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April 30, 2018

Office of Pesticide Programs
Docket number EPA-HQ-OPP-2009-0361
Environmental Protection Agency Docket Center (EPA/DC)
(28221T)
1200 Pennsylvania Ave. NW.
Washington, DC 20460-0001

Re: Comments on EPA Draft Risk Assessment Documents – Glyphosate (Docket #: EPA-HQ-OPP-2009-0361)

Please accept the following comments on behalf of the Center for Biological Diversity, Beyond Toxics, Center for Food Safety, American Bird Conservancy, National Latino Farmers & Ranchers Trade Association, U.S. PIRG, National Family Farm Coalition, Environment America, Kansas Rural Center, Organic Consumers Association, Citizens Regeneration Lobby, and The City Project in response to the Environmental Protection Agency's ("EPA") risk assessment documents for products containing a pesticide ingredient under the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA").

Unfortunately, there are serious issues with these risk assessment documents that absolutely need to be addressed in order for risk to accurately be reflected. As these draft documents stand now, risk is almost certainly underestimated – putting all species, including humans, at risk of unreasonable harm from the labeled uses of glyphosate. Issues that must be addressed are outlined below.

1. Increase In Glyphosate Loading In The Environment Must Be Assessed

Glyphosate is currently the most widely used pesticide in the U.S. with about 300 million pounds used in the agricultural sector every year.[1] Add on top of that home, commercial and government

[1] U.S. Geological Survey: National Water-Quality Assessment (NAWQA) Program. Pesticide National Synthesis Project, pesticide use maps – glyphosate. Accessed Nov. 29, 2017; Available at: https://water.usgs.gov/nawqa/pnsp/usage/maps/show_map.php?year=2015&map=GLYPHOSATE&hilo=L&disp=Glyphosate.

use and the total is much higher. For some perspective, the nation's second most widely used pesticide is atrazine, at around 70 million pounds per year – four fold lower than glyphosate.[2]

Glyphosate is truly in a category of its own, yet EPA is analyzing it like it would any other pesticide. A pesticide used at this magnitude cannot be accurately assessed by simply looking at risk quotients calculated from estimated environmental concentrations (EECs) from a single user. In 1993, the last time an ecological risk assessment was completed for glyphosate, there was roughly 20 million pounds used per year. Now there is 15-fold more pesticide used, yet the analytical tools the EPA is using remain nearly identical. The estimated environmental concentration from a single person using the pesticide is compared to a toxicological endpoint. This completely ignores the cumulative impact of the hundreds of millions of pounds of glyphosate that is used throughout the country year after year.

The total glyphosate load in the environment has increased dramatically in the last 20 years. A risk assessment analysis that is designed for pesticides with much lower overall use is not going to give an accurate reflection of risk for a pesticide that is used on a level of this magnitude. The current risk assessment process treats a pesticide used at 100 pounds per year the same as a pesticide that is used at 100 million pounds per year. Ecological concerns that result from increased total use of pesticide nationwide are simply not taken into account with this risk assessment methodology. Ultimately this underestimates risk for a pesticide like glyphosate.

Furthermore, risk quotient ("RQ") exceedances are going to indicate something much different for a pesticide like glyphosate than another pesticide that is used at a lower level. Even *very slight* exceedances in RQs are extremely worrisome for a pesticide used at this magnitude because those exceedances will be on a much larger scale and affect a much broader geographical area. In multiple places in the ecological risk assessment, the agency has sought to downplay RQ exceedances because the exceedance was only very minimal – calling the risk "low."[3] This is an incorrect interpretation for RQ exceedances for glyphosate. Even slight RQ exceedances when present on this scale can have profound effects on populations of plants and animals. Therefore, even modest RQ exceedances will necessitate significant mitigation measures for the EPA to remain compliant with FIFRA.

[2] U.S. Geological Survey: National Water-Quality Assessment (NAWQA) Program. Pesticide National Synthesis Project, pesticide use maps – atrazine. Accessed Nov. 29, 2017; Available at: https://water.usgs.gov/nawqa/pnsp/usage/maps/show_map.php?year=2015&map=ATRAZINE&hilo=L&disp=Atrazine.

[3] EPA. Preliminary Ecological Risk Assessment for Glyphosate and Its Salts. Sept. 8, 2015. See section 5.3.

2. The Drinking Water Assessment Incorrectly Excludes Bias Factors in Monitoring Data

Multiple governmental agencies have monitoring data available for glyphosate in surface water that the EPA has included in its analysis of drinking water concentrations.[4] Although these monitoring studies provide a good comparison for EPA's modelling estimations, ultimately they underestimate peak glyphosate concentrations. This is because the monitoring data were taken on a regular basis and not in response to a recent nearby application or storm event. Therefore, these studies may have missed peak concentrations that were considerably higher than those identified. Recent quantification of bias factors needed to offset this underestimation indicate that the differences in actual peak concentrations and identified peak concentrations could be very large.[5] Since data from the Water Quality Portal ("WQP") and the USGS National Water Quality Assessment Program ("NAWQA") have a median sample frequency of 14 days, peak glyphosate concentrations could be as high as 24 - 39 times the recorded peak values. Furthermore, even the 90-day average concentrations could be undervalued by as much as 4-fold.[6]

Despite actually having a rough quantification of the extent of underestimation in the monitoring data, the EPA has opted to not use bias factors in its analysis. Since the non-bias factor adjusted monitoring data is more or less similar to EPA's modelled data, the agency takes this to indicate that its model is sufficiently protective of glyphosate concentrations. Yet comparing to bias factor adjusted monitoring data indicates that EPA's modelling may be under-representative of peak and chronic glyphosate concentrations. Therefore risk from drinking water exposure is likely underestimated.

3. Significant Buffers Must be Implemented for Aerial and Ground Applications

The EPA's ecological risk assessment indicates that considerable no-spray buffers would be needed to keep off-target plants from being harmed by glyphosate use, more than 1000 feet for certain aerial applications and nearly 400 feet for certain ground applications.[7] Even when using other plant species that are not the most sensitive, buffer distances of hundreds of feet are necessary for keeping those plants from harm.[8]

Plants that exist on the edges of agricultural fields, in roadside ditches and on marginal agricultural land are some of the only sources of plant diversity in agricultural areas. Since non-

[4] EPA. Drinking Water Assessment for the Registration Review of Glyphosate. June 15, 2017. Pg. 19.
[5] Mahler, B.J., P.C. Van Metre, T.E. Burley, K. A. Loftin, M. T. Meyer, and L.H. Nowell. 2017. Similarities and differences in occurrence and temporal fluctuations in glyphosate and atrazine in small Midwestern streams (USA) during the 2013 growing season. Science of the Total Environment. Volume 579.
[6] EPA. Drinking Water Assessment for the Registration Review of Glyphosate. June 15, 2017. Page 23.
[7] *Id.* page 92.
[8] *Id.*

crop plants are eradicated from fields year after year, these small remaining slivers of land in regions dominated by agriculture are extremely important habitat for all kinds of plants and animals. Because of that it is vital that they remain as untouched as possible and that all life is able to thrive there.

Pesticide drift and runoff is a direct threat to these important habitats. Due to the magnitude of its use, glyphosate poses a significant threat to these habitats and it is important that measures are taken to ensure that glyphosate will not leave agricultural fields. One well-documented way of doing that is to impose in-field buffers where pesticide cannot be sprayed.

Ecological incident data also reinforce the finding that the current labelled uses of glyphosate are having devastating effects to plant and animal life outside of the sprayed field.[9] Approximately 600 incidents have been reported and logged on the EIIS and AIMS databases. A separate IDS database has identified 269 separate aggregate incident reports. Ecological incidents are also significantly underreported for pesticides so this should be viewed as the absolute bare minimum of ecological incidents that involve glyphosate.

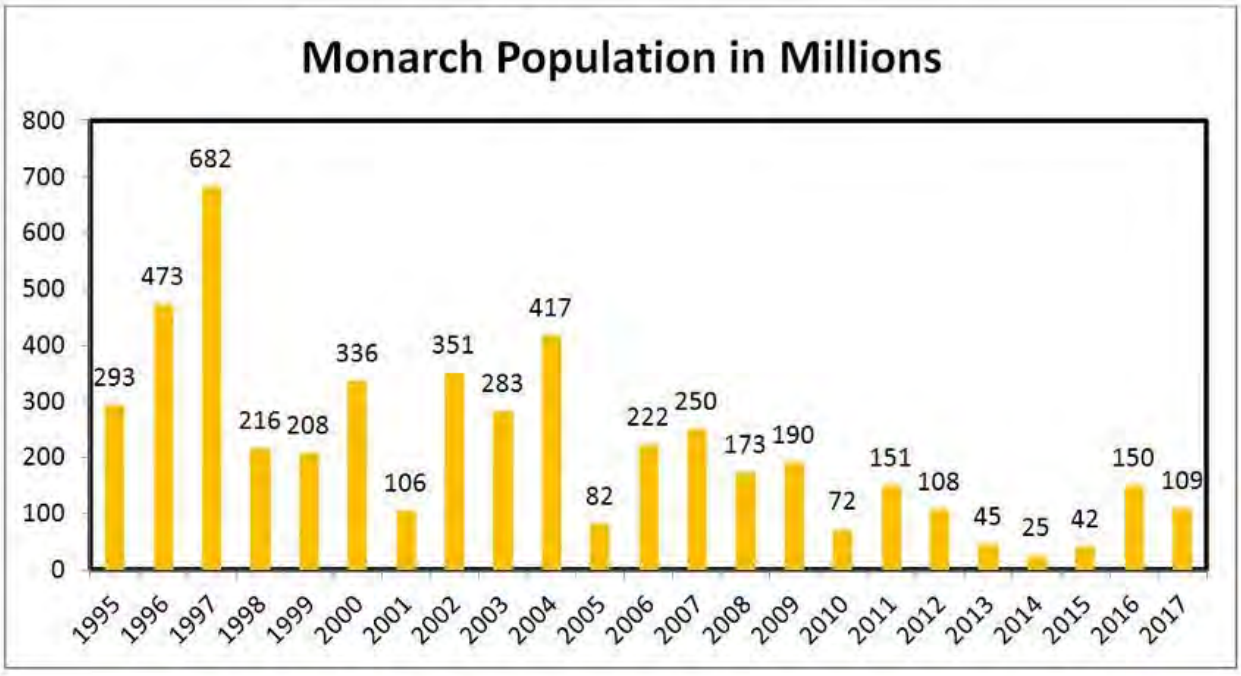
The EPA's analysis indicates that not only are buffers warranted, but they are necessary to keep non-target plants from being harmed by glyphosate use. We urge the agency to put in place mandatory in-field no spray buffers of 1000 feet for aerial applications of glyphosate and 400 feet for ground applications. This would not be an outrageous mandate. The states of California and Arkansas both have mandatory no-spray buffers of 500 feet for aerial applications.[10] These are two heavy agricultural states that are able to grow agricultural products just fine. The buffers in these two states must be expanded and mandated across the U.S.

