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April 14, 2017

Pest Management Regulatory Agency
Health Canada
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Ottawa, Ontario K1A 0K9
Address Locator: 6607D

BY E-MAIL to PMRA.publications@hc-sc.gc.ca

Re: Proposed Cumulative Risk Assessment Framework, PRO2017-01

To Whom It May Concern:

In response to the Proposed Cumulative Risk Assessment Framework, PRO2017-01 (posted March 1, 2017), these are the comments of the Canadian Association of Physicians for the Environment, Canadian Environmental Law Association, the David Suzuki Foundation, Ecojustice, Environmental Defence, Équiterre and Prevent Cancer Now. Our organizations have a long-standing interest in the regulation of pesticides to protect human health and the environment. In general, while recognizing the limits of the risk assessment paradigm,¹ we welcome the proposed framework as progress toward implementing at last the legal requirement to consider cumulative effects when evaluating the health risks of pesticides. We offer several recommendations, detailed below, that would strengthen the framework and ensure its relevance within the regulatory system.

1. Assessment of cumulative pesticide risks is legally required and long overdue

The preamble to the *Pest Control Products Act* (PCPA) states:

WHEREAS it is in the national interest that the primary objective of the federal regulatory system be to prevent unacceptable risks to individuals and the environment from the use of pest control products, [...]

¹ McClenaghan, T., K. Cooper, L. Vanderlinden, P. Muldoon, A. Abelsohn, K. Khatter, and K. Keenan. (2003) Environmental Standard Setting and Children's Health: Injecting Precaution into Risk Assessment, *J. Env'l Law and Practice* 12(2): 141-279.

in assessing risks to individuals, consideration be given to aggregate exposure to pest control products, cumulative effects of pest control products and the different sensitivities to pest control products of major identifiable subgroups...

Sections 7, 11 and 19 of the Act require consideration of “cumulative effects of the pest control product and other pest control products that have a common mechanism of toxicity” in relation to evaluating health risks. This requirement applies to decisions with respect to applications for registration or amendment (section 7), maximum residue limits (section 11), special reviews and re-evaluations (section 19).

Despite these legal requirements (in place since 2006), the PMRA has not assessed the cumulative health effects of pesticides approved for use in Canada. In contrast, in other scientific and regulatory contexts, recognition of cumulative impacts/risk is not new; efforts have been made to assess cumulative impacts/risks for many years.

The proposed Cumulative Risk Assessment Framework for pesticides marks an important milestone, and we are encouraged by this progress. We recommend that the PMRA finalize the framework and operationalize it without further delay. We also recommend that the PMRA establish timelines for addressing the backlog of currently registered pesticides for which cumulative risks have not been assessed.

2. Embedding cumulative risk assessment within the regulatory process

The proposed framework does not clearly specify how cumulative risk assessments will relate to and inform decisions concerning individual pesticide registrations/registration amendments, maximum residue levels, re-evaluations and special reviews. The consultation document implies that individual pesticide re-evaluations will be completed prior to assessing — ergo, without considering — cumulative risks:

Currently, the PMRA is completing individual assessments for pesticides within the same common mechanism group through its re-evaluation program. It is essential that toxicological and exposure assessments of individual chemicals are up-to-date prior to undertaking the complex task of cumulative assessment.

In our view, the re-evaluation of individual pesticides within the same common mechanism group should not be considered complete until cumulative risks have been assessed. Furthermore, consideration of cumulative risks, where applicable, should factor into decisions on individual pesticide registrations/registration amendments, maximum residue levels and special reviews, as well as re-evaluations. Sections 7, 11 and 19 of the PCPA require consideration of cumulative effects in evaluating the health risks of individual pesticides.

We recommend including a decision tree with the framework setting out the points in the decision-making process when cumulative risk assessments may be triggered and how conclusions about cumulative risk will influence regulatory action on individual pesticides.

In consideration of the uncertainties involved in assessing cumulative risks, we further recommend that the PMRA clearly set out in the framework how the legislative requirement for precaution (in conducting special reviews and re-evaluations) applies.

