Proposed Maximum Residue Limit PMRL2024-21

Clethodim

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Health Canada is consulting the public and seeking your feedback on:

- A proposed maximum residue limit (MRL) increase for the use of clethodim on lowbush blueberries.

1.0 Pesticides in Canada

Pesticides provide both organic and conventional growers in Canada with a variety of options to help minimize damage from pests to their crops and livestock. Pesticides 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). This includes regulating pesticide residues that may be present on food commodities imported into Canada. Health Canada reviews all new pesticide applications and re-evaluates existing pesticides on a regular basis to help ensure the protection of human health.

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 scientists set (or specify) MRLs after a robust scientific review of the pesticide, provided that the risks meet Health Canada's requirements for the protection of human health. This means that the scientists first make sure the amount of pesticide residue on or in food commodities is low enough that there are no effects on human health. Health Canada is responsible for setting 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.

An MRL is a scientific calculation that estimates the maximum potential concentration of residues on food commodities. It is **not** a measurement of pesticide toxicity or safety. It accounts for the highest potential amount of residue that may remain on a food commodity when label directions are followed. More information about these calculations is in Section 5.0 on Calculating the proposed MRL. Often, the residues that remain are much lower than the MRL 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 reports and journal articles page on Canada.ca.

Food commodities grown in Canada

Before making any registration decision for a pesticide in Canada, Health Canada must evaluate the chemistry of a pesticide, how well a pesticide works, and the pesticide's potential impact on human health and the environment. This is the full pesticide assessment process as directed in the *Pest Control Products Act*. This is to ensure there are no health or environmental concerns from the potential pesticide exposure to Canadians through this use, and that the pesticide 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 clethodim residues on lowbush blueberries grown in Canada.

Clethodim is a herbicide currently registered for use in Canada on various fruit, vegetable, grain, herb and spice commodities.

A proposal was submitted by the New Brunswick Department of Agriculture, Aquaculture and Fisheries, and supported by the registrant UPL Agrosolutions Canada Inc., to register the foliar use of clethodim on lowbush blueberries on the Clethodim 360EC Herbicide and Select Emulsifiable Concentrate Post-Emergence Herbicide labels (*Pest Control Products Act* Registration Numbers 31496 and 22625, respectively). This MRL increase would allow treated lowbush blueberries to be sold in Canada.

Health Canada is proposing to accept this MRL increase. This is because Health Canada conducted a thorough scientific assessment and found that the health risk from eating food commodities treated with clethodim meets Health Canada's requirements for the protection of human health. The main health assessment required for this consultation was the dietary risk assessment, which was conducted in accordance with sections 10 and 11 of the *Pest Control Products Act*. This assessment involves a thorough evaluation of health risks that considered the toxicity and dietary exposure of clethodim, and follows strict regulatory standards. Further details on the dietary risk assessment can be found in Section 3.0 Dietary risk assessment.

Proposed Canadian MRL for clethodim

Table 1 summarizes the revised MRL proposed for clethodim, and the reason for the proposed MRL.

MRLs are based on a residue definition that typically includes the pesticide itself and may also include 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.

The following MRL is based on the following residue definition: 2-[1-[[[(2*E*)-3-chloro-2-propen-1-yl]oxy]imino]propyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one, including metabolites containing the 2-cyclohex-1-enone moiety (expressed as parent equivalents)

Table 1 Current and proposed MRL for clethodim

Food commodity	Current MRL (ppm)[1]	Proposed MRL (ppm)[1]	Reason for the proposed MRL
Lowbush blueberries	0.2	0.5	**Increased MRL on lowbush blueberries,** to support the Canadian use of clethodim on lowbush blueberries with cranberry data that better represent the proposed use than the highbush blueberry data used to calculate the previously established MRL.

1 ppm = parts per million

Based on the results from the dietary risk assessment, Health Canada **is proposing to accept** the revised MRL request for clethodim. This is because this revised MRL **meet Health Canada's requirements** for the protection of human health.

