



COMMENTS ON PROPOSED INCREASES OF MAXIMUM RESIDUE LIMITS (MRLS) UNDER PMRL 2023-41 Mefentrifluconazole

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Introduction

We herein provide comments to PMRL 2023-41 concerning Mefentrifluconazole (the Active). The comments relate to both the expansion of the Active in Canada for use on new commodities, and to the specification of maximum residue limits (MRLs) on imported commodities.

No Jurisdiction to Approve Import MRLs

Section 6 of the *Pest Control Products Act* (the Act) indicates that a pest control product cannot be imported or used unless it has been registered or authorized under the Act. With respect to MRLs for pest control products, the Act contemplates two scenarios: specifying an MRL when the Minister is "making a decision regarding the registration of a pest control product" (Section 9), and specifying an MRL with respect to uses that have not been registered (Section 10). It follows that, with respect to a Section 10 MRL and because of section 6, a Section 10 MRL use has to be authorized under the Act.

The Act allows authorizations under sections 41(1), 21(5), 48, 51 and 53-59 and the Regulations. **None of these provisions contemplate authorizing an MRL on an imported food commodity (an "Import MRL").** This means that PMRA's approval of the use of Import MRLs in is *ultra vires* and without jurisdiction. In other words, it is illegal.

Failure to Assess Whole Product

PMRA does not assess the full pesticide product but only the active ingredient. PMRA has the legal authority to assess the entire co-formulated product, and its mandate to protect Canadians from the risk of pesticide requires it to take the most protective approach in its assessment. This is particularly problematic here, because the formulated product contains allergen(s) that have not apparently been assessed.

Highly Uncertain MRL Estimates

In setting the proposed residue levels for both chemicals, PMRA used the OECD Calculator. This statistical approach "overestimates" or inflates values in situations where the data sets are small, as explained in the OECD [White Paper](#). Many of the data sets supporting the proposed MRLs were small and the OECD MRL Calculator Output for the relevant commodities reported in red:

"High uncertainty of MRL estimate due to small dataset".

EXPANDED USE: The affected proposed expanded use MRLs are for the following commodities: green onion, head lettuce without wrapper, mustard greens and non-bell pepper.

IMPORT MRL: The affected proposed Import MRLs are for the following commodities: radish root, radish tops, turnip tops, green onion, head lettuce without wrapper, mustard greens and non-bell pepper.

PMRA is required to assess a pesticide using a scientifically based approach, and have a reasonable certainty, based on its scientific assessment, that no harm to human health from the pesticide will arise. PMRA cannot have such reasonable scientific certainty because the proposed MRLs are based on small datasets and are highly uncertain.



Unjustified Use of Residue Data from Decline Studies

For carrot root, non-bell pepper, banana and coffee Import MRLs, PMRA used data from decline studies in the OECD Calculator. This was not justified. As explained by PMRA in its [MRL information](#), the field trials show results when the pesticide is used according to label directions. The Pre-harvest interval for Mefentrifluconazole is zero, so use of residues at PHIs other than 0 are not justified based upon the scientific process employed for setting MRLs.

Field Trials from US not Appropriate for Canadian expansion

The proposed MRLs for the Use Expansion of the Active on fruiting vegetables, melon, squash/cucumber, bushberries, and low growing berries are based on field trials conducted in the United States, not Canada. The agricultural practise used in the trials for all was 450 g/ha and 0 day pre-harvest interval (PHI) (except the non-bell paper also had a 3 day PHI).

This agricultural practise is not applicable to the Canadian context. The current Canadian label has an application rate of 0.25 – 0.375 L/ha for these commodities.

Increases Not Needed for Canadian expansions

The current Canadian label already includes the relevant commodities, so there is no need for expansion. The expanded use application is described in PMRL2023-41 as an “application to add new commodities”. However, almost all the commodities are not new, and are covered by the existing, current label.

The only exceptions may be spinach and mustard greens. As noted, with respect to mustard greens, the OECD Calculator states that the proposed MRL estimate is highly uncertain, due to the small dataset.

With respect to spinach, the data set contains 8 data points. This is also a small dataset. Although this commodity did not attract the “high uncertainty” statement, it contains only one data point more than the datasets for radish roots and radish tops, which did present the “high uncertainty” statements based on 7 data points. Speaking generously, the proposed MRL for spinach is at best medially uncertain. It is not supported with any reasonable certainty.

Health Risk Assessment

- PMRA is obligated to conduct a full health risk assessment when setting MRLs. This includes a toxicology assessment, dietary exposure assessment, aggregate risk assessment and an occupational and residential risk assessment.

There was no evidence that PMRA updated the last health risk assessments, including evidence that it ran a new dietary exposure or aggregate risk assessment.

- In PRD2019-09, PMRA noted the “serious effect” observed in a rat dietary 2-generation reproductive toxicity study, namely that there were a decreased number of implantation sites in F1 dams was observed and that as a consequence, a decreased number of pups were delivered per dam as well as a decreased gestation index in F1 dams were observed. These effects were adverse and treatment related. They were also qualitatively different than other adverse effects observed and, as such, the PCPA Factor should have been retained, as outlined in *Science Policy Note SPN2008-01 The Application of Uncertainty Factors and the Pest Control Products Act Factor in the Human Health Risk Assessment of Pesticides*. PMRA suggests that there is some kind of “intrinsic margin” in the assessment, such that the PCPA factor could be reduced to one. This is not a valid scientific rationale.



- There was also no evidence that PMRA conducted a review of the scientific literature for purposes of updating the previous health assessment. New evidence of the toxicological potential of the active is in the literature is available, and was available after the previous assessment.

By way of example, the September 2023 publication *“Mefentrifluconazole exposure disrupted hepatic lipid metabolism disorder tightly associated with gut barrier function abnormal in mice”*, found at <https://www.sciencedirect.com/science/article/abs/pii/S0048969723059442> cites recent studies that show it has the potential to bioaccumulate, and also that there has been gradual accumulation [of azole fungicides] in the environment and excessive exposure to fungicides may induce various diseases, such as impaired metabolic function, endocrine disruption, and even induction of cancer, in animals and humans. It provides cites of “Cui et al., 2022; Giavini and Menegola, 2010; Hu et al., 2022; Hu et al., 2023; Sancho et al., 2010”. On the basis of this evidence and these studies, there is evidence of carcinogenicity and other concerns that should have been considered in the health risk assessment.

- PMRA has not conducted a cancer risk assessment for this Active or its full product even though the literature shows cancer risks are present. This represents a failure to assess risk.

- The current Canadian label indicates the full product contains the allergen soy. It also states that the product is a “Potential Skin Sensitizer”. No assessment of the allergic potential of the product, because of its soy component or dermal has been conducted. The health risks associated with an allergy to soy can be high and warrant assessment.

Import MRL Removes Canadian Standard

- By inflating the Canadian MRL to align with the higher proposed Import MRL, PMRA is removing the Canadian standard for residues of the Active– it leaves no measure for pesticide residue that may remain on or in food **grown in Canada** when the product is used according to **Canadian** label directions. As such, PMRA is **removing a measure and check for the exposure of Canadians to pesticides**, a key measure of risk. This opens the door for allowing higher pesticide levels to occur on Canadian foods without adequate checks.