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File No.: 2115

October 28, 2022

Sent via e-mail to pmra.publications-arla@hc-sc.gc.ca
Submitted by online form to: https://pest-control.canada.ca/public-engagement-portal/en/forms/notice-objection

Registration Evaluation Co-Ordinator
Pest Management Regulatory Agency (PMRA)
Health Canada
2720 Riverside Drive
Ottawa, Ontario
Address Locator: 6607D
K1A 0K9

Dear Registration Evaluation Co-ordinator:

Re: Tiafenacil Notice of Objection (RD2022-09)

This notice of objection is sent on behalf of Ecojustice, Prevent Cancer Now, Friends of the Earth and Safe Food Matters Inc..

Please note that with respect to the submissions on the appropriate legal test for consideration of objections set out in Appendix A (or otherwise referenced herein) Safe Food Matters Inc. reserves the right to make additional submissions or take differing positions on these issues.

We are objecting to the registration of products containing tiafenacil. This objection raises a scientifically founded doubt about the validity of the evaluations of the risks to human health and the environment. This information could change the PMRA's conclusion about whether there is reasonable certainty – to a scientific standard – that tiafenacil will cause no harm to human health or the environment. The Pest Management Regulatory Agency's (**PMRA**) evaluation failed to address cumulative effects of exposures to Canadians of multiple sources of protoporphyrinogen IX oxidase (PPO) inhibitors in drinking water, raising questions about whether all subpopulations are protected from multiple sources of exposure. The PMRA has not assessed whether tiafenacil is an endocrine disruptor. The PMRA failed to assess the toxicity of trifluoroacetic acid (TFA), or the potential for long-term, multigenerational accumulation of TFA in the environment at toxic levels. The registrant has not established that there is acceptable risk from TFA to future generations and the PMRA cannot be assured of acceptable risk. The PMRA

has also failed to assess the effects of TFA on climate change, which should form part of the evaluation of environmental risks.

Nature and scope of this submission

This submission was prepared during the 60-day notice of objection period provided for under s.35 of the *Pest Control Products Act* (**PCPA**). Although there are provisions for the review by the public of confidential test data during the objection period, and the objectors requested these materials in early October, no extension was granted.[1] Objectors were advised that once they were provided with confidential test data, they would have only 14 days to submit additional information in support of the notices of objection. Accordingly, the objectors were prejudiced by the failure of the PMRA to provide confidential test data in a timely way or to provide relevant extensions and cannot speak to any of the specifics of the data considered by the PMRA in its evaluation in this submission. The objectors also state that 14 days is not a reasonable period of time to review and comment on thousands of pages of confidential test data, particularly given the format constraints of the way the data is provided to objectors (non-OCR, non-indexed etc.). We also do not know in advance when we are likely to receive the test data.

We are also submitting this objection as public comments opposing the pending registration of tiafenacil for an additional tiafenacil product in application 2022-2051 which is listed as "pending" on the public registry and appears to be an end-use product intended for use on field corn, soybeans, spring wheat, grape, fallow and non-crop areas.[2] As the public registry keeps various aspects of the application confidential we do not know if this amendment is at higher application rates or uses different application methods potentially posing different risks than the end use products which were registered as a result of PRD2022-01 and RD2022-09. The PMRA did not include this product in the public consultation documents. As there is not usually a public consultation or comment period on a new end use product where the technical active is already registered for similar uses, this is our only way to provide this information to the PMRA. The content of this submission should also be considered to be public comments on the registration amendments, renewals and new registrations for other PPO inhibitors and TFA-producing pest control products including but not limited to those listed in Appendices B and C.

About tiafenacil

The PMRA's registration decisions propose to register the active ingredient tiafenacil (Tergeo Technical Herbicide) along with two end-use products Tiafenacil 70WG Herbicide and Tiafenacil 339SC Herbicide. It is proposed to be used as a preplant and/or pre-emergence broadcast spray on field corn, soybean and spring wheat, postemergence on grape and post emergence on non-crop areas and summerfallow. Two applications per-year are anticipated.[3]

[1] Email communication Meagan Maloney (PMRA) to Mary Lou McDonald (Safe Food Matters) dated October 14, 2022 denying extension request to review confidential test data.
[2] Health Canada, PCPA public registry (old version) Application No. 2022-2051 https://pr-rp.hc-sc.gc.ca/pi-ip/adoc-ddoc-eng.php?p_app_id=2022-2051
[3] PRD2022-01 Table 27 "list of supported uses"

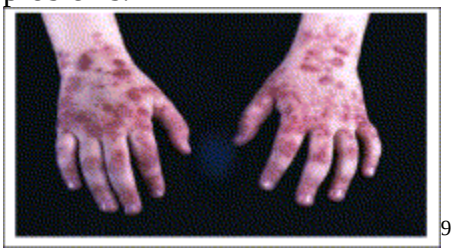
Additionally the registration decision would allow maximum residue limits of tiafenacil (MRLs) on food for certain commodities (fat, meat, milk, eggs) of 0.01 ppm. For all other commodities the default general MRL of 0.1 ppm would apply.

Scientific rationale

Evidence – toxicity profile of PPO inhibitors is incomplete

Tiafenacil is a herbicide belonging to the pyrimidione class of chemicals. The primary pesticidal mode of action (**MOA**) of tiafenacil is inhibition of protoporphyrinogen IX oxidase (**PPO**) in plants which in turn disrupts chlorophyll synthesis. The same enzyme PPO is involved in the production of hemoglobin in mammals.[4] PPO inhibition in humans can result in light sensitivity due to the accumulation of protoporphyrinogen in the liver and decreased erythrocytes, hemoglobin, hematocrrit, mean cell volume, mean corpuscular hemoglobin concentrations and increases in reticulocyte counts. Toxicity is expressed as hunched posture, loss of body weight, abnormal respiration, piloerection and vomiting.[5] PPO inhibition can also result in increased or decreased liver weight and pathology.[6]

Porphyria can be caused by PPO inhibition. Porphyria arises as a result of a malfunction in one of the eight steps in the body's synthesis of a complex molecule called heme. Heme is essential for the transport of oxygen to cells in the body. If any step in the synthesis of heme is blocked, an intermediate chemical accumulates in the cell. Those intermediate chemicals, known as porphyrins or porphyrin precursors, are the substances of which heme is composed. Each type of Porphyria represents a deficiency of a specific enzyme needed for the synthesis of heme.[7] Porphyria is a serious illness that presents as skin lesions, pain in the abdomen, back, arms or legs, digestive symptoms, mental changes, anemia, high blood pressure and liver and kidney problems.[8]

 [9]

[4] Rio, B et al, “Effects of a diphenyl-ether herbicide, oxyfluorfen, on human BFU-E/CFU-E development and haemoglobin synthesis” (1997) 16:2 Hum Exp Toxicol 115–122.
[5] Proposed registration decision Tiafenacil PRD2022-01, p.11, 13, 26.
[6] PRD, p.13. Krijt, Jan et al, “Herbicide-induced experimental variegate porphyria in mice: tissue porphyrinogen accumulation and response to porphyrogenic drugs” (1997) 75 7.
[7] American Porphyria Foundation “About Porphyria” https://porphyriafoundation.org/for-patients/about-porphyria/
[8] National Institute of diabetes and Digestive and Kidney Diseases “Porphyria” https://www.niddk.nih.gov/health-information/liver-disease/porphyria
[9] Iftikhar Ahmed, Childhood Porphyrias, Mayo Clinic Proceedings, Volume 77, Issue 8, 2002, Pages 825-836, ISSN 0025-6196, https://doi.org/10.4065/77.8.825.
https://www.sciencedirect.com/science/article/pii/S0025619611620259

The PMRA has not considered the line of evidence establishing that PPO inhibition is linked to anemia and developmental toxicity in rats.[10] Porphyria caused by PPO inhibition is also linked to liver cancer risk.[11] With respect to other PPO inhibitors it has been observed that PPO inhibition could potentially explain developmental toxicity findings in PPO inhibitors as follows:

> The proposed MOA would be the inhibition of the enzyme protoporphyrinogen oxidase (PPO) interfering with normal haem synthesis and resulting in anaemia. This condition would lead to hypoxia in fetal tissues followed by impairment of other liver functions including protein synthesis and ultimately fetal oedema and anaemia. Concurrently, the fetus would compensate for the anaemia by pumping a greater volume of blood leading to the observed enlargement of the heart. The acceptability of the additional mechanistic data and the different sensitivity humans/rats to PPO inhibition was discussed at the Pesticides Peer Review Experts' Meeting 109: the experts considered the proposed mechanism for flumioxazin-induced developmental toxicity via inhibition of PPO plausible, but the experts could not clearly exclude other mechanisms.[12]

The PMRA did not assess whether tiafenacil, or other PPO inhibitors are endocrine disruptors. Recently the European Food Safety Authority engaged in a detailed review of another PPO inhibitor and concluded that they were unable to assess for endocrine disruption.[13] This information is needed to establish reasonable certainty of no harm.

In summary, the PMRA appears not to have developed a full toxicity profile for tiafenacil that includes whether it has endocrine disrupting properties or is linked to developmental toxicity through anemia associated with PPO inhibition. The PMRA therefore has not applied its own requirements with respect to a scientifically based approach, has not concluded a valid evaluation and lacks reasonable certainty that no harm will occur using the existing reference dose.

[10] Iwashita, Katsumasa et al, "Flumioxazin, a PPO inhibitor: A weight-of-evidence consideration of its mode of action as a developmental toxicant in the rat and its relevance to humans" (2022) 472 Toxicology 153160
[11] Jakubek, Milan et al, "PPO-Inhibiting Herbicides and Structurally Relevant Schiff Bases: Evaluation of Inhibitory Activities against Human Protoporphyrinogen Oxidase" (2021) 9:2 Processes 383.
[12] https://efsa.onlinelibrary.wiley.com/doi/full/10.2903/j.efsa.2020.6246.
[13] https://efsa.onlinelibrary.wiley.com/doi/full/10.2903/j.efsa.2020.6246.

Evidence – the PMRA has not assessed potential cumulative risks to human health from multiple PPO inhibitors in drinking water

The proposed registration decision stated in relation to PPO inhibitors that: "further consideration for potential cumulative health effects is warranted" and that "A cumulative risk assessment *will be conducted* separately" (emphasis added). A similar commitment to conduct a cumulative risk assessment for all PPO inhibitors was included in the recent decision to register trifludimoxazin.[14] In the final registration decision for tiafenacil, no cumulative risk assessment was conducted. However, the final registration decision contains a further discussion of cumulative effects. The PMRA states in the registration decision that "as part of the process in *determining the need to conduct a cumulative risk assessment* (CRA), other important considerations must be explored such as defining and comparing the use patterns of the different chemicals…" Accordingly the PMRA appears to acknowledge in the proposed registration decision for tiafenacil that a cumulative risk assessment was required - but once it was pointed out that this must occur prior to registration under section 7 of the PCPA by Ecojustice and Friends of the Earth, the PMRA switched approaches and engaged in a new screening which now appears to determine that no cumulative risk assessment for PPO inhibitors is needed.

It is ultimately unclear from the combination of the proposed and final decisions whether the PMRA is actually proposing to do a further cumulative risk assessment of PPO inhibitors – and if so when – or whether it has now determined that a cumulative risk assessment is not warranted. This should have been clearly stated in the registration decision - which should have clearly explained why the PMRA changed its mind from the proposed registration decision and from commitments to conduct a cumulative risk assessment of PPO-inhibitors found in other recent PMRA decisions including the recent decision to register trifludimoxazin in 2020-2021.[15]

Section 7(7)(b)(i) of the *Pest Control Products Act* requires the PMRA to consider available information on aggregate exposure to the pest control product, namely dietary exposure from other non-occupational sources, including drinking water and use in and around homes and schools and cumulative effects of the pest control product and other pest control products that have a common mechanism of toxicity. This must take place, and must be "scientifically based" during the evaluation and hence prior to of a pest control product. Once the PMRA has identified a common mechanism of toxicity, it has no jurisdiction to register a pest control product without considering available information on cumulative effects. For the consideration of available information on cumulative effects to be scientifically based, the PMRA must conduct an aggregate risk assessment because the question it is statutorily required to answer is whether there is reasonable certainty that no harm will occur to human health from cumulative effects.

The PMRA has developed a policy to guide its assessment of cumulative health risks. In SPN2018-02 *Cumulative Health Risk Assessment Framework*, the PMRA asserts that it has discretion to "screen out" cumulative risk assessments stating that the Act requires the following:

[14] Trifludimoxazin, vulcarus and voraxor PRD-2020-15, RD2021-01.
[15] Trifludimoxazin, vulcarus and voraxor PRD-2020-15, RD2021-01.

> These assessments may consist of a qualitative or quantitative cumulative risk assessment or result in a determination that a cumulative risk assessment is not required. For example, situations in which no common mechanism of toxicity exists or that do not involve co-exposures, would not require a cumulative risk assessment.[16]

We do not agree that the PMRA can decide *whether or not to* assess cumulative risk, as the PCPA provides no such discretion. To the extent that the PMRA declines to consider available information on cumulative risks, using a scientifically based approach to risk assessment,[17] such a registration is unlawful and the evaluation underlying it is not scientifically valid. To the extent that the decision on tiafenacil and the PMRA's cumulative risk assessment framework suggests that the PMRA can "screen out" the need to consider available information on cumulative risks, this is non-compliant with the Act and is not a scientifically based approach. The cumulative risk assessment framework needs to be revised. We note that none of this "screening" language was provided in the original consultation documents on the cumulative risk assessment framework.[18]

The Act requires available information on cumulative exposures to be part of a the PMRA's "scientifically based" risk assessment. The Act does not allow the PMRA to implement a screening process to determine whether to conduct a cumulative risk assessment. **Although the PMRA has now determined multiple times that it needs to conduct a cumulative health assessment of all the pest control products that are PPO inhibitors**, it has failed to do so since implementing the cumulative risk assessment framework in 2018. The final registration decision for tiafenacil appears to backtrack from these other prior conclusions by expanding the screening process in order to support this particular registration decision without a cumulative risk assessment.

