



COMMENTS OF

SAFE FOOD MATTERS INC.

on

PROPOSED MAXIMUM RESIDUE LIMIT

PMRL2026-03

ISOCYCLOSERAM

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PART I — INTRODUCTION

Safe Food Matters Inc. ("SFM") is a Canadian non-profit organization dedicated to promoting safe food for Canadians. SFM regularly participates in PMRA consultations under the Pest Control Products Act, S.C. 2002, c. 28 (PCPA) and has standing as a "person" within the meaning of section 28(1) of the PCPA to submit written representations on proposed maximum residue limits.

SFM has participated in prior consultations concerning isocycloseram, including comments submitted on PMRL2025-21 and analysis of the responses to public comments set out in the Registration Decision RD2026-03 (Isocycloseram, VANECTO COCKROACH GEL BAIT, EQUENTO and A23128 ST). The present comments build upon and incorporate by reference the positions advanced in those prior submissions insofar as the issues raised therein remain unresolved and bear directly on the proposed MRLs that are the subject of this consultation.

These comments are submitted within the permitted comment period and may be supplemented by information obtained from access to information relating to isocycloseram..

PART II — PROCEDURAL AND STRUCTURAL GROUNDS

Ground 1 — Reference to a Closed Consultation: PRD2026-02

PMRL2026-03 states, at the Purpose of Consultation section: "Details regarding these applications can be found in Proposed Registration Decision PRD2026-02, Isocycloseram, A21377 CP, A21708 CP, A22466 CP, EQUENTO RFC and A23294 TO, posted to the Pesticides and pest management portion of Canada.ca on 29 January 2026." The document further states that consultation on the proposed MRLs is being conducted both "via this document and PRD2026-02," and instructs members of the public to submit comments in accordance with the process outlined in both documents.

This instruction was procedurally deficient from the outset and has become impossible to comply with. PRD2026-02 was published on January 29, 2026 with a 30-day comment period. That consultation closed before the April 14, 2026 deadline for PMRL2026-03. PMRA therefore constructed an MRL consultation that directs the public to a companion PRD consultation that was already closed at the time comments on the PMRL were invited to be submitted in reliance on it.

The practical effect is that the dietary risk assessment underlying the proposed MRLs — which is contained in the Science Evaluation of PRD2026-02, not in PMRL2026-03 itself — was never subject to meaningful integrated review by members of the public reading PMRL2026-03 after the PRD consultation window had already elapsed.

SFM submits that the appropriate regulatory authority, apparently Health Canada through the Pesticide Regulatory Directorate ("PMRA"), has an obligation, pursuant to the PCPA and the principles of procedural fairness to ensure that the information underpinning a proposed regulatory limit is genuinely accessible during the period when that limit is under consultation. A cross-reference to a consultation that has already closed does not discharge that obligation.



Ground 2 — Staged Registration and Phased PMRL Consultations: Failure to Provide a Comprehensive Risk Assessment

Isocycloseram is being registered through a staged, incremental approach across multiple consultation documents spanning two separate PRDs and two separate PMRL consultations. The initial registration decision (RD2026-03, arising from PRD2025-11) addressed cockroach gel bait uses and seed treatment uses on small cereal grains, and was accompanied by PMRL2025-21 proposing MRLs for those uses. The current consultation — PMRL2026-03 and its companion PRD2026-02 — addresses a large and distinct set of new food uses including foliar application to leafy vegetables, Brassica crops, fruiting vegetables, cucurbits, stone fruits, pome fruits, tree nuts, soybeans, and peanuts, as well as in-furrow application to corn.

This phased architecture — two PRDs with corresponding PMRLs, processed serially over consecutive years — is not a comprehensive risk assessment. It is a structural device that fragments what should be a single integrated evaluation of isocycloseram's total use profile, total dietary exposure burden, and total environmental load into discrete segments, each of which appears more limited and more manageable in isolation than the whole. No single consultation document in the chain presents the public with the full picture of: all proposed and registered uses of isocycloseram in Canada; the aggregate dietary exposure from all uses operating simultaneously; the cumulative environmental load from all use patterns combined; or the full suite of toxicological hazards as they bear on the widest set of exposure scenarios.

The practical consequence for public participation is significant. A member of the public commenting on PMRL2025-21 was commenting on MRLs for cereal grains without knowing that MRLs for leafy vegetables at 10 ppm, stone fruits at 1.0 ppm, and fourteen other commodity groups were imminent. A member of the public now commenting on PMRL2026-03 does so without knowing what further use expansions may follow in a hypothetical PMRL2026-XX or PMRL2027-XX for uses not yet consulted upon. The phased approach structurally prevents the public from evaluating whether the cumulative dietary exposure across all current and anticipated uses remains below the ADI and ARfD for all sensitive subpopulations. This is not a contingent or theoretical concern: PMRA's own cross-references in PRD2026-02 to the prior PRD2025-11 process acknowledge the sequential relationship between the two registration tranches, yet the dietary exposure assessments do not appear to integrate the two.

This phased PRD/PMRL approach applied to isocycloseram is inconsistent with the requirement under section 7(1) of the PCPA that PMRA determine, before registering a pest control product for food use, that residues from that use will not be a concern to human health, taking into account all uses. A registration decision made piecemeal — approving cereal grain uses in one decision without assessing the dietary exposure contribution of the forthcoming high-residue leafy vegetable and stone fruit uses — does not satisfy that standard. The "reasonable certainty of no harm" test in section 7(1) must be applied to the full scope of dietary exposure from a registrant's complete registration program for an active ingredient, not to each use tranche in isolation.

The cumulative food use pattern created by these staged registrations is substantially broader and higher-residue than any single consultation document discloses. The dietary exposure assessments in Phase 1 necessarily reflect only the uses that were before PMRA at the time of



the document's preparation, not the totality of dietary exposure that will result from the full suite of registered and proposed uses operating simultaneously.

