the Search Product Label.
- Under the header "Filter", select the field "Active Ingredient – English".
- Enter "fludioxonil" in the Value area.
- Click the Search button.

3.0 Dietary risk assessment

Before an MRL can be set, scientists from Health Canada make sure the amount of pesticide residue on or in food commodities is low enough that there are no effects on human health. Scientists evaluate the relevant scientific information on the toxicity and dietary exposure of the pesticide. This process is called a dietary risk assessment.

Overview of the dietary risk assessment process

The **dietary risk assessment** process involves four distinct steps:

1. Evaluate the relevant scientific data and information and then identify the toxicological hazards of the pesticide.

2. Determine the **acceptable daily intake (ADI)** level and the **acute reference dose (ARfD)**, when applicable.

   ADI: the amount of a specific pesticide residue a person could eat every day over their entire lifetime without any negative health effects. This is set considering all vulnerable people such as pregnant people, infants, children, and seniors.

   ARfD: the amount of a specific pesticide residue that a person can eat on any given day without any negative health effects. This is set considering all vulnerable people such as pregnant people, infants, children, and seniors.

3. Estimate the **potential daily intake (PDI)** level.

   PDI: the total amount of a specific pesticide residue that might be eaten. When determining the PDI for a pesticide, scientists consider **all** registered uses on food commodities (both domestic and import), and how diets can vary between people in Canada.

4. Characterize the human health risk by comparing the PDI level with the ADI level, and ARfD level, if applicable.

If the PDI level is lower than the ADI level and the ARfD level, the scientists at Health Canada conclude that all food commodities that could be treated with this pesticide are safe to eat.

When assessing dietary risk, both acute, if applicable, and chronic dietary intakes are estimated for the general population and several sub-populations such as pregnant people, infants, children, and seniors.

Summary of the dietary risk assessment results for fludioxonil

This summary is focussed on key aspects of the dietary risk assessment that are potentially of greatest interest to people in Canada. It is written to help improve the understanding of Health Canada's pesticide decisions. Further technical details and how to request additional information about the dietary risk assessment can be found in Section 7.0, Next steps and in Appendix I.

The results from the dietary risk assessment show that when fludioxonil is used according to the label directions for the sugar beet root use registered in the US, the dietary risks continue to meet Health Canada’s requirements for the protection of human health.

There were **no acute or short-term health effects observed** in the fludioxonil toxicology data and an ARfD was not necessary. **This means that acute exposure to fludioxonil will not affect your health.** The toxicology information for fludioxonil relevant to the dietary risk assessment is reported in Table A1-1 of Appendix I.

The chronic or long-term dietary risk assessment results showed that exposure to fludioxonil is **less than 68%** of the ADI level. **This means that chronic exposure to fludioxonil will not affect your health.** The dietary risk for each subpopulation is reported in Appendix I, Table A1-2.

- Health Canada's level of concern for chronic risk is when exposure is greater than 100% of the ADI. When the chronic dietary risk assessment is lower than 100% of the ADI, it means that there are no long-term human health concerns from eating foods treated with fludioxonil every day over a person's lifetime.

For more information on how Health Canada's PMRA assesses and manages risk from pesticides, refer to this guidance document: PMRA Guidance Document, A framework for risk assessment and risk management of pest control products

4.0 Summary of residue data to support the proposed MRL

The required residue data for fludioxonil were submitted and reviewed to support the MRL on imported sugar beet roots. In addition, experimental processing data on treated sugar beet roots were reviewed to determine the potential for the concentration of fludioxonil residues in processed food commodities. Examples of a processed food commodity from sugar beet root are molasses and refined sugar.

In the submitted study, fludioxonil was applied at a range of 3.86–4.26 g a.i./2000 lb of sugar beet roots (or 907 kg of sugar beet roots), which aligns with the US registered label rate of 4.08 g a.i./2000 lb of sugar beet roots.

Table 2 summarizes the residue data used to calculate the proposed MRL for imported sugar beet roots.

Table 2 Summary of residue trial and processing data used to support the MRL

Commodity	Application method/ Total application rate [g a.i./2000 lb (or 907 kg) roots][1]	Lowest average field trial residues (ppm)[2]	Highest average field trial residues (ppm)	Experimental processing factor[3]
Sugar beet roots	Post-harvest application/ 3.86–4.26	0.64	1.9	Molasses: 0.6-fold [0.6 × 1.6 ppm (which is the average concentration of residues in treated sugar beet roots) = 0.96 ppm] Refined Sugar: 0.1-fold [0.1 × 1.6 ppm (which is the average concentration of residues in treated sugar beet roots) = 0.16 ppm]

[1] g a.i./2000 lb (or 907 kg) roots = grams of active ingredient per 2000 pounds (or 907 kilograms) of sugar beet roots.

