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May 4, 2020

Office of Pesticide Programs
Docket numbers EPA-HQ-OPP-2012-0329, EPA-HQ-OPP-2011-0865, EPA-HQ-OPP-2011-0920, EPA-HQ-OPP-2008-0844, EPA-HQ-OPP-2011-0581
Environmental Protection Agency Docket Center (EPA/DC)
(28221T)
1200 Pennsylvania Ave. NW.
Washington, DC 20460-0001
SUBMITTED VIA ELECTRONIC UPLOAD TO DOCKET ONLY

Re: Comments on EPA's Proposed Interim Registration Review Decision for Acetamiprid, Clothianidin, Thiamethoxam, Imidacloprid and Dinotefuran (Dockets: EPA-HQ-OPP-2012-0329, EPA-HQ-OPP-2011-0865, EPA-HQ-OPP-2011-0920, EPA-HQ-OPP-2008-0844, and EPA-HQ-OPP-2011-0581)

Please accept the following comments on behalf of the Center for Biological Diversity ("Center") and Pesticide Action Network in response to the Environmental Protection Agency's ("EPA") proposed interim registration review decision for products containing a pesticide ingredient under the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA"). This letter applies to each of the five neonicotinoids (or "neonics") under the EPA's Proposed Interim Registration Review Decision: acetamiprid, clothianidin, dinotefuran, imidacloprid, and thiamethoxam. These comments also hereby incorporate by reference all additional materials submitted to EPA-HQ-OPP-2008-0844 in to all five dockets.

The U.S. Environmental Protection Agency (EPA) licenses the sale and use of the herbicides and insecticides under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA, 7 U.S.C. § 136 et seq). FIFRA directs EPA to register a pesticide only upon determining that "when used in accordance with widespread and commonly recognized practice it will not generally cause unreasonable adverse effects on the environment" (7 U.S.C § 136a(c)(5)(D)).

Unfortunately, there are serious issues with this proposed decision that absolutely need to be addressed in order for EPA to be in compliance with FIFRA and the Endangered Species Act ("ESA"). As this draft decision stands now, risk is underestimated – putting all species, including humans, at risk of unreasonable harm from the labeled uses of the five neonicotinoids under consideration. Neonicotinoids are amongst the most harmful and controversial types of pesticides

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in use in the United States today, and the cost of EPA's failures are not abstract. Right now, we are in the midst of what leading scientists describe as an insect apocalypse, and countless studies point to neonicotinoid pesticides, including the five at issue here, as a leading cause. This is not the right time for the EPA to ignore the threats posed by these pesticides. We strongly urge EPA to ban all outdoor uses of these five neonicotinoid insecticides. However, if the agency decides to re-register these insecticides, it must address the issues outlined below.

1. The proposed mitigations are inadequate to prevent unreasonable adverse effects to wildlife and water sources

a. Vegetative buffer strips are inadequate and unenforceable

EPA has proposed to implement vegetative filter strips (VFS) of 10 feet for these neonics. VFS are used generally to remove some contaminants from run-off, however, their effectiveness is difficult to predict because of the variability in soil types, the amount of organic material in the soil, the properties of the contaminant itself, and other variables.[1] Based on available lab and field studies, vegetative buffer strips can range from no removal to complete removal of moderately adsorptive contaminants like neonicotinoids.[2] The EPA's mitigation measures lack specificity and guidance for how these buffers should be maintained, which is just as important functionally important as the existence of these buffers themselves. Available field studies on neonicotinoids have mixed results for buffer effectiveness. One study found that prairie strips resulted in no significant difference in runoff concentration.[3] If EPA decides to pursue a VFS requirement, it should at least meet the National Resource Conservation Service (NRCS) standard of a minimum of 30 feet and require other best management practices to capture pesticides.[4] In fact, EPA has even proposed to increase the 10 foot VFS that is currently in place for pyrethroids to 25 feet due to water quality concerns.[5] It is very noteworthy that neonicotinoids are much more widespread water contaminants than pyrethroids, yet EPA is proposing a less stringent runoff mitigation. The EPA's proposed VFS requirement is arbitrary and insufficient to mitigate risks to a "no unreasonable adverse effect" standard.

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[1] Congrong Yu et al., "Experimental and Model Investigations of Vegetative Filter Strips for Contaminant Removal: A Review," *Ecological Engineering* 126 (January 1, 2019): 25–36, https://doi.org/10.1016/j.ecoleng.2018.10.020.
[2] Yu et al., 27.
[3] Michelle L. Hladik et al., "Neonicotinoid Insecticide Removal by Prairie Strips in Row-Cropped Watersheds with Historical Seed Coating Use," *Agriculture, Ecosystems & Environment* 241 (April 1, 2017): 160–67, https://doi.org/10.1016/j.agee.2017.03.015.
[4] Natural Resource Conservation Service, "Conservation Practice Standard: Filter Strip Code 393" (US Department of Agriculture, 2016), https://www.nrcs.usda.gov/Internet/FSE_DOCUMENTS/stelprdb1241319.pdf.
[5] EPA. Pyrethroids and Pyrethrins Ecological Risk Mitigation Proposal For 23 Chemicals. September 2019. Available here: https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0331-0096.

b. The Effectiveness of EPA's Proposed Mitigations are not Supported by Substantial Evidence

In supporting its proposed registration decision, EPA has devised a host of mitigation schemes that the agency believes will reduce risk to the point where the pesticides can still be legally re-registered under FIFRA. However, there is no confirmation or follow up by EPA that this is the case. EPA does not re-run its models or do any refined analysis to look at whether any of these mitigations will reduce the harm to environmental receptors. It simply makes subjective guesses. The EPA must have substantial evidence to indicate that its actions won't result in unreasonable adverse effects to the environment. The agency cannot reach that bar by proposing mitigations, some mandatory, some voluntary, that it has not vetted or analyzed.

For proposed mitigations like rate reductions, EPA claims that they will result in a decrease in overall risk because they will result in a decrease in environmental loading.[6] This fundamentally misunderstands the definition of risk. Risk is the probability or likelihood that an impact (harm, in this case) will occur. EPA's ecological risk assessment has already established that many different taxa may be exposed to levels of neonics that are tens to thousands of times higher than the concentrations known to cause harm. When the agency is identifying LOC exceedances of that magnitude, proposing mitigations that will somewhat lower those exceedances does not give the EPA any evidence whatsoever that risk is being reduced. The National Academy of Sciences (NAS) has made several significant statements about EPA's ecological risk assessment process and its use of "risk quotients" (RQs), including:

- The EPAs "concentration-ratio approach" for its ecological risk assessments "is ad hoc (although commonly used) and has unpredictable performance outcomes."[7]
- "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."[8]
- "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."[9]

[6] U.S. EPA. Clothianidin and Thiamethoxam Proposed Interim Registration Review Decision Case Numbers 7620 and 7614. January 2020. Pg 57. Available here: https://www.regulations.gov/document?D=EPA-HQ-OPP-2011-0865-1190.
[7] National Academy of Sciences. 2013. *Assessing Risks to Endangered and Threatened Species from Pesticides*, 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). Pg 149.
[8] *Id*. at 15.
[9] *Id*. at 14.

What the NAS is saying is that risk quotients are unpredictable and don't tell the agency anything about risk. EPA could impose a mitigation measure for a high risk neonic use that reduces its risk quotient by 100-fold, but it may still result in high risk. Whether an animal is exposed to 1000-times the concentration of a neonic known to cause mortality or 10-times the concentration known to cause mortality, the risk of death is the same. The exposed animal has a 100% chance of dying.

Use rate reductions may indicate that less neonic will be put into the environment, but it cannot tell you that risk will be reduced to a specific non-target taxon. For EPA to make that determination it must first analyze risk and then identify how the probability of harm would change following implementation of a specific mitigation measure. For the EPA to claim that its mitigation measures result in risk reduction is simply not supported by any available data and greatly oversimplifies the incredibly complex interaction between a poison and environmental receptors.

In addition to EPA's inability to support its claims that the proposed mitigations will result in reduced risk, many of these required mitigations really do nothing above and beyond the current status quo. For instance, most neonic labels already require a VFS of 10 feet - making this "mitigation" even more ineffective at mitigating the current known harm from the runoff of neonics.[10,11]

Furthermore, there are also previous mitigations that are being taken away. For instance, Thiamethoxam currently has a wind speed cutoff of 10 mph and the EPA is proposing to raise it to 15 mph.[12] Additionally the boom length for helicopter is proposed to be increased to 90 percent of the rotor diameter, a change that will result in more pesticide being sprayed in a single pass.[13]

The EPA has simply not demonstrated that any of the proposed mitigations, combined with the weakening of other mitigations, will achieve a reduction in risk to the point that no unreasonable adverse effects will be seen. EPA's own language casts doubt that these mitigations will achieve any mitigation at all. When talking about VFS, the agency states: "they may have some utility in reducing movement of pesticides, particularly those bound to sediments into natural waters."[14] That is not a statement by an agency that is confident in the effectiveness of its actions.

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[10] *Id*. at 69.
[11] U.S. EPA. Imidacloprid Proposed Interim Registration Review Decision Case Number 7605. January 2020. Pg 55. Available here: https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0844-1619.
[12] U.S. EPA. Clothianidin and Thiamethoxam Proposed Interim Registration Review Decision Case Numbers 7620 and 7614. January 2020. Pg 70. Available here: https://www.regulations.gov/document?D=EPA-HQ-OPP-2011-0865-1190.
[13] *Id.*
[14] U.S. EPA. Imidacloprid Proposed Interim Registration Review Decision Case Number 7605. January 2020. Pg 52. Available here: https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0844-1619.

In fact there is absolutely no evidence that any of these mitigations will achieve the desired outcome. Without any evidence, the agency certainly cannot claim to support its decision with substantial evidence. Therefore, EPA must provide an analysis or evidence that the proposed mitigation measures will actually reduce risk to acceptable levels before a registration decision is made or it will be in violation of FIFRA.

c. Drift mitigations are unenforceable and ineffective

The agency has proposed rate reductions for a several crops across the five neonicotinoids under review, as well as some boilerplate "drift reduction" measures that the agency seems to have put in place for nearly every pesticide currently under registration review.[15] This includes boom height restrictions, wind speed restrictions and droplet size restrictions that are already common practice.

Notably, the agency is also proposing to relax some drift mitigations that are already in place, like reducing the allowable wind speed for aerial applications of thiamethoxam from the current 10 mph cutoff to a more permissive 15mph cutoff.[16] And increasing the boom length for helicopter applications to 90 percent of the rotor diameter, a change that will result in more pesticide being sprayed in a single pass.[17]

The EPA has proposed a mix of increased and decreased safeguards in the current proposed IRED, yet the agency has absolutely no clue how this will all interact to impact people and the environment. For instance, in the final bee risk assessment for clothianidin and thiamethoxam, EPA found that those pesticides could still harm bees more than 1000 feet from treated fields due to drift.[18] However, EPA estimated drift using droplet sizes that are smaller than those proposed in EPA's required mitigations (very fine to fine for ground applications and fine to medium for aerial applications compared to the medium or coarser requirement on the proposed label).[19] EPA does not even attempt to refine its AgDrift modelling to analyze how a coarser droplet spectrum would impact its predictions about how far off field harm was expected. This is essential information for EPA to know if it's to base this registration decision on substantial evidence. This is a simple adjustment in EPA's AgDrift model that it has commonly done in other pesticide assessments.

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[15] U.S. EPA. Clothianidin and Thiamethoxam Proposed Interim Registration Review Decision Case Numbers 7620 and 7614. January 2020. Pgs 68-69. Available here: https://www.regulations.gov/document?D=EPA-HQ-OPP-2011-0865-1190.
[16] *Id.* at 70.
[17] *Id.*
[18] U.S. EPA, "Final Bee Risk Assessment to Support the Registration Review of Clothianidin and Thiamethoxam" (Washington, D.C.: U.S. Environmental Protection Agency, January 14, 2020). Pg 111.
[19] *Id.*

In fact, the EPA did model how a 0.5X application rate would affect the drift of clothianidin and thiamethoxam and found that even when the allowable application rate was reduced by half, bees could still be harmed more than 1000 feet off field for aerial and ground applications.[20] So the mitigation of rate reduction still resulted in harm to bees all the way out to the limit of EPA's model (1000 ft). That is an example of a mitigation that has no measurable effect on how far off-field the pesticide will harm bees based on the limits of EPA's tools. It is important to understand how other mitigations will impact this measurement, but EPA does not even attempt to perform any relevant analysis to that end.

Therefore, the EPA does not know that these mitigation measures, together with the purported benefits, will lead to "no unreasonable adverse effects" on the environment. There has been no scientific assessment of these proposed increased and decreased safeguards. This is rife with subjectivity. EPA will be in violation of FIFRA if this proposed IRED is finalized.

d. Runoff mitigations are nonexistent

There is not one mitigation measure proposed to mitigate runoff. Most neonic labels already require a 10 ft VFS, so this cannot be considered a mitigation.[21,22] All of the weak mitigations proposed are for pesticide drift only and will not do anything to decrease the widespread contamination to surface water in this country from neonic use. The vast amount of data on water contamination and exceedances of vital safety thresholds documented over the last 20 years is significant and the EPA did not even discuss potential benefits or costs associated with mitigation measures that could decrease runoff, like a larger VFS, larger buffers from water sources and seasonal restrictions.

e. Treated seed mitigations are voluntary and ineffective

EPA's mitigations for neonic-treated seeds are voluntary measures that growers should take to prevent exposure. EPA cannot assume that voluntary measures will be taken if they are not clearly stated, legally enforceable requirements. These advisory statements are little more than simple suggestions. EPA even states that this language is meant to "…encourage the adoption of best management practices when handling and planting clothianidin- and/or thiamethoxam-treated seeds that will reduce the exposure of birds and mammals to treated seeds."[23]

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[20] *Id.*
[21] *Id*. at 69.
[22] U.S. EPA. Imidacloprid Proposed Interim Registration Review Decision Case Number 7605. January 2020. Pg 55. Available here: https://www.regulations.gov/document?D=EPA-HQ-OPP-2008-0844-1619.
[23] U.S. EPA. Clothianidin and Thiamethoxam Proposed Interim Registration Review Decision Case Numbers 7620 and 7614. January 2020. Pg 67. Available here: https://www.regulations.gov/document?D=EPA-HQ-OPP-2011-0865-1190

The EPA has the ability to mandate use of these best practices, but it neglects to. It is also impossible to ensure that all seeds remain covered while planting a large acreage. A scan of 71 fields found seeds present at the surface in 35% of them.[24] Neonicotinoid treated seed constitutes a major exposure scenario for non-target birds.[25] EPA discounts exposure to birds from larger seeds like corn and potato, by stating that they are too big to be ingested by smaller birds. Yet researchers have documented smaller birds breaking up larger seeds into smaller pieces in order to consume.[26] This must be taken into account in EPA's registration decision and the EPA absolutely must mandate more than voluntary half-measures to be taken to prevent the widespread harm to birds from treated seeds.

2. Honeybees are an Unsuitable Surrogate Species for Terrestrial Invertebrates

a. Other Flying Insects

The EPA's final bee risk assessment presents strong evidence for a high risk to honeybees from neonicotinoid exposure on most crops grown in the United States. This assessment found that some crops present more of a risk than others, however EPA decided there was not enough of a risk to severely restrict neonicotinoid usage across flowering crops. While this bee risk assessment provides a more detailed risk assessment than the EPA has put forth for other pesticides, the effects to non-apis bees are still omitted. The EPA wholly and completely relies on honeybees as the surrogate for all terrestrial invertebrate species. The bee risk assessment also states that "Tier 1 conclusions for honeybees are also used to represent risks to solitary bees…"[27] This risk assumption perpetuates an ignorance of the life history and exposure pathways of non-apis bees and other insects.

Non-apis bees have exposure pathways that are different that honeybees primarily in their increased contact with soil, social structure, and differences in feeding habits. The vast majority of native bees are solitary and ground-nesting[28] which has many implications for the exposure of these bees to neonicotinoids. Neonicotinoids are long-lasting pesticides that can contaminate soil

[24] Roy, C. L., Coy, P. L., Chen, D., Ponder, J., & Jankowski, M. (2019). Multi-scale availability of neonicotinoid-treated seed for wildlife in an agricultural landscape during spring planting. *Science of The Total Environment, 682*, 271-281. doi:10.1016/j.scitotenv.2019.05.010.
[25] Roy, C, Chen, D, Ponder, J, Jankowski, M. Neonicotinoids on the landscape: evaluating avian exposure to treated seeds in agricultural landscapes. MN Department of Natural Resources.2016. Found here: https://files.dnr.state.mn.us/wildlife/research/summaries/forest/2016_neonictoids.pdf.
[26] *Id*. and Roy, C. L., Coy, P. L., Chen, D., Ponder, J., & Jankowski, M. (2019). Multi-scale availability of neonicotinoid-treated seed for wildlife in an agricultural landscape during spring planting. *Science of The Total Environment, 682*, 271-281. doi:10.1016/j.scitotenv.2019.05.010.
[27] U.S. EPA, 226.
[28] David Fischer and Thomas Moriarty, eds., *Pesticide Risk Assessment for Pollinators*, 1st ed. (John Wiley & Sons, Ltd, 2014), 10–11, https://doi.org/10.1002/9781118852408.

in and around fields for years after application, particularly when applied via treated seeds. Ground nesting bees need loose, bare soil for their nests and this contact with contaminated soil is not considered in the EPA's bee risk assessment even though many native bees spend a great deal of their lives in contact with the soil. Non-apis bees are largely solitary whereby one female provisions her own nest. EPA underestimates risk to these native bees because the acute and chronic effects to individual honeybees are buffered at the colony level – so even if one bee is highly exposed, the colony can still be at low risk. Non-apis bees tend to be smaller, therefore can be harmed at a lower concentration.[29] If one solitary bee is exposed and dies that means that her colony will stop growing and thereby reduce the effective population. Non-apis, solitary bees forage differently that honeybees which are extreme generalists. Non-apis bees often forage on a restricted range of plants[30] and on more marginal floral resources than honeybees that are likely to be found in field margins.

Bumble bee physiology, behavior, and life cycle characteristics also differ from honeybees in ways that are not considered when tests are applied only to honeybees. For example, bumble bee larvae are fed raw pollen and nectar whereas honey bees process nectar and pollen within nurse bees' digestive systems before feeding larvae[31] Bumble bee larvae are also in direct contact with raw nectar and pollen provisions rather than in individual cells like honey bees and therefore have a different exposure profile.[32] Furthermore, the persistent residues of pesticides in soil can contaminate bumble bee nests and overwintering sites, but this is not considered by the EPA when assessing risk of pesticides to bumble bees.

Many other insect species rely on nectar that can be contaminated with neonicotinoids. Neonicotinoids are known to be very harmful to many butterfly species.[33,34,35] Monarch butterflies feed on milkweed that is often found in field margins and this can weaken larvae and adults and impair their life cycle.[36] Very few insects use workers to gather nectar and pollen

[29] Fischer and Moriarty, 53–54.
[30] Fischer and Moriarty, 53.
[31] Fischer and Moriarty, 53.
[32] Fischer and Moriarty, 53.
[33] Forister, M. L., Cousens, B., Harrison, J. G., Anderson, K., Thorne, J. H., Waetjen, D., … Shapiro, A. M. (2016). Increasing neonicotinoid use and the declining butterfly fauna of lowland California. Biology Letters, 12(8), 20160475. doi:10.1098/rsbl.2016.0475.
[34] Braak, N., Neve, R., Jones, A. K., Gibbs, M., & Breuker, C. J. (2018). The effects of insecticides on butterflies – A review. *Environmental Pollution*, *242*, 507-518. doi:10.1016/j.envpol.2018.06.100.
[35] Whitehorn PR, Norville G, Gilburn A, Goulson D. (2018). Larval exposure to the neonicotinoid imidacloprid impacts adult size in the farmland butterfly Pieris brassicae. PeerJ 6:e4772 https://doi.org/10.7717/peerj.4772.
[36] Niranjana Krishnan et al., "Assessing Field-Scale Risks of Foliar Insecticide Applications to Monarch Butterfly (Danaus Plexippus) Larvae," *Environmental Toxicology and Chemistry* n/a, no. n/a (January 21, 2020), https://doi.org/10.1002/etc.4672; Jacob R. Pecenka and Jonathan G. Lundgren, "Non-Target Effects of Clothianidin on Monarch Butterflies," *The Science of Nature* 102, no. 3 (April 3, 2015): 19, https://doi.org/10.1007/s00114-015-1270-y.

which puts individuals at greater risk. Each individual lost is a loss to the genetic diversity of a species. Lady beetles are also highly susceptible to harm from neonics.[37]

b. Soil Dwelling Organisms and Ground-nesting Pollinators

See **Appendix A** below for a discussion on the available research on how neonics affect soil-dwelling organisms, ground-nesting pollinators and overall soil health.

Importantly, EPA uses honeybees as a surrogate for toxicity to all other terrestrial invertebrates. We believe this approach is dangerous, as it will necessarily underestimate harm to some other terrestrial invertebrates. This is no better exemplified than with soil dwelling invertebrates. Research has shown soil organisms to be extremely sensitive to neonicotinoids (Appendix A). Further, these organisms have a very different exposure potential than above-ground flying insects like the honeybee.

These organisms are just about as different from each other than fish and mammals, yet EPA recognizes that fish and mammals must be analyzed differently with respect to their exposure potential and sensitivity to neonics.

In addition to honeybees being poor surrogates for soil-dwelling invertebrates, EPA's mitigations for terrestrial invertebrate toxicity are tailored towards preventing exposure to above-ground pollinators. These include things like preventing drift and preventing spraying during flowering. These mitigations will have absolutely no impact on soil-dwelling invertebrates This is despite EPA's conclusion that terrestrial invertebrates (represented by the honeybee) require harm to be mitigated.

EPA must, at the very least, put in place mitigations to prevent soil organisms from being exposed to concerning amounts of neonics. These should include things like <u>mandatory</u> mitigations for treated seed and soil drench uses. Voluntary measures or guidance is not sufficient.

If the EPA does not, at the very least, implement mitigations to reduce the harm that it found to be unacceptable for honeybees for soil dwelling organisms, the agency will be in violation of FIFRA. It is imperative that mitigations put in place for terrestrial invertebrates encompass all exposure routes for all terrestrial invertebrates, not just some. The use of surrogate species has consequences. Harm found to the surrogate must be assumed for every species it is supposed to

[37] Jiang, J., Zhang, Z., Yu, X., Yu, C., Liu, F., & Mu, W. (2019). Sublethal and transgenerational effects of thiamethoxam on the demographic fitness and predation performance of the seven-spot ladybeetle Coccinella septempunctata L. (Coleoptera: Coccinellidae). *Chemosphere*, *216*, 168-178. doi:10.1016/j.chemosphere.2018.10.126.

represent. That means harm that is mitigated for the surrogate species but also be mitigated for the other species it represents. That is currently not done in this proposed IRED.