In Science Policy Note SPN2018-02 the PMRA is required to consider co-exposures including the route of exposure, identification of use patterns and modeling. Further, the PMRA has to start with a tier 1 assessment of hazards of each pesticide in the common mechanism group. An exposure assessment is required using semi-quantitative estimates and considering the worst case scenario. No such analysis is included in the registration decision or proposed registration decision for tiafenacil.

For example, the consideration of available information on use patterns is not included in the final registration decision for tiafenacil. The registration decision then goes on to consider "available monitoring data." This data consists solely of food residue monitoring data for

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[16] SPN2018-02 *Cumulative Health Risk Assessment Framework,* p.2 https://www.canada.ca/content/dam/hc-sc/documents/services/consumer-product-safety/reports-publications/pesticides-pest-management/policies-guidelines/science-policy-notes/2018/cumulative-health-risk-assessment-framework-spn2018-02/spn2018-02-eng.pdf Note that this language was not included in the original framework that was consulted on in 2017 PRO2017-01 https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/cps-spc/alt_formats/pdf/pest/part/consultations/pro2017-01/pro2017-01-eng.pdf

[17] PMRA's "A Framework for Risk Assessment and Risk Management of Pest Control Products" (July 2021) associated PMRA science policy notes and guidance documents provide for its scientifically-based approach to risk assessment.

[18] PRO2017-01 Proposed Cumulative Health Risk Assessment Framework.

registrations of other PPO inhibitors and examines levels of food residue and residential exposure. This section does not explain if the residues are on the same crops or on other crops than are proposed for tiafenacil uses and does not model cumulative dietary risk from all exposures to PPO inhibitor residues on crops. Further, the registration decision does not explain whether the PMRA conducted a dietary risk assessment that would allow anyone to compare the residues in Table A of the registration decision with an acute or chronic dietary endpoint based on PPO inhibition. In many cases, Table A contains no Canadian data for food residues from these active ingredients. It is also unclear if the PDP residue data from the United States are relevant since we do not know anything from the registration decision about the use patterns involved on or how they compare to Canadian ones. The table does not include trifludimoxazin, which is also a PPO inhibitor that was recently registered in Canada.[19] The PMRA did not consider available information on the cumulative effects of all registered PPO inhibitors. Accordingly, the PMRA appears to lack a comprehensive list of registered PPO inhibitors and is registering them one-by-one in isolation without considering cumulative effects - despite making public commitments to do so.

The analysis of cumulative effects from PPO inhibitors in the registration decision for tiafenacil is limited to food residue and residential exposure. The *Pest Control Products Act* (**PCPA**) requires that the PMRA consider aggregate exposures from food, residential and drinking water.[20] Drinking water exposure to multiple PPO inhibitors is not included in the discussion of cumulative risks in the registration decision even though the majority of dietary exposure to tiafenacil was modelled to be from drinking water. The PMRA did not address whether there are drinking water exposures from multiple PPO inhibitors and whether they exceed chronic or acute reference doses when considered cumulatively.

The PMRA has now registered tiafenacil to control weeds in field corn, soybean, spring wheat, grapes, summerfallow and non-crop areas. Many of the other PPO inhibitors that are registered are also used or proposed to be used on wheat, corn, soybean and non-crop areas. In response to questions during the objection period, the PMRA has admitted that the use patterns for other PPO inhibitors are "very similar".[21] In some cases, the PMRA found that the modelled dietary and aggregate exposure for these PPO inhibitors filled up significant portions of the "risk cup" of either the chronic or acute reference doses or both. These other pesticides were also observed to have effects on the liver and blood by the same mechanism of toxicity as tiafenacil.

Active ingredient	**%ADI (chronic**	**%ARfD**	**Effects Summary**	**Sales (c.2018)[22]**

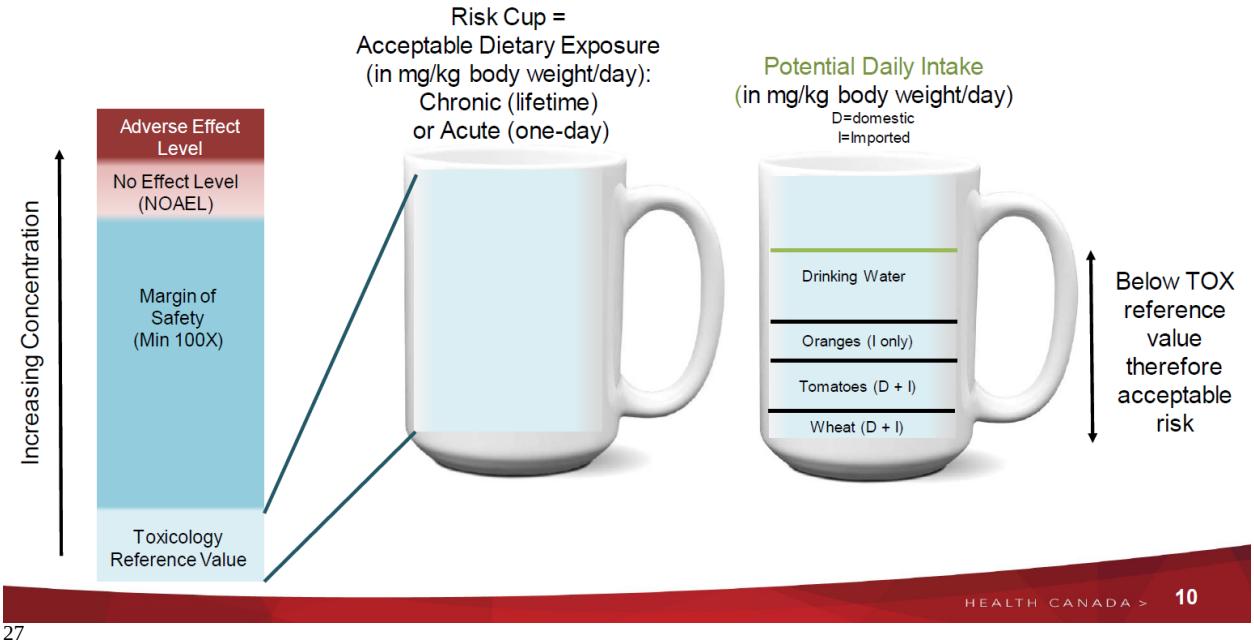
[19] Trifludimoxazin, vulcarus and voraxor PRD-2020-15, RD2021-01.
[20] PCPA s.7(7)(b)(i)
[21] Email from Robert Martin (PMRA) to Laura Bowman (Ecojustice) dated October 14, 2022.
[22] PMRA sales reports, 2018.

	reference dose)	**(acute reference dose)**		
Flumioxazin[23]	6% (children 1-2 years)	15% (females 13-49)	PPO inhibition resulting in effects on blood and liver, effects on developing fetus.	>25,000 kg/yr
Saflufenacil[24]	51% (infants < 1 year 41% (females 13-49)	100% (Females 13-49)	Target organs included blood, liver, spleen, and bone marrow. Increased susceptibility of the young.	>25,0000 kg/yr
Carfentrazone-ethyl[25]	50% (children 1-2 years)	n/a	Organ toxicity "invariably involved the liver and the kidneys. … porphyrin metabolism, which resulted in increased urinary excretion of various porphyrin components."	>25,000 kg/yr
Sulfentrazone[26]	PRD2011-01 only says that food plus water for all subpopulations are less than 57% of ADI	21.13% (Females 13-49)	Virtually all blood parameters were negatively affected by high doses of sulfentrazone.Developmental and neurotoxicity toxicity was also observed, along with fetal malformations. Health effects in animals given sulfentrazone on a daily basis for prolonged periods of time included clinical anaemia, liver and kidney effects.	>25,000 kg/yr

It is evident from these other risk assessments that these PPO inhibitors all act on liver and heme systems and that significant portions of the reference dose are taken up by each one when assessed individually. This raises the prospect that the "risk cup" for PPO inhibition could be filled by combinations of PPO inhibitors. Therefore, this raises a scientifically founded doubt about the conclusion of the evaluation that the risk to human health from drinking water exposure combined with food exposure is acceptable for tiafenacil.

[23] Flumioxazin, PRD2013-20.
[24] Saflufenacil PRD2017-07.
[25] Carfentrazone-ethyl RD2009-11; ERC2008-05.
[26] Sulfentrazone ERC2010-08; PRD2011-01.

Risk Cup Concept



[27]

For several other PPO inhibitors that are currently registered in Canada, the publicly available risk assessment documentation is incomplete. As a result, it is not clear whether complete data was actually submitted to the PMRA or whether the PMRA ever did a dietary risk assessment at all, let alone a quantitative aggregate risk assessment including drinking water for PPO relevant effects. The potential for cumulative exposures through food and drinking water for these other registered PPO inhibitors is effectively unknown.[28]

Further, the PMRA risk assessments lack transparency about how the endpoints were derived and whether they are directly related in each case to PPO inhibition-associated effects, and there appear to be significant uncertainties about which effects are PPO-related. Estimated environmental concentrations in surface, groundwater and drinking water are not publicly available for all of the relevant PPO inhibitors making the PMRA's assessment of cumulative risks unintelligible.

Although in responses to questions the PMRA indicates that in some cases the reference doses are based on reproductive and developmental toxicity, and not PPO inhibition, it is not established that these effects result from a mechanism separate from PPO inhibition and specifics of how each PPO endpoint was derived were not provided. Known processes have been identified in the published literature attributing developmental and reproductive toxicity to PPO

[27] Isabelle Pilotte, presentation to the Scientific Advisory Committee of the PMRA (October 21, 2022).
[28] This is the case for acifluorfen-sodium (PACR2006-12, RRD2006-20), Pyraflufen-ethyl (PRD2016-32, ERC2014-03), Oxyfluforfen (PACR2005-03, RRD2006-19).

inhibition in rats.[29] The ECHA RAC discussed this issue in relation to flumioxazin in 2019 and found that "uncertainties still exist including unresolved questions related to the suggested link between anemia and developmental toxicity."[30] Given the species-specific responses to PPO inhibitors and the lack of epidemiological literature on the effects of pesticide PPO inhibitor exposure in humans and a known mechanism of action for developmental and reproductive toxicity, there are significant uncertainties that are not addressed with the standard 100-fold uncertainty factor for uncertainties in using animal toxicology data. Since reproductive and developmental toxicity are potentially linked to PPO inhibition there is good reason to consider the reference dose exposures to each PPO inhibitor could be related to the common mechanism.

The potential exposure to these active ingredients is relatively high as each of them have significant domestic sales higher than 25,000 kg/yr.[31] The chronic risks from previously predicted exposures to infants, children and women are significant for at least four of them, leading to the potential that these exposures could be added to the potential exposures from tiafenacil and result in PPO-related effects at well over 100% of both the acute and chronic reference doses for females, children and/or infants. This is particularly concerning given that the modelling of aggregate food and drinking water exposure for tiafenacil alone already exceeds 100% of the chronic reference dose for infants at 102%. The acute reference dose for saflufenacil alone is also already at 100% for females. Added together, exposures to multiple PPO inhibitors raise the prospect of much more substantial reference dose exceedances and accordingly potential impacts on the livers and heme systems for the affected subpopulations such as infants, children and women.

While the PMRA has indicated in responses to questions that it considered the available information on drinking water exposures to multiple PPO inhibitors, this information was not provided or discussed in either the proposed or final registration decision for tiafenacil and the public was not consulted on this in accordance with s.28(1) of the PCPA.[32] It is unclear whether the PMRA considered this issue prior to the registration decision or only when it was raised by the objectors in September 2022. No health evaluation division memo or peer reviewed monograph explaining how PMRA scientists evaluated this issue has been provided. When pressed, the PMRA would only provide the bare EEC calculations for tiafenacil alone.

The PMRA appears to consider that saflufenacil is the only PPO inhibitor that is expected to contribute significantly to drinking water. The basis for this conclusion is unintelligible. The public risk assessments are for many of the other PPO inhibiting registered pest control products are incomplete.

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[29] Iwashita, Katsumasa et al, "Flumioxazin, a PPO inhibitor: A weight-of-evidence consideration of its mode of action as a developmental toxicant in the rat and its relevance to humans" (2022) 472 Toxicology 153160
[30] ECHA (European Chemicals Agency) 2019 Minutes of the 48th Meeting of the Committee for Risk Assessment (RAC 48), RAC/48/2019, Final 28 May 2019 https://echa.europa.eu/documents/10162/2166400/RAC-48_final_minutes.pdf/d976ab5d-33b4-7d2d-eedf-2e0c0913b3b0?t=1559040934934
[31] PMRA sales data (2018) which is the most recent year published for PMRA sales. Additional and more up-to date sales data were requested but were not provided in time to include in this submission.
[32] Email from Robert Martin (PMRA) to Laura Bowman (Ecojustice) dated October 14, 2022 – Question 1.