4. Protections Must be Put in Place for Monarch Butterflies

Researchers have found negative associations between glyphosate use and monarch population size.[11] Use of glyphosate has been tied to widespread declines of milkweed, which is essential to monarch butterfly survival.[12] The threat this habitat loss poses to the continued existence of

[9] EPA. Preliminary Ecological Risk Assessment for Glyphosate and Its Salts. Sept. 8, 2015. Pgs 59-62.
[10] EPA. Drinking Water Assessment for the Registration Review of Glyphosate. June 15, 2017. Pg. 16.
[11] Semmens, B. X., D. J. Semmens, W. E. Thogmartin, R. Wiederholt, L. Lopez-Hoffman, J. E. Diffendorfer, J. M. Pleasants, K. S. Oberhauser and O. R. Taylor (2016). "Quasi-extinction risk and population targets for the Eastern, migratory population of monarch butterflies (Danaus plexippus)." Sci Rep 6: 23265.
[12] Center for Biological Diversity, Petition to Protect the Monarch Butterfly (*Danaus Plexippus Plexippus*) Under the Endangered Species Act, 7 (2014), available at http://www.biologicaldiversity.org/species/invertebrates/pdfs/Monarch_ESA_Petition.pdf ("A primary threat to the monarch is the drastic loss of milkweed caused by increased and later season use of the herbicide glyphosate in conjunction with widespread planting of genetically engineered, herbicide-resistant corn and soybeans in the Corn Belt region of the United States and to planting of genetically-engineered cotton in California. In the Midwest, nearly ubiquitous adoption of, glyphosate-resistant 'Roundup Ready' corn and soybeans has caused a precipitous decline of common milkweed, and thus of monarchs, which lay their eggs only on milkweeds. The majority of the

eastern monarch population cannot be overstated. The estimated overwintering population of monarchs in 2017 was just 109 million, down 27 percent from 2016 and down more than 80 percent from counts in the mid-1990s.[13]



Monarch butterfly population graph by Tierra Curry, Center for Biological Diversity.

EPA's current analysis has also identified concerns. Using milkweed toxicity data, the agency identified considerable in-field buffers would be necessary to adequately protect nearby milkweed plants. The agency erroneously did not use the most sensitive study of sufficient quality and instead relied on an IC_{25} value of 0.126 lb/Acre.[14] If the agency correctly used the more sensitive study, which found and IC_{25} value of 0.04 lb/Acre, the necessary buffers would be much more considerable.[15] The above proposed no spray buffers of 1000 feet for aerial application and 400 feet for ground application would help to mitigate some of this harm to monarch habitat and we encourage the EPA to immediately make these buffers mandatory label requirements.

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world's monarchs originate in the Corn Belt region of the United States where milkweed loss has been severe, and the threat that this habitat loss poses to the resiliency, redundancy, and representation of the monarch cannot be overstated.").

[13] Center for Biological Diversity, *Monarch Butterfly Population Drops by Nearly One-Third: Iconic Butterfly has Declined by More than 80 Percent in Recent Decades* (Feb.9, 2017), *available at* https://www.biologicaldiversity.org/news/press_releases/2017/monarch-butterfly-02-09-2017.php.

[14] EPA. Preliminary Ecological Risk Assessment for Glyphosate and Its Salts. Sept. 8, 2015. Pgs 93-93.

[15] *Id.*

5. Toxicity values are not based on best available science

The EPA has decided once again to ignore peer-reviewed studies by independent researchers in favor of unpublished studies by pesticide registrants. For instance, despite multiple open literature studies finding sublethal effects at 0.0074 and 0.003 lb/Acre glyphosate for different species of plants, the EPA elected to go with the higher value of 0.074 lb/Acre from an unpublished, industry sponsored study.[16] Every single one of the open literature studies was suitable for quantitative use (albeit with reproductive endpoints rather than the typical vegetative vigor endpoints), yet the EPA chose to use the less protective value identified in a study that has a clear funding bias.

Good Laboratory Practices ("GLPs") were enacted to prevent fraud in industry science, now they are being used as a way to rely almost exclusively on industry research. When you take away the incentive for fraud, GLPs are no longer necessary to ensure that research can be effectively relied upon. Providing raw data, using extensive replicates, or only analyzing certain endpoints and not others is rarely a requirement for scientific publication, yet published research is how most scientists communicate their findings and it is the way science is able to progress in every single field.

A 2012 Scientific Advisory Panel ("SAP") on atrazine agreed, stating that: "In the view of the Panel, the test design elements should not be applied so strictly to the published literature as to disqualify all studies that do not meet all of these criteria... In the Panel's analysis, the EPA's strict application of the test design elements to the published literature was flawed and many of the test design elements should be relaxed for review of the published literature."[17] Although this statement was made in regards to the atrazine ecological risk assessment, the same could be said for any ecological risk assessment process.

The 2012 Atrazine SAP further states: "The Panel determined that the EPA's test design elements are very useful to use in designing new studies, but not when they are applied retroactively to the published literature"[18] and "The Panel stressed that a study could be considered a high quality study and very useful in risk assessment (even quantitative assessment), even if some of these design elements are not met."[19]

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[16] EPA. Preliminary Ecological Risk Assessment for Glyphosate and Its Salts. Sept. 8, 2015. Pgs 55-56.
[17] FIFRA Scientific Advisory Panel. (2012) SAP Minutes No. 2012-05. A Set of Scientific Issues Being Considered by the Environmental Protection Agency Regarding: Problem Formulation for the Reassessment of Ecological Risks from the Use of Atrazine. Document ID EPA-HQ-OPP-2012-0230-0220 Pg. 15 https://www.regulations.gov/document?D=EPA-HQ-OPP-2012-0230-0220
[18] *Id.* at 29.
[19] *Id.* at 30.

GLP guidelines are simply not necessary for establishing a cause and effect relationship. The precarious funding of most academic and governmental research precludes the inclusion of many of these good practices, but in no way makes the conclusions less scientifically valid. Much of the research that EPA deems "qualitative," and therefore not valid for use in establishing thresholds, has been funded by the United States government. This double standard, being good enough to fund and publish but not good enough to help guide regulations, is ultimately biasing against third-party, independent research.

The EPA must use the most sensitive study of acceptable quality for use in establishing protective thresholds.[20] GLP's are not an acceptable way of judging scientific quality and should only be used as an inclusion criterion for research that has the incentive for fraud.[21]

Furthermore, many peer-reviewed studies have been left out of this analysis altogether. The last time the EPA searched for published studies on glyphosate for the ecological risk assessment was in August of 2013.[22] There are more than four years' worth of published data that have not even been analyzed by the EPA. Before the ecological risk assessment is finalized the EPA must perform an updated search of the ECOTOX database and properly incorporate any studies on glyphosate into this analysis.

6. The EPA Wrongly Concludes That Glyphosate Does Not Cause Cancer

The World Health Organization's International Agency for Research on Cancer ("IARC") conducted an exhaustive review of the publically available scientific literature in 2015 and concluded that glyphosate is "probably carcinogenic to humans" (Group 2A).[23] IARC carefully weighed evidence in three areas, and found that: 1) There was sufficient evidence to conclude that glyphosate causes cancer in animal studies; 2) There was limited evidence that exposure to glyphosate causes cancer (non-Hodgkin lymphoma) in humans; and 3) There was strong evidence that glyphosate can damage DNA and induce oxidative stress,[24] two well characterized pathways that can lead to cancer.[25]

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[20] U.S. EPA Evaluation Guidelines for Ecological Toxicity Data in the Open Literature https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/evaluation-guidelines-ecological-toxicity-data-open#_2_1_2

[21] Vom Saal FS, Myers JP. "Good Laboratory Practices Are Not Synonymous with Good Scientific Practices, Accurate Reporting, or Valid Data." *Environmental Health Perspectives*. 2010 118 (2), A60

[22] EPA. Preliminary Ecological Risk Assessment for Glyphosate and Its Salts. Sept. 8, 2015. Pg 36.

[23] WHO. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 112: Some Organophosphate Insecticides and Herbicides. Glyphosate. 2017. Available at: http://monographs.iarc.fr/ENG/Monographs/vol112/mono112.pdf

[24] *Id.*

[25] Klaunig, J.E., et al., The role of oxidative stress in chemical carcinogenesis. Environ Health Perspect, 1998. 106 Suppl 1: p. 289-95; and Lee, S.J., et al., Distinguishing between genotoxic and non-genotoxic hepatocarcinogens by gene expression profiling and bioinformatic pathway analysis. Sci Rep, 2013. 3: p. 2783.

IARC's finding that glyphosate causes cancer in animals prompted California's Office of Environmental Health Hazard Assessment to list glyphosate as a known carcinogen under California's Proposition 65 law.[26] The agency has also finalized a No Significant Risk Level for glyphosate, which estimated the daily exposure level that will result in a 1/100,000 chance of developing cancer, of 1.1 mg/day.[27]

If the EPA used its own guidelines for carcinogen risk assessment, the agency would have concluded that glyphosate displays "Suggestive Evidence of Carcinogenic Potential." Instead, the agency has ignored its own guidelines[28] and those of the internationally recognized Organisation for Economic Co-operation and Development ("OECD")[29] to conclude that glyphosate is "Not Likely to Be Carcinogenic to Humans."

The FIFRA Scientific Advisory Panel ("SAP") that analyzed the EPA's preliminary carcinogen analysis for glyphosate unanimously concluded that EPA did not follow its own cancer risk assessment guidelines.[30] In response to this highly relevant criticism of the EPA's analysis, the agency has simply ignored it and has failed to make any effort to comply with its guidelines. The agency went so far as to state: "The 2005 EPA Guidelines for Carcinogen Risk Assessment are intended as a guidance only…"[31] and do not necessarily need to be followed verbatim.

Using predetermined guidelines is the preferred way for scientists and government agencies to prevent biases from swaying the analysis towards one conclusion or another. It is simply unacceptable for the EPA to have guidelines in place that have been rigorously vetted, but pick and choose which elements it wants to follow each time it does an analysis.

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[26] OEHHA. The California Environmental Protection Agency's Office of Environmental Health Hazard Assessment. Glyphosate Listed Effective July 7, 2017, as Known to the State of California to Cause Cancer. Available at: https://oehha.ca.gov/proposition-65/crnr/glyphosate-listed-effective-july-7-2017-known-state-california-cause-cancer.

[27] OEHHA. The California Environmental Protection Agency's Office of Environmental Health Hazard Assessment. Amendment to Section 25705 No Significant Risk Level - Glyphosate April 10, 2018. Available at: https://oehha.ca.gov/proposition-65/crnr/amendment-section-25705-no-significant-risk-level-glyphosate-april-10-2018.

[28] EPA. Guidelines for Carcinogen Risk Assessment. March 2005. Pgs 2-20 and 2-21. Available at: https://www.epa.gov/sites/production/files/2013-09/documents/cancer_guidelines_final_3-25-05.pdf.

[29] OECD. 2012. Guidance Document 116 On The Conduct And Design Of Chronic Toxicity And Carcinogenicity Studies, Supporting Test Guidelines 451, 452 And 453 2nd Edition. Series on Testing and Assessment No. 116. Available at: http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/JM/MONO(2011)47&doclanguage=en.

[30] FIFRA Scientific Advisory Panel Meeting Minutes and Final Report No. 2017-01. (2017). A Set of Scientific Issues Being Considered by the Environmental Protection Agency Regarding: EPA's Evaluation of the Carcinogenic Potential of Glyphosate. Pg 18. Available at https://www.epa.gov/sites/production/files/2017-03/documents/december_13-16_2016_final_report_03162017.pdf

[31] 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. Pgs 6-7.

The flaws in the EPA's analysis have been brought to the attention of the agency in many prior public comment periods. These flaws, which remain unchanged in the final draft, include:

- The agency repeatedly used a lack of monotonic dose response in tumor incidence as justification to discount statistically significant findings. Nowhere in EPA's or OECD's guidelines are there any mention of carcinogens needing to follow a monotonic dose response pattern, and the recent glyphosate SAP rejected this as an invalid criterion. In fact, comments were made during the SAP meeting that throwing out dose responses that are non-monotonic "should not be a criterion at all."[32] The valid criterion for dose-response is a statistically significant result from a trend test, and statistically significant trends are quite often found even when the dose-response pattern is not monotonic. In addition, we know that endocrine disruptors, which can be involved in carcinogenesis, often have effects at low but not higher doses, highlighting the importance of putting protections in place to protect the public from chemicals that do not follow the typical "dose makes the poison" paradigm.[33]

- The agency uses non-significance in one statistical test to discount significance in another. For some of the tumors in the mouse and rat studies, there was a statistically significant finding in the Cochran-Armitage Trend Test or in the Fisher's Exact Test for pairwise comparisons but not in both. The EPA erroneously used this as justification to discount the statistical significance that was present. EPA's Guidelines for Carcinogen Risk Assessment state that, in reference to the trend test and pairwise test, "[s]ignificance in either kind of test is sufficient to reject the hypothesis that chance accounts for the result."[34] Therefore, using the results of one test to cancel out the results of the other test is a violation of the agency's own guidelines and is not a scientifically appropriate course of action for study analysis.

