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PETITION FOR RULEMAKING TO EVALUATE SYNERGISTIC EFFECTS OF PESTICIDES DURING REGISTRATION AND REGISTRATION REVIEW

July 28, 2016

The Honorable Gina McCarthy
Administrator
Environmental Protection Agency
Office of the Administrator, MC 1101A
1200 Pennsylvania Avenue NW
Washington, DC 20004

Jack Housenger
Director
Office of Pesticide Programs
Environmental Protection Agency
2777 South Crystal Drive
Arlington, VA 22202

Dear Administrator McCarthy and Director Housenger,

Pursuant to the to the right to petition the government clause in the First Amendment to the United States Constitution[1] and the Administrative Procedure Act,[2] the Center for Biological Diversity ("Center") submits this petition to the Environmental Protection Agency ("EPA") to revise its regulations and restore the requirement that all applicants and registrants provide data on the potential synergistic effects of pesticides during the registration process and provide a clear, science-based definition of "synergistic effects" to comply with its duties under the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA").

Beginning in 1984, the EPA's regulations at 40 C.F.R. § 158.75(b) expressly provided that the agency could request additional data and testing from a pesticide applicant or registrant regarding the potential synergistic effects of a pesticide active ingredient with other active

[1] "Congress shall make no law . . . abridging . . . the right of the people . . . to petition the Government for a redress of grievances." U.S. Const. Amend. I. The right to "petition for a redress of grievances [is] among the most precious of the liberties safeguarded by the Bill of Rights." *United Mine Workers of Am. Dist. 12 v. Ill. State Bar Ass'n*, 389 U.S. 217, 222 (1967). The Supreme Court has recognized that the right to petition is logically implicit in and fundamental to the very idea of a republican form of government. *United States v. Cruikshank*, 92 U.S. 542, 552 (1875).

[2] The Center and its members are "interested persons" within the meaning of the APA. *See* 5 U.S.C. § 553(e) (granting any "interested person the right to petition for the issuance, amendment, or repeal of a rule"); *see also* 5 U.S.C. § 702 & § 551(13) (providing that "agency action" includes "the whole or a part of an agency rule, … or the equivalent or denial thereof, or failure to act"); *id*. § 706(1) & (2)(A) (granting a reviewing court the authority to "compel agency action unlawfully withheld or unreasonably delayed" and/or to "hold unlawful and set aside agency action … found to be… arbitrary, capricious, an abuse of discretion"). Should the EPA fail to respond to this petition in a timely manner, the Center may pursue relief in federal court.

ingredients, inert ingredients or any additional substance that could act as a synergist.[3] In 2007, the EPA revised its regulations and deleted § 158.75(b), with a cursory explanation: "Paragraph (b) deleted as unnecessary. This material is covered by paragraph (a)."[4] Events over the last several years — including the registration of new, multiple-active-ingredient products like Enlist Duo — illustrate that this decision was a mistake that the EPA can rectify through targeted rulemaking.

Without expressly requiring applicants to provide information on synergy, it is highly likely that the EPA is underestimating the negative impacts on the environment of pesticide exposure in its analyses. Pesticide companies claim that their pesticide products have synergistic impacts in their patent applications to the U.S. Patent Office, while apparently not disclosing similar information to the EPA.[5] In addition to patent claims, it is highly likely that pesticide companies have information pertaining to the potential synergistic effects of pesticide products through research and development of those products. This petition requests that the EPA restore and strengthen these regulatory requirements, thereby providing the agency with information necessary for it to comply with its duty under FIFRA to ensure that its registration of pesticides will not result in unreasonable adverse effects on the environment.[6]

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 one million members and online activists dedicated to the protection and restoration of endangered species and wild places. For 26 years, the Center has worked to protect imperiled plants and wildlife, open space, air and water quality, and overall quality of life. The Center's Environmental Health Program and Pesticides Reduction Campaign aim to improve pesticide regulation in order to reduce the harms of pesticides to the environment as a whole, and threatened and endangered species in particular.