3. Harm to bats is not adequately discussed, analyzed or mitigated in the proposed IRRD

EPA has used sensitivity and exposure measures for mammals that are based on rats and mice for sensitivity and the typical land mammal for the exposure scenario. This is not inclusive of bats, a highly specialized mammal that cannot be accurately assessed via EPA's surrogate species approach. The European Food Safety Authority (EFSA) Panel on Plant Protection Products and their Residues recently published its findings on risk assessment procedures common to Europe and the U.S. and found that "…bats are not adequately covered by the current risk assessment approach, and that there is a need to develop a bat-specific risk assessment scheme."[38]

There is considerable evidence that neonics are very harmful to bats and EPA's surrogate risk assessment approach does not adequately account for this harm.[39,40,41] For instance neonics are well-documented to impair echolocation, an effect that is not relevant to any of the surrogate animals analyzed by EPA. For instance EFSA found that "A large variation in toxicological sensitivity and no relationship between sensitivity of bats and bird or mammal test-species to pesticides could be found."[42] There is simply no evidence that EPA's risk assessment has given the agency an accurate reflection of risk to these animals. In fact, the available evidence indicates that it hasn't. Harm to listed and non-listed bats must be adequately analyzed and mitigated before the EPA can make decision to re-register neonicotinoids. The serious flaws in EPA's risk assessment indicate that the agency has not supported its proposed decision with substantial evidence and cannot be certain that this decision won't result in unreasonable adverse effects to bats.

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[38] EFSA. 2019. Scientific statement on the coverage of bats by the current pesticide risk assessment for birds and mammals. EFSA Journal 2019;17(5):5758. 10.2903/j.efsa.2019.5758. Available here: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2019.5758.

[39] Wu, C., Lin, C., Wang, S., & Lu, C. (2020). Effects of imidacloprid, a neonicotinoid insecticide, on the echolocation system of insectivorous bats. *Pesticide Biochemistry and Physiology*, *163*, 94-101. doi:10.1016/j.pestbp.2019.10.010.

[40] Hsiao, C., Lin, C., Lin, T., Wang, S., & Wu, C. (2016). Imidacloprid toxicity impairs spatial memory of echolocation bats through neural apoptosis in hippocampal CA1 and medial entorhinal cortex areas. *NeuroReport*, *27*(6), 462-468. doi:10.1097/wnr.0000000000000562.

[41] Mineau, P. and C. Callaghan 2018. Neonicotinoid insecticides and bats: an assessment of the direct and indirect risks. Canadian Wildlife Federation. 87 pp.

[42] EFSA. 2019. Scientific statement on the coverage of bats by the current pesticide risk assessment for birds and mammals. EFSA Journal 2019;17(5):5758. 10.2903/j.efsa.2019.5758. Available here: https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2019.5758.

4. Insect decline and ripple effects associated with neonicotinoids present unreasonable adverse effects to the environment

Since the risk assessments were completed for these neonicotinoids, evidence continues to mount demonstrating the impacts of neonicotinoid pesticides beyond the field. Minute doses produce sublethal effects to insects with ripple effects up the food chain, yet the EPA does not include these cumulative, ecosystem level effects of increased pesticide load in the environment. The popularity, ubiquity, and toxicity of neonicotinoid pesticides has led to increasing levels of pesticides in the environment, resulting in an overall 48-fold increase in the honey bee oral toxic loading and a four-fold increase in contact loading.[43] Neonicotinoids are responsible for at least 60% of this increased toxicity for honey bees.[44] At a more regional level, farmland in the central U.S. has seen even higher increases in total toxic load, 121-fold, largely because of neonicotinoid treated corn and soybean seeds.[45]

Risk to honeybees is not restricted to only the treated crop. Because of their popularity and persistence, neonicotinoids contaminate nearby flowering plants and increase the risk to honeybees and other pollinators.[46] By only focusing on the toxicity to honeybees from exposure to treated crops and only targeting mitigations to the treated crops themselves, the EPA dismisses exposure via nearby flowering crops. Furthermore, by mitigating exposure to pollinators by prohibiting spraying during or before the crop blooms, EPA ignores nearby flowering plants that may be in full bloom at the time of application. This can result in high exposures to pollinators and is completely discounted in EPA's mitigation measures and analysis.

Measurable levels of neonicotinoids have been found in the wild-flowers on field margins which undermine the biological and pollination value of these plants.[47] Field margins are often the only refuge for grassland insects and birds, but they can be harmed because the systematic nature of these pesticides means that they can be present in nectar, pollen and plant tissue. Native bees surveyed in Colorado were found to have clothianidin at an average concentration of 40ng/g and

[43] Michael DiBartolomeis et al., "An Assessment of Acute Insecticide Toxicity Loading (AITL) of Chemical Pesticides Used on Agricultural Land in the United States," ed. Simone Tosi, *PLOS ONE* 14, no. 8 (August 6, 2019): e0220029, https://doi.org/10.1371/journal.pone.0220029.
[44] *Id.*
[45] Margaret R. Douglas et al., "County-Level Analysis Reveals a Rapidly Shifting Landscape of Insecticide Hazard to Honey Bees (Apis Mellifera) on US Farmland," *Scientific Reports* 10, no. 1 (January 21, 2020): 1–11, https://doi.org/10.1038/s41598-019-57225-w.
[46] Scott H. McArt et al., "High Pesticide Risk to Honey Bees despite Low Focal Crop Pollen Collection during Pollination of a Mass Blooming Crop," *Scientific Reports* 7, no. 1 (April 19, 2017): 1–10, https://doi.org/10.1038/srep46554.
[47] Cristina Botías et al., "Contamination of Wild Plants near Neonicotinoid Seed-Treated Crops, and Implications for Non-Target Insects," *Science of The Total Environment* 566–567 (October 1, 2016): 269–78, https://doi.org/10.1016/j.scitotenv.2016.05.065.

found in 24% of samples.[48] Common farmland butterflies are also negatively affected by neonicotinoid contamination.[49] Other native butterflies also show abundance declined with increasing neonic usage in California.[50] These observations all point to consistent negative impact to insects from the widespread over-use of these pesticides which can feed the declines of other species that rely on insects for food.

All exposure scenarios are not taken into account. Things such as abraded seed dust, guttation fluid, dew, soil, water are all relevant exposure scenarios that the EPA has simply not modelled or made any effort to estimate. Bees and other insects can be exposed through many pathways other than pollen and nectar consumption and EPA must take that into account.

Neonicotinoids end up in water bodies at alarming rates. Recent water quality monitoring surveys have found clothianidin in 24% of sampled streams across the United States[51] and found in 85% of wetlands in Nebraska.[52] There are significant negative associations between neonic concentrations and aquatic invertebrate biomass across sites.[53] Neonicotinoids applied to cotton seed made their way into wetlands and exceeded the chronic safety thresholds for certain macroinvertebrates in 28% of the samples.[54] Chronic neonicotinoid exposure changes aquatic invertebrate communities[55] by reducing sensitive species which are often indicators of ecosystem degradation.[56] New analysis shows that the time of exposure can matter even more to toxicity than the dosage of these pesticides.[57] This evidence indicates that EPA seriously underestimates the harm posed to insects at minute quantities over long periods of time.

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[48] Michelle L. Hladik, Mark Vandever, and Kelly L. Smalling, "Exposure of Native Bees Foraging in an Agricultural Landscape to Current-Use Pesticides," *Science of The Total Environment* 542 (January 15, 2016): 469–77, https://doi.org/10.1016/j.scitotenv.2015.10.077.
[49] Penelope R. Whitehorn et al., "Larval Exposure to the Neonicotinoid Imidacloprid Impacts Adult Size in the Farmland Butterfly *Pieris Brassicae*," *PeerJ* 6 (May 18, 2018): e4772, https://doi.org/10.7717/peerj.4772.
[50] Matthew L. Forister et al., "Increasing Neonicotinoid Use and the Declining Butterfly Fauna of Lowland California," *Biology Letters* 12, no. 8 (August 31, 2016): 20160475, https://doi.org/10.1098/rsbl.2016.0475.
[51] Michelle Hladik and Dana W. Kolpin, "First National-Scale Reconnaissance of Neonicotinoid Insecticides in Streams across the USA," *Environmental Chemistry* 13, no. 1 (2015): 1220, https://doi.org/10.1071/EN15061.
[52] Travis J. Schepker et al., "Neonicotinoid Insecticide Concentrations in Agricultural Wetlands and Associations with Aquatic Invertebrate Communities," *Agriculture, Ecosystems & Environment* 287 (January 1, 2020): 106678, https://doi.org/10.1016/j.agee.2019.106678.
[53] Schepker et al.
[54] Kristina L. Kohl et al., "Tracking Neonicotinoids Following Their Use as Cotton Seed Treatments," *PeerJ* 7 (April 19, 2019): e6805, https://doi.org/10.7717/peerj.6805.
[55] Daisuke Hayasaka, Koji Kobashi, and Koya Hashimoto, "Community Responses of Aquatic Insects in Paddy Mesocosms to Repeated Exposures of the Neonicotinoids Imidacloprid and Dinotefuran," *Ecotoxicology and Environmental Safety* 175 (July 15, 2019): 272–81, https://doi.org/10.1016/j.ecoenv.2019.03.051.
[56] Koya Hashimoto et al., "Long-Term Monitoring Reveals among-Year Consistency in the Ecological Impacts of Insecticides on Animal Communities in Paddies," *Ecological Indicators* 113 (June 1, 2020): 106227, https://doi.org/10.1016/j.ecolind.2020.106227.
[57] Francisco Sánchez-Bayo and Henk A. Tennekes, "Time-Cumulative Toxicity of Neonicotinoids: Experimental Evidence and Implications for Environmental Risk Assessments," *International Journal of Environmental Research and Public Health* 17, no. 5 (March 3, 2020): 1629, https://doi.org/10.3390/ijerph17051629.

Decreases in terrestrial and aquatic insects undermines the function of ecosystems and recent research implicates neonicotinoids in the declines of bird populations and fish stocks. Neonicotinoids have been linked for years to declines in bird populations through indirect effects on food chains.[58] Alarmingly, a recent review indicates that North America has lost nearly 30% of our birds with nearly 75% of grassland birds in decline with neonicotinoids as a contributing factor.[59] Fisheries have also been affected showing that the introduction of neonicotinoid pesticides into rice patties coincided with a decline in zooplankton and a collapse in the fish harvest.[60]

It's clear that EPA's risk assessments do not account for the widespread declines in bird and fish populations that many independent scientists associate with increased usage of neonicotinoid pesticides at a broad scale. The EPA discounts the vast majority of studies for a handful of GLP studies done by the registrant. A weight of evidence approach would undoubtedly find that neonicotinoids cannot possibly be expected to result in no unreasonable adverse effects to the environment. However, the EPA ignores the totality of evidence in favor of a minority of studies. This does not meet the "substantial evidence" standard in FIFRA and the proposed registration decision is unlawful.

5. EPA does not consider synergistic or cumulative effects on toxicity for any environmental receptor.

See previous comments attached at the end of this document. EPA has still not attempted to do any analysis on cumulative or synergistic effects, so our previous comments are still relevant more than four years later.

6. The risks to invertebrate communities and drinking water outweigh the benefits of these pesticides

Reregistering these five neonicotinoid pesticides presents significant risks to invertebrates and vertebrates with negligible or even negative effects to crop yield. Neonicotinoid seed treatments are often not effective, yet prophylactic seed treatment is where the majority of neonicotinoid applications occur. The EPA itself, as well as several other labs, have analyzed the benefits of neonicotinoid usage and found that seed treatments are unnecessary and consequently raise farmer's input costs and result in massive amounts of pesticide in the environment.

[58] Dave Goulson, "Pesticides Linked to Bird Declines," *Nature* 511, no. 7509 (July 2014): 295–96, https://doi.org/10.1038/nature13642.
[59] Kenneth V. Rosenberg et al., "Decline of the North American Avifauna," *Science* 366, no. 6461 (October 4, 2019): 120–24, https://doi.org/10.1126/science.aaw1313.
[60] Masumi Yamamuro et al., "Neonicotinoids Disrupt Aquatic Food Webs and Decrease Fishery Yields," *Science* 366, no. 6465 (November 1, 2019): 620–23, https://doi.org/10.1126/science.aax3442.

Independent research continues to demonstrate that neonicotinoid seed treatments produce marginal economic benefits for the farmer and often do not produce a yield improvement. Across multiple crops, the value of prophylactic neonicotinoid usage as a seed treatment is nil and multiple cultural and alternative methods exist that can produce similar effect when pest pressure is high.[61] We found 14 studies that showed no yield gain from neonicotinoid treated seeds for the worst offending crops-corn and soybeans. The most damning study yet from 2019—the largest study of its kind—showed that across 14 states the use of neonicotinoid treated soybean seeds produced negligible benefits to yield. [62] Neonicotinoid treated corn seed controls early season pests but studies show that most of the time the early season pest pressure on corn is not economically detrimental to the yield at the end of the season.[63] Not only does corn seed treatment not result in yield benefits, but the dust created from seeding neonicotinoid treated corn is documented to substantially drift from corn fields potentially exposing more than 94% of honey bees in the state of Indiana alone.[64] Several other crops also fail to produce consistent yield benefits from neonicotinoid treated seeds including: cotton,[65] sugar beets,[66] sunflowers,[67] and rice.[68]

There is overwhelming evidence that neonicotinoids have non-target impacts on beneficial arthropods and especially natural enemies (see attached studies). Neonicotinoids disrupt predator/prey interactions which weakens the natural controls that regulate pest species. For example, seed treatments produced a transgenerational effect of lowered egg fertility and generational survival in predatory species.[69] Thiamethoxam seed treatment in cotton had transgenerational effects that reduced the second generation survival of predatory insects.[70] Corn

[61] William Quarles, "Neonic Seeds Are Not Needed," *The IPM Practioner* XXXVI, no. 11/12 (2019): 16.
[62] Spyridon Mourtzinis et al., "Neonicotinoid Seed Treatments of Soybean Provide Negligible Benefits to US Farmers," *Scientific Reports* 9, no. 1 (September 9, 2019): 1–7, https://doi.org/10.1038/s41598-019-47442-8.
[63] Geneviève Labrie et al., "Impacts of Neonicotinoid Seed Treatments on Soil-Dwelling Pest Populations and Agronomic Parameters in Corn and Soybean in Quebec (Canada)," ed. Nicolas Desneux, *PLOS ONE* 15, no. 2 (February 26, 2020): e0229136, https://doi.org/10.1371/journal.pone.0229136.
[64] C. H. Krupke et al., "Planting of Neonicotinoid-Treated Maize Poses Risks for Honey Bees and Other Non-Target Organisms over a Wide Area without Consistent Crop Yield Benefit," ed. Sarah Diamond, *Journal of Applied Ecology* 54, no. 5 (October 2017): 1449–58, https://doi.org/10.1111/1365-2664.12924.
[65] J. H. North et al., "Value of Neonicotinoid Insecticide Seed Treatments in Mid-South Cotton (Gossypium Hirsutum [Malvales: Malvaceae]) Production Systems," *Journal of Economic Entomology* 111, no. 1 (February 9, 2018): 10–15, https://doi.org/10.1093/jee/tox324.
[66] R. J. Pretorius et al., "Response of Pemphigus Betae (Hemiptera: Aphididae) and Beneficial Epigeal Arthropod Communities to Sugarbeet Plant Density and Seed-Applied Insecticide in Western Nebraska," *Environmental Entomology* 46, no. 1 (February 1, 2017): 107–17, https://doi.org/10.1093/ee/nvw157.
[67] Michael M. Bredeson and Jonathan G. Lundgren, "Thiamethoxam Seed Treatments Have No Impact on Pest Numbers or Yield in Cultivated Sunflowers," *Journal of Economic Entomology* 108, no. 6 (December 1, 2015): 2665–71, https://doi.org/10.1093/jee/tov249.
[68] S. K. Lanka et al., "Impact of Thiamethoxam Seed Treatment on Growth and Yield of Rice, Oryza Sativa," *Journal of Economic Entomology* 110, no. 2 (March 2017): 479–86, https://doi.org/10.1093/jee/tox043.
[69] Rafaella R. Sâmia et al., "Sublethal and Transgenerational Effects of Thiamethoxam Applied to Cotton Seed on Chrysoperla Externa and Harmonia Axyridis," *Pest Management Science* 75, no. 3 (2019): 694–701, https://doi.org/10.1002/ps.5166.
[70] Sâmia et al.

seed treatments reduce the amounts of natural enemies and predatory insects that keep pest species in check.[71] Another showed that declining predatory species caused by neonicotinoid treatment allowed for an increase of slug populations that damaged the corn crop and led to **lower** yield.[72] When neonicotinoids reduce the fitness of natural enemies it may carry the risk of increasing the amount of pest species that the farmer was trying to get rid of in the first place. We have put together a survey of the most recent independent research on the yield benefits (or lack thereof) and harms to natural enemies of neonicotinoid treaded seeds and have submitted it as a supporting material.

Neonicotinoids clearly are not compatible with Integrated Pest Management (IPM) because of the impacts to natural enemies, yet alternative cropping systems and IPM techniques exist that suppress early season pests and produce competitive yields, which can effectively replace neonicotinoid usage. High-diversity/IPM cropping systems fosters beneficial arthropod populations which keep pest pressure low and produce competitive corn yield.[73] Regenerative approaches to corn production can also increase organic material in the soil and lower pest pressure relative to conventional corn.[74] Encouraging natural enemies and preserving farmland insects doesn't just help corn. Mass flowering crops like rapeseed and canola can perform better (15-40% increase in yield) when there is a higher abundance of pollinating bees compared to fields that treat with pesticides to reduce pests.[75]

Furthermore, the agency has not discussed anywhere in its cost-benefit analysis the costs to water managers, municipalities and ratepayers due to increased water filtration requirements necessary to remain compliant with federal drinking water standards. Midwestern cities are already seeing neonicotinoids in their drinking water and drinking water treatment facilities are struggling to cope with their removal.[76] It has been exhaustively documented that many communities across the country have had to spend a lot of money upgrading their water filtration systems to deal with the onslaught of pesticides that get dumped into drinking water sources.

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[71] Heather H. Disque et al., "Effects of Clothianidin-Treated Seed on the Arthropod Community in a Mid-Atlantic No-till Corn Agroecosystem," *Pest Management Science* 75, no. 4 (April 2019): 969–78, https://doi.org/10.1002/ps.5201.

[72] Margaret R. Douglas, Jason R. Rohr, and John F. Tooker, "Neonicotinoid Insecticide Travels through a Soil Food Chain, Disrupting Biological Control of Non-Target Pests and Decreasing Soya Bean Yield," ed. Ian Kaplan, *Journal of Applied Ecology* 52, no. 1 (February 2015): 250–60, https://doi.org/10.1111/1365-2664.12372.

[73] Anna K. Busch et al., "A High-Diversity/IPM Cropping System Fosters Beneficial Arthropod Populations, Limits Invertebrate Pests, and Produces Competitive Maize Yields," *Agriculture, Ecosystems & Environment* 292 (April 15, 2020): 106812, https://doi.org/10.1016/j.agee.2019.106812.

[74] Claire E. LaCanne and Jonathan G. Lundgren, "Regenerative Agriculture: Merging Farming and Natural Resource Conservation Profitably," *PeerJ* 6 (February 26, 2018): e4428, https://doi.org/10.7717/peerj.4428.

[75] Rui Catarino et al., "Bee Pollination Outperforms Pesticides for Oilseed Crop Production and Profitability," *Proceedings of the Royal Society B: Biological Sciences* 286, no. 1912 (October 9, 2019): 20191550, https://doi.org/10.1098/rspb.2019.1550.

[76] Kathryn L. Klarich et al., "Occurrence of Neonicotinoid Insecticides in Finished Drinking Water and Fate during Drinking Water Treatment," *Environmental Science & Technology Letters* 4, no. 5 (May 9, 2017): 168–73, https://doi.org/10.1021/acs.estlett.7b00081.

These costs get passed on to ratepayers and perpetuate on an ongoing basis due to the need to replace filters regularly. These costs must be taken into account as one of the costs associated with continued neonicotinoid registration. In fact, EPA even has a tool on its website designed to do specifically that, estimate water filtration costs to filter out common contaminants: "The [work breakdown structure] model for [Granular activated carbon] includes standard designs to estimate costs for treatment of a number of different contaminants, including atrazine and various VOCs."[77]

Further, EPA does not discuss other alternatives to these five neonics that may be less harmful to the environment. Part of any weighing of costs and benefits must include integration of information on alternatives. There are many non-chemical alternatives that exist that could replace many neonic uses. Furthermore, EPA's own analyses for other pesticides have found that neonics are not the safest insecticides that are approved for use on many crops.[78,79,80] Therefore, EPA must discuss alternatives to neonic use and if there are other alternatives available, take that into account in its cost-benefit analysis.

The EPA's registration analysis clearly overvalues neonicotinoids by overstating their benefits and not taking into account all of the costs associated with their use. Without an accurate accounting of costs and benefits, EPA cannot come to a "no unreasonable adverse effects" determination and will be in violation of FIFRA.

7. The EPA must comply with duties under Section 7 of the ESA,[81] including completion of consultation

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 ensure that its action does not jeopardize the continued existence of imperiled species across the country or adversely modify or destroy their

[77] EPA. Drinking Water Treatment Technology Unit Cost Models and Overview of Technologies Drinking Water Treatment Technology Unit Cost Models. Last updated July 3, 2019. Available here: https://www.epa.gov/dwregdev/drinking-water-treatment-technology-unit-cost-models-and-overview-technologies.
[78] EPA. Sulfoxaflor: Hazard Comparison for Several Alternative Insecticides. July 10, 2019. Available here: https://www.regulations.gov/document?D=EPA-HQ-OPP-2010-0889-0567.
[79] EPA. Benefits for New Uses of Sulfoxaflor on Alfalfa, Avocado, Citrus, Corn, Cotton, Cucurbits, Fruiting Vegetables, Pineapple, Pome Fruit (pre-bloom), Rice, Sorghum, Soybean, Strawberry, Ornamentals and Home Fuit Trees (DP#442401). March 7, 2019. Available here: https://www.regulations.gov/document?D=EPA-HQ-OPP-2010-0889-0569.
[80] EPA. Proposed Registration Decision of the New Active Ingredient Flupyradifurone. September 24, 2014. Available here: https://www.regulations.gov/document?D=EPA-HQ-OPP-2013-0226-0015.
[81] 16 U.S.C. § 1536.

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 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."[82] The EPA must initiate consultation under Section 7 whenever its action "may affect" a listed species or critical habitat.[83] 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."[84] 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.

The Fish and Wildlife service has produced at least two Special Status Assessments (SSA) for wildlife listed under the act that explicitly detail the impacts of neonicotinoids on the rusty patched bumble bee and the Dakota skipper. These two species have broad ranges in the upper Midwest near areas that have documented large amounts of neonicotinoid usage. The Special Status Assessment for the rusty patched bumble bee demonstrates a close association between neonicotinoid use increase and the decline of the rusty patched bumble bee.[85] The Special Status Assessment for the Dakota skipper cites neonicotinoid pesticides as a threat and cites a study that found clothianidin in Dakota skipper prairie habitat in Minnesota and South Dakota.[86] The EPA must consult with the FWS on the continued registration of these pesticides that have clear harms to native insect fauna. Based on species range and habitat we have put together a list of the ESA listed species that will be most directly and indirectly affected by the continued use of neonicotinoid pesticides (see Table 1.). **This list is not exhaustive and does not represent all species that may be affected by this action**.

[82] 16 U.S.C. § 1536(a)(2) (emphasis added).
[83] 50 C.F.R. § 402.14(a).
[84] *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).
[85] Jennifer Szymanski et al., "Rusty Patched Bumble Bee (Bombus Affinis) Species Status Assessment" (U.S. Fish and Wildlife Service, June 2016), 47, https://ecos.fws.gov/ServCat/DownloadFile/120109.
[86] U.S. Fish and Wildlife Service, "Dakota Skipper (Hesperia Dacotae) Report on the Species Status Assessment Version 2 - September 2018" (U.S. Fish and Wildlife Service, 2018), 47.