3. Identifying common mechanism groups

The framework sets out a step-wise approach to identify pesticides that belong to a common mechanism group as the precondition for assessing cumulative risks. The consultation document states that PMRA follows a “weight-of-evidence” approach to support the development of hypotheses pertaining to mechanisms of toxicity. However, when the Commissioner of the Environment and Sustainable Development audited the PMRA in 2015, the audit identified inconsistencies:

The Agency concluded that a cumulative risk assessment was not warranted in 6 of the 10 re-evaluations we examined. However, in some of the 6 cases, we found no evidence to support the Agency’s conclusion that there was no common mechanism of toxicity. For 2 of the other 4 re-evaluations, we found that the Agency had yet to determine whether a cumulative risk assessment was warranted. For the 2 remaining re-evaluations, the Agency had determined that the assessment was warranted, but it had not completed the work.²

According to the Commissioner’s 2015 report, the PMRA told the auditors “that information was typically not available to determine which chemicals act in the same manner.”³

We are concerned that failure to identify common mechanism groups will thwart assessment of cumulative risks. In keeping with the PCPA requirement for application of the precautionary principle, we recommend the PMRA adopt a precautionary approach to grouping pesticides for cumulative risk assessment. If there is uncertainty about mechanisms of toxicity, the PMRA should proceed with a cumulative risk assessment. The onus should be on the registrant to disprove hypotheses about common mechanisms of toxicity.

Furthermore, we question whether the proposed framework will be applicable to certain types of adverse health outcomes, including endocrine disruption, neurodevelopmental effects and cancer. For example, several pesticides and pesticide groups/classes are identified in the peer-reviewed literature as being causally linked to specific cancer outcomes, yet the relevant mechanism of toxicity remain only partially elucidated. For this reason, we recommend applying a weight-of-evidence approach that considers epidemiological data, in addition to in vivo cancer studies in model animals, in vitro genotoxic assays, and mechanistic studies. To ensure transparency, rigour and confidence in “weight of evidence” approaches, it is necessary to use systematic review methods and reporting,⁴ particularly to advance from simplistic biochemical groupings to more meaningful but complex outcomes. To support the data requirements of cumulative risk assessment, external surveillance programs that calculate lifetime cancer risk and average daily lifetime exposures of selected pesticides may be useful (see CAREX

² *Fall 2015 Reports of the Commissioner of the Environment and Sustainable Development. Report 1 – Pesticide Safety*, paragraph 1.41. < http://www.oag-bvg.gc.ca/internet/English/parl_cesd_201601_01_e_41015.html>

³ *Ibid*, paragraph 1.42.

⁴ e.g., Rooney, A. A., A. L. Boyles, M. S. Wolfe, J. R. Bucher, and K. A. Thayer. “Systematic Review and Evidence Integration for Literature-Based Environmental Health Science Assessments.” *Environ Health Perspect* 122, no. 7 (July 2014): 711–18. doi:10.1289/ehp.1307972.

Canada's indicators of environmental exposure to carcinogens:
http://www.carexcanada.ca/en/profiles_and_estimates/).

Toxic mechanisms and effects are defined differently among various jurisdictions, and are quickly evolving with advancing science. The North American grouping method as conducted by the U.S. Environmental Protection Agency has to date been very narrowly defined at the level of a particular biochemical reaction, and these assessments have resulted in no action taken against any pesticide as a result of cumulative assessments conducted to date. The European Union approach to examine effects such as neurotoxicity is more complex, but more relevant. We recommend that the PMRA initiate cumulative assessments with a view to rapid development of expertise to be applied within broader frameworks on a tissue rather than a biochemical basis. We further recommend that the PMRA consult regarding proposed groupings of pesticides for cumulative assessments.

When a pesticide has more than one mechanism of toxicity identified (for example, an acute response and a chronic carcinogenicity), this raises an important question of how the chemical groupings will be prioritized and regulated. Quantitative assessment of cancer risk is a different approach compared to the margin-of-safety approach used for non-cancerous endpoints. If a pesticide grouping is being assessed in a cumulative risk assessment for a non-cancer mechanism of toxicity, it may not capture an appropriate level of safety without a separate cumulative risk assessment for its cancerous mechanism of toxicity. We recommend that the PMRA clarify in the framework how such situations will be addressed.

To improve transparency, we further recommend the PMRA maintain a publicly accessible database of pesticide toxic effects and associated hypotheses about mechanisms of toxicity, including groupings of pesticides for cumulative risk assessments.

4. Assessing cumulative exposure

The consultation document states, "In assessing cumulative exposure, it is appropriate to integrate only those exposures that are likely to co-occur within the critical time window for the common toxicological effect." In our view, sequential exposures over time to different pesticides within a common mechanism group should be considered in assessing cumulative chronic risks. We recommend that the PMRA define "critical time window" and clarify its approach to assessing cumulative chronic exposure to multiple pesticides within a common mechanism group.

