April 30, 2018

COMMENTS SUBMITTED FROM

THE NATURAL RESOURCES DEFENSE COUNCIL

On the Draft Human Health and Ecological Risk Assessments for Glyphosate

EPA-HQ-OPP-2009-0361-0066

On the EPA's Preliminary Ecological Risk Assessment for Glyphosate and its Salts

Docket EPA-HQ-OPP-2009-0361-0077

Submitted to the docket and by email to glyphosateRegReview@epa.gov

We submit these comments on behalf of the Natural Resources Defense Council (NRDC) and our more than 3 million members and activists. The Environmental Protection Agency (EPA) has utterly failed to evaluate the human health risks including cancer and noncancer risks, and the ecological risk that glyphosate poses to wildlife including monarch butterflies. Since the last ecological risk assessment was completed for glyphosate in 1993, its use has skyrocketed resulting in glyphosate being the most widely used pesticide in the US. In that time, mounting evidence has pointed to adverse human health effects as well as the precipitous decline of the North American monarch butterfly population. Based on the combined data, the EPA needs to severely restrict the use of glyphosate and glyphosate-based products immediately.

NRDC has submitted previous comments to EPA on glyphosate and its mixes and formulations including Enlist Duo. Our previous comments are incorporated in full by reference herein, and the following documents are attached:

- Portier C. 2017. Rebuttal report. Exhibit 96. Case 3:16-md-02741-VC Document 655-6 Filed 10/28/17 https://usrtk.org/wp-content/uploads/2017/10/Rebuttal-report-of-chris-potier.pdf
- Comment submitted by the Jennifer Sass, PhD, to the December 13-16, 2016 FIFRA SAP meeting. Document ID: EPA-HQ-OPP-2016-0385-0501. www.regulations.gov/document?D=EPA-HQ-OPP-2016-0385-0501
- Additional Comments of Christopher J. Portier. PhD. to the December 13-16, 2016 FIFRA SAP meeting. Document ID: EPA-HQ-OPP-2016-0385-0501. www.regulations.gov/document?D=EPA-HQ-OPP-2016-0385-0501

EPA CONTINUES TO DENY SCIENTIFIC EVIDENCE, EXPERT RECOMMENDATIONS OF CANCER RISKS

EPA is classifying glyphosate as "Not Likely" to cause cancer in humans, despite studies reporting elevated cancer risk in humans and laboratory animals. EPA is disregarding the recommendations of some FIFRA SAP Panelists that "Overall" rejected EPA's classification of "not likely" carcinogenic, and instead recommended it be classified as having a suggestive link to cancer (SAP 2017 p. 47-48). Some SAP Panelists referenced the EPA (2005) Cancer Guidelines as supporting the conclusion of 'Suggestive Evidence of Cancer Potential' (SAP, p. 48). EPA should classify glyphosate and its formulated products as posing a risk of cancer, consistent with overall recommendations of some SAP Panelists, its own Cancer Guidelines, and the International Agency for Research on Cancer that classified it as "probably" carcinogenic to humans (Group 2A) (IARC 2017, Vol 112).

Previous Cancer Assessments: EPA Denies Agency Scientists and Scientific Evidence of Cancer Risks

In 1985 EPA proposed to classify glyphosate as a possible human carcinogen (Group C), based on evidence of a rare form of kidney tumors (renal tubule adenomas) in male CD-1 mice in a Monsanto-sponsored two-year chronic feeding study (Knezevich and Hogan, 1983).[1] The studies reported: 0/49 in the control group; 0/49 at the low-dose; 1/50 at the mid-dose; 3/50 at the high dose (TXR No. 0004370). In an Agency memo in February, 1984, EPA toxicologist William Dykstra concluded that, "Review of the mouse oncogenicity study indicates that glyphosate is oncogenic, producing renal tubule adenomas, a rare tumor, in a dose-related manner."(Dykstra memo, Feb 1984)

Monsanto, the Registrant, opposed the EPA expert conclusions, claiming that historical data from Bio/dynamics lab and two other test labs showed that the kidney tumors were a more common occurrence than indicated by the experimental results (no tumors in the control and low-dose groups), and therefore not treatment-related. But, EPA statistician Herbert Lacayo of the toxicology branch pushed back (Lacayo memo, Feb 1985):

- "With respect to historical data we note the large number and variety of factors which influence the life history of rodents in chronic studies. Hence, it is generally agreed that the most relevant

[1] Knezevich and Hogan, 1983, Study MRID 00130406

historical controls are experiments from the subject laboratory studied within a 3 to 4 year 'window'.

- "We disagree with the Registrants position. First, even if one did analyze the study at the .01 level as they [Monsanto] suggest it would still result (using the same mathematics as before) in seeing 18 mice out of 100 with tumors."
- "The Registrant wishes to avoid false positives while those concerned with the public health wish to avoid false negatives. Hence, for this reason alone Monsanto's argument is unacceptable."
- "False positive results are less likely to occur with rare tumors… and the tumors in question are rare."
- "Finally, we mention that none of the tumors occurred in the control or low dose groups. Instead there was one at 5000 ppm and 3 at 30000 ppm dose level. This together with the previous comments make it likely that there is a dose-tumor relationship for Glyphosate."

The EPA internal memo concludes with the following: "Viewpoint is a key issue. Our [EPA] viewpoint is one of protecting the public health when we see suspicious data. it [sic] is not our job to protect registrants from false positives. We sympathyze [sic] with the Registrants problem; but they will have to demonstrate that this positive result is false." (Lacayo memo, Feb 1985)

The following month an 8-member team from the Toxicology Branch of EPA issued a "consensus review of glyphosate" that the kidney cancers seen in the male CD-1 mice were due to glyphosate treatment, "since their frequency was not consistent with the historical controls and there is a trend indicating dose dependency" (underline in original) (Tox Branch Consensus memo, March 1985).

Thus, in 1985 EPA classified glyphosate as a "possible human carcinogen" (Group C) (SAP Feb 1986; Monsanto memo April 1985) This is similar to the 2015 classification by IARC of "probable human carcinogen" (Group 2A) based on limited evidence for non-Hodgkin lymphoma (NHL) in humans, and sufficient evidence of carcinogenicity in animal studies (IARC 2015 press release; IARC 2017 Vol 112).[2]

In order to weaken the scientific evidence of cancer in animal studies, Monsanto had to show there is no statistical differences between the control or unexposed groups, and the groups treated with

[2] Note that the IARC assessment was conducted and completed in 2015, and made public at that time. The final Monograph was published in 2017, in Volume 112

glyphosate. It could do this by either increasing the number of tumors in the control groups or decreasing the number of tumors in the treatment groups. It did the former. In 1985 the registrant, Monsanto hired a pathologist "to persuade the agency that the observed tumors are not related to glyphosate" according to an internal Monsanto memo written prior to the pathologist's review (Monsanto memo April 1985). As expected, the pathologist determined that glyphosate did not cause the observed tumors in the exposed mice by identifying new, very small, almost invisible tumors in the control group of mice (see Gillam, 2017).[3]

A review by EPA's Scientific Advisory Panel the next year recommended classifying glyphosate as "not classifiable as to human carcinogenicity" (Group D) and recommended additional research. (SAP Feb 1986) The SAP particularly noted that the tumors in the high dose group were rare, and remained statistically significant when compared to either concurrent (within the experiment) or historical controls, although the Panel recommended that EPA use concurrent controls, following standard procedures.