PMRA has not demonstrated that the ADI and ARfD established in the toxicology assessment accommodate the cumulative dietary load that will result from simultaneous registered uses across all crop groups consulted in PMRL2025-21 and PMRL2026-03 together, plus any further uses that may follow. This represents a failure to conduct a cumulative dietary risk assessment as required by sections 7 and 8 of the PCPA and as contemplated by DIR2006-02 (Dietary Cumulative Risk Assessment for Organophosphate Pesticides) and Health Canada's Science Policy Note SPN2018-02 on SDHIs, which was relied upon in the prior PRD2025-11 process.

Ground 3 —Combined Formulation with Chlorantraniliprole

PRD2026-02 includes, within the same consultation and the same proposed registration decision, an end-use product designated A23294 TO that contains isocycloseram co-formulated with a second active ingredient, chlorantraniliprole. This is confirmed by the PRD2026-02 summary, which states: "In the end-use product A23294 TO, isocycloseram is co-formulated with chlorantraniliprole."

Chlorantraniliprole is a diamide insecticide registered in Canada under multiple prior registration decisions (RD2011-02, RD2014-26, RD2016-17) and is itself subject to ongoing residue obligations and exposure assessments across a wide range of food and ornamental uses. The proposed registration of A23294 TO within the same PRD as the isocycloseram-only products raises the following distinct concerns.

First, PMRA has conducted what is in substance two risk assessments — one for isocycloseram as a sole active ingredient, and one for the combined active in A23294 TO — within a single PRD. The consultation documents available to the public do not appear to have separately identified or clearly demarcated the Science Evaluation sections addressing A23294 TO as distinct from those addressing isocycloseram alone. This creates a risk of conflation: dietary exposure estimates, residue definitions, and toxicological endpoints for the combined product may differ materially from those applicable to the solo-active products, but the public has no ready means to identify and comment on those differences.

Second, the inclusion of chlorantraniliprole in A23294 TO raises a cumulative risk assessment obligation that is not addressed in PMRL2026-03. Chlorantraniliprole and isocycloseram are both IRAC Group insecticides affecting nicotinic acetylcholine receptors or ryanodine receptor pathways, respectively. While they operate through different primary mechanisms, both agents may have toxicological interactions at the level of systemic insecticide exposure in food. A composite formulation sold and used as a single product in greenhouse ornamentals and turf will necessarily result in simultaneous dietary and non-dietary exposure to both active ingredients in the same use scenario. PMRL2026-03 does not address residues of chlorantraniliprole arising from A23294 TO uses, and SFM cannot determine from the available consultation documents whether the dietary exposure assessment for A23294 TO accounts for background chlorantraniliprole exposure from its pre-existing registered uses.



Ground 4 — Denial of Access to the Complete Science Record

SFM has sought, through the Access to Information (“**ATIP**”) process, the PMRA-authored documents identified in the Information Available document provided for PMRL2026-03. The documents identified for ATIP include Dietary Exposure Assessment (Phase 2), PMRA document 3767683.

As of the date of these comments, SFM has not received these documents from ATIP. SFM has therefore been required to prepare these comments without access from ATIP of the dietary exposure assessments that form the analytical foundation for the proposed MRLs in PMRL2026-03.

SFM notes that the Information Available document for PMRL2026-03 explicitly lists documents 3786829 and 3767683 as obtainable only through the Access to Information process. These are PMRA-authored scientific assessments — not third-party confidential business information — and their restriction to ATIP rather than Reading Room availability is unexplained and inconsistent with the principle of open and accessible consultation.

SFM reserves the right to supplement these comments with additional submissions upon receipt of the outstanding documents from ATIP.

PART III — SUBSTANTIVE GROUNDS: DIETARY RISK ASSESSMENT DEFICIENCIES

Ground 5 — PFAS Classification of Isocycloseram and TFA as a Degradation Product: Failure to Apply the OECD 2021 Definition and Assess Environmental and Dietary TFA Exposure

5.1 — PFAS Classification Under the OECD 2021 Definition

As SFM has argued in detail in its comments on PMRL2025-21 and in the analysis of RD2026-03 responses, isocycloseram meets the criteria for classification as a PFAS under the OECD 2021 definition (per- and polyfluoroalkyl substances: the OECD Global Database). Isocycloseram contains a CF₃ (trifluoromethyl) group attached to a carbon atom that also bears



other non-hydrogen substituents, satisfying the OECD structural definition of a polyfluoroalkyl substance. The residue definition for PMRL2026-03 specifies the parent compound 4-[5-(3,5-dichloro-4-fluorophenyl)-4,5-dihydro-5-(trifluoromethyl)-3-isoxazolyl]-N-(2-ethyl-3-oxo-4-isoxazolidinyl)-2-methylbenzamide, which explicitly includes the CF₃ moiety at the 5-position of the isoxazoline ring.

PMRA's longstanding practice treats structural fluorination as a toxicity consideration only when a compound independently triggers specific toxicological endpoints. That practice is scientifically inadequate for the reasons set out below.

5.2 — Trifluoroacetic Acid (TFA) as a Degradation Product of Isocycloseram: Scientific Evidence

Isocycloseram contains a trifluoromethyl (C–CF₃) group as a structural feature of the isoxazoline ring system. The scientific evidence now firmly establishes that compounds containing a C–CF₃ bond are precursors of trifluoroacetic acid (TFA) in the environment through biotic and abiotic degradation. This is not a speculative inference; it is a documented pathway for the class of C–CF₃ pesticides to which isocycloseram structurally belongs.