The PDP data for saflufenacil, which is only for the United States, included only 627 samples of groundwater-only samples. When we searched the PDP database we retrieved different groundwater monitoring data than is cited by the PMRA in its responses to questions.[33] There is no water monitoring data at all for the other PPO inhibitors listed above. The relevance of the non-detects for saflufenacil, the conditions leading to the detects and reliability of the monitoring data is not established for these samples. For example, we do not know whether they were taken in areas where saflufenacil was used in a Canadian use pattern, or at the time of year or during environmental conditions when saflufenacil would be expected in groundwater, let alone peak concentrations. We do not know if it was shallow or deep groundwater. There is no sampling of surface water, bottled water, or treated drinking water for saflufenacil. The PMRA appears to have ignored the drinking water modeling conducted by the USEPA for saflufenacil which predicted higher concentrations in drinking water which are as follows:

Table 5.3. Tiered EDWCs for Proposed Saflufenacil Uses.

Source (Tier: Model)	1-in-10-year Peak Exposure (ppb)	1-in-10-year Annual Mean Exposure (ppb)
Surface water (Tier I: Rice Model)	133 (used in acute analysis)	120 (used in chronic analysis)
Ground water (Tier II: PRZM GW)	69.2	51.5

[34]

While two of the PMRA's public risk assessments for other PPO inhibitors do include some estimated environmental concentration (EEC) modeling for exposures in groundwater and surface water. information this information is incomplete and as between different risk assessments appears to use different units of measurement internally and compared to monitoring data.[35] For the majority of PPO inhibitors, public documents do not provide details of the EEC modeling. The EEC modeling and the drinking water levels of comparison that the PMRA uses to identify aggregate risks from food and drinking water are also not provided in a transparent way in all of the PPO inhibitor risk assessments nor in the tiafenacil final registration decision. The public are prejudiced in being able to prepare an objection as a result. To make matters worse, in the case of sulfentrazone, the PMRA appears to have registered sulfentrazone without information on metabolites necessary to conduct a drinking water assessment for groundwater.[36] Although a section 12 notice was apparently issued for this registration, it has not been included

[33] Saflufenacil groundwater PDP data for two detects were 4.95 and 5.4 ppt.
[34] USEPA "Saflufenacil. Human-Health Risk Assessment" (Jun 24, 2014)
[35] In Saflufenacil PRD2017-07 some EECs are expressed in mg/L and some are expressed in µg a.i./L, others are expressed in ppm or ppt (US models and monitoring). Trifludimoxazin Table 3 of PRD2020-15 does provide some EECs but these are in µg a.i./L. Molecular weights are required to properly convert between some of these, making it hard for the public to understand what the relative contributions of drinking water are. The PMRA has not included drinking water levels of comparison in the public facing PPO risk assessments and therefore it is impossible to compare total EECs with DWLOCs to determine if there would be a cumulative reference dose exceedance.
[36] Sulfentrazone was registered under ERC2010-08 and no new assessment of dietary exposure was included in PRD2011-01.

in the PMRA's public list of conditional registrations.[37] It is unclear what the status of outstanding groundwater information is for sulfentrazone and whether it could change the drinking water risk assessment.

The PMRA places heavy emphasis on monitoring in the tiafenacil registration decision and responses to questions. It does so even though tiafenacil and some other PPO inhibitors are new products with limited to no monitoring available. The PMRA does not appear to have considered any drinking water monitoring or modeling data for the other major PPO inhibitors registered in Canada. Use data such as sales data does not appear to be considered in understanding exposure. With such minimal monitoring (without proper context to establish reliability), limited modeling, no use data, no published sales data for the last four years, and using only very limited monitoring in water from other jurisdictions, the PMRA does not have a clear picture of - and has not transparently advised the public regarding - potential drinking water exposures to PPO inhibitors. The PMRA fails to acknowledge these limitations in its decision-making. Given that significant portions of the chronic reference doses for infants and other sub-populations are utilized for several of these products, we do not understand how the PMRA can conclude that exposures to multiple PPOs in drinking water are not going to cause harm to the standard of reasonable scientific certainty. Without transparent modeling of co-exposure to drinking water the PMRA cannot have determined this. The PMRA also does not appear to have any drinking water monitoring program whatsoever in Canada for PPO inhibitors, nor any plans to create one and has not requested any water monitoring or biomonitoring data from the registrants.

In this regard the assessment fails to comply with the PMRA's Science Policy Note SPN2003-04 entitled "General principles for performing aggregate exposure and risk assessments." As a result, the PMRA's evaluation does not utilize the scientifically based approach espoused by the PMRA. This document states that "it is essential to estimate pesticide concentrations (including transformation products of toxicological concern) in both groundwater and surface water sources." and provides that "the PMRA uses established computer models to estimate pesticide concentrations in both surface water and groundwater sources of drinking water." It also acknowledges that: "Valid monitoring data would be considered preferable to estimates generated using water models; however, for new chemicals, monitoring data will be unavailable. In such cases, where monitoring data would be essential for conducting a refined exposure assessment, registrants would be requested to conduct field studies." We are not aware of any modelling of drinking water co-exposures for PPO inhibitors, we are not aware of field studies having been submitted or required to validate whether co-exposures in drinking water could be occurring. As many of the PPO inhibitors are new, with limited or no surface and groundwater monitoring, the emphasis on monitoring data in the registration decision for tiafenacil is inconsistent with this policy.

To the extent that the PMRA considered, whether before or after the registration decision, the water monitoring data from the US PDP program for groundwater and saflufenacil the PMRA

[37] PMRA "Conditional Registrations" https://www.canada.ca/en/health-canada/services/consumer-product-safety/pesticides-pest-management/public/protecting-your-health-environment/conditional-registrations.html

does not discuss whether it considered the limitations of available water monitoring in accordance with SPN2003-04 which cautions against over-reliance on monitoring:

> In evaluating, characterizing and interpreting water monitoring data, the PMRA attempts to collect as much information as is readily available on the design of the studies. This includes information on how the samples were collected and analysed, why they were collected, and where and when they were collected. In evaluating the quality of monitoring data, the Agency considers the spatial and temporal conditions under which the monitoring was conducted. Spatial considerations include whether the data originate from areas of pesticide use and temporal considerations include information relating the timing of pesticide application to the timing of sampling. Other important ancillary data include accurate weather data, hydrological data (size and type of receiving water body, depth of groundwater), and geochemical and geophysical characteristics (topography, soil characterization).
>
> The level of variability and uncertainty associated with existing monitoring data in Canada means that the use of these data to predict EECs can be challenging. Reported concentrations may vary considerably over time at the same location and from one area to the next. Without having specific information on the history of use of the pesticide in the sampled area, it is very difficult to fully understand the reasons for these differences. Further, the PMRA is not always able to discern whether samples were taken from potential drinking water sources or waters that would be representative of such drinking water sources. The frequency with which samples are taken in monitoring studies is often insufficient to allow a determination of peak concentrations. Peak concentrations, by nature, occur over short times, and sampling frequencies in many studies are quarterly or monthly, giving a low probability of sampling during the period of peak concentration.

Similar statements can be found in other PMRA policies such as SPN2004-01 "Estimating the water component of a dietary exposure assessment."[38] These policies confirm that the weight to be given to water monitoring data is context-specific, and that non-detections are to be given less weight than those that exceed modeled levels.[39] The PMRA does not explain how it assigns weight to the saflufenacil PDP groundwater monitoring that is sufficient to allow it to find that co-exposure in drinking water (including in surface water) is unlikely to a standard of reasonable certainty.

The PMRA has not modeled the potential cumulative effects of exposures to multiple PPO inhibitors in drinking water. Instead, in responses to questions, the PMRA appears to qualitatively guess that "generally" drinking water is not a major contributor to exposures for PPO inhibitors and that in general, when drinking water exposures are modelled for any group of pesticides it is "unlikely" that there would be co-occurrence of high-end residues. However, the

[38] SPN2004-01 "Estimating the water component of a dietary exposure assessment." (2004) pp.2, 10-12.
[39] SPN2004-01 p.12.

PMRA has not actually conducted the relevant modeling. This is not a scientifically based approach required by section 7 of the PCPA.[40]

The PMRA acknowledges that drinking water is a significant part of the dietary exposure for both saflufenacil and tiafenacil (unknown for other PPO inhibitors). Given that co-exposure to these two actives alone could result in 153% of the ADI for infants, the PMRA should have quantitatively modeled this - along with the contributions from other PPO inhibitors - to confirm whether co-exposures could result in harm to the livers and heme systems of Canadian infants. Given the similarity in use patterns between all registered PPO inhibitors we do not understand the PMRA's conclusion that "it is highly unlikely that there will be co-occurrence of high-end residues" for infants for these two products. The assessment of risks to infants is unintelligible. The assessment appears to be based on unfounded and unjustified speculation.

The PMRA has also ignored the potential cumulative effects of exposure of workers to multiple PPO inhibitors, this is a major gap given that many of the currently registered PPO inhibitors with similar use patterns and which could be used on the same crops. This issue is applicable not only for saflufenacil but for all of the other registered PPO inhibitors to which workers may be co-exposed. While the cumulative risk assessment framework purports to allow the PMRA to "focus" its evaluation of cumulative effects on non-occupational risks, we remind the PMRA that the definition of "health" in the PCPA is broad and includes occupational exposures. A valid, scientifically based cumulative risk evaluation would include the potential for occupational co-exposure. The PMRA must have reasonable certainty that no harm will occur to the health of workers from co-exposures.

The proposed registration decision relies heavily on the absence of residential exposures to find that no cumulative risk assessment is required. Reliance on residential exposures as a basis for whether or not to complete a cumulative risk assessment is non-compliant with the PCPA. For example, the PCPA requires that the PMRA consider aggregate risks of diet, drinking water and residential exposures, not just residential exposures alone. Further, residential exposure is only one of many possible exposures that can impact human health, including occupational (inhalation, dermal, oral), residential, bystander, diet and drinking water. While aggregate risk assessments do not have to include occupational risks, cumulative assessments do have to include them.

The PMRA has accordingly unlawfully registered tiafenacil without considering available information on aggregate and cumulative risks, or alternatively has failed to ensure that information on potential drinking water exposures and occupational co-exposures was provided by the registrants. The evaluation of risks is not a valid scientifically based approach. The PMRA needs to urgently remedy this by conducting a cumulative risk assessment of PPO inhibitors on occupational exposure, food and drinking water. The PMRA must not continue to register PPO inhibitors without completing these evaluations.

[40] Robert Martin email, supra.

Evidence- TFA – nature and toxicity

Tiafenacil transforms into the transformation product/metabolite trifluoracetic acid (TFA) also known as metabolite M-32. TFA is a highly persistent forever chemical. TFA is chemically similar to nitric or hydrochloric acid.[41] Like other strong acids, such as sulfuric, nitric, or hydrochloric acid, high concentrations of TFA produce damage to organisms by virtue of its acidity. This mode of toxicity is relevant to organisms exposed to TFA in precipitation or via dry deposition (if any) from the atmosphere.[42]

> TFA is formed through degradation from a large number of fluorinated substances containing one or more trifluoromethyl groups (C-CF3). In the environmentally relevant pH range, the molecule occurs as trifluoroacetate. TFA is highly soluble in water and adsorbs poorly to soil, sediment and organic matter. Thus, the substance is very mobile; it is introduced into the natural water cycle very rapidly from the atmosphere, soils and through wastewater, and is thereby dispersed in the environment. As a result, TFA can be detected even in waters at some distance from input sources. Given the strong carbon–fluorine bond and its poor oxidisability, TFA is very stable. There are no currently known environmental conditions in which TFA degrades. TFA is thus a very persistent substance.[43]

Although the PMRA has stated in section 6 of the proposed registration decision that it has reviewed tiafenacil and its transformation products for TSMP Track 1 criteria, it does not provide any further details on how it determined that TFA is not persistent or bioaccumulative. In the proposed re-evaluation decision for flufenacet, the PMRA determined that TFA was CEPA-toxic, predominantly anthropogenic, and persistent. This evaluation also indicated that the PMRA had lacked complete information on bioaccumulation for TFA.[44] It has been previously observed that TFA bioaccumulates in terrestrial higher plants.[45] No equivalent table is provided in the proposed or final registration decisions for tiafenacil, and the decision lacks transparency about how the PMRA determined that TFA was not persistent or bioaccumulative.[46]

In responses to questions the PMRA indicates that the PMRA determined that TFA is not likely to bioaccumulate "based on the log K_{OW} value of 0.502, estimated using the Estimation Program Interface (EPI) Suite (Ver.3.12) from the USEPA. A bioaccumulation study was not required because this log K_{OW} value is less than the trigger value of 3 described in PMRAs environmental data requirements for DACO 9.5.6." We note that the log K_{OW} value is only relevant to fatty

[41] Solomon et al "sources, fates, toxicity, and risks of trifluoroacetic acid and its salts: relevance to substances regulated under the Montreal and Kyoto Protocols" *Journal of Toxicology and Environmental Health* Part B (2016) DOI: 10.1080/10937404.2016.1175981.
[42] Solomon et al (2016) above.
[43] German Environment Agency "Reducing the input of chemicals into waters: trifluoroacetate (TFA) as a persistent and mobile substance with many sources" (Nov 2021), p.9.
[44] Flufenacet PVRD2021-01 (Table 23).
[45] Jean Charles Boutonnet et al. (1999) Environmental Risk Assessment of Trifluoroacetic Acid, Human and Ecological Risk Assessment: An International Journal, 5:1, 59-124, DOI: 10.1080/10807039991289644.
[46] Tiafenacil PRD2022-01 (Table 26).

tissues and that K_{OW} has little if any relationship to bioaccumulation in bones, muscle, liver or kidneys.

