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May 4, 2020

Office of Pesticide Programs
Environmental Protection Agency, (28221T)
1200 Pennsylvania Ave., NW
Washington, DC 20460-0001

Re: Pesticide Registration Review: Proposed Interim Decisions (PID) for Several Neonicotinoid Pesticides (EPA-HQ-OPP-2008-0844-1608)

Dear Madam/Sir,

These comments are submitted by Beyond Pesticides on behalf of the City of Boulder (Colorado), Central Maryland Beekeepers Association, Farmworker Association of Florida, Friends of the Earth, Hawaii Alliance for Progressive Action, Herbicide-Free Campus, Kansas Rural Center, LEAD for Pollinators, Maryland Pesticide Education Network, National Latino Farmers & Ranchers Trade Association, Northeast Organic Farming Association - Massachusetts Chapter, Northwest Center for Alternatives to Pesticides, Organic Consumers Association, People and Pollinators Action Network, and Toxic Free NC.

Founded in 1981 as a national, grassroots, membership organization that represents community-based organizations and a range of people seeking to bridge the interests of consumers, farmers and farmworkers, Beyond Pesticides advances improved protections from pesticides and alternative pest management strategies that reduce or eliminate a reliance on pesticides. Our membership and network span the 50 states and the world.

We are writing with serious concerns in response to the proposed interim decisions on registration of five neonicotinoid pesticides including imidacloprid (EPA-HQ-OPP-2008-0844), clothianidin (EPA-HQ-OPP-2011-0865), thiamethoxam (EPA-HQ-OPP-2011-0581), acetamiprid (EPA-HQ-OPP-2012-0329), and dinotefuran (EPA-HQ-OPP-2011-0920). These neonicotinoids are highly mobile and persistent in the environment and have been linked to numerous adverse health and environmental effects, which have motivated numerous public interest campaigns to ban their use in the U.S. as they have been in Canada and the EU. Based on the agency's own findings of serious risk and growing evidence in the peer-reviewed literature describing adverse impacts to pollinators, aquatic invertebrates, and other wildlife we urged the agency, in previous comments, to revoke the registration of these compounds. With emerging human health concerns being documented, we reiterate our appeal for the agency to adhere to the Federal Insecticide, Fungicide, and Rodenticide Act's (FIFRA) statutory mandate and withdraw the registration of these pesticides that clearly pose unreasonable adverse health and environmental effects. It is important for the agency to recognize that the putative benefits listed in its benefit assessments do not outweigh the ecological harm and existential threat

these compounds pose to pollinators alone, but the added adverse effects expected to aquatic organisms, wildlife, and human health further diminish the ratio of benefits in comparison to the extensive threats. Moreover, the agency's benefits assessment fails to include the many negative externalities (detailed below) that greatly reduce the overall benefits asserted by the agency and dissolves its basis for accepting the demonstrated serious adverse environmental and health risks as reasonable.

Neonicotinoid Extensive Environmental and Health Risks

Pollinator Risks

Multiple studies have confirmed that the environmental concentrations of neonicotinoid pesticides that bees encounter in the environment are toxic enough to impair foraging,[1] navigational,[2,3] and learning behaviors,[4] as well as suppress immune responses.[5] These individual impacts are compounded at the level of social colonies, weakening collective resistance to common parasites, pathogens, and other pesticides, and thus leading to colony losses and mass population declines.[6,7] In 2018, more than two hundred scientists co-authored a "Call to restrict neonicotinoids" on the basis of the breadth of evidence implicating neonicotinoids in mass pollinator and beneficial insect declines.[8] Pollinator exposure to neonicotinoids is widespread, as demonstrated in one survey showing that all fruit and vegetable samples (except nectarine and tomato) and 90% of honey samples were found to be positive for at least one neonicotinoid; 72% of fruits, 45% of vegetables, and 50% of honey samples contained at least two different neonicotinoids in one sample, with imidacloprid, the most widely used neonicotinoid, having the highest detection rate among all samples.[9]

Overall, the agency's assessments confirm that all neonicotinoids considered, including the nitroguanidine neonicotinoids imidacloprid, clothianidin, thiamethoxam, dinotefuran, and the chloropyridinyl neonicotinoid acetamiprid, are highly toxic to honey bees, and contaminate nectar and pollen of crops to which bees are exposed. EPA's assessments focused on

