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COMMENTS ON PROPOSED MAXIMUM RESIDUE LIMITS FOR CYANTRANILIPROLE UNDER PMRL 2025-09

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Introduction

We herein provide comments to PMRL 2025-09 concerning Cyantraniliprole (CY) and the addition of hops to the product label for use in Canada. We are very concerned about this pesticide and its increased use on a crop highly esteemed by Canadians, particularly because it is a relatively new pesticide

Lack of a Proper "Value" Assessment

Under section 2(1) of the Pest Control Products Act, "value" includes:

(a) efficacy,

(b) effects on host organisms, and

(c) health, safety, environmental, social, and economic impacts.

No value rationale or assessment was provided for this application. First and foremost, no rationale for the need for this pesticide has been provided. It appears that PMRA is just proposing this use because the US wants it to. PMRA must also demonstrate that an evaluation under at least these 3 criteria was conducted before accepting the new use pattern on hops. On these criteria:

(a) efficacy: the label wording shows efficacy has not been proven:

> "Crop varieties can differ in their responsiveness, and environmental conditions can have an influence. It is not possible to test EXIREL® insecticide alone or with all possible tank mix combinations on all crop varieties under all environmental conditions".

In addition, the label points out that resistance to CY can be a problem. Evidence on resistance management offered by CY is required, as compared with alternatives, needs to be part of the value assessment. The label states:

> "Any insect population may contain individuals naturally resistant to EXIREL® insecticide and other Group 28 insecticides. The resistant individuals may dominate the insect population if this group of insecticides is used repeatedly in the same fields. Other resistance mechanisms that are not linked to site of action but are specific for individual chemicals, such as enhanced metabolism, may also exist".

(b) Effect on host organism. The tolerance of hops to CY is an important factor and an adequate margin of crop safety is required. This is particularly important since the labels ask for the highest rate of application, and because the quality of hops is important for good brewing and medicinal uses.

(c) Health, safety, environmental, social and economic impacts:

The environmental impacts of this pesticide are very adverse. See the discussion on Environmental Impacts and Species at Risk below. The social impacts will be negative. Hops are used in the production of beer, and the beer brewing industry, particularly the craft beer segment, is growing. Beer growing standards want reductions in the impact of insecticides on pollinators, yet the impact on pollinators, including those which are at risk, is clearly toxic. According to the Beer Council of B.C.:.

> "The Canadian Hop Growers Association sets industry standards that promote best practices related to hops farming that allow producers to effectively balance quality production with environmental responsibility. These standards include:
>
> - Reducing the negative impact of insecticides on important pollinator species."

In a craft and/or specialized industry like beer the impacts on offending industry standards can be quite harmful in society, and carry over to reduced purchases and reduced marketability, causing negative economic impacts.

Environmental Impacts Unacceptable

The assessment of environmental risks associated with CY shows the risks are unacceptable. The label, the science, the courts and risk assessments are clear it is toxic to aquatic organisms, non-target terrestrial plants, certain beneficial anthropods and bees. In 2013, the EPA found that CY is "highly or very highly toxic" to hundreds of endangered species: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0668-0008

In being toxic, the pesticide crosses the assessment threshold for "acceptable risk" in the risk assessment, rendering the risk unacceptable. It must be shown that an unacceptable risk has been rendered acceptable by the conditions of registration before registration, amendment or approval can occur. This has not been shown using a scientifically based approach, and therefore the onus for considering the risks acceptable has not been met.

Litigation in the US has caused amendments to product labels. The label in issue does not reflect these amendments, and, again, it must be shown that any label amendments render the risk acceptable. Evidence is required.

Risk Assessment on Species at Risk Lacking – including Bees

The PMRA does not indicate whether an assessment of species at risk has occurred for the new use. Various bees are listed under the Species at Risk" Act (SARA):

- The Rusty-patched bumble bee ("Bombus affinis") is listed as "Endangered" under SARA and is also federally listed as Endangered in the United States It is also classified as Endangered under Ontario's Endangered Species Act

- The Gypsy cuckoo bumble bee ("Bombus bohemicus") and the ""Macropis cuckoo bee"" are listed as ""Endangered""

- The ""American bumble bee"" ("Bombus pensylvanicus") and the ""Yellow-banded bumble bee"" ("Bombus terricola") are listed as ""Special Concern""

- The ""Western bumble bee occidentalis subspecies"" ("Bombus occidentalis occidentalis") was added to SARA as ""Threatened"" in December 2023

- The "Western bumble bee mckayi subspecies"" ("Bombus occidentalis mckayi") was added to SARA as ""Special Concern"" in December 2023

Additionally, the **Monarch butterfly** (*Danaus plexippus*), while not a bee, was reclassified from Special Concern to **Endangered** under SARA in 2023.

