



Know your environment.
Protect your health.

Environmental Working Group Comments to
The Agency for Toxic Substance and Disease Registry (ATSDR) on
The Draft Toxicological Profile for Glyphosate

Docket ID: ATSDR-2019-0001

Submitted on May 8, 2019

The Environmental Working Group (EWG), a nonprofit research and policy organization with headquarters in Washington, D.C., is pleased to provide comments on the ATSDR Draft Toxicological Profile for Glyphosate that was published in April 2019.

EWG commends ATSDR on providing a thorough and comprehensive review of the current science regarding exposure to glyphosate as well as to glyphosate-based formulations and toxicological effects associated with this herbicide. There are three areas where we would like to provide additional comment, which will strengthen the Toxicological Profile for glyphosate and add further scientific depth to this important risk assessment document.

1. EWG disagrees with the minimal risk level (MRL) of 1 mg/kg/day established by ATSDR and recommends that ATSDR adopt a risk level that would protect against cancer risk due to glyphosate.
2. EWG urges ATSDR to include recent studies on glyphosate cancer risk and on harm to reproductive health due to glyphosate exposure.
3. EWG supports the recommendation of increased monitoring of glyphosate exposure via food and water, especially for children. We particularly recommend further study of children's exposure to glyphosate from food sprayed with glyphosate prior to harvesting.

1. EWG disagrees with the minimal risk level (MRL) of 1 mg/kg/day established by ATSDR and recommends that ATSDR adopt a risk level that would protect against cancer risk due to glyphosate.

EWG strongly agrees with ATSDR's statement that "a possible association between exposure to glyphosate and risk of non-Hodgkin's lymphoma could not be ruled out." As summarized by ATSDR, eight epidemiological studies have assessed the use of glyphosate-based herbicides by agricultural workers and risk of non-Hodgkin's lymphoma (Table 2-8 and Figure 2-4). Most of these studies find some association between glyphosate exposure and elevated risk of non-Hodgkin's lymphoma.



Know your environment.
Protect your health.

Importantly, the increased risk identified in two individual studies was greatest when exposure dose, such as number of application days, was considered. Correlation between risk and exposure dose points toward the possibility of defining a dose-response relationship between glyphosate and cancer, a key component used in risk assessment and weight of evidence evaluations.^{1,2}

Four separate meta-analyses published between 2014 and 2019 have identified a statistically significant 30 to 50 percent increase in the risk of non-Hodgkin's lymphoma due to glyphosate exposure.^{3,4,5,6} ATSDR's draft profile for glyphosate includes discussion of three meta-analyses assessing glyphosate exposure and cancer risk in agricultural workers, all with positive findings, and a fourth meta-analysis should be included in the references (see Section 2 below).

Additionally, glyphosate exposure has been associated with other lymphohematopoietic cancers, including acute myeloid leukemia as reported in a recent publication from the Agricultural Health Study,⁷ and multiple myeloma.⁵ Lastly, the association between glyphosate and cancer is supported by several studies in rats and mice that reported elevated rates of malignant tumors in animals treated with glyphosate.

In light of glyphosate's cancer risk, EWG disagrees with the ATSDR's proposal to derive a risk level for glyphosate based on a non-cancer endpoint. Instead, we urge the agency to derive an MRL using a cancer-based study.

We particularly recommend that the ATSDR follow the example of the glyphosate assessment published by the California Office of Environmental Health Hazard Assessment (OEHHA). The state of California has published a cancer-based "No Significant Risk Level" for glyphosate.⁸ This cancer-based risk level is significantly

¹ Eriksson M, Hardell L, Carlberg M, et al. 2008. Pesticide exposure as risk factor for non-Hodgkin lymphoma including histopathological subgroup analysis. *Int J Cancer* 123(7):1657-1663. 10.1002/ijc.23589.