Overriding its own Agency experts and its external scientific advisors, EPA ultimately sided with Monsanto and downgraded the classification to evidence of non-carcinogenicity in humans (Group E) in 1991 – two Agency reviewers did not sign the report, one wrote in 'non-concur' where a signature was expected (EPA Oct 1991).

Subsequently, documents released through litigation reveal that the EPA Pesticide Office had a disturbing level of communication and collaboration between Monsanto and senior EPA official Jess Rowland, who headed up the EPA Cancer Assessment Review Committee for glyphosate and many other pesticides. Monsanto internal emails note that Rowland "could be useful as we move forward with ongoing glyphosate defense". Rowland has since left EPA, but concerns of collusion sparked an investigation by the EPA Inspector General that is still ongoing and may, unfortunately, never be made public. As several retired US government cancer experts recently wrote, "the interference by economic interests in cancer evaluations conducted by public heath institutions do not bode well for the free flow

[3] Gillam C. Of Mice, Monsanto And A Mysterious Tumor. HuffPost 06/08/2017. https://www.huffingtonpost.com/entry/of-mice-monsanto-and-a-mysterious-tumor_us_5939717fe4b014ae8c69de40

of scientific information that informs and protects the public and workers from clear risks of cancer" (Infante et al 2018).[4]

Current Cancer Assessment: EPA Fails to Consider Evidence of Blood-based (Non-Solid) Tumors in People Exposed to Glyphosate-Based Products, Ignores SAP Recommendations

Six epidemiologic studies that evaluated a link between real-world exposure to glyphosate-based products and the risk of non-Hodgkin's Lymphoma (NHL) in people were reviewed by EPA in its Revised Glyphosate Issue Paper of Carcinogenic Potential (EPA 2017, Document ID EPA-HQ-OPP-2009-0361-0073, herein referred to as EPA 2017 Cancer Issue Paper)[5] – five retrospective case-control studies and one prospective cohort study. The same studies were also reviewed by non-Agency scientific experts, with the following results:

- The International Agency for Research on Cancer (IARC 2017)[6] concluded in a consensus report that the cancer evidence from studies of people comprised "limited evidence" for risk of cancer (NHL), which was supported by "sufficient" evidence of carcinogenicity in animal studies;
- A Monsanto-sponsored meta-analysis by Chang and Delzell (2016) reported a positive and marginally statistically significant association between any versus no use of glyphosate and risk of NHL (meta-RR = 1.3, 95% confidence interval (CI) = 1.0–1.6, based on six studies) and multiple myeloma (meta-RR = 1.4, 95% CI = 1.0–1.9; four studies);[7]
- The EPA FIFRA Scientific Advisory Panel did not reach a consensus, but a large proportion of Panelists concluded that there is suggestive evidence that glyphosate is a human carcinogen (SAP 2017, p. 45).

In October 2017 the Lancet Commission on Pollution and Health issued a consensus statement identifying pollution from chemicals and pesticides as the "largest environmental cause of disease and death in the world today, responsible for an estimated 9 million premature deaths" (Landrigan et al

[4] Infante PF, Melnick R, Vainio H, Huff J. Commentary: IARC Monographs Program and public health under siege by corporate interests. Am J Ind Med. 2018;61:277–281. https://doi.org/10.1002/ajim.22811

[5] All EPA documents available at: https://www.epa.gov/ingredients-used-pesticide-products/draft-human-health-and-ecological-risk-assessments-glyphosate

[6] IARC 2017. Volume 112. Some Organophosphate Insecticides and Herbicides. http://monographs.iarc.fr/ENG/Monographs/vol112/index.php

[7] Chang ET, Delzell E. Systematic review and meta-analysis of glyphosate exposure and risk of lymphohematopoietic cancers. J Environ Sci Health 2016;51(6):402-34.

2017). [8] The paper devotes two paragraphs to glyphosate, highlighting cancer concerns: "Epidemiological studies of agricultural workers who were exposed occupationally to glyphosate and other herbicides have found evidence for increased occurrence of non-Hodgkin lymphoma in these people." The authors of this report represent dozens of recognized medical and scientific experts from around the world, and the report is published in the Lancet, one of the most prestigious medical journals in the world.

Oddly, even EPA seems to acknowledge that the studies are all positive for an elevated risk of NHL cancer in exposed people. EPA presents the following figure in its most recent cancer assessment (EPA 2017 Cancer Issue Paper, p. 65 Fig. 3.2):

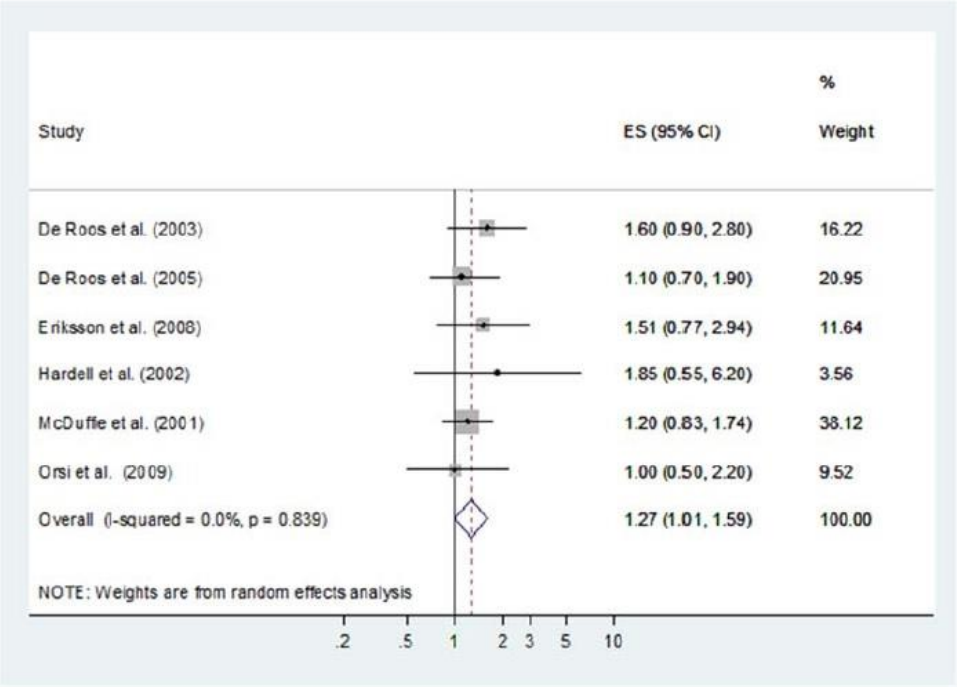

Figure 3.2. Forest plot of effect estimates (denoted as ES for effect sizes) and associated 95% confidence intervals (CI) for non-Hodgkin lymphoma (NHL).