I. The EPA's Failure to Properly Evaluate Synergistic Effects Under FIFRA is a Direct Result of its Failure to Specifically Require that Applicants and Registrants Provide Relevant Data and Testing

On November 24, 2015, the EPA requested that the Ninth Circuit Court of Appeals remand and vacate the registration decision for the new pesticide product Enlist Duo — a combination of glyphosate and 2,4-D — based on new information that the EPA obtained regarding the potential adverse synergistic effects on non-target organisms when these two pesticide active ingredients are combined together. According to the EPA, this information was discovered while reviewing the patent filings for Enlist Duo, in which Dow AgroSciences asserted that the product exhibited

[3] The EPA included 40 C.F.R. § 158.75(b) in 1984 when it originally promulgated the data requirements necessary to make regulatory judgments with respect to the safety of each pesticide proposed for registration in 40 C.F.R. Part 158. 49 Fed. Reg. 42856 (Oct. 24, 1984). The EPA stated that it is "concerned about problems of potential synergism of inerts with actives and other ingredients in formulations." *Id.*

[4] 72 Fed. Reg. 60934 (Oct. 26, 2007) (final rule revision); 70 Fed. Reg. 12275, 12284 (Mar. 11, 2005) (notice of proposed rulemaking providing cursory explanation for removal of paragraph (b)).

[5] Donley, N. (2016). Toxic Concoctions: How The EPA Ignores The Dangers Of Pesticide Cocktails. Enclosed and available at: http://www.biologicaldiversity.org/campaigns/pesticides_reduction/pdfs/Toxic_concoctions.pdf.

[6] 7 U.S.C. § 136a(c)(5).

"synergism, i.e., the herbicidal active ingredients are more effective in combination than when applied individually."[7] Because information relating to the synergistic effects of Enlist Duo was not presented to the EPA during the registration process, the EPA could no longer assure that Enlist Duo would not cause "unreasonable adverse environmental effects" as required under FIFRA.[8] The Ninth Circuit granted the remand to the EPA so that it could reevaluate Enlist Duo's impacts on the environment, particularly whether these synergistic effects could cause unreasonable harm to non-target plants.

It is now clear that Enlist Duo is just the tip of the iceberg of a much larger problem regarding the pesticide registration process. Because evidence of synergistic effects is not specifically required in the registration process or the registration review process, pesticide applicants and registrants are not providing the EPA with this vital information.[9] As a result, the EPA is systemically underestimating the adverse effects of pesticide products on the environment. Moreover, because a pesticide product *must* generally demonstrate synergistic effects in order to be eligible for patent protection and many pesticide products are patented, it is possible that pesticide companies are routinely claiming a synergistic effect to the U.S. Patent Office, while omitting that synergistic effects exist in communications with the EPA pertaining to registration of their products. Aside from the patent context, it is also likely that pesticide companies have testing, data or information concerning synergistic effects of combined ingredients that are not currently disclosed to the EPA. Accordingly, we believe that the EPA should revisit its pesticide product approval process, as well as its permissive approach to allowing tank mixtures, in order to fully protect the environment from these unknown synergistic effects.

A. Pesticide Product Mixtures

Pesticide products are defined in the FIFRA regulations as "a pesticide in the particular form (including composition, packaging, and labeling) in which the pesticide is, or is intended to be, distributed or sold. The term includes any physical apparatus used to deliver or apply the pesticide if distributed or sold with the pesticide."[10] Almost by definition, all pesticide products contain at least one active ingredient and one or more inert ingredients.[11]

Under the U.S. Patent System established by the Constitution, and detailed by the Congress and U.S. Courts,[12] a patent can be issued to protect the intellectual property of an active ingredient's composition, as well as for pesticide products. However, the requirements to successfully patent an active ingredient appear to be very different from the requirements to successfully patent a

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[7] Letter from Susan Lewis, Division Director, Registration Division, Office of Pesticide Programs, United States Environmental Protection Agency to Diego Fonseca, Dow AgroSciences LLC (October 13, 2015).
[8] 7 U.S.C. § 136a(c)(5).
[9] The EPA's regulations currently require registrants to submit information that they reasonably should know that EPA might regard the information as raising concerns about the appropriate terms and conditions of registration of a product. 40 C.F.R. § 159.195(a). However, Dow AgroSciences did not provide the information concerning synergy.
[10] 40 C.F.R. § 152.3. "End-use products are those products for which the label "Does not state that the product may be used to manufacture or formulate other pesticide products." *Id*.
[11] The Center is unaware of any pesticide end-use product where the active ingredient represents 100% of the product composition.
[12] Article I, § 8; *see also* 35 U.S.C. § 103.