In PMRA guidance document "Toxic substances management policy : persistence and bioaccumulation criteria : final report of the Ad Hoc Science Group on Criteria." (1995) the *ad hoc* science committee commented that:

> The potential for a substance to bioaccumulate can be expressed in terms of the bioconcentration factor (BCF), the bioaccumulation factor (BAF) or for lipophilic substances, the octanol-water partition coefficient (K_{ow}). BCF and BAF are environmentally more relevant that K_{ow} because they take into account the response of the organism, including metabolism, steric effects at the gill/water interface, etc. In addition, bioavailability of the substance is considered especially for BAF. Field data (eg BAFs) are preferred over laboratory data (eg BCFs) which, in turn are preferred over chemical properties (eg, log K_{ow}). The ad hoc science group recommended the use of BCF over log K_{ow} because of its greater environmental relevance.[47]

It is unclear what the PMRA is referencing when it states that there is a trigger of 3 for the K_{ow} in the data requirements for data code 9.5.6. The PMRA has only published criteria for data codes 1-7 and 10. In the 1997 Backgrounder document, which pre-dates the current PCPA, it says that "For the majority of cases, the PMRA will use the log K_{ow} $3 [sic], the bioconcentration/ bioaccumulation in fish and the metabolism data in plants, rats, cows , goats and chickens to assess the bioaccumulation in other organisms." This document does not support waiving a bioaccumulation study for all organisms based on log K_{ow} - only for earthworms.[48] It appears that the PMRA has failed to assess bioaccumulation, beyond identifying the log K_{ow}, which as its own guidance document notes, is simply a chemical property assessment and is not laboratory data on bioaccumulation. Given that there is published literature on bioaccumulation of TFA the PMRA should have considered this literature. The PMRA has not explained how this reliance on the log K_{ow} is consistent with the requirement that the PMRA give effect to the toxic substances management policy in subsections 2(1) and subsection 7(8) of the PCPA.

In contrast to the PMRA's assessment for flufenacet last year that found that TFA is predominantly anthropogenic, the final registration decision for tiafenacil takes a different approach which appears to accept that TFA is a partially a "natural" substance. This conclusion is contradicted by the published literature.[49] The PMRA must weigh this evidence and if it did so it would have changed the PMRA's conclusion on the sources of environmental TFA. The PMRA has not explained why it gave no weight to that literature.

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[47] https://publications.gc.ca/collections/collection_2019/eccc/En40-499-2-1995-eng.pdf at p.11
[48] B97-02 Backgrounder "Harmonization of Environmental Data REquirements under NAFTA for Registration of Chemical Pesticides" (June 2, 1997) https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/cps-spc/alt_formats/pacrb-dgapcr/pdf/pubs/pest/pol-guide/bgr_b/bgr_b97-02-eng.pdf
[49] Joudan, Shira, Amila O De Silva & Cora J Young, "Insufficient evidence for the existence of natural trifluoroacetic acid" (2021) 23:11 Environ Sci: Processes Impacts 1641–1649; Nielsen, Ole John et al, "Trifluoroacetic acid in ancient freshwater" (2001) 35:16 Atmospheric Environment 2799–2801.

The PMRA has previously determined that TFA is highly mobile and has the potential to leach through soils and reach groundwater.[50] TFA is an extremely polar, persistent, and highly water-soluble substance.[51] However, in the tiafenacil decision, these properties of TFA are not mentioned. This is particularly concerning since another significant TFA-producing pest control product, flufenacet, is currently also registered for corn and soybean uses which are now also approved for tiafenacil.

Further, there is a line of evidence that TFA accumulates in plants and can be detected in beer and tea in relatively high concentrations of up to 51 µg/L.[52] This issue is irrespective of the log $K_{ow.}$ This research found that the average concentrations in beer and tea exceeded the ones in tap water by a factor of approximately ten. Therefore, beverages can contribute to a considerable share to the total intake of TFA. There is also evidence of bioaccumulation of TFA in humans and this accumulation is associated with glycemic biomarkers.[53] Based on the registration decisions and the responses to our questions the PMRA appears not to have considered this information nor has it justified why it gave this information little weight. These studies raise uncertainties about the conclusions of the PMRA's assessment.

We are not aware of any published, peer-reviewed studies on the carcinogenicity or reproductive toxicity of TFA.[54] There are also no known published toxicity tests for TFA in terrestrial vertebrates such as birds.[55] The only toxicity data we could find in published PMRA studies for TFA is contained in the 2021 flufenacet proposed re-evaluation decision. This includes a table which indicates that the PMRA has nine studies on the toxicity of TFA. The only developmental toxicity study on TFA is listed as "supplemental". None of these studies on the toxicity of TFA appear to have been considered in the tiafenacil registration decision. The PMRA therefore has an incomplete toxicity database on TFA and no reference dose for TFA and should not be registering or renewing products for which TFA is a metabolite. The PMRA has not complied with its own residue chemistry guidelines and has not completed a valid evaluation by its own standards.

[50] Flufenacet PVRD2021-01.
[51] Scheurer, Marco & Karsten Nödler, "Ultrashort-chain perfluoroalkyl substance trifluoroacetate (TFA) in beer and tea – An unintended aqueous extraction" (2021) 351 Food Chemistry 129304.
[52] Scheurer "Ultrashort-chain perfluoroalkyl substancetrifluoroacetate (TFA) in beer and tea – an unintended aqueous extraction Food Chemistry 351 (2021) 129304.
[53] Duan, Yishuang et al, "Distribution of novel and legacy per-/polyfluoroalkyl substances in serum and its associations with two glycemic biomarkers among Chinese adult men and women with normal blood glucose levels" (2020) 134 Environment International 105295 .
[54] https://ozone.unep.org/sites/default/files/2019-08/TFA2016.pdf p.14.
[55] Ibid. https://ozone.unep.org/sites/default/files/2019-08/TFA2016.pdf p.14.

Evidence - PMRA does not cite any evidence for its contention that pest control products would not contribute to potentially harmful TFA contamination in the environment over time.

TFA is persistent and the use of tiafenacil will increase this persistent chemical in the environment. A study by the German Environment Agency attempted to quantify the contribution of plant protection products including flufenacet and other pest control products registered in Canada to the annual emissions of TFA comparted to other sources. Because flufenacet sales are relatively high they estimated that approximately 200 tonnes of TFA releases could be attributed to flufenacet sales alone in that country and that plant protection products exceeded many other sources totalling 504 tonnes per year.[56] Given the lack of information on potential sources, the United Nations Environment Program has concluded as recently as last year that it is not possible to quantify the proportion of each anthropogenic source of TFA.[57] No such research is cited in the tiafenacil decision, raising a scientifically founded doubt about how the PMRA calculated or identified the potential contribution of pest control products to environmental TFA in Canada relative to other sources. Tiafenacil is a new pest control product, which could have future sales of unknown quantities. Since the PMRA does not collect use data and has not required the registrant to provide it the PMRA has no plan to monitor TFA contributions from pest control products that degrade into TFA.

The PMRA has not attempted to ascertain in its registration decision the environmental exposure to TFA arising from other pest control products that degrade into TFA. Increases in sales do not trigger any regulatory actions by the PMRA or any specific monitoring or research program by the PMRA. Merely speculating that tiafenacil will be a minor source relative to other sources is not a scientifically based approach and fails to address the potential cumulative effect of multiple pest control products degrading into TFA. It also does not address whether TFA contributions by tiafenacil are reasonably certain not to cause harm, either individually or cumulatively, and over multiple generations. Further the registration decision fails to address significant multiple potential sources of TFA. Tiafenacil, flufenacet, TFM, and numerous other sources may be combined contributors to TFA in drinking water and surface water. The PMRA has also not addressed how it will protect future generations from increasing environmental levels TFA pursuant to section 4.1 of the PCPA. All of this raises a scientifically founded doubt about the validity of the evaluations and a proper assessment of these factors could change the outcome of the PMRA's risk assessment.

Evidence – PMRA has not assessed the potential impact of TFA on climate change

Nothing in the PCPA limits the assessment of harm to human health and the environment to toxicological harm. "Environment" as defined in the PCPA explicitly includes all layers of the atmosphere.

[56] GEA "reducing the input" above.
[57] UNEP "Summary Update 2021 for Policymakers" UNEP Environmental Effects Assessment Panel.

The formation of the potent greenhouse gas fluoroform (**CHF3**) has been observed during TFA degradation.[58] The formation of aerosols from atmospheric TFA could have a significant impact on climate change.[59] The PMRA has not assessed the impact of pest control products that degrade into TFA on climate change and ozone depletion and has therefore failed to establish that it has reasonable certainty that no harm will occur to the environment or human health.

Evidence – PMRA has not assessed the potential cumulative risks from TFA combined with background levels of TFA and other pest control products containing TFA

The German Environment Agency, in a discussion of the potential effects of TFA, noted that there are limitations to using short-term risk assessment to assess the potential long-term effects of exposures to a forever-chemical like TFA that is highly persistent in the environment. They stated:

> the modelling programs used in the assessment of [individual] chemicals are not usually designed for persistent substances: by simulating only limited periods, they do not consider any long-term accumulation and thus tend to underestimate the concentrations to be expected in the environment in the long term. Nor do the studies on health and ecotoxicological assessments usually provided for the registration and approval of chemicals cover the special risks of very persistent substances. These are usually short-term studies and cannot account for (potential) long-term effects that may occur after several decades, affecting future generations. The effects of mixtures with TFA and other substances or their behaviour under different environmental conditions and media are also not considered by these tests This, however, would be advisable, particularly for very persistent substances such as TFA. Given its persistence, mobility in the water cycle and the impossibility of reversing existing contamination, TFA will persist for a long time and spread far in the environment. Thus, in practice, it will come into contact with other substances and various environmental media. An adequate risk assessment would therefore have to cover much longer timescales and much greater spatial scales than those used by standard methods. Probability-based approaches show that even very rare risks become more probable the longer it takes for a substance to degrade, since the period of time during which a substance remains in the environment is greatly increased (Cousins et al., 2019). For TFA, this period is practically indefinite: the risk increases accordingly and is left to future generations. These are not mere

[58] GEA "reducing the input" p.9 citing Visscher et al., 1994; Castro et al., 2014; Lu, Y.; Liu, L.; Ning, A.; Yang, G.; et al "Atmospheric Sulfuric Acid-Dimethylamine Nucleation Enhanced by Trifluoroacetic Acid. Geophys. Res. Lett. 2020, 47, GL08562.

[59] Holland, Rayne et al, "Investigation of the Production of Trifluoroacetic Acid from Two Halocarbons, HFC-134a and HFO-1234yf and Its Fates Using a Global Three-Dimensional Chemical Transport Model" (2021) 5:4 ACS Earth Space Chem 849–857; Lu, Yiqun et al, "Atmospheric Sulfuric Acid-Dimethylamine Nucleation Enhanced by Trifluoroacetic Acid" (2020) 47:2 Geophys Res Lett, online: <https://onlinelibrary.wiley.com/doi/10.1029/2019GL085627>.

> theoretical considerations: there are many examples of risks that had been overlooked and later became apparent in practice, often decades after use.[60]

The PMRA has not considered the long-term risks or probabilities of those risks from TFA. In the 2021 proposed re-evaluation decision for flufenacet, another pest control product that metabolizes into TFA, the PMRA noted that because the PMRA was *proposing* to cancel all registrations of flufenacet no cumulative assessment of the risk of TFA was required. It is a year later and there is no final decision for flufenacet and it has still not been cancelled or phased out and - although the PMRA is now registering a new active (tiafenacil) that degrades to TFA - the PMRA is still not completing a cumulative risk assessment as required by the PCPA.

There are several pending renewals and proposed new registrations for flufenacet that the PMRA appears poised to grant at the end of 2022 despite the outstanding re-evaluation decision finding unacceptable risks (these are listed in Appendix C). The proposed re-evaluation decision for flufenacet also states that "Health Canada will *continue to monitor the status of pesticide-related contributions of TFA* to the environment." (emphasis added). However, this monitoring, if it ever existed, has not been used in the evaluation for tiafenacil. In responses to questions the PMRA has seemingly confirmed that it actually does not monitor TFA in the environment and has no plans to do so.[61] The registration decisions for tiafenacil and flufenacet are misleading as they suggest that the PMRA is reviewing an ongoing monitoring program for TFA that either does not exist or which the PMRA now says would not be relevant.

Drinking water supply carries a specific risk in connection with TFA. Being highly soluble in water and spreading along the water cycle, TFA will eventually find its way into drinking water sources.[62] Biomonitoring in China also suggests widespread human exposure to TFA is already a reality.[63] The Great Lakes provide drinking water for millions of people, and the PMRA has also approved a number of other pest control products that produce potentially significant levels of TFA. 4-nitro-3-(trifluoromethyl)phenol or sodium salt (also known as TFM) is used for lamprey control in the Great Lakes and produces TFA as one of its metabolites. TFM has been reported to be photolytically degraded to TFA with a yield of about 17%.[64] TFM is applied to nursery streams in the Great Lakes containing larval sea lampreys. The PMRA has registered TFM since 1970 without addressing the risks associated with the TFA producing properties of

[60] GEA "reducing the input" Page 30-31.
[61] Email from Robert Martin (PMRA) to Laura Bowman (Ecojustice) dated October 14, 2022 (Question 6) "Tiafenacil was not included in the [proposed water monitoring program] method given its recent registration. Given that there are multiple non-pesticidal sources that contribute to the presence of TFA in the environment, monitoring for TFA in the environment would not allow the PMRA to determine the contribution of TFA from the use of tiafenacil or other pesticides."
[62] GEA p.34; Scheurer, Marco et al, "Small, mobile, persistent: Trifluoroacetate in the water cycle – Overlooked sources, pathways, and consequences for drinking water supply" (2017) 126 Water Research 460–471.
[63] Yishuang Duan, Hongwen Sun, Yiming Yao, Yue Meng, Yongcheng Li, Distribution of novel and legacy per-/polyfluoroalkyl substances in serum and its associations with two glycemic biomarkers among Chinese adult men and women with normal blood glucose levels, Environment International, Volume 134, 2020, 105295, ISSN 0160-4120, https://doi.org/10.1016/j.envint.2019.105295.
[64] Ellis D, Mabury SA. 2000. The aqueous photolysis of TFM and related trifluoromethylphenols. An alternate source of trifluoroacetic acid in the environment. Environ Sci Technol 34:632-637.