[2] ppm = parts per million

[3] An Experimental Processing Factor that is less than 1.0-fold indicates that residues of fludioxonil do not concentrate in the processed commodity, and a separate MRL does not need to be set for the processed commodity, as it will be covered off by the proposed MRL for sugar beet roots.

5.0 Calculating the proposed MRL

The proposed MRL of 4.0 ppm for fludioxonil was calculated using the residues observed in the residue trials and the guidance provided in the OECD MRL Calculator. This statistically based calculator is used by many international regulatory authorities to set MRLs on food commodities either grown domestically or imported from different countries. Full residue datasets are required to run the OECD MRL calculator, not just the highest and lowest residues reported in Table 2 above.

Pesticide MRLs established for each food commodity, including those imported into Canada, may be found using the Maximum Residue Limit Database. The database allows users to search for established MRLs, regulated under the *Pest Control Products Act*, for pesticides or food commodities.

6.0 International considerations

Internationally, MRLs are used to facilitate trade of food commodities. MRLs may vary from one country to another for several reasons, which may include:

- differences in the way pesticides are used between countries
- different geographical locations of the field residue studies, except certain indoor uses such as post-harvest uses
- different environmental and weather conditions and pests between the countries, except certain indoor uses such as post-harvest uses.

For fludioxonil, the proposed MRL increase is caused by a difference in use of the pesticide between Canada and the US, as in bullet 1 above. In the US, fludioxonil is sprayed after harvest directly on sugar beet roots to prevent fungal diseases during storage or transport.

Table 3 compares the MRL proposed for fludioxonil in Canada with the corresponding American tolerance. There is no international Codex MRL for fludioxonil on sugar beet roots. The Codex Alimentarius Commission is an international organization under the auspices of the United Nations that develops international food standards, including MRLs.

- The American tolerance is listed by pesticide in the Electronic Code of Federal Regulations, 40 CFR Part 180
- The Codex MRL is listed by pesticide or commodity on the Codex Alimentarius Pesticide Index

Table 3 Comparison of proposed Canadian MRL, American Tolerance and Codex MRL

Food commodity	Canadian MRL (ppm)[1]	American Tolerance (ppm)[1]	Codex MRL (ppm)[1]
Sugar beet roots	4.0	4.0	none

[1] ppm = parts per million

International consultation on the proposed MRL also occurs as a result of Canada notifying the World Trade Organization. This is coordinated by Canada's Notification Authority and Enquiry Point in order to comply with Canada's international trade obligations.

7.0 Next steps

Health Canada invites the public to submit written comments on the proposed increase to the MRL for fludioxonil up to 75 days from the date of publication of this document.

Please submit your comments to the PMRA Publications Section.

Health Canada considers all comments received before making a final science-based decision about the proposed MRL. Comments received will be addressed in a separate document linked to this proposed MRL. If no comments are received, or the comments do not result in a change to the proposed MRL, the established MRL will be legally in effect on the date it is entered into the Maximum Residue Limit Database.

If you would like to request additional information on the supporting scientific documents for this proposed MRL, here is the information you will need to help identify the request:

- Active ingredient: fludioxonil
- Published document number: PMRL2023-34
- Submission number: 2020-2152
- Related re-evaluation decisions: PRVD2016-03 and RVD2018-04

Appendix I Excerpt of the dietary risk assessment

The technical details of the dietary risk assessment are available in Proposed Re-evaluation Decision PRVD2016-03, Fludioxonil. If you would like to read the document, please visit the Request Publication page for the Proposed Re-evaluation Decision PRVD2016-03, Fludioxonil. The details of the final re-evaluation decision for fludioxonil are available here, Re-evaluation Decision RVD2018-04, Fludioxonil and Its Associated End-Use Products.

Table A1-1 Summary of toxicology information for fludioxonil for use in dietary exposure assessment

Exposure scenario	Toxicology reference value used in risk assessment	Study	Toxicological endpoint
Acute Dietary **General population**	No ARfD[1] required	Not applicable	None
Chronic Dietary **All populations**	NOAEL[1] = **3.7** mg/kg bw/day CAF[1,2] = **100**[2] **ADI**[1] = **0.037** mg/kg bw/day	Two-year chronic study in rats	NOAEL[1] = 3.7 mg/kg bw/day Based on liver lesions (degeneration, atrophy / necrosis / inflammation) that were noted at the LOAEL[1] of 37 mg/kg bw/day in a chronic toxicity study in rats (i.e., 10-fold greater dose than the NOAEL)

[1] ARfD = Acute Reference Dose; NOAEL = No Observed Adverse Effect Level; LOAEL = Lowest Observed Adverse Effect Level; CAF = Composite Assessment Factor; ADI = Acceptable Daily Intake. PCPA-factor = *Pest Control Products Act-factor*. Reference values and endpoints cited in PRVD2016-03 and finalized via decision document RVD2018-04.