pesticide product. In order to patent a pesticide product, one must claim that the combination of ingredients within the formulated product have a synergistic effect — they "result in an effect greater than the sum of the several effects taken separately."[13] In addition, one must show that an invention is "nonobvious" — that the inventor demonstrates that the combination of previous inventions goes beyond the "the level of ordinary skill in the pertinent art."[14]

Accordingly, if a pesticide registrant wishes to patent a particular pesticide product, then it must demonstrate both synergistic effects and non-obviousness in its patent application. Indeed, our investigation of the U.S. Patent Office database revealed that many patent applications for pesticide formulations, mixtures, adjuvants, and surfactants, among others, routinely claim that synergistic effects exist for these pesticide products.[15] More than two-thirds, or 96 out of 140, of the products with multiple active ingredients that the EPA registered for just four agrochemical companies in the last six years had at least one patent that claimed synergy between the active ingredients in the product.[16] As the case of Enlist Duo showed, it is quite possible that this patent information or other relevant data or testing is not being disclosed to the EPA. This means that the EPA likely is not considering all adverse effects on the environment during the risk assessment and is, therefore, unable to make valid final registration decisions for these pesticides.

B. Pesticide Tank Mixtures

In addition to products that contain either multiple active or inert ingredients that result in synergism, pesticide products can often be mixed in the field in a way that results in synergistic effects. The EPA has broadly permitted tank mixtures — the mixing of two or more pesticide products in the spray tank, immediately before treatment application in the field — with few to no restrictions on which tank mixtures can be applied without unreasonable adverse effects on the environment. These unregulated chemistry experiments can result in pesticide products having synergistic effects with almost no oversight or awareness of the scope of impacts to non-target organisms. For example, in the recent pollinator risk assessment for imidacloprid, the EPA noted that this pesticide was often mixed with fungicides in tank mixtures.[17] In the risk assessment, the EPA stated:

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[13] *Anderson's-Black Rock, Inc. v. Pavement Salvage Co.*, 396 U.S. 57, 61 (1969).
[14] *Graham v. John Deere Co*., 383 U. S. 1, 18 (1966).
[15] *See, e.g*. Syngenta Limited, U.S. Patent 9,173,397 (filed April 26, 2010). ("The efficacy of the active ingredients (AIs) in an agrochemical composition can often be improved by the addition of further ingredients. The observed efficacy of the combination of ingredients can sometimes be significantly higher than that which would be expected from the individual ingredients used (synergism). An adjuvant is a substance which can increase the biological activity of and AI but is itself not significantly biologically active. The adjuvant is often a surfactant, and can be included in the formulation or added separately, e.g. by being built into emulsion concentrate formulations, or as tank mix additives.").
[16] Donley, N. (2016). Toxic Concoctions: How The EPA Ignores The Dangers Of Pesticide Cocktails. Enclosed and available at: http://www.biologicaldiversity.org/campaigns/pesticides_reduction/pdfs/Toxic_concoctions.pdf.
[17] EPA Pollinator Ecological Risk Assessments: Imidacloprid Registration Review. Docket # EPA-HQ-OPP-2008-0844 (Jan. 15, 2016).

> "fungicides, particularly those of the sterol biosynthesis inhibitor class that include the triazole fungicides were detected with high frequency. There are reports in the literature that these chemicals may exhibit a greater than additive (e.g., synergistic) effect on toxicity when bees are exposed simultaneously with neonicotinoid chemicals like imidacloprid. While the extent of this relationship is beyond the scope of this assessment, it highlights the complex nature of interactions of different stressors that exist in the hive.[18]