Table 1. ESA listed species likely to be most affected by continued neonicotinoid application.

Common Name	Species Name	Status	Class
Bachman's warbler	*Vermivora bachmanii*	E	Bird
Ivory-billed woodpecker	*Campephilus principalis*	E	Bird
Least Tern Interior	*Sternula antillarum athalassos*	E	Bird
Piping Plover	*Charadrius melodus*	T	Bird
Red Knot	*Calidris canutus rufa*	T	Bird
Red-cockaded Woodpecker	*Picoides borealis*	E	Bird
Southwest Willow flycatcher	*Empidonax traillii extimus*	E	Bird
Whooping crane	*Grus americana*	E	Bird
Wood stork (U.S. DPS)	*Mycteria americana (U.S. DPS)*	T	Bird
Yellow-billed cuckoo (Western DPS)	*Coccyzus americanus (Western DPS)*	T	Bird
American Burying Beetle	*Nicrophorus americanus*	E	Insect
Dakota Skipper	*Hesperia dakotae*	T	Insect
Delta green ground beetle	*Elaphrus viridis*	T	Insect
Fender's blue butterfly	*Plebejus icarioides fenderi*	E	Insect
Hine's emerald dragonfly	*Somatochlora hineana*	E	Insect
Karner blue butterfly	*Plebejus melissa samuelis*	E	Insect
Mitchell's satyr butterfly	*Neonympha mitchellii mitchellii*	E	Insect
Powesheik skipperling	*Oarisma powesheik*	T	Insect
Rusty Patched Bumble Bee	*Bombus affinis*	E	Insect
Valley Elderberry Longhorn beetle	*Desmocerus californicus dimorphus*	T	Insect
Florida bonneted bat	*Eumops floridanus*	E	Mammal

Gray Bat	*Myotis grisescens*	E	Mammal
Indiana bat	*Myotis sodalis*	E	Mammal
Northern long-eared bat	*Myotis septentrionalis*	T	Mammal
Virginia big-eared bat	*Corynorhinus townsendii virginianus*	E	Mammal

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.

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."[87] 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."[88] The EPA cannot meet this standard without requiring, evaluating and considering all information that causes adverse effects from the 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.

[87] 7 U.S.C. § 136a(c)(5)(C), (D); 40 C.F.R. § 152.112(e).
[88] 7 U.S.C. § 136(bb).

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These comments are supported by Pesticide Action Network

Appendix A

EFFECTS ON SOIL ORGANISMS IN LAB STUDIES:

In the lab, acetamiprid negatively affected the survival and reproduction of collembola and enchytraeids,[1] and the survival,[1,2,3] reproduction,[1,3] cellulase activity, [3] and epidermal and midgut cells[3] of earthworms. Clothianidin negatively affected survival of collembola[4] and earthworms.[2,3,4,5,6] Imidacloprid negatively affected survival and reproduction of acari[7] and collembola,[7] biochemical biomarkers in collembola,[8] and reproduction in the nematode, *Caenorhabditis elegans*.[9] In earthworm tests, imidacloprid negatively affected survival, [2, 3,7,10,11,12,13 14,15,16,17,18,19,20,21,22] reproduction, [3,7,8,10,19,21,22,23] biochemical biomarkers, [3,14,16,19,,21,22,23,24,25,26,27] burrowing behavior,[28,29,30] cast production,[31,32] biomass,[32,33] and caused sperm deformities[15] and tissue damage to the epidermal and midgut cells.[3] In isopods, imidacloprid negatively affected the mortality,[7] feeding rate,[7,34] growth,[34] epithelial thickness,[34] and Glutathione S-transferase enzyme activity.[34] Imidacloprid at environmentally relevant concentrations impaired navigation and foraging success in the ant, *Pogonomyrmex occidentalis*.[35] Another ant study revealed that the activity and foraging behavior of *Lasius flavus and Lasius niger* were both negatively impacted by imidacloprid.[36] A significant increase in aggressive behavior in *L. flavus* toward other nest-mates reduced survival probability down to 60% due to altered established dominance hierarchies and the dynamic and structure of ant communities.[28] Thiamethoxam negatively affected survival and reproduction of collembola, [4,37,38] and survival [4] and reproduction [10] of earthworms. A seed treatment containing thiamethoxam and the fungicides mefenoxam and fludioxonil, killed over 60% of *Chlaenius tricolor* (coleoptera) when beetles ingested contaminated slugs.[39] Behavioral impairment, including twitching, paralysis, and mild motor difficulty, was observed in up to 89% of the population, and the beetles that survived required several days to recover.[39] Dinotefuran impaired multiple enzymatic activities, gene expression, proteins and lipids, and caused DNA damage in the earthworm, *Eisenia fetida*, resulting in destruction of the structure and function of cells.[40] A combined analysis of neonicotinoid treatments containing acetamiprid, clothianidin, dinotefuran, imidacloprid, and thiacloprid negatively affected reproduction and caused DNA damage in the earthworm, *Eisenia andrei*.[41]

EFFECTS ON SOIL ORGANISMS IN FIELD STUDIES:

In the field, clothianidin negatively affected the survival of Staphylinidae (coleoptera) and total invertebrate populations.[42] Clothianidin reduced the survival and biomass of earthworms by 32% and 39%, respectively, and the survival of Acari by 52-66%.[43] When

applied with bifenthrin, clothianidin nearly eradicated collembola populations (89-92% decrease), and reduced the survival and biomass of coleoptera by 67% and 83%, respectively.[43] Clothianidin and bifenthrin additionally decreased Formicidae and Staphylinidae predation of target pest eggs by 37% to 47%.[43] A treatment containing clothianidin and imidacloprid on genetically engineered corn seeds negatively affected the population of carabids.[44]

Imidacloprid suppressed total coleoptera populations by 2.4 fold,[45] with 60% reductions in staphylinidae abundance and 85.5% in carabidae abundance.[46] Imidacloprid seed treatment in corn fields over a 5 year period had a moderately negative effect on carabidae through visual sampling, and a strongly negative effect on staphylinidae through pitfall trips.[47] *Harpalus pennsylvanicus* abundance and fecundity were also negatively affected.[48] Imidacloprid reduced the abundance,[43,49,50] casting production,[49,50] litter decomposition,[51,52] feeding activity,[53,50] surface activity,[54] and weight [43,51] of Oligochaetes. Imidacloprid decreased the abundance of Diptera,[55] collembola, [55,56,57,58] acari,[55] and prostigmata mites.[56,43] In treatments on the beneficial wasp, *Tiphia vernalis*, that parasitizes and feeds on agricultural pests, imidacloprid negatively affected the survival,[59] reproduction,[60] and ability to locate, recognize, and parasitize hosts.[60] An imidacloprid seed dressing containing the fungicides, prothioconazole, difenoconazole, and fludioxonil, significantly reduced plant decomposition of detritivores.[61] Imidacloprid seed treatment was detrimental to Thysanoptera abundance in one out of three study years in grain crop rotations.[41] Imidacloprid suppressed the total hexapod population by 54-62%.[45] Imidacloprid and thiamethoxam applied as both seed treatment and foliar spray reduced the population density of Oribatida, Actinedida, and Gamasid mites, and Psocoptera when applied at field rates.[57]

When thiamethoxam seed treatments containing the fungicides mefenoxam and fludioxonil were applied to Soybean fields to treat slugs, there was a decrease in activity-density of *Chlaenius tricolor* and slug predation was reduced by 33%, causing a 67% increase in slug activity and a 19% and 5% decrease in soybean yield and density, respectively.[39] Thysanoptera populations were reduced by thiamethoxam seed treatments in two out of three study years in soybean fields.[55] Psocoptera populations were negatively affected by thiamethoxam seed treatment.[57] The diversity of combined functional guilds (detritivores, predators, and herbivores) were reduced in thiamethoxam and fungicide seed treatments.[58] Additionally, the study found that the intended target of the seed treatment, the herbivore guild, was unaffected, and that crop yields in the thiamethoxam treatment remained the same as the control.[46]

Neonicotinoid seed treatments of clothianidin, imidacloprid, and thiamethoxam caused nearly complete mortality for all but one of the 14 carabid species tested.[62] The feeding period of carabids was two days longer in neonicotinoid treatments than the control, and treated carabids consumed less of the target pest, corn rootworm.[62]

EFFECTS ON GROUND-NESTING POLLINATORS:

Neonicotinoids arguably pose the greatest risk to pollinators, but pollinators that nest in the ground, such as ground-nesting bees and most bumblebees, have even greater exposure to pesticide residues. Willis Chan et al.[63] found that neonicotinoids represented 99% of total insecticide hazard in the soil sites tested, with imidacloprid detected in 10.97% of sites, thiamethoxam in 81.48% and clothianidin in 96.34%. In pollen tests, only imidacloprid was detected, but residues of imidacloprid in soil (41.6 ng/g) were nearly ten times greater than the maximum residue of imidacloprid in pollen (4.3 n/g).[63] The authors analyzed the probabilistic chronic and acute risk of neonicotinoid residues to hoary squash bees, *Peponapis pruinosa,* that nest in the ground.[63] For chronic risk, clothianidin, thiamethoxam, and imidacloprid risk exceeded 5%, which the authors considered significant in their hazard quotient.[63] In acute scenarios, clothianidin and thiamethoxam risk was also greater than 5%.[63] This study provides evidence that ground nesting bees are at greater risk to neonicotinoid exposure than non-ground nesting bees.[63] Neonicotinoid residues from seed dressings containing clothianidin, imidacloprid, or thiamethoxam were detected in 87% and 100% of treated agricultural field soils at pre-seeding and after application at harvest time, respectively.[64] In untreated field soil, neonicotinoid residues were 22% and 56% at pre-seeding and after application and harvest, respectively.[64] Neonicotinoid residues in the soil of field margins surrounding treated fields ranged from 53-93% and residues in the soil of field margins surrounding untreated fields ranged from 33-56%, depending on pre-treatment or post-treatment.[64] By comparison, neonicotinoid residues in wildflowers of field margins was only 7%.[64] Overall, the abundance of wild, ground-nesting bees was not negatively affected by neonicotinoid concentrations, however, populations did significantly decline with time as the seed treatments were applied.[64] Wild bee richness was negatively associated with field margin soils containing higher neonicotinoid residues.[64] When neonicotinoid residues were very low while fungicide concentrations in wildflowers were high, bee richness was greater in field margins, indicating a more significant impact of pesticides to bees through soil residues than from pollen intake.[64] In a study analyzing colony development and foraging in *Bombus terrestris*, clothianidin and imidacloprid were applied to oilseed rape fields but were not detected above the limit of quantitation, while thiamethoxam, which was not applied, was detected.[65]

Bombus terrestris that were fed field levels of neonicotinoids accumulated between 4 and 10 nM of imidacloprid and clothianidin in their brains within 3 days.[66] Clothianidin showed acute effects on brain mitochondrial dysfunction at 10 nM, and imidacloprid had chronic effects as low as 1 nM over multiple weeks of exposure.[66] Both clothianidin and thiamethoxam activated the nicotinic acetylcholine receptors and neural kenyon cells in *B. terrestris* and imidacloprid, thiamethoxam, and clothianidin all delivered neuroactive levels of clothianidin to the bumblebee brain either as a parent form or a metabolite.[67]

Imidacloprid caused acute mortality in *B. terrestris* when ingested after 72 hours,[68] and negatively affected *Bombus* spp. survival.[69,70,71,72,73] Imidacloprid reduced worker production,[74] colony growth, [67,75] brood production [69,74] and viability,[66] and reproduction,[71,75] with an 85% decrease in new queen production.[75]. Imidacloprid reduced the average amount of pollen

consumed by *Bombus impatiens* and fully prevented *B. impatiens* from ovipositing and reproducing.[76] Imidacloprid had a negative impact on bumble bee worker fecundity, due, in part, to the reduced feeding of the treated bees, as control bees that ate more syrup and pollen produced more brood.[77] Imidacloprid applied without irrigation negatively impacted *B. impatiens* foraging activity and worker's defensive response.[78] *Bombus terrestris* foragers treated with imidacloprid brought back pollen in 40% of trips versus 63% in control, and overall 31% less per hour than control,[79] while foraging trips for *B. impatiens* took 42.6% longer than the control.[80] Cresswell et al.,[81] reported that bumblebees were more sensitive to imidacloprid than honeybees, with negative effects on feeding and locomotory activity, a lower limit of detection (0.10 ug/bee), greater intake of contaminated syrup, and slower ability to eliminate toxins. The authors note that *B. terrestris* is negatively affected after ingesting 1 ug of imidacloprid per day, and under normal circumstances, are capable of clearing 5 ug from their system daily.[81] Imidacloprid caused hyperactivity in flight velocity of *B. terrestris*, which resulted in negative effects on flight distance and duration, indicating that bees may have become worn out by increased flight performance.[82] *Bombus impatiens* treated with imidacloprid demonstrated a dose-dependent delay in completing a flower handling task.[83]

In the lab, clothianidin negatively affected survival of *B. impatiens* [72], and gene expression in *B. terrestris*.[84] In the field, clothianidin was highly acutely toxic to *B. impatiens*,[72] and significantly reduced the number of workers.[85] Clothianidin negatively affected flight activity,[86] flower visitation,[86] and neural function [66,67] in *B. terrestris* colonies. Clothianidin seed treatment containing the pyrethroid, cyfluthrin, negatively impacted *B. terrestris* reproduction and colony development.[87] In combination with additional stress caused by harnessing bees for Proboscis Extension Response (PER) learning assays, clothianidin led to an increase in mortality of *B. terrestris*.[88,89] Both clothianidin and thiamethoxam seed treatments negatively affected *B. terrestris* egg cell production via nest residue toxicity, and queen and drone production were also reduced.[90]

Thiamethoxam negatively affected the nest structure mass of *B. terrestris* colonies,[67] reduced the number of viable brood cells by 70%,[67], and altered the weight [70] and sex ratio of males, with more males produced than in the control.[67] Chronic exposure of field relevant levels of thiamethoxam caused *B. terrestris* foragers to have longer foraging bouts (68 vs 55 minutes in control), and bring back pollen less frequently.[91] Although a higher number of treated bees returned to nests after being released 1 km from nests, there was no effect on homing success when bees were released 2 km from nests.[91] The increased homing ability in the 1 km test may have been due to bees experiencing increased orientation practice during longer foraging frequency bouts that were previously caused by thiamethoxam treatment.[91] While thiamethoxam treated *B. terrestris* foragers collected pollen more often than control, untreated bees learned to handle flowers more efficiently after fewer visits to the flowers.[92] Untreated bees preferred to forage on *Trifolium repens* and exposed bees preferred *Lotus corniculatus*, which demonstrates pollinator preferences in neonicotinoid treated bees that could have lasting effects on pollination services.[92]

BIBLIOGRAPHY:

1. Renaud, M., Akeju, T., Natal-da-Luz, T., Leston, S., Rosa, J., Ramos, F., Sousa, J. P., & Azevedo-Pereira, H. M. V. S. (2018). Effects of the neonicotinoids acetamiprid and thiacloprid in their commercial formulations on soil fauna. *Chemosphere*, *194*, 85–93. https://doi.org/10.1016/j.chemosphere.2017.11.102
2. Wang, Y., Cang, T., Zhao, X., Yu, R., Chen, L., Wu, C., & Wang, Q. (2012). Comparative acute toxicity of twenty-four insecticides to earthworm, *Eisenia fetida*. *Ecotoxicology and Environmental Safety*, *79*, 122–128. https://doi.org/10.1016/j.ecoenv.2011.12.016
3. Wang, K., Pang, S., Mu, X., Qi, S., Li, D., Cui, F., & Wang, C. (2015). Biological response of earthworm, *Eisenia fetida*, to five neonicotinoid insecticides. *Chemosphere*, *132*, 120–126. https://doi.org/10.1016/j.chemosphere.2015.03.002
4. Ritchie, E. E., Maisonneuve, F., Scroggins, R. P., & Princz, J. I. (2019). Lethal and Sublethal Toxicity of Thiamethoxam and Clothianidin Commercial Formulations to Soil Invertebrates in a Natural Soil. *Environmental Toxicology and Chemistry*, *38*(10), 2111–2120. https://doi.org/10.1002/etc.4521
5. Wang, Y., Wu, S., Chen, L., Wu, C., Yu, R., Wang, Q., & Zhao, X. (2012). Toxicity assessment of 45 pesticides to the epigeic earthworm *Eisenia fetida*. *Chemosphere*, *88*(4), 484–491. https://doi.org/10.1016/j.chemosphere.2012.02.086
6. Yang, G., Chen, C., Wang, Y., Peng, Q., Zhao, H., Guo, D., Wang, Q., & Qian, Y. (2017). Mixture toxicity of four commonly used pesticides at different effect levels to the epigeic earthworm, *Eisenia fetida*. *Ecotoxicology and Environmental Safety*, *142*, 29–39. https://doi.org/10.1016/j.ecoenv.2017.03.037
7. de Lima e Silva, C., Brennan, N., Brouwer, J. M., Commandeur, D., Verweij, R. A., & van Gestel, C. A. M. (2017). Comparative toxicity of imidacloprid and thiacloprid to different species of soil invertebrates. *Ecotoxicology*, *26*(4), 555–564. https://doi.org/10.1007/s10646-017-1790-7
8. Sillapawattana, P., & Schäffer, A. (2017). Effects of imidacloprid on detoxifying enzyme glutathione S-transferase on Folsomia candida (Collembola). *Environmental Science and Pollution Research*, *24*(12), 11111–11119. https://doi.org/10.1007/s11356-016-6686-1
9. Gomez-Eyles, J. L., Svendsen, C., Lister, L., Martin, H., Hodson, M. E., & Spurgeon, D. J. (2009). Measuring and modelling mixture toxicity of imidacloprid and thiacloprid on *Caenorhabditis elegans* and *Eisenia fetida*. *Ecotoxicology and Environmental Safety*, *72*(1), 71–79. https://doi.org/10.1016/j.ecoenv.2008.07.006
10. Alves, P. R. L., Cardoso, E. J. B. N., Martines, A. M., Sousa, J. P., & Pasini, A. (2013). Earthworm ecotoxicological assessments of pesticides used to treat seeds under tropical conditions. *Chemosphere*, *90*(11), 2674–2682. https://doi.org/10.1016/j.chemosphere.2012.11.046

11. Cang, T., Dai, D., Yang, G., Yu, Y., Lv, L., Cai, L., Wang, Q., & Wang, Y. (2017). Combined toxicity of imidacloprid and three insecticides to the earthworm, *Eisenia fetida* (Annelida, Oligochaeta). *Environmental Science and Pollution Research*, *24*(9), 8722–8730. https://doi.org/10.1007/s11356-017-8627-z
12. Capowiez, Y., Rault, M., Costagliola, G., & Mazzia, C. (2005). Lethal and sublethal effects of imidacloprid on two earthworm species (*Aporrectodea nocturna* and *Allolobophora icterica*). *Biology and Fertility of Soils*, *41*(3), 135–143. https://doi.org/10.1007/s00374-004-0829-0
13. Chen, C., Wang, Y., Zhao, X., Wang, Q., & Qian, Y. (2014). Comparative and combined acute toxicity of butachlor, imidacloprid and chlorpyrifos on earthworm, *Eisenia fetida*. *Chemosphere*, *100*, 111–115. https://doi.org/10.1016/j.chemosphere.2013.12.023
14. Dittbrenner, N., Capowiez, Y., Köhler, H.-R., & Triebskorn, R. (2012). Stress protein response (Hsp70) and avoidance behaviour in *Eisenia fetida*, Aporrectodea caliginosa and Lumbricus terrestris when exposed to imidacloprid. *Journal of Soils and Sediments*, *12*(2), 198–206. https://doi.org/10.1007/s11368-011-0437-1
15. Faheem, M., & Khan, M. F. (2010). Toxicity of Imidacloprid (Nicotinoid) against earthworm, *Pheretima posthuma* with reference to its effects on protein. *J Basic Appl Sci*, *6*(1), 55-62.
16. Luo, Y., Zang, Y., Zhong, Y., & Kong, Z. (1999). Toxicological study of two novel pesticides on earthworm *Eisenia foetida*. *Chemosphere*, *39*(13), 2347–2356. https://doi.org/10.1016/S0045-6535(99)00142-3
17. Mostert, M. A., Schoeman, A. S., & Merwe, M. van der. (2002). The relative toxicities of insecticides to earthworms of the Pheretima group (Oligochaeta). *Pest Management Science*, *58*(5), 446–450. https://doi.org/10.1002/ps.473
18. Velki, M., & Ečimović, S. (2015). Changes in exposure temperature lead to changes in pesticide toxicity to earthworms: A preliminary study. *Environmental Toxicology and Pharmacology*, *40*(3), 774–784. https://doi.org/10.1016/j.etap.2015.09.009
19. Wang, K., Qi, S., Mu, X., Chai, T., Yang, Y., Wang, D., Li, D., Che, W., & Wang, C. (2015). Evaluation of the Toxicity, AChE Activity and DNA Damage Caused by Imidacloprid on Earthworms, *Eisenia fetida*. *Bulletin of Environmental Contamination and Toxicology*, *95*(4), 475–480. https://doi.org/10.1007/s00128-015-1629-y
20. Wang, Y., An, X., Shen, W., Chen, L., Jiang, J., Wang, Q., & Cai, L. (2016). Individual and combined toxic effects of herbicide atrazine and three insecticides on the earthworm, *Eisenia fetida*. *Ecotoxicology*, *25*(5), 991–999. https://doi.org/10.1007/s10646-016-1656-4
21. Wang, X., Zhu, X., Peng, Q., Wang, Y., Ge, J., Yang, G., Wang, X., Cai, L., & Shen, W. (2019). Multi-level ecotoxicological effects of imidacloprid on earthworm (*Eisenia fetida*). *Chemosphere*, *219*, 923–932. https://doi.org/10.1016/j.chemosphere.2018.12.001