[2] To account for uncertainties (inter- and intra-species variations), a CAF of 100-fold (10-fold for differences between animals and humans, 10-fold for variation between humans, and a onefold PCPA factor was applied to the NOAEL for potential liver toxicity to calculate the Toxicology Reference Value – in this case the ADI. Therefore, 3.7 mg/kg bw/day ÷ 100 = 0.037 mg/kg bw/day). This is 1000-fold lower than the dose where toxicological effects were observed in animals (LOAEL).

Dietary exposure assessments are conducted using a database called the Dietary Exposure Evaluation Model - Food Commodity Intake Database (DEEM-FCID) which is explained in Science Policy Note SPN2014-01, General Exposure Factor Inputs for Dietary, Occupational, and Residential Exposure Assessments. This is a food recipe and consumption database used by Canada and the US for dietary exposure modelling that incorporates food consumption data from the US National Health and Nutritional Examination Survey, What We Eat in America (NHANES/ WWEIA) dietary survey. This survey is made available through the National Center for Health Statistics (NCHS), which is part of the Centers for Disease Control and Prevention (CDC). The NHANES survey, which uses interviews and physical examinations to assess the health and nutritional status of adults and children in the United States, is updated periodically and is also reflective of the large variety of food consumption patterns in the Canadian population.

Results of the acute dietary risk assessment

An acute dietary exposure assessment was not required as there were no acute or short-term health effects observed. **This means that acute exposure to fludioxonil will not affect your health.**

Results of the chronic dietary risk assessment

There are no dietary risks of concern when the PDI is less than the ADI (see Section 3.0), which is the result shown in Table A1-2. The DEEM-FCID (NHANES) analyses estimate the dietary exposure of the general population and various population subgroups. The results reported in Table A1-2 are for the general population (all ages), all infants (<1 year old), children 1–2 years old, children 3–5 years old, children 6–12 years old, youth 13–19 years old, adults 20–49 years old, females 13–49 years old and adults 50+ years old. When including the use of fludioxonil on imported sugar beet roots, the estimated dietary exposure to fludioxonil for all population subgroups is less than 68% of the ADI. **This means that chronic exposure to fludioxonil will not affect your health.**

Table A1-2 Summary of chronic dietary risk for fludioxonil

Population subgroup	Food only[1]		Food and drinking water[1,3]	
	Previous assessment (% ADI[4,5])	Updated to include the proposed MRL[2] (% ADI[4])	Previous assessment (% ADI[4,5])	Updated to include the proposed MRL[2] (% ADI[4])
General Population	19.6	**20.4**	20.5	**21.3**
All Infants	40.4	**41.3**	43.9	**44.8**
Children 1–2 years old	64.2	**66.2**	65.5	**67.5**
Children 3–5 years old	46.2	**48.4**	47.2	**49.4**
Children 6–12 years old	23.7	**25.4**	24.5	**26.1**
Youth 13–19 years old	12.9	**13.7**	13.5	**14.3**
Adults 20–49 years old	15.3	**15.9**	16.2	**16.8**
Adults 50+ years old	17.6	**18.1**	18.5	**19.0**
Females 13–49 years old	15.7	**16.4**	16.6	**17.3**

1 "Food Only" represents all foods that could be treated with fludioxonil, including imported foods. "Food and Drinking Water" represents all Canadian-grown and imported foods that could be treated with fludioxonil, as well as the dietary contribution from consuming water that may be impacted by Canadian agricultural uses of fludioxonil.

2 Proposed MRL for sugar beet roots is also included in the risk assessment for sugar beet molasses.

3 Estimated Environmental Concentration (EEC) of fludioxonil in drinking water was 17 µg active ingredient/L, from surface water. There were no EECs from groundwater. Note: for an import MRL there is no change to drinking water EECs from the previous assessment, as the pesticide for the specific use is not applied in Canada.

4 Values are below 100% (PDI ÷ ADI × 100), therefore, there are no dietary concerns for any segment of the population.

5 Previous assessment from submission 2017-3384/3385.