TFM. It is simply unclear from the registration decision or the proposed registration decision what the sales of these other pest control products are, and whether they locally contribute to potential TFA contamination or whether cumulatively their contributions to either local or global TFA contamination over time have the potential to be significant. The PMRA has also failed to assess the line of evidence establishing that TFA accumulates in the Arctic.[65] It is irrelevant if there are other anthropogenic sources of TFA that may need to be controlled as well. The relative contribution of TFA from pest control products does not provide reasonable certainty that no harm will occur.

Simply ignoring the increasing levels of forever chemicals in Canadian surface and drinking water is not a reasonable approach and does not adequately identify or assess risks. No practicable and economical method exists for removing TFA from water once it is released into the environment.[66] The PMRA is required to consider the effects of pest control products on future generations under section 4.1 of the PCPA and it has not done so. It is evident from the research we have cited here that concentrations of TFA are increasing in the environment over time, and that tiafenacil will add to this contribution in unknown amounts. The PMRA has failed to consider the potential effects of future widespread use of tiafenacil and the cumulative effects of exposure to tiafenacil metabolites such as TFA combined with other pesticides which degrade into TFA and other sources of TFA in the environment. The PMRA has not conducted a complete evaluation of risks. The PMRA does not have reasonable certainty that no harm will occur to human health and the environment from the registration of active ingredients like tiafenacil that degrade into TFA.

Evidence – chronic dietary exceedance for infants

The registration decision acknowledges that when the fate properties of TFA are grouped with the other metabolites of tiafenacil the result is an exceedance of the acute reference dose or "acceptable dietary intake" (**ADI**) for infants. PMRA policies equate an ADI exceedance with unacceptable risks.[67] ADI is the reference dose chosen based on animal studies and uncertainty factors to account for the differences between animals and humans. The 100-fold uncertainty factors applied to account for the differences between animal and human studies and responses are not perfect, they do not account for differences between animals and humans necessarily, they are only a rough approximation.

The registration decision for tiafenacil indicated that the PMRA applied uncertainty factors and determined target margins of exposure for chronic dietary risk in a manner consistent with SPN2008-01. We disagree. This document requires that a minimum 100-fold uncertainty factor

[65] Pickard, H. M., Criscitiello, A. S., Persaud, D., Spencer, C., Muir, D. C. G., Lehnherr, I., et al. (2020). Ice core record of persistent short-chain fluorinated alkyl acids: Evidence of the impact from global environmental regulations. *Geophysical Research Letters*, 47, e2020GL087535. https://doi.org/10.1029/2020GL087535.
[66] GEA p.34
[67] Science Policy Note SPN2003-01 "Choosing a percentile of acute dietary exposure as a threshold of concern" (PMRA: July 2003) also see "A Framework for Risk Assessment and Risk Management of Pest Control Products" (2021) p.9; Science Policy Note "Technical Paper, a decision framework for risk assessment and risk management in the Pest Management Regulatory Agency" SPN200-01 p.7.

be applied to address uncertainties arising from extrapolation from animal studies to develop human reference doses. Additionally, the PCPA requires the application of a 10-fold safety factor to take into account completeness of the data with respect to the exposure of and toxicity to infants and children (known as the PCPA factor). The approach taken in the risk assessment differs from this in significant ways.

The proposed registration decision (Table 6 and section 3.2.4) states that the repeated dietary 78-week mouse carcinogenicity study found this same NOAEL (0.35 mg/kg bw/day) without any additional factors and this study is cited as the basis for the ADI of 0.004 mg/kg/bw per day (i.e. 0.35 with a 100-fold safety factor/composite assessment factor applied). Accordingly, the PMRA applied only the 100 composite assessment factor which is used to account for the uncertainty in extrapolation of animal studies. No additional PCPA factor was applied to account for uncertainty of toxicity or exposure to children and infants.

The registration decision takes a completely different approach. Instead of using the repeat dietary study it instead cites the lowest offspring NOAEL in a different rat reproductive toxicity study of 2.6 mg/kg/day for parental toxicity in males (PMRA#286604). It is unclear what the relevance of the cited rat developmental study is to chronic toxicity if any and it is not clear if it is a repeat dietary study. We are unable to confirm its relevance as we were not provided with the actual study prior to the end of the notice of objection period.[68] On this basis the final registration decision makes claims that additional safety factors were applied. However, this is clearly not the case as the proposed registration decision makes it clear that only the standard 100 safety factor was applied and that the critical effect identified in the risk assessment was 0.35 mg/kg bw/day.

The registration decision does not explain why the PMRA changed the study relied upon to calculate the ADI. Australian regulators and the USEPA have used the original repeat dietary study in mice that the PMRA used in the proposed registration decision.[69] Using a higher critical effect than appears in the database would not be consistent with SPN2008-01 which states that "The endpoint selected for risk assessment, known as the critical effect, is typically the first adverse effect that occurs in the toxicity database with increasing dose." Without any explanation, the PMRA selected a much higher dose to derive the ADI in the final registration decision. Further, where the PMRA extrapolates short term data to long term effects, SPN2008-01 requires an additional 10-fold factor. It does not appear that – if the rat reproductive toxicity study is relied on – the PMRA actually applied any additional factor to address this. None of this is explained in the PMRA's decision.

[68] Confidential test data was requested but as of the date of this submission drafting had not yet been provided.
[69] Australian Pesticides and Veterinary Medicines Authority "Public Release on the evaluation of tiafenacil…" (November 2020) https://apvma.gov.au/sites/default/files/publication/75726-public_release_summary_on_the_evaluation_of_the_tiafenacil_in_the_product_terrador_700_wg_herbicide.pdf at p.9; and USEPA, Memorandum supporting decision to approve registration for new active ingredient tiafenacil (September 2020) p.7.

Therefore, in our view, it is not accurate for the PMRA to suggest that risk assessors applied an additional 7.4- and 57-fold safety factor. Taking into account the way the ADI was actually derived, **there is no additional factor that could replace or approximate the PCPA factor of 10 to account for the vulnerability of children and infants**. The composite assessment factor of 100 represents uncertainties for interspecies extrapolation (**UFA**) and intraspecies variability (**UFH**) pursuant to SPN2008-01. The uncertainty factor applied to address the particular vulnerabilities of children is a separate uncertainty factor of 10 pursuant to section 7 of the PCPA. Accordingly, the PMRA has not applied any additional factor to account for the uncertainty around exposure to children and infants.

In the final registration decision Health Canada states that it made conservative assumptions in calculating potential dietary exposure. The registration decision correctly states that the purpose of using conservative assumptions is to "ensure that dietary exposure is not underestimated for any segment of the population." It notes that the risk assessment was a tier 1 assessment only using "high-end or worst-case assumptions were applied".

The PMRA's approach of utilizing tier 1 assumptions and then dismissing the results *because* they were tier 1 assumptions is not a scientifically based approach. The logic that the PMRA utilizes in this decision to disregard the findings of the tier 1 assessment could be used to disregard any tier 1 assessment finding. By design a tier 1 assessment is conservative, it is conservative for a specific purpose which is to ensure that exposures are not under-estimated.

If a tier 1 assessment shows risks of concern, as was the case for the ADI exceedance from tiafenacil for infants, the PMRA's own policies state that a refined assessment is required to ensure that when more accurate assumptions are used, the risk of concern disappears. For example, Science Policy Note SPN2004-01 states that "a level one assessment resulting in unacceptable pesticide concentrations in sources of drinking water advances to a level 2 assessment.[70] The PMRA has not explained the failure to refine the assessment given the ADI exceedance for infants. The commentary in the final registration decision about this issue essentially repudiates the findings of the Tier 1 assessment but does not replace it with a more accurate assessment finding acceptable risks to infants.

The registration decision fails to transparently explain any basis upon which the PMRA refused or failed to complete a refined tier 2 or 3 assessment of chronic dietary risk to infants. This is particularly alarming given that no additional 10-fold uncertainty factor was applied to address the uncertain exposure of infants and children. Given the identified exceedance for infant exposure, this factor should have been applied.

The lack of a further refined assessment of drinking water exposure is also not justified under SPN2008-01. This policy requires that an uncertainty factor for children (referred to herein as the PCPA factor) must be applied to deal with uncertainty of exposure, not just uncertainty around

[70] Science Policy Note SPN2004-01 "Estimating the Water Component of a Dietary Exposure Assessment" at pp.2-3. https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/cps-spc/alt_formats/pacrb-dgapcr/pdf/pubs/pest/pol-guide/spn/spn2004-01-eng.pdf

toxicity. Given the ADI exceedance, and the absence of any refined assessment of exposure to infants, it is obvious that there are uncertainties around exposure to infants. The uncertainty around exposure to and potential harm to infants raises a scientifically founded doubt about the validity of the PMRA's assessment. This doubt could be addressed in a transparent manner by a review panel.

SPN2008-01 states that "Determination of the magnitude of the [PCPA factor] involves evaluating the completeness of the data with respect to exposure of and toxicity to infants and children as well as potential for prenatal or postnatal toxicity." (emphasis added). It also provides that "presumptive application of the 10-fold factor for the protection of infants and children. In other words, the onus is on the PMRA to provide a reliable scientific rationale in those cases where the 10-fold PCPA factor is reduced." And that "Separate decisions on the magnitude of the PCPA factor may be necessary for different routes of exposure, different durations of exposure or different subpopulations." Without doing a refined assessment of drinking water exposure for chronic toxicity to infants, and having found that the chronic ADI was exceeded for infants, the PMRA has not met this onus and the PCPA factor should not be reduced to 1.

Adding significantly to this uncertainty about chronic toxicity to infants is the failure of the PMRA to address combined exposures of infants to other PPO inhibitors and its failure to consider future generations respecting the cumulative effects of TFA in drinking water. The refusal to apply a 10-fold uncertainty factor for infants in this situation is not justified by the registration decision, is not scientifically based, and is not reasonable.

The Ontario College of Family Physicians who previously submitted to the PMRA that current knowledge was insufficient to rely on the standard 100-fold safety factors:

> There is an ongoing difficulty that the results of epidemiological studies of potential human health effects of exposure to pesticides do not appear to be consistent with pesticide risk assessment study conclusions. Thus, limitations in extrapolation of animal test results under experimental laboratory conditions must be recognized and the reliability of such extrapolations ought not to be overstated. … Until the hypotheses generated by toxicological risk assessment are validated by monitoring of human and environmental contamination, epidemiological research and other basic science studies, Canada's regulatory system is not truly "science-based."
>
> It is our view that present knowledge is insufficient to conclude that a default factor of 10-fold to extrapolate from laboratory animals to humans is protective for all outcomes.… Given the wide variability among the human population in susceptibilities to toxicities at various ages and stages, it is our view that current knowledge is insufficient to use a default factor of 10-fold for intraspecies variability.[71]

[71] Sears and Findlay et al., "Comments on the Pest Management Regulatory Agency's Use of Uncertainty and Safety Factors in the Human Health Risk Assessment of Pesticides".

While the registration decision seems to imply that the use of the 100-fold uncertainty factor provides some sort of guarantee or assurance that there will be no effects on human infants - the PMRA's own policy documents acknowledge that use of this factor is at best a crude guess as to whether there would ultimately be human effects.

Evidence – Exposure: Tiafenacil is a new pest control product which may become widely used to deal with glyphosate resistance

Increasingly PPO inhibitor pesticides are being used to manage resistance to the herbicide glyphosate in certain weeds. As glyphosate resistance increases over time, so too will the use of PPO inhibitors. These products may well be mixed with glyphosate since they have different modes of action and have allowable uses on the same crops. The PMRA has not assessed the potential effects on human health, including worker protection and drinking water, and the environment from mixtures of tiafenacil and glyphosate.

Part II – A review panel should be appointed

In the PMRA's recent response to the notice of objection of Safe Food Matters Inc. for glyphosate, the PMRA took the view that uncertainty in an aspect of the evaluation of risks, when considered with other scientifically reliable information, can establish scientifically founded doubt sufficient to ground a review panel request.

Doubt about the exposure of infants to tiafenacil, combined with other PPO inhibitors, is sufficient to establish both scientifically founded doubt and that a review panel could assist.

The primary purpose of the PCPA is to prevent unacceptable risks to human health and the environment before they occur. This is a new registration decision for a new product for which the PMRA has no monitoring data. The only thing that an objector should need to show is that there is doubt about whether tiafenacil may cause harm to human health or the environment, and that there is a scientific foundation for that doubt. There is no onus on the objector to show that harm is likely. In this case, there is doubt about whether tiafenacil may cause harm to human health from chronic exceedances of the reference dose to infants from tiafenacil alone, and to all sub-populations and workers from the combined exposure to PPO inhibitors.

A review panel will assist the PMRA because a properly charged review panel can assess whether there are potential cumulative effects on human health from multiple PPO inhibitors in drinking water and for occupational risks. A review panel could also propose adequate monitoring regimes to ensure that PPO inhibitors and TFA do not exceed reference doses in real-world exposure scenarios.

Doubt about long-term exposure to TFA in the environment as well as the toxicity profile of TFA, and the absence of reference doses for TFA, and the lack of monitoring of TFA is sufficient to establish scientifically founded doubt and that a review panel could assist.