All of the listed bumble bee species in Canada are ground-nesting or primarily use underground sites for nesting:

- Rusty-patched bumble bee (*Bombus affinis*): Nests are typically 1 to 4 feet underground in abandoned rodent burrows or other underground cavities. Over 95% of observed nests are underground.
- Gypsy cuckoo bumble bee (*Bombus bohemicus*): As a social parasite, it does not build its own nest but invades host bumble bee nests, which are typically underground in abandoned rodent burrows.
- American bumble bee (*Bombus pensylvanicus*): Most often nests on the ground surface among long grass or haystacks, but occasionally nests underground.

- Yellow-banded bumble bee (*Bombus terricola*): Nests underground in preexisting holes like abandoned rodent burrows, often under rocks or fallen logs.
- Western bumble bee (*Bombus occidentalis*): Typically nests underground, often using abandoned rodent holes or other subterranean cavities.

Thus, all these species rely on ground-based nesting habitats, either directly or through their host species in the case of the cuckoo bee.

Review and Assessment of Current Science Required

PMRA is obligated to review current science on CY as part of its assessment for this proposed new use, which results in an amendment to the registration. The new science reviewed by PMRA was not listed in the Reference section of the PMRL, and it should be provided.

A Canadian scientist, Sabrine Rondeau makes the case that residues of pesticides in soil are harmful but are overlooked in assessments. The paper, Digging below the surface: Hidden risks for ground-nesting bees [Science 14 Nov 2024 Vol 386, Issue 6723 p. 739 DOI: 10.1126/science.adt899 , cites previous research [S. Rondeau, N. E. Raine, *Sci. Total Environ.* **948**, 174852 (2024)], and states:

> "My research revealed size-dependent effects for bumble bee queens exposed to cyantraniliprole-treated soil. Heavier queens exhibited increased mortality and delayed brood emergence and produced smaller workers. These larger queens likely face greater vulnerability to cyantraniliprole because of their greater muscle mass (cyantraniliprole disrupts insect muscle function), greater surface area in contact with soil, and lower metabolic detoxification capacity. My findings suggest that cyantraniliprole impairs heavier queens' ability to feed their brood and highlight potential cascading impacts on bumble bee populations, as larger queen size is key to successful overwintering and colony establishment in the spring."

This paper provide a new line of evidence on methodologies for assessing risks in the current context and must be accorded due weight in the assessment of risks.

Cumulative Assessment with Other Diamides Required

Cyantraniliprole is a diamide insecticide, chemically related to chlorantraniliprole, and it has a common mechanism of toxicity: [Carl T. Redmond and Daniel A. Potter, Chlorantraniliprole: Reduced-risk Insecticide for Controlling Insect Pests of Woody Ornamentals with Low Hazard to Bees, Arboriculture & Urban Forestry (AUF) November 2017, 43 (6) 242-256; DOI: https://doi.org/10.48044/jauf.2017.020] PMRA is obligation to conduct a cumulative risk assessment given this common mechanism of toxicity. Other pesticides may have a similar mechanism and should be included.

Health Risk Assessment Problems

We have requested and are awaiting the dietary risk assessment and results, including results reported at the 95th, 99 and 99.9 percentiles, so may have additional comments on health risk assessment. We received what was characterized as confidential test data (CTD) from PMRA, and note that PMRA #3548026 is a Joint Review with the EPA for a label expansion under the URMULE Program. It has a very limited number of redactions; plus the redactions appeared to be for locations, which does not qualify as CTD or as personal information that attracts protection as information that is "integral to the dignity or identity of a person, over which they would want to retain control, and in relation to which they would have a reasonable expectation of privacy". Reviews by PMRA relevant to PMRLs must be provided to members of the public when requested without the need for the reading room process, unless they directly copy and

include the CTD set out in registrant studies. Transparency and public participation are not served when PMRA evaluations are held back as here.

Chronic Dietary Risk Assessment – Margin too Narrow

A first concern is that In the PMRL the PMRA reports that chronic dietary intake for all populations is "less than 96% of the acceptable daily intake (ADI)." This margin is unacceptably narrow to ensure a "reasonable certainty of no harm," particularly considering uncertainties and problems with the dietary risk assessment.

We reviewed the URMULE D.3.2. application which is a joint review with the EPA.

Concerns with the Dietary Risk Assessment

We asked for the dietary exposure assessment, but it was not provided. The URMULE review indicated a DEA was conduced in 2022 but this was not updated because the dietary share of hops is low. No evidence was provided for this statement.

Uncertainties and problems with the dietary risk assessment likely include the following. These can be confirmed once the assessment is received.

- the URMULE indicates an **intermediate refinement** provided a refined aggregate assessment ranging from **16-95%** of the ADI. Date on the findings without the refinement were not provided, but given the high level of 95% with refinement, there were likely exceedances.

- An ADI of 95.4% was found for children 1 to 2 years, which is very high. This value crosses the line of scientific certainty/ scientific confidence level of 5%.