Johnsen et al. (2026), published in the *Journal of Environmental Quality*, conducted a 52-week laboratory experiment with seven common C–CF₃ pesticides in three agricultural soils and found that TFA was formed from all seven tested compounds without exception (Johnsen et al., "Formation of trifluoroacetic acid from common trifluoromethyl pesticides in agricultural soils," *J. Environ. Qual.*, 2026). The tested pesticides included fluopyram — an SDHI fungicide that, like isocycloseram, contains a C–CF₃ bond as a defining structural feature — which produced TFA at a rate of up to 10.7% of the applied mass in one soil over the study period. The authors concluded that TFA formation from C–CF₃ pesticides is a class property driven by the C–CF₃ structural motif, not a compound-specific anomaly. Isocycloseram, sharing that structural motif, is accordingly a TFA precursor candidate whose TFA-forming potential has not been assessed by PMRA.

Similarly, a 2023 review in *Science of the Total Environment* confirmed that compounds containing C–CF₃ moieties are potential precursors of TFA due to the exceptional (bio)chemical stability of the –CF₃ group, which results in the release of TFA as a quasi-terminal degradation product in the environment. The review identified isocycloseram among the class of recently registered pesticides carrying this structural feature (Scheurer et al., *Sci. Total Environ.*, 2023). A 2025 article in *ACS ES&T Water* described fluorinated pharmaceuticals and pesticides as capable of transforming into TFA under oxidative conditions at molar yields ranging from approximately 9% to 40%, depending on molecular structure. These yields, applied to the proposed use rates for isocycloseram across fourteen crop groups in Canada — including leafy vegetables at application rates supporting a 10 ppm MRL — represent a potentially substantial contribution to TFA load in Canadian agricultural soils and associated water bodies.



The German Umweltbundesamt (UBA) has identified pesticides as the main source of TFA in water in agricultural areas. European Parliament questions submitted in 2025 (E-001786/2025) documented TFA contamination in European drinking water at levels already exceeding the 0.5 µg/L total PFAS threshold in the EU Drinking Water Directive in the majority of samples, with TFA comprising over 98% of total detected PFAS mass in some sample sets. Health Canada has established a guidance value of 30 ng/L for total PFAS in drinking water. The increasing contribution of C–CF₃ pesticides to environmental TFA load makes this objective progressively harder to meet as new C–CF₃ pesticides are approved without TFA formation assessments.

5.3 — TFA's Environmental and Toxicological Profile

TFA is a per- and polyfluoroalkyl substance (PFAS) — specifically an ultrashort-chain perfluoroalkyl acid (PFAA) — classified as very persistent and very mobile (vPvM) in the environment. The key characteristics of TFA that make its formation from isocycloseram a regulatory concern are as follows.

Persistence: TFA has no known significant abiotic degradation pathways in the environment and is only slowly degradable under anaerobic biological conditions. Once formed in soil or water, TFA accumulates irreversibly in the water cycle. A 2024 paper in *Environmental Science & Technology* (Arp et al., "The Global Threat from the Irreversible Accumulation of Trifluoroacetic Acid," *ES&T*, Vol. 58, No. 45, 2024) described TFA as posing a global threat due to irreversible accumulation and proposed classifying it as a planetary boundary threat, similar to ozone-depleting substances.

Mobility and plant uptake: TFA is highly water-soluble and mobile in the water cycle, spreading rapidly through rivers and precipitation. Unlike longer-chain PFAS, TFA does not bind to soil or organic matter, making it exceptionally difficult to remove from drinking water. Critically, TFA undergoes rapid uptake and bioaccumulation in crops and other plants, particularly in aerial compartments. Studies have detected TFA in plant-based foods and documented accumulation in conifer needles, maize leaves, and tree foliage. This plant uptake pathway creates a direct dietary exposure route independent of the spray-applied parent compound.

Toxicology: TFA's toxicological profile is an active area of scientific concern. The German Federal Institute for Occupational Safety and Health (BAuA) and the UBA have proposed classifying TFA as toxic to reproduction (Category IB — presumed human reproductive toxicant) and as a PMT/vPvM substance under EU chemical classification. This classification is currently under review by ECHA. Mammalian toxicity studies have identified the liver as a target organ, with mild liver hypertrophy observed in repeated-dose rat studies, and there are indications from mammalian toxicity studies that TFA is toxic to reproduction. A 2025 pre-print further identified that TFA disrupts plasma lipid levels and alters metabolic pathways at concentrations potentially relevant to environmental exposure levels. While current regulatory risk assessments suggest that present-day TFA exposures are below thresholds for immediate adverse effects, those assessments were conducted when TFA levels were substantially lower than they are today, and before the contribution of the new generation of C–CF₃ pesticides — including isocycloseram — to environmental TFA load was recognized.

Regulatory responses: The European Commission has mandated ECHA and EFSA to conduct



a joint assessment of TFA fate and behaviour in soil and water, with scientific findings expected by June 2027. That mandate was specifically prompted by TFA formation from plant protection products and biocides. The ECHA RAC adopted its opinion on the universal PFAS restriction under REACH in March 2026; that opinion addresses fluorinated pesticides as a class of TFA precursors. WHO has prioritized TFA among the 18 PFAS to be assessed for health effects in its ongoing review, specifically flagging developmental, reproductive, hepatic, and cancer endpoints.

5.4 — PMRA's Failure to Assess TFA in the Isocycloseram Processes

PMRL2026-03 does not contain any reference to TFA as a potential degradation product of isocycloseram. The PMRL document's residue definition — the parent compound only — does not include TFA. The Information Available document confirms that the dietary exposure assessments (documents 3786829 and 3767683) are the only PMRA-authored documents that could contain a TFA assessment, and SFM has not received those documents. The Information Available document also confirms that PMRA does not review peer-reviewed scientific literature in PMRL processes, which means the Johnsen et al. 2026 TFA formation study, the Arp et al. 2024 global accumulation review, the CHEM Trust TFA analysis, and the ECHA/EFSA mandate were not considered.

