



COMMENTS ON PROPOSED REGISTRATION DECISION FOR Fluoxapiprolin and Xivana Prime UNDER PRD 2025-07

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Introduction

We herein provide comments to PRD 2025-07 concerning Fluoxapiprolin (Active) and Xivana Prime.

The proposal is to register the Active and end-use product for for the control of late blight on potatoes, and against downy mildew and certain *Phytophthora* diseases on brassica head and stem vegetables, bulb vegetables, cucurbit vegetables, fruiting vegetables, leafy vegetables, leafy petiole vegetables, grapes and Amur river grapes. romaine lettuce and as a soybean seed treatment.

Background: Appropriate PMRA Approach

The legislative goal under the PCPA is for the Minister of Health/ PMRA to have a reasonable certainty that no harm to human health, future generations or the environment will result from exposure to or use of the product, taking into account its conditions or proposed conditions of registration. This goal sets the legislative standard for “acceptable risk” (See Health Canada Decision-Making Framework for Identifying, Assessing, and Managing Health Risks and Section 1(2), 4 and 7(6) of the PCPA).

A pest control product (PCP) is defined as either the active ingredient, the end-product, or both. The PMRA, on behalf of the Minister of Health, must apply a scientifically based approach when evaluating the risks of the PCP. A scientifically based approach considers both the toxicity or hazard and the level of exposure to characterize risk ([PMRA Guidance Document, a Framework for Risk Assessment and Risk Management of Pest Control Products](#)).

Because the approach is “scientifically based”, it gathers knowing using the scientific method and is evidence-based. The scientific method develops and then test theories/hypothesis with scientific data and evidence. The method consists of gathering evidence through rigorous repeatable procedures, and the evidence must be empirical, interpretable according to the scientific method, and capable of being verified or falsified through observation and experimentation.

PMRA reflects this approach in it Mission, which is: “To protect the health and environment of Canadians by using modern, evidence-based, scientific approaches to pesticide regulation, in an open and transparent manner”.

Additional Information Requested

We have requested and are awaiting information from Access to Information. We may have additional comments following our receipt of such information.

Health Risk Assessment Concerns

Cancer

The assessment found equivocal evidence of cancer. Equivocal means uncertain, which means there is no reasonable certainty that it does not pose cancer. The “no harm” standard that is the legislative goal cannot be met.

We were not able to review the confidential test data for the assessment, but the Centre for Food Safety in the US has reviewed the data and concludes that the PCP causes cancer. We adopt this analysis.

It is found at: https://www.centerforfoodsafety.org/files/cfs-fluoxapiprolin-comments--9-12-25-corrected_45232.pdf

Other

There is a lack of data on the toxicological endpoints of acute toxicity and skin corrosion, so the risk assessment is not sufficient.



- The registrant used a kinetically-derived maximum dose (KMD) / saturation argument to choose high doses in several core studies. The PMRA flagged issues with that rationale (uncertainty about the inflection point, sex differences in TK) and did not accept the KMD rationale wholesale. The review indicates the KMD justification “was not accepted due to a number of issues,” and the agency considered dose selection on a study-by-study basis.

- There was sensitivity of the young, which means there was developmental/reproductive toxicity. The rat developmental gavage study (up to limit dose) showed bent tails and short 14th thoracic ribs in fetuses in absence of maternal toxicity. PMRA characterises these as “well-characterized and not serious” but also notes sensitivity of the young.

Malformations are serious endpoint according to PMRA’s own policy, SPN2008-01. The safety factor of 10 must be retained under SPN2008-01.

- PMRA accepted waivers for subchronic neurotoxicity and immunotoxicity. This is a new PCP so the database is limited. Such waivers are not appropriate.

Metabolites

- PMRA concluded BCS-BP32808 (fluoxapiprolin-BDM-pyrazole) is more toxic than the parent and established separate, much lower toxicological reference values (ADI for BCS-BP32808 uses a NOAEL of 2 mg/kg with a composite CAF of 3000).

Plus soil/field dissipation data show BCS-BP32808 is present among transformation products (e.g., up to ~6% AR in some studies), and it is “non-persistent to slightly persistent” in aerobic soils in some tests. However but PMRA modelled BCS-BP32808 conservatively in drinking water (spray-direct assumption) rather than using measured field formation fractions in refined scenarios.

Metabolites with higher toxicity than the parent demand a complete chronic/toxicokinetic database or conservative aggregate handling. PMRA applied heavy CAFs for this metabolite, but exposure modelling assumptions (spraying the metabolite directly) are a rough proxy and may either over- or under-estimate real exposure pathways if metabolite formation in crops, soil, or water differs regionally. The “reasonable certainty of no harm” standard has not been met.

Concerns with the Dietary Risk Assessment

Uncertainties and problems with the dietary risk assessment include the following.

- the PCPA Factor of 10 was not applied, even though the Act requires it, particularly because of the serious endpoint as described above. No “reliable scientific data” was provided to reduce the factor, to the contrary. Even the requirements based on PMRA’s own interpretation are not met: there were concerns with sensitivity of the young.

- the consumption data is based on DEEM, which measures what Americans, not Canadians consume.

Field Trial Data

The field trial data was fully or partially located outside of Canada. These regions differ in terms of climate and applications than Canada, rendering the trials inadequate for the Canadian context.



Environmental Risk Assessment

- Persistence, mobility and transformation product profile are mixed. Fluoxapiprolin is non-persistent to moderately persistent in aerobic soils and persistent under anaerobic conditions; it adsorbs strongly to soils (low mobility), and partitions rapidly to sediments in water bodies.

Several transformation products (including BCS-BP32808 and others) are present in soil after one year (field dissipation data show metabolites at measurable proportions); some TPs are detected in the 0–15 cm soil layer and at trace depths.

Although the parent adsorbs strongly, persistent metabolites in upper soil layers can be available for runoff or crop uptake and might affect aquatic organisms or contribute to long-term load in soil.

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.

In addition, PMRA must demonstrate that an evaluation under at least the 3 legislated criteria was conducted.

This resistance risk is considered medium to high because fluoxapiprolin is a single-site inhibitor, meaning resistance can develop relatively easily if not managed properly.

Conclusion

The scientific evaluation did not adequately assess the risk arising to human health and the environment from the Active and its end-product, or showed that they pose risks to human health and the environment, including cancer. Mitigation by labels does not guarantee the “no harm” standard. The value assessment was lacking in that there was no need for the PCP provided, and also the 3 criteria for value set out in the Act were not established.

Safe Food Matters urges PMRA to not register this Active or its end-products, given these problems with the risk and value assessment.