- The agency improperly used historical control data to discount significant differences between treated animals and the concurrent control cohort for tumors in multiple mouse and rat studies. EPA's guidelines caution against the use of historical controls except in very extreme circumstances, stating "[g]enerally 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. Random assignment of animals to

[32] FIFRA Scientific Advisory Panel (SAP) Open Meeting Federal Insecticide, Fungicide, and Rodenticide Act December 13-16, 2016. Meeting transcript, line 14, pg. 993. Document ID EPA-HQ-OPP-2016-0385-0500. Available at: https://www.regulations.gov/document?D=EPA-HQ-OPP-2016-0385-0500.
[33] Vandenberg LN, Colborn T, Hayes TB, et al. Hormones and Endocrine-Disrupting Chemicals: Low-Dose Effects and Nonmonotonic Dose Responses. *Endocrine Reviews*. 2012; 33(3):378-455. doi:10.1210/er.2011-1050.
[34] EPA. Guidelines for Carcinogen Risk Assessment. March 2005. Pg 2-19. Available at: https://www.epa.gov/sites/production/files/2013-09/documents/cancer_guidelines_final_3-25-05.pdf.

groups and proper statistical procedures provide assurance that statistically significant results are unlikely to be due to chance alone."[35] The guidance further goes on to recommend caution for relying solely on concurrent control data when "…incidence rates in concurrent controls are unusually low in comparison with historical controls."[36]

For instance, in the case of the Stout and Ruecker, 1990 study,[37] the EPA uses historical control data from 7 earlier studies indicating a range of 1.8 - 8.3 % spontaneous pancreatic adenoma formation in male Sprague-Dawley rats as a means to cast doubt on the concurrent control value of 2%.[38] The concurrent control spontaneous tumor formation is on the low end, but well within the range of historical controls. It is certainly not "unusually low," which is the bar that must be met using EPA guidance.

Further, EPA guidance also states that "[w]hen historical control data are used, the discussion should address several issues that affect comparability of historical and concurrent control data, such as genetic drift in the laboratory strains, differences in pathology examination at different times and in different laboratories (e.g., in criteria for evaluating lesions; variations in the techniques for the preparation or reading of tissue samples among laboratories), and comparability of animals from different suppliers. The most relevant historical data come from the same laboratory and the same supplier and are gathered within 2 or 3 years one way or the other of the study under review; other data should be used only with *extreme* caution."[39]

For instance, the historical control data EPA utilized were from studies up to 7 years older than the Stout and Ruecker, 1990 study.[40] In addition, there was no discussion of possible genetic drift, pathological differences and what suppliers the animals came from. Without these data, it is impossible to know whether these are acceptable historical control cohorts. And the age of many of the studies certainly indicate that they are not.

- Some significant increases in tumor formation were ignored because there was no indication of preneoplastic lesions to indicate a progressive disease. Dr. Chris Portier, former director of the National Center for Environmental Health at the Centers for Disease Control and Prevention and former associate director of the National Institute of

[35] *Id.* at 2-21.
[36] *Id.*
[37] Stout, L. D. and Ruecker, P.A. (1990). Chronic Study of Glyphosate Administered in Feed to Albino Rats. MRID No. 41643801; Historical Controls. MRID 41728700.
[38] EPA. Office of Pesticides Programs. Revised Glyphosate Issue Paper: Evaluation of Carcinogenic Potential. Dec. 12, 2017. Pg 76.
[39] EPA. Guidelines for Carcinogen Risk Assessment. March 2005. Pg 2-21. Emphasis added. Available at: https://www.epa.gov/sites/production/files/2013-09/documents/cancer_guidelines_final_3-25-05.pdf.
[40] EPA. Office of Pesticides Programs. Revised Glyphosate Issue Paper: Evaluation of Carcinogenic Potential. Dec. 12, 2017. Pg 76, Table 4-3.

Environmental Health Sciences chastises EPA for use of this criterion in its analysis, stating in his comments to the FIFRA SAP: "This presumes that all mechanisms by which chemicals induce tumors in animals will involve enough stages that there would be a histologically identifiable preneoplastic lesion from which final tumors are formed. This simply is not the case and this criteria is applied without any concern for its validity by the EPA."[41] Cancer is a progressive disease, but that does not mean that every stage will be readily identifiable on a visual level or even a molecular level given the limited number of tools pathologists currently have. Lack of identifiable pre-neoplastic lesions is simply not a justifiable reason to discount significant data.

- EPA utilizes two-sided P values to test for significance in pairwise comparisons, when one-sided P tests are more appropriate and should be used in this context.[42]

The EPA must comply with duties under Section 7 of the Endangered Species Act (ESA),[43] including completion of consultation (Also see APPENDIX A)

As a separate, discretionary action that may affect endangered and threatened species, the EPA cannot register a pesticide prior to the completion of consultations with the U.S. Fish and Wildlife Service and the National Marine Fisheries Service ("the Services"). Without such consultation, the EPA cannot satisfy its duty to insure that its action does not jeopardize the continued existence of imperiled species across the country or adversely modify or destroy their critical habitat. Moreover, unless and until the EPA completes ESA consultation, any taking of protected species from the use of this pesticide is unlawful.

Section 7(a)(2) of the Endangered Species Act ("ESA") requires that "each federal agency *shall*, in consultation with and with the assistance of the Secretary, insure that any action authorized, funded, or carried out by such agency is not likely to jeopardize the continued existence of any endangered species or threatened species or result in the destruction or adverse modification of habitat of such species which is determined by the Secretary . . . to be critical."[44] Under the Services' joint regulations implementing the ESA, the EPA is required to review its actions "at the earliest possible time" to determine whether the action may affect listed species or critical habitat.[45] Indeed, the EPA's recently finalized policy *Enhancing Stakeholder Input in the*

[41]Comments of Christopher J. Portier, PhD on the Glyphosate Issue Paper: Evaluation of Carcinogenic Potential. October 4, 2016. Pg 2. Document ID EPA-HQ-OPP-2016-0385-0371. Available at: https://www.regulations.gov/document?D=EPA-HQ-OPP-2016-0385-0371.
[42] Ludbrook, J. 2013. Should we use one-sided or two-sided P values in tests of significance? Clinical and Experimental Pharmacology and Physiology 40(6): 357-361.
[43] 16 U.S.C. § 1536.
[44] 16 U.S.C. § 1536(a)(2) (emphasis added).
[45] 50 C.F.R. § 402.14(a).

Pesticide Registration Review and ESA Consultation Processes envisions informal consultations with the Services beginning at the preliminary risk assessment stage.[46] The EPA must initiate consultation under Section 7 whenever its action "may affect" a listed species or critical habitat.[47] The phrase "may affect" has been interpreted broadly to mean that "any possible effect, whether beneficial, benign, adverse, or of an undetermined character, triggers the formal consultation requirement."[48] Accordingly, the EPA must consult with the Services on its continuing and ongoing authority over this pesticide to satisfy its duty to insure that its use will not jeopardize or adversely modify protected species or their critical habitat well *before* it proposes a registration review decision. *See* Endangered Species Act Consultation Obligations for Pesticide Approvals by the Environmental Protection Agency (enclosed).

The EPA must consult on all synergistic and cumulative uses. The EPA must insure that all uses of this pesticide do not jeopardize species protected by the ESA or adversely modify or destroy their critical habitat, including uses with other ingredients or other pesticides. Absent information or data to determine whether this pesticide will act synergistically with other ingredients, such uncertainty requires that the EPA decline to re-register any end use products containing more than one active ingredient and prohibit tank mixing on the labels.

At a minimum, where a product may affect listed species, all product labels must contain the following language:

> This product may have effects on federally listed threatened or endangered species or their critical habitat in some locations. When using this product, you must follow the measures contained in the Endangered Species Protection Bulletin for the county or parish in which you are applying the pesticide. To determine whether your county or parish has a Bulletin, and to obtain that Bulletin, consult *http://www.epa.gov/espp/*, or call 1-800-447-3813 no more than 6 months before using this product. Applicators must use Bulletins that are in effect in the month in which the pesticide will be applied. New Bulletins will generally be available from the above sources 6 months prior to their effective dates.[49]

[46] http://www.epa.gov/oppfead1/cb/csb_page/updates/2013/esa-regreview.html
[47] 50 C.F.R. § 402.14(a).
[48] *Western Watersheds Project v. Kraayenbrink*, 632 F.3d 472, 496 (9th Cir. 2011) (brackets omitted) (quoting 51 Fed. Reg. at 19,949). The threshold for triggering ESA consultation "is relatively low." *Lockyer v. U.S. Dep't of Agric.*, 575 F.3d 999, 1018 (9th Cir. 2009).
[49] *Endangered Species Protection Program Field Implementation*, 70 Fed. Reg. 66392 (Nov. 2, 2005).

7. **Require that that the registrant provide all necessary data and studies**

The EPA must have substantial evidence to re-register this pesticide. To do so, the EPA must require all necessary data and studies, including, but not limited to any previously identified data or study gaps, additional studies to evaluate effects on pollinators in accordance with the *Guidance for Assessing Pesticide Risks to Bees,*[50] information concerning estrogen or other endocrine disruption effects,[51] and any information that this pesticide or products containing this pesticide may have synergistic effects.

This is information that the EPA must require from the applicant in the first instance pursuant to 40 C.F.R. § 159.195(a), which require registrants to submit information that they reasonably should know that EPA might regard as raising concerns about the appropriate terms and conditions of registration of a product. The applicant may have information regarding synergy, whether in a U.S. Patent Application or as a result of its research and development. Failure to require any of the above information will result in the EPA underestimating adverse effects and lacking substantial evidence to support registration.

8. Incorporate necessary factors into evaluation and any proposed decision

These factors should include the following, at a minimum:

a. effects on species listed as protected under the ESA and their critical habitat,
b. effects on pollinators and other beneficial insects, including indirect effects,
c. effects on human health or environmental safety concerning endocrine disruption, and
d. any additive, cumulative or synergistic effects of the use of this pesticide.

EPA cannot satisfy its legal duties unless it requires sufficient information and evaluates it for adverse effects before reaching any conclusions. Congress tasked the EPA with regulation of pesticides for safe use. FIFRA authorizes EPA to register a pesticide only upon determining that the pesticide "will perform its intended function without unreasonable adverse effects on the environment," and that "when used in accordance with widespread and commonly recognized practice it will not generally cause unreasonable adverse effects on the environment."[52] The statute defines "unreasonable adverse effects on the environment" to include "any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide."[53] The EPA cannot meet this standard without requiring, evaluating and considering all information that causes adverse effects from the

[50] EPA 2014. Guidance for Assessing Pesticide Risks to Bees. Available at https://www.epa.gov/sites/production/files/2014-06/documents/pollinator_risk_assessment_guidance_06_19_14.pdf
[51] *See* 21 U.S.C. §§ 346a(d)(2)(A)(x) and 346a(p).
[52] 7 U.S.C. § 136a(c)(5)(C), (D); 40 C.F.R. § 152.112(e).
[53] 7 U.S.C. § 136(bb).

additional use of this pesticide. *Pollinator Stewardship Council v. U.S. E.P.A.*, Case No. 13-72346, Dkt. No. 58-1 at 6, 2015 WL 5255016, *1.

9. Place appropriate restrictions on uses to avoid and minimize adverse effects

The EPA has broad authority to restrict uses and place strong mitigation language on labels to avoid adverse effects and when there is uncertainty.