There is a high level of doubt about whether the PMRA validly assessed whether future generations are protected from potentially high and increasing levels of environmental TFA exposure. PMRA did not assess cumulative exposures to TFA or provide a complete toxicity profile for TFA which raises a doubt that the evaluation identified relevant risks and assessed those risks. There is also uncertainty about whether TFA from tiafenacil will contribute to climate change with related environmental and human health harms. These issues merit examination by a review panel to ensure that TFA does not become widely used without these issues being addressed.

A review panel could also assess cumulative effects on human health including to future generations from multiple sources of TFA including other registered pest control products. An independent review panel is needed because even when the objectors commented on the proposed registration decision the PMRA declined to address these issues.

A review panel can assist whenever there is information about a pest control product relevant to acceptable risk which the PMRA did not assess in its risk assessment. Further, a review panel can assist where the methods or weight used by the PMRA with respect to evidence already considered, or the conclusions reached by the PMRA are scientifically flawed. A review panel can independently review the PMRA's methodologies and identify potential uncertainties to enhance public confidence in the federal regulatory regime for pest management.

These submissions meet the criteria in DIS2007-01 and establish scientifically founded doubt and that a review panel would assist.

We acknowledge that the PMRA has, in a recent decision to deny a notice of objection for glyphosate, set out other criteria for how it will implement and apply the criteria for establishing a review panel in the *Review Panel Regulations*. We disagree with the PMRA that these criteria are consistent with the Act's purpose or with the fundamental elements of section 7 of the PCPA which set out the methods that the PMRA must use to assess products. These issues are set out in Appendix A to this submission.

Evidence – Value is not demonstrated

Canada has registered other herbicides with the same PPO inhibition mode of action, so there is no unique trait in that regard. A recent report, reviews resistance against PPO inhibitors, and concludes that the same mechanism for resistance against other PPO inhibitors negates or blunts

herbicidal action of tiafenacil. The PMRA has not explained or justified how tiafenacil registrants have demonstrated value.[72]

Proposed mandate for the review panel

The review panel should address the following questions:

1. What is the cumulative risk of exposure to multiple registered PPO inhibitors from drinking water?
2. What user data and monitoring date is necessary to monitor for those cumulative risks?
3. What gaps exist in the toxicological information on PPO inhibitors particularly with respect to reproductive toxicity?
4. What is the cumulative risk of occupational exposure to multiple PPO inhibitors?
5. What uncertainty factor should have been applied by the PMRA in respect of uncertainties around exposure to infants and what refinements to the assessment of chronic risks to infants should have been done?
6. What gaps exist in the toxicological profile for TFA?
7. What are the trends in TFA exposure in humans?
8. Is TFA bioaccumulative?
9. What climate change effects could TFA have if amounts in the environment continue to follow current trends?
10. Is there reasonable certainty that no harm will occur from the cumulative exposure to PPO inhibitors?
11. Is there reasonable certainty that TFA will not cause harm to future generations or the environment of future generations?
12. What are the potential human health and environmental effects of mixtures of PPO inhibitors and glyphosate?

The Minister of Health should suspend the registration of tiafenacil until the review panel is complete due to the serious and irreversible harm that PPO inhibitors and TFA could pose to human health and the environment. The PMRA should not renew registrations of PPO inhibitors or products with TFA metabolites until the review panel has completed its review.

Deadline for response

The objectors acknowledge that there is no fixed timeline for a response to this objection under section 35(1) of the PCPA. However, for objections to be a meaningful mechanism for public participation under the Act, and to ensure that the PMRA is only registering products where acceptable risk has been demonstrated, it is necessary for the PMRA to respond expeditiously to notices of objection. Further, an expeditious response is necessary for the PMRA to uphold the primary purpose of the PCPA to prevent unacceptable risks from occurring.

[72] Cha JY, Shin GI, Ahn G, Jeong SY, Ji MG, Alimzhan A, et al. "Loss-of-function in GIGANTEA confers resistance to PPO-inhibiting herbicide tiafenacil through transcriptional activation of antioxidant genes in Arabidopsis" Applied Biological Chemistry. 2022 Oct 8;65(1):66 https://doi.org/10.1186/s13765-022-00734-6

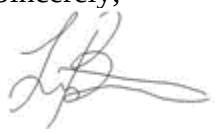
There have been cases where the PMRA has taken three years to respond to notices of objection.[73] The PCPA does not stay decisions of the PMRA pending resolution of an objection request. The issues raised in this objection are serious questions of human health and environmental protection that are within the expertise of the PMRA to quickly determine whether they raise doubts about acceptable risk that an independent review panel could address. TFA is a forever chemical and once tiafenacil is widely used, irreversible environmental contamination will already have occurred. Subsection 20(2) of the PCPA provides that where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent adverse health impact or environmental degradation. Moreover, under subsection 35(5) of the PCPA the Minister is required to provide reasons where an objection is rejected "without delay." Where a review panel is appointed, the Minister must exercise his discretion under section 36 of the PCPA to decide whether to suspend the registration of tiafenacil while the review panel completes its review, and this should also be done expeditiously.

Taking all of this into consideration the objectors submit that a reasonable time to respond to this objection and determine whether a review panel will be convened is no more than six months. If no response is provided within that time the objectors reserve the right to bring a judicial review application in respect of the PMRA's failure to respond and provide reasons without delay for the refusal to convene a review panel to address the potentially serious and irreversible damage caused by the registration of tiafenacil.

Application number 2022-2051 should not be granted

Until such time as the PMRA corrects the deficiencies in its assessment, in particular the failure to conduct cumulative risk assessments and aggregate drinking water assessments for tiafenacil and other products with PPO inhibitor or TFA degradation properties the PMRA should not register any further end use products for tiafenacil. The PMRA should also provide public access to confidential test data and allow further comment periods on new tiafenacil registrations. The same considerations apply with respect to PPO inhibitors with pending registrations including those listed in Appendix B and the proposed renewals of flufenacet registrations in Appendix C. These prospective registrations and renewals should also not be granted.

Sincerely,



Laura Bowman
Staff Lawyer
Ecojustice

[73] The PMRA took three years to respond to the notices of objection in respect of registrations of clothianidin and only responded when the objectors commenced a judicial review. A response to the chlorpyrifos objection has been outstanding since early 2021.

Appendix A - Test for when a review panel should be convened

The PCPA is built on the premise that pest control products pose potential risks to human health and the environment. The PCPA's primary purpose is to "prevent unacceptable risks to individuals and the environment from the use of pest control products."[74] To achieve this goal, the PCPA requires the Minister of Health/PMRA to evaluate risks using a scientifically-based, high-threshold approach.[75] The PCPA reflects that approach in its risk prevention regime through a strong, fundamental presumption against registration. The PCPA prohibits the use, manufacture, sale, and other dealing in any pest control product until the PMRA has determined that the product's risks are acceptable. At the same time, the PCPA imposes an onus on the would-be registrant to provide enough scientific information to establish that the product's risks are acceptable.[76]

Reinforcing its precautionary approach, the PCPA sets a very stringent standard for "acceptable" risks. Under subsection 2(2), a product's risks are acceptable only where there is "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."[77]

This extremely high threshold for the registration of pest control products reflects Parliament's concern that only the safest and most useful pest control products should be registered for use in Canada. Parliament adopted this high threshold in the context of pressure from three opposition parties to apply stricter risk standards to pesticides, including recommendations from the Standing Committee on Environment and Sustainable Development to completely phase out cosmetic pesticides.[78]

To give effect to its very low tolerance for risk under the PCPA, Parliament intentionally used terms such as "certainty" and "no harm" to define acceptable risk. Its intent, in using those terms, was to impose the highest possible level of protection for human health and the environment, just short of an outright ban. Parliament did not charge the PMRA with determining whether harm was likely or whether harm was proven to a scientific-standard.

For example, Parliament was advised by officials from the PMRA and Department of Justice that not only did the PCPA take a precautionary approach to protecting human health and the environment, but that its definition of acceptable risk was stronger than the precautionary principle recognized in Supreme Court of Canada in *Spraytech* because it used a threshold that did not require evidence of serious or irreversible harm to deny registration. The threshold adopted in subsection 2(2) was

[74] *Pest Control Products Act*, SC 2002, c 28, Preamble, s 4(1).
[75] *Pest Control Products Act*, Preamble, ss 7(7), 19(2), 20(2).
[76] *Pest Control Products Act*, ss 2(2), 6, 7(6)(a), 8(1), 8(4), 20, 21(1), 21(2), 25.
[77] *Pest Control Products Act*, s 2(2).
[78] *House of Commons Debates*, 37th Parl, 1st Sess, Vol 137, No 163 (8 Apr 2002) pp. 10109-10120,; House of Commons, Standing Committee on Environment and Sustainable Development, *Pesticides: Making the Right Choice for the Protection of Health and the Environment* (May 2000), paras 12.7-12.8.

repeatedly described in Parliamentary proceedings as the highest level of protection for human health and the environment possible short of an outright ban.[79]

Thus, the term "no harm" reflects Parliament's intent to impose a stringent standard that does not require evidence of serious or irreversible harm or "likely' harm to deny registration. The "no harm" standard can be triggered by any potential harm, not just significant or extremely likely harm, or harm that is a policy priority. Likewise, the term "reasonable certainty" reflects a high degree of scientific confidence. The "certainty" in subsection 2(2) must be both "reasonable" and "scientifically based."[80]

The PCPA's scientifically-based, strict reverse-onus approach to pesticide regulation does not end with registration. Rather, the Minister must consider, on an ongoing basis, whether the risks of a pest control product remain acceptable. Pest control products may only be registered for five years and upon renewal must provide acceptable risk information. The Minister can re-evaluate a pest control product where the information required or procedures used to evaluate the product's health or environmental risks have changed. Periodic 15-year re-evaluations of some pest control products are required. Similarly, the Minister must initiate a special review of a pest control product if there are reasonable grounds to believe that the product poses unacceptable risks or if there is a ban in another Organization for Economic Co-operation and Development country.[81]

At all times throughout the regulatory process, the burden of showing that a product's risks are acceptable, to the point of reasonable certainty that no harm will occur, lies with the registrant. The registrant expressly bears this burden when applying to register, amend or renew a pest control product; when the Minister re-evaluates a pest control product; and when the Minister conducts a special review of a pest control product.[82] If the registrant cannot meet its burden and show that its product's risks are acceptable, the Minister must deny registration or, following a re-evaluation or special review, must amend the registration to make the product's risks acceptable or else cancel the registration.[83]

To further its primary purpose of preventing unacceptable risks from pest control products, the PCPA sets out four ancillary objectives, including that of "encourag[ing] public awareness in relation to pest control products by informing the public, facilitating public access to relevant information and public participation in the decision-making process."[84]

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[79] Canada, House of Commons, *Evidence of the Standing Committee on Health*, 37th Parl, 1st Sess, No 79 (21 May 2002) pp. 9-11; Canada, House of Commons, *Evidence of the Standing Committee on Health*, 37th Parl, 1st Sess, No 80 (23 May 2002), p. 17; *114957 Canada Ltée (Spraytech, Société d'arrosage) v Hudson (Town)*, [2001] 2 S.C.R. 241, 2001 SCC 40 at paras 30-32.
[80] *Pest Control Products Act*, ss 2(2), 7(7), 19(2).
[81] *Pest Control Products Act*, ss 8(1)(c), 16, 17, 19; *Pest Control Products Regulations*, SOR/2006-124, ss 13, 16.
[82] *Pest Control Products Act*, ss 2(2), 7(6)(a), 8, 19(1)(b); *Pest Control Products Regulations*, s 16.
[83] *Pest Control Products Act*, ss 8(4), 21(2).
[84] *Pest Control Products Act*, s 4(2)(c); *House of Commons Debates*, 37th Parl, 1st Sess, Vol 137, No 163 (8 Apr 2002) pp. 10101, 10103-4; House of Commons, Standing Committee on Environment and Sustainable Development, *Pesticides: Making the Right Choice for the Protection of Health and the Environment* (May 2000), paras 13.30-13.31.

Consistent with the PCPA's ancillary objective, public participation plays an important role in the Minister's decision-making process. Among other public participation opportunities, the Minister must actively consult the public before she decides:

- whether to register a pest control product that is or contains an unregistered active ingredient (subparagraph 28(1)(a)(i));

- whether to register, or amend the registration of, a pest control product where the Minister considers that doing so may result in significantly increased health or environmental risks (subparagraph 28(1)(a)(ii));
- whether to confirm, amend, or cancel the registration of a pest control product on completion of a re-evaluation or special review (paragraph 28(1)(b)); and
- any other matter if the Minister considers it is in the public interest to consult (paragraph 28(1)(c)).

The PCPA's public participation scheme culminates in the statutory reconsideration process under section 35.[85] Section 35 of the PCPA permits notices of objection to any decision where public consultation was required under paragraphs 28(1)(a) or (b). Notices must be filed within 60 days. The decisions that may be subject to a notice of objection include decisions to grant or deny an application to register a pest control product that is or contains an unregistered active ingredient, to register or amend the registration of a pest control product if the Minister considers that registration or amendment of the registration may result in significantly increased health or environmental risks, or any decision about the registration of a pest control product on completion of a re-evaluation or special review. Where a review panel is convened subsection 35(7) provides the public with special privileges to participate in the panel review, not simply passively comment on the outcome. The hearings of a review panel are also open to the public under subsection 35(8). The ability of the public to actually participate in the review enhances public confidence in the review process. This special function of the review panel must factor into the PMRA's decision whether a review panel could assist, since a review panel is not simply a panel of independent experts, but is a process that fosters enhanced public participation as compared to the notice and comment provisions in the rest of the Act. Thus, where the public express a lack of confidence in the final outcome of PMRA decision-making a review panel is the ideal forum to allow a transparent examination of those concerns, before a truly independent panel. The result would, in our submission be enhanced public confidence in pesticide regulation.