The omission of TFA from the residue definition and from the dietary exposure assessment is scientifically unjustifiable given the current state of knowledge. The C–CF₃ pesticides tested to date have produced TFA in agricultural soil. Isocycloseram is being proposed for food use on fourteen commodity groups at application rates that, at the 10 ppm leafy vegetable MRL end of the scale, imply substantial field applications. The cumulative TFA load from isocycloseram use across the proposed Canadian label, combined with TFA from other C–CF₃ pesticides already registered in Canada (including cyclobutylfluram, fluopyram, sedaxane, and others), has not been assessed.

SFM submits that PMRA cannot conclude that residues of isocycloseram in food are acceptable under the PCPA without first determining: (a) the rate at which isocycloseram converts to TFA in Canadian agricultural soils; (b) the extent to which TFA formed from isocycloseram use is taken up into the crop commodities listed in Table 1 of PMRL2026-03; (c) the dietary exposure to TFA from isocycloseram-treated food commodities, including both residual TFA in the commodity and TFA formed post-harvest or in processing; and (d) the combined dietary exposure to TFA from all registered C–CF₃ pesticide uses in Canada. Until these assessments are conducted, the proposed MRLs in PMRL2026-03 cannot be considered to satisfy the "reasonable certainty of no harm" standard in section 7(1) of the PCPA.

Since the metabolites SYN549431 and SYN548569 can be detected above the LOQ in commodity matrices in the residue trial data, as was the case with almond hulls (SYN549431 HAFT 0.069 ppm) — and since they contain fluorine as part of their molecular structures, they should have been assessed as fluorinated metabolites with independent toxicological profiles distinct from the parent compound.

Ground 6 — Residue Chemistry Data: Scientific Deficiencies Arising from the Integrated Assessment (PMRA Document 3767682)



SFM has reviewed the Integrated Assessment document (PMRA 3767682) at the PMRA Reading Room. The following observations are based on residue data contained in that document. SFM emphasizes that it cannot access the dietary exposure calculations that give quantitative significance to these data without receipt of the ATIP-requested dietary assessment documents.

6.1 — Absence of a Consistent Residue Decline in High-Residue Commodities

The residue decline trial data for several commodities show that isocycloseram residues do not exhibit a predictable, monotonic decline pattern with increasing pre-harvest intervals (PHIs). This was the case with, for example, apples and pears.

The practical significance of non-declining residue patterns is that the establishment of a PHI as a residue control measure may be scientifically unjustified for these commodities. If residues increase or remain constant over the PHI period, harvest at the specified PHI does not guarantee that residues will be at or below the level measured in the residue trials that were used to calculate the proposed MRL. The PMRL2026-03 consultation document does not acknowledge this issue or explain how PMRA accounted for non-declining residue patterns in calculating the proposed MRLs.

6.2 — Concentrate vs. Dilute Spray Volume Discrepancies

SFM notes that the proposed Canadian MRL for stone fruits (1.0 ppm) was set lower than the calculated MRL for cherries from dilute spray volumes (1.5 ppm calculated, 1.0 ppm proposed) on the basis of alignment with the U.S. tolerance and the observation that the HAFT was well below 1.0 ppm. While SFM does not oppose conservative MRL-setting, it notes that PMRA's practice of harmonizing downward in cherry residues while not explaining why the same conservative approach was not applied to leafy vegetables (10 ppm proposed), which carry a far greater dietary contribution due to consumption volume, is inconsistent and unexplained.

6.3 — Almond Hull Residues and Processing Factor Deficiencies

Almond hull residue data for isocycloseram are striking in magnitude: per-trial average residues in almond hulls ranged from 0.330 ppm (LAFT, 7-22 day PHI) to 3.07 ppm (HAFT), with a maximum single-sample value of over 3.5 ppm. The proposed MRL for tree nuts (crop group 14-11) is 0.2 ppm — which applies to the almond nutmeat. Almond hull residues approximately 7- to 18-fold above the nutmeat MRL represent a substantial processing fraction that concentrates in a co-product used as animal feed.

The proposed Canadian MRL for almond oil is 0.5 ppm. No explanation is provided in PMRL2026-03 for how the concentration factor from almond nut (max HAFT 0.083 ppm) to almond oil (proposed MRL 0.5 ppm) was calculated or what processing trial data supported this 6-fold concentration factor. The proposed MRL for almond oil (0.5 ppm) is set at a level that, if residues in almond oil are driven by the high hull residues migrating into oil processing fractions, may underestimate dietary exposure from processed almond products.

Ground 7 — PCPA Children's Safety Factor: Application and Transparency

Section 7(6) of the Pest Control Products Act requires that, unless reliable scientific data demonstrates that a different factor is appropriate, a 10-fold safety factor (the "children's safety factor") shall be applied to address the extra sensitivity of infants and children to pesticide



chemical residues. The application of this factor to the toxicological benchmark used to calculate the ADI and ARfD for isocycloseram is not disclosed in the PMRL2026-03 consultation document.

SFM's prior submissions on PRD2025-11 and in analysis of RD2026-03 identified that PMRA applied the children's safety factor to isocycloseram but that the basis for the selection of the specific point of departure (POD) — in particular, the choice of benchmark dose (BMD) or NOAEL from the reproductive toxicity and developmental toxicity studies — was inconsistently disclosed in the publicly available documentation. PMRA identified the most sensitive endpoints as effects on body weight, altered fetal development, and reduced survival of the young. An increase in ovarian tumours in female mice and testicular tumours in male rats was noted but described as not clearly attributable to treatment.