- Moreover, the PCPA Factor of 10 was not applied and, contrary to policy and the requirement in the Act, no scientific data was provided to justify the failure to apply the PCPA Factor. Particularly since that this is a new pesticide, such disregard for the health of our young is not justified, not protective and infringes the requirements of and protective approach mandated under the Act.

- the consumption data is likely based on DEEM, which measures what Americans, not Canadians consume, and the fact that there is a difference in consumption patterns of beer between Americans and Canadians. For example, draft beer holds a 70% share of volume in the on-premise market whereas this is only 52% share in the US, and Canadians show an 11% higher preference for draft (41%) than Americans (30) [CGA, Spirits and Beer performance in North America: The distinct differences between US and Canada's On Premise].

- the fact that residues on dried hops may carry through to beer and other brewed products. PMRA must provide measured **processing factors** (hops → beer) for the parent compound and metabolites. Without these, the dietary exposure estimate is incomplete and may underestimate real-world exposure.

- the fact that the numerical ADI was not provided nor were the studies on which it was based.

Health Risks because Systemic and an Allergen

A further concern is that CY is a systemic pesticide, which means that it is translocated to growing areas of the plant. Research has shown that systemic pesticides are taken up by hop plants and translocated upward through the xylem, making them bioavailable in the leaves and thus the developing cones. [Brent Warneke, Pesticide redistribution: an

important aspect of synthetic pesticides, Sprayers 101, January 25, 2022] The particular risk arising because of the systemic nature of CY as it relates to the measurement of the residue levels must be accounted for. Evidence on its metabolism in plants is needed in this regard.

Another risk arises because, as the label reports, the product may contain soy, a potential allergen. The health risk associated with this potential allergen must be assessed.

A cancer risk assessment was not conducted because of lack of methodology. This is not an appropriate rationale for conducting a review for cancer.

Problems with MRL Calculations Use

It is not clear if the OECD MRL Calculator was used to calculate the MRLs. However the Appendix to the URMULE review provides information similar to an OECD MRL Calculator output page. There were only six data points, which makes the data set was very small. The White Paper on the OECD Caculator indicates that the problem with a dataset between 5 and 8 is "most MRL proposals lie between 0.5 and 2.5 of the HR" (highest residue), indicating it is not an accurate representative limit. In the instant case, it was about 2.0 times the HR of 36 ppm. The statistical tool used on a small dataset can yield misleadingly high values when limited or heterogeneous residue trials are use. The MRL was inflated by virtue of the statistical treatment of small datasets.

Plus, the estimate of 70 ppm was rounded up from an unrounded estimate of 62.887. This is not justified.

Failure to Assess the Whole Product and Tank Mixtures

To understand the actual risks to health and environment arising from use of the pesticide, as is required, the full product as applied and absorbed must be assessed, and the mixture of the product with other products as applied and absorbed must also be assessed.

PMRA has jurisdiction to assess the entire co-formulated product and mixtures, and its mandate to protect Canadians from the risk of pesticide requires it to take the most protective approach in its assessment. In addition, an evaluation of metabolites and transformation products is required, particularly because independent studies show that metabolites are toxic to insects as well.

The label shows that tank mixtures can be harmful:

> "In some cases, tank mixing pest control products can result in reduced pesticide efficacy or increased host crop injury".

The label speaks to "adverse crop response", "increase the potential for crop injury' . As mentioned, it states "It is not possible to test EXIREL® insecticide alone or with all possible tank mix combinations on all crop varieties under all environmental conditions".

Proposed MRL (70 ppm) Excessive

The proposed MRL of **70 ppm** for dried hops is high. The PMRL indicates the residues in supporting field trials reportedly ranged from 6.7 ppm to **36 ppm** with a **1-day preharvest interval (PHI),** meaning the proposed MRL is almost twice the highest average level. This is no in keeping with the required approach for MRLs. Moreover, a PHI this short cannot reasonably be assumed to yield safe consumer residues, particularly given cyantraniliprole's persistence. PMRA should

publish the **residue decline data** and the rationale for selecting this PHI. Without this information, the consumer safety determination is not scientifically supportable.

Conclusion

We have various concerns with this pesticide, as set out above, and including the following. The scientific evidence indicates that cyantraniliprole poses unacceptable risks to the environment and species at risk. The dietary risk assessment has not been updated or provided, but the URMULE review of it shows there are problems and concerns that do not align with a scientifically based approach. The % of ADI present for young children is unacceptable scientifically. The 10 fold PCPA Factor must be applied. The margin of risk for the chronic assessment is too narrow to provide a reasonable certainty of no harm, and the proposed MRL has been inflated by the MRL Calculations because of a small dataset. A cumulative risk assessment is required, and assessments of the risk arising because the product contains an allergen and is systemic are required. A case has not been made that CY has value, or that PMRA has conducted a review of current science.

Safe Food Matters urges PMRA to suspend finalization of this MRL until the concerns raised in these comments are addressed.