22. Zang, Y., Zhong, Y., Luo, Y., & Kong, Z. M. (2000). Genotoxicity of two novel pesticides for the earthworm, *Eisenia fetida*. *Environmental Pollution*, *108*(2), 271–278. https://doi.org/10.1016/S0269-7491(99)00191-8
23. Baylay, A. J., Spurgeon, D. J., Svendsen, C., Griffin, J. L., Swain, S. C., Sturzenbaum, S. R., & Jones, O. A. H. (2012). A metabolomics based test of independent action and concentration addition using the earthworm *Lumbricus rubellus*. *Ecotoxicology*, *21*(5), 1436–1447. https://doi.org/10.1007/s10646-012-0897-0
24. Capowiez, Y., Rault, M., Mazzia, C., & Belzunces, L. (2003). Earthworm behaviour as a biomarker – a case study using imidacloprid. *Pedobiologia*, *47*(5–6), 542–547. https://doi.org/10.1078/0031-4056-00226
25. Wang, J., Wang, J., Wang, G., Zhu, L., & Wang, J. (2016). DNA damage and oxidative stress induced by imidacloprid exposure in the earthworm *Eisenia fetida*. *Chemosphere*, *144*, 510–517. https://doi.org/10.1016/j.chemosphere.2015.09.004
26. Zhang, Q., Zhang, B., & Wang, C. (2014). Ecotoxicological effects on the earthworm *Eisenia fetida* following exposure to soil contaminated with imidacloprid. *Environmental Science and Pollution Research*, *21*(21), 12345–12353. https://doi.org/10.1007/s11356-014-3178-z
27. Velki, M., & Hackenberger, B. K. (2012). Species-specific differences in biomarker responses in two ecologically different earthworms exposed to the insecticide dimethoate. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology*, *156*(2), 104–112. https://doi.org/10.1016/j.cbpc.2012.05.001
28. Capowiez, Y., Bastardie, F., & Costagliola, G. (2006). Sublethal effects of imidacloprid on the burrowing behaviour of two earthworm species: Modifications of the 3D burrow systems in artificial cores and consequences on gas diffusion in soil. *Soil Biology and Biochemistry*, *38*(2), 285–293. https://doi.org/10.1016/j.soilbio.2005.05.014
29. Capowiez, Y., & Bérard, A. (2006). Assessment of the effects of imidacloprid on the behavior of two earthworm species (*Aporrectodea nocturna* and *Allolobophora icterica*) using 2D terraria. *Ecotoxicology and Environmental Safety*, *64*(2), 198–206. https://doi.org/10.1016/j.ecoenv.2005.02.013
30. Dittbrenner, N., Moser, I., Triebskorn, R., & Capowiez, Y. (2011). Assessment of short and long-term effects of imidacloprid on the burrowing behaviour of two earthworm species (*Aporrectodea caliginosa* and *Lumbricus terrestris*) by using 2D and 3D post-exposure techniques. *Chemosphere*, *84*(10), 1349–1355. https://doi.org/10.1016/j.chemosphere.2011.05.011
31. Capowiez, Y., Dittbrenner, N., Rault, M., Triebskorn, R., Hedde, M., & Mazzia, C. (2010). Earthworm cast production as a new behavioural biomarker for toxicity testing. *Environmental Pollution*, *158*(2), 388–393. https://doi.org/10.1016/j.envpol.2009.09.003
32. Dittbrenner, N., Triebskorn, R., Moser, I., & Capowiez, Y. (2010). Physiological and behavioural effects of imidacloprid on two ecologically relevant earthworm species

(Lumbricus terrestris and Aporrectodea caliginosa). *Ecotoxicology*, *19*(8), 1567–1573. https://doi.org/10.1007/s10646-010-0542-8
33. Dittbrenner, N., Schmitt, H., Capowiez, Y., & Triebskorn, R. (2011). Sensitivity of Eisenia fetida in comparison to Aporrectodea caliginosa and Lumbricus terrestris after imidacloprid exposure. Body mass change and histopathology. *Journal of Soils and Sediments*, *11*(6), 1000–1010. https://doi.org/10.1007/s11368-011-0397-5
34. Drobne, D., Blažič, M., Van Gestel, C. A. M., Lešer, V., Zidar, P., Jemec, A., & Trebše, P. (2008). Toxicity of imidacloprid to the terrestrial isopod *Porcellio scaber* (Isopoda, Crustacea). *Chemosphere*, *71*(7), 1326–1334. https://doi.org/10.1016/j.chemosphere.2007.11.042
35. Sappington, J. D. (2018). Imidacloprid alters ant sociobehavioral traits at environmentally relevant concentrations. *Ecotoxicology*, *27*(9), 1179–1187. https://doi.org/10.1007/s10646-018-1976-7
36. Thiel, S., & Köhler, H.-R. (2016). A sublethal imidacloprid concentration alters foraging and competition behaviour of ants. *Ecotoxicology*, *25*(4), 814–823. https://doi.org/10.1007/s10646-016-1638-6
37. Alves, P. R. L., Cardoso, E. J. B. N., Martines, A. M., Sousa, J. P., & Pasini, A. (2014). Seed dressing pesticides on springtails in two ecotoxicological laboratory tests. *Ecotoxicology and Environmental Safety*, *105*, 65–71. https://doi.org/10.1016/j.ecoenv.2014.04.010
38. de Lima e Silva, C., Mariette, J., Verweij, R. A., & van Gestel, C. A. M. (2018). Assessing the toxicity of thiamethoxam, in natural LUFA 2.2 soil, through three generations of *Folsomia candida*. *Ecotoxicology*, *27*(7), 764–771. https://doi.org/10.1007/s10646-018-1922-8
39. Douglas, M. R., Rohr, J. R., & Tooker, J. F. (2015). EDITOR'S CHOICE: Neonicotinoid insecticide travels through a soil food chain, disrupting biological control of non-target pests and decreasing soya bean yield. *Journal of Applied Ecology*, *52*(1), 250–260. https://doi.org/10.1111/1365-2664.12372
40. Liu, T., Wang, X., Xu, J., You, X., Chen, D., Wang, F., & Li, Y. (2017). Biochemical and genetic toxicity of dinotefuran on earthworms (Eisenia fetida). *Chemosphere*, *176*, 156–164. https://doi.org/10.1016/j.chemosphere.2017.02.113
41. Chevillot, F., Convert, Y., Desrosiers, M., Cadoret, N., Veilleux, É., Cabana, H., & Bellenger, J.-P. (2017). Selective bioaccumulation of neonicotinoids and sub-lethal effects in the earthworm *Eisenia andrei* exposed to environmental concentrations in an artificial soil. *Chemosphere*, *186*, 839–847. https://doi.org/10.1016/j.chemosphere.2017.08.046
42. Babendreier, D., Jeanneret, P., Pilz, C., & Toepfer, S. (2015). Non-target effects of insecticides, entomopathogenic fungi and nematodes applied against western corn rootworm larvae in maize. *Journal of Applied Entomology*, *139*(6), 457–467. https://doi.org/10.1111/jen.12229

43. Larson, J. L., Redmond, C. T., & Potter, D. A. (2012). Comparative impact of an anthranilic diamide and other insecticidal chemistries on beneficial invertebrates and ecosystem services in turfgrass. *Pest Management Science*, *68*(5), 740–748. https://doi.org/10.1002/ps.2321
44. Leslie, T. W., Biddinger, D. J., Rohr, J. R., & Fleischer, S. J. (2010). Conventional and Seed-Based Insect Management Strategies Similarly Influence Nontarget Coleopteran Communities in Maize. *Environmental Entomology*, *39*(6), 2045–2055. https://doi.org/10.1603/EN10049
45. Peck, D. C. (2009a). Comparative impacts of white grub (Coleoptera: Scarabaeidae) control products on the abundance of non-target soil-active arthropods in turfgrass. *Pedobiologia*, *52*(5), 287–299. https://doi.org/10.1016/j.pedobi.2008.10.003
46. Peck, D. C. (2009b). Long-term effects of imidacloprid on the abundance of surface- and soil-active nontarget fauna in turf. *Agricultural and Forest Entomology*, *11*(4), 405–419. https://doi.org/10.1111/j.1461-9563.2009.00454.x
47. Albajes, R., López, C., & Pons, X. (2003). Predatory Fauna in Cornfields and Response to Imidacloprid Seed Treatment. *Journal of Economic Entomology*, *96*(6), 1805–1813. https://doi.org/10.1093/jee/96.6.1805
48. Kunkel, B. A., Held, D. W., & Potter, D. A. (2001). Lethal and Sublethal Effects of Bendiocarb, Halofenozide, and Imidacloprid on *Harpalus pennsylvanicus* (Coleoptera: Carabidae) Following Different Modes of Exposure in Turfgrass. *Journal of Economic Entomology*, *94*(1), 60–67. https://doi.org/10.1603/0022-0493-94.1.60
49. Ghosal, A., & Hati, A. (2019). Impact of some new generation insecticides on soil arthropods in rice maize cropping system. *The Journal of Basic and Applied Zoology*, *80*(1), 6. https://doi.org/10.1186/s41936-019-0077-3
50. Tu, C., Wang, Y., Duan, W., Hertl, P., Tradway, L., Brandenburg, R., Lee, D., Snell, M., & Hu, S. (2011). Effects of fungicides and insecticides on feeding behavior and community dynamics of earthworms: Implications for casting control in turfgrass systems. *Applied Soil Ecology*, *47*(1), 31–36. https://doi.org/10.1016/j.apsoil.2010.11.002
51. Kreutzweiser, D. P., Good, K. P., Chartrand, D. T., Scarr, T. A., & Thompson, D. G. (2008). Are Leaves that Fall from Imidacloprid-Treated Maple Trees to Control Asian Longhorned Beetles Toxic to Non-target Decomposer Organisms? *Journal of Environment Quality*, *37*(2), 639. https://doi.org/10.2134/jeq2007.0278
52. Kreutzweiser, D. P., Thompson, D. G., & Scarr, T. A. (2009). Imidacloprid in leaves from systemically treated trees may inhibit litter breakdown by non-target invertebrates. *Ecotoxicology and Environmental Safety*, *72*(4), 1053–1057. https://doi.org/10.1016/j.ecoenv.2008.09.017
53. Larink, O., & Sommer, R. (2002). Influence of coated seeds on soil organisms tested with bait lamina. *European Journal of Soil Biology*, *38*(3–4), 287–290. https://doi.org/10.1016/S1164-5563(02)01161-5

54. Van Hoesel, W., Tiefenbacher, A., König, N., Dorn, V. M., Hagenguth, J. F., Prah, U., Widhalm, T., Wiklicky, V., Koller, R., Bonkowski, M., Lagerlöf, J., Ratzenböck, A., & Zaller, J. G. (2017). Single and Combined Effects of Pesticide Seed Dressings and Herbicides on Earthworms, Soil Microorganisms, and Litter Decomposition. *Frontiers in Plant Science*, *8*. https://doi.org/10.3389/fpls.2017.00215
55. Dubey, A., Lewis, M. T., Dively, G. P., & Hamby, K. A. (2019). Evaluating the ecological impacts of pesticide seed treatments on arthropod communities in a grain crop rotation. *bioRxiv*, 689463.
56. Knoepp, J. D., Vose, J. M., Michael, J. L., & Reynolds, B. C. (2012). Imidacloprid Movement in Soils and Impacts on Soil Microarthropods in Southern Appalachian Eastern Hemlock Stands. *Journal of Environment Quality*, *41*(2), 469. https://doi.org/10.2134/jeq2011.0306
57. El-Naggar, J. B., & Zidan, N. E.-H. A. (2013). FIELD EVALUATION OF IMIDACLOPRID AND THIAMETHOXAM AGAINST SUCKING INSECTS AND THEIR SIDE EFFECTS ON SOIL FAUNA. *Journal of Plant Protection Research*, *53*(4), 375–387. https://doi.org/10.2478/jppr-2013-0056
58. Atwood, L. W., Mortensen, D. A., Koide, R. T., & Smith, R. G. (2018). Evidence for multi-trophic effects of pesticide seed treatments on non-targeted soil fauna. *Soil Biology and Biochemistry*, *125*, 144–155. https://doi.org/10.1016/j.soilbio.2018.07.007
59. Oliver, J. B., Reding, M. E., Moyseenko, J. J., Klein, M. G., Mannion, C. M., & Bishop, B. (2006). Survival of Adult *Tiphia vernalis* (Hymenoptera: Tiphiidae) After Insecticide, Fungicide, and Herbicide Exposure in Laboratory Bioassays. *JOURNAL OF ECONOMIC ENTOMOLOGY*, *99*(2), 7.
60. Rogers, M. E., & Potter, D. A. (2003). Effects of Spring Imidacloprid Application for White Grub Control on Parasitism of Japanese beetle (Coleoptera: Scarabaeidae) by Tiphia vernalis (Hymenoptera: Tiphiidae). *JOURNAL OF ECONOMIC ENTOMOLOGY*, *96*(5), 8.
61. Zaller, J. G., König, N., Tiefenbacher, A., Muraoka, Y., Querner, P., Ratzenböck, A., Bonkowski, M., & Koller, R. (2016). Pesticide seed dressings can affect the activity of various soil organisms and reduce decomposition of plant material. *BMC Ecology*, *16*(1), 37. https://doi.org/10.1186/s12898-016-0092-x
62. Mullin, C. A., Saunders, M. C., Leslie, T. W., Biddinger, D. J., & Fleischer, S. J. (2005). Toxic and Behavioral Effects to Carabidae of Seed Treatments Used on Cry3Bb1- and Cry1Ab/c-Protected Corn. *Environmental Entomology*, *34*(6), 1626–1636. https://doi.org/10.1603/0046-225X-34.6.1626
63. Willis Chan, D. S., Prosser, R. S., Rodríguez-Gil, J. L., & Raine, N. E. (2019). Assessment of risk to hoary squash bees (*Peponapis pruinosa*) and other ground-nesting bees from systemic insecticides in agricultural soil. *Scientific Reports*, *9*(1), 11870. https://doi.org/10.1038/s41598-019-47805-1

64. Main, A. R., Webb, E. B., Goyne, K. W., & Mengel, D. (2020). Reduced species richness of native bees in field margins associated with neonicotinoid concentrations in non-target soils. *Agriculture, Ecosystems & Environment*, *287*, 106693. https://doi.org/10.1016/j.agee.2019.106693
65. Thompson, H. M. (2003). Behavioural effects of pesticides in bees–their potential for use in risk assessment. *Ecotoxicology*, *12*(1-4), 317-330.
66. Moffat, C., Pacheco, J. G., Sharp, S., Samson, A. J., Bollan, K. A., Huang, J., Buckland, S. T., & Connolly, C. N. (2015). Chronic exposure to neonicotinoids increases neuronal vulnerability to mitochondrial dysfunction in the bumblebee (*Bombus terrestris*). *The FASEB Journal*, *29*(5), 2112–2119. https://doi.org/10.1096/fj.14-267179
67. Moffat, C., Buckland, S. T., Samson, A. J., McArthur, R., Chamosa Pino, V., Bollan, K. A., Huang, J. T.-J., & Connolly, C. N. (2016). Neonicotinoids target distinct nicotinic acetylcholine receptors and neurons, leading to differential risks to bumblebees. *Scientific Reports*, *6*. https://doi.org/10.1038/srep24764
68. Marletto, F., Patetta, A., & Manino, A. (2003). Laboratory assessment of pesticide toxicity to bumblebees. *Bulletin of insectology*, *56*(1), 155-158.
69. Tasei, J.-N., Lerin, J., & Ripault, G. (2000). Sub-lethal effects of imidacloprid on bumblebees, *Bombus terrestris* (Hymenoptera: Apidae), during a laboratory feeding test. *Pest Manag Sci*, 5.
70. Stanley, D. A., & Raine, N. E. (2017). Bumblebee colony development following chronic exposure to field-realistic levels of the neonicotinoid pesticide thiamethoxam under laboratory conditions. *Scientific Reports*, *7*(1), 8005. https://doi.org/10.1038/s41598-017-08752-x
71. Mommaerts, V., Reynders, S., Boulet, J., Besard, L., Sterk, G., & Smagghe, G. (2010). Risk assessment for side-effects of neonicotinoids against bumblebees with and without impairing foraging behavior. *Ecotoxicology*, *19*(1), 207–215. https://doi.org/10.1007/s10646-009-0406-2
72. Scott-Dupree, C. D., Conroy, L., & Harris, C. R. (2009). Impact of Currently Used or Potentially Useful Insecticides for Canola Agroecosystems on *Bombus impatiens* (Hymenoptera: Apidae), *Megachile rotundata* (Hymentoptera: Megachilidae), and *Osmia lignaria* (Hymenoptera: Megachilidae). *Journal of Economic Entomology*, *102*(1), 177–182. https://doi.org/10.1603/029.102.0125
73. Incerti, F., Bortolotti, L., Porrini, C., & Sbrenna, A. M. (n.d.). *An extended laboratory test to evaluate the effects of pesticides on bumblebees. Preliminary results*. 6.
74. Gill, R. J., Ramos-Rodriguez, O., & Raine, N. E. (2012). Combined pesticide exposure severely affects individual- and colony-level traits in bees. *Nature*, *491*(7422), 105–108. https://doi.org/10.1038/nature11585
75. Whitehorn, P. R., O'Connor, S., Wackers, F. L., & Goulson, D. (2012). Neonicotinoid Pesticide Reduces Bumble Bee Colony Growth and Queen Production. *Science*, *336*(6079), 351–352. https://doi.org/10.1126/science.1215025

76. Gradish, A. E., Scott-Dupree, C. D., Shipp, L., Harris, C. R., & Ferguson, G. (2009). Effect of reduced risk pesticides for use in greenhouse vegetable production on *Bombus impatiens* (Hymenoptera: Apidae). *Pest Management Science*, n/a-n/a. https://doi.org/10.1002/ps.1846
77. Laycock, I., Lenthall, K. M., Barratt, A. T., & Cresswell, J. E. (2012). Erratum to: Effects of imidacloprid, a neonicotinoid pesticide, on reproduction in worker bumble bees (*Bombus terrestris*). *Ecotoxicology*, *21*(7), 1946–1946. https://doi.org/10.1007/s10646-012-0974-4
78. Gels, J. A., Held, D. W., & Potter, D. A. (2002). Hazards of Insecticides to the Bumble Bees *Bombus impatiens* (Hymenoptera: Apidae) Foraging on Flowering White Clover in Turf. *Journal of Economic Entomology*, *95*(4), 722–728. https://doi.org/10.1603/0022-0493-95.4.722
79. Feltham, H., Park, K., & Goulson, D. (2014). Field realistic doses of pesticide imidacloprid reduce bumblebee pollen foraging efficiency. *Ecotoxicology*, *23*(3), 317–323. https://doi.org/10.1007/s10646-014-1189-7
80. Morandin, L. A., & Winston, M. L. (2003). Effects of Novel Pesticides on Bumble Bee (Hymenoptera: Apidae) Colony Health and Foraging Ability. *Environmental Entomology*, *32*(3), 555–563. https://doi.org/10.1603/0046-225X-32.3.555
81. Cresswell, J. E., Robert, F.-X. L., Florance, H., & Smirnoff, N. (2014). Clearance of ingested neonicotinoid pesticide (imidacloprid) in honey bees (*Apis mellifera*) and bumblebees (*Bombus terrestris*). *Pest Management Science*, *70*(2), 332–337. https://doi.org/10.1002/ps.3569
82. Kenna, D., Cooley, H., Pretelli, I., Rodrigues, A. R., Gill, S. D., & Gill, R. J. (2019). Pesticide exposure affects flight dynamics and reduces flight endurance in bumblebees. *Ecology and Evolution*, *9*(10), 5637–5650. https://doi.org/10.1002/ece3.5143
83. Phelps, J. D., Strang, C. G., & Sherry, D. F. (2020). Imidacloprid impairs performance on a model flower handling task in bumblebees (*Bombus impatiens*). *Ecotoxicology*. https://doi.org/10.1007/s10646-020-02182-8
84. Colgan, T. J., Fletcher, I. K., Arce, A. N., Gill, R. J., Ramos Rodrigues, A., Stolle, E., Chittka, L., & Wurm, Y. (2019). Caste- and pesticide-specific effects of neonicotinoid pesticide exposure on gene expression in bumblebees. *Molecular Ecology*, *28*(8), 1964–1974. https://doi.org/10.1111/mec.15047
85. Christopher Cutler, G., & Scott-Dupree, C. D. (2014). A field study examining the effects of exposure to neonicotinoid seed-treated corn on commercial bumble bee colonies. *Ecotoxicology*, *23*(9), 1755–1763. https://doi.org/10.1007/s10646-014-1340-5
86. Dietzsch, A. C., Kunz, N., Wirtz, I. P., Stähler, M., Heimbach, U., & Pistorius, J. (2019). Does winter oilseed rape grown from clothianidin-coated seeds affect experimental populations of mason bees and bumblebees? A semi-field and field study. *Journal of Consumer Protection and Food Safety*, *14*(3), 223–238. https://doi.org/10.1007/s00003-019-01225-5

87. Rundlöf, M., Andersson, G. K. S., Bommarco, R., Fries, I., Hederström, V., Herbertsson, L., Jonsson, O., Klatt, B. K., Pedersen, T. R., Yourstone, J., & Smith, H. G. (2015). Seed coating with a neonicotinoid insecticide negatively affects wild bees. *Nature*, *521*(7550), 77–80. https://doi.org/10.1038/nature14420
88. Piiroinen, S., & Goulson, D. (2016). Chronic neonicotinoid pesticide exposure and parasite stress differentially affects learning in honeybees and bumblebees. *Proceedings of the Royal Society B: Biological Sciences*, *283*(1828). https://doi.org/10.1098/rspb.2016.0246
89. Piiroinen, S., Botías, C., Nicholls, E., & Goulson, D. (2016). No effect of low-level chronic neonicotinoid exposure on bumblebee learning and fecundity. *PeerJ*, *4*. https://doi.org/10.7717/peerj.1808
90. Woodcock, B. A., Bullock, J. M., Shore, R. F., Heard, M. S., Pereira, M. G., Redhead, J., Ridding, L., Dean, H., Sleep, D., Henrys, P., Peyton, J., Hulmes, S., Hulmes, L., Sárospataki, M., Saure, C., Edwards, M., Genersch, E., Knäbe, S., & Pywell, R. F. (2017). Country-specific effects of neonicotinoid pesticides on honey bees and wild bees. *Science*, *356*(6345), 1393–1395. https://doi.org/10.1126/science.aaa1190
91. Stanley, D. A., Russell, A. L., Morrison, S. J., Rogers, C., & Raine, N. E. (2016). Investigating the impacts of field-realistic exposure to a neonicotinoid pesticide on bumblebee foraging, homing ability and colony growth. *The Journal of Applied Ecology*, *53*(5), 1440–1449. https://doi.org/10.1111/1365-2664.12689Tu, C., Wang, Y., Duan, W., Hertl, P., Tradway, L.,
92. Stanley, D. A., & Raine, N. E. (2016). Chronic exposure to a neonicotinoid pesticide alters the interactions between bumblebees and wild plants. *Functional Ecology*, *30*(7), 1132–1139. https://doi.org/10.1111/1365-2435.12644

Past Neonic Comments to the Agency

April 21, 2018

Office of Pesticide Programs
Docket numbers EPA-HQ-OPP-2011-0865, EPA-HQ-OPP-2011-0920, EPA-HQ-OPP-2008-0844, EPA-HQ-OPP-2011-0581
Environmental Protection Agency Docket Center (EPA/DC)
(28221T)
1200 Pennsylvania Ave. NW.
Washington, DC 20460-0001

Re: Comments on EPA Draft Ecological Risk Assessments – Imidacloprid, Thiamethoxam, Clothianidin, and Dinotefuran (Dockets: EPA-HQ-OPP-2011-0865, EPA-HQ-OPP-2011-0920, EPA-HQ-OPP-2008-0844, EPA-HQ-OPP-2011-0581)

Please accept the following comments on behalf of the Center for Biological Diversity ("Center"), Prairie Rivers Network, National Latino Farmers & Ranchers Trade Association, Maryland Latino Farmers & Ranchers Trade Association, Central Maryland Beekeepers Association, American Bird Conservancy, Maryland Pesticide Education Network, Friends of the Earth, Pollinate Minnesota, Center for Food Safety, Avaaz, and the Sierra Club in response to the Environmental Protection Agency's ("EPA") ecological risk assessment for products containing a pesticide ingredient under the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA").

Unfortunately, there are serious issues with these ecological risk assessments 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 at risk of unreasonable harm from the labeled uses of clothianidin, thiamethoxam, imidacloprid and dinotefuran. Issues that must be addressed are outlined below.

1. The cumulative effects of neonicotinoids must be measured

The EPA states "Imidacloprid is in the N-nitroguanidine group of neonicotinoids (IRAC subclass 4A) along with clothianidin, thiamethoxam and dinotefuran. Its mode of action on target insects involves out-competing the neurotransmitter, acetylcholine for available binding sites on the nAChRs. At low concentrations, neonicotinoids cause excessive nervous stimulation and at high concentrations, insect paralysis and death will occur."[89] In addition, CropLife's Insecticide

[89] US EPA. Office of Pesticide Programs Environmental Fate and Effects Division. Preliminary Terrestrial Risk Assessment to Support the Registration Review of Imidacloprid. 2017. Page 11.