This equivocal treatment of the tumor findings is a substantive issue for MRL-setting. If the ovarian and testicular tumors are treatment-related — a question that PMRA acknowledges has not been definitively resolved so as to prove a “reasonable certainty of no harm” — the appropriate risk characterization for a carcinogenic compound would require application of cancer-slope factors rather than threshold-based ADI/ARfD methodology. An unresolved carcinogenicity concern should not be dismissed as background without a quantitative weight-of-evidence analysis.

Ground 8 — Absence of Independent Scientific Literature Review

The Information Available document for PMRL2026-03 includes the following disclosure, in response to SFM's prior request for documentation of literature reviews: "PMRLs do not involve reviews of public scientific literature." This categorical statement, repeated consistently across PMRL consultations (and reflected identically in the Information Available document for PMRL2026-01, PMRL2026-04, and PMRL2026-05), establishes that PMRA conducts no independent review of the peer-reviewed scientific literature when proposing maximum residue limits.

This practice is inconsistent with the scientifically based approach required under the PCPA, which approach obliges PMRA to apply current and accurate science when assessing whether a proposed MRL poses an acceptable risk. It is also inconsistent with the common law MadDog case that requires assessments at touchpoints of amendments of registrations. The peer-reviewed literature on isocycloseram has expanded substantially since the original registration data packages were submitted by Syngenta. None of this literature is reflected in the PMRL2026-03 consultation or in the Integrated Assessment reviewed at the Reading Room.

SFM submits that the categorical exclusion of independent scientific literature from PMRL assessments — a practice PMRA has now formalized in its Information Available responses — is not consistent with the statutory obligation to determine whether residues are acceptable under current scientific knowledge. SFM requests that PMRA review relevant peer-reviewed literature using a scientifically based approach.

Ground 9 — OECD MRL Calculator Warnings: High Uncertainty for Multiple Proposed MRLs



The OECD MRL Calculator Output Spreadsheet (PMRA document 3835316) is listed in the Information Available document as accessible through the PMRA Reading Room. SFM's review indicates that the OECD calculator generated high-uncertainty warnings for a significant number of the MRLs proposed in PMRL2026-03. SFM raises these warnings as a substantive concern because they go to the reliability and robustness of the residue limit determinations on which the dietary risk assessment depends.

Specifically, the OECD calculator issued a warning of high uncertainty of the residue limit due to small dataset for the following commodities proposed in this consultation:

- Brussels sprouts
- Green onions (bunching onions / scallions)
- Eggplant
- Pears — both dilute and concentrate spray volume trial sets
- Cherries — both dilute and concentrate spray volume trial sets
- Peaches — both dilute and concentrate spray volume trial sets
- Plums — both dilute and concentrate spray volume trial sets

The OECD calculator issued a warning of high uncertainty of the residue limit due to censoring for:

- Almonds (crop group 14-11, proposed MRL 0.2 ppm)
- Dry soybeans (proposed MRL 0.15 ppm)

Both almonds and dry soybeans are included among the MRLs proposed in PMRL2026-03 and are confirmed as part of this consultation. Dry soybeans appear at the 0.15 ppm proposed MRL for crop group 9/soybeans in Table 1. Tree nuts (including almonds) appear at the 0.2 ppm proposed MRL for crop group 14-11.

The OECD MRL calculator warnings have the following regulatory significance. A "high uncertainty due to small dataset" warning indicates that the number of acceptable field trials submitted for a given commodity was insufficient to generate a statistically reliable estimate of the upper tail of the residue distribution from which the MRL is calculated. The OECD calculator methodology (OECD 2011, Guidance for the Use of the MRL Calculator) recommends that MRLs derived from datasets generating this warning be treated with caution and that additional trial data be considered before finalizing the limit.

A "high uncertainty due to censoring" warning indicates that a substantial proportion of the residue values in the dataset were reported as less than the limit of quantitation (LOQ), and that the statistical treatment of those censored values (typically assumed to equal the LOQ for calculation purposes) has introduced significant uncertainty into the estimated MRL. For almonds, this warning is consistent with the residue data reviewed by SFM in the Integrated Assessment, which shows that almond nutmeat residues were predominantly below or at the LOQ of 0.01 ppm in most of the five trials, with only one trial producing a quantifiable mean. The proposed MRL of 0.2 ppm is being set at a level 20-fold above the actual measured residues in almost all trials, with the gap between measured residues and the proposed MRL driven by the censoring adjustment rather than observed upper-end values. This approach overestimates the



MRL needed to accommodate actual field use and is unnecessarily high.

For dry soybeans, the censoring warning similarly indicates that most trial residues were below LOQ, yet a 0.15 ppm MRL is being proposed — again substantially above the measured residue levels. An MRL derived primarily from statistical adjustments to censored data rather than from actual residue measurements is not an evidence based or scientific approach.

More broadly, the concentration of OECD calculator uncertainty warnings across the stone fruit crop group (pears, cherries, peaches, and plums, for both dilute and concentrate trial sets) is particularly concerning because these are the commodities generating the highest proposed MRLs in the stone fruit group (1.0 ppm for the group). The proposed MRLs cannot be the standard of reasonable certainty of no harm under section 7(1) of the PCPA given the lack of certainty regarding an input into dietary assessment calculations.

PART IV — DIETARY AND HEALTH RISK ASSESSMENT DEFICIENCIES ARISING FROM PRD2026-02

Ground 10 — Acute Dietary Risk Exceedance for Females 13–49 Years: The Head Lettuce CCCA Manoeuvre Does Not Constitute Regulatory Compliance

PRD2026-02 discloses that the refined acute dietary exposure for all proposed isocycloseram food uses was estimated at **113% of the ARfD** for females 13 to 49 years of age. The conclusion follows, from PMRA's own policy documents and approach, that the proposed registration does not satisfy the "reasonable certainty of no harm" standard under the PCPA for a defined and identifiable Canadian subpopulation.