3.0 Dietary risk assessment

Before an MRL can be set, Health Canada scientists make sure the amount of pesticide residue on or in food commodities is low enough that there are no effects on human health. They 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 toxicology hazards of the pesticide;

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

   ARfD: the amount of a specific pesticide residue that a person can eat and drink **on any given day** without any negative health effects. The ARfD is used to estimate acute dietary risk, which considers the potential for health effects after a single day of exposure to the pesticide.

   ADI: the amount of a specific pesticide residue a person could eat and drink **every** day over their entire lifetime without any negative health effects. The ADI is used to estimate chronic dietary risk, which considers the potential for health effects after a lifetime of exposure to the pesticide.

Health Canada scientists estimate both acute (single day) and chronic (lifetime) dietary intakes, where applicable, for the general population and several subpopulations such as pregnant people, infants, children and seniors.

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

   PDI: the total amount of a specific pesticide residue that might be eaten. When determining the PDI for a pesticide, scientists consider **all** food commodities (both registered (domestic) and imported), drinking water (where applicable), and how diets can vary between people in Canada. The PDI is the potential dietary exposure to a specific pesticide.

4. Characterize the **acute dietary risk** by comparing the PDI with the ARfD, and characterize the **chronic dietary risk** by comparing the PDI with the ADI, where applicable.

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

Summary of the dietary risk assessment results for clethodim

This summary focusses on key aspects of the dietary risk assessment that are potentially of greatest interest to people in Canada. It is intended to help improve the understanding of Health Canada's pesticide decisions. Technical details and how to request additional information about the dietary risk assessment can be found in Section 7.0 on How to get involved and in Appendix I.

The results from the dietary risk assessment show that when clethodim is used according to the Canadian label directions for the proposed use, the dietary risks from clethodim on food commodities continue to meet Health Canada’s requirements for the protection of human health. The toxicology information for clethodim relevant to the dietary risk assessment is reported in Table A1-1 of Appendix I.

The acute dietary risk assessment results showed that exposure to clethodim is **less than 8%** of the ARfD. Health Canada's level of concern for acute risk is when exposure is greater than 100% of the ARfD. **This means that acute exposure to clethodim will not affect your health**. The dietary risk for each subpopulation is reported in Table A1-2 of Appendix I.

- Health Canada considers that acute risk may be of concern when exposure is greater than 100% of the ARfD. When the acute dietary risk assessment is lower than 100% of the ARfD, it means that on a given day there are no human health concerns from eating foods treated with clethodim.

The chronic dietary risk assessment results showed that exposure to clethodim is **less than 28%** of the ADI. **This means that chronic exposure to clethodim will not affect your health**. The dietary risk for each subpopulation is reported in Table A1-3 of Appendix I.

- Health Canada considers that chronic risk may be of concern 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 human health concerns from eating foods treated with clethodim every day over a person's lifetime.

For more information on how Health Canada 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

For more information on the MRL process, refer to Section 19 *Maximum Residue Limits* found within this guideline:

- Residue chemistry guidelines: Revised 2022 PMRA guidance document - Canada.ca

4.0 Summary of residue data to support the proposed MRL

Health Canada scientists reassessed previously reviewed residue data from field trials conducted for clethodim on cranberries for these petitions, as cranberry is the representative commodity for crop subgroup 13-07H (low growing berries, except strawberries) which includes lowbush blueberries.

Table 2 summarizes the residue data used to calculate the proposed MRL for lowbush blueberries.

Table 2 Summary of field trial data used to support the maximum residue limit (MRL)

Commodity	Application method	Total application rate (g a.i./ha)[1]	Preharvest interval (days)	Lowest average field trial residues (ppm)[2,3]	Highest average field trial residues (ppm)[2,3]	Proposed MRL (ppm)[2]
Cranberry fruit	Foliar application	551–614	29–30	0.16	0.31	0.5

[1] g a.i./ha = grams of active ingredient per hectare
[2] ppm = parts per million
[3] . The combined residues of clethodim and all metabolites containing the 2-cyclohex-1-enone moiety (expressed as parent equivalents).