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[1] Feltham, H., Park, K. & Goulson, D. 2014. Field realistic doses of pesticide imidacloprid reduce bumblebee pollen foraging efficiency. Ecotoxicology 23, 317–323.
[2] Schneider, C. W., Tautz, J., Gruenewald, B. & Fuchs, S. 2012. RFID Tracking of Sublethal Effects of Two Neonicotinoid Insecticides on the Foraging Behavior of *Apis mellifera*. Plos One 7, 10.1371/journal.pone.0030023.
[3] Fischer, J., Mueller, T., Spatz, A.K., Greggers, U., Gruenewald, B. and Menzel, R., 2014. Neonicotinoids interfere with specific components of navigation in honeybees. *PloS one*, *9*(3).
[4]Piiroinen, S. and 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), p.20160246.
[5] Brandt, A., Gorenflo, A., Siede, R., Meixner, M. and Büchler, R., 2016. The neonicotinoids thiacloprid, imidacloprid, and clothianidin affect the immunocompetence of honey bees (Apis mellifera L.). *Journal of insect physiology*, *86*, pp.40-47.
[6] Sandrock, C. et al. 2014. Impact of Chronic Neonicotinoid Exposure on Honeybee Colony Performance and Queen Supersedure. Plos One 9, 10.1371/journal.pone.0103592.
[7] Gill, R. J., Ramos-Rodriguez, O. & Raine, N. E. 2012. Combined pesticide exposure severely affects individual- and colony-level traits in bees. Nature 491, 105–108.
[8] https://www.beyondpesticides.org/programs/bee-protective-pollinators-and-pesticides/what-the-science-shows
[9] Chen, M., Tao, L., McLean, J. and Lu, C., 2014. Quantitative analysis of neonicotinoid insecticide residues in foods: implication for dietary exposures. *Journal of agricultural and food chemistry*, *62*(26), pp.6082-6090.

quantitative estimates of exposure via contact from foliar applications and oral ingestion of pollen and nectar only. While EPA acknowledges that honey bees can be exposed through various pathways, including soil, surface water, and guttation droplets, the agency asserts that it lacks sufficient information to quantify the risks from these other exposure routes that would certainly magnify quantitative estimates of risk. Similarly, the agency focuses its pollinator assessment on honey bees, as a surrogate for other bee species, and ignores relevant exposure routes and susceptibility to the many other bee species or insect pollinators (e.g., butterflies, etc.). Since 70 percent of native bee species in the U.S. have ground/soil nests[10] and can come into contact with persistent neonicotinoid residues, especially in agricultural regions, neonicotinoid-contaminated soil becomes a perilous source of exposure to much of the nation's bee populations. In addition, neonicotinoid metabolites such as imidacloprid-olefin have higher toxicity than the parent compound and are also linked to bee mortalities.[11] Neonicotinoids can persist in the environment from previous applications and impact pollinator populations even though not applied in a particular season. Such toxic residues of parent compound or metabolites can be found not only in soil but also in plants.[12]

Neonicotinoids pose high risk to non-bee insect pollinators as mentioned. Monarch butterflies (*Danaus plexippus*), for instance, frequently consume milkweed in and near agroecosystems and consequently may be exposed to pesticides like neonicotinoids. The neonicotinoid clothianidin in milkweed plants impedes normal development of monarchs even at low levels that can be found in milkweed growing adjacent to neonicotinoid treated fields.[13]

Aquatic Risks

In addition to the risks to non-target pollinators, neonicotinoids pose substantial risks to aquatic environments. According to EPA, "all neonicotinoid insecticides are expected to exhibit a high toxicity to aquatic invertebrates, particularly insect larvae, in part due to their common mode of action."[14] According to the "Worldwide Integrated Assessment on Systemic Pesticides," a meta-analysis published by several distinguished scientists, systemics like neonicotinoids are persistent in the environment "at levels that are known to cause lethal and sublethal effects on a wide range of terrestrial (including soil) and aquatic microorganisms, invertebrates and vertebrates."[15] With the U.S. Geological Survey (USGS) finding neonicotinoid

[10] Vaugh, M, Hopwood, J, Mader, EL, et al. 2015. Farming for Bees: Guidelines for Providing Native Bee Habitat on Farms. The Xerces Society. Available at http://www.xerces.org/wp-content/uploads/2008/11/farming_for_bees_guidelines_xerces_society.pdf

[11] Suchail, S., Debrauwer, L. & Belzunces, L. P. 2004. Metabolism of imidacloprid in Apis mellifera. Pest Manag Sci 60, 291–296.

[12] Seifrtova, M., Halesova, T., Sulcova, K., Riddellova, K. and Erban, T., 2017. Distributions of imidacloprid, imidacloprid-olefin and imidacloprid-urea in green plant tissues and roots of rapeseed (Brassica napus) from artificially contaminated potting soil. *Pest management science*, *73*(5), pp.1010-1016.

[13] Pecenka, J.R. and Lundgren, J.G., 2015. Non-target effects of clothianidin on monarch butterflies. *The Science of Nature*, *102*(3-4), p.19.

[14] USEPA. 2017. Thiamethoxam -Transmittal of the Preliminary Aquatic and Non-Pollinator Terrestrial Risk Assessment to Support Registration Review. Office of Pesticide Programs. Washington DC.

