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Proposed Maximum Residue Limit

PMRL2023-46

Cyclaniliprole

(publié aussi en français)

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Publications
Pest Management Regulatory Agency
Health Canada
2 Constellation Drive
8th floor, A.L. 2608 A
Ottawa, Ontario K1A 0K9

Internet: canada.ca/pesticides
pmra.publications-arla@hc-sc.gc.ca

Information Service:
1-800-267-6315
pmra.info-arla@hc-sc.gc.ca

Canada 

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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 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 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 MRLs after a robust scientific review and provided that the risks meet Health Canada's requirements for the protection of human health. 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.

An MRL is a scientifically based calculation that estimates the maximum potential concentration of residues on food commodities. It is not a measure 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 [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 reports and journal articles page](#) on Canada.ca.

Food commodities grown in Canada

Prior to any registration decision for use of a pesticide in Canada, Health Canada must evaluate multiple studies from various scientific disciplines to conduct full assessments of the potential impact of the proposed use on human health and the environment as well as its value, as directed in the [Pest Control Products Act](#). This is to ensure there are no health or environmental concern 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 MRL increases to address potential cyclaniliprole residues on various food commodities grown in Canada.

Cyclaniliprole is an insecticide currently registered for use in Canada on various field-grown fruit, nut and vegetable commodities. A proposal was submitted by the Pest Management Centre of Agriculture and Agri-Food Canada (AAFC), and supported by the registrant ISK BioSciences Corporation, to conduct a joint review with the United States of America (US) to register the use of cyclaniliprole on greenhouse-grown tomatoes and greenhouse-grown peppers in the two countries at approximately the same time. These MRL changes would allow these greenhouse-grown commodities, or any of their derived processed food commodities that may contain cyclaniliprole residues, to be grown and sold in Canada.

The following outlines the reasons for the proposed revised MRLs:

- A proposed cyclaniliprole MRL **increase** for peppers and eggplants (crop subgroup 8-09B) is a result of new residue data on greenhouse-grown bell and non-bell peppers that were submitted by AAFC and reviewed by PMRA. Bell peppers and non-bell peppers are the representative crops for crop subgroup 8-09B which includes eggplants.
- A proposed cyclaniliprole MRL **increase** for greenhouse tomatoes (crop subgroup 8-09A) is a result of new residue data on greenhouse-grown tomatoes that were submitted by AAFC and reviewed by the PMRA.

The revised MRLs are proposed, because the health risk from eating food commodities treated with cyclaniliprole 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 cyclaniliprole, and follows strict regulatory standards. Further details on the dietary risk assessment can be found in [Section 3.0](#).

Proposed Canadian MRLs for cyclaniliprole

Table 1 summarizes the proposed revised MRLs for cyclaniliprole.

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: 3-bromo-*N*-[2-bromo-4-chloro-6-[[[(1-cyclopropylethyl)amino]carbonyl]phenyl]-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxamide.

Table 1 Proposed maximum residue limits for cyclaniliprole

Food commodity	Current MRL (ppm)¹	Proposed MRL (ppm)¹
Peppers/Eggplants (crop subgroup 8-09B)	0.2 for Fruiting vegetables (crop group 8-09), which includes peppers, eggplants and tomatoes	1.5
Tomatoes (crop subgroup 8-09A)		0.7

¹ppm = parts per million

Based on the results from the dietary risk assessment, Health Canada is proposing to accept the revised MRL requests for cyclaniliprole. This is because these revised MRLs meet Health Canada’s requirements for the protection of human health.

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 and drink 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 and drink 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** food commodities (both registered (domestic) and imported) and drinking water, and how diets can vary between people in Canada. The PDI level is the potential dietary exposure to a specific pesticide.

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 cyclaniliprole

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 [7.0 Next steps](#) and in [Appendix I](#).

The results from the dietary risk assessment show that when cyclaniliprole is used according to the Canadian label directions for the various proposed uses, 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 cyclaniliprole toxicology data relevant to acute dietary exposure and an ARfD was not necessary. **This means that acute exposure to cyclaniliprole will not affect your health.** The toxicology information for cyclaniliprole 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 cyclaniliprole is **less than 7%** of the ADI level. **This means that chronic exposure to cyclaniliprole will not affect your health.** The dietary risk for each subpopulation is reported in [Table A1.2](#) of [Appendix I](#).

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 cyclaniliprole 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 MRLs

The required residue data from greenhouse trial studies for cyclaniliprole were submitted and reviewed to support the proposed MRLs on the following commodities: bell peppers and non-bell peppers (as part of crop subgroup 8-09B), and tomatoes (crop subgroup 8-09A).