In contrast, when the PMRA purports to do an "independent" internal review of objections, without any iterative discussions with the objectors, and without affording objectors the opportunity to see confidential test data this is not a transparent or independent process. Although the PMRA may provide a scientific rationale to reject the objection, none of the objectives of s.35 are met. In such an instance, the PMRA's additional reasons simply bootstrap the PMRA's existing rationale. This rationale was frequently not disclosed during the original public comment period, working an unfairness to members of the public who cannot respond.

[85] *House of Commons Debates*, 37th Parl, 1st Sess, Vol 137, No 163 at p. 10103 (8 Apr 2002).

In our experience as objectors, the PMRA's responses to objections frequently chastise objectors for failing to prove that harms are likely with sufficient or sufficiently reliable new evidence to change the weight of evidence. They do not address the level of uncertainty or doubt about the PMRA's methods or conclusions, they do not do additional work to fill gaps identified by objectors, are not transparent and are not truly independent of the PMRA's internal culture, attitudes or management structure. They do not therefore enhance public confidence in the PMRA regulatory regime.

Notices of objection are available in a wide range of circumstances including when a pest control product is cancelled or amended to restrict uses, when a new active ingredient is registered, when an amendment to a specific use or condition of use would result in significantly increased health or environmental risks. Parliament's decision to make notices of objection available in this diverse range of decisions reflected their intention to allow a robust appeal process within the four corners of the legislation.[86]

Subsection 35(3) of the PCPA provides that: after receiving a notice of objection, the Minister may, in accordance with the regulations, if any, establish a panel of one or more individuals to review the decision and to recommend whether the decision should be confirmed, reversed or varied.

In deciding whether or not to establish a review panel in response to a notice of objection, under the *Review Panel Regulations*, SOR/2008-22, section 3, the Minister shall consider two factors:

> (a) whether the information in the notice of objection raises scientifically founded doubt as to the validity of the evaluations, on which the decision was based, of the health and environmental risks and the value of the pest control product; and
> (b) whether the advice of expert scientists would assist in addressing the subject matter of the objection.

The broader statutory context demonstrates that Parliament did not intend to require objectors to provide a peer-reviewed study or a "new" study or evidence to make a successful objection under s. 35. There is requirement to provide a scientific foundation for doubt, but not new evidence. The PCPA's primary purpose is to prevent environmental risks, and the scheme aims to ensure that registrants provide the PMRA with enough information to achieve reasonable certainty.

It is important that the onus is not on the objector to prove on the balance of probabilities that a product will cause or is likely to cause harm. Nor is any evidence or argument provided by an objector to be evaluated for whether it fundamentally changes the weight of evidence – as this question is properly the role of an independent review panel. The central issue in the objection process is whether there are scientifically founded doubts about the methods, weight, or

[86] House of Commons, Standing Committee on Environment and Sustainable Development, *Pesticides: Making the Right Choice for the Protection of Health and the Environment* (May 2000), paras 13.30-13.31.

conclusion of the evaluation of the pest control product that a review panel could assist in resolving or addressing.

Furthermore, s. 3(a) of the Review Panel Regulations specifically requires the Minister to consider whether the information raises doubt about the validity of the evaluations on which the decision was based. The objector is not required to establish that the evaluation was wrong or likely wrong. This further demonstrates that Parliament intended to permit the public to object based on the quality, completeness, credibility or validity of existing evaluations undertaken by the PMRA, without needing to rely on the provision of new data or studies which the registrant failed to produce in support of its application.

Therefore, on a reading of the *Review Panel Regulations* consistent with the modern principle of statutory interpretation, a doubt could be "scientifically founded" if the existing research (including research already considered by the PMRA and identified in the objection) provides an objective basis for a possible risk, without sufficient study of that risk to determine with a high degree of scientific confidence (i.e. "reasonable certainty") that the harm will not occur.

The objection threshold should be read generously such that the PMRA has the broadest possible jurisdiction to correct its mistakes and ensure its risk acceptability standards are met through independent review panels under s. 35. An overly narrow or restrictive set of criteria for considering objections under s.35 would undermine the objectives of the PCPA and s.35 by restricting public participation and allowing unacceptable risks to persist.

The PMRA has developed other criteria for the determination of the two factors in the *Review Panel Regulations*. These criteria are elaborated upon in the recent response to the notice of objection of Safe Food Matters to the registration of glyphosate.[87] These criteria are markedly different from the criteria published in Discussion Document DIS2007-01. It is unclear what criteria our notice of objection should address as a result.

In respect of scientifically founded doubt, the PMRA has included new criteria in the response to the Safe Food Matters Inc.'s glyphosate objection that gives weight to whether information was available and considered in the assessment as follows:

1. Does the information in the notice of objection raise a scientifically founded doubt as to the validity of the evaluations, on which the decision was based, of the health and environmental risks and value of the pest control product? To assess whether there is scientifically founded doubt, PMRA will consider:
    a. Is the scientific basis for the objection directly linked to the evaluation of the pest control product?
    b. Was the evidence supporting the objection considered in the evaluation?
        i. Was the information available prior to publishing the decision? If the information was available, was it considered in the assessment?

[87] Letter, Frederic Bissonnette, Chief Registrar PMRA to Mary Lou McDonald, Safe Food Matters Re Notice of Objection to Re-evaluation Decision RVD2017-01, Glyphosate dated September 29, 2022 (PMRA application no. 2017-3047).

ii. If the evidence was not considered, does the information meet the criteria for scientific acceptability for use in the evaluation of a pest control product?

c. Does the scientific basis of the objection and the evidence provided in support of the objection, when considered with all scientifically reliable information available and considered by PMRA at the time of decision, present uncertainty in an aspect of the evaluation?

The above criteria are directed at a science-based review of the objection and will inform whether there may be scientifically-founded doubt raised by the objection concerning an aspect of the evaluation on which the final decision was based.

It is our submission that this set of criteria is overly onerous and is not consistent with the primary purpose of the PCPA to prevent unacceptable risks or the ancillary purpose of public participation. In light of the purpose and context of subsection 35(1) it is self-evident that objections are likely to engage the question of whether the existing evidence before the PMRA, provided by the registrant, meets the PCPA's high risk prevention threshold for all known potential risks. This includes questions of whether the PMRA employed a scientifically-based methodology and whether it has actually concluded that it has reasonable certainty that no harm will occur in relation to all scientifically plausible hazards and exposures. Further criteria 1(c) appears to require an objector to provide new evidence that fundamentally changes the weight of evidence. Once again, we say that the question of newly evaluating the weight of evidence is properly the role of the review panel. The only issue in an objection is whether the objection raises a scientifically founded doubt. The objector is not required to prove that harm is likely to occur.

That an objection may validly address existing evidence, methods, weight and conclusions is confirmed in DIS2007-01. DIS2007-01, which is currently on the PMRA's website as an active discussion document, with the stated purpose of advising members of the public on the criteria the PMRA will use in evaluating notices of objection. This document provides that the PMRA would consider the following factors relevant to scientifically founded doubt:

- whether the information in the notice raises doubt as to the interpretation of the scientific information, on which the decision was based;
- whether the information in the notice raises any disagreements as to the applied methodology of the scientific information, on which the decision was based;
- whether the information in the notice raises concern(s) as to the relative weights given to data impacting on the risk assessment of the scientific information, on which the decision was based;
- whether the information in the notice raises concern(s) regarding the conclusion reached during the decision making process;

DIS2007-01 correctly identifies that in considering an objection, it is the process of scientific consideration, not the ultimate conclusion, that is at issue. This includes whether the PMRA correctly identified relevant hazards and exposures and whether the PMRA employed a scientific methodology in assessing those hazards and exposures. This objection meets all of these criteria. The information

in this notice raises doubt as to the identification of, and interpretation of scientific information on cumulative effects and other issues. It raises doubt as to the methodology of assessing cumulative effects of PPO inhibitors, the toxicity of PPO and TFA, and bioaccumulation. It raises concerns as to the weight given to specific information considered in the PMRA's assessment. It actively questions the conclusions of the PMRA's decision-making process and contrasts the methods employed by the PMRA with the scientifically based methods that the PMRA purports to use.

A high threshold for "scientifically founded doubt," requiring new evidence, or information that the PMRA did not yet consider, would preclude an objection from resulting in a review panel even on the basis that the PMRA had no scientific information or did no analysis of a scientifically credible potential risk, and registered the product anyway. Similarly, a threshold that required an objector to prove that harm was likely – using a full weight of evidence - would prevent an objector from raising doubts based on scientifically relevant gaps in the PMRA's risk assessment. Since objectors frequently are not provided access to confidential test data within the 60-day period, this prejudices their ability to address the full weight of evidence. Without full and timely access, an objector cannot fairly speak to the weight that the PMRA should place on the evidence it has already considered relative to any additional evidence that is presented in the objection.
This cannot be what Parliament intended in s.35 of the PCPA. In providing objectors with access to confidential test data and in providing that objectors have only 60 days to submit an objection, Parliament was clearly signalling that objectors should have access to the other evidence the PMRA considered. Sixty days is not enough time for an objector to conduct a full weight of evidence analysis. That objections are for the public, whether or not they have detailed expertise – is suggestive that a detailed weight of evidence analysis demonstrating likely harm is not the purpose of objections. Rather the issue in an objection is whether there is scientifically founded doubt and whether an independent review panel should review the weight of evidence. The PMRA appears to be requiring new evidence when it considers whether the evidence supporting the objection was already considered in the evaluation. Accordingly, although we do provide new evidence in this objection, we object to criteria b. and c. of the PMRA's "new" test for notices of objection.

Parliament did not intend to shift the onus to prove harm from pesticides onto the public when it enacted section 35. The public's role under the PCPA is not to provide "new" information about whether a risk is acceptable, or supplement insufficient information provided by the registrant. Such a role would be inconsistent with the registrant's clear onus to establish acceptable risk and the PMRA's clear obligation to ensure that the high threshold of scientifically based reasonable certainty is met when making the registration decision that is being objected to.

Information can be available and considered in the assessment but nevertheless there can be a scientifically valid basis for objecting to the reliability or weight given to that information or to the methods used in the PMRA's interpretation of that information, including whether it is sufficiently complete or reliable. To the extent that the PMRA demands new information to be provided in objections, this is contrary to the purpose of the Act and unreasonably places the onus on the objector to provide evidence that should have been provided by the registrant. Further, requiring new evidence – particularly evidence that meets all of the PMRA's criteria - is not reasonable in a 60-day objection period provided for in the Act. Reasonable members of the public may disagree with the way the PMRA has used existing studies and whether they are sufficient – from a scientific methodology point of view – to establish "reasonable certainty" that

no harm will occur. Once doubt about this issue is established by an objector they have in our submission made out the criteria for "scientifically founded doubt."

We note the incorporation of uncertainty into criteria 1(c) in the PMRA's evaluation criteria. However, under the *Review Panel Regulations* an objector does not need to present an uncertainty, only raise a doubt. It is for the review panel to examine uncertainty. In employing this criteria, the PMRA seems to require more than that the objection raise a doubt, but rather that the objection establish an uncertainty persists when the evidence provided in support of the objection is considered along with "all scientifically reliable" information available and considered by the PMRA at the time of the decision. The PMRA defines "scientifically reliable" as science that is credible and unbiased. This criteria of being "unbiased" would exclude many sources of information the PMRA has relied upon in its assessment of tiafenacil as they are nearly all non peer reviewed confidential studies sponsored by the registrant. It also appears to exclude a wide range of peer-reviewed published research that does not follow specific OECD protocols. This approach is overly restrictive. The PMRA should grant objections when the objector raises a scientifically founded doubt, and leave the "reconsideration" of the decision – in other words the examination of the weight of evidence - for the review panel. In taking on the reconsideration role itself when assessing an objection, the PMRA is usurping the role of the review panel.

Additionally, it must be the case that an objection can present areas that the PMRA did not evaluate or consider in the registration decision, even without any "new" evidence. Here we raise objections based on the absence of review by the PMRA of entire categories of information and evidence, some of which are required by the PCPA or which the PMRA states are required in its own policies. It is sufficient that there be a scientific basis for the relevance of the information that was not considered to raise a scientifically-founded doubt.

Nothing in the Act or regulations suggests that the onus is on the objector to provide new evidence addressing gaps in the assessment sufficient to establish likely harm, as at all times it is the registrant's obligation to prove acceptable risk. This situation does not change simply because the PMRA's evaluations have been completed or public consultations have already occurred. An objection is valid and should be referred to a review panel if it raises scientifically founded doubt as to the conclusion of the PMRA's determination of acceptable risk. Here, there are significant scientifically relevant but unevaluated issues raised in the objection and we submit that it meets the criteria of establishing scientifically-founded doubt. If the PMRA had considered these issues, they might have reached a different conclusion on acceptable risk. If the PMRA agrees that these issues are relevant, then it should refer them to a review panel to reconsider the PMRA's decision. The PMRA's assessment role concluded when it made the final registration decision. The objectors raised the cumulative risk issues with the PMRA during the public comment period based on the information that the PMRA made available at that time. The PMRA has already provided a response in the final registration decision and in supplementary answers to the objectors. If the reasoning in that decision does not resolve the doubts about the evaluation, it is not proper for the PMRA to supplement the registration analysis now or purport to do an internal peer review – the PMRA should refer the matter to a review panel to enhance

transparency and public confidence in its scientific decision-making and respect the process that Parliament set out for reconsideration of decisions.