[8] The Lancet Commission on pollution and health. Philip J Landrigan, Richard Fuller, Nereus J R Acosta, Olusoji Adeyi, Robert Arnold, Niladri (Nil) Basu, Abdoulaye Bibi Baldé, Roberto Bertollini, Stephan Bose-O'Reilly, Jo Ivey Boufford, Patrick N Breysse, Thomas Chiles, Chulabhorn Mahidol, Awa M Coll-Seck, Maureen L Cropper, Julius Fobil, Valentin Fuster, Michael Greenstone, Andy Haines, David Hanrahan, David Hunter, Mukesh Khare, Alan Krupnick, Bruce Lanphear, Bindu Lohani, Keith Martin, Karen V Mathiasen, Maureen A McTeer, Christopher J L Murray, Johanita D Ndahimananjara, Frederica Perera, Janez Potočnik, Alexander S Preker, Jairam Ramesh, Johan Rockström, Carlos Salinas, Leona D Samson, Karti Sandilya, Peter D Sly, Kirk R Smith, Achim Steiner, Richard B Stewart, William A Suk, Onno C P van Schayck, Gautam N Yadama, Kandeh Yumkella, Ma Zhong. The Lancet, Vol. 391, No. 10119

EPA dismisses the evidence from these half-dozen studies shown in its Figure 3.2 in part by noting that the studies fail to adjust for occupational exposure to diesel exhaust fumes, solvents, livestock and other farm animals, UV radiation, and 'unknown factors' which EPA proposes as "highly likely confounders in NHL studies" that could cause the increased risk of NHL among study subjects (EPA 2017 Cancer Issue Paper, p.65). This is a mistaken understanding of a confounder – such factors could only confound the results if they cause NHL, and if they are not randomly distributed across both the exposed and unexposed populations. EPA has presented no information that would suggest that the study subjects with high glyphosate exposures are in the sunlight or around livestock any more than the study subjects with little or no glyphosate exposures. In addition, EPA has presented no information that would suggest that any potential confounding would be in the direction of artificially inflating the cancer risks, rather than in the direction of masking them. The SAP specifically disagreed with EPA's presumption that the direction of confounding is to inflate any true effect of glyphosate; the Panel emphasized that confounding can be in either direction, to inflate or mask a true cancer risk (SAP 2017, p. 29).

EPA also rationalizes its dismissal of the epidemiologic evidence of cancer by noting that recall bias and missing data are frequent limitations in studies (EPA 2017 Cancer Issue Paper, p.66). This concern seems to come primarily from one SAP member, and the SAP report makes it clear that it does not apply to all the epidemiologic studies; "This analysis does not imply that these or all case-control studies in general suffer from recall bias" (SAP p. 31). In other words, EPA has presented no evidence to support or suggest that there is recall bias or missing data at sufficient amounts to alter the study results. EPA should not dismiss evidence of harm based on unsubstantiated suppositions. "Declaring a chemical as not hazardous, or reducing a level of health protection, should require validation, not speculation" (Melnick et al 2003).[9]

Both Monsanto and EPA frequently support their no-cancer position by citing a long-term prospective epidemiologic study of pesticide applicators in the Midwest, called the Agriculture Health Study (AHS), conducted by the NIH National Cancer Institute, that does not report a link between glyphosate exposure and NHL.[10] However, a recent update of the cohort did report a possible association between

[9] Melnick RL, Kamel F, Huff J. Declaring chemicals "not carcinogenic to humans" requires validation, not speculation. Environ Health Perspect. 2003 Apr;111(4):A203-4.
[10] EPA ranks the quality of this study as "moderate". EPA 2017 Cancer Issue Paper, Table 3.2, p. 34.

glyphosate and another type of blood cancer called acute myeloid leukemia (AML) (Andreotti et al 2017).[11] The study authors warn that, "Given the prevalence of use of this herbicide worldwide, expeditious efforts to replicate these findings are warranted" (Andreotti et al 2017).[12] The increase risk of AML in the study was over 2-fold higher in highest exposed applicators compared with the never exposed applicators. The possible link with leukemia should be very concerning to the public and particularly to pesticide applicators, because AML is a very serious fast-growing cancer, with only about one-quarter of the people that have it surviving longer than 5 years. Although EPA acknowledges these new data, it considers them too limited to inform the assessment and simply states it will continue to follow the literature (EPA 2017 Cancer Issue Paper, Section 3.5.2 (1), p. 53). However, at the very least, these data should prevent EPA from classifying glyphosate as posing no cancer risk.

SAP Panelists recommended that EPA put more weight on the meta-analyses as they are useful for overcoming the limitations, biases, and potential confounding across many of the epidemiology studies (SAP 2017 p. 40, 42, 44, 47). The meta-analysis pools data across studies and thereby provides increased the statistical power, strengthened by the observation of a dose-response relationship in two studies, Eriksson et al (2008) and McDuffie et al (2001) (SAP 2017 p. 40, 42, 44, 47). Other than adding a meta-risk value to its Figure 3.2, EPA disregarded the SAP recommendations (EPA 2017 Response to SAP, p. 6). At the very least, the meta-analysis of pooled studies showing elevated NHL risk in exposed people should prevent EPA from classifying glyphosate as posing no cancer risk.

In its final Issue Paper, EPA dismisses much of the systematic reviews and meta-analyses by proposing – again without any evidence – that, "publication bias may play a role in this evaluation given there is a tendency to only publish positive results [data showing a cancer risk] and potential concerns regarding glyphosate have only been raised in recent years" (EPA 2017 Cancer Issue Paper, p. 64). EPA provides no reference or support for this statement, which is not only pure conjecture but there is evidence that the opposite is true. That is, there is a bias for published industry-sponsored studies to report no harm associated with toxic chemicals - see for example: Bero et al 2016; Sass 2006; Vom Saal and Hughes

[11] Andreotti G, Koutros S, Hofmann JN, Sandler DP, Lubin JH, Lynch CF, Lerro CC, De Roos AJ, Parks CG, Alavanja MC, Silverman DT, Beane Freeman LE. Glyphosate Use and Cancer Incidence in the Agricultural Health Study. J Natl Cancer Inst. 2017 Nov 9. doi: 10.1093/jnci/djx233.

[12] Andreotti G, Koutros S, Hofmann JN, Sandler DP, Lubin JH, Lynch CF, Lerro CC, De Roos AJ, Parks CG, Alavanja MC, Silverman DT, Beane Freeman LE. Glyphosate Use and Cancer Incidence in the Agricultural Health Study. J Natl Cancer Inst. 2017 Nov 9. doi: 10.1093/jnci/djx233.

2005; Hayes 2004; Ong and Glantz 2001; Deerfield et al 1993.[13] EPA has no basis to disregard the published evidence linking glyphosate and glyphosate-based products to NHL cancer, and no justification for disregarding the recommendations of its SAP to consider the cancer evidence in the available studies and meta-analyses.

Many SAP Panelists specifically disagreed with EPA's conclusions, emphasizing that, "assessing potential bias is a challenge that makes the overall evidence base preliminary; overall the NHL result is suggestive of the carcinogenic potential of glyphosate" (SAP 2017, p. 47, underline not in original). Many Panelists rejected EPA's classification of "not likely" carcinogenic, instead recommended it be classified as having a suggestive link to cancer while acknowledging that "study limitations and concerns of potential biases remain" (SAP 2017 p. 47-48). The Panelists noted that this is supported by the EPA Cancer Guidelines, that define suggestive evidence as, "evidence of a positive response in studies whose power, design, or conduct limits the ability to draw a confident conclusion" (SAP 2017, p. 48; EPA 2005, p. 83). One Panelist, Dr. Lianne Sheppard, emphasized that, "It is clear to me that we can't conclude, as the Agency has done, that it's not a carcinogen. That's just completely inappropriate based on their criteria" (SAP Transcript, p. 1192)