5. Characterization of the "PCPA factor"

In reference to the Hazard Index Method for assessing cumulative risk (and elsewhere), the consultation document states, "The approach allows for the application of chemical-specific uncertainty factors regardless of whether they are applied for scientific reasons (such as the extrapolation of short-term data to a long-term scenario) or for policy considerations (such as the PCPA factor)." We strongly disagree with this distinction between "scientific" and "policy" uncertainty factors. The so-called PCPA factor is required by the Act "to take into account potential pre- and post-natal toxicity and completeness of the data with respect to the exposure of, and toxicity to, infants and children"; in other words, to address uncertainties in assessing risks to infants and children, with life-long implications. The PCPA factor is based on the scientific understanding of infants and children's increased vulnerability to

toxic exposures. We recommend the PMRA revise references to uncertainty factors in the framework to avoid stating or implying that application of the PCPA factor lacks scientific basis.

6. Assessing cumulative environmental risks

Although the PCPA explicitly mandates consideration of cumulative effects only in relation to evaluation of health effects, in general the act requires parallel consideration of risks to health and the environment. In our view, consideration of cumulative effects is equally relevant in determining whether risks to the environment are acceptable. The proposed framework applies only to the assessment of cumulative human health risks, although the same methodologies could be applied to assess cumulative risks to the environment. For example, the PMRA is currently re-evaluating risks to pollinators from a group of neonicotinoid insecticides, which might support a cumulative assessment of environmental risks. We recommend expanding the framework to enable assessment of cumulative environmental risks.

7. Complementary measures to monitor exposure

We note that the strength of cumulative risk assessment depends on the availability and quality of cumulative exposure data. Operationalization of the proposed framework would benefit from improved and expanded monitoring of human and environmental exposures to pesticides, including pesticide residues in foods and drinking water — and public access to the data. Although beyond the scope of the proposed Cumulative Risk Assessment Framework, we recommend the Government of Canada increase funding and strengthen reporting requirements for monitoring programs, including the Canadian Food Inspection Agency sampling programs, the Canadian Health Measures Survey, the House Dust Survey, and environmental monitoring conducted by Environment and Climate Change Canada, and ensure co-ordination between these programs and the data needs of the PMRA pesticide evaluation program.

8. Future directions

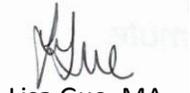
The consultation document presents the proposed framework as “a starting point upon which the methodology will be further developed as approaches and scientific understanding progress.” Recognizing that cumulative risk assessment methodologies are rapidly developing, we encourage the PMRA to build on the proposed framework to develop complementary approaches in the following related areas:

- Consideration of cumulative risks associated with mixtures of pesticides with disparate mechanisms of toxicity but the same toxic effect;
- Consideration of synergistic effects associated with mixtures of pesticides, regardless of mechanisms of toxicity and individual toxic effects;
- Consideration of cumulative risks associated with pesticide formulations (beyond active ingredients); and,
- Mixture risk assessments to consider cumulative risks associated with pesticides in combination with other chemicals with common toxic effects and/or mechanisms of toxicity.⁵

⁵ Evans, R. M., O. V. Martin, et al. (2016). "Should the scope of human mixture risk assessment span legislative/regulatory silos for chemicals?" *Science of The Total Environment* 543, Part A: 757-764. <http://www.sciencedirect.com/science/article/pii/S0048969715309785>

We appreciate the opportunity to comment on the proposed Cumulative Risk Assessment Framework. Do not hesitate to contact us should you require clarification or to discuss these matters further.

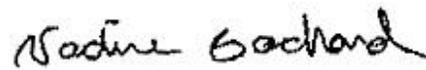
Sincerely,



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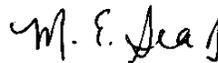
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About our organizations:

The **Canadian Association of Physicians for the Environment (CAPE)** is a non-profit organization run by physicians that seeks to better human health by protecting the planet.

The **Canadian Environmental Law Association** works to protect human health and our environment by seeking justice for those harmed by pollution and by working to change policies to prevent such problems in the first place.

The **David Suzuki Foundation** collaborates with Canadians from all walks of life to conserve our environment and find solutions that will create a sustainable Canada through science-based research, education and policy work.

Leading the legal effort for a brighter future, **Ecojustice** is Canada's only national environmental law charity. Ecojustice has a staff of lawyers and scientists who use the power of the law to defend nature, slow climate change, and stand up for the health of our communities.

Environmental Defence is a national charity that challenges and inspires change in government, businesses and people to ensure a greener, healthier and prosperous life for all.

Équiterre helps build a social movement by encouraging individuals, organizations and governments to make ecological and equitable choices, in a spirit of solidarity.

Prevent Cancer Now works to stop cancer before it starts by eliminating preventable contributors to cancer, with research, public education and advocacy.