In respect of the second criteria, whether the advice of expert scientists would assist, the PMRA has set out the following new criteria in the response to the glyphosate notice of objection:

2. Would the advice of expert scientists assist in addressing the subject matter of the objection? To assess this question, PMRA will consider:

a) Is there is a lack of agreement among federal government regulatory scientists with respect to the evidence presented in the objection, and could it affect the outcome of the evaluation?
b) Is the area of science relatively new and the regulatory approach still under development globally and, in this context, does the PMRA believe that the advice of the panel will aid in the regulatory decision-making process?
c) Is there a lack of uniformity in global regulatory evaluations related to the health or environmental risks, or value, of the pest control product that is the subject matter of the objection?
    i. Does the lack of uniformity concern an aspect of the evaluation that is relevant to the Canadian use pattern?'
    ii. Does the lack of uniformity relate to the scientific risk assessment or a legislative requirement in the foreign jurisdiction that is not applicable to the Canadian context?

It is not clear if these new criteria are conjunctive or disjunctive or what weight the PMRA gives to the different criteria. The PMRA now appears to require a lack of agreement among federal government regulatory scientists with respect to "evidence presented in the objection." This disagreement, in the view of the PMRA must be one that, in the opinion of the PMRA itself, could affect the outcome of the evaluation. This criteria is circular and is impossible to meet.

With respect, what is in the minds of PMRA federal regulatory scientists – writ large – is not a reasonable criteria for whether to grant a notice of objection. The purpose of a review panel is to permit a transparent review that is fully independent from the PMRA. This independent review has not just a scientific purpose but a purpose of facilitating public participation and public confidence. PMRA regulatory consultation documents are not transparent about internal agreement or lack thereof of federal scientists. The PMRA's consultation documents present conclusions without disclosing if there is internal disagreement among federal scientists. PMRA registration decisions are reviewed by a select PMRA scientists and are sometimes – but not always – peer reviewed and the conclusions of the peer review – if one even occurs – are not well documented and are not made public.

As this information is not within the knowledge of an objector either before or after the submission of an objection it is not a procedurally fair or sufficiently transparent criteria to include when considering a notice of objection. If the PMRA wishes to rely on this type of criteria it should provide prospective objectors with all evaluation memos, emails, meeting

recordings etc. from the health evaluation division and environmental assessment division during the objection period. Further, since this criteria appears limited to the "evidence provided in the objection" this criteria prejudices objectors who will have no prior knowledge of what federal regulatory scientists *will* think about any new evidence presented in an objection, and no such evidence is disclosed even after the objection is reviewed. The criteria presumes that new evidence is required to support an objection. Thus as framed in the glyphosate response this criteria would allow the PMRA to deny an objection even if the PMRA had internal disagreements about the existing evaluation it conducted. Further, it is not the case that the PMRA consults *all* federal regulatory scientists about every issue, and so the PMRA would not know whether there is consensus in the first place. The use of this criteria is conclusory, it amounts to the PMRA indicating that if the specific scientists it consulted do not document disagreement amongst each other then the objection will not be granted. Ironically, if all of the PMRA reviewers agreed that the objection raised a scientifically founded doubt it would appear that this criteria would also preclude granting an objection.

In our experience the PMRA also heavily edits the opinions of scientists where they differ from the conclusions of PMRA management. Scientists at the PMRA are not permitted to reach conclusions on acceptable risk, only senior managers are.[88] Decisions about acceptable risk conclusions are only made by senior managers at the science management committee or directors committees. Often these are managers without requisite expertise and who did not participate in the evaluations. Any disagreement among senior managers when they meet to discuss registration decisions is not documented, as the PMRA produces one-line minutes providing only the conclusions of those conversations which occur among directors or the science management committee. Even briefing notes prepared by scientific staff are edited to match the conclusions of senior managers after the meetings conclude. Monographs are sometimes peer reviewed but any changes or comments from the reviewer are not included and often the monographs are kept in perpetual draft form. Thus, even if an objector sought the record of decision from the PMRA it would not disclose whether there was any underlying disagreement among federal scientists as these are not documented by the PMRA. The new criteria appears to be an attempt to judicial-review proof objection decisions. Ecojustice requested the underlying scientific briefing notes and draft briefing notes for tiafenacil in early 2022 and even though these are comprised of only a handful of documents and are likely less than 50 pages the associated access to information request is subject to a 360-day extension.[89]

[88] Memo from Peter Delorme (PMRA) to PMRA staff "Briefing Notes for SMC" dated July 8, 2005. This memo directs scientific staff documenting proposed registration and re-evaluation decisions for decisions by the Science Management Committee (a committee of directors) that "no comments should be made with respect to registration recommendations - this is the role of SMC" it further states that the director should be briefed before the points are sent to the science team lead for inclusion in the Briefing note. It also states that scientists should "avoid being overly conservative - provide the bottom line - e.g. if we assume 100% of diet is contaminated but think this is an unreaslistic assumption and do not think there is a real risk, then a risk should not be identified. - I recognize we will have to work on how to handle this aspect." Typical briefing notes from scientists leave the "recommendations" section blank or provide options that are then selected by the senior managers, after which the briefing note is edited and finalized. Scientists provide general discussion and the PMRA managers determine if the risks are acceptable.
[89] A-2021-002140 revised timeline for narrowed request has been outstanding since September 13, 2022.

Forcing the public to prove harm to a high standard under s. 35 of the PCPA in support of an objection would create another absurdity in that the review panel itself, if appointed, would be rendered redundant and would serve no clear purpose. This problem is compounded by the PMRA's practice of internally reviewing notices of objection instead of permitting a truly independent review by a review panel. A test that requires internal disagreement usurps the role of the review panel and undermines Parliament's intention that reconsiderations of pesticide registration decisions be independent.

In our view this criteria as framed in the glyphosate notice of objection response amounts to a total bar on the granting and consideration of objections given the evaluation context in which PMRA operates, the refusal of the PMRA to allow scientists to give explicit opinions on acceptable risk, and the fact that the PMRA does not have any practice of documenting or disclosing internal disagreements. Since it is impossible for us to speculate whether federal scientists selected by PMRA managers will happen to disagree or not about any new information we submit herein, and we do not know if they will be allowed to document any disagreement if it exists, we cannot fairly speak to this issue in the objection. However, we do submit that there is obvious disagreement among PMRA staff about whether a cumulative risk assessment is needed for TFA and PPO and that this is reflected in the difference between the proposed and final registration decisions for tiafenacil and the commentary in the proposed decisions for trifludimoxazin and flufenacet.[90]

Criteria 2b) in the PMRA's new test for notices of objection in the glyphosate objection response is that the "area of science" must be "relatively new" with a "regulatory approach still under development globally". This criteria is absurd. The PMRA appears to be asserting that the only time a review panel could assist is when an entirely new area of science is involved with no clear regulatory approach *globally*. The review panel process is meant to be a check and balance on PMRA decision-making and this criteria effectively precludes the objection and review panel mechanism from being used as such. Instead, it defers to the processes and regulatory analysis in other countries. The PMRA is attempting to convert review panels from a check and balance on specific decisions on pest control products and their use in Canada into a general research forum for novel scientific issues. In the glyphosate notice of objection decision, the PMRA asserted that because it had experience with "herbicides" generally this criterion was not met. The fact that a herbicide may pose particular risks or be different than other herbicides in terms of mechanisms of action or exposure modeling is not considered. Particularly given the way this criteria was applied in the glyphosate objection response, we consider this criteria to be a near total bar on granting all notices of objection for all herbicides and insecticides as well as entire other categories of pest control products and are of the view that it is not a reasonable criteria. This criteria is entirely inconsistent with the role Parliament intended review panels to play under the statutory scheme.

[90] Trifludimoxazin, vulcarus and voraxor PRD-2020-15, RD2021-01; Flufenacet PVRD2021-01 "the dietary exposure assessment has identified health risks of concern from exposure to flufenacet and its metabolites, thereby requiring the proposed decision to cancel all uses. Therefore, a cumulative assessment for TFA is not required as part of this re-evaluation."

Tiafenacil is a herbicide, but it is an entirely new herbicide with a mode of action for which only a handful of herbicides have been previously registered in Canada. Neither the common mechanism of PPO inhibition nor significant issues with metabolites like TFA have been well studied, and indeed the issues raised in this notice of objection were largely ignored in previous registrations of related products. Tiafenacil is not currently registered in several jurisdictions including OECD jurisdictions in Europe. Although the PMRA has been required to complete cumulative assessments of pest control products with common mechanisms of action since 2007 it has yet to complete any - making such an assessment novel. Tiafenacil was only recently registered in the United States and Australia. The PPO inhibition issue was not identified as a common mechanism of toxicity, and TFA as a metabolite was not addressed at all in those assessments. Although we disagree with the criteria as framed by the PMRA, we submit that this should be sufficient to establish that a review panel could assist.

Criteria 2c) of the PMRA's new test for notices of objection queries whether there is a "lack of uniformity" in global regulatory evaluations and whether this lack of uniformity concerns an issue relevant to Canadian use patterns and regulatory criteria. The way these criteria are framed appears to be intended to sidestep hazard-based assessments from Europe – even where European regulators have identified toxicological aspects of concern relevant to Canadian use patterns. Indeed, any regulator with a different conclusion that uses a slightly different statutory test or process than the Canadian *Pest Control Products Act* might be ignored the way this criterion are framed, which would be nearly all regulators. Where basic questions of toxicology are at issue, this criterion makes little sense since if there are major questions about what reference dose should be used, or whether one can even be identified – similarities or differences in use patterns are not necessarily relevant. Use patterns are only relevant where questions are raised about exposures in another jurisdiction. In many cases other jurisdictions have slightly different use patterns due to climate. That does not automatically mean that their exposure evaluations are irrelevant as they may use different assumptions or methodologies that if used in Canada could change the outcome of Canadian exposure assessments.

Tiafenacil is registered in the United States and Australia but is not registered in Europe. There is therefore no consistent regulatory finding on the acceptability of tiafenacil across OECD countries. In this objection we are raising scientifically founded doubts about how the PMRA calculated exposures to Canadians and whether the PMRA adequately addressed cumulative Canadian exposures over multiple generations. This is a question of how the PMRA is considering and weighing Canadian modeling and comparing it to Canadian reference doses, Canadian policy criteria and Canadian legislative standards. These new criteria if applied to a notice of objection could preclude a review panel from being appointed to deal with issues specific to Canada. This cannot be consistent with the purpose of the PCPA which is to prevent Canadian risks. Where the issue is not specific to Canada, the PMRA's new criteria permits a review panel in incredibly narrow circumstances where legislative criteria and use patterns are extremely similar but foreign regulators reached a different conclusion. We object to this criteria. It is not consistent with the preventative purpose of the PCPA or with the intent of section 35 of the PCPA and is incongruent with Canadian-based risk assessment. While an objector can legitimately point out that for example, exposures were modeled differently elsewhere or that

reference doses were calculated differently elsewhere – and indeed a review panel might assist with those methodological issues – the criteria in 2c) are not directed at such questions. Rather this criteria is framed to only find that a review panel will assist in extreme and exceptional situations involving closely tracking regulatory decisions in another jurisdiction.

A review panel could assist because there are significant unaddressed doubts about cumulative risks from multiple PPO inhibitors to certain subpopulations such as infants, children, and women. Further, the PMRA has not attempted to deal with non-toxicological environmental and health harms from TFA such as climate change and such questions are not within standard PMRA methodologies. The PMRA has an incomplete toxicological profile for PPO inhibitors and TFA. Finally, the PMRA has not considered future generations as required by section 4.1 of the PCPA and has not addressed the potential long-term and cumulative impacts of TFA on human health or the environment. An independent review panel could assist the PMRA to resolve each of these issues.

Appendix B - pending registration decisions for PPO inhibitors to which this submission applies

Active ingredient	Pending application numbers	proposed new uses*
Flumioxazin	2022-4973 2022-4278	Succulent shelled edible podded peas (pisum spp and pigeon pea), celery, lowbush blueberry, alfalfa.[91]
Saflufenacil	2022-4487 2022-4485 2022-3872	Barley, canary seed, chickpeas, creeping red fescue, timothy and bromegrass, seedling (seed production, forage and hay, faba beans, lentils, oats, peas (dried field) wheat (spring, winter and durum), corn, soybeans, canola, chickpeas, dry common beans, faba beans, flax, lentils (red), mustard, field peas, soybeans, sunflower, broadleaf and grass weeds.
Carfentrazone-ethyl	2022-5443 2022-3751 2022-3771	"labelled crops"**
Sulfentrazone	2022-4585 2022-3887 2022-3781 2022-3785 2022-3279 2022-3077 2022-2122 2022-2094 2022-1813	"labelled crops"** chickpeas, field pea, flax, sunflower, fababean, soybeans, wheat (spring and durum), asparagus, strawberry, brassica, head and stem (crop group 5-13), leafy greens, tomato, horseradish, tree nuts, tame mustard.

[91] https://pr-rp.hc-sc.gc.ca/1_1/view_label?p_ukid=251296538

*Note that not all proposed new uses or amendment terms are disclosed on the public registry
** it is not clear from the public registry if higher application rates, different application methods etc. are applied for as this information is not disclosed.

Appendix C - pending renewals for products with TFA metabolites

Active ingredient	Pending application numbers	proposed new uses
FLUFENACET	2022-4400 2022-4410 2022-4414 2021-0692 2019-6340 2019-6316 2019-6160	renewals New registrations for use site categories 13 and 14 (terrestrial feed crops and terrestrial food crops).