10. The EPA must take into account real-world scenarios

The EPA often claims that it is acting conservatively by using the maximum labeled use rates when estimating exposure to plants and animals. These upper-level exposure scenarios, however, do not take into account accidental spills and illegal uses of the pesticide. An assumption of 100 percent label compliance underestimates risk and is unsupported by state-collected data.[54]

A recent survey of farmers in Missouri indicated that less than half -- only 43 percent -- actually read the label each time they use pesticides.[55] Sixteen percent only read the label half the time or less and 1.2 percent have never read the label at all. Pesticide labels also have wind speed requirements that are meant to reduce drift and are used in the EPA's risk assessment process to estimate off-site exposure. Four percent of pesticide applicators never checked the wind speed before application and 40 percent of applicators checked wind speed by looking at trees, a very unreliable form of measurement that is often inaccurate.

The Centers for Disease Control and Prevention studied acute injuries related to use of fogging insect killers in residential homes.[56] While the overall injury rate was low, there were many human health harms associated with the use of these products. More importantly, the CDC measured the number of injuries before and after a mandatory label change the EPA required in 2012 to address the many incidents reported with these products. The label change, which was designed to make the products safer to use, had no effect on the number of pesticide related injuries. This indicates that some users either did not read the label instructions or failed to follow them.

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[54] Practical Farmers of Iowa. 2013. Summary of Public Record: IDALS Pesticide Bureau Case Files for Alleged Spray Drift to Organic, Fruits and Vegetables, and Horticulture. 2008-2012. Ames, IA. Available at: http://practicalfarmers.org/app/uploads/2014/01/IDALSsummary_1-14-14NN3.pdf.

[55] Randall. July 13th, 2016. State news. *57 percent of those applying pesticides in Missouri do not read label instructions*. Available at: http://www.kttn.com/57-percent-of-those-applying-pesticides-in-missouri-do-not-read-label-instructions/.

[56] Liu R, Alarcon WA, Calvert GM, et al. Acute Illnesses and Injuries Related to Total Release Foggers — 10 States, 2007–2015. MMWR Morb Mortal Wkly Rep 2018;67:125–130. Available here: https://www.cdc.gov/mmwr/volumes/67/wr/mm6704a4.htm?s_cid=mm6704a4_w

Therefore, the ever-present possibility of an accidental spill or improper disposal indicates that this is a reasonably foreseeable event that should be accounted for when estimating peak exposure concentrations. In addition, the data that are available on label compliance indicate that it is unreasonable to assume that pesticides are always applied in accordance with the label. We feel that when communicating findings to a risk manager, the EPA should no longer refer to its use of maximum labeled rates as "conservative" or accurately estimating peak exposures that may occur. And modeling off of maximum use rates should absolutely never be used to discount level of concern ("LOC") or population adjusted dose ("PAD") exceedances.

11. **The EPA must assess the enhanced toxicity of pesticide mixtures**

The Center for Biological Diversity recently released a report[57] analyzing an unconventional new source of much needed data – patent applications. When a company or individual wants to patent a chemical mixture in the United States, the United States Patent and Trademark Office ("USPTO") has to determine whether there is something non-obvious about the mixture that could presumably only be found through research and development done by the applicant. For chemical mixtures of pesticides, the applicant will often demonstrate this by claiming that the chemicals have synergistic activity. Therefore, when a chemical company applies for patent protection on a mixture of multiple pesticides, it is often accompanied by data that demonstrate synergistic toxicity to the organisms that are going to be targeted by the pesticide mixture.

We conducted an intensive search of patent applications that were germane to all pesticide products containing two or more active ingredients approved by the EPA in the past six years from four major agrochemical companies (Bayer, Dow, Monsanto and Syngenta). Our key finding was that 69 percent of these products (96 out of 140) had at least one patent application that claimed or demonstrated synergy between the active ingredients in the product.

There were 16 multi-ingredient products containing glyphosate that were approved in the past six years from Bayer, Dow and Monsanto.[58] Of those 16, 11 have evidence of synergy between the active ingredients in the product. The identified patent applications in our report found synergistic toxicity to insects from the combinations of

1) Glyphosate and indaziflam (U.S. patent application number 12506456)[59]
2) Glyphosate and 2,4-D (U.S. patent application numbers 12147853 and 14567574).[60]
3) Glyphosate and dicamba (U.S. patent application number 13099552 and 13751021).[61]

[57] Donley, N. (2016). Toxic Concoctions: How The EPA Ignores The Dangers Of Pesticide Cocktails. Retrieved from The Center for Biological Diversity website: http://www.biologicaldiversity.org/campaigns/pesticides_reduction/pdfs/Toxic_concoctions.pdf. Submitted to the docket with comment letter.
[58] *Id.* at Appendix B
[59] Submitted to the docket with comment letter as Patent #12506456
[60] Submitted to the docket with comment letter as Patent #12147853 and 14567574

Since most products that contain glyphosate were approved more than six years ago, our analysis would not have identified other patent applications that may be relevant to other multi-ingredient glyphosate products. In addition, the mixture of glyphosate and dicamba has been shown to produce synergistic toxicities in numerous other studies.[62] None of these studies or patent applications was discussed in the draft ERA or in any other documents in the docket despite being directly relevant to the analysis at hand.

We recognize that the EPA is embarking on a new process of evaluating pesticide synergy. The discovery that patent applications harbor a wealth of information about how individual pesticides interact with each other and with inert ingredients has given the agency a much needed source of data to analyze the heightened toxicities of certain chemical mixtures and proof that pesticide companies have information on synergism that they have historically failed to provide to the agency. The EPA has begun taking into account synergy data from patent applications for new pesticide registrations and has taken initial steps towards limiting some tank mixtures on pesticide labels.[63] This is a step in the right direction and we commend the EPA for the great work they have put into this process. However, recent language from the EPA and a greater understanding by our organization of how this process is being carried out has given us cause for concern that the EPA's analysis may not fully analyze and account for the wide spectrum of potential adverse effects on the environment that may result from synergism.

In the registration decision for halauxifen-methyl, the agency stated: "…the Agency views true synergism to be a rare event and intends to follow the National Research Council's recommendation for government agencies to proceed with estimating effects of pesticide mixtures with the assumption that the components have additive effects in the absence of any data to support the hypotheses of a synergistic interaction between pesticide active ingredients."[64]

The phrase "true synergism" insinuates that the data contained in applications to the United States Patent and Trademark Office ("USPTO") may somehow be easily disregarded, not taken seriously, or treated as requiring more scrutiny than other data generated by pesticide registrants. This is unacceptable. Any patent application submitted to the USPTO is a publicly available

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[61] Submitted to the docket with comment letter as Patent #13099552 and #13751021

[62] Kruger, GR, Johnson, WG, Weller, SC. The Effect of Glyphosate Plus Dicamba Drift Rates on Commercial Processing Tomatoes. Poster Presentation. Available at: https://ag.purdue.edu/btny/weedscience/slidesandposters/GKruger08-02.pdf; Soloneski, S., Ruiz de Arcaute, C. & Larramendy, M.L. Environ Sci Pollut Res (2016) 23: 17811. Available at: https://link.springer.com/article/10.1007%2Fs11356-016-6992-7.

[63] See final registration decisions for halauxifen-methyl (regulations.gov docket ID EPA-HQ-OPP-2012-0919-0024) and sulfoxaflor (regulations.gov docket ID EPA-HQ-OPP-2010-0889-0563).

[64] EPA. Final Registration Decision of the New Active Ingredient Halauxifen-methyl. 2016. Pg. 8. Regulations.gov docket ID EPA-HQ-OPP-2012-0919-0024.

document containing claims made to a government agency of the United States. Since it is unlawful to knowingly submit false information to the government,[65] any data or claims contained within a document submitted to a government agency should be assumed to be accurate unless there is specific evidence to indicate otherwise.

Synergy is synergy – it has a very precise and well-established definition and EPA's statement indicates a reckless disregard of this reality. In fact, the Colby equation,[66] which has been the standard benchmark method for establishing herbicide synergy for nearly 50 years, is often the analysis used to demonstrate synergy in patent applications. The data on synergy in patent applications is gathered on plants, fungi and insects. These are not complex organisms and these are not complex experiments. Some level of statistical analysis may be warranted to show that the synergy identified was not a result of chance alone, but there is absolutely no indication that these data should not receive full consideration in a registration decision. In most cases, the same companies that submit all of the toxicity studies that the EPA uses in its risk assessments in the first place performed the experiments that demonstrate synergy in patent applications. It's coming from the same source, likely using the same protocols and methodology used to meet EPA's data requirements under FIFRA. The agency cannot justify applying two different standards to the same data source. These data are without a doubt sufficient to support the hypothesis of a synergistic interaction and should not be met with skepticism, but rather as an opportunity for the agency to adhere to its mission and mandate under FIFRA – to ensure that the pesticides it registers do not cause unreasonable adverse effects to the environment.

In addition, we agree with the Agency that synergy is a rare event in the context of a random assortment of chemicals. However, the EPA's fundamental assumption that synergy is a rare event is unsupportable in the context of pesticide products. Pesticides aren't a random assortment of chemicals – different classes of pesticides are designed to be toxic to a specific group of organisms through different modes of action. This greatly increases the likelihood that synergy will occur with combinations of pesticides because the toxicity is already tailored to a specific group of organisms and pesticides with different modes of action can concomitantly disrupt different vital cellular pathways used for detoxification, maintaining homeostasis and repairing injury.

In addition, the mixtures that have been identified by their synergistic action in patents are not a random assortment of pesticides. These mixtures were chosen based on their patentability and since patentability of mixtures usually relies on the presence of synergy, this is not a random assortment of pesticide mixtures. This is an assortment of pesticide mixtures that is biased towards the presence of synergy. Therefore, the number of pesticide synergy claims should not

[65] 18 U.S.C. 1001.
[66] Colby, S.R. (1967) Calculating Synergistic and Antagonistic Responses of Herbicide Combinations. *Weeds*, 15(1), 20-22.

be taken as evidence that most of them must somehow be incorrect, but that registrants have invested a lot of time and energy in identifying novel and patentable pesticide mixtures. The sheer number of combinations of possible pesticide mixtures is immense. This is a very important point to understand. Given how many pesticide mixtures are possible, the ones that have evidence of synergy only represent a fraction of a percent. Assuming that there are 2000 pesticide active ingredients that are currently registered and allowed for use, then that means there are nearly 2 million unique combinations of two that can be formed from that pool of active ingredients and more than a billion unique combinations of three. The number of synergy claims identified in patent applications pales in comparison to those numbers. Therefore, pesticide synergy will still be an *extremely* rare event even if every single patent claim of synergy reflects "true synergism."

The protocol that is currently being used to identify claims of synergy and place restrictions on pesticide use is a step above how the agency has utilized synergy data in the past, yet many steps in the process appear arbitrary and poorly executed. Therefore, we have outlined the steps that the EPA must take to ensure that its process for evaluating pesticide synergy is scientifically robust, defensible and compliant with FIFRA.

1) The EPA must request <u>all</u> data regarding the toxicity of mixtures containing the pesticide under consideration from the pesticide registrant/applicant, including all data on possible synergy. The Agency has stated in the past that it cannot be confident whether issuance of registration can meet the standard in FIFRA without prior analysis of all available data regarding synergy.[67] However, the EPA now appears to be limiting itself in the type of data it is requesting from pesticide registrants. It is our understanding that in the registration of halauxifen-methyl, the agency only requested synergy data from the pesticide registrants that were submitted to the USPTO. This is inadequate because pesticide registrants likely possess additional information regarding pesticide synergy that they do not include in their patent applications to the USPTO, as extensive experimentation is typically done before a company will invest the time and money to develop a product that they intend to market. If any other synergy data exist *in addition* to what was submitted to the USPTO, this would be directly relevant to the registration decision at hand. Registrants are required to submit information to the EPA that could raise concerns about the continued registration of a product or about the appropriate terms and conditions of registration.[68] For example, pursuant to 40 CFR §159.195(a)(3), the registrant is required to submit information that indicates "[u]se of a pesticide may

[67] Respondents' Motion for Voluntary Vacatur and Remand filed in N*atural Resources Defense Council, Inc. v. U.S. EPA*, No. 14-73353 (consolidated with 14-73359), ECF Dkt. No. 121 (filed November 24, 2015 9th Cir.).
[68] 40 C.F.R. § 159.195(a).

pose any greater risk than previously believed or reported to the Agency." Any data on chemical synergy would certainly fall into that category.

