Proposed Maximum Residue Limit PMRL2024-10

Cyflumetofen

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Canada

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

- A proposed maximum residue limit (MRL) increase for the use of cyflumetofen on tomatoes.
- Setting new MRLs on cucurbit vegetables (like cucumbers) (crop group 9), bell peppers and non-bell peppers.

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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.

When setting MRLs on related food commodities, Health Canada uses crop groups. Individual crops can be allocated to a crop group based on botanical or taxonomic criteria as well as on cultivation practices. Crop groups simplify the establishment of MRLs by using residue data for crops that are representative of the whole group to extend to all crops within the crop group. Crop groups can also contain smaller and more closely related crop subgroups.

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 proposed new and revised MRLs to address potential cyflumetofen residues on various food commodities grown in Canada.

Cyflumetofen is a miticide currently registered for use in Canada on field-grown tomatoes, hops and various fruit commodities. Miticides are chemical substances designed to control and manage mites and ticks.

A proposal was submitted by the Pest Management Centre of Agriculture and Agri-Food Canada, and supported by the registrant BASF Canada Inc., to conduct a joint review with the United States (U.S.) to register the use of cyflumetofen on greenhouse-grown tomatoes, greenhouse-grown peppers and greenhouse cucumbers in the two countries at approximately the same time. In Canada, the use would be registered on the Nealta Miticide label (Registration number 31284). These MRL changes, including new MRLs, would allow these greenhouse-grown commodities, or any of their derived processed commodities that may contain cyflumetofen residues, to be sold in Canada.

A second proposal was submitted by the Pest Management Centre of Agriculture and Agri-Food Canada and supported by BASF Canada Inc. to add the new commodities of cucurbit vegetables (crop group 9) from field uses to the product label of Nealta Miticide (Registration number 31284).

Health Canada is proposing to accept these MRL changes (including new MRLs). This is because Health Canada conducted a thorough scientific assessment and found that the health risk from eating food commodities treated with cyflumetofen 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 cyflumetofen, and follows strict regulatory standards. Further details on the dietary risk assessment can be found in Section 3.0 on Dietary risk assessment.

Proposed Canadian maximum residue limits (MRLs) for cyflumetofen

Table 1 summarizes the proposed new and revised MRLs for cyflumetofen, and the reason for each 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 MRLs are based on the following residue definition: 2-methoxyethyl α-cyano-α-[4-(1,1-dimethylethyl)phenyl]-β-oxo-2-(trifluoromethyl)benzenepropanoate

Table 1 Current and proposed maximum residue limits (MRLs) for cyflumetofen

Food commodity	Current MRL (ppm)[1]	Proposed MRL (ppm)[1]	Reason for the proposed MRL
Bell peppers, non-bell peppers	None	2.0	**New MRLs on bell and non-bell peppers**, because of new greenhouse uses on these peppers
Tomatoes	0.4	0.7	**Increased MRL on tomatoes,** because of new data on greenhouse-grown tomatoes
Cucurbit vegetables (crop group 9)	None	0.3	**New MRL on cucurbit vegetables**, as a result of new greenhouse use on cucumbers, and new field uses on cucurbit vegetables (crop group 9)

[1]ppm = parts per million

Based on the results from the dietary risk assessment, Health Canada **is proposing to accept** the new and revised MRL requests for cyflumetofen. This is because these new and revised MRLs **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 sub-populations 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 cyflumetofen

This summary focuses 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 cyflumetofen is used according to the Canadian label directions for the various proposed uses, the dietary risks from cyflumetofen on food commodities continue to meet Health Canada's requirements for the protection of human health. The toxicology information for cyflumetofen relevant to the dietary risk assessment is reported in Appendix I, Table A1-1.

The acute dietary risk assessment results showed that exposure to cyflumetofen is **less than 2%** of the ARfD. **This means that acute exposure to cyflumetofen will not affect your health**. The dietary risk for the relevant subpopulation that may be more susceptible to potential acute effects of cyflumetofen is reported in Appendix I, Table A1-2.

- 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 cyflumetofen.

The chronic dietary risk assessment results showed that exposure to cyflumetofen is **less than 7%** of the ADI. **This means that chronic exposure to cyflumetofen will not affect your health**. The dietary risk for each subpopulation is reported in Appendix I, Table A1-3.