The Center notes that the EPA has proposed to prohibit tank mixing of an herbicide product containing dicamba (M1691) with all other herbicides because "the topic of synergy and multiple stressors is an uncertainty in assessing risk to non-target plants including endangered species."[19] This is certainly a step in the right direction and the Center is supportive of this approach. However, less than a month later, the EPA again recognized "an uncertainty in assessing risk with tank-mix combinations," but it did not propose a tank mix ban and only invited comments on the issue of synergism for its consideration in deciding whether to register products with the new active ingredient halauxifen methyl.[20] So in the case of dicamba, the associated uncertainty was sufficient for the EPA to propose a ban on certain tank mixtures, but in the case of halauxifen methyl the same uncertainty was not sufficient for the EPA to propose a ban on tank mixing. The EPA must take a consistent approach concerning synergistic effects and prohibit tank mixes on the labels until any uncertainty concerning potential synergistic effects is adequately addressed by the applicant or registrant.

C. Conclusion

Most pesticide products on the market are likely more harmful than the EPA has previously assumed because some of the most common combinations of ingredients cause synergistic effects, and most pesticide product labels do not meaningfully limit tank mixtures. Therefore, it is imperative that the EPA consider synergistic effects of pesticide products during its registration and registration review process, and include protective label restrictions to eliminate or mitigate adverse, synergistic environmental impacts. In addition, the EPA should prohibit tank mixes on the labels unless there is sufficient information demonstrating that no synergistic effects will occur.

For too long, the pesticide industry has been gaming the system, saying one thing to the U.S. Patent Office or internally and another to the EPA. It is time that the EPA takes a serious look at synergistic effects from pesticide products in order to meet FIFRA's mandate that no unreasonable adverse environmental effects are occurring when pesticides are used. To achieve this result, the Center proposes the following rule language.

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[18] *Id*. at 100.

[19] EPA 2016. Proposed Registration of Dicamba for New Use on Herbicide-tolerant Cotton and Soybean at 21-22 (March 31, 2016), EPA Docket# EPA-HQ-OPP-2016-0187-0016. Unfortunately, the EPA ignores the potential for synergistic effects from mixing pesticides other than herbicides.

[20] EPA 2016. Proposed Registration Decision of the New Active Ingredient Halauxifen-methyl at 9 (April 28, 2016), EPA Docket# EPA-HQ-OPP-2012-0919-0013.

II. Proposed Rule Language

The Center hereby petitions the EPA to amend its regulations as follows:

A. At 50 C.F.R. § 152.3, add the following regulatory language:

Synergistic effect means an effect or effects arising between two or more active ingredients, or an active ingredient and one or more inert ingredients, that is greater than the sum of their individual effects.

B. At 50 C.F.R. § 158.75, replace the existing section with the following regulatory language:

(a) *General policy.* The data required by part 158 must be supplemented if the applicant is aware that a pesticide product or active ingredient may cause synergistic effect, or, if the information required under this part is not sufficient for EPA to evaluate the potential of the product or active ingredient to cause unreasonable adverse effects on humans or the environment, additional data requirements shall be imposed.

(b) *Policy on test substance.* In general, where the technical grade of the active ingredient is specified as the substance to be tested, tests may be performed using a technical grade which is substantially similar to the technical grade used in the product for which registration is sought. In addition to or in lieu of the testing required in subparts C and D of this part the Administrator shall, when required by subsection (a) or otherwise on a case-by-case basis, require testing to be conducted with:

(1) An analytical pure grade of an active ingredient, with or without radioactive tagging.
(2) The technical grade of an active ingredient.
(3) The representative technical grade of an active ingredient.
(4) An intentionally added inert ingredient in a pesticide product.
(5) A contaminant or impurity of an active or inert ingredient.
(6) A plant or animal metabolite or degradation product of an active or inert ingredient.
(7) The end-use pesticide product.
(8) The end-use pesticide product plus any recommended vehicles and adjuvants.
(9) Any additional substance which could act as a synergist to the product for which registration is sought, or
(10) Any combination of substances in paragraphs (b) (1) through (9) of this section.

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For all the reasons provided above, the Center requests that the EPA grant this petition and begin to revise its regulations expeditiously. Given the narrow and focused request of this petition, we believe that the EPA should be able to process and respond to this request before the end of the year. If the EPA fails to timely respond, the Center may pursue relief through litigation.

Sincerely,

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Enclosure

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