Unfortunately, EPA uses the limitations in the studies as its excuse to discard cancer evidence. EPA instead concludes that since, "the agency cannot exclude chance and/or bias as an explanation for observed associations in the database", it cannot draw a conclusion regarding the association between glyphosate exposure and risk of non-Hodgkin's Lymphoma in people (EPA 2017 Cancer Issue Paper, p. 68). However, not being able to make confident conclusions is not a valid reason to classify glyphosate as posing no cancer risk; calling glyphosate safe is a conclusion, and it is one that puts the health of people and wildlife at significant risk! EPA, in its efforts to bury cancer evidence, is terribly misusing the Bradford Hill criteria, particularly for a series of studies with small rate ratios or where bias including

[13] Bero L, Anglemyer A, Vesterinen H, Krauth D. The relationship between study sponsorship, risks of bias, and research outcomes in atrazine exposure studies conducted in non-human animals: Systematic review and meta-analysis. Environment international. 2016;92-93:597-604.
Dearfield KL, Stack HF, Quest JA, Whiting RJ, Waters MD. A survey of EPA/OPP and open literature data on selected pesticide chemicals tested for mutagenicity. I. Introduction and first ten chemicals. Mutat Res. 1993;297(3):197–233.
Hayes T. There is no denying this: defusing the confusion about atrazine. BioScience. 2004;54(12):1138–1149.
Sass J. Credibility of Scientists: Conflict of Interest and Bias. Environmental Health Perspectives. 2006;114(3):A147-A148.
Ong EK, Glantz SA. Constructing "sound science" and "good epidemiology": tobacco, lawyers, and public relations firms. Am J Public Health. 2001;91(11):1749–1757.
vom Saal FS, Hughes C. An extensive new literature concerning low-dose effects of bisphenol A shows the need for a new risk assessment. Environ Health Perspect. 2005;113:926–933.

confounding is possible. In those instances, Hill states, "We must not be too ready to dismiss a cause-and-effect hypothesis merely on the grounds that the observed association appears to be slight. There are many occasions in medicine when this is in truth so" (reported in Neutra, Cranor, Gee 2018). This is directly applicable to the NHL studies shown in EPA's Figure 3.2 above, where the cancer effect size is not large, but the confidence interval is clearly weighted towards a positive association (elevated cancer risk) with exposure to glyphosate-based products.

EPA Disregards Evidence of Blood-based Tumors in Male CD-1 Mice, Ignores SAP Recommendations

EPA concludes that "none of the tumors evaluated in individual rat and mouse carcinogenicity studies are treatment-related" due to a (a) lack of pairwise statistical significance, (b) lack of a monotonic dose response, (c) absence of preneoplastic or related non-neoplastic lesions, (d) no evidence of tumor progression, (e) and/or historical control information (when available) (EPA 2017 Cancer Issue Paper, p. 97). This conclusion is a rejection of the recommendation of some SAP Panelists to: "Discuss the suggestive association of NHL risk and glyphosate exposure in humans, with the supporting evidence in mouse studies (the positive and monotonic trends of increased lymphomas reported in Wood 2009b, Sugimoto 1997, Knezevich and Hogan 1983 in female mice, as well as Kumar 2001 in male and female mice) and recent findings on non-genotoxic mechanistic action (e.g. reported from Ford et al 2017)" (SAP, p. 48).

Below I address each of EPA's excuses for discarding experimental evidence of cancer risk:

(a) Statistical test cherry-picking - EPA stated that the results were statistically significant with a trend test but not with other statistical tests (EPA 2017 Cancer Issue Paper, p. 88). However, the SAP pointed out that this violates EPA's Cancer Guidelines, which state that significance in either a trend test or a pairwise test is sufficient to establish significance (EPA 2005 p.46). (SAP, p. 53) EPA responds to the SAP by arguing that this "does not imply that statistical significance alone in an individual test is sufficient to determine that observed tumors are treatment-related… the Agency included both the trend and pairwise analyses" (EPA 2017 SAP Response, p. 7). This argument seems to turn the Cancer Guidelines on its head – EPA is using it to eliminate cancer evidence, not to identify it. EPA is using the test that shows no cancer risk, in lieu of the tests that show cancer risks.

(b) Undue emphasis on lack of clear monotonic response - EPA rejected cancer evidence if it the dose-response was not also monotonic, meaning a steady increase in the number of tumors with an increase in the treatment dose. The EPA Cancer Guidelines say in reference to the Bradford Hill criteria for epidemiologic information that "the absence of an exposure-response relationship does not exclude a causal relationship" (EPA 2005, p. 41). EPA should not have dismissed evidence of harm for this reason. The Cancer Guidelines are consistent with the National Academies report on non-monotonic dose-response relationships for endocrine disruptors (NRC 2014), which recommended that EPA explicitly consider non-monotonic dose-response relationships.[14] Glyphosate in particular has raised red flags among scientific researchers and endocrine experts because it has not been properly tested for endocrine disruption activity, despite some in vitro and whole animal studies suggested that it may interfere with hormone activity.[15]

(c) Undue emphasis on lack of preneoplastic observations - EPA dismissed tumors if preneoplastic changes were not also reported (for example, EPA Cancer Issue Paper, Table 4.20). EPA violated its Cancer Guidelines by turning them upside down regarding the relevance of pre-neoplastic (pre-cancer) tumors. The Guidelines wisely note that the presence of pre-neoplastic tumors may "lend support to the significance of findings for animal carcinogenicity" (EPA 2005 p. 48), whereas EPA uses the lack of reported pre-neoplastic tumors as an excuse to disregard observed tumors. In other words, EPA is interpreting the lack of supporting evidence as confirmative evidence of no harm, even when presented with evidence of harm.

(d) Absence of evidence of tumor progression is not absence of cancer – EPA has dismissed evidence of tumors in mice due to what it describes as a lack of evidence that the tumor would progress from pre-neoplastic to malignancy (EPA 2017 Cancer Issue Paper, p. 90). Three of the mouse studies lasted only 18 months: Kumar 2001 reported dose-dependent increases in renal tubular adenoma and malignant lymphoma; Wood et al 2009 reported dose-dependent increases in malignant lymphoma; Sugimoto 1997 reported a statistically significant trend test increase in malignant lymphoma, hemangiosarcoma,

[14] NRC 2014. Review of the Environmental Protection Agency's State-of-the-Science Evaluation of Nonmonotonic Dose-Response Relationships as they Apply to Endocrine Disruptors. National Research Council. National Academies Press, Washington DC.

[15] Myers JP, Antoniou MN, Blumberg B, Carroll L, Colborn T, Everett LG, Hansen M,Landrigan PJ, Lanphear BP, Mesnage R, Vandenberg LN, Vom Saal FS, Welshons WV,Benbrook CM. Concerns over use of glyphosate-based herbicides and risks associated with exposures: a consensus statement. Environ Health. 2016 Feb 17;15:19.

and renal tubular adenoma.[16] A mouse of 18 months is equivalent to a human of about 30 to 50 years old, hardly long enough to reliably predict a human cancer risk, since about 80% of all human cancers occur in people over the age of 60 (Bucher 2002[17]; Haseman et al. 2001[18]; Kodell et al. 2000[19]). For this reason, the NIEHS cancer experts include higher doses and consider various statistical methods when interpreting study results, with the goal of identifying agents that pose a cancer risk to humans. EPA should not disregard evidence of early cancer or pre-cancer lesions on the basis that it occurred in a test that was likely too short to give the lesions time to progress to full cancer. We would falsely believe that many carcinogens were safe if we only looked in people under the age of 40.