Resistance Action Committee (IRAC) lists neonicotinoids as having the same mechanism of action as nicotinic acetylcholine receptor (nachr) competitive modulators.[90]

Neonicotinoids are known to produce neuronal toxicities in insects via a common mechanism of action, that being the disruption of acetylcholine/nAChR signaling. Therefore, the combined exposure to all neonicotinoids via all sources must be addressed for the agency to come to a scientifically defensible conclusion that no unreasonable adverse effects will occur with the re-registration of these ingredients. For agents that act by the same mode of action, "dose addition" can be applied to that group according to agency documents.[91] This is not an impossible task, as the EPA currently does this when analyzing risk to another group of neurotoxins, the organophosphates, to humans.

Additionally, patent applications from pesticide companies have found that some neonicotinoids act synergistically with one another to kill insects (U.S. patent application numbers 12093299 and 10575276).[92] This makes it all the more important to measure the cumulative effects of exposure.

Given the extent of use, most species will generally be exposed to multiple neonicotinoids throughout the span of their lives. These exposures need to be accounted for and anticipated in a thorough risk assessment; anything less will underestimate risk. The EPA understands that compounds with a common mode of action often act additively to produce toxicities in all species but currently only take this into account in the human health risk assessment. A cumulative neonicotinoid risk assessment must be performed for all taxa before a re-registration decision can be made.

2. The EPA does not account for harm to terrestrial invertebrates

In the current registration review for four neonicotinoids, the EPA has currently analyzed ecological risk to aquatic invertebrates, fish (used as a surrogate for aquatic phase amphibians), mammals, birds (used as a surrogate for reptiles and terrestrial phase amphibians), and aquatic and terrestrial plants. Pollinator risk assessment documents (which only analyzed harm to managed honeybees – not other bees or any other pollinators) were released previously.

It is notable, and unacceptable, that the EPA has not analyzed ecological risk to any terrestrial invertebrate other than managed honeybees. Terrestrial invertebrates are a key part of the ecological risk assessment process. The specialized risk assessment document that analyzed risk to honeybees does not somehow preclude the agency from analyzing risk to other terrestrial

[90] Insecticide Resistance Action Committee. Modes of Action. Available at: http://www.irac-online.org/modes-of-action/. Accessed 1/28/2016.
[91] U.S. EPA. Framework for Cumulative Risk Assessment. Risk Assessment Forum. May 2003. Accessed at: http://www.epa.gov/sites/production/files/2014-11/documents/frmwrk_cum_risk_assmnt.pdf
[92] Submitted to the docket with comment letter as Patent #1 and #2.

invertebrates. Managed honeybees cannot be used as a surrogate for all other terrestrial invertebrates, they are simply too specialized and too unique in their life cycles and diets to accurately reflect risk to other invertebrate species. In fact, this is one reason that pollinators were targeted for the specialized risk assessment in the first place.

Honeybees are not the only terrestrial insects that are being harmed by the use of neonicotinoids. There are myriad examples in the peer-reviewed literature of harm to other terrestrial invertebrates – invertebrates that differ from honeybees not only in physiology but diet, lifecycle, nesting and mating. Beetles, butterflies, true bugs, crickets and grasshoppers have all been left out of the risk assessment. Of particular concern is the monarch butterfly, a species that has declined by more than 80 percent in the last two decades and is known to be harmed by neonicotinoid use. We have submitted many of these papers to the docket for EPA to review.

Therefore the ecological risk assessment profile for this registration review is incomplete. Any attempt to identify mitigation measures or make a registration decision based solely on the ecological risk analysis that has been done to date will be arbitrary and capricious and will not satisfy EPA's obligations under FIFRA.

3. Exposure through diet was not considered for aquatic invertebrates

The EPA's analysis of neonicotinoid exposure to aquatic invertebrates only accounted for exposure through the water phase. Some invertebrates are detritivores and obtain nutrients by ingesting decaying organic material from plants. Neonicotinoids are systemic pesticides that make their way through the plants' vascular system to all parts of the plant, thus contaminating all of the organic material. This contaminated plant material can make its way into water bodies and be directly consumed by some invertebrates. This will increase exposure to many invertebrates beyond simple exposure through the water phase. This will increase aggregate exposures and not taking this exposure scenario into account will underestimate risk. This issue is nicely summed up in Englert et. al,[93] which has been submitted to the docket.

Additionally, neonicotinoids can leach through contaminated organic material into water bodies in addition to directly contaminating water bodies through runoff[5]. This fact was not taken into account in EPA's modeling for this risk assessment.

Not only are these exposure scenarios not taken into account in the quantitative risk assessment, they are not even mentioned as sources of uncertainty in any risk assessment documents posted to the docket. This omission is troubling and indicates that EPA does not have a firm grasp of the

[93] Dominic Englert, Jochen P. Zubrod, Moritz Link, Saskia Mertins, Ralf Schulz, and Mirco Bundschuh. "Does Waterborne Exposure Explain Effects Caused by Neonicotinoid-Contaminated Plant Material in Aquatic Systems?" *Environmental Science & Technology* 2017 51 (10), 5793-5802.

exposure pathways that can affect these animals. These exposure scenarios must be taken into account in these risk analyses, otherwise EPA will not be upholding its duties under FIFRA.

4. Toxicity values for aquatic invertebrates 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 4 separate open literature studies finding toxicity values of 4.4, 2.83, 2.32, 2, and 1.85 ug a.i./L for different species of aquatic insects to clothianidin, the EPA elected to go with the higher value of 22 ug a.i./L from an industry sponsored study[94]. Every single one of the open literature studies was suitable for quantitative use, 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 or using extensive replicates 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."[95] 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" 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."

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

[94] US EPA. Office of Pesticide Programs Environmental Fate and Effects Division. Preliminary Aquatic and Non-Pollinator Terrestrial Risk Assessment to Support Registration Review of Clothiaidin. 2017.
[95] 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

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 in use in establishing protective thresholds[96]. 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[97].

5. Comply with duties under Section 7 of the Endangered Species Act (ESA),[98] including completion of consultation.

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."[99] 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.[100] Indeed, the EPA's recently finalized 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 stage.[101] The EPA must initiate consultation under Section 7 whenever its action "may affect" a listed species or critical

[96] 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
[97] 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
[98] 16 U.S.C. § 1536.
[99] 16 U.S.C. § 1536(a)(2) (emphasis added).
[100] 50 C.F.R. § 402.14(a).
[101] http://www.epa.gov/oppfead1/cb/csb_page/updates/2013/esa-regreview.html

habitat.[102] 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."[103] 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.[104]

6. 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

[102] 50 C.F.R. § 402.14(a).
[103] *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).
[104] *Endangered Species Protection Program Field Implementation*, 70 Fed. Reg. 66392 (Nov. 2, 2005).

Guidance for Assessing Pesticide Risks to Bees,[105] information concerning estrogen or other endocrine disruption effects,[106] 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.

7. 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."[107] 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."[108] The EPA cannot meet this standard without requiring, evaluating and considering all information that causes adverse effects from the 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.

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

[105] 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
[106] *See* 21 U.S.C. §§ 346a(d)(2)(A)(x) and 346a(p).
[107] 7 U.S.C. § 136a(c)(5)(C), (D); 40 C.F.R. § 152.112(e).
[108] 7 U.S.C. § 136(bb).

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

9. 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.[109]

A recent survey of farmers in Missouri indicated that less than half -- only 43 percent -- actually read the label each time they use pesticides.[110] 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.[111] 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 users either did not read the label instructions or failed to follow them.

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

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[109] 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.

[110] 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/.

[111] 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

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.

10. The EPA must assess the enhanced toxicity of pesticide mixtures.

The Center for Biological Diversity recently released a report[112] 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 44 multi-ingredient products containing thiamethoxam, imidacloprid or clothianidin that were approved in the past six years from Bayer and Syngenta.[113] Of those 44, 42 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) Thiamethoxam or clothianidin and abamectin, emanectin benzoate or spinosad (U.S. patent application number 11028776)[114]
2) Thiamethoxam or clothianidin and *Bacillus firmus* CNCM I-1582 (U.S. patent application number 12936700).[115]
3) Thiamethoxam or clothianidin and benalaxyl M, pyraclostrobin or metalaxyl M (U.S. patent application number 11793763 and 13209926).[116]

[112] 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.
[113] *Id.* at Appendix B
[114] Submitted to the docket with comment letter as Patent #3
[115] Submitted to the docket with comment letter as Patent #4
[116] Submitted to the docket with comment letter as Patent #5 and #6

4) Thiamethoxam or clothianidin and trifloxystrobin (U.S. patent application number 10486663).[117]
5) Thiamethoxam or clothianidin and cyantraniliprole (U.S. patent application number 11628145).[118]
6) Thiamethoxam and any pyrethrin or pyrethroid (U.S. patent application number 10486663, 12633063 and 14215205).[119]
7) Clothianidin and penflufen (U.S. patent application number 11912773).[120]
8) Thiamethoxam and azoxystrobin, sedaxane and fludioxonil (U.S. patent application number 12306870).[121]
9) Imidacloprid and any pyrethrin or synthetic pyrethroid (U.S. patent application number 09968175)[122]
10) Imidacloprid and spirotetramat (U.S. patent application number 13790375).[123]

Since most products that contain thiamethoxam, clothianidin, imidacloprid or dinotefuran were approved more than six years ago, our analysis would not have identified other patent applications that may be relevant to other multi-ingredient neonic products. In addition, the mixture of neonicotinoid insecticides and ergosterol biosynthesis inhibitor (EBI) fungicides has been shown to produce synergistic toxicities in numerous studies in the peer-reviewed literature.[124] Chronic exposure to combinations of neonicotinoids and pyrethroids impairs bees' natural foraging behavior, increases worker mortality, and accordingly, hurts brood development and colony success.[125] 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.

The scope of this issue is immense. The number of products that just contain imidacloprid mixed with another active ingredient is stunning. According to the Public National Pesticide Information Retrieval System maintained by Purdue University, over 70 products have been approved by the EPA that contain imidacloprid and at least one other active ingredient. The list of other active ingredients mixed with imidacloprid include: Lambda-Cyhalothrin, Cyfluthrin, Metalaxyl, Tebuconazole, Imazallil, Thiodicarb, Clothianidin, Spirotetramat, Fluopyram,

[117] Submitted to the docket with comment letter as Patent #7
[118] Submitted to the docket with comment letter as Patent #8
[119] Submitted to the docket with comment letter as Patent #9, #10 and #11
[120] Submitted to the docket with comment letter as Patent #12
[121] Submitted to the docket with comment letter as Patent #13
[122] Submitted to the docket with comment letter as Patent #14.
[123] Submitted to the docket with comment letter as Patent #15.
[124] Wood, T. J., & Goulson, D. (2017). The environmental risks of neonicotinoid pesticides: a review of the evidence post 2013. *Environmental Science and Pollution Research*. https://link.springer.com/article/10.1007%2Fs11356-017-9240-x.
[125] Gill, R. J., et al. (2012). Combined pesticide exposure severely affects individual- and colony-level traits in bees. Nature 491(7422): 105-108. Submitted to docket

Bifenthrin, Captan, Carboxin, Ipconazole, Phenothrin, MGK 264, Pyriproxyfen, Copper carbonate (basic), Boron sodium oxide, Carbendazim, 2-(2-Ethoxyethoxy)ethyl 2-benzimidazole carbamate (115001), Fludioxonil, cis-9-Tricosene, diphacinone, Bromadiolone, Warfarin, Abamectin, 3(2H)-Isothiazolone, 4,5-dichloro-2-octyl- (128101). This is also just the list of active ingredients that have been premixed in a formulated product and does not represent the extensive amount of tank mixing of active ingredients that happens out in the field before application.

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.[126] 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."[127]

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 document containing claims made to a government agency of the United States. Since it is unlawful to knowingly submit false information to the government,[128] any data or claims

[126] 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).
[127] EPA. Final Registration Decision of the New Active Ingredient Halauxifen-methyl. 2016. Pg. 8. Regulations.gov docket ID EPA-HQ-OPP-2012-0919-0024.
[128] 18 U.S.C. 1001.

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,[129] 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 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

[129] Colby, S.R. (1967) Calculating Synergistic and Antagonistic Responses of Herbicide Combinations. *Weeds*, 15(1), 20-22.

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.[130] 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.[131] 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 pose any greater risk than previously believed or reported to the Agency." <u>Any</u> data on chemical synergy would certainly fall into that category.

[130] 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.).
[131] 40 C.F.R. § 159.195(a).

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.[132] Since end-use products often contain chemicals that are not considered active ingredients (commonly called "inert" ingredients), synergy between <u>any</u> 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.[133]
    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.[134] 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 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

[132] *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)).
[133] 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.
[134] EPA. Final Registration Decision of the New Active Ingredient Halauxifen-methyl. 2016. Pg. 9. Regulations.gov docket ID EPA-HQ-OPP-2012-0919-0024.

Ninth Circuit Court of Appeals to vacate its registration of Enlist Duo.[135] 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.[136] 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,[137] 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 needs to 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.[138] 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.

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

[135] 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.).
[136] 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. Untied States patent publication no. US 20110275517 A1. Application number US 13/099,552. 10 November 2011.
[137] 18 U.S.C. 1001.
[138] 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.

restrictions.[139] 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.[140] 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.
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

[139] 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).
[140] EPA. Final Registration Decision of the New Active Ingredient Halauxifen-methyl. 2016. Pg. 9. Regulations.gov docket ID EPA-HQ-OPP-2012-0919-0024.

to make multiple passes through their fields to apply pesticides individually, thus increasing fuel consumption, costs and soil compaction.[141] 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.[142] 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 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 unfounded practice should have the opposite effect. Maybe, finally,

[141] 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.

[142] See submitted comments from the USDA for "Sulfoxaflor; New Active Ingredient." Docket ID: EPA-HQ-OPP-2010-0889.

some realization that this has gotten way out of hand and tank mixing is something that the 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.[143] 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[144]. 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.[145] 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 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

[143] 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.
[144] Daniel Cooley, Susan Futrell, Lyn Garling, Edwin Rajotte, Grace Gershuny, Jeff Moyer, Abby Seaman, and Stephen Young. Organic Agriculture and Integrated Pest Management: Synergistic Partnership Needed to Improve the Sustainability of Agriculture and Food Systems, 2015. Available at: https://organicipmwg.files.wordpress.com/2015/07/white-paper.pdf
[145] 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.

select for these multiple-pesticide-resistant pests."[146] 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."[147]

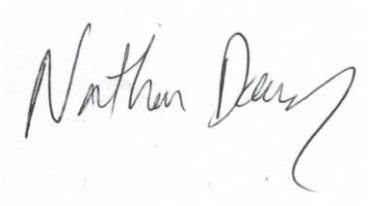
Recent modelling studies looking at how pesticide mixtures or sequential pesticide use would influence resistance development in mosquitoes found both methods to provide a similar delay in resistance compared to using just one pesticide year after year.[148] However the sequential use scenario had the added benefit of increasing the time it takes for resistance to both insecticides to develop, effectively extending the useful life of both pesticides.

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.

Respectfully submitted,

[146] 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.
[147] 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.
[148] 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



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These comments are fully supported by
Prairie Rivers Network
National Latino Farmers & Ranchers Trade Association
Maryland Latino Farmers & Ranchers Trade Association
Central Maryland Beekeepers Association
American Bird Conservancy
Maryland Pesticide Education Network
Friends of the Earth
Pollinate Minnesota
Center for Food Safety
Avaaz
Sierra Club

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."[149] 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.[150] The consultation requirement applies to any discretionary agency action that may affect listed species.[151] 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.[152]

The EPA must initiate consultation under Section 7 whenever its action "may affect" a listed species or critical habitat.[153] 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.[154] 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 stage.[155] The Services define "may affect" as "the appropriate conclusion when a proposed action may pose ***any*** effects on listed species or

[149] 16 U.S.C. § 1536(a)(2) (emphasis added).
[150] 50 C.F.R. § 402.14.
[151] *National Association of Home Builders v. Defenders of Wildlife*, 551 U.S. 644 (2007).
[152] *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.").
[153] 50 C.F.R. § 402.14(a).
[154] 50 C.F.R. § 402.14(a).
[155] 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

designated critical habitat."[156] 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."[157] 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."[158]

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.[159]

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."[160]

[156] 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).
[157] *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).
[158] CONSULTATION HANDBOOK at 3-13.
[159] 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).
[160] *Id*. at 107.

- "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."[161]
- "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."[162]
- "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."[163]

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.[164] 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*,[165] and (2) *Interim Approaches for National-level Pesticide Endangered Species Act Assessments Based on Recommendations of the National Academy of Science April 2013*.[166] The agencies made clear at a November 15, 2013 public meeting that these new procedures and approaches would be "day forward" in their implementation.[167] 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

[161] *Id*. at 11.
[162] *Id*.
[163] *Id*.
[164] *Id*. at 107.
[165] 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).
[166] Available at https://www.epa.gov/sites/production/files/2015-07/documents/interagency.pdf
[167] 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).

As laid out in the National Academy of Sciences and *Interim Approaches* guidance, the risk assessment and consultation process should follow three steps.[168] 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.[169]

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.[170] 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 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.[171] In addition, many State governments collect detailed information on non-game species through their State Wildlife Action Plans.[172] 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

[168] NAS REPORT at 37-38.
[169] 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.
[170] US Fish and Wildlife Service Environmental Conservation Online System. http://ecos.fws.gov
[171] NatureServe Get data. http://www.natureserve.org/getData/index.jsp
[172] State Wildlife Action Plans. http://teaming.com/state-wildlife-action-plans-swaps

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.

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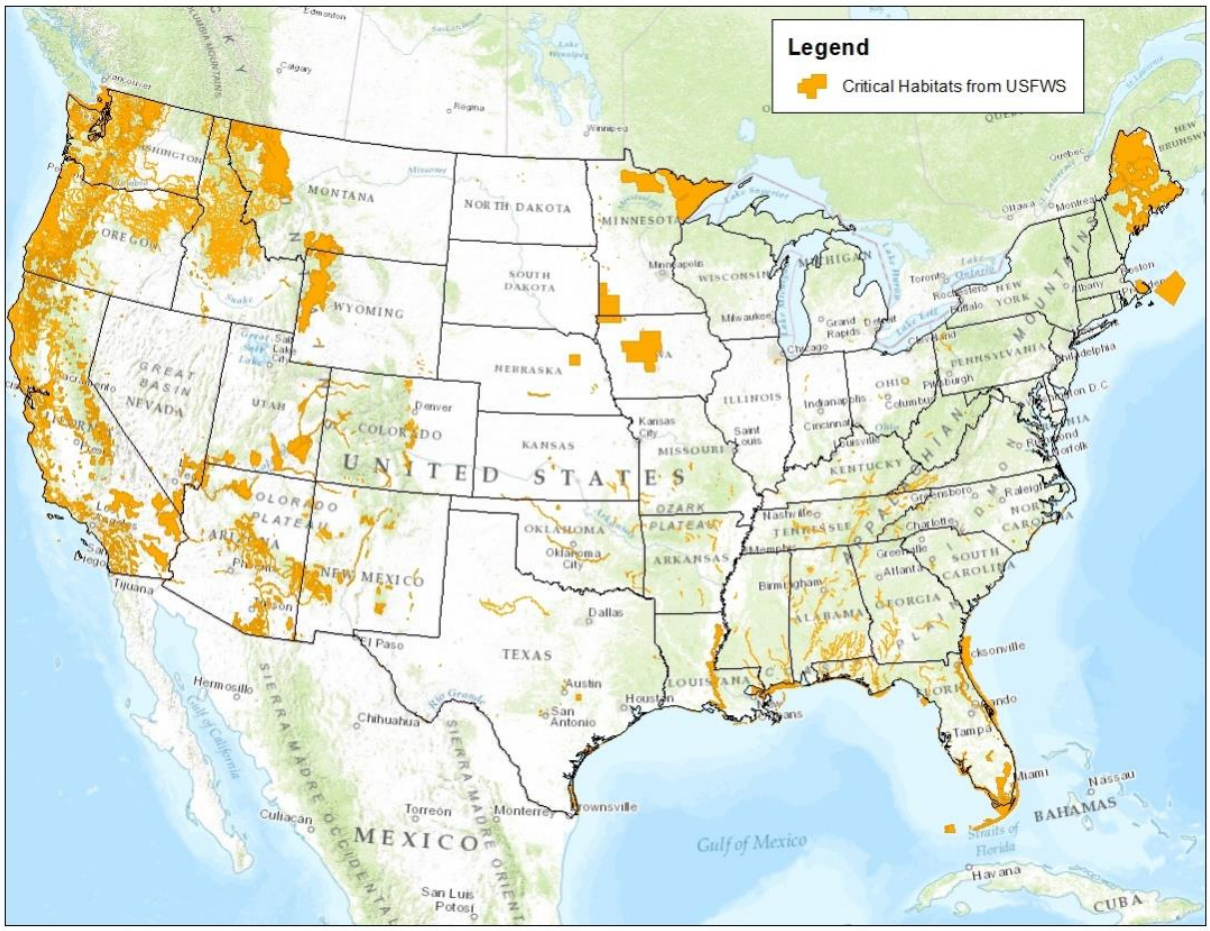
Figure One – Base Composite Map of Critical Habitat in the United States[173]



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[174] 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 Two and Step

[173] US Fish and Wildlife Service Environmental Conservation Online System. http://ecos.fws.gov
[174] 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/

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.[175] 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.[176]

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

[176] *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.[177] 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[178] 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."[179] 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

[177] 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.
[178] *Id*. at xv.
[179] *Id*. at xiv.

subject to consultation."[180] 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."[181] 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.[182] 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.[183] The mixtures of these chemicals can combine to have additive or synergistic effects that are substantially more dangerous and increase the toxicity to wildlife.[184] 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 *current* water quality conditions nationwide. In particular, the use of pesticides in watersheds that contain threatened

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[180] *Id*. at xiii.

[181] 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.

[182] 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.

[183] 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/.

[184] 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.

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."[185] 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*[186] 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.[187] 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 necessary to safeguard the species from ongoing and future threats. Therefore, Section 7 requires that critical

[185] 16 U.S.C. § 1536(a)(2).
[186] 437 U.S. 153 (1978)
[187] *See* Owen, D. 2012. *Critical Habitat and the Challenge of Regulating Small Harms*. Florida Law Review 64:141-199.

habitat not be adversely modified in ways that would hamper the *recovery* of listed species.[188] 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 Toxics Coalition v. U.S. Dept. of Interior*, "other ingredients" within a pesticide end product may cause negative impact to

[188] *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)

listed species even if they are less toxic than the active ingredient being reviewed.[189] "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.[190] 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.

March 16, 2018

Office of Pesticide Programs
Docket number EPA-HQ-OPP-2012-0329
Environmental Protection Agency Docket Center (EPA/DC)
(28221T)
1200 Pennsylvania Ave. NW.
Washington, DC 20460-0001

Re: Comments on EPA Draft Ecological Risk Assessment – Acetamiprid (Docket #: EPA-HQ-OPP-2012-0329)

Please accept the following comments on behalf of the Center for Biological Diversity ("Center") in response to the Environmental Protection Agency's ("EPA") ecological risk

[189] 457 F. Supp. 2d 1158 (W.D. Wash 2006).
[190] 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.

assessment for products containing a pesticide ingredient under the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA").