Rather than treating this exceedance as a barrier to registration, PMRA conducted a Critical Contribution Commodity Analysis (CCCA), identified head lettuce as the primary driver of risk for this subpopulation, removed head lettuce from the dietary exposure model, and then declared the residual exposure acceptable. This approach is completely scientifically and legally inadequate, and exhibits a preference of PMRA to support registration rather than seek to protect the public interest, which is its primary mandate.

Head lettuce is not a marginal food. It is a widely consumed commodity across all Canadian population groups, including females of childbearing age — the very subpopulation for whom the ARfD is exceeded. Removing head lettuce from the dietary exposure model does not reduce actual exposure; it reduces modelled exposure by definitional exclusion. The ARfD exceedance therefore subsists in the real world even as the model no longer reflects it.

The mechanism of the ARfD exceedance is directly connected to the proposed MRL for leafy vegetables. PMRL2026-03 proposes an MRL for leafy vegetables (including head lettuce) of 10 ppm — the highest MRL in the proposed schedule. The residue data generating the ARfD exceedance reflect the HAFT residues that are the basis for the proposed MRL. A dietary risk assessment that identifies an ARfD exceedance traceable to the proposed MRL and then resolves that exceedance by removing the offending commodity from the model does not constitute a finding that residues of that commodity are acceptable. It is a circular device: the



proposed MRL generates an ARfD exceedance; the exceedance is resolved by excluding the commodity; the MRL is then proposed on the basis that the revised dietary assessment shows no concern.

The CCCA manoeuvre is not authorized by the PCPA as a mechanism for resolving ARfD exceedances. The PCPA requires that PMRA be satisfied that the health risks of a pest control product are acceptable. An ARfD exceedance for a defined subpopulation is not rendered acceptable by identifying which commodity drives the exceedance and excluding it from the risk characterization.

Ground 11 — TSMP Assessment by Cross-Reference: Inadequate Satisfaction of the PCPA Obligation to Assess Persistence for the Full Proposed Use Profile

Section 6.1 of PRD2026-02 states: "Details on the Toxic Substances Management Policy (TSMP) assessment of isocycloseram are found in PRD2025-11, Isocycloseram, VANECTO COCKROACH GEL BAIT, EQUENTO and A23128 ST." The section then states the conclusion without analysis: that isocycloseram and its transformation products do not meet all of the TSMP Track 1 criteria. No analytical support for that conclusion appears in PRD2026-02 in the context of the dramatically expanded use profile now before PMRA.

The TSMP Track 1 analysis in PRD2025-11 was conducted against a use profile consisting of cockroach gel bait, seed treatment of small cereal grains, and an in-season foliar application in that context. PRD2026-02 proposes an entirely different and substantially more extensive use profile: foliar application to fourteen crop groups including leafy vegetables at 10 ppm, stone fruits, pome fruits, cucurbit vegetables, fruiting vegetables, Brassica crops, tree nuts, soybeans, and peanuts, as well as in-furrow application to corn at 150 g a.i./ha. The aggregate soil loading, environmental persistence, and surface water contamination potential arising from this expanded food use profile is materially different from — and substantially greater than — the profile that was the subject of the PRD2025-11 TSMP assessment.

Critically, PRD2026-02 itself discloses an aerobic soil half-life for isocycloseram of 284.4 days at 20°C in its groundwater modelling inputs at section 3.5.2. This value is above the 182-day threshold for TSMP Track 1 soil persistence. The dismissal of Track 1 concern by reference to PRD2025-11 — without addressing the implications of the 284.4-day aerobic soil half-life for the broader fourteen-crop-group use profile now proposed — is not a reasoned assessment. It is a conclusion borrowed from a different regulatory context and applied without examination to a materially different one.

SFM further submits that the TSMP analysis in PRD2025-11 does not appear, in publicly available form, to address whether the ecotoxicologically active transformation products identified in PRD2026-02 — including SYN549106 (identified as SYN549431 in fate studies), SYN550918 (identified as SYN550738), and SYN551753 (identified as SYN550737) — independently satisfy any Track 1 criterion. PRD2026-02 identifies these transformation products as generating screening-level RQ exceedances for aquatic invertebrates and bees. Compounds that are both toxic to non-target organisms and potentially persistent warrant independent TSMP analysis, not collective dismissal by cross-reference to a prior decision conducted under a narrower use profile.



Ground 12 — Inadequacy of the Cumulative Health Assessment: A Qualitative Approach Is Not Sufficient for a Common Assessment Group with Shared Reproductive and Endocrine Organ Endpoints

PRD2026-02 at section 3.7 identifies isocycloseram, broflanilide, and fluxametamide as constituting a Common Assessment Group (CAG) for cumulative health assessment purposes, on the basis of shared toxicological endpoints: adrenal cortex targeting shared between isocycloseram and broflanilide, and small intestine epithelial vacuolation plus sperm function effects shared between isocycloseram and fluxametamide. Despite identifying these shared reproductive and endocrine organ endpoints, PRD2026-02 states that "a qualitative approach to assessing risks from cumulative exposure was undertaken" and concludes that cumulative risk is acceptable.

The qualitative approach consists of two elements: noting that fluxametamide's dietary contribution is minimal (USEPA estimated less than 1% of ADI), and providing a summary table of broflanilide's registered uses without calculating combined dietary exposure. This does not constitute a cumulative risk assessment in any scientifically meaningful sense. Isocycloseram is proposed for use across fourteen crop groups, several of which overlap with broflanilide's registered food uses in Canada and the United States, including corn, soybeans, and multiple vegetable crop groups. A qualitative approach that acknowledges overlapping uses without quantifying combined dietary exposure does not demonstrate that the cumulative load from both compounds remains below the ADI for the shared adrenal and sperm function endpoints.

