



## Submission to the Pest Management Regulatory Agency regarding PRVD 15-01 Re-evaluation of Glyphosate

[www.preventcancer.ca](http://www.preventcancer.ca)

June 12<sup>th</sup>, 2015

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### Overview

Prevent Cancer Now is pleased to submit the following comments, to assist with the re-evaluation of glyphosate – the most commonly used herbicide globally, and in Canada. PRVD2015-01 would improve workers' protection, but would not change substantially the permitted uses, frequencies, application rates, or permitted levels in foods or water.

We offer recommendations to improve scientific validity and credibility, as well as protection of agriculture, and environmental and public health, presently and into the future.

- PVRD 2015-01 is not a comprehensive, systematic scientific review by the PMRA, in terms of process, examination of all relevant publicly available literature, reporting of deliberations and findings, and weighing of evidence. Carcinogenicity was dismissed with a paragraph, and an unsubstantiated claim that a weight of evidence process was used.
- Implementation of systems for thorough systematic review offer potential for streamlining, improving efficiency and transparency, and potentially better actions for public health;
- Scaling from small animals to humans is such that the Pest Control Products Act (2002) factor cannot be eliminated;
- The review fails to examine important features and actions of glyphosate, such serious implications of its chelation activity, and antimicrobial properties;
- The present *re*-evaluation has neither explored nor addressed the impacts of the use of glyphosate over past decades, as its use has soared. No historical data is presented to judge the effectiveness of previous conditions of use (labels) on Canadians' water, soil, biodiversity or sustainability of agriculture. There is no data on foods. Thus, there is nothing to distinguish the present approach from an evaluation of a new pesticide, for which we have little real life experience. This is a wasted opportunity to protect all that is listed above.

When a poor quality review misidentifies negligible risk when a risk is actually present, then public health is impaired (with attendant hardships and costs) when it should not have been. We expect that this may be the case with glyphosate. Prevent Cancer Now sees that it is necessary to curtail the use of toxic herbicides, and to support farmers in transition to more sustainable agricultural practices.

### Scientific Review

The path taken determines the destination, and in scientific review it is imperative that rigorous, transparent methods are in place to minimize risk of bias, and to ensure accuracy of conclusions. Systematic review of scientific literature was first developed for medical interventions, but is now extended to environmental health <sup>1</sup>. These procedures have been test-run on substances such as bisphenol-A, and are the preferred approach to pesticide re-evaluation.

Systematic review is applied to a specific question or set of questions, with extensive professional searching of the literature, screening, data extraction and synthesis. Health Canada's evidence base is clearly incomplete, as evidenced by lack of the bulk of the peer-reviewed literature. Some

examples include, the work of Prof. Séralini's laboratory; examination of populations in South America and Asia who are suffering spontaneous abortions, birth defects, kidney disease, DNA damage and diverse other ailments associated with glyphosate spraying; several independent reports of endocrine disruption; diverse reports of effects of glyphosate on microbes in the environment and in the "microbiome"; and effects on aquatic organisms. These are but a few examples of the broad, compelling body of evidence that is conspicuous by its absence in PVRD 2015-01.

Only after systematic review and synthesis of the evidence is it possible to weigh it. Vague claims of using a weight of evidence approach are meaningless when the evidence base is not established, the framework for weighing is not stated, and weighing is not presented<sup>2</sup>. Carcinogenicity, a very serious outcome, was discussed in a paragraph, with an unsubstantiated claim regarding weight of evidence.

It is a step forward to see tables of outcomes with lists of studies, but the tables and references provided are of limited usefulness. Considerable judgment enters into distinguishing between an "effect" and an "adverse effect," so effects should be tabulated. In previous examinations of data in the Reading Room, it has been seen that significant effects seen at lower doses are dismissed as not "adverse," but the effect is that Canadians are potentially exposed to much more pesticides. As well, many bibliographic records are incomplete, so are not readily identifiable, and many are not referenced in the document so it is unknown what was relevant, and how they were incorporated into the review. There is no indication of methods or judgements involved in weighing of evidence

The Statutory Review of the Pest Control Products Act, 2015, *Report of the Standing Committee on Health*, Ben Lobb Chair, April 2015 states in Recommendation 3: "That the PMRA review the openness and transparency of its processes to register pest control products with a view to ensuring that Canadians are able to provide meaningful and informed input into the decision-making process and clearly understand decisions once they are made." PVRD 2015-01 fails to meet this goal.

### **Review Scoping**

The re-evaluation is narrowly scoped, based almost exclusively on confidential, industry-supplied animal test data. Although a subset of the environmental peer reviewed literature is listed among the references, the epidemiological evidence research is not actually presented or discussed.