The Center for Biological Diversity ("Center") is a non-profit environmental organization dedicated to the protection of native species and their habitats through science, policy, and environmental law. The Center has over 1.6 million members and online activists dedicated to the protection and restoration of endangered species and wild places. The Center has worked for twenty-six years to protect imperiled plants and wildlife, open space, air and water quality, and overall quality of life. The Center's Environmental Health Program aims to secure programmatic changes in the pesticide registration process and to stop toxic pesticides from contaminating fish and wildlife habitats. We appreciate the opportunity to provide comment.

Before the EPA can make a supportable decision to authorize products containing this pesticide, it must first accomplish all of the following:

1. Comply with duties under Section 7 of the Endangered Species Act (ESA),[191] including completion of consultation.

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."[192] 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.[193] Indeed, the EPA's recently finalized 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 stage.[194] The EPA must initiate

[191] 16 U.S.C. § 1536.
[192] 16 U.S.C. § 1536(a)(2) (emphasis added).
[193] 50 C.F.R. § 402.14(a).
[194] http://www.epa.gov/oppfead1/cb/csb_page/updates/2013/esa-regreview.html

consultation under Section 7 whenever its action "may affect" a listed species or critical habitat.[195] 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."[196] 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.[197]

2. 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

[195] 50 C.F.R. § 402.14(a).
[196] *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).
[197] *Endangered Species Protection Program Field Implementation*, 70 Fed. Reg. 66392 (Nov. 2, 2005).

Guidance for Assessing Pesticide Risks to Bees,[198] information concerning estrogen or other endocrine disruption effects,[199] 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.

3. 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."[200] 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."[201] The EPA cannot meet this standard without requiring, evaluating and considering all information that causes adverse effects from the 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.

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

[198] 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
[199] *See* 21 U.S.C. §§ 346a(d)(2)(A)(x) and 346a(p).
[200] 7 U.S.C. § 136a(c)(5)(C), (D); 40 C.F.R. § 152.112(e).
[201] 7 U.S.C. § 136(bb).

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

5. 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.[202]

A recent survey of farmers in Missouri indicated that less than half -- only 43 percent -- actually read the label each time they use pesticides.[203] 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 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.[204] 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.

Therefore, the ever-present possibility of an accidental spill or improper disposal indicates that this is a reasonably forseeable 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 no longer refer to its use of

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[202] 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.
[203] 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/.
[204] 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

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.

6. The EPA must assess the enhanced toxicity of pesticide mixtures.

We recognize that 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.[205] 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."[206]

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 publically 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,[207] 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.

[205] 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).
[206] EPA. Final Registration Decision of the New Active Ingredient Halauxifen-methyl. 2016. Pg. 8. Regulations.gov docket ID EPA-HQ-OPP-2012-0919-0024.
[207] 18 U.S.C. 1001.

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,[208] 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 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

[208] Colby, S.R. (1967) Calculating Synergistic and Antagonistic Responses of Herbicide Combinations. *Weeds*, 15(1), 20-22.

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.

6) 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.[209] 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.[210] 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 pose any greater risk than previously believed or reported to the Agency." <u>Any</u> data on chemical synergy would certainly fall into that category.

7) 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.

[209] 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.).
[210] 40 C.F.R. § 159.195(a).

e) 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.[211] 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.

f) This includes studies from government or any third party 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.[212]

g) 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.[213] 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 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.[214] 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

[211] *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)).

[212] 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.

[213] EPA. Final Registration Decision of the New Active Ingredient Halauxifen-methyl. 2016. Pg. 9. Regulations.gov docket ID EPA-HQ-OPP-2012-0919-0024.

[214] 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.).

restrictions for a product containing dicamba.[215] 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 publically 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,[216] 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 needs to analyze any patent application that has been approved, denied or is still pending.

h) 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.[217] 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.

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.[218] 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

[215] 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. Untied States patent publication no. US 20110275517 A1. Application number US 13/099,552. 10 November 2011.
[216] 18 U.S.C. 1001.
[217] 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.
[218] 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).

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.

8) 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.[219] 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.

9) 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.
10) 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.[220] Not only is the "multiple pass" scenario highly unlikely (because no farmer in their right mind would elect to make

[219] EPA. Final Registration Decision of the New Active Ingredient Halauxifen-methyl. 2016. Pg. 9. Regulations.gov docket ID EPA-HQ-OPP-2012-0919-0024.
[220] 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.

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.[221] 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 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 silly exercise 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

[221] See submitted comments from the USDA for "Sulfoxaflor; New Active Ingredient." Docket ID: EPA-HQ-OPP-2010-0889.

prevent pest resistance from occurring.[222] 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. 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.[223] 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 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."[224] 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."[225]

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[222] 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.

[223] 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.

[224] 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.

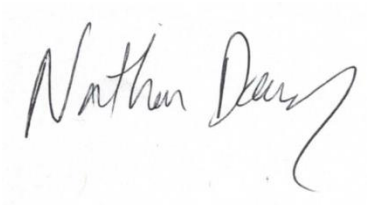
[225] University of Massachusetts Amherst Extension. The Center for Agriculture, Food and the Environment. Pest Management: Proper Use of Pesticides. Available at: https://ag.umass.edu/greenhouse-floriculture/greenhouse-best-management-practices-bmp-manual/pest-management-proper-use.

Recent modelling studies looking at how pesticide mixtures or sequential pesticide use would influence resistance development in mosquitos found both methods to provide a similar delay in resistance compared to using just one pesticide year after year.[226] 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.

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.

Respectfully submitted,



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[226] 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

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

V. 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."[227] 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.[228] The consultation requirement applies to any discretionary agency action that may affect listed species.[229] 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.[230]

The EPA must initiate consultation under Section 7 whenever its action "may affect" a listed species or critical habitat.[231] 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.[232] 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 stage.[233] The Services define "may affect" as "the appropriate conclusion when a proposed action

[227] 16 U.S.C. § 1536(a)(2) (emphasis added).
[228] 50 C.F.R. § 402.14.
[229] *National Association of Home Builders v. Defenders of Wildlife*, 551 U.S. 644 (2007).
[230] *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.").
[231] 50 C.F.R. § 402.14(a).
[232] 50 C.F.R. § 402.14(a).
[233] 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

may pose ***any*** effects on listed species or designated critical habitat."[234] 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."[235] 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."[236]

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.[237]

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:

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[234] 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).

[235] *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).

[236] CONSULTATION HANDBOOK at 3-13.

[237] 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).

- The EPA "concentration-ratio approach" for its ecological risk assessments "is ad hoc (although commonly used) and has unpredictable performance outcomes."[238]
- "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."[239]
- "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."[240]
- "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."[241]

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.[242] 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,*[243] and (2) *Interim Approaches for National-level Pesticide Endangered Species Act Assessments Based on Recommendations of the National Academy of Science April 2013*.[244] The agencies made clear at a November 15, 2013 public meeting that these new procedures and approaches would be "day forward" in their implementation.[245] Accordingly, approvals of pesticides and uses *must* follow these new *Interim Approaches* and comply with the requirements of the ESA.

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[238] *Id*. at 107.
[239] *Id*. at 11.
[240] *Id*.
[241] *Id*.
[242] *Id*. at 107.
[243] 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).
[244] Available at https://www.epa.gov/sites/production/files/2015-07/documents/interagency.pdf
[245] 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).

C. 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.[246] 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.[247]

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.[248] 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 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.[249] In addition, many State governments

[246] NAS REPORT at 37-38.
[247] 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.
[248] US Fish and Wildlife Service Environmental Conservation Online System. http://ecos.fws.gov
[249] NatureServe Get data. http://www.natureserve.org/getData/index.jsp

collect detailed information on non-game species through their State Wildlife Action Plans.[250] 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.

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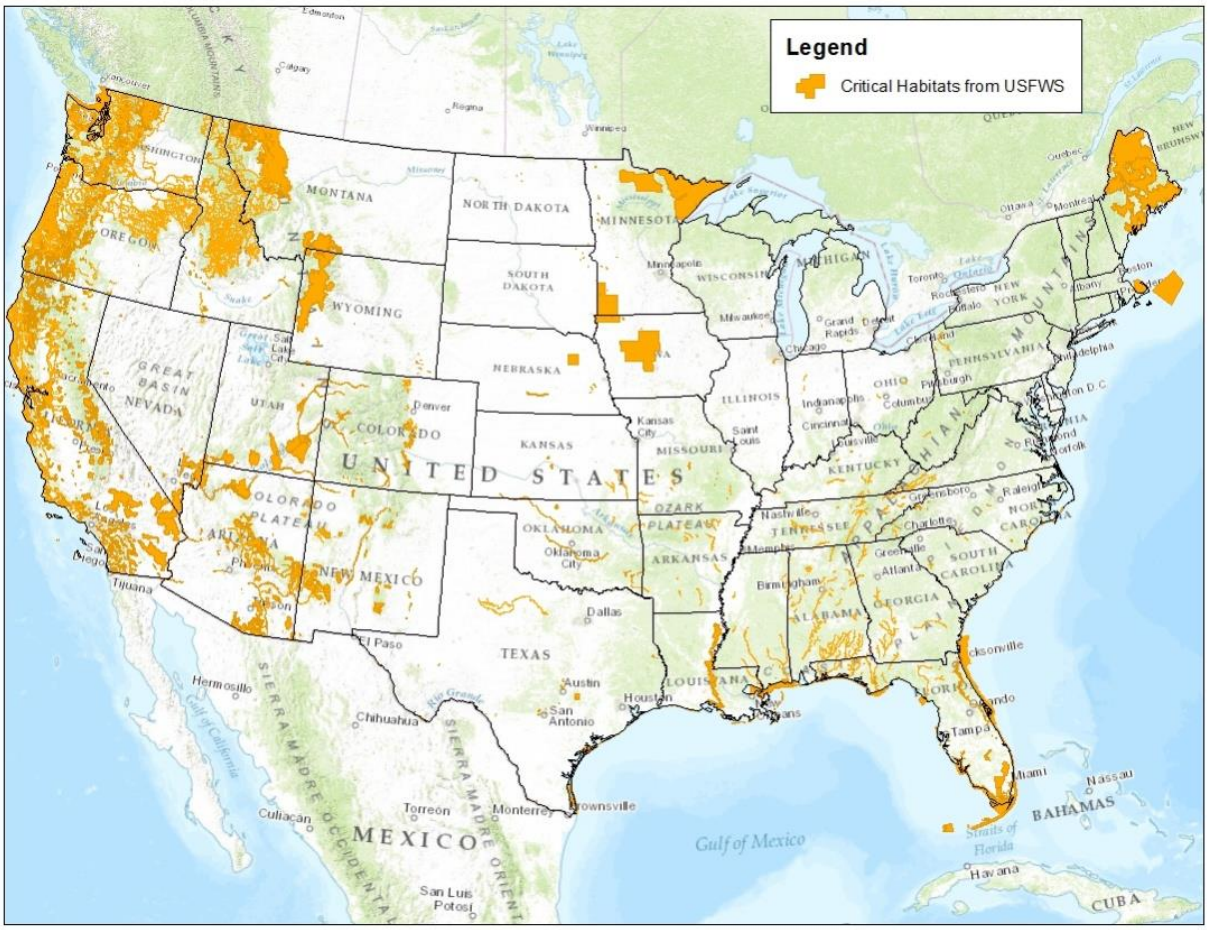
[250] State Wildlife Action Plans. http://teaming.com/state-wildlife-action-plans-swaps

Figure One – Base Composite Map of Critical Habitat in the United States[251]



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[252] 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

[251] US Fish and Wildlife Service Environmental Conservation Online System. http://ecos.fws.gov
[252] 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.

D. 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.[253] 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.[254]

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

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

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VI. 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.[255] 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[256] 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

[255] 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.
[256] *Id*. at xv.

are contemporaneous with the consultation in process."[257] 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 consultation."[258] 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."[259] 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.[260] 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.[261] The mixtures of these chemicals can combine to have additive or synergistic effects that are substantially more

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[257] *Id*. at xiv.
[258] *Id*. at xiii.
[259]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.
[260] 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.
[261] 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/.

dangerous and increase the toxicity to wildlife.[262] 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 *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.

VII. 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."[263] 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*[264] 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.[265] 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.

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[262] 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.
[263] 16 U.S.C. § 1536(a)(2).
[264] 437 U.S. 153 (1978)
[265] *See* Owen, D. 2012. *Critical Habitat and the Challenge of Regulating Small Harms*. Florida Law Review 64:141-199.

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 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.[266] 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.

VIII. 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.

[266] *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)

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 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.[267] "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.[268] 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.

July 24, 2017

Office of Pesticide Programs Docket # EPA-HQ-OPP-2011-0920, EPA-HQ-OPP-2011-0865, EPA-HQ-OPP-2011-0581
Environmental Protection Agency Docket Center (EPA/DC)
1200 Pennsylvania Ave NW
Washington, DC 20460-0001

Re: Comments on EPA Pollinator Ecological Risk Assessments: Clothianidin, Thiamethoxam and Dinetofuran Registration Reviews (Docket #: EPA-HQ-OPP-2011-0920, EPA-HQ-OPP-2011-0865, EPA-HQ-OPP-2011-0581).

[267] 457 F. Supp. 2d 1158 (W.D. Wash 2006).
[268] 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.

Please accept the following comments on behalf of the Center for Biological Diversity ("Center") in response to the Environmental Protection Agency's ("EPA") preliminary pollinator assessment to support the registration review of clothianidin, thiamethoxam and dinetofuran as part of its registration review process under the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA").

The Center is a non-profit environmental organization dedicated to the protection of native species and their habitats through science, policy, and environmental law. The Center has more than 1.3 million members and online activists dedicated to the protection and restoration of endangered species and wild places. The Center has worked for many years to protect imperiled plants and wildlife, open space, air and water quality, and overall quality of life. The Center's Pesticides Reduction Campaign aims to secure programmatic changes in the pesticide registration process and to stop toxic pesticides from contaminating fish and wildlife habitats. We appreciate the opportunity to provide comment.

We commend the EPA for taking on this much needed analysis. Many pesticides, including neonicotinoids, pose serious threats to pollinator species and this cannot be accurately accounted for in the typical ecological risk assessment process. Having a specialized risk assessment document that takes into account the different exposure pathways, life stages and heightened toxicities of many different kinds of pollinators is a step in the right direction. Furthermore, the essential pollination services that these species provide make them not only important from an ecological point of view, but also from a food security point of view.

Unfortunately, there are serious issues with these preliminary pollinator assessments 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 pollinator species at risk of unreasonable harm from the labeled uses of clothianidin, thiamethoxam and dinetofuran. Issues that need to be addressed are outlined below.

1) <u>Uncertainty is not dealt with appropriately</u>

Despite efforts to appear as though this risk assessment is thorough and complete, we are stunned at just how many data gaps there are. In fact, this risk assessment raises more questions than answers. We understand that EPA has to make due with the information that is available, but the standard that EPA has to meet in order to re-register clothianidin, thiamethoxam and dinetofuran is a "reasonable certainty of no harm." Given the extent of data gaps in this risk assessment that have not been offset with uncertainty factors, that standard surely cannot be met.

EPA has a habit of assuming uncertainty equals no risk. Simply acknowledging uncertainty at the end of a risk assessment without *quantitatively* taking it into account is unacceptable for an agency tasked with protecting human and environmental health. A narrative of uncertainty is an

insufficient way to convey the potential risks involved in registering a pesticide to a risk manager. The National Academy of Sciences has chastised EPA on this approach, stating that "….changing uncertainty analysis from a narrative addendum to an integral part of the assessment is possible and necessary to provide realistic, objective estimates of risk."[269]

When there are data deficiencies in a risk assessment, there are two options: you can err on the side of caution or err on the side of risk. The EPA constantly does the latter, and with many data deficient pesticides currently in use, the cumulative effects of these decisions are putting humans and wildlife at risk.

In this pollinator risk assessment, some of these uncertainties can be addressed through more study, others can be addressed with uncertainty factors or a more refined analysis. Where Tier II data are unavailable, it may be necessary to rely on Tier I data for any reregistration decision, which is to acknowledge substantial risks. But simply treating uncertainty as something to be mentioned but not addressed quantitatively is a shirking of EPA's responsibilities as a regulator.

2) <u>The cumulative effects of neonicotinoids need to be measured</u>

The EPA states "Clothianidin and thiamethoxam are in the N-nitroguanidine group of neonicotinoids (IRAC subclass 4A) along with imidacloprid and dinotefuran. Their mode of action on target insects involves out-competing the neurotransmitter, acetylcholine for available binding sites on the nAChRs. At low concentrations, neonicotinoids cause nervous stimulation and at high concentrations, insect paralysis and death will occur."[270] In addition, CropLife's Insecticide Resistance Action Committee (IRAC) lists neonicotinoids as having the same mechanism of action as nicotinic acetylcholine receptor (nAChR) competitive modulators.[271]

Neonicotionoids are known to produce neuronal toxicities in insects via a common mechanism of action, that being the disruption of acetylcholine/nAChR signaling. Therefore, the combined exposure to <u>all</u> neonicotinoids via pollen, nectar, water and other sources must be addressed for the agency to come to a scientifically defensible conclusion that no unreasonable adverse effects will occur with the re-registration of these ingredients. For agents that act by the same mode of action, "dose addition" can be applied to that group according to agency documents.[272] This is

[269] National Academy of Sciences. 2013. *Assessing Risks to Endangered and Threatened Species from Pesticides*, 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). Page 44.
[270] US EPA. Office of Pesticide Programs Environmental Fate and Effects Division. Preliminary Bee Risk Assessment to Support the Registration Review of Clothianidin and Thiamethoxam. 2017. Page 27.
[271] Insecticide Resistance Action Committee. Modes of Action. Available at: http://www.irac-online.org/modes-of-action/. Accessed 7/11/2017.
[272] U.S. EPA. Framework for Cumulative Risk Assessment. Risk Assessment Forum. May 2003. Accessed at: http://www.epa.gov/sites/production/files/2014-11/documents/frmwrk_cum_risk_assmnt.pdf

not an impossible task, as the EPA currently does this when analyzing risk to another group of neurotoxins, the organophosphates, to humans.

Additionally, patent applications from pesticide companies have found that some neonicotinoids act synergistically with one another to kill insects (U.S. patent application numbers 12093299 and 10575276).[273] This makes it all the more important to measure the cumulative effects of exposure.

Given the extent of use, pollinators will generally be exposed to multiple neonicotinoids throughout the span of their lives. These exposures need to be accounted for and anticipated in a thorough risk assessment; anything less will underestimate risk. The EPA understands that compounds with a common mode of action often act additively to produce toxicities in all species but currently only take this into account in the human health risk assessment. Now that the draft risk assessments are complete for the 4 major neonicotinoid pesticides, a cumulative neonicotinoid risk assessment needs to be performed for insect pollinators before a re-registration decision can be made. Interim restrictions will, of course, need to be put in place while this analysis takes place. This cannot wait another 20 years for the next re-registration to happen.

3) <u>EPA needs to assess risks to pollinators other than honey bees</u>

These draft pollinator risk assessments completely ignore pollinators other than *Apis mellifera*, which is a poor surrogate for the vast majority of bee species as the colony can buffer against some negative effects of pesticides.[274] Some space is given to discussing the difficulties of doing a proper risk assessment to native bees, despite the fact that the majority of native bees are solitary -- making them a much more convenient model for fitness than social bees as there is a direct link between an individual female's performance and reproductive success.[275] The EPA cites studies indicating that native bees are at much greater risk from neonicotinoid exposure than *Apis mellifera*, yet without factoring this into a quantitative value that estimates risk to these species, then risk cannot be accurately determined. If the EPA cannot be certain that unreasonable adverse effects will not occur, then it cannot re-register these pesticides. Ultimately, without an analysis of risk to pollinators other than *Apis mellifera*, a reasonable certainty of no harm cannot be attained. Lack of analysis does not indicate safety, it indicates uncertainty.

[273] Submitted to the docket with comment letter as Patent #1 and #2.
[274] Suryanarayanan, S. 2015. Pesticides and pollinators: a context-sensitive policy approach. Current Opinion in Insect Science, 10: 149-155.
[275] Sandrock, C., Tanadini, L. G., Pettis, J. S., Biesmeijer, J. C., Potts, S. G., and Neumann, P. 2014. Sublethal neonicotinoid insecticide exposure reduces solitary bee reproductive success. Agricultural and Forest Entomology, 16(2): 119-128.

EPA's lack of assessing risk to native and wild bees is especially glaring in light of a recent Government Accountability Office (GAO) report on bee health,[276] which took issue with EPA's lackadaisical approach in assessing harm to non-honeybee species. Below are statements made on page 53 of that report:

- "The [White House Pollinator Health Task Force's] research action plan calls for EPA to develop tools for assessing risks to a variety of bee species, including nonhoney bee species, such as other managed or wild, native bees"
- "FIFRA authorizes EPA to require pesticide registrants to submit data from tests on nonhoney bee species using methods that meet EPA's approval"
- "By developing a plan for obtaining data from pesticide registrants on pesticides' effects on nonhoney bee species until the standardized guidelines are developed, EPA could increase its confidence that it is reducing the risk of unreasonable harm to these important pollinators."

Ultimately, the GAO report stated that "To better ensure that EPA is reducing the risk of unreasonable harm to important pollinators, we recommend that the Administrator of EPA direct the Office of Pesticide Programs to develop a plan for obtaining data from pesticide registrants on the effects of pesticides on nonhoney bee species, including other managed or wild, native bees,"[277] a recommendation that the EPA ultimately agreed with.[278] Obviously, these recommendations change things, and the EPA should take them to heart before making a decision on re-registration of these neonicotinoids. However, further study will take a considerable amount of time, so in the interim, measures need to be taken to reduce any potential risk to non-honeybee pollinators that currently exist.

Pollination is an essential function of plant reproduction. Bees provide the bulk of these services for agricultural crops but there are many other pollinators that are not even mentioned in this risk assessment that are invaluable for the propagation of non-agricultural plants that are an essential part of a healthy ecosystem. Beetles, moths, butterflies, hummingbirds, bats and many other species also provide pollination services. Since these neonicotinoids are present in the pollen of treated crops as well as most plants in the vicinity of treated fields and in the same watershed as treated fields, exposure to all pollinators is likely. Where exposure is likely, risk needs to be estimated. The ecological risk assessment is insufficient to estimate risk to these other pollinators, because the pollen exposure source is not taken into account.

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[276] United States Government Accountability Office. Report to Congressional Requesters. Bee Health. USDA and EPA Should Take Additional Actions to Address Threats to Bee Populations. 2016. Available at: http://www.gao.gov/assets/680/675109.pdf.

[277] *Id*. at 55.
[278] *Id*. at 57.

All species that provide pollination services need to be included in this much needed assessment. If not, we recommend a document title that does not mislead the public, like: "Preliminary *Apis mellifera* assessment to support the registration review of clothianidin, thiamethoxam and dinotefuran."