2) Before any registration decision is made, the EPA must do a comprehensive patent application and literature search for any evidence or claims that the active ingredient under consideration produces any synergistic toxicities with any chemical with which it may be co-applied.
    a) This includes patent applications or publications that find synergy with the active ingredient under consideration and any chemical that is not considered an active ingredient. Currently, it appears that the agency is only considering data on synergy of *active ingredient* combinations. The EPA has a duty under FIFRA to ensure that end-use products do not cause unreasonable adverse effects on the environment.[69] Since end-use products often contain chemicals that are not considered active ingredients (commonly called "inert" ingredients), synergy between any ingredients in the product must be analyzed and considered in the context of a registration decision.
    b) This includes studies from government or any non-industry researchers and patent applications that are assigned to entities other than the pesticide registrant. Patent applications from companies or individuals other than the pesticide registrant/applicant are relevant information that the EPA must analyze and consider in the context of a registration decision. The EPA has done this is the past, specifically for the new use registration of dicamba on herbicide resistant cotton and soybean. Studies in the primary literature, as well as a patent application from Dow (the applicant for the new use was Monsanto), were both identified as lines of evidence to propose tank-mixing restrictions.[70]
    c) This includes patent applications that have been approved, are still pending or have been denied. Recently, we have been troubled by what we see as the agency arbitrarily disregarding certain pieces of key information in making registration decisions. In the case of halauxifen-methyl, the EPA only took into account synergy data from approved patents, writing off data in pending patent applications or denied patent applications.[71] This practice is not only indefensible, but contradicts earlier, common-sense practices used by the EPA to analyze data on synergy. Following registration of the Enlist Duo pesticide product, the EPA identified a *pending* patent application that made a claim of synergy between the

[69] *Reckitt Benckiser Inc. v. EPA*, 613 F.3d 1131, 1133 (D.C. Cir. 2010) (citing 7 U.S.C. § 136a(a), (c)-(e) and 7 U.S.C. § 136a(c)(5)(C), (D)).
[70] EPA. Memorandum. Dicamba DGA: Second Addendum to the Environmental Fate and Ecological Risk Assessment for Dicamba DGA salt and its Degradate, 3,6-dichlorosalicylic acid (DCSA) for the Section 3 New Use on Dicamba-Tolerant Soybean. Docket ID EPA-HQ-OPP-2016-0187-0007. Page 22.
[71] EPA. Final Registration Decision of the New Active Ingredient Halauxifen-methyl. 2016. Pg. 9. Regulations.gov docket ID EPA-HQ-OPP-2012-0919-0024.

active ingredients in the product. This pending patent application (that was ultimately abandoned by the applicant) was the sole reason that the EPA asked the Ninth Circuit Court of Appeals to vacate its registration of Enlist Duo.[72] The EPA has also used a patent application that was rejected by the USPTO and ultimately abandoned by the applicant as one line of evidence to propose tank-mixing restrictions for a product containing dicamba.[73] At one point, the EPA understood that the status of a patent application had no bearing on the underlying accuracy of the synergy claims. The job of a patent examiner is to determine whether a patent application is covered by prior art or makes novel claims. They do not provide peer-review or judge whether claims of synergy are real or not, they simply decide whether a patent application overlaps with other patented material. Any patent application submitted to the USPTO is a publicly available document containing claims made to a government agency of the United States. Since it is unlawful to knowingly submit false information to the government,[74] any data or claims contained within a document submitted to a government agency should be assumed to be accurate unless there is specific evidence to indicate otherwise. Therefore, the EPA must analyze any patent application that has been approved, denied or is still pending.

d) This includes patent applications submitted to other countries or the World Intellectual Property Organization ("WIPO"). Many other countries and the European Union have counterparts to the USPTO and most patent applicants will submit applications to multiple organizations to gain patent protection throughout the countries they intend to market their products. Unfortunately, it can be up to 18 months before a patent application submitted to the USPTO is published and made available to the public.[75] Therefore, patent applications submitted to other organizations generally contain relevant information, often in a timelier manner. This information is crucial to have, especially in the case of new active ingredients, which are often newer chemistries that may have patent applications not yet made available to the public by the USPTO.

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[72] Respondents' Motion for Voluntary Vacatur and Remand filed in N*atural Resources Defense Council, Inc. v. U.S. EPA*, No. 14-73353 (consolidated with 14-73359), ECF Dkt. No. 121 (filed November 24, 2015 9th Cir.).

[73] EPA. Memorandum. Dicamba DGA: Second Addendum to the Environmental Fate and Ecological Risk Assessment for Dicamba DGA salt and its Degradate, 3,6-dichlorosalicylic acid (DCSA) for the Section 3 New Use on Dicamba-Tolerant Soybean. Docket ID EPA-HQ-OPP-2016-0187-0007. Page 22. Referencing Satchivi, N and Wright, T. Synergistic herbicidal composition containing a dicamba derivative and a glyphosate derivative. United States patent publication no. US 20110275517 A1. Application number US 13/099,552. 10 November 2011.

[74] 18 U.S.C. 1001.

[75] USPTO. USPTO Will Begin Publishing Patent Applications. November 27th , 2000. Available at: https://www.uspto.gov/about-us/news-updates/uspto-will-begin-publishing-patent-applications.

3) The EPA should identify which patent applications or studies were analyzed for claims of synergy. In recent registration decisions for halauxifen-methyl and sulfoxaflor, the EPA did not indicate which patent applications were used to support the proposed tank mix restrictions.[76] This information is necessary for the public to understand what lines of evidence were used to support tank mix restrictions and also give the public a chance to provide the EPA with more information that may have been missed or wrongly discounted. Public review and comment should be done at the earliest possible point in the registration process, but -- at the very least -- at the time of a proposed registration decision. It is absolutely imperative that all dangerous chemical combinations be restricted before a registration decision is made and this can only happen if the EPA is transparent with the information that it has used, or not used, to support the proposed restrictions.

3) Any change in tank-mix restrictions post-registration needs to go through public review and comment. For the registration of halauxifen-methyl, the EPA has indicated that, as more information is analyzed, some chemicals may be removed from the list of prohibited tank mixing partners.[77] If any evidence exists that contradicts claims or data provided in patent applications, then that information needs to be made available to the public or discussed in a public forum, as this is not only of interest to stakeholders but also the USPTO. This information could have major consequences for approved or pending patent applications in the United States and in other countries. It is vitally important that patent organizations stay up-to-date on whether any claims of synergy are contradicted by newly provided registrant studies or recent analyses by the EPA.

4) A synergy analysis needs to be performed for all new ingredient registrations and during all registration reviews. It appears that the EPA has begun to institute a synergy analysis for all new ingredient registrations, which we fully support; however, it is still unclear whether the agency intends to do this for all active ingredients under registration review. Active ingredients that are up for registration review have been in use for at least 15 years. This means they are generally available in a wider variety of end-use products (containing more combinations of active and inert ingredients) and, because they have been studied longer, there is more synergy information associated with them than with new active ingredients. Therefore, an intensive synergy analysis on any active ingredient must be done during registration review in order for the EPA to remain compliant with FIFRA.

[76] See final registration decisions for halauxifen-methyl (regulations.gov docket ID EPA-HQ-OPP-2012-0919-0024) and sulfoxaflor (regulations.gov docket ID EPA-HQ-OPP-2010-0889-0563).
[77] EPA. Final Registration Decision of the New Active Ingredient Halauxifen-methyl. 2016. Pg. 9. Regulations.gov docket ID EPA-HQ-OPP-2012-0919-0024.

5) Tank mix prohibitions are not protective enough when evidence of synergy exists; prohibitions on "co-application in the same growing season" are needed to ensure no unreasonable adverse effects on the environment. The USDA and industry groups that oppose tank mix restrictions are eager to assert that tank mixing bans will force farmers to make multiple passes through their fields to apply pesticides individually, thus increasing fuel consumption, costs and soil compaction.[78] Not only is the "multiple pass" scenario highly unlikely because farmers would not reasonably (or rationally) elect to make multiple passes when they can just choose a new tank mix partner that is not prohibited, but also it completely misses the point of what the EPA is trying to achieve with these prohibitions. The same dangerous synergistic toxicity will be present whether these chemicals are applied at the exact same time (as with a tank mix) or whether they are applied within a couple of days of one another (as with multiple passes in a field). The half-lives of nearly all pesticides extend beyond a couple of days and many are in the hundreds of days under normal environmental conditions. As long as the pesticide label allows synergistically acting chemicals to be applied in the same geographical location in the same growing season, then the EPA cannot reasonably assume that these chemicals will never be encountered at the same time by non-target plants or animals. Restrictions solely on tank mixing are inadequate and leave the agency open to absurd criticisms about increased fuel use and soil compaction. It's important to keep in mind that while a prohibition on co-applying a handful of certain pesticides in the same growing season may be painted as restrictive by opponents, it is anything but. This involves a *very* small fraction of pesticides that will not be able to be used in combination. Any benefit to the farming community of being able to use *these specific combinations* of pesticides and/or "inert" ingredients is far outweighed by the environmental costs associated with their use.

   The USDA decided to do a case study on apple production on the east coast and west coast in order to bolster its position against common-sense tank mix restrictions.[79] The agency found that an astonishing 51 active ingredients are applied to Washington apples every year and east coast apples are sprayed 15-25 times a year with tank mixes of around 3 pesticides. The USDA then concluded that a blanket tank mix ban would result in farmers having to make 51 to 75 passes each year to spray their crops.

   First of all, there has never been a blanket tank mix ban proposed by EPA. The tank mix restrictions are very modest and only for ingredients with demonstrated synergy. Second, the fact that apple farmers are spraying more than 50 active ingredients on a single crop each year is absolutely frightening. Under no scenario should this be okay. This is a

[78] See submitted comments from the USDA and industry groups for "New Active Ingredient Halauxifen-Methyl for Use on Wheat, Barley, and Triticale (PP# 2F8086)." Docket ID: EPA-HQ-OPP-2012-0919.
[79] See submitted comments from the USDA for "Sulfoxaflor; New Active Ingredient." Docket ID: EPA-HQ-OPP-2010-0889.

practice that has been enabled by the EPA's lax restrictions on tank mixing, not one that is threatened by EPA's current actions. Rather than providing evidence against action on tank mixes, we believe the USDA's case study should have the opposite effect. Maybe, finally, some realization that this has gotten way out of hand and tank mixing is something that EPA must get a handle on.

The USDA and industry groups have said in the past that prohibiting the co-application of certain pesticide ingredients will impair the ability of the farming community to prevent pest resistance from occurring.[80] This is not true. First of all, there are many proven methods for discouraging resistance, including: reducing pesticide use by spraying in response to a pest or weed infestation and not prophylactically, integrating other control methods in addition to chemical control (such as beneficial insects/nematodes) and pesticide rotation in conjunction with crop rotation, among others.[81] Mixing multiple different chemicals in the same tank is not the most effective way of preventing resistance and is inconsistent with Integrative Pest Management ("IPM") techniques that promote sustainable agricultural techniques over harmful ones. Furthermore, tank mixes can actually promote pest resistance if the mixed pesticides share the same mode of action.