In the wake of the classification of glyphosate as a probable human carcinogen by the International Agency for Research on Cancer (IARC),<sup>3</sup> it is disappointing to see carcinogenicity dismissed with a single paragraph in PVRD 2015-01. This serious endpoint merits much more serious consideration, and should be acted upon on the basis of the IARC determination. The "weight of evidence" claim regarding carcinogenicity is unsubstantiated.

### **Scaling from animals to humans**

As is commonly done, comparisons of effects are on the basis of pesticide dose (mg/kg body weight /day). Scaling to humans is fraught, because small animals eat proportionally much more per kilogram body weight, so chow with much lower levels of pesticides are used in toxicological experiments. In consequence, rodents fed glyphosate at a unit dose would receive the pesticide diluted in much more food, and consume many times more nutrients along with the pesticide. Studies by the Séralini laboratory found organ damage and tumours in animals fed food and water with Roundup at "acceptable" concentrations for people, albeit at higher concentrations than typically used in rodent research.

Although the dose-based approach is preferred by industrial stakeholders, the inter-species extrapolation factor of 10-fold barely covers the difference in pesticide concentrations in foods, let alone fundamental differences between rodents and humans. These types of considerations featured in the justification for introduction of an additional 10-fold extrapolation factor in the Pest Control Products Act (2002). This factor has been eliminated via bureaucratic maneuvers as PMRA consulted with industry; this is unjustifiable and amounts to circumvention of the will of Parliament.

### **Key reference doses**

The PMRA indicates that over 30 mg/kg body weight /day is the “no observable adverse effect level,” but the US Integrated Risk Information System (<http://www.epa.gov/iris/subst/0057.htm>) indicates a NOEL of 10 mg/kg/day based upon increased incidence of renal tubular dilation in F3b offspring, at a “lowest effect level” (LEL) of 30 mg/kg/day. Had the Monsanto 1981a study referenced by the US EPA been incorporated into the re-evaluation, current glyphosate exposures would have had to have been reduced by two thirds.

A two stage process was used for exposure assessment. The preliminary approach indicated excessive levels, whereupon refinements brought exposures below the reference dose. At this point, dietary estimates for the two youngest age groups were approximately 70% of the maximum. Thus, use of the IRIS data would have meant that the reference dose would have still been too low for uses of glyphosate to result in sufficiently low exposures.

### **Extraordinary chemical properties of glyphosate**

Glyphosate’s chemical properties, actions and subsequent implications of its use are not mentioned, let alone incorporated in a transparent weighing of the scientific evidence. For example, although neither antibacterial effects nor chelation are mentioned in PRVD2015-01, there is strong evidence that:

- As an antibiotic, glyphosate
    - affects the human bacterial microbiome (with implications for health, child development, and cancers, particularly haematological and colorectal, as well as others);
    - potentially contributes to antibiotic resistance and “super bugs”;
    - kills micro-organisms in the soil including beneficial bacteria, eventually impairing plant growth, and contributing to toxic fungal crop disease.
  - As a chelator, glyphosate
    - may mobilize toxic heavy metals (e.g. cadmium, arsenic and lead) from the soil into water and plants, which humans and animals consume;
    - may limit absorption of essential trace elements from foods. (In more diluted experimental rodent diets, a surfeit of essential elements may negate chelation effects of glyphosate, whereas a threshold may be surpassed in human diets where Maximum Residue Levels (MRLs – see below) permit higher concentrations of glyphosate.)
- Recent research demonstrates higher cadmium levels in “conventional” than in “organic” foods.<sup>4</sup>

### **Endocrine disruption**

Multiple in vitro and in vivo studies indicate that glyphosate may disrupt the body’s chemical messaging system – the actions of hormones, or the endocrine system. Endocrine disruption is an extremely important effect, as is protecting public health from chemicals that alter fundamental processes such as foetal and child development, metabolism, reproduction, and development of cancers in sensitive tissues such as the breast or prostate. The EU was on track to take actions on endocrine disruptors,

which would have particularly affected pesticides – many pesticides exert these effects – until the effort was derailed by complex corporate-sponsored interventions.

The PMRA is not currently incorporating this important endpoint, instead waiting until the US has completed its screening for endocrine disruption. It is not clear that this screening should trump observations in animals, particularly when glyphosate-associated downstream effects related to the microbiome or toxic elements, that may also contribute to endocrine disruption, will be missed during this screening.

### **Extrapolation Factors**

Continuing all permitted uses of glyphosate is justified by the PMRA, using “safety” factors to extrapolate from animal data to human health. The PRVD incorporates a scientifically unjustifiable bare minimum, that does not encompass the diverse adverse actions of glyphosate, nor the inherent susceptibilities of the young that was introduced to the Pest Control Products Act in 2002. The assessment was refined to achieve “acceptable” exposures, and even so it is estimated that young children may be receiving 70% of the [high] permitted daily glyphosate dose from their diets. An additional extrapolation factor would render the use of glyphosate “unacceptable,” and preclude re-registration.