4) EPA Must Assess the Enhanced Toxicity of Pesticide Mixtures

No effort was made to analyze risks to pollinators from commonly encountered pesticide mixtures. Simply acknowledging that such risks may be present is wholly inadequate. This lack of assessing risk to pollinators from pesticide mixtures is especially glaring in light of a recent GAO report on bee health, which chastised EPA for not taking a more real world approach. Below are relevant statements and conclusions that came from that report:

- "The [White House Pollinator Health Task Force's] research action plan generally called for research on the effects mixtures of pesticides can have on bees and, in particular, directed EPA to develop appropriate assessment tools for sublethal effects of pesticides, adjuvants, and combinations of pesticides with other products on the health of managed and wild pollinators."[279]
- "According to stakeholders GAO interviewed, sources for data on commonly used or recommended mixtures are available and could be collected from farmers, pesticide manufacturers, and others"[280]
- "According to senior EPA officials, if the agency has information about certain combinations being used regularly, it could require that pesticide registrants provide testing data on those combinations."[281]
- "If an assessment of commonly-used pesticide mixtures found synergistic effects on bees, FIFRA authorizes EPA to take regulatory actions to reduce risks, such as requiring label language warning of those effects."[282]

Once again the EPA has declined to do an analysis of the toxicity of neonicotinoid mixtures. It has long been the EPA's policy to not do a mixture analysis because it's just too darn hard. Yet there is never any mention that this decision essentially results in the default assumption that all mixtures involving neonicotinoids have the exact same toxicity as the neonic alone, a completely

[279] United States Government Accountability Office. Report to Congressional Requesters. Bee Health. USDA and EPA Should Take Additional Actions to Address Threats to Bee Populations. 2016. Page 53. Available at: http://www.gao.gov/assets/680/675109.pdf.
[280] United States Government Accountability Office. Highlights from the report on Bee Health. 2016. Available at: http://www.gao.gov/products/GAO-16-220.
[281] United States Government Accountability Office. Report to Congressional Requesters. Bee Health. USDA and EPA Should Take Additional Actions to Address Threats to Bee Populations. 2016. Page 48. Available at: http://www.gao.gov/assets/680/675109.pdf.
[282] *Id*.

scientifically-unjustified assumption. The EPA is constantly saying that there are never enough data and that they lack the methodology to do a robust analysis. But the agency completely ignores the fact that by approving so many multi-ingredient formulations and allowing countless numbers of tank mixtures to occur, it is essentially enabling the existence of all of these mixtures without any indication whatsoever that it can be done safely. These are not the actions of an agency that is confident in its abilities to protect the health of humans and the environment; these are the actions of an agency that is in way over its head.

The Center for Biological Diversity recently released a report[283] 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 nonobvious 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 37 multi-ingredient products containing thiamethoxam or clothianidin that were approved in the past six years from Bayer and Syngenta.[284] Of those 37, 36 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

2) Thiamethoxam or clothianidin and abamectin, emanectin benzoate or spinosad (U.S. patent application number 11028776)[285]
2) Thiamethoxam or clothianidin and *Bacillus firmus* CNCM I-1582 (U.S. patent application number 12936700).[286]

[283] 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.
[284] *Id.* at Appendix B
[285] Submitted to the docket with comment letter as Patent #3
[286] Submitted to the docket with comment letter as Patent #4

3) Thiamethoxam or clothianidin and benalaxyl M, pyraclostrobin or metalaxyl M (U.S. patent application number 11793763 and 13209926).[287]
4) Thiamethoxam or clothianidin and trifloxystrobin (U.S. patent application number 10486663).[288]
5) Thiamehtoxam or clothianidin and cyantraniliprole (U.S. patent application number 11628145).[289]
6) Thiamethoxam and any pyrethrin or pyrethroid (U.S. patent application number 10486663, 12633063 and 14215205).[290]
7) Clothianidin and penflufen (U.S. patent application number 11912773).[291]
8) Thiamethoxam and azoxystrobin, sedaxane and fludioxanil (U.S. patent application number 12306870).[292]

Since most products that contain thiamethoxam, clothianidin or dinotefuran were approved more than six years ago, our analysis would not have identified other patent applications that may be relevant to other multi-ingredient neonic products. In addition, the mixture of neonicotinoid insecticides and ergosterol biosynthesis inhibitor (EBI) fungicides has been shown to produce synergistic toxicities in numerous studies in the peer-reviewed literature.[293] Chronic exposure to combinations of neonictoinoids and pyrethroids impairs bees' natural foraging behavior, increases worker mortality, and accordingly, hurts brood development and colony success.[294] 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 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.[295] This is a step in the right direction and we commend the EPA for the great

[287] Submitted to the docket with comment letter as Patent #5 and #6
[288] Submitted to the docket with comment letter as Patent #7
[289] Submitted to the docket with comment letter as Patent #8
[290] Submitted to the docket with comment letter as Patent #9, #10 and #11
[291] Submitted to the docket with comment letter as Patent #12
[292] Submitted to the docket with comment letter as Patent #13
[293] Wood, T. J., & Goulson, D. (2017). The environmental risks of neonicotinoid pesticides: a review of the evidence post 2013. *Environmental Science and Pollution Research*. https://link.springer.com/article/10.1007%2Fs11356-017-9240-x.
[294] Gill, R. J., et al. (2012). Combined pesticide exposure severely affects individual- and colony-level traits in bees. Nature 491(7422): 105-108. Submitted to docket
[295] 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).

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."[296]

The phrase "true synergism" insinuates that the data contained in applications to the 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 publically 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,[297] 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,[298] 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. 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.

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[296] EPA. Final Registration Decision of the New Active Ingredient Halauxifen-methyl. 2016. Pg. 8. Regulations.gov docket ID EPA-HQ-OPP-2012-0919-0024.
[297] 18 U.S.C. 1001.
[298] Colby, S.R. (1967) Calculating Synergistic and Antagonistic Responses of Herbicide Combinations. *Weeds*, 15(1), 20-22.

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 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.

11) 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.[299] However, the EPA now appears to be limiting itself in the type of

[299] 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.).

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

12) 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.

    i) 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.[301] 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.

    j) This includes studies from government or any third party 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

[300] 40 C.F.R. § 159.195(a).
[301] *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)).

application from Dow (the applicant for the new use was Monsanto), were both identified as lines of evidence to propose tank-mixing restrictions.[302]

k) 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.[303] 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 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.[304] 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.[305] 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 publically 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,[306] 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.

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[302] 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.

[303] EPA. Final Registration Decision of the New Active Ingredient Halauxifen-methyl. 2016. Pg. 9. Regulations.gov docket ID EPA-HQ-OPP-2012-0919-0024.

[304] 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.).

[305] 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. Untied States patent publication no. US 20110275517 A1. Application number US 13/099,552. 10 November 2011.

[306] 18 U.S.C. 1001.

Therefore, the EPA needs to analyze any patent application that has been approved, denied or is still pending.

l) 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.[307] 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.

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.[308] 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.

4) 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.[309] Not only is the "multiple pass" scenario highly unlikely (because no farmer in their right mind would elect to make

[307] 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.
[308] 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).
[309] 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.

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.

5) 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.

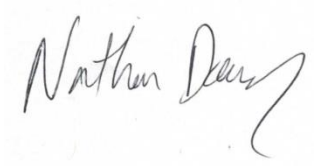
This should not be viewed as a comprehensive list of all ingredients that synergize with neonics, as others likely exist. These ingredient combinations need to be prohibited through language on the pesticide label stating that the identified pesticides may not be tank mixed or co-applied in the same growing season as the used neonicotinoid. We would like to be clear that a prohibition solely on tank mixing is insufficient to ensure that these combinations will not be encountered by non-target organisms in the environment; a prohibition on "co-application in the same growing season" is the proper language that needs to be used on pesticide labels.

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.[310] 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), conservation tillage (not "boogeyman" tillage that chemical companies vilify, but responsible tilling techniques that mechanically disrupt weeds while promoting little to no erosion) and pesticide rotation in conjunction with crop rotation, among others. 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 allow the farming community to more sustainably work their land. Furthermore, tank mixes can actually promote pest resistance if the mixed pesticides share the same mode of action. 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.

Therefore, in order to be compliant with FIFRA, the EPA must do an analysis of mixture toxicity with mixtures containing thiamethoxam, clothianidin or dinotefuran before a 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 these neonics through label changes and cancelling certain products that contain these mixtures 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 the continued use of thiamethoxam, clothianidin or dinotefuran will not have unreasonable adverse effects on the environment.

Respectfully submitted,



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Center for Biological Diversity

[310] 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.

July 24, 2017

Office of Pesticide Programs Docket # EPA-HQ-OPP-2008-0844
Environmental Protection Agency Docket Center (EPA/DC)
1200 Pennsylvania Ave NW
Washington, DC 20460-0001

Re: Comments on EPA Preliminary Aquatic Risk Assessment: Imidacloprid Registration Review (Docket #: EPA-HQ-OPP-2008-0844).

Please accept the following comments on behalf of the Center for Biological Diversity ("Center") in response to the Environmental Protection Agency's ("EPA") preliminary aquatic risk assessment to support the registration review of imidacloprid as part of its registration review process under the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA").

The Center is a non-profit environmental organization dedicated to the protection of native species and their habitats through science, policy, and environmental law. The Center has more than 1.3 million members and online activists dedicated to the protection and restoration of endangered species and wild places. The Center has worked for many years to protect imperiled plants and wildlife, open space, air and water quality, and overall quality of life. The Center's Pesticides Reduction Campaign aims to secure programmatic changes in the pesticide registration process and to stop toxic pesticides from contaminating fish and wildlife habitats. We appreciate the opportunity to provide comment.

We commend the EPA for taking on this much needed analysis. Many pesticides, including neonicotinoids, pose serious threats to aquatic species and this cannot be accurately accounted for in the typical ecological risk assessment process. Having a specialized risk assessment document that takes into account the different exposure pathways, life stages and heightened toxicities of many different kinds of aquatic species is a step in the right direction. Furthermore, the essential role that these species provide to aquatic and terrestrial ecosystems make them extremely important from an ecological point of view.

Unfortunately, there are serious issues with this preliminary aquatic assessment that absolutely need to be addressed in order for risk to accurately be reflected. As this draft document stands now, risk is almost certainly underestimated – putting aquatic species at risk of unreasonable harm from the labeled uses of imidacloprid. Issues that need to be addressed are outlined below.

5) Uncertainty is not dealt with appropriately

Despite efforts to appear as though this risk assessment is thorough and complete, we are stunned at just how many data gaps there are. In fact, this risk assessment raises more questions than

answers. We understand that EPA has to make due with the information that is available, but the standard that EPA has to meet in order to re-register imidacloprid is a "reasonable certainty of no harm." Given the extent of data gaps in this risk assessment that have not been offset with uncertainty factors, that standard surely cannot be met.

EPA has a habit of assuming uncertainty equals no risk. Simply acknowledging uncertainty at the end of a risk assessment without *quantitatively* taking it into account is unacceptable for an agency tasked with protecting human and environmental health. A narrative of uncertainty is an insufficient way to convey the potential risks involved in registering a pesticide to a risk manager. The National Academy of Sciences has chastised EPA on this approach, stating that "….changing uncertainty analysis from a narrative addendum to an integral part of the assessment is possible and necessary to provide realistic, objective estimates of risk."[311]

When there are data deficiencies in a risk assessment, there are two options: you can err on the side of caution or err on the side of risk. The EPA constantly does the latter, and with thousands of data deficient chemicals currently in use, the cumulative effects of these decisions are putting humans and wildlife at risk.

In this aquatic risk assessment, some of these uncertainties can be addressed through more study, others can be addressed with uncertainty factors or a more refined analysis. But simply treating uncertainty as something to be mentioned but not addressed quantitatively is an avoidance of EPA's responsibilities as a regulator.

6) <u>The cumulative effects of neonicotinoids need to be measured</u>

The EPA states "Imidacloprid [is] in the N-nitroguanidine group of neonicotinoids (IRAC subclass 4A) along with clothianidin, thiamethoxam and dinotefuran. Its mode of action on target insects involves out-competing the neurotransmitter, acetylcholine for available binding sites on the nAChRs. At low concentrations, neonicotinoids cause excessive nervous stimulation and at high concentrations, insect paralysis and death will occur."[312] In addition, CropLife's Insecticide Resistance Action Committee (IRAC) lists neonicotinoids as having the same mechanism of action as nicotinic acetylcholine receptor (nachr) competitive modulators.[313]

Neonicotionoids are known to produce neuronal toxicities in insects via a common mechanism of action, that being the disruption of acetylcholine/nAChR signaling. Therefore, the combined

[311] 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). Page 44.
[312] US EPA. Office of Pesticide Programs Environmental Fate and Effects Division. Preliminary Aquatic Risk Assessment to Support the Registration Review of Imidacloprid. 2016. Pages 12-13.
[313] Insecticide Resistance Action Committee. Modes of Action. Available at: http://www.irac-online.org/modes-of-action/. Accessed 1/28/2016.

exposure to all neonicotinoids via all sources must be addressed for the agency to come to a scientifically defensible conclusion that no unreasonable adverse effects will occur with the re-registration of this ingredient. For agents that act by the same mode of action, "dose addition" can be applied to that group according to agency documents.[314] This is not an impossible task, as the EPA currently does this when analyzing risk to another group of neurotoxins, the organophosphates, to humans.

Additionally, patent applications from pesticide companies have found that some neonicotinoids act synergistically with one another to kill insects (U.S. patent application numbers 12093299 and 10575276).[315] This makes it all the more important to measure the cumulative effects of exposure.

Given the extent of use, aquatic species will generally be exposed to multiple neonicotinoids throughout the span of their lives. These exposures need to be accounted for and anticipated in a thorough risk assessment; anything less will underestimate risk. The EPA understands that compounds with a common mode of action often act additively to produce toxicities in all species but currently only take this into account in the human health risk assessment. Once the aquatic risk assessments for the other neonicotinoids are complete, a cumulative neonicotinoid risk assessment needs to be performed for aquatic species before a re-registration decision can be made. Interim restrictions will, of course, need to be put in place while this analysis takes place. This cannot wait another 20 years for the next re-registration to happen.

7) EPA must assess all home uses, not just outdoor uses of imidacloprid

Recent studies have indicated that imidacloprid is not removed from wastewater treatment plants.[316] This means that any imidacloprid that makes its way into the sewer system will remain in the effluent and eventually contaminate rivers, lakes and streams. In its recent aquatic risk assessment for 20 pyrethroids and pyrethrins, EPA did an analysis on many of the home uses of this pesticide class and found significant risks to aquatic invertebrates from just the indoor uses alone.[317] Imidacloprid is a very common ingredient found in flea treatments for pets, both as a spot-on treatment and in flea collars. The resulting residues can migrate from pet fur via multiple pathways and eventually end up in the wastewater system. This will be contributing to the imidacloprid loading in the environment and is an exposure source that must be analyzed.

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[314] U.S. EPA. Framework for Cumulative Risk Assessment. Risk Assessment Forum. May 2003. Accessed at: http://www.epa.gov/sites/production/files/2014-11/documents/frmwrk_cum_risk_assmnt.pdf

[315] Submitted to the docket with comment letter as Patent #1 and #2.

[316] Sadaria, A. M., Supowit, S. D., & Halden, R. U. (2016). Mass Balance Assessment for Six Neonicotinoid Insecticides During Conventional Wastewater and Wetland Treatment: Nationwide Reconnaissance in United States Wastewater. Environ Sci Technol, 50(12), 6199-6206. doi:10.1021/acs.est.6b01032.

[317] EPA. 2016. Preliminary Comparative Environmental Fate and Ecological Risk Assessment for the Registration Review of Eight Synthetic Pyrethroids and the Pyrethrins. Document ID EPA-HQ-OPP-2010-0384-0045.

8) EPA must address toxicities of pesticide mixtures

No effort was made to analyze risks to aquatic species from commonly encountered pesticide mixtures. Simply acknowledging that such risks may be present is wholly inadequate.

The scope of this issue is immense. The number of products that contain imidacloprid mixed with another active ingredient is stunning. According to the Public National Pesticide Information Retrieval System[318] maintained by Purdue University, over 70 products have been approved by the EPA that contain imidacloprid and at least one other active ingredient. The list of other active ingredients mixed with imidacloprid include: Lambda-Cyhalothrin, Cyfluthrin, Metalaxyl, Tebuconazole, Imazallil, Thiodicarb, Clothianidin, Spirotetramat, Fluopyram, Bifenthrin, Captan, Carboxin, Ipconazole, Phenothrin, MGK 264, Pyriproxyfen, Copper carbonate (basic), Boron sodium oxide, Carbendazim, 2-(2-Ethoxyethoxy)ethyl 2-benzimidazole carbamate (115001), Fludioxonil, cis-9-Tricosene, diphacinone, Bromadiolone, Warfarin, Abamectin, 3(2H)-Isothiazolone, 4,5-dichloro-2-octyl- (128101). This is also just the list of active ingredients that have been premixed in a formulated product and does not represent the extensive amount of tank mixing of active ingredients that happens out in the field before application.

The EPA has declined to do an analysis of the toxicity of neonicotinoid mixtures. It has long been the EPA's policy to not do a mixture analysis because it's just too darn hard. Yet there is never any mention that this decision essentially results in the default assumption that all mixtures involving neonicotinoids have the exact same toxicity as the neonic alone, a completely scientifically-unjustified assumption. The EPA is constantly saying that there are never enough data and that they lack the methodology to do a robust analysis. But the agency completely ignores the fact that by approving so many multi-ingredient formulations and allowing countless numbers of tank mixtures to occur, it is essentially enabling the existence of all of these mixtures without any indication whatsoever that it can be done safely. These are not the actions of an agency that is confident in its abilities to protect the health of humans and the environment; these are the actions of an agency that is in way over its head.

The Center for Biological Diversity recently released a report[319] 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 nonobvious about the mixture that could presumably only be found through research and development done by the applicant. For

[318] National Pesticide Information Retrieval System. Federal Pesticide Product Database. Purdue University. Available at: http://npirspublic.ceris.purdue.edu/ppis/.
[319] 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.

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 7 multi-ingredient products containing imidacloprid that were approved in the past six years from Bayer.[320] Of those 7, 6 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

3) Imidacloprid and any pyrethrin or synthetic pyrethroid (U.S. patent application number 09968175)[321]
2) Imidacloprid and spirotetramat (U.S. patent application number 13790375).[322]

Since most products that contain imidacloprid were approved more than six years ago, our analysis would not have identified other patent applications that may be relevant to other multi-ingredient neonic products. In addition, the mixture of neonicotinoid insecticides and ergosterol biosynthesis inhibitor (EBI) fungicides has been shown to produce synergistic toxicities in numerous studies in the peer-reviewed literature.[323] Chronic exposure to combinations of neonictoinoids and pyrethroids impairs bees' natural foraging behavior, increases worker mortality, and accordingly, hurts brood development and colony success.[324] 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 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

[320] *Id.* at Appendix B
[321] Submitted to the docket with comment letter as Patent #3.
[322] Submitted to the docket with comment letter as Patent #4.
[323] Wood, T. J., & Goulson, D. (2017). The environmental risks of neonicotinoid pesticides: a review of the evidence post 2013. *Environmental Science and Pollution Research*. https://link.springer.com/article/10.1007%2Fs11356-017-9240-x.
[324] Gill, R. J., et al. (2012). Combined pesticide exposure severely affects individual- and colony-level traits in bees. Nature 491(7422): 105-108. Submitted to docket

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.[325] 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."[326]

The phrase "true synergism" insinuates that the data contained in applications to the 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 publically 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,[327] 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,[328] 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

[325] 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).
[326] EPA. Final Registration Decision of the New Active Ingredient Halauxifen-methyl. 2016. Pg. 8. Regulations.gov docket ID EPA-HQ-OPP-2012-0919-0024.
[327] 18 U.S.C. 1001.
[328] Colby, S.R. (1967) Calculating Synergistic and Antagonistic Responses of Herbicide Combinations. *Weeds*, 15(1), 20-22.

coming from the same source. 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 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.

13) 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.[329] 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.[330] 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 pose any greater risk than previously believed or reported to the Agency." Any data on chemical synergy would certainly fall into that category.

14) 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.

    m) 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.[331] 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.

    n) This includes studies from government or any third party 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

[329] 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.).
[330] 40 C.F.R. § 159.195(a).
[331] *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)).

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.[332]

o) 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.[333] 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 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.[334] 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.[335] 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 publically 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,[336] any data or claims

[332] 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.
[333] EPA. Final Registration Decision of the New Active Ingredient Halauxifen-methyl. 2016. Pg. 9. Regulations.gov docket ID EPA-HQ-OPP-2012-0919-0024.
[334] 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.).
[335] 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. Untied States patent publication no. US 20110275517 A1. Application number US 13/099,552. 10 November 2011.
[336] 18 U.S.C. 1001.

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 needs to analyze any patent application that has been approved, denied or is still pending.

p) 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.[337] 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.

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.[338] 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.

4) 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.[339] Not only is the "multiple pass"

[337] 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.
[338] 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).
[339] 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.

scenario highly unlikely (because no farmer in their right mind would 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.

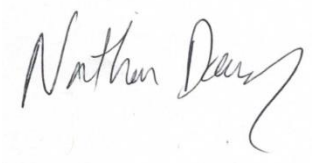
5) A synergy analysis needs to be performed for all new ingredient registrations and during all registration reviews. It appears that the EPA has begun to institute a synergy analysis for all new ingredient registrations, which we fully support; however, it is still unclear whether the Agency intends 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.

This should not be viewed as a comprehensive list of all ingredients that synergize with neonics, as others likely exist. These ingredient combinations need to be prohibited through language on the pesticide label stating that the identified pesticides may not be tank mixed or co-applied in the same growing season as the used neonicotinoid. We would like to be clear that a prohibition solely on tank mixing is insufficient to ensure that these combinations will not be encountered by non-target organisms in the environment; a prohibition on "co-application in the same growing season" is the proper language that needs to be used on pesticide labels.

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.[340] 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), conservation tillage (not "boogeyman" tillage that chemical companies vilify, but responsible tilling techniques that mechanically disrupt weeds while promoting little to no erosion) and pesticide rotation in conjunction with crop rotation, among others. 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 allow the farming community to more sustainably work their land. Furthermore, tank mixes can actually promote pest resistance if the mixed pesticides share the same mode of action. 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.

Therefore, in order to be compliant with FIFRA, the EPA must do an analysis of mixture toxicity with mixtures containing imidacloprid before a 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 these neonics through label changes and cancelling certain products that contain these mixtures 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 the continued use of imidacloprid will not have unreasonable adverse effects on the environment.

Respectfully submitted,



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[340] 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.

Center for Biological Diversity

April 14, 2015

Office of Pesticide Programs Docket # EPA-HQ-OPP-2008-0844
Environmental Protection Agency Docket Center (EPA/DC)
1200 Pennsylvania Ave NW
Washington, DC 20460-0001

Re: Comments on EPA Pollinator Ecological Risk Assessments: Imidacloprid Registration Review (Docket #: EPA-HQ-OPP-2008-0844).

Please accept the following comments on behalf of the Center for Biological Diversity ("Center") in response to the Environmental Protection Agency's ("EPA") preliminary pollinator assessment to support the registration review of imidacloprid as part of its registration review process under the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA").

The Center is a non-profit environmental organization dedicated to the protection of native species and their habitats through science, policy, and environmental law. The Center has more than 990,000 members and online activists dedicated to the protection and restoration of endangered species and wild places. The Center has worked for many years to protect imperiled plants and wildlife, open space, air and water quality, and overall quality of life. The Center's Pesticides Reduction Campaign aims to secure programmatic changes in the pesticide registration process and to stop toxic pesticides from contaminating fish and wildlife habitats. We appreciate the opportunity to provide comment.

We commend the EPA for taking on this much needed analysis. Many pesticides, including neonicotinoids, pose serious threats to pollinator species and this cannot be accurately accounted for in the typical ecological risk assessment process. Having a specialized risk assessment document that takes into account the different exposure pathways, life stages and heightened toxicities of many different kinds of pollinators is a step in the right direction. Furthermore, the essential pollination services that these species provide make them not only important from an ecological point of view, but also from a food security point of view.