Many state extension offices promote the use of the above methods for controlling resistance and allowing for either pesticide rotation or tank mixing if necessary.[82] Pesticide rotation, which involves using rotating pesticides with different MOAs over consecutive years is more effective at preventing pest resistance to a single chemical than tank mixing (and it does not necessitate the use of mixtures). In fact the University of California Agriculture and Natural Resources Department materials on managing pest resistance state: "Key elements of resistance management include minimizing pesticide

[80] See submitted comments from the USDA and industry groups for "New Active Ingredient Halauxifen-Methyl for Use on Wheat, Barley, and Triticale (PP# 2F8086)." Docket ID: EPA-HQ-OPP-2012-0919.

[81] See Report, Organic Agriculture and Integrated Pest Management: Synergistic Partnership Needed to Improve the Sustainability of Agriculture and Food Systems, 2015. Authors: Dr. Daniel Cooley, University of Massachusetts Amherst; Susan Futrell, Red Tomato; Lyn Garling and Dr. Edwin Rajotte, Penn State University; Grace Gershuny, GAIA Services; Jeff Moyer, Rodale Institute; Abby Seaman, Cornell University; and Dr. Stephen Young of the Northeastern IPM Center. This work is supported by the USDA National Institute of Food and Agriculture, North Central IPM Center projects AG 2012-51120-20252 and AG 2014-70006-22486
Available at: https://organicipmwg.files.wordpress.com/2015/07/white-paper.pdf

[82] University of California Agriculture and Natural Resources Statewide Integrated Pest Management Program. How to Manage Pests, UC Pest Management Guidelines. Floriculture and Ornamental Nurseries Managing Pesticide Resistance. March 2009. Available at: http://ipm.ucanr.edu/PMG/r280390311.html; Michigan State University Extension. Growers need to think "rotation" to prevent pesticide resistance. Posted on February 26, 2013 by Bruce MacKellar. Available at: http://msue.anr.msu.edu/news/growers_need_to_think_rotation_to_prevent_pesticide_resistance; University of Massachusetts Amherst Extension. The Center for Agriculture, Food and the Environment. Pest Management: Proper Use of Pesticides. Available at: https://ag.umass.edu/greenhouse-floriculture/greenhouse-best-management-practices-bmp-manual/pest-management-proper-use.

use, avoiding tank mixes, avoiding persistent chemicals, and using long-term rotations of pesticide from different chemical classes" and "In some cases, mixing pesticides from two different classes provides superior control. However, long-term use of these two-class pesticide mixes can also give rise to pesticide resistance, if resistance mechanisms to both pesticides arise together in some individuals. Continued use of the mixture will select for these multiple-pesticide-resistant pests."[83] The University of Massachusetts Extension office further states: "Avoid tank mixes (mixing two or more insecticides together to control a single pest) except in cases where research has demonstrated improved efficacy."[84]

Recent modelling studies looking at how pesticide mixtures or sequential pesticide use would influence resistance development in mosquitoes found both methods to provide a similar delay in resistance compared to using just one pesticide year after year.[85] However the sequential use scenario had the added benefit of increasing the time it takes for resistance to both insecticides to develop, effectively extending the useful life of both pesticides compared to mixing them.

We hope the irony of the "we need to mix more chemicals to prevent resistance" argument is not lost on the EPA. We have gotten to the point where farmers are being told that they need to mix multiple chemicals together – **not** to combat a pest pressure – but to maintain the efficacy of one of the chemicals in the mixture. Tank mixing is not the most effective way of preventing resistance – that would be reducing pesticide use altogether and spraying in response to a pest problem instead of prophylactically.

For the reasons outlined above, in order to be compliant with FIFRA, the EPA must do an analysis of mixture toxicity with mixtures containing this active ingredient before any registration decision can be made. If the EPA does not think that it has the proper methodology in place to do this analysis, prohibiting the co-application of certain pesticides with this active ingredient is another way the EPA can ensure that any registration decision is compliant with FIFRA. Otherwise, the EPA will not be able to conclude that registration of this ingredient will not have unreasonable adverse effects on the environment.

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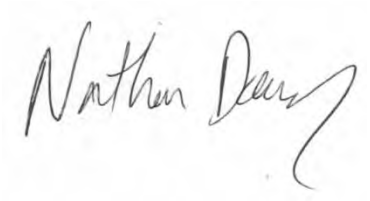
[83] University of California Agriculture and Natural Resources Statewide Integrated Pest Management Program. How to Manage Pests, UC Pest Management Guidelines. Floriculture and Ornamental Nurseries Managing Pesticide Resistance. March 2009. Available at: http://ipm.ucanr.edu/PMG/r280390311.html.

[84] University of Massachusetts Amherst Extension. The Center for Agriculture, Food and the Environment. Pest Management: Proper Use of Pesticides. Available at: https://ag.umass.edu/greenhouse-floriculture/greenhouse-best-management-practices-bmp-manual/pest-management-proper-use.

[85] Levick B, South A, Hastings IM (2017) A Two-Locus Model of the Evolution of Insecticide Resistance to Inform and Optimise Public Health Insecticide Deployment Strategies. PLoS Comput Biol 13(1): e1005327. Available at: http://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1005327 and South, A and Hastings, IM (2018) Insecticide resistance evolution with mixtures and sequences: a model-based explanation. Malaria Journal. 17(80). Available at: https://malariajournal.biomedcentral.com/articles/10.1186/s12936-018-2203-y

Respectfully submitted,



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These comments are fully supported by

Beyond Toxics
Center for Food Safety
American Bird Conservancy
National Latino Farmers & Ranchers Trade Association
U.S. PIRG
National Family Farm Coalition
Environment America
Kansas Rural Center
Organic Consumers Association
Citizens Regeneration Lobby
The City Project

APPENDIX A

ENDANGERED SPECIES ACT CONSULTATION OBLIGATIONS FOR PESTICIDE APPROVALS BY THE ENVIRONMENTAL PROTECTION AGENCY

I. EPA Has an Independent Duty Under the Endangered Species Act to Consult with the U.S. Fish and Wildlife Service and National Marine Fisheries Service on Pesticide Approvals.

Section 7(a)(2) of the ESA requires that "each federal agency *shall*, in consultation with and with the assistance of the Secretary, insure that any action authorized, funded, or carried out by such agency is not likely to jeopardize the continued existence of any endangered species or threatened species or result in the destruction or adverse modification of habitat of such species which is determined by the Secretary… to be critical."[86] Under Section 7(a)(2), the EPA must consult with the U.S. Fish and Wildlife Service and National Marine Fisheries Service (collectively the "Services") to determine whether its actions will jeopardize listed species' survival or adversely modify designated critical habitat, and if so, to identify ways to modify the action to avoid that result.[87] The consultation requirement applies to any discretionary agency action that may affect listed species.[88] Because the EPA may decline to approve pesticides and uses, its decision represents a discretionary action that clearly falls within the ESA's consultation requirement.[89]

The EPA must initiate consultation under Section 7 whenever its action "may affect" a listed species or critical habitat.[90] Under the Services' joint regulations implementing the ESA, the EPA is required to review its actions "at the earliest possible time" to determine whether the action may affect listed species or critical habitat.[91] Indeed, the EPA's policy *Enhancing Stakeholder Input in the Pesticide Registration Review and ESA Consultation Processes* envisions informal consultations with the Services beginning at the preliminary risk assessment

[86] 16 U.S.C. § 1536(a)(2) (emphasis added).
[87] 50 C.F.R. § 402.14.
[88] *National Association of Home Builders v. Defenders of Wildlife*, 551 U.S. 644 (2007).
[89] *See Washington Toxics Coalition v. EPA*, 413 F. 3d 1024, 1032 (9th Cir. 2005) ("even though EPA registers pesticides under FIFRA, it must also comply with the ESA when threatened or endangered species are affected.").
[90] 50 C.F.R. § 402.14(a).
[91] 50 C.F.R. § 402.14(a).

stage.[92] The Services define "may affect" as "the appropriate conclusion when a proposed action may pose ***any*** effects on listed species or designated critical habitat."[93] This inquiry even includes beneficial effects. The phrase "may affect" has been interpreted broadly to mean that "any possible effect, whether beneficial, benign, adverse, or of an undetermined character, triggers the formal consultation requirement."[94] For this initial stage of review, exposure to a pesticide does not require that effects reach a pre-set level of significance or intensity to trigger the need to consult (e.g. effects do not need to trigger population-level responses). As the Services' joint consultation handbook explains, an action agency such as the EPA may make a "no effect" determination, and thus avoid undertaking informal or formal consultations, only when "the action agency determines its proposed action will not affect listed species or critical habitat."[95]

Because the use of these pesticide formulations and products "may affect" listed species and "may affect" the critical habitat of listed species, the EPA must consult with the Services regarding its pesticide approvals in order to comply with the ESA.

Fortunately the National Academy of Sciences ("NAS") has provided guidance regarding the obligations of EPA and other wildlife agencies in analyzing pesticide approvals under the ESA. The NAS committee provided a report to the EPA and Services in April of 2013 providing specific recommendations relating to the use of "best available data;" methods for evaluating sublethal, indirect, and cumulative effects; the state of the science regarding assessment of mixtures and pesticide inert ingredients; the development, application, and interpretation of results from predictive models; uncertainty factors; and what constitutes authoritative geospatial and temporal information for the assessment of individual species, habitat effects and probabilistic risk assessment methods.[96]

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[92] U.S. Environmental Protection Agency 2013, Office of Chemical Safety and Pollution Prevention- Office of Pesticide Programs, Enhancing Stakeholder Input in the Pesticide Registration Review and ESA Consultation Processes and Development of Economically and Technologically Feasible Reasonable and Prudent Alternatives, Docket ID #: EPA-HQ-OPP-2012-0442-0038 (March 19, 2013) at p. 8

[93] U.S. Fish and Wildlife Service and National Marine Fisheries Service 1998. *Endangered Species Consultation Handbook: Procedures for Conducting Consultation and Conference Activities Under Section 7 of the Endangered Species Act* (hereafter CONSULTATION HANDBOOK) at xvi (emphasis in original).

[94] *Western Watersheds Project v. Kraayenbrink*, 632 F.3d 472, 496 (9th Cir. 2011) (brackets omitted) (quoting 51 Fed. Reg. at 19,949). The threshold for triggering ESA consultation "is relatively low." *Lockyer v. U.S. Dep't of Agric.*, 575 F.3d 999, 1018 (9th Cir. 2009).

[95] CONSULTATION HANDBOOK at 3-13.

[96] National Academy of Sciences 2013. *Assessing Risks to Endangered and Threatened Species from Pesticides* (hereafter NAS REPORT), Committee on Ecological Risk Assessment under FIFRA and ESA Board on Environmental Studies and Toxicology Division on Earth and Life Studies National Research Council (April 30, 2013).

While the NAS report outlines areas for all three agencies to improve, the NAS report made several significant conclusions about the current ecological risk assessment process and its use of risk quotients ("RQs"), including:

- The EPA "concentration-ratio approach" for its ecological risk assessments "is ad hoc (although commonly used) and has unpredictable performance outcomes."[97]
- "RQs are not scientifically defensible for assessing the risks to listed species posed by pesticides or indeed for any application in which the desire is to base a decision on the probabilities of various possible outcomes."[98]
- "The RQ approach does not estimate risk…but rather relies on there being a large margin between a point estimate that is derived to maximize a pesticide's environmental concentration and a point estimate that is derived to minimize the concentration at which a specified adverse effect is not expected."[99]
- "Adding uncertainty factors to RQs to account for lack of data (on formulation toxicity, synergy, additivity, or any other aspect) is unwarranted because there is no way to determine whether the assumptions that are used overestimate or underestimate the probability of adverse effects."[100]

According to the NAS, the EPA concentration-ratio approach contrasts sharply with a probabilistic approach to assessing risk, which the NAS describes as "technically sound." The NAS's underlying conclusion is that EPA should move towards a probabilistic approach based on population modeling, an approach that the NMFS already utilizes.[101] The NAS also recommends that the FWS move towards a probabilistic approach in its consultations.