### **Maximum Residue Levels (MRLs)**

Following from the acceptable exposure (based upon industry-provided animal toxicology studies, that are not available for public review until after the final re-registration), the PMRA sets maximum residue limits (MRLs) for foods and water. MRLs are arrived at by apportioning various estimated contributions to the total permissible exposure. (Pragmatic considerations are also clearly important, as 2015 MRLs for pesticides not registered in Canada are set to accommodate levels in imported foods, with no consideration of health and safety.)

Although MRLs are set not to interfere with agricultural practices in Canada, they may impact trade. For example, pre-harvest desiccation, can result in exceeding MRLs for [barley](#), and suppress germination for making malt. Similarly, grain cadmium may exceed foreign tolerance levels. Of note, Canada sets no standards for this very toxic metal in foods. Canadian foods already contain cadmium exceeding other nations’ standards, and it is urgent to address whether levels of toxic metals are increasing in foods as a result of glyphosate use. Interestingly, [cadmium is restricted in cosmetics](#).

In a process of circular reasoning, the MRLs are factored into data similar to that that was used to create the MRLs in the first place, and then the aggregate exposures are found to be “acceptable.” In a re-evaluation, the effects of MRLs might better be measured against food contamination levels and trends (of both herbicide and toxic elements), biomarkers (e.g. DNA damage, and glyphosate in bodily fluids), and health endpoints seen elsewhere such as kidney disease, cancers, and birth defects.

### **A Data-Deficient Re-Assessment**

Despite generalized statements in the PVRD, the federal government is not monitoring glyphosate in crops (Canadian Grains Commission), in foods (Canadian Food Inspection Agency), in citizens (Canadian Health Measures survey), nor water (although a small Quebec study reported increasing levels over time in waterways, associated with soybean crops). PCN has been repeatedly requesting data from the PMRA on glyphosate in the environment, foods, wildlife, people, anywhere in Canada, since November 2014, with no data in response. It was noted in PRVD 2015-01 that 1990s US dietary data fulfilled data requirements, but it is inconceivable that a pesticide that is used in many-fold greater quantities than in the 1990s would not have increased in food as well.

## The Opportunity of a Re-Evaluation

A *re*-evaluation is an opportunity to assess effectiveness of previously set limits for pesticide use. Measured levels and trends in foods, water, people and the environment, and pesticides sales and use should be reported. Some of these aspects are currently contained in the US Registration Evaluation Documents. As well, levels and trends of toxic elements (e.g. cadmium, that is naturally high in areas of the prairies, and in Canadian potash), and trends of associated biomarkers and diseases are required to assess real-life impacts. Ecological/agronomical measures might include yields over the long term with and without glyphosate, weed resistance, crop diseases (e.g. *Fusarium* levels) and need for inputs. Nothing of the sort is in PRVD2015-01.

A re-evaluation is also an opportunity to revisit the value of a pesticide, that may be affected by resistant weeds, killing non-target species, and needs for other crop inputs over time.

Going forward, it is essential to monitor pesticides and public health so ensure that we have in hand necessary information for future decision-making.

## In conclusion

Canada is missing out. In Europe, South America and Asia, glyphosate uses are being restricted to protect public health, for reasons that are not broached by the PMRA.

PVRD2015-01 is not a scientifically credible re-evaluation of glyphosate hazards or risks. Substantial issues are not addressed, and crucial data is absent (and we fear non-existent). This PVRD does not demonstrate, as the PCPA (2002) requires, “reasonable certainty that **no** harm to human health, future generations or the environment will result from exposure to or use of the product ...” (emphasis added). In the interim, as evidence accrues and PMRA review processes and capacity improve, while further evidence and evidence-gathering is set up, steps in the right direction would include comprehensive, transparent, systematic review and weighing of evidence in all the PMRAs endeavours; and ongoing data collection with public availability, to monitor regulated substances and whether measures are indeed protecting the environment, and health of Canadians.

We wrote further on the topic of glyphosate here: <http://www.preventcancer.ca/the-worlds-most-used-weed-killer-is-probably-carcinogenic-so-what>

Please do not hesitate to ask, if we may assist further in this matter. We have an extensive references database, with which to justify all statements you feel require substantiation.

Prevent Cancer Now is a Canadian national group with over 6000 followers, working to eliminate preventable causes of cancer.

Respectfully submitted,

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## References (more available upon request)

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3. Barański M, Srednicka-Tober D, Volakakis N, Seal C, Sanderson R, Stewart GB, et al. Higher antioxidant and lower cadmium concentrations and lower incidence of pesticide residues in organically grown crops: a systematic literature review and meta-analyses. *Br J Nutr*. 2014 Jun 26;118:1–18.