5.0 Calculating the proposed MRL

Health Canada scientists calculated the proposed MRL for clethodim using the residues observed in the residue trials, and the guidance provided in the OECD MRL Calculator. Many international regulatory authorities use this statistical calculator to set MRLs on food commodities that are 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 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 between countries. Canadian MRLs are established or amended based on a robust scientific risk assessment that demonstrates safety for people in Canada. Table 3 compares the MRL proposed for clethodim in Canada with the corresponding U.S. tolerance and international Codex MRL. The Codex Alimentarius Commission is an international organization under the auspices of the United Nations that develops international food standards, including MRLs.

The tolerance in the United States is listed by pesticide in the Electronic Code of Federal Regulations, 40 CFR Part 180. The term **"tolerance"** is used in the United States as another name for MRLs.

The Codex MRL is listed by pesticide or commodity on the Codex Alimentarius Pesticide Index webpage.

The U.S. tolerance and Codex MRL for clethodim are listed in Table 3 below.

Table 3 Comparison of proposed Canadian MRLs, U.S. tolerances and Codex MRLs

Food commodity	Proposed Canadian MRL (ppm)[1]	Established U.S. tolerance (ppm)[1]	Established Codex MRL (ppm)[1]
Lowbush blueberries	0.5	0.20 (Bushberry subgroup 13-07B) 3.0 (Berry, low growing, subgroup 13–07G, except cranberry)	Not established

[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 How to get involved

Health Canada invites the public to submit written comments on the proposed MRL change for clethodim 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 up to 75 days from the date of publication of this document (by 16 December 2024) before making a final science-based decision about the proposed MRL. Comments received within this 75 day period will be addressed in a response to comments document found in Pesticides and pest management consultations. If no comments are received, or the comments do not result in a change to the proposed MRL, the MRL will be set and legally in effect on the date they are 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 identify the request:

Active ingredient:	clethodim
Published document number:	PMRL2024-21
Submission number:	2022-5047, 2022-5049
Related re-evaluation decisions:	PRVD2016-11, RVD2017-10

Appendix I Excerpt of the dietary risk assessment

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

Exposure scenario	Toxicology reference value used in risk assessment	Study	Toxicological endpoint
Acute Dietary **All populations**	NOAEL[1] = 100 mg/kg bw CAF[1] = 100[2] ARfD[1] = 1.0 mg/kg bw	Rat acute neurotoxicity study	LOAEL[1] = 1000 mg/kg bw Based on decreased spontaneous activity, hunched posture, ruffled fur, head tilt and abnormal gait and salivation in females (10-fold greater dose than the NOAEL)
Chronic Dietary **All populations**	NOAEL[1] = 16 mg/kg bw/day CAF[1] = 100[3] ADI[1] = 0.16 mg/kg bw/day	Chronic toxicity/oncogenicity study in the rat	LOAEL[1] = 86 mg/kg/day based on decreases in body weight gain, increases in liver weight, and increased incidence of centrilobular hypertrophy, binucleated cells in the liver and chronic pancreatis (5.4-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 = *Pest Control Products Act*; bw = body weight. Reference values and endpoints cited in PRVD2016-11 and finalized via decision document RVD2017-10.

[2] To account for uncertainties including 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 decreased spontaneous activity, hunched posture, ruffled fur, head tilt and abnormal gait and salivation in females to calculate the ARfD. Therefore, NOAEL÷CAF = 100 mg/kg bw ÷ 100 = 1.0 mg/kg bw. This is 1000-fold (LOAEL ÷ ARfD) lower than the lowest dose where toxicological effects were observed in animals (at the LOAEL = 1000 mg/kg bw/day).

[3] To account for uncertainties including 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 1-fold PCPA factor) was applied to the NOAEL based on decreases in body weight gain, increases in liver weight, and increased incidence of centrilobular hypertrophy, binucleated cells in the liver and chronic pancreatis, in order to calculate the ADI. Therefore, NOAEL ÷ CAF = 16 mg/kg bw/day ÷100 = 0.16 mg/kg bw/day. This is 538-fold (LOAEL÷ADI) lower than the lowest dose where toxicological effects were observed in animals (at the LOAEL = 86 mg/kg bw/day).