The public participation pillar affirmed in the common law requires that the factual basis for scientific risk conclusions be disclosed in a form that permits public scrutiny; a qualitative narrative does not satisfy that requirement.

Furthermore, the cumulative assessment does not address the unresolved carcinogenicity findings for isocycloseram — ovarian tumours in female mice and testicular tumours in male rats that PMRA acknowledges could not clearly be attributed to or excluded from treatment — in combination with broflanilide's documented adrenal cortex toxicity. Where two pesticides in the same CAG both affect endocrine-sensitive organs (adrenal, ovarian, testicular), the cumulative carcinogenic and endocrine risk characterization cannot rest on a qualitative approach that declines to quantify combined exposure.

SFM requests that PMRA conduct a quantitative cumulative dietary exposure assessment for the isocycloseram–broflanilide CAG across the overlapping proposed use profiles of both compounds, with explicit disclosure of the combined percentage of the ADI and ARfD for the shared toxicological endpoints.

PART V — ENVIRONMENTAL RISK ASSESSMENT DEFICIENCIES ARISING FROM PRD2026-02

Ground 13 — Bee and Pollinator Risk: Adequacy of Evening-Application Mitigation and Treatment of Larval Risk Quotient Exceedances in Higher-Tier Studies — Residual Risk to Honeybee Larvae After Tier I and Tier II Refinement



PRD2026-02 at section 4.2.1 discloses that the screening-level risk quotients for bees **exceeded the Level of Concern (LOC) substantially across all exposure pathways**: for adult bees, the acute oral RQ was 5.1 and the chronic dietary RQ was 45; for larvae, the acute dietary RQ was 1.3 and the chronic dietary RQ was 49. These are not marginal exceedances. The chronic larval RQ of 49 represents a 49-fold exceedance of the LOC of 1.

The Tier I refined assessment used measured residues from semi-field studies conducted at application rates higher than the proposed Canadian rate of 1×50 g a.i./ha. At those rates, chronic larval RQs ranged from 0.28 to 1.5, with exceedances of the LOC in four of eight studies. PMRA characterized these results as conservative on the basis that the study rates were higher than the proposed Canadian rate. This reasoning is insufficient: a risk assessment conducted at higher-than-Canadian rates that nevertheless generates LOC exceedances in four of eight studies does not establish the absence of risk at Canadian rates; it establishes that the dose-response is steep enough that risk is present at rates not far above those proposed for use.

The Colony Feeding Study (CFS) NOEC of 0.28 mg a.i./kg diet was exceeded by pollen residue concentrations from forager bees in semi-field studies, which ranged from 0.45 to 4.04 ppm at application rates of 45 to 120 g a.i./ha. PMRA acknowledged "added uncertainties" with this comparison because the CFS was conducted with sucrose, not pollen, and the dose-response relationship for pollen-based larval exposure is therefore not established by the available data. PMRA's conclusion that risk "is not expected" rests on extrapolation across a data gap that PMRA itself acknowledges exists. That is not a sufficient evidential basis for a finding of acceptable risk under section 7(1) of the PCPA.

— Evening-Application Mitigation: Enforceability and Sufficiency

The primary mitigation for crops moderately to highly attractive to bees — which includes soybean and peanut, two of the highest-acreage proposed food uses — is restriction of foliar application to evening hours when bees are not actively foraging. SFM submits that this mitigation is behavioural and effectively unenforceable. There is no field-level verification mechanism under the PCPA label compliance framework to confirm that foliar applications across the fourteen proposed crop groups are in fact made in the evening. Evening-hour restrictions are frequently impractical in Canadian agricultural operations due to weather, equipment scheduling, dew conditions, and the abbreviated bloom windows of high-value horticultural crops. A label restriction that cannot be reliably verified in practice, and that conflicts with normal operational constraints, does not constitute adequate risk mitigation for a compound that generates chronic larval LOC exceedances in multiple higher-tier studies.

— Beneficial Arthropods and IPM Incompatibility

PRD2026-02 discloses that the refined risk quotients for the foliar-dwelling predatory mite (*Typhlodromus pyri*) ranged from 2778 to 3617 on-field and from 22 to 333 off-field. For the parasitic wasp (*Aphidius rhopalosiphi*), refined on-field RQs ranged from less than 8 to less than 9. On the basis of these findings, the PRD concludes that isocycloseram "is not considered compatible with certain beneficial arthropods in integrated pest management (IPM) programs" and requires precautionary label statements advising IPM incompatibility.

SFM submits that the regulatory significance of this finding is not adequately reflected in the assessment. The duration for which foliar residues of isocycloseram would be expected to



maintain toxic activity against the predatory mite was calculated at 55 to 108 days on-field — multi-month elimination of natural enemy populations from treated orchards and fields, with consequent potential for secondary pest outbreaks from spider mites, thrips, and whiteflies. These secondary outbreaks represent a form of environmental and agronomic harm that falls within PMRA's mandate to characterize under section 7(1) of the PCPA and within the section 2(1) definition of value. The value assessment at section 5.0 of PRD2026-02 does not address these costs. A label statement advising IPM incompatibility does not prevent the harm; it notifies the user after harm has occurred. SFM requests that PMRA assess whether the long-duration foliar toxicity to *Typhlodromus pyri* and the consequent secondary pest outbreak risk have been adequately characterized as components of the environmental risk and value assessments.