EPA discounted tumors in the highest treatment groups, stating that it exceeded guideline dose recommendations. This violates its Cancer Guidelines which state that "effects seen at the highest doses are assumed to be appropriate for assessment . . . [unless] data demonstrate that the effects are solely the result of excessive toxicity rather than carcinogenicity of the tested agent per se" (EPA 2005 p.140). EPA provides no evidence of excessive toxicity at the high doses and should not have dismissed the cancer evidence for this unsubstantiated claim.

Dr. Christopher Portier, cancer assessment expert and Retired Director of the National Center for Environmental Health/Agency for Toxic Substances and Disease Registry, submitted comments to the SAP presenting the mouse tumor data with standard statistical adjustments for less-than-lifetime bioassays used by the NIEHS National Toxicology Program (Portier 2016, p. 15).[20] After adjusting the study lengths and combining the data for a pooled analysis, the data demonstrated a highly significant trend for excess cancer risk for male mouse kidney cancer, male mouse malignant lymphoma, and hemangiosarcoma in male mice; in addition, trends remain even when high doses are removed from the analysis.[21] Thus, whether or not EPA considers the highest treatment groups, EPA should have considered the tumors in lower treatment groups as providing evidence of cancer risk.

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[16] Clausing P, Robinson C, Burtscher-Schaden H Pesticides and public health: an analysis of the regulatory approach to assessing the carcinogenicity of glyphosate in the European Union J Epidemiol Community Health Published Online First: 13 March 2018. doi: 10.1136/jech-2017-209776

[17] Bucher JR. The National Toxicology Program rodent bioassay: designs, interpretations, and scientific contributions. Ann NY Acad Sci.2002;982:198–207

[18] Haseman J, Melnick R, Tomatis L, Huff J. Carcinogenesis bioassays: study duration and biological relevance. Food Chem Toxicol. 2001;39:739–744

[19] Kodell RL, Lin KK, Thorn BT, Chen JJ. Bioassays of shortened duration for drugs: statistical implications. Toxicol Sci. 2000;55:415–432.

[20] See Docket ID EPA-HQ-OPP-2016-0385-0501, NRDC comments to SAP, and Portier 2016, Table 3

[21] See Docket ID EPA-HQ-OPP-2016-0385-0501, NRDC comments to SAP, and Portier 2016, Table 3

(e) Misuse of historical control data - EPA stated that the tumors were within the range of historical control data. This violates EPA Cancer Guidelines that state, "Generally speaking, statistically significant increases in tumors should not be discounted simply because incidence rates in the treated groups are within the range of historical controls or because incidence rates in the concurrent controls are somewhat lower than average." (EPA 2005 p. 48; EPA 2016 p. 73). The SAP suggested to EPA that it may be using historical control data "subjectively" only in situations where it would reduce the impact of the cancer evidence, "which may potentially introduce biases", and further, that due to genetic drift the Panelists felt that data more than three to five years old may not be representative of animals in current experiments. In response, EPA has presented the historical control data where it is available, but continues to use it where it results in downgrading or reducing statistically significant increases in tumors in glyphosate-treated animals (EPA 2017 Response to SAP, p. 8). As the SAP noticed, it seems that in many instances where EPA believes it has an option to interpret the data, it chose the interpretation that reduces or negates the evidence of cancer risk. One panelist in particular, Dr. Zhang, points out to EPA that even a small significant increase in risk is still a significant risk, and that public servants should serve the public trust and protect public health, to which EPA Senior Science Advisor Dr. Anna Lowitt registers her offense at the suggestion that her team are not being good public servants (SAP Transcript, p. 1224).[22]

A re-analysis of the rodent tumor data has recently been conducted by Dr. Christopher Portier, retired US government cancer expert. Dr. Portier reports an excessively high number of malignant lymphomas and hemangiosarcomas in the male mice in multiple studies of CD-1 strain of mice (See Portier Rebuttal Report, Oct 2017); these are blood-based tumors, as are the non-Hodgkin's Lymphoma (NHL) cases seen in the human epidemiologic studies.[23] These are the analyses that EPA – an Agency charged with protecting human health and the environment – should have come up with.

EPA Should Not Disregard Potential Acute and Chronic Risks of Glyphosate-Based Products

[22] FIFRA SAP Transcript of meeting, Dec 13-16, 2016. Docket ID EPA-HQ-OPP-2016-0385. https://www.epa.gov/sites/production/files/2017-02/documents/glyphosate_transcript.pdf

[23] Portier C. 2017. Rebuttal report. Exhibit 96. https://usrtk.org/wp-content/uploads/2017/10/Rebuttal-report-of-chris-potier.pdf

A report submitted under contract to USDA in 1997 – twenty years ago – warned that surfactants added to glyphosate products make them much more toxic, and that very little toxicity information is available about the formulated products. (Diamond and Durkin 1997)[24]

More recently, in July 2016, European Union member states banned POE-tallowamine from glyphosate-based products including Roundup. This followed the conclusions of the European Food Safety Authority that tallowamine ingredients are more toxic than glyphosate in terms of acute, short term, reproductive, and developmental toxicity, and that there is some evidence of DNA damage in vitro at high doses (EFSA 2015).[25]

Even Monsanto experts agree in internal memos that the glyphosate-based products carry additional health risks, compared with glyphosate alone. A 2002 internal Monsanto email states, "Glyphosate is OK but the formulated product (and thus the surfactant) does the damage" (Monsanto email, April 25, 2002). And, in another corporate email from Donna Farmer, Ph.D., Monsanto's Manager of Toxicology Programs, "You cannot say that Roundup is not a carcinogen… we have not done the necessary testing on the formulation to make that statement". (Monsanto email, November 22, 2003) These corporate disclosures represent a disturbing level of understanding of the potential health harms from its products, while making public assurances of the safety of its products.

EPA considers adjuvants such as the tallowamines to be "inerts", effectively treating them as if they were free of adverse effects. POE-tallow amine is approved by EPA for both food and non-food uses, at up to 25% in herbicide formulations, without any evaluation of its safety either alone or when combined with active ingredients (EPA List of Inerts).[26] It seems willfully irresponsible for EPA to ignore the dangers of the formulated glyphosate-based products that are used to widely on fields, food crops, playgrounds, and residential homes and gardens.

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[24] Diamond GL, Durkin PR. Effects of Surfactants on the Toxicitiy of Glyphosate, with Specific Reference to RODEO Report submitted to Leslie Rubin, COTR, Animal and Plant Health Inspection Service (APHIS). Biotechnology, Biologics and Environmental Protection, Environmental Analysis and Documentation, United States Department of Agriculture, February 6, 1997 http://www.fs.fed.us/foresthealth/pesticide/pdfs/Surfactants.pdf

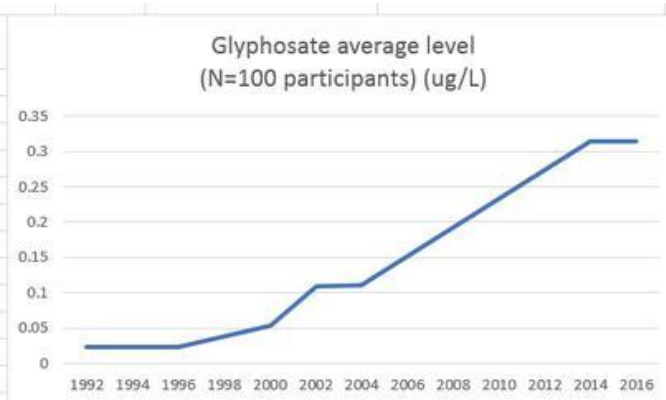
[25] http://www.efsa.europa.eu/sites/default/files/4302_glyphosate_complementary.pdf