² McDuffie HH, Pahwa P, McLaughlin JR, et al. 2001. Non-Hodgkin's lymphoma and specific pesticide exposures in men: Cross-Canada study of pesticides and health. *Cancer Epidemiol Biomarkers Prev* 10(11):1155-1163. _

³ Zhang L, Rana I, Shaffer RM, Taiolo E, Sheppard L. 2019. Exposure to glyphosate-based herbicides and risk for non-Hodgkin Lymphoma: a meta-analysis and supporting evidence. *Mutation Research/Reviews in Mutation Research*, in press. Available at <https://www.sciencedirect.com/science/article/pii/S1383574218300887>

⁴ Schinasi L, Leon ME. 2014. Non-Hodgkin lymphoma and occupational exposure to agricultural pesticide chemical groups and active ingredients: A systematic review and meta-analysis. *Int J Environ Res Public Health* 11(4):4449-4527.

⁵ Chang ET, Delzell E. 2016. Systematic review and meta-analysis of glyphosate exposure and risk of lymphohematopoietic cancers. *J Environ Sci Health Part B* 51(6):402-434.

⁶ IARC. 2017. Glyphosate. Some organophosphate insecticides and herbicides. In: *IARC monographs on the evaluation of carcinogenic risks to humans*. Volume 112. International Agency for Research on Cancer. <http://monographs.iarc.fr/ENG/Monographs/vol112/mono112.pdf>. June 4, 2018.

⁷ Andreotti G, Koutros S, Hofmann JN, et al. 2018. Glyphosate use and cancer incidence in the Agricultural Health Study. *J Natl Cancer Inst* 110(5):509-516.

⁸ California Office of Environmental Health Hazard Assessment, Initial Statement of Reasons Title 27, California code of regulations proposed amendment to: section 25705(b) specific regulatory levels posing no significant risk glyphosate safe



more protective compared to the ATSDR's proposed Minimal Risk Level for glyphosate, which is based on a non-cancer endpoint.

Furthermore, EWG scientists recommend adding an additional tenfold children's health safety factor to account for the potential increased susceptibility to glyphosate exposures occurring before birth and in the early years of life. Such a safety factor is supported by the 1993 National Research Council Report, "Pesticides in the Diets of Infants and Children,"⁹ and the 2009 OEHHA study, "In Utero and Early Life Susceptibility to Carcinogens."¹⁰ Finally, EWG recommends a one-in-one-million cancer risk standard for glyphosate, a risk level health agencies and risk assessors typically consider *de minimis*.

Overall, EWG believes that a children's health-protective, one-in-one-million cancer risk benchmark for glyphosate exposure should be set at an intake dose of 0.01 mg/day.

2. EWG urges ATSDR to include recent studies on glyphosate cancer risk and on harm to reproductive health due to glyphosate exposure.

Three additional research articles should be added to the final ATSDR assessment. Since the publication of the draft report, a fourth meta-analysis of glyphosate exposure and cancer risk by Zhang et al. (2019) found a 41 percent increase in risk of non-Hodgkin's lymphoma for individuals in the highest glyphosate exposure group.¹¹ These findings corroborate those of previous meta-analyses and provide more scientific evidence linking glyphosate exposure to cancer risk.

In addition, the report reviews the non-cancer health effects resulting from glyphosate exposure, including gastrointestinal effects, harm to the liver and kidney, and developmental impacts. A recent publication from scientists at the Ramazzini Institute found significant adverse reproductive outcomes with low dose glyphosate exposure.¹² Such findings included increased anogenital distance and increased

drinking water and toxic enforcement act of 1986 proposition 65. 2017. Available at <https://oehha.ca.gov/media/downloads/proposition-65/chemicals/glyphosate032917isor.pdf>

⁹ National Research Council of National Academies, Pesticides in the Diets of Infants and Children. 1993. Available at www.nap.edu/catalog/2126/pesticides-in-the-diets-of-infants-and-children

¹⁰ California Office of Environmental Health Hazard Assessment, In Utero and Early Life Susceptibility to Carcinogens. The Derivation of Age-at-Exposure Sensitivity Measures. 2009. Available at oehha.ca.gov/media/downloads/cnr/appendixjearly.pdf

¹¹ Zhang L, Rana I, Shaffer RM, Taiolo E, Sheppard L. 2019. Exposure to glyphosate-based herbicides and risk for non-Hodgkin Lymphoma: a meta-analysis and supporting evidence. Mutation Research/Reviews in Mutation Research, in press. Available at <https://www.sciencedirect.com/science/article/pii/S1383574218300887>