Following the publication of the NAS report, the agencies have developed two policy documents to guide consultations on pesticide review and approvals moving forward: (1) *Enhancing Stakeholder Input in the Pesticide Registration Review and ESA Consultation Processes*,[102] and (2) *Interim Approaches for National-level Pesticide Endangered Species Act Assessments Based on Recommendations of the National Academy of Science April 2013*.[103] The agencies made clear at a November 15, 2013 public meeting that these new procedures and approaches would

[97] *Id*. at 107.
[98] *Id*. at 11.
[99] *Id*.
[100] *Id*.
[101] *Id*. at 107.
[102] U.S. Environmental Protection Agency 2013, Office of Chemical Safety and Pollution Prevention- Office of Pesticide Programs, Enhancing Stakeholder Input in the Pesticide Registration Review and ESA Consultation Processes and Development of Economically and Technologically Feasible Reasonable and Prudent Alternatives, Docket ID #: EPA-HQ-OPP-2012-0442-0038 (March 19, 2013).
[103] Available at https://www.epa.gov/sites/production/files/2015-07/documents/interagency.pdf

be "day forward" in their implementation.[104] Accordingly, approvals of pesticides and uses *must* follow these new *Interim Approaches* and comply with the requirements of the ESA.

A. Completion of Step One under Interim Approaches

As laid out in the National Academy of Sciences and *Interim Approaches* guidance, the risk assessment and consultation process should follow three steps.[105] These steps generally follow the three inquiries of the ESA consultation process: (1) the "no effect"/ "may affect" determination (2) the "not likely to adversely affect"/ "likely to adversely affect" determination (3) the jeopardy/no jeopardy and adverse modification/no adverse modification of critical habitat determination. Step One generally follows the requirements of the ESA and will in most cases identify those species at risk from pesticides that need additional review through the informal and formal consultation process. At Step One, the EPA must gather sufficient data to complete the following two related inquiries: (1) the EPA must determine whether pesticide use areas will overlap with areas where listed species are present, including whether a use area overlaps with any listed species' critical habitat (2) the EPA must determine whether off-site transport of pesticides will overlap with locations where listed species are present and/or critical habitat is designated. Off-site transport must include considerations of downstream transport due to runoff as well as downwind transport due to spray drift when the best available science indicates such transport is occurring.[106]

What the EPA should do to meet the legal requirements of the ESA is use the best available spatial data regarding the pesticide use patterns and the distribution and range of listed species to determine whether a pesticide's use overlaps with species, and then make a "may affect"/"no effect" determination. The Fish and Wildlife Service ECOS website provides GIS-based data layers for each listed species with designated critical habitat.[107] These maps are scalable and can achieve the precision needed to make accurate effects determinations regarding whether a pesticide will have "no effect" or "may affect" a listed species and are certainly accurate enough to make determinations as to whether the use of a pesticide represents adverse modification of

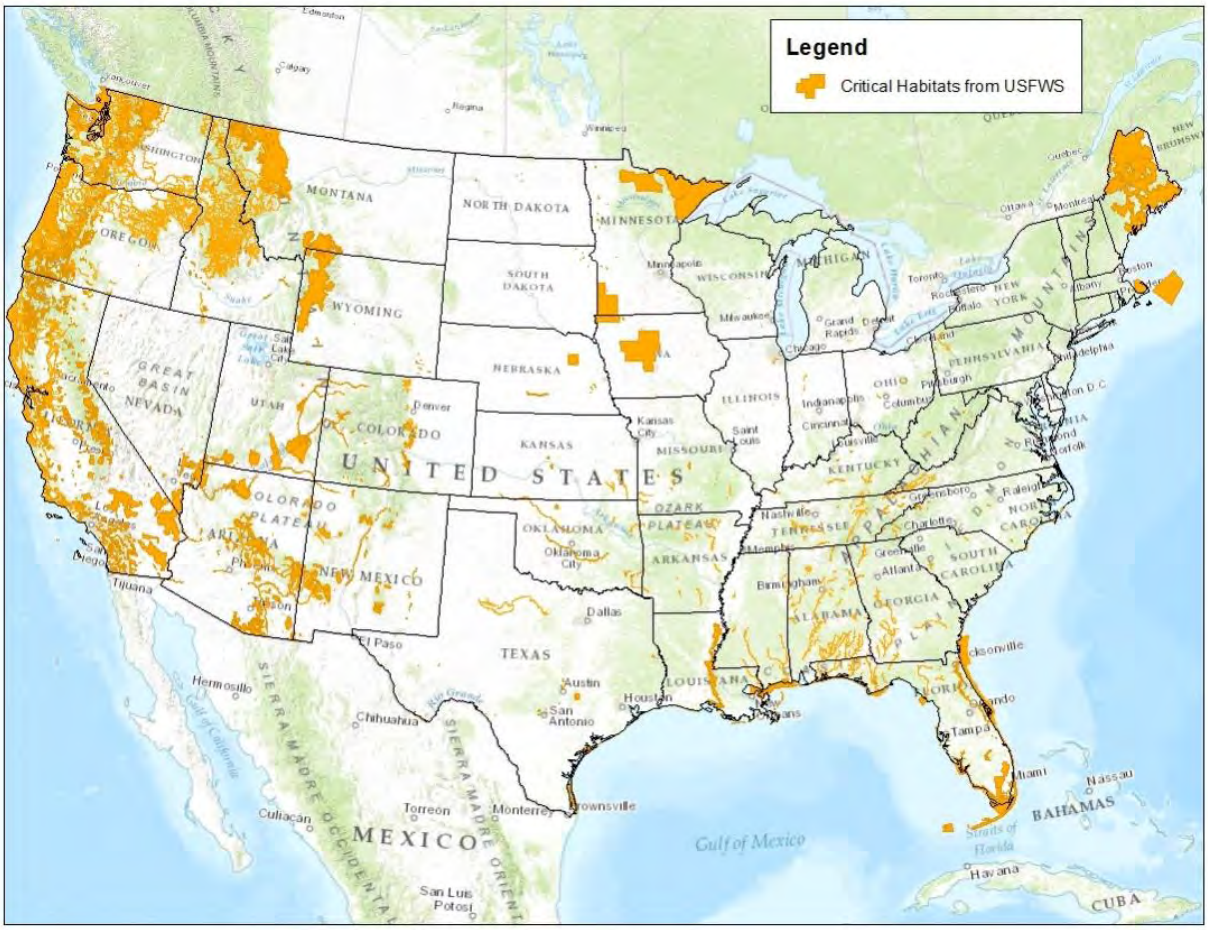
[104] INTERAGENCY APPROACH FOR IMPLEMENTATION OF NATIONAL ACADEMY OF SCIENCES REPORT: ASSESSING RISKS TO ENDANGERED AND THREATENED SPECIES FROM PESTICIDES, Public Meeting Silver Spring NOAA Auditorium (Nov. 15, 2013).
[105] NAS REPORT at 37-38.
[106] The Center acknowledges that in many areas, atmospheric transport is difficult to model and assess. However, in some areas, the impacts of atmospheric transport of pesticides are well understood. A recent study found that a variety of pesticides are accumulating in the Pacific chorus frogs (*Pseudacris regilla*) through atmospheric deposition at remote, high-elevation locations in the Sierra Nevada mountains, including in Giant Sequoia National Monument, Lassen Volcanic National Park, and Yosemite National Park Smalling, K.L., et al. 2013. *Accumulation of Pesticides in Pacific Chorus Frogs (Pseudacris regilla) from California's Sierra Nevada Mountains*, Environmental Toxicology and Chemistry, 32:2026–2034.
[107] US Fish and Wildlife Service Environmental Conservation Online System. http://ecos.fws.gov

critical habitat. Figure One provides an overlay map from ECOS of all critical habitat that has been designated for listed species thus far.

Other sources provide additional data on the distribution and life history of threatened and endangered species. NatureServe provides detailed life history information, including spatial distribution, for native species across the United States.[108] In addition, many State governments collect detailed information on non-game species through their State Wildlife Action Plans.[109] In short, there are many sources of data that can provide EPA with the detailed information it needs to conduct an effects determination for each species. If there is a subset of species where it believes information is still lacking, EPA should make that clear to all stakeholders which species specifically it believes such data are lacking early in the process such that this information can be collected from the Services and other sources.

[108] NatureServe Get data. http://www.natureserve.org/getData/index.jsp
[109] State Wildlife Action Plans. http://teaming.com/state-wildlife-action-plans-swaps

Figure One – Base Composite Map of Critical Habitat in the United States[110]



To make scientifically valid effects determinations, EPA will also need the best available spatial data regarding the use of pesticides. The U.S. Department of Agriculture and the U.S. Geological Survey[111] collect data on an enormous suite of pesticide active ingredients each year, as do several private organizations. Thus, it should be possible to determine where areas of geographic overlap between species and pesticide usage occur. If empirical data on pesticide use or persistence in the environment is lacking geospatial modeling can be used to determine where pesticide use may overlap with affected endangered species.

With the completion of the problem formulations for Ecological Risk, the EPA should now move quickly to begin the informal consultation process for pesticides, starting with a spatial analysis as envisioned as Step one. If this information is collected and assessed properly, then it should then be relatively straightforward for the EPA to begin to develop geographic restriction on the use of pesticides wherever designated critical habitat for a listed species exists as parts of Step

[110] US Fish and Wildlife Service Environmental Conservation Online System. http://ecos.fws.gov
[111] USGS, National Water-Quality Assessment (NAWQA) Program, Pesticide National Synthesis Project, Annual Pesticide Use Maps: 1992-2013, available at https://water.usgs.gov/nawqa/pnsp/usage/maps/

Two and Step Three. However, because not all threatened and endangered species have critical habitat, the EPA will also have to collect data on the distribution and range of species that do not yet have critical habitat to determine whether the use of these pesticides will jeopardize any of those species.

B. Label Requirements.

FIFRA requires that the EPA evaluate and reregister a pesticide every 15 years. During that 15 year period, crop distributions change, use patterns for pesticides change, and listed species change. By the time the registration review process is complete several years from now, additional species will almost certainly be protected by the ESA. Of the species currently listed, some may move towards recovery and become more common while others may become even more imperiled.

Product labels must be able to adapt to changing conditions on the ground to ensure that the use of these pesticides do not cause unanticipated adverse impacts that result in levels of take not authorized through the Section 7 consultation process. Fortunately, the EPA has already developed a system that can address impacts to endangered species and that provides for geographically-targeted conservation measures on the ground through its *Bulletins Live! Two* website.[112] The Center recommends that whenever a pesticide may affect listed species, both as a precautionary matter and as a mechanism to implement any conservation measures that are implemented in the informal and formal consultation process, the EPA use the *Bulletins Live! Two* system to incorporate these measures. Accordingly, all product labels for pesticides affecting endangered species must contain the following language:

> This product may have effects on federally listed threatened or endangered species or their critical habitat in some locations. When using this product, you must follow the measures contained in the Endangered Species Protection Bulletin for the county or parish in which you are applying the pesticide. To determine whether your county or parish has a Bulletin, and to obtain that Bulletin, consult *http://www.epa.gov/espp/*, or call 1-800-447-3813 no more than 6 months before using this product. Applicators must use Bulletins that are in effect in the month in which the pesticide will be applied. New Bulletins will generally be available from the above sources 6 months prior to their effective dates.[113]

[112] U.S. Environmental Protection Agency Endangered Species Protection Bulletins. http://www.epa.gov/espp/bulletins.htm

[113] *Endangered Species Protection Program Field Implementation*, 70 Fed. Reg. 66392 (Nov. 2, 2005).

II. The EPA Must Make Defensible "Not Likely to Adversely Affect" and "Likely to Adversely Affect" Determinations as a Prerequisite for Defensible "Jeopardy" and "No Jeopardy" Determinations.