Unfortunately, there are serious issues with this preliminary pollinator assessment that absolutely need to be addressed in order for risk to accurately be reflected. As this draft document stands now, risk is almost certainly underestimated – putting pollinator species at risk of unreasonable harm from the labeled uses of imidacloprid. Issues that need to be addressed are outlined below.

9) Uncertainty is not dealt with appropriately

Despite efforts to appear as though this risk assessment is thorough and complete, we are stunned at just how many data gaps there are. In fact, this risk assessment raises more questions than answers. We understand that EPA has to make due with the information that is available, but the standard that EPA has to meet in order to re-register imidacloprid is a "reasonable certainty of no harm." Given the extent of data gaps in this risk assessment that have not been offset with uncertainty factors, that standard surely cannot be met.

EPA has a habit of assuming uncertainty equals no risk. Simply acknowledging uncertainty at the end of a risk assessment without *quantitatively* taking it into account is unacceptable for an agency tasked with protecting human and environmental health. A narrative of uncertainty is an insufficient way to convey the potential risks involved in registering a pesticide to a risk manager. The National Academy of Sciences has chastised EPA on this approach, stating that "….changing uncertainty analysis from a narrative addendum to an integral part of the assessment is possible and necessary to provide realistic, objective estimates of risk."[341]

When there are data deficiencies in a risk assessment, there are two options: you can err on the side of caution or err on the side of risk. The EPA constantly does the latter, and with thousands of data deficient chemicals currently in use, the cumulative effects of these decisions are putting humans and wildlife at risk.

In this pollinator risk assessment, some of these uncertainties can be addressed through more study, others can be addressed with uncertainty factors or a more refined analysis. Where Tier II data are unavailable, it may be necessary to rely on Tier I data for any reregistration decision, which is to acknowledge substantial risks. But simply treating uncertainty as something to be mentioned but not addressed quantitatively is a shirking of EPA's responsibilities as a regulator.

10) <u>The cumulative effects of neonicotinoids need to be measured</u>

The EPA states "Imidacloprid [is] in the N-nitroguanidine group of neonicotinoids (IRAC subclass 4A) along with clothianidin, thiamethoxam and dinotefuran. Its mode of action on target insects involves out-competing the neurotransmitter, acetylcholine for available binding sites on the nAChRs. At low concentrations, neonicotinoids cause excessive nervous stimulation and at high concentrations, insect paralysis and death will occur."[342] In addition, CropLife's Insecticide

[341] 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). Page 44.
[342] US EPA. Office of Pesticide Programs Environmental Fate and Effects Division. Preliminary Pollinator Assessment to Support the Registration Review of Imidacloprid. 2016. Page 25.

Resistance Action Committee (IRAC) lists neonicotinoids as having the same mechanism of action as nicotinic acetylcholine receptor (nachr) competitive modulators.[343]

Neonicotionoids are known to produce neuronal toxicities in insects via a common mechanism of action, that being the disruption of acetylcholine/nAChR signaling. Therefore, the combined exposure to all neonicotinoids via pollen, nectar, water and other sources must be addressed for the agency to come to a scientifically defensible conclusion that no unreasonable adverse effects will occur with the re-registration of this ingredient. For agents that act by the same mode of action, "dose addition" can be applied to that group according to agency documents.[344] This is not an impossible task, as the EPA currently does this when analyzing risk to another group of neurotoxins, the organophosphates, to humans.

Given the extent of use, pollinators will generally be exposed to multiple neonicotinoids throughout the span of their lives. These exposures need to be accounted for and anticipated in a thorough risk assessment; anything less will underestimate risk. The EPA understands that compounds with a common mode of action often act additively to produce toxicities in all species but currently only take this into account in the human health risk assessment. Once the risk assessments for the other neonicotinoids are complete, a cumulative neonicotinoid risk assessment needs to be performed for insect pollinators before a re-registration decision can be made. Interim restrictions will, of course, need to be put in place while this analysis takes place. This cannot wait another 20 years for the next re-registration to happen.

11) Imidacloprid exposure is dramatically underestimated.

The EPA states that, in addition to contact and oral routes, "Bees may also be exposed to imidacloprid through other routes, such as contaminated surface water, plant guttation fluids, honey dew, soil (for ground-nesting bees), and leaves; however, there is high uncertainty regarding the importance of some of these exposure routes, and the Agency lacks information to understand the relative importance of these other routes of exposure and/or to quantify risks from these other routes."[345] Tier I studies considered contact and oral routes, yet the only exposure route analyzed for quantitative risk assessment (what ultimately will guide regulatory decisions) was through ingestion of spiked nectar. So of all of the potential exposure sources that should have been considered in aggregate, only one was actually measured. This is absolutely unacceptable, and exposes the most prominent weakness in this assessment.

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[343] Insecticide Resistance Action Committee. Modes of Action. Available at: http://www.irac-online.org/modes-of-action/. Accessed 1/28/2016.

[344] U.S. EPA. Framework for Cumulative Risk Assessment. Risk Assessment Forum. May 2003. Accessed at: http://www.epa.gov/sites/production/files/2014-11/documents/frmwrk_cum_risk_assmnt.pdf

[345] US EPA. Office of Pesticide Programs Environmental Fate and Effects Division. Preliminary Pollinator Assessment to Support the Registration Review of Imidacloprid. 2016. Page 14.

Throughout this entire document the EPA keeps trying to downplay the significance of pollen in the bee diet. Pollen in the main source of protein for bees and is an absolutely essential part of their early diet. Pollen is also present in royal jelly, an important food source for future queens. Instead of trying to discount the importance of exposure through pollen, more effort needs to go into how to estimate the effects of contaminated pollen.

In fact, foliar spray on cherries and oranges resulted in imidacloprid residues in pollen that were 1-2 orders of magnitude higher than in nectar, with levels as high as 500-600 ppb.[346] Use of imidacloprid on strawberries yielded residues in pollen that were higher than estimated toxicity values and residues in nectar were not analyzed.[347]

Estimates of residues on cotton due to foliar spray were estimated using only 20% of maximum labeled use, a major underestimate.[348] Studies on other crops, like cucurbit vegetables, also used lower than maximum labeled uses.[349] And even though the majority of imidacloprid use is on soybeans, residues on legumes were not analyzed in Tier II studies.

To address exposure to the substantial amount of seed dust, the EPA states that "Rather than assess the risks of abraded seed coat dust, the Agency is focusing its resources on mitigating risks from this exposure pathway through best management practices and working with the regulated community in the development of alternative technologies to reduce dust-off during planting."[350] This logic is completely off base. Without measuring risk before and after mitigation measures, there is absolutely no way of telling whether such mitigation measures have the intended effect of reducing risk. If the EPA does not accurately assess risk from exposure to seed dust in this assessment, then it cannot be certain that any best management practices will reduce risk to acceptable levels.

Furthermore, following spray and harvest many bees will remain exposed to neonicotinoids over the assumed 6 week period by continuing to visit wildflowers that exist on field margins.[351,352] This can be a significant source of exposure for many bees, particularly native bees and was completely ignored in this assessment.

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[346] *Id*. Page 217.
[347] *Id*. Page 246.
[348] *Id*. Page 74.
[349] *Id*. Page 234.
[350] US EPA. Office of Pesticide Programs Environmental Fate and Effects Division. Preliminary Pollinator Assessment to Support the Registration Review of Imidacloprid. 2016. Page 37.
[351] Botías, C, David, A, Horwood, J, Abdul-Sada, A, Nicholls, E, Hill, E, Goulson, D. Neonicotinoid Residues in Wildflowers, a Potential Route of Chronic Exposure for Bees. Environmental Science & Technology 2015 49 (21), 12731-12740.
[352] David, A, Botías, C, Abdul-Sada, A, Nicholls, E, Rotheray, EL, Hill, EM, Goulson, D, Widespread contamination of wildflower and bee-collected pollen with complex mixtures of neonicotinoids and fungicides commonly applied to crops. Environment International 2016 88, 169-178.

12) Imidacloprid toxicity is dramatically underestimated.

The toxicity of multiple sources of imidacloprid in aggregate needs to be addressed. The only Tier II study (Bromenshenk *et al*., 2012; MRID 48962001, deemed qualitative) that fed bees spiked sucrose and pollen at the same time found that 50 ppb *of each* were associated with negative effects on the hive. So while the EPA is analyzing risk in terms of pollen and nectar toxicity *separately* (LOAEL in nectar of 50 ppb and a (supplemental) LOAEL in pollen of 100 ppb), in reality the aggregate exposure of the two (a more realistic scenario) will likely drop those values significantly. Add exposure through water and seed dust to that, and the EPA's approach to analyzing risk to pollinators drastically underestimates toxicity.

While the Tier II (MRID 49510001) study design has some strengths, overall it underestimates risk:

- The most glaring deficiency with this study is the lack of contaminated pollen, water and seed dust exposure. These exposure sources are expected to have a significant effect on bees, especially since they are encountered in aggregate.
- Nectar was taken from sources other than the spiked sucrose, diluting the imidacloprid and underestimating exposure.
- The existence of pesticides other than imidacloprid in the hive nectar indicates that control animals were exposed to a pesticide cocktail. In fact, it would be hard to find a place in the U.S. to carry out this experiment that would not result in environmental exposure to pesticides. This should be a wake-up call to the EPA -- that pesticides are so prevalent in the U.S. that there is really nowhere left to conduct a proper field experiment.
- Many sub-lethal effects, such as foraging behavior and immune deficiencies, were not measured. Although these sub-lethal effects may not have caused mortality or reduced pollen collection in the Tier II experiment that was analyzed, these effects could have dramatic consequences for bees in times of stress.

This assessment is not designed to look at cascading stressors – how pesticide use could weaken a colony and make it more susceptible to Varroa mite infestation or the effects of global climate change. These are real world possibilities, and in many ways, these cascading stressors may be having more of an impact on bee and pollinator populations than outright pesticide-induced mortality.

13) The carry-over of imidacloprid over subsequent years needs to be accounted for.

The EPA cited two studies where imidacloprid was shown to accumulate in soil from year-to-year. This, combined with modeling data indicating that an accumulation of about 5 times the

annual rate is possible after 10 years of treatment, is a good indication that imidacloprid can accumulate in soil year-to-year.

However, the EPA comes to the conclusion that "there is limited indication of a carryover effect from year-to-year accumulation of imidacloprid resides in soil that translates to increased residues in pollen and nectar."[353] For two of the three studies that the EPA analyzed, a single surrogate plant (white clover) was used to analyze nectar and pollen accumulation year-to-year (it was unclear what was used in the soil applied blueberry study). Since there is large variation between plant species, there is considerable uncertainty associated with using a single surrogate species to make sweeping assumptions about all food crops. Although this is necessitated by the lack of studies available for analysis, this uncertainty needs to be accounted for. And the greater the uncertainty, the less likely EPA can come to a defensible conclusion that the continued use of imidacloprid will not result in higher residues in nectar and pollen year-after-year.

Furthermore, EPAs own modeling demonstrated that soil accumulation of imidacloprid could be about 5 times the annual rate in 10 years. Since the analyzed studies only spanned two years, it is possible that statistically significant increases of imidacloprid in pollen and nectar would not be evident in that span of time, depending on how well-powered the studies were. Accordingly, studies spanning at least 3-5 years would be necessary to identify trends on that scale.

14) Consideration of future usage increases needs to be taken into account

In the Tier II risk evaluation, the EPA considers Screening Level Usage Analysis (SLUA) of current imidacloprid usage on certain crops. SLUA takes into account data on crop usage from the last 10 years to estimate current usage. It is important that EPA use SLUA data to forecast future usage. It will probably be a couple of years until EPA makes a decision on reregistration and, if imidacloprid is reregistered, it may be another 15-20 years until another risk assessment will be conducted. Therefore, estimating what imidacloprid use will be in the next 20 years is more appropriate. There is obviously a lot of uncertainty with forecasting future use, however, trends in imidacloprid usage indicate that it will keep rising in the future. Furthermore, as further restrictions on insecticides, like organophosphates, get implemented due to their extreme toxicity to humans (e.g. chlorpyrifos), demand for other insecticides, like neonics, will likely increase. This future rise in use should be considered in the Tier II evaluations.

15) EPA needs to assess risks to pollinators other than honey bees

This draft pollinator risk assessment completely ignores pollinators other than *Apis mellifera*, which is a poor surrogate for the vast majority of bee species as the colony can buffer against

[353] US EPA. Office of Pesticide Programs Environmental Fate and Effects Division. Preliminary Pollinator Assessment to Support the Registration Review of Imidacloprid. 2016. Page 98.

some negative effects of pesticides.[354] Some space is given to discussing the difficulties of doing a proper risk assessment to native bees, despite the fact that the majority of native bees are solitary -- making them a much more convenient model for fitness than social bees as there is a direct link between an individual female's performance and reproductive success.[355] The EPA cites studies indicating that native bees are at much greater risk from imidacloprid exposure than *Apis mellifera*, yet without factoring this into a quantitative value that estimates risk to these species, then risk cannot be accurately determined. If the EPA cannot be certain that unreasonable adverse effects will not occur, then it cannot re-register this pesticide. Ultimately, without an analysis of risk to pollinators other than *Apis mellifera*, a reasonable certainty of no harm cannot be attained. Lack of analysis does not indicate safety, it indicates uncertainty.

What is known is that, while nectar consumption is similar, pollen consumption by bumble bees can be 750 times that of the *Apis mellifera* honeybee.[356] Futhermore, Tier II studies on *Bombus* species indicate that negative effects can happen at imidacloprid concentrations 71 times lower than those that affect *Apis mellifera* (0.7 ppb compared to 50 ppb).[357] Whitehorn et. al[358] found that field realistic levels of 6ng/g of imidacloprid in the pollen of *Bombus terrestris* lead to an 85% drop in queen production with population level impacts. So, for bumble bees at least, toxicity and exposure are both considerably elevated compared to honeybees.

EPA's lack of assessing risk to native and wild bees is especially glaring in light of a recent Government Accountability Office (GAO) report on bee health,[359] which took issue with EPA's lackadaisical approach in assessing harm to non-honeybee species. Below are statements made on page 53 of that report:

- "The [White House Pollinator Health Task Force's] research action plan calls for EPA to develop tools for assessing risks to a variety of bee species, including nonhoney bee species, such as other managed or wild, native bees"
- "FIFRA authorizes EPA to require pesticide registrants to submit data from tests on nonhoney bee species using methods that meet EPA's approval"

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[354] Suryanarayanan, S. 2015. Pesticides and pollinators: a context-sensitive policy approach. Current Opinion in Insect Science, 10: 149-155.
[355] Sandrock, C., Tanadini, L. G., Pettis, J. S., Biesmeijer, J. C., Potts, S. G., and Neumann, P. 2014. Sublethal neonicotinoid insecticide exposure reduces solitary bee reproductive success. Agricultural and Forest Entomology, 16(2): 119-128.
[356] US EPA. Office of Pesticide Programs Environmental Fate and Effects Division. Preliminary Pollinator Assessment to Support the Registration Review of Imidacloprid. 2016. Table 6-58.
[357] *Id*. Page 282.
[358] Whitehorn, P. R., O'Connor, S., Wackers, F. L., & Goulson, D. 2012. Neonicotinoid pesticide reduces bumble bee colony growth and queen production. *Science*, *336*(6079), 351-352.
[359] United States Government Accountability Office. Report to Congressional Requesters. Bee Health. USDA and EPA Should Take Additional Actions to Address Threats to Bee Populations. 2016. Available at: http://www.gao.gov/assets/680/675109.pdf.

- "By developing a plan for obtaining data from pesticide registrants on pesticides' effects on nonhoney bee species until the standardized guidelines are developed, EPA could increase its confidence that it is reducing the risk of unreasonable harm to these important pollinators."

Ultimately, the GAO report stated that "To better ensure that EPA is reducing the risk of unreasonable harm to important pollinators, we recommend that the Administrator of EPA direct the Office of Pesticide Programs to develop a plan for obtaining data from pesticide registrants on the effects of pesticides on nonhoney bee species, including other managed or wild, native bees,"[360] a recommendation that the EPA ultimately agreed with.[361] Obviously, these recommendations change things, and the EPA should take them to heart before making a decision on re-registration of imidacloprid. However, further study will take a considerable amount of time, so in the interim, measures need to be taken to reduce any potential risk to non-honeybee pollinators that currently exist.

Pollination is an essential function of plant reproduction. Bees provide the bulk of these services for agricultural crops but there are many other pollinators that are not even mentioned in this risk assessment that are invaluable for the propagation of non-agricultural plants that are an essential part of a healthy ecosystem. Beetles, moths, butterflies, hummingbirds, bats and many other species also provide pollination services. Since imidacloprid is present in the pollen of treated crops as well as most plants in the vicinity of treated fields and in the same watershed as treated fields, exposure to all pollinators is likely. Where exposure is likely, risk needs to be estimated. The ecological risk assessment is insufficient to estimate risk to these other pollinators, because the pollen exposure source is not taken into account.

All species that provide pollination services need to be included in this much needed assessment. If not, we recommend a document title that does not mislead the public, like: "Preliminary *Apis mellifera* assessment to support the registration review of imidacloprid."

16) <u>EPA must address toxicities of pesticide mixtures</u>

No effort was made to analyze risks to pollinators from commonly encountered pesticide mixtures. Simply acknowledging that such risks may be present is wholly inadequate. This lack of assessing risk to pollinators from pesticide mixtures is especially glaring in light of a recent GAO report on bee health, which chastised EPA for not taking a more real world approach. Below are relevant statements and conclusions that came from that report:

[360] United States Government Accountability Office. Report to Congressional Requesters. Bee Health. USDA and EPA Should Take Additional Actions to Address Threats to Bee Populations. 2016. Page 55. Available at: http://www.gao.gov/assets/680/675109.pdf.
[361] *Id*. Page 57.

- "The [White House Pollinator Health Task Force's] research action plan generally called for research on the effects mixtures of pesticides can have on bees and, in particular, directed EPA to develop appropriate assessment tools for sublethal effects of pesticides, adjuvants, and combinations of pesticides with other products on the health of managed and wild pollinators."[362]
- "According to stakeholders GAO interviewed, sources for data on commonly used or recommended mixtures are available and could be collected from farmers, pesticide manufacturers, and others"[363]
- "According to senior EPA officials, if the agency has information about certain combinations being used regularly, it could require that pesticide registrants provide testing data on those combinations."[364]
- "If an assessment of commonly-used pesticide mixtures found synergistic effects on bees, FIFRA authorizes EPA to take regulatory actions to reduce risks, such as requiring label language warning of those effects."[365]

The scope of this issue is immense. The number of products that contain imidacloprid mixed with another active ingredient is stunning. According to the Public National Pesticide Information Retrieval System[366] maintained by Purdue University, over 70 products have been approved by the EPA that contain imidacloprid and at least one other active ingredient. The list of other active ingredients mixed with imidacloprid include: Lambda-Cyhalothrin, Cyfluthrin, Metalaxyl, Tebuconazole, Imazallil, Thiodicarb, Clothianidin, Spirotetramat, Fluopyram, Bifenthrin, Captan, Carboxin, Ipconazole, Phenothrin, MGK 264, Pyriproxyfen, Copper carbonate (basic), Boron sodium oxide, Carbendazim, 2-(2-Ethoxyethoxy)ethyl 2-benzimidazole carbamate (115001), Fludioxonil, cis-9-Tricosene, diphacinone, Bromadiolone, Warfarin, Abamectin, 3(2H)-Isothiazolone, 4,5-dichloro-2-octyl- (128101). This is also just the list of active ingredients that have been premixed in a formulated product and does not represent the extensive amount of tank mixing of active ingredients that happens out in the field before application.

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[362] United States Government Accountability Office. Report to Congressional Requesters. Bee Health. USDA and EPA Should Take Additional Actions to Address Threats to Bee Populations. 2016. Page 53. Available at: http://www.gao.gov/assets/680/675109.pdf.
[363] United States Government Accountability Office. Highlights from the report on Bee Health. 2016. Available at: http://www.gao.gov/products/GAO-16-220.
[364] United States Government Accountability Office. Report to Congressional Requesters. Bee Health. USDA and EPA Should Take Additional Actions to Address Threats to Bee Populations. 2016. Page 48. Available at: http://www.gao.gov/assets/680/675109.pdf.
[365] *Id*.
[366] National Pesticide Information Retrieval System. Federal Pesticide Product Database. Purdue University. Available at: http://npirspublic.ceris.purdue.edu/ppis/.

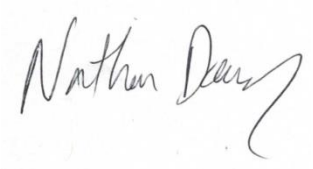
The EPA has approved at least two products from Bayer in the last 5 years, 12ESP703 SC Insecticide (reg # 432-1530) and Movento RC (reg # 264-1170), that contain both imidacloprid and spirotetramat—two insecticides. As it turns out, Bayer was recently issued a patent by the United States Patent and Trademark Office entitled "Combination and methods for controlling turfgrass pests" (USPTO patent number 9,241,486). In this patent, Bayer Cropscience LP states that "The good insecticidal activity of the active substance combinations according to the invention can be seen from the examples which follow. While the individual active substances show weaknesses in their activity, the combinations show an activity which exceeds a simple additive effect," and "A true synergistic effect has been found which could not have been predicted exists, not simply a complementation of action." The active substance combination referred to in the patent is imidacloprid and spirotetramat and it is accompanied by experimental evidence of synergy in controlling insects. Therefore, it appears that the imidacloprid registrant, Bayer, is in possession of experimental evidence that these two ingredients act synergistically with one another to kill insects. It is unclear whether Bayer furnished these highly relevant data to the EPA as they are required to under FIFRA. Since many pollinators are insects, these data are necessary to inform a pollinator risk assessment and an ecological risk assessment. The EPA needs to make it clear to registrants that any information relevant to a risk assessment needs to be furnished to the EPA, even if it may result in greater restrictions on use.

To be clear, this patent is not the only one that makes assertions of synergy between imidacloprid and other ingredients with which it is commonly mixed. In fact, with just ten minutes of searching the U.S. Patent and Trademark Office database, we found many patents that identify synergistic interactions between imidacloprid and other pesticides and/or adjuvants. Since imidacloprid is used to control insect pests, the vast majority of claims of synergism were specifically for the synergistic action of the mixture to kill insects. Every patent claim is accompanied by experimental evidence of synergism of the mixture. It is also likely that the patent assignee would have additional data on synergism in their possession, as the experimental data required to be submitted for a patent application are not very extensive. This, of course, is in addition to the extensive number of studies in the primary literature showing synergy of neonicotinoids and other pesticides.

In the past, the EPA has been reluctant to analyze the effects of chemical mixtures, citing lack of experimental data to come to a scientifically defensible conclusion. Fortunately, it is evident from patent applications that pesticide registrants have these data available for the EPA to analyze. This is a previously unknown and unappreciated source of much needed data. There is now experimental evidence that the EPA can access that can inform an accurate assessment of health effects of exposure to chemical mixtures. The demonstrated toxicity of imidacloprid to insects and invertebrates makes the analysis of these synergistic interactions even more important. Therefore, the existence of scientific data that shows synergistic effects to insects, and possibly other organisms, makes this lack of analysis scientifically indefensible. The EPA cannot come to the conclusion that no unreasonable adverse effects to pollinators or the environment

will result from the re-registration of this pesticide until an analysis of synergistic and/or additive effects is performed.

Respectfully submitted,



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