[26] Polyoxyethylene tallow amine (CAS No. 61791-26-2), is on the U.S. EPA List of Inert Ingredients of Pesticides, where it is classified as cleared for both food and nonfood uses.
Chemical Data Access Tool (CDAT): https://java.epa.gov/oppt_chemical_search/?redirectFrom=InertFinder&casno=61791-26-2
EPA Inert Finder here: https://iaspub.epa.gov/apex/pesticides/f?p=INERTFINDER:3:::NO::P3_ID:6708

The SAP highlighted that EPA had only solicited SAP input on the carcinogenic potential of glyphosate, not glyphosate-based products (SAP 2017, p. 23), and specifically recommended that EPA expand its scope to identify and discuss toxicity studies of glyphosate-based formulations (SAP 2017, p. 14). However, EPA did not do this. In its response to the SAP report, EPA identifies that it "has been collaborating with the National Toxicology Program (NTP) to evaluate potential differences in formulation toxicity and the results of this research will be considered when available" (EPA Response to SAP 2017 p. 3).[27] While NRDC is pleased that this important collaborative research has been initiated, we note that EPA's failure to include an assessment of potential acute and chronic adverse impacts of glyphosate formulations is a major data gap that should be addressed with the use of additional uncertainty factors.

WIDESPREAD AND INCREASING HUMAN EXPOSURE

Recently published research by medical experts from the University of California reports on the startling evidence that glyphosate—the main ingredient in Monsanto's weed-killer, Roundup—is not only getting into our bodies, but has been doing so at increasing levels for decades.[28] The researchers measured levels of glyphosate in the urine of one hundred people. The study subjects had been involved in a study since the 1970's which allowed the researchers to go back and look at historical and current levels of glyphosate in urine over decades. And, the trend is rising, as glyphosate crop uses rise across the country.



Sample year	ug/L glyphosate in urine
1993-1996	0.024
1999-2000	0.053
2001-2002	0.11
2004-2005	0.111
2014-2016	0.314

[27] EPA Response to the Final Report of the Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (FIFRA SAP) on the Evaluation of the Human Carcinogenic Potential of Glyphosate, December 12, 2017. Document ID EPA-HQ-OPP-2009-0361-0072

[28] JAMA October 24/31, 2017 Volume 318, Number 16

The SAP raised concern at the potential for the general population including young children to be exposed to glyphosate at occupational levels. In its report, the SAP noted that the Agency's presumption that pesticide applicators had significantly higher exposures than the general population is incorrect; EPA's high-end exposure estimate for 1-2 year old children (presuming all relevant foods have glyphosate residues at the maximum allowable limit) is 0.47 mg/kg/day, which is much higher than the exposure estimates for applicators and within the range of exposure estimates for pesticide mixers and loaders (0.03-7 mg/kg/day) (SAP 2017).

A 2014 report of the Government Accountability Office (GAO) was critical of FDA and USDA for both a failure to launch an effective pesticide residue testing program, and for failing to make public its findings of glyphosate in foods (GAO 2014).[29] In response, the FDA finally started testing for residues of glyphosate in common foods only in the past two years, and no results have been officially made public yet. Collapsing consumer confidence in the regulatory agencies led to consumer groups and academics doing their own testing, reporting glyphosate residues in breast milk, honey, cereal including oatmeal marketed for kids, infant formula, soy sauce, flour, and other food products (Reuters 2015; HuffPost Dec 6, 2017; US RTK Apr 18, 2018; Guardian, Apr 30 2018).[30] Now reports in the Guardian reveal FDA internal documents showing that almost every food FDA has tested has been shown to be contaminated with glyphosate residues. "I have brought wheat crackers, granola cereal and corn meal from home and there's a fair amount [of glyphosate] in all of them," wrote FDA chemist Richard Thompson to colleagues in a 2017 mail[31] reported in the Guardian (Guardian, Apr 30 2018).[32] The Guardian also reported on an email from FDA chemist Narong Chamkasem that glyphosate was detected in corn at levels exceeding the legal tolerance limit; this should have been reported to EPA but, "an FDA supervisor wrote to an EPA official that the corn was not considered an official sample" so it wasn't reported (FDA email Jan 3, 2017; Guardian, Apr 30 2018).[33] This denies the public's right to know about pesticide residues in foods, it

[29] US GAO. FDA and USDA Should Strengthen Pesticide Residue Monitoring Programs and Further Disclose Monitoring Limitations. GAO-15-38; Oct 2017. https://www.gao.gov/products/GAO-15-38
[30] Gillam C. Fears over Roundup herbicide residues prompt private testing. Reuters, April 10, 2015. https://www.reuters.com/article/us-food-agriculture-glyphosate-idUSKBN0N029H20150410
[31] Glyphosate method. Email from Richard L. Thompson to Eugene Chang and Chris A. Sack. January 4, 2017. Available at https://usrtk.org/wp-content/uploads/2018/04/FDA-Richard-Thompson-wheat-crackers-email.pdf
[32] Gillam C. Weedkiller found in granola and crackers, internal FDA emails show. The Guardian, Apr 30, 2018. https://www.theguardian.com/us-news/2018/apr/30/fda-weedkiller-glyphosate-in-food-internal-emails
[33] Glyphosate. Email from Chris A. Sack, FDA to David Hrdy, EPA. January 3, 2017

thwarts the ability of EPA to follow its legal authorities to address tolerance exceedances, and it further shatters the public confidence in government generally, and EPA specifically.

The failure of the agencies to initiate and incorporate comprehensive glyphosate residue testing results into its assessment is a major data gap that should be addressed with the use of additional uncertainty factors. Under the Food Quality Protection Act, 21 U.S.C. §346a, the agency must prohibit any use for which the registrant has failed to demonstrate that there is a reasonable certainty of no harm to vulnerable populations including infants and children from cumulative and aggregate exposure (from the diet and all other sources.) EPA must apply an "additional tenfold margin of safety for the pesticide chemical residue and other sources of exposure…for infants and children to take into account potential pre- and post-natal toxicity and completeness of the data with respect to exposure and toxicity to infants and children." EPA may use a different additional margin safety for the pesticide "only if, on the basis of reliable data, such margin will be safe for infants and children." 21 U.S.C. §346a(b)(2)(C). EPA must ensure that it is meeting its FQPA responsibilities in evaluating the exposure and risks to vulnerable populations as well as to the general population from both cancer and non-cancer risks, and has failed to do so.