- 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 cyflumetofen 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:

- PMRA Guidance Document, Updated Residue Chemistry Guidelines - Canada.ca

4.0 Summary of residue data to support the proposed maximum residue limits (MRLs)

Health Canada scientists reviewed the residue data from greenhouse trial studies for cyflumetofen that were submitted to support the proposed MRLs on the following commodities: cucumbers, bell peppers, non-bell peppers and tomatoes. Health Canada also reviewed residue data from field trial studies for cyflumetofen on cantaloupes, cucumbers and summer squash to support the proposed MRL on cucurbit vegetables (crop group 9).

Experimental processing data were not required for greenhouse cucumbers, greenhouse peppers and greenhouse non-bell peppers as these commodities are not processed. Experimental processing data were not required for greenhouse tomatoes, as they are sold for consumption in their whole form, and not for commercial processing (unlike field-grown tomatoes).

Table 2 summarizes the residue data used to calculate the proposed MRLs for the various commodities.

Table 2 Summary of greenhouse and field trial data used to support the maximum residue limits (MRLs)

Commodity	Application method	Total application rate (g a.i./ha)[1]	Preharvest interval (days)	Lowest average field trial residues (ppm)[2]	Highest average field trial residues (ppm)[2]	Proposed MRL (ppm)[2]
Greenhouse tomatoes	Foliar application	396-410	1	0.077	0.38	0.7 (tomatoes)
Greenhouse bell peppers	Foliar application	387-415	1	0.135	0.398	2.0 (bell peppers)
Greenhouse non-bell peppers	Foliar application	410-427	1	0.293	0.865	2.0 (non-bell peppers)
Greenhouse cucumbers	Foliar application	391-423	1	0.026	0.11	0.3 (cucurbit vegetables, crop group 9)
Field Cucumbers	Foliar application	399-415	1	<0.01	0.030	
Field Cantaloupes	Foliar application	398-410	1	<0.018	0.068	
Field Summer squash	Foliar application	399-416	1	<0.01	0.078	

[1] g a.i./ha = grams of active ingredient per hectare

[2] ppm = parts per million

5.0 Calculating the proposed maximum residue limits (MRLs)

Health Canada scientists calculated the proposed MRLs for cyflumetofen 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.

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 MRLs proposed for cyflumetofen in Canada with the corresponding U.S. tolerances and international Codex MRLs. The Codex Alimentarius Commission is an international organization under the auspices of the United Nations that develops international food standards, including MRLs.

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

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

The MRLs proposed for cyflumetofen in Canada are the same as corresponding tolerances that are now in place in the U.S. as a result of this joint review. The Codex MRLs for cyflumetofen are listed in Table 3.

Table 3 Comparison of 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]
Bell peppers and non-bell peppers	2.0	2 (Pepper/eggplant subgroup 8–10B)	Not established
Tomatoes	0.7	0.7 (Tomato subgroup 8–10A)	0.3
Cucurbit vegetables (crop group 9)	0.3	0.3 (Vegetable, cucurbit, group 9)	Not established

[1] ppm = parts per million

International consultation on the proposed MRLs 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 changes (including new MRLs) for cyflumetofen 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 25 August 2024) before making a final science-based decision about the proposed MRLs. 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 MRLs, the MRLs 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 these proposed MRLs, here is the information you will need to identify the request:

Active ingredient:	cyflumetofen
Published document number:	PMRL2024-10
Submission number:	2018-6336, 2018-6337, 2018-6338, 2022-5710, 2022-5711, 2022-5712
Related registration decisions:	PRD2014-10, RD2014-24
Related consultation:	PRD2024-07, *Nealta Miticide, containing Cyflumetofen*