At the informal consultation stage, the EPA must determine whether the use of a pesticide is either "not likely to adversely affect" ("NLAA") a listed species or is "likely to adversely affect" ("LAA") a listed species.[114] The Services define NLAA as "when effects on listed species are expected to be discountable, insignificant, or completely beneficial." Discountable effects are those that are extremely unlikely to occur and that the Services would not be able to meaningfully measure, detect, or evaluate" because of their insignificance[115] In the context of pesticides, only if predicted negative effects are discountable or insignificant can the EPA avoid the need to enter formal consultations with the Services. This is *not* a high threshold. The EPA is not required to make a determination as to whether exposure to a pesticide results in population level changes in order to request formal consultations. The Center believes that the Step Two approach described is generally compatible with the mandates of the ESA regarding actions that may affect listed species. The one in a million mortality threshold for "likely to adversely affect" reflects the ESA's and the Consultation Handbook's requirements. The decision to consider 1) sublethal effects to species, 2) additive, synergistic and cumulative effects of all chemicals and non-chemical stressors present in the pesticide formulation, tank mixture, and the environment, 3) and the fate and action of pesticide degradates at Step Two is also consistent with the ESA's requirements and represents an important change from the previous EPA approach, in which the EPA was making policy judgments at Step Two as to whether known, adverse, population-level impacts crossed a severity threshold to warrant consultations.

Finally, the Center notes that at Step Three, the formal consultation process, the EPA and Services must consider the environmental baseline as well as all cumulative effects when determining if the approval pesticides, formulations, or uses will jeopardize any threatened or endangered species. The Services define environmental baseline as "the past and present impacts of all Federal, State, or private actions and other human activities in an action area, the anticipated impacts of all proposed Federal projects in an action area that have already undergone formal or early section 7 consultation, and the impact of State or private actions that are contemporaneous with the consultation in process."[116] Cumulative effects are defined as "those effects of future State or private activities, not involving Federal activities, that are reasonably certain to occur within the action area of the Federal action subject to

[114] U.S. Fish and Wildlife Service and National Marine Fisheries Service. 1998. *Endangered Species Consultation Handbook: Procedures for Conducting Consultation and Conference Activities Under Section 7 of the Endangered Species Act*. at 3-1.
[115] *Id*. at xv.
[116] *Id*. at xiv.

consultation."[117] Pesticide consultations must consider the interactions between the active ingredient under review and other pollutants in the present in the environment.

The Food Quality Protection Act of 1996 ("FQPA") requires EPA to measure risk of a pesticide based on "… available information concerning the cumulative effects on infants and children of such residues and other substances that have a common mechanism of toxicity." The EPA has interpreted this to mean that only pesticides with a common mechanism of action be assessed in a cumulative risk assessment. We strongly disagree with this interpretation. First, the term "other substances" can include chemicals other than pesticides and also stressors that are not chemicals, like radiation and climate change. The EPA itself defines cumulative risk as "the combined risks from aggregate exposures to multiple agents or stressors," where agents or stressors can be chemicals or "may also be biological or physical agents or an activity that, directly or indirectly, alters or causes the loss of a necessity such as habitat."[118] Second, the term "common mechanism of toxicity" does not dictate that the EPA only consider agents or stressors with a common mechanism of action. The National Research Council has recommended that the EPA use the endpoint of common adverse outcome rather than common mechanism of action to group agents that could act cumulatively.[119] As for how this relates to EPA's duty under the ESA, cumulative risk in the ESA needs to be interpreted very broadly as this piece of legislation is a precautionary document meant to ensure that no harm comes to listed species. Although the EPA interprets the scope of cumulative risk assessments under FQPA to be limited to the common mechanism effect, **there is absolutely no such written or intended limit in the ESA**. The EPA needs to begin discussions on how it will test true cumulative risk, the way it is broadly defined in the ESA, because current metrics and protocols that measure cumulative risk under FQPA are inadequate for the EPA to meet its legal obligations under the ESA.

Pesticide and their residues and degradates do not occur in single exposure situations and many different mixtures of pesticides occur in water bodies at the same time.[120] The mixtures of these chemicals can combine to have additive or synergistic effects that are substantially more dangerous and increase the toxicity to wildlife.[121] Thus, to fully understand the ecological effects and adverse impacts, the EPA and the Services must consider the pesticide's use in the context of

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[117] *Id*. at xiii.

[118] U.S. Environmental Protection Agency 2003. Framework for Cumulative Risk Assessment. U.S. Environmental Protection Agency, Office of Research and Development, National Center for Environmental Assessment, Washington Office, Washington, DC, EPA/600/P-02/001F, 2003. Pg. xvii.

[119] National Research Council (US) Committee on the Health Risks of Phthalates. Phthalates and Cumulative Risk Assessment: The Tasks Ahead. Washington (DC): National Academies Press (US); 2008. Page 4.

[120] NMFS 2011, *Endangered Species Act Section 7 Consultation Draft Biological Opinion for the Environmental Protection Agency's Pesticide General Permit for Discharges from the Application of Pesticides (*hereafter Draft BiOp) at 118-119, lines 4209-31; Gilliom, R.J. et al. 2006. *Pesticides in the Nation's Streams and Ground Water, 1992–2001—A Summary*, available at http://pubs.usgs.gov/fs/2006/3028/.

[121] Draft BiOp at 127-129, lines 4471-4515; Gilliom, R.J. 2007. *Pesticides in the Nation's Streams and Ground Water*; Environmental Science and Technology, 413408–3414.

current water quality conditions nationwide. In particular, the use of pesticides in watersheds that contain threatened or endangered species and where water quality is already impaired could be particularly problematic. Therefore, the agencies must use the best available data to fully inform its ecological risk assessment by considering water quality.

In conclusion, the EPA should move quickly to assemble the needed spatial data to make an informed "no effect" or "may affect" finding for *each* listed species that will likely overlap with the use of these pesticides or come into contact with its environmental degradates. If there is overlap, EPA must at a minimum conclude that the use of these pesticides "may affect" listed species. Where this occurs, EPA has a choice—(1) the EPA can elect to complete an informal consultation through a biological assessment (also known as a biological evaluation), or (2) the EPA can undergo formal consultation with the Services. If EPA completes a biological assessment and implements geographically-tailored conservation measures through *Bulletins Live! Two*, it may be able to reach NLAA determinations via the informal consultation process and alleviate the need for formal consultations. In the alternative, the EPA can move directly to formal consultation after making "may affect" determinations for species where the impacts of pesticides are more complex and will take additional expertise to develop sufficient conservation measures. Cumulative effects need to be measured in Steps 2 and 3.

III. EPA and the Services Must Assess the Adverse Impacts on Critical Habitat.

Section 7 of the ESA prohibits agency actions that would result in the "destruction or adverse modification of [critical] habitat."[122] This inquiry is separate and distinct from the question as to whether a pesticide approval will result in jeopardy to any listed species. A no jeopardy finding (or a Not Likely to Adversely Affect finding in an informal consultation) is *not* equivalent to a finding that critical habitat will not be adversely modified. While there is much overlap between these two categories (for example, as in *Tennessee Valley Authority v. Hill*[123] where the proposed agency action to build a dam would both destroy a species' habitat and kill individual members of the species in the same time) many agency actions do result in adverse modification to critical habitat without causing direct harms to species that do rise to the level of jeopardy.[124] Indeed, the ESA's prohibition on "destruction or adverse modification" of critical habitat does not contain any qualifying language suggesting that a certain species-viability threshold must be reached prior to the habitat modification prohibition coming into force.

As three federal circuit courts have made abundantly clear, avoiding a species' immediate extinction is not the same as bringing about its recovery to the point where listing is no longer

[122] 16 U.S.C. § 1536(a)(2).
[123] 437 U.S. 153 (1978)
[124] *See* Owen, D. 2012. *Critical Habitat and the Challenge of Regulating Small Harms*. Florida Law Review 64:141-199.

necessary to safeguard the species from ongoing and future threats. Therefore, Section 7 requires that critical habitat not be adversely modified in ways that would hamper the *recovery* of listed species.[125] These potent pesticides with known adverse ecological effects have the potential to adversely modify critical habitat by altering ecological community structures, impacting the prey base for listed species, and by other changes to the physical and biological features of critical habitat. Accordingly, the informal consultation must separately evaluate whether these pesticide products and formulations will adversely modify critical habitat regardless of whether these pesticide products jeopardize a particular listed species. For example, if plant communities alongside a water body that has been designated as critical habitat suffer increased mortality, and this then results in increased temperatures or increased sedimentation, that would represent adverse modification of critical habitat. Likewise, if pesticides are toxic to species lower in the food chain, and a threatened or endangered species feeds on those affected prey species, this impact to the food web would represent a clear example of adverse modification to critical habitat.

EPA's evaluation must address impacts to critical habitat even if the direct effects on listed species fall below the NLAA or jeopardy thresholds. The Center recommends that the EPA design conservation measures—and implement those measures using *Bulletins Live! Two* — specifically to protect critical habitat of listed species from exposure to pesticides, and where appropriate, prohibit its use altogether in critical habitat where necessary. Doing so would provide meaningful, on-the-ground protections for hundreds of listed species, and may in some cases, help the EPA and the Services then reach a defensible NLAA or "no jeopardy" opinion.

IV. EPA Has an Independent Duty Under the Endangered Species Act to Consult with the U.S. Fish and Wildlife Service and National Marine Fisheries Service on the Approval of All End-use Product Labels.

Just as the EPA must consult with the Services regarding the reregistration of an active pesticide ingredient, EPA must also consult with the Services regarding the registration or approval of end use and technical pesticide products. Such consultations must also occur at the earliest possible time to ensure that specific product formulations do not result in jeopardy for a listed species or adversely modify critical habitat.

In addition, because end use formulations may result in mixes of the active ingredient with "other ingredients" before application, the EPA must consider during the consultation process the effects of these "inert" or "other" ingredients together with the active ingredient on listed species and set appropriate conservation restrictions accordingly. As noted in *Washington*

[125] *See Gifford Pinchot Task Force v. FWS*, 378 F.3d 1059, 1069-71 (9th Cir. 2004) (finding a FWS regulation conflating the requirements of survival and recovery to be unlawful); *see also N.M. Cattle Growers Ass'n v. FWS*, 248 F.3d 1277, 1283 n.2 (10th Cir. 2001); *Sierra Club v. FWS*, 245 F.3d 434, 441-42 (5th Cir. 2001)

Toxics Coalition v. U.S. Dept. of Interior, "other ingredients" within a pesticide end product may cause negative impact to listed species even if they are less toxic than the active ingredient being reviewed.[126] "Other ingredients," such as emulsifiers, surfactants, anti-foaming ingredients, and fillers may harm listed species and adversely modify critical habitat. Many of the more than 4,000 potentially hazardous additives allowed for use as pesticide additives are environmental contaminants and toxins that are known neurotoxins and carcinogens.[127] The EPA has routinely failed to consult with the Services on the registration of "other ingredients," potentially compounding harms to listed species by allowing such ingredients to be introduced widely into the environment. EPA must, as part of the consultation process, consider the range of potential impacts by using different concentrations and different formulations of the active ingredient, as well as the potential negative impacts of "other ingredients" used in end use products.

The National Academy of Science report recognized that without real-world considerations of where listed species are located, the relative conservation status of listed species, the environmental baseline, and the interaction of pesticides with other active ingredients, pesticide degradates, and other pollutants, the EPA risk assessment process will not be able to make meaningful predictions about which endangered species will be adversely affected. Until the EPA can conduct realistic assessments, it should take a precautionary approach and enter into formal consultations with the Services as outlined in the *Interim Approaches* document.

[126] 457 F. Supp. 2d 1158 (W.D. Wash 2006).
[127] Draft BiOp at 113, lines 4062-68; 120-121, lines 4262-308; 127, lines 4445-4455; Northwest Coalition for Alternatives to Pesticides, et al., Petition to Require Disclosure of Hazardous Inert Ingredients on Pesticide Product Labels. 2006. http://www.epa.gov/opprd001/inerts/petition_ncap.pdf.