WILDLIFE IMPACTS

Glyphosate poses an existential threat to North American monarch butterflies

There is broad consensus amongst monarch butterfly experts that the driving force behind the butterfly's decline is the loss of milkweed in the United States due to the widespread use of glyphosate.[34] While other factors affect the butterfly population— such as weather, climate, and deforestation in the Mexican overwintering sites— experts agree that the loss of milkweed is one of the largest contributing factors, if not the leading factor. A recent study examining the various threats to the monarch population concluded that, "[w]hile climatic factors, principally breeding season temperature,

[34] *See* Thogmartin, W. E et al. 2017. *Monarch butterfly population decline in Norther America: identifying the threatening processes*. Royal Society Open Sci 4: 170760 [hereafter Thogmartin et al. 2017a]; John M. Pleasants, *Monarch Butterflies and Agriculture*, *in Monarchs in a Changing World: Biology and Conservation of an Iconic Insect* (Karen Oberhauser et al. eds., forthcoming 2015), at 15-16 [hereinafter Pleasants]; D.T. Tyler Flockhart et al., *Unravelling the Annual Cycle in a Migratory Animal: Breeding-season Habitat Loss Drives Population Declines of Monarch Butterflies*, J. Animal Ecology, 2014, at 7-8 [hereinafter Flockhart et al.]; John M. Pleasants & Karen S. Oberhauser, *Milkweed Loss in Agricultural Fields Because of Herbicide Use: Effect on the Monarch Butterfly Population*, Insect Conservation & Diversity, 2012, at 8 [hereinafter Pleasants & Oberhauser]; Lincoln P. Brower et al., *Decline of Monarch Butterflies Overwintering in Mexico: Is the Migratory Phenomenon at Risk?*, 5 Insect Conservation & Diversity, 2011, at 1-4 [hereinafter Brower et al.].

were important determinants of annual variation in abundance, our results indicated strong negative relationships between population size and habitat loss variables, *principally glyphosate use*, but also weaker negative effects from the loss of overwinter forest and breeding season use of neonicotinoids[35]" (emphasis added). Another study concluded that "[r]ecent population declines stem from reduction in milkweed host plants in the United States that arise from increasing adoption of genetically modified crops and land-use change, not from climate change or degradation of forest habitats in Mexico."[36] The authors further concluded that "[c]onserving monarch butterflies by addressing the negative impacts of changing land-use and the adoption of genetically modified, herbicide-resistant crops on host plant abundance is the highest conservation priority."[37] Clearly, the scientific consensus is that the loss of milkweed due to the widespread use of glyphosate is responsible for the decline in the monarch population.

The loss of milkweed, particularly in the agricultural Midwest, has been well documented, and is the direct result of increased glyphosate use.[38] A survey of milkweed in corn and soybean fields in 1999 documented milkweed in at least fifty percent of fields. By 2009, milkweed was documented in only eight percent of the fields. Additionally, the overall area occupied by milkweed within the fields decreased by ninety percent.[39] Relying on this and other data, another study extrapolated the loss of milkweed in both agricultural and non-agricultural areas across the entire Midwest and found a sixty-four percent decline in milkweed from 1999 to 2012.[40]

Monarchs tend to lay more eggs in agricultural areas than in non-agricultural areas. Accordingly, the decline of milkweed in the largely agricultural Midwest has caused a greater-than-proportional reduction in successful monarch reproduction.[41] While there has been a sixty-four percent loss of milkweed in the Midwest, researchers estimate that this has corresponded with an eighty-eight percent

[35] Thogmartin, W. E. et al. 2017a.
[36] Flockhart et al. at 1; *see also* The Xerces Society for Invertebrate Conservation & U.S. Dep't of Agric. Natural Resources Conservation Serv., Pollinator Plants of the Central United States: Native Milkweeds (2013), at 5 ("[D]ocumented declines in milkweed habitat and monarch breeding potential illustrate the urgent need to protect existing milkweed populations."), *available at* http://www.nrcs.usda.gov/Internet/FSE_PLANTMATERIALS/publications/mopmcpu11905.pdf.
[37] Flockhart et al. at 8.
[38] Pleasants, at 15-16.
[39] Robert G. Hartzler, *Reduction in Common Milkweed (*Asclepias Syriaca*) Occurrence in Iowa Cropland from 1999 to 2009*, 29 Crop Protection 1542, 1543 (2010).
[40] Pleasants at 1.
[41] Pleasants & Oberhauser; Pleasants at 1.

decrease in monarch production.[42] During the same time period that researchers have measured the declines in milkweed and monarch production in the Midwest, there has also been a corresponding, statistically significant decline in the monarch overwintering population in Mexico.[43] The overwintering population has dropped from a high of approximately one billion butterflies in 1997 to a low of approximately 33.5 million butterflies.[44] Scientists have warned that the monarch migration is at risk of vanishing.[45]

The EPA has failed to act on glyphosate

In its ecological risk assessment, EPA failed to evaluate the risk of glyphosate to monarch butterflies due to habitat destruction. EPA claims that it has "identified an approach" to protecting monarch butterflies and points to its "Risk management approach to identifying options for protecting the monarch butterfly."[46] This risk management approach is a general document that solicits input from "diverse stakeholders" regarding steps that EPA could take, but it does not outline any "approach" for doing so. In the nearly three years since this document was posted, the EPA has not taken any measures to protect monarch butterflies from glyphosate or any other pesticide. In evaluating the registration of glyphosate, EPA must evaluate its risk to monarch butterflies and enact restrictions to prevent their demise.

The EPA should immediately restrict the use of glyphosate

In 2014, NRDC submitted a petition to the EPA requesting the EPA review the use of glyphosate in light of the impact it is having on monarch butterflies[47]. In July of 2015, the EPA denied this petition stating, in part, that "any actions taken to protect the monarch butterfly and its resources should not be focused on just glyphosate"[48]. The EPA argues that restricting glyphosate could lead to the intensification of other herbicides. While we agree that the EPA should also consider the impact of other herbicides on

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[42] Pleasants at 1.
[43] *See generally* Brower et al., at 1-4.
[44] *Monarch Population Status*, Monarch Watch.org (Jan. 29, 2014, 12:10 PM), http://monarchwatch.org/blog/2014/01/monarch-population-status-20/ (expressing monarch population in terms of hectares colonized; one colonized hectare contains approximately 50 million butterflies).
[45] *See generally* Brower et al. at 1-4; Semmens et al. 2016. Quasi-extinction risk and population targets for the Eastern migratory population of monarch butterflies (*Danaus plexippus*). Nature Scientific Reports 6:23265.
[46] http://www.eswr.com/docs/science/EPA-HQ-OPP-2015-0389-0002.pdf
[47] NRDC 2014 Petition to conduct interim administrative review for the pesticide glyphosate, in light of serious harm to monarch butterflies. Petition to EPA.
[48] EPA 2015 Response to Natural Resources Defense Council's (NRDC) February 24th , 2014 Petition Requesting Interim Administrative Review for Glyphosate.

the monarch butterfly that does not release the EPA from its obligation to immediately issue restrictions on the use of glyphosate.

The reason that glyphosate (rather than any other herbicide) has contributed so significantly to the decline of the monarchs is because of its use in connection with crops that have been genetically engineered to resist glyphosate. After the introduction of these crops, the use of glyphosate increased dramatically. For example, between 1989 and 1991, before the genetically engineered crops were developed, 18.7 million pounds of glyphosate were used on between thirteen and twenty million acres annually; between 2008 and 2009, 182 million pounds were used on over 261 million acres— an approximate tenfold increase.[49] Given that the majority of herbicide tolerant crops are engineered to resist glyphosate, it is unlikely that limiting glyphosate would automatically lead to a significant increase in other herbicides for which there are not tolerant crops as EPA has argued.