¹² Manservigi F, Lesseur C, Panzacchi S, Mandrioli D, Falcioni L, Bua L, Manservigi M, Spinaci M, Gaeleati G, Mantovani A, Lorenzetti D, Miglio R, Andrade AM, Kristensen DM, Perry MJ, Swan SH, Chen J, Belpoggi F. 2019. The Ramazzini Institute 13-week pilot study glyphosate-based herbicides administered at human-equivalent dose to Sprague Dawley rats: effects on development and endocrine system. Environ Health. 18(1):15.



plasma thyroid stimulating hormone in glyphosate-treated males. We urge ATSDR to include these important findings in the final toxicological profile for glyphosate, given that they occurred in animals treated with 1.75 mg/kg/day of glyphosate, a dose less than double the ATSDR's proposed minimal risk level (1 mg/kg/day) and 100 times lower than the ASTDR identified point of departure. Another recent study found harm to the male reproductive system, also in animals treated with low doses of glyphosate.¹³

3. EWG supports the recommendation of increased monitoring of glyphosate exposure via food and water, especially for children. We particularly recommend further study of children's exposure to glyphosate from food sprayed with glyphosate prior to harvesting.

In the past decade, the use of glyphosate has soared, with more than 250 million pounds sprayed in the U.S. annually, as data from the U.S. Geological Survey show.¹⁴ Yet the EPA and the Agriculture Department do not monitor glyphosate residues on most food crops, though Americans' exposures have increased dramatically. Between 2014 and 2016, at least 70 percent of American adults surveyed had detectable traces of glyphosate in their bodies, compared to 12 percent of American adults between 1993 and 1996.¹⁵ The actual current exposure levels might be higher because glyphosate has not been included in nationwide biomonitoring studies and there are no comprehensive datasets on glyphosate intake for young children and teenagers.

We agree with the agency's recommendations for improved biomonitoring of glyphosate in humans as well as "monitoring of children's exposure to glyphosate." To fill this data gap, EWG has pursued its own testing of products made with oats, a crop often treated with glyphosate pre-harvest, especially products marketed to children, and we determined that glyphosate contamination of such foods is widespread.¹⁶ In total, EWG has tested 73 samples of 41 conventional oat-based products in the past year. Ninety-seven percent of products had detectable levels of glyphosate. Approximately 75 percent of products had glyphosate levels that, in the assessment of EWG scientists, are higher than the *de minimis* cancer risk. This

¹³ Pham TUH, Derian L, Kervarrec C, Kernanec P, Jegou B, Smagulova F, Gely-Pernot A. 2019. Perinatal Exposure to Glyphosate and a Glyphosate-Based Herbicide Affect Spermatogenesis in Mice. *Toxicological Sciences*. 169(1): 260-271.

¹⁴ U.S. Geological Survey. 2018. Estimated Annual Agricultural Pesticide Use. Available at <https://water.usgs.gov/nawqa/pnsp/usage/maps/>

¹⁵ Mills PJ, Kania-Korwel I, Fagan J, McEvoy LK, Laughlin GA, Barrett-Connor E. 2017. Excretion of the Herbicide Glyphosate in Older Adults Between 1993 and 2016. *JAMA*. 318(16): 1610-1611.

¹⁶ Environmental Working Group. Complete Results of EWG's 2018 Glyphosate tests in oat cereals and snacks. Available at https://cdn3.ewg.org/sites/default/files/u352/EWG_Glyphosate-2_Table_Full_C02.pdf?_ga=2.30478655.1691627321.1556114025-1166909982.1546543464



Know your environment.
Protect your health.

research by EWG, as well as studies conducted by other researchers, points to an immediate need for glyphosate-exposure monitoring studies in the general population, and especially for children.

We thank you for this opportunity to comment.

Submitted on behalf of Environmental Working Group,

Alexis Temkin, Ph.D.
Toxicologist
Environmental Working Group
1436 U St NW, Suite 100
Washington DC 20009