Experimental processing data were not required for 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 considered 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 trial data used to support the MRLs

Commodity	Application method	Total application rate (kg a.i./ha) ¹	Preharvest interval (days)	Lowest average field trial residues (ppm) ²	Highest average field trial residues (ppm) ²
Greenhouse tomatoes	Foliar application	0.240–0.250	1–7	0.062	0.30
Greenhouse bell peppers	Foliar application	0.298–0.304	0–3	0.159	0.252
Greenhouse non-bell peppers	Foliar application	0.306–0.307	0	0.158	0.588

¹ kg a.i./ha = kilograms of active ingredient per hectare

² ppm = parts per million

5.0 Calculating the proposed MRLs

The proposed MRLs for cyclaniliprole were 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 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. Canadian MRLs are established or amended on the basis of a robust scientific risk assessment that demonstrates safety for people in Canada. The MRLs may be aligned to the extent possible with the Codex Alimentarius MRLs and US tolerances, provided that the risks meet Health Canada's requirements for the protection of human health. Table 3 compares the MRLs proposed for cyclaniliprole in Canada with the corresponding American tolerances and international Codex MRLs.

The American tolerance is listed by pesticide in the [Electronic Code of Federal Regulations](#), 40 CFR Part 180. The term “tolerance” is used in the US to describe the maximum residue limit.

The Codex MRL is listed by pesticide or commodity on the Codex Alimentarius [Pesticide Index](#) webpage. The Codex Alimentarius Commission is an international organization under the auspices of the United Nations that develops international food standards, including MRLs.

The MRLs proposed for cyclaniliprole in Canada are the same as corresponding tolerances that are now in place in the United States as a result of this joint review. The Codex MRLs for cyclaniliprole are listed in Table 3 below.

Table 3 Comparison of Canadian MRLs, American Tolerances and Codex MRLs

Food commodity	Proposed Canadian MRL (ppm) ¹	Established American Tolerance (ppm) ¹	Established Codex MRL (ppm) ¹
Peppers/Eggplants (crop subgroup 8-09B)	1.5	1.5	0.15 (eggplants subgroup, peppers subgroup)
Tomatoes (crop subgroup 8-09A)	0.7	0.7	0.08 (tomatoes subgroup)

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 revised MRLs for cyclaniliprole 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 19 February 2024) before making a final science-based decision about the proposed MRLs. Comments received will be addressed in a separate document linked to these proposed MRLs. If no comments are received, or the comments do not result in a change to the proposed MRLs, the established MRLs will be 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 help identify the request:

Active ingredient:	cyclaniliprole
Published document number:	PMRL2023-46
Submission number:	2019-4395 and 2021-0361
Related re-evaluation decisions:	PRD2017-12, RD2017-17
Related consultation:	PRD2023-11

Appendix I Excerpt of the dietary risk assessment

Table A1.1 Summary of Toxicology Information for Cyclaniliprole for Use in Dietary Exposure Assessment

Exposure Scenario	Toxicology Reference Value Used in Risk Assessment	Study	Toxicological Endpoint
Acute Dietary All populations	No ARfD ¹ required ³	Not applicable	None
Chronic Dietary All populations	NOAEL ¹ = 27 mg/kg bw CAF ¹ = 100 ² ADI ¹ = 0.3 mg/kg bw	1 year dog oral toxicity study, co-critical with the 90-day study dog oral toxicity study	LOAEL ¹ = 259 mg/kg bw/day (males) based on increased liver weights, hepatocellular hypertrophy, increased alkaline phosphatase, and decreased albumin (in other words, 9.6-fold greater dose than the NOAEL)

¹ARfD = 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 PRD2017-12 and finalized via decision document RD2017-17.

²To 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 for liver effects to calculate the ADI. Therefore, $NOAEL \div CAF = 27 \text{ mg/kg bw} \div 100 = 0.3 \text{ mg/kg bw}$. This is 863-fold ($LOAEL \div ADI$) lower than the lowest dose where toxicological effects were observed in animals (at the $LOAEL = 259 \text{ mg/kg bw/day}$).

³ No ARfD is required as there were no acute health effects observed.

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

An acute dietary exposure assessment was not required as there were no acute health effects observed relevant to dietary exposure. **This means that acute exposure to cyclaniliprole will not affect your health.**

Results of the Chronic Dietary Risk Assessment

The results of the most recent chronic dietary exposure assessment for cyclaniliprole are shown in [Table A1-2](#). 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 A1-2](#) 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 cyclaniliprole on the various food commodities, the estimated dietary exposure to cyclaniliprole for all population subgroups is less than 7% of the ADI. **This means that chronic exposure to cyclaniliprole will not affect your health.**

Table A1.2 Summary of Chronic Dietary Risk for Cyclaniliprole

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	2.9	3.2
All Infants	3.9	4.1
Children 1-2 years old	5.8	6.5
Children 3-5 years old	4.6	5.3
Children 6-12 years old	2.9	3.3
Youth 13-19 years old	2.2	2.4
Adults 20-49 years old	2.7	3.0
Adults 50+ years old	2.9	3.1
Females 13-49 years old	2.8	3.1

Bolded values indicate updated risk assessments.

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

² Estimated Environmental Concentrations (EECs) of cyclaniliprole have been calculated for drinking water at 79 µg a.i./L from ground water.

³ Values are below 100% ($PDI \div ADI \times 100$), therefore, there are no dietary concerns for any segment of the population.

⁴ Previous assessment from submission number [2018-1692](#).