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 U.S. for dietary exposure modelling that incorporates food consumption data from the U.S. 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

The results of the most recent acute dietary exposure assessment for clethodim are shown in Table A1-2. There are no dietary risks of concern when the PDI is less than the ARfD (see Section 3.0). 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, adults 50+ years old, and females 13–49 years old. When including the use of clethodim on the various food commodities and levels of clethodim found in drinking water, the estimated dietary exposure to clethodim for all population subgroups is less than 8% of the ARfD. **This means that acute exposure to clethodim will not affect your health.**

Table A1-2 Summary of acute dietary risk for clethodim

Population subgroup	Basic assessment food and drinking water [1,2] – Previous assessment	Basic assessment food and drinking water [1,2] – Updated to include the proposed MRL
	% ARfD[3,4]	% ARfD[3]
General Population	3.7	**3.7**
All Infants	7.1	**7.1**
Children 1–2 years old	7.7	**7.7**
Children 3–5 years old	7.0	**7.0**
Children 6–12 years old	4.4	**4.4**
Youth 13–19 years old	2.7	**2.7**
Adults 20–49 years old	2.7	**2.7**
Adults 50+ years old	2.5	**2.5**
Females 13–49 years old	2.6	**2.6**

Bolded values indicate updated risk assessments.

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

2 Estimated Environmental Concentrations (EECs) of clethodim have been calculated for drinking water at 41 µg a.i./L (micrograms of active ingredients per litre) from ground water.

[3] Values are below 100% (PDI ÷ ARfD × 100), therefore, there are no dietary concerns for any segment of the population.
[4] Previous assessment from 2019-5540, 2019-5544, 2019-5546, and 2019-5547.

Results of the chronic dietary risk assessment

The results of the most recent chronic dietary exposure assessment for clethodim are shown in Table A1-3. There are no dietary risks of concern when the PDI is less than the ADI (see Section 3.0). The DEEM-FCID (NHANES) analyses estimate the dietary exposure of the general population and various population subgroups. The results reported in Table A1-3 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, adults 50+ years old, and females 13–49 years old. When including the use of clethodim on the various food commodities and levels of clethodim found in drinking water, the estimated dietary exposure to clethodim for all population subgroups is less than 28% of the ADI. **This means that chronic exposure to clethodim will not affect your health.**

Table A1-3 Summary of chronic dietary risk for clethodim

Population subgroup	Basic assessment food and drinking water [1,2] – Previous assessment	Basic assessment food and drinking water [1,2] – Updated to include the proposed MRL
	% ADI[3,4]	% ADI[3]
General Population	9.0	**9.0**
All Infants	19.4	**19.4**
Children 1-2 years old	27.8	**27.8**
Children 3-5 years old	20.5	**20.5**
Children 6-12 years old	12.3	**12.3**
Youth 13-19 years old	7.4	**7.4**
Adults 20-49 years old	7.3	**7.3**
Adults 50+ years old	7.0	**7.1**
Females 13-49 years old	7.2	**7.2**

Bolded values indicate updated risk assessments.
[1] "Food and Drinking Water" represents all Canadian-grown and imported foods that could be treated with clethodim, as well as the dietary contribution from consuming water that may be impacted by Canadian agricultural uses of clethodim.
[2] Estimated Environmental Concentrations (EECs) of clethodim have been calculated for drinking water at 41 µg a.i./L from ground water.
[3] Values are below 100% (PDI ÷ ADI × 100), therefore, there are no dietary concerns for any segment of the population.
[4] Previous assessment from 2019-5540, 2019-5544, 2019-5546, and 2019-5547.

For more information

PRVD2016-11, Clethodim – available through this publication request page
RVD2017-10, Clethodim – available through this publication request page