Appendix I Excerpt of the dietary risk assessment

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

Exposure scenario	Toxicology reference value used in risk assessment	Study	Toxicological endpoint
Acute Dietary **Females 13-49 years old**	NOAEL[1] = 250 mg/kg bw/day CAF[1] = 300[2] ARfD[1] = 0.8 mg/kg bw/day	Rabbit developmental toxicity study	LOAEL[1] = 1000 mg/kg/day based on increased incidence of fetal malformations (birth defects)
Acute Dietary **All populations (except females 13-49 years old)**	Studies in laboratory animals showed that acute health effects are unlikely to occur in any other population subgroup except females 13-49 years old.		
Chronic Dietary **All populations**	NOAEL[1] = 16.5 mg/kg bw/day CAF[1] = 100[3] ADI[1] = 0.2 mg/kg bw/day	90 day and 2 year rat oncogenicity study	LOAEL[1] = 54.5 mg/kg/day (males) based on adrenal cortical cell vacuolation and increased liver weight (effects on the adrenal gland and liver) (90 day study) LOAEL[1] = 49.5 mg/kg/day (males) based on adrenal cortical cell hypertrophy and hyperplasia (effects on the adrenal gland) (2 year study)

[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; bw = body weight; PCPA = *Pest Control Products Act*. Reference values and endpoints cited in PRD2014-10 and finalized via decision document RD2014-24.

[2] To account for uncertainties including inter- and intra-species variations, a CAF of 300-fold (10-fold for differences between animals and humans, 10-fold for variation between humans, and a 3-fold PCPA factor) was applied to the NOAEL for increased incidence of fetal malformations (birth defects) to calculate the ARfD. Therefore, NOAEL÷CAF = 250 mg/kg bw ÷300 = 0.8 mg/kg bw (rounded value). This is 1250-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 adrenal cortical cell vacuolation and increased liver weight (effects on the adrenal gland and liver) (90 day study) and adrenal cortical cell hypertrophy and hyperplasia (effects on the adrenal gland) (2 year study), in order to calculate the ADI. Therefore, NOAEL÷CAF = 16.5 mg/kg bw ÷100 = 0.2 mg/kg bw (rounded value). This is 248 -fold (LOAEL÷ADI) lower than the lowest dose where toxicological effects were observed in animals (at the LOAEL = 49.5 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 for pesticides 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 (Information Note – Comparing food and drink consumption data from Canada and the United States).

Results of the acute dietary risk assessment

Table A1-2 shows that the PDI is less than 100% of the ARfD (see Section 3.0), therefore there are no acute dietary risks of concern. 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 females 13-49 years old only, as studies in laboratory animals showed that acute health effects are unlikely to occur in any other population subgroup. When including the use of cyflumetofen on the various food commodities, the estimated dietary exposure to cyflumetofen for females 13-49 years old is less than 2% of the ARfD. **This means that potential acute exposure to cyflumetofen will not affect your health.**

Table A1-2 Summary of acute dietary risk for cyflumetofen

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 MRLs
	% ARfD[3,4]	% ARfD[3]
Females 13-49 years old	0.75	**1.03**

Bolded values indicate updated risk assessments.

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

[2] Estimated Environmental Concentrations (EECs) of cyflumetofen have been calculated for drinking water at 20 µg a.i./L from surface 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 2012-0156. Published documents can be accessed in the link by choosing "Application Number" in the "Filter" field, and entering the submission number in the "Value" field.

Results of the chronic dietary risk assessment

Table A1-3 shows that the PDI is less than 100% of the ADI (see Section 3.0), therefore there are no chronic dietary risks of concern. 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, females 13-49 years old and adults 50+ years old. When including the use of cyflumetofen on the various food commodities, the estimated dietary exposure to cyflumetofen for all population subgroups is less than 7% of the ADI. **This means that potential chronic exposure to cyflumetofen will not affect your health.**

Table A1-3 Summary of chronic dietary risk for cyflumetofen

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 MRLs
	% ADI[3,4]	% ADI[3]
General Population	1.6	**1.8**
All Infants	3.2	**3.0**
Children 1-2 years old	6.3	**6.5**
Children 3-5 years old	4.5	**4.8**
Children 6-12 years old	2.3	**2.4**
Youth 13-19 years old	1.3	**1.4**
Adults 20-49 years old	1.1	**1.4**
Adults 50+ years old	1.1	**1.4**
Females 13-49 years old	1.1	**1.4**

Bolded values indicate updated risk assessments.

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

[2] Estimated Environmental Concentrations (EECs) of cyflumetofen have been calculated for drinking water at 12 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 2012-0156. Published documents can be accessed in the link by choosing "Application Number" in the "Filter" field, and entering the submission number in the "Value" field.

For more information

PRD2014-10, *Cyflumetofen* – available through this publication request page
RD2014-24, *Cyflumetofen* – available through this publication request page