There are currently few to no meaningful restrictions on the agricultural use of glyphosate. The label, for example, does not even provide guidance on how to apply glyphosate so as to reduce drift. EPA can and should impose immediate restrictions on the agricultural use of glyphosate. In addition to providing guidance to reduce drift, the EPA could require farmers that use glyphosate in connection with glyphosate tolerant crops to institute pesticide free buffer zones in and alongside their fields and/or land set asides where milkweed can be grown. Promising research out of Idaho State University, for example, demonstrates that planting strips of native prairie within or on the edge of agricultural fields provides significant benefits to farmers including reducing soil erosion and enhancing soil quality in addition to providing habitat for pollinators[50]. A recent study determined that agricultural land, particularly in the Midwest, is critical to the survival of monarch butterflies and therefore a portion of agricultural land will need to support milkweed in order to recover a sustainable population of monarch butterflies[51]. The authors conclude that it may be possible to cultivate milkweed within agricultural land "if issues with pesticides can be overcome.[52]" The EPA should at a minimum restrict the use of glyphosate while requiring buffers or areas where milkweed can grow to mitigate the effect of glyphosate use on monarchs.

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[49] Comments of the Natural Resources Defense Council on Dow Agrosciences' Application to Register Enlist Duo Herbicide Containing the Choline Salt of 2,4-D and Glyphosate (June 30, 2014), at 7-9.
[50] *See* http://www.nrem.iastate.edu/research/STRIPs/
[51] Thogmartin, W. E. et al. 2017. Restoring monarch butterfly habitat in the Midwestern US: all hands on deck. Environmental Research Letters 12:074005. [hereafter Thogmartin et al. 2017b]
[52] Id

The EPA should require the use of Integrated Pest Management

Rather than promote the use of increased herbicides for weed management, EPA should require Integrated Pest Management to reduce reliance on pesticides and prevent the evolution of herbicide-resistant weeds. Integrated pest management focuses on weed control, rather than weed eradication, in an effort to control weeds using the least environmentally destructive means possible. Methods to decrease weed abundance include rotating crops, cleaning equipment to remove plant residue, mechanical weed control, and using cover crops during the off-season. By preventing weed growth, integrated pest management can dramatically reduce herbicide use and herbicide resistance. EPA should mandate some or all of these methods for farmers using glyphosate to reduce the volume of glyphosate needed.

By reducing glyphosate use through integrated pest management, EPA would also help prevent development of glyphosate resistant weeds, a major threat to agriculture. The USDA's own research has shown that "an overreliance on glyphosate and a reduction in the diversity of weed management practices adopted by crop producers have contributed to the evolution of glyphosate resistance in 14 weed species and biotypes in the United States"[53]. Seed companies have responded by developing crops that are resistant to both glyphosate and a second herbicide like 2,4-D. But this is an unsustainable solution that magnifies the environmental consequences of herbicide use. EPA's mission is to protect human health and the environment. Consistent with that mission, EPA must take steps to reduce herbicide use, rather than increase it. Requiring integrated pest management practices is a simple step EPA can take to move our agricultural system towards a more sustainable and monarch-friendly future.

The EPA can and should act now

The monarch population is currently so precariously small that the continued loss of milkweed, even over a single migration cycle, could compromise the population's ability to rebound. Continued losses could also endanger the entire population's ability to withstand stressors such as adverse climate events, freezing temperatures, disease, and deforestation. In 2002, for example, a single storm killed more than 450 million monarchs, which constituted approximately 75 percent of the overwintering

[53] USDA 2014 Genetically engineered crops in the United States. Economic Research Service Report 162.

population—and exceeded, by over three times, the 150 million monarchs overwintering in Mexico during the 2015-2016 season.[54] Were a comparable storm to hit the current monarch population now, it could wipe out the entire North American population. The smaller the population becomes, the more vulnerable it is to these kinds of random events. Even the losses sustained over a single migratory season could critically impair the surviving population. Any additional destruction of milkweed habitat in the United States only further endangers the population.

The migrating monarch population continues to be in danger of collapse and requires immediate relief from the primary cause of its decline: the loss of milkweed due to the use of glyphosate. As the agency that regulates the use of glyphosate and other herbicides, the EPA needs to act immediately to address the unprecedented decline of monarch butterflies.

EPA must account for cumulative and synergistic effects

As with all of EPA's risk assessments, the agency must evaluate the synergistic effects of glyphosate. Glyphosate is often mixed with other active ingredients in patented products and the cumulative and synergistic effect of this combination must be evaluated. The EPA's risk assessment is not complete until both cumulative and synergistic effects are accounted for.

EPA must consult with the U.S. Fish and Wildlife Service (FWS) and National Marine Fisheries Service (NMFS) under Section 7 of the Endangered Species Act (ESA)

EPA must consult with FWS and NMFS under Section 7 of the ESA on its registration review decisions. Under the ESA, all federal agencies must ensure that their actions do not jeopardize the existence of federally threatened or endangered (listed) species or adversely modify their critical habitat.[55] In practice, this requires agencies to consult with FWS and NMFS on actions that "may affect" such species.[56] Accordingly, EPA must consult on glyphosate before issuing its final registration review determination.

CONCLUSION

[54] Lincoln P. Brower et al., *Catastrophic Winter Storm Mortality of Monarch Butterflies in Mexico during January 2002*, *in The Monarch Butterfly: Biology and Conservation* 151, 151-66 (Karen S. Oberhauser & Michelle J. Solensky eds., 2004).
[55] 16 U.S.C. § 1536(a)(2).
[56] Id.; 50 C.F.R. § 402.14(a).

Despite massive glyphosate over-use leading to widespread weed resistance, Monsanto and other agrochemical companies are simply pushing increased uses and new chemical mixes. For example, in 2014 EPA approved Dow AgroSciences' new Enlist Duo herbicide, which combines glyphosate and 2,4-D as active ingredients. Monsanto rushed to market its new "Xtend" herbicide-tolerant soybean seeds engineered to resist both glyphosate and dicamba. The result of all this herbicide use, misuse, and overuse is an agricultural system that leaves farmers economically challenged and woefully underprepared, with only one main tool in their toolbox - more toxic chemicals.[57]

Meanwhile, consumer confidence in regulatory agencies is shattered by assessments such as this one, that leave EPA and Monsanto standing together, in conflict with the EPA Scientific Advisory Panel, the IARC, and non-industry cancer and wildlife experts around the world that have sounded the alarm over glyphosate-based products. The European Union has been unable to get sufficient support from Member Countries to re-approve glyphosate except for a very time-limited approval that will sunset in five years (Hakim, NYT Nov 2017). The iconic ice cream company Ben & Jerry's recently introduced a new line of organic ice cream that doesn't contain glyphosate, in response to public concern after glyphosate residues were found in its products. Food products from wheat, barley, rye and oats have also been reported to contain glyphosate, and at levels hundreds of times higher than those reported in ice cream.

Despite public concern and scientific evidence of harm, it seems that EPA and Monsanto are continuing to deny cancer risks from exposure to glyphosate products. EPA should not be on the side of Monsanto, as, "The Registrant wishes to avoid false positives while those concerned with the public health wish to avoid false negatives. Hence, for this reason alone Monsanto's argument is unacceptable" (Lacayo memo, Feb 1985). EPA should reverse course, and re-assess glyphosate including cancer and non-cancer risks, potential adverse effects posed by exposure to glyphosate-based formulated products, and the irrefutable evidence that the escalating use of glyphosate is devastating the flora that supports many beneficial insects including pollinators and the iconic monarch butterflies. Severe restrictions on glyphosate use are warranted by the evidence to date – there is no excuse for rubber stamping this highly damaging herbicide any longer.

[57] http://cjonline.com/news/business/2016-09-10/herbicide-resistant-weeds-challenge-farmers-bottom-lines

Respectfully,

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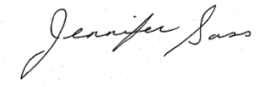

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