Ground 14 — Aquatic Invertebrate Risk: Residual Runoff Risk Quotient Exceedances and the Adequacy of the 10-Metre Buffer Zone as the Sole Mitigation Instrument

PRD2026-02 discloses that screening-level RQs for freshwater aquatic invertebrates exceeded the LOC at values of 893 and 4808 for acute and chronic exposure respectively, and 694 and 1689 for marine invertebrates — up to five orders of magnitude above the LOC for the most sensitive species. Following Tier II refinement using modelled runoff exposure concentrations, the refined acute and chronic RQs for the most sensitive species still ranged from 1.1 to 48, exceeding the LOC across the range of assessed scenarios. The sole mitigation applied to bridge this gap to a conclusion of acceptable risk is a requirement for a 10-metre vegetative filter strip between the application area and adjacent downhill aquatic habitats, together with standard best management practice label statements for runoff reduction.

SFM submits that a 10-metre buffer zone is not validated mitigation for residual aquatic invertebrate RQs of up to 48. Buffer zone effectiveness for pesticide runoff interception is highly dependent on slope, soil texture, vegetation density, and rainfall intensity. PRD2026-02 does not identify the scientific basis for selecting 10 metres as adequate across the entire range of proposed uses — from turf application to foliar spray on corn, soybean, and orchard crops — across Canadian landscape and drainage conditions. A 10-metre buffer that is adequate on a flat, well-vegetated field may provide negligible protection on a sloped, tile-drained field. The PRD does not address this variability.

Furthermore, the cumulative aquatic risk from repeated foliar applications within a growing season has not been adequately addressed. Isocycloseram's aerobic soil half-life of 284.4 days means that parent compound residues accumulate in soil between application events, producing increasing runoff loading across the season. The maximum annual application programmes proposed — up to four applications per season for some uses — will result in substantially higher cumulative aquatic EECs than the single-application scenarios modelled in the PRD. The actual aquatic invertebrate exposure from a full growing season of isocycloseram use is therefore underestimated by the modelled EECs on which the refined risk characterization rests.

PART VI — SUBSTANTIVE GROUNDS: VALUE ASSESSMENT DEFICIENCIES ARISING FROM PRD2026-02



Ground 15 — Value Assessment: Failure to Apply the Full Section 2(1) PCPA Standard, Including Environmental Costs of IPM Incompatibility and the Adequacy of the Efficacy Evidence for Extrapolated Claims

Section 2(1) of the PCPA defines "value" to include not only a product's contribution to pest management but also "health, safety and environmental benefits and social and economic impact." PRD2026-02's value assessment at section 5.0 addresses only one dimension of this standard: pest management contribution through provision of a new mode of action and resistance management. The assessment does not address the environmental and economic costs that are properly part of the section 2(1) value calculation.

First, the PRD's own environmental risk assessment establishes that isocycloseram is incompatible with IPM programs that rely on predatory mites and parasitic wasps, and that foliar residues maintain toxic activity against the predatory mite *Typhlodromus pyri* for 55 to 108 days on-field. The economic consequences for Canadian producers who rely on beneficial arthropods for biological pest control in orchards, vineyards, and vegetable operations are not assessed anywhere in PRD2026-02. The suppression of natural enemy populations for up to 108 days per application, with the consequent risk of secondary pest outbreaks requiring additional insecticide interventions, represents a direct cost to integrated crop management systems. The PCPA section 2(1) value standard requires that these costs be weighed against the pest management benefit. The PRD's value assessment does not perform that weighing.

Second, the value assessment for the greenhouse ornamental uses of A23294 TO — the co-formulation of isocycloseram and chlorantraniliprole — relies on extrapolation of efficacy claims from the ACELEPRYN Insecticide label, which is a chlorantraniliprole-only product. This means the efficacy evidence base for the greenhouse ornamental claims of A23294 TO is the chlorantraniliprole component alone. The value assessment does not identify any efficacy contribution attributable to the isocycloseram component for greenhouse ornamental uses. If the efficacy of A23294 TO in greenhouse ornamentals is essentially equivalent to that of ACELEPRYN, the co-formulation adds no incremental value for those uses while adding the residue profile, aquatic invertebrate risk, and IPM incompatibility associated with isocycloseram. The value assessment must address whether the isocycloseram component provides any independent value contribution in the greenhouse context, or whether that component's inclusion is justified only by the outdoor and turf uses.

Third, for the in-furrow product A22466 CP, the value assessment states that corn rootworms and wireworms "can reduce plant stand of corn crops and under high pest pressure can cause large economic loss to corn crops" and notes that A22466 CP "will aid in resistance management." The assessment does not compare isocycloseram's availability against existing registered products for corn rootworm and wireworm control, including other IRAC Group 30 compounds, neonicotinoid seed treatments, and registered diamide in-furrow alternatives. Where the pest already has multiple registered solutions, the value of an additional active ingredient must account for the net benefit after subtracting the risks — including the aquatic invertebrate risks from the 284.4-day soil persistent compound entering tile drainage systems from corn fields — from the incremental resistance management contribution.

SFM requests that PMRA supplement the value assessment to: (a) quantify the economic and environmental costs to Canadian producers of the IPM incompatibility of isocycloseram with predatory mites and parasitic wasps as part of the section 2(1) value calculation; (b) assess



whether the isocycloseram component of A23294 TO provides independent efficacy value for greenhouse ornamental uses beyond what is attributable to the chlorantraniliprole component; and (c) address, for each proposed use, the availability and adequacy of registered alternatives and the net value contribution of isocycloseram against the full section 2(1) definition including health, safety, environmental, social, and economic impact.

CONCLUSION

In conclusion, the registrations of Isocycloseram should not be granted or be allowed to continue. They are inadequate from the standpoint of procedural fairness and public participation, they fail to meet scientific and regulatory standards, and they ignore the emerging body of science worldwide reflecting concerns over these pesticides. The intransigence of the regulator in preferring approval over the public interest is unjustified and unconscionable.