[15] Van der Sluijs J.P., et al. 2014. Conclusions of the Worldwide Integrated Assessment on the risks of neonicotinoids and fipronil to biodiversity and ecosystem functioning. *Environ Sci Pollut Res*, doi:10.1007/s11356-014-3229-5.

residues in U.S. waterways,[16] which threaten not just pollinators but especially aquatic organisms, the agency must take a firm position to prevent the dispersal of systemic, mobile, and persistent pesticides that contaminate surface waters and groundwater at such extremely toxic levels.

Wildlife Risks

Like the other neonicotinoids, imidacloprid as representative of the class is highly water soluble and persistent in both terrestrial and aquatic environments, and poses potential risks to birds and mammals, especially from seed treatment. Imidacloprid is already classified as highly toxic to birds on an acute oral basis, and chronic toxicity results in effects on egg production, egg hatchability, and body weight. EPA's overall risk conclusion states, "For the registered agricultural and non-agricultural foliar spray applications, there is a potential for acute risk above the level of concern (LOC) to non-listed birds for all uses modeled when evaluated on an acute, oral basis." For mammals, "a potential for chronic risks is identified when evaluated on an oral basis."[17] Alarmingly, as little as 1 to 6 percent of a bird's diet of treated seed is enough to trigger acute and chronic risks. Reproduction impairment has also been demonstrated from neonicotinoid exposure in wild mammals, including rabbits and white-tailed deer.[18,19]

Human Health Risks

Although neonicotinoids are considered low toxicity to mammals and humans in comparison with traditional insecticides, more and more studies show exposure to neonicotinoids do indeed pose potential risk to mammals and even humans. In recent years, neonicotinoids and their metabolites have been successfully detected in various human biological samples. Meanwhile, many studies have focused on the health effects of neonicotinoids on humans.[20] Given the wide-scale use of neonicotinoids, more studies are needed to fully understand their effects on human health.[21] Investigations, conducted mostly on laboratory rats, have shown adverse effects of imidacloprid on the reproductive ability in both parental and offspring generations as well as on the development of the offspring. Like many pesticides, imidacloprid may also act as an endocrine disrupting chemical (EDC). It may disrupt the metabolic homeostasis, contribute to obesity, and disrupt steroidogenesis by inhibiting cytochrome P450 (CYP) enzyme activities. All these endocrine associated adverse

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16 Hladik, M, Kolpin, D and Kuivila, K. 2014. Widespread occurrence of neonicotinoid insecticides in streams in a high corn and soybean producing region, USA. *Environ Poll*. 193: 189–196.

17 USEPA. 2017. Imidacloprid -Transmittal of the Preliminary Terrestrial Risk Assessment to Support the Registration Review.

18 Memon, S.A., Memon, N., Mal, B., Shaikh, S.A. and Shah, M.A., 2014. Histopathological changes in the gonads of Male rabbits (Oryctolagus cuniculus) on exposure to imidacloprid insecticide. *J Entomol Zool Stud*, *2*, pp.159-63.

19 Berheim, E.H., Jenks, J.A., Lundgren, J.G., Michel, E.S., Grove, D. and Jensen, W.F., 2019. Effects of neonicotinoid insecticides on physiology and reproductive characteristics of captive female and fawn white-tailed deer. *Scientific reports*, *9*(1), pp.1-10.

20 Han, W., Tian, Y. and Shen, X., 2018. Human exposure to neonicotinoid insecticides and the evaluation of their potential toxicity: An overview. *Chemosphere*, *192*, pp.59-65.

21 Cimino, A.M., Boyles, A.L., Thayer, K.A. and Perry, M.J., 2017. Effects of neonicotinoid pesticide exposure on human health: a systematic review. *Environmental health perspectives*, *125*(2), pp.155-162.

effects of imidacloprid may pose a serious risk for reproduction and development with long-term consequences in adulthood.[22]

Proposed Interim Decisions

Imidacloprid (EPA-HQ-OPP-2008-0844)

Risks of concern to honey bees were identified in EPA's assessments. Although the focus of the pollinator risk assessments is on honey bees, the agency recognizes that numerous other species of bees occur in North America and that these non-Apis bees have ecological importance in addition to commercial importance in some cases. For example, it is important to note that several species of non-Apis bees are commercially managed for their pollination services, including bumblebees (*Bombus spp*.), leaf cutting bees (*Megachile rotundata*), alkali bees (*Nomia melanderi*), blue orchard bees (*Osmia lignaria*), and the Japanese horn-faced bee (*Osmia cornifrons*). The agency recognizes a growing body of information that indicates native bees also play an important role in crop and native plant pollination, in addition to their overall ecological importance via maintaining biological diversity. However, EPA is only proposing limited mitigation to reduce exposure and potential impact to honey bees that are also expected to benefit other pollinating insects. Of these measures, reductions in maximum application rates for certain crops where pollinator/bee exposure may occur, or crop stage restrictions which limit exposure during critical periods in the growing season, are expected to have the highest potential impact in reducing risks to all pollinators. On the other hand, for certain critical uses, like citrus and cotton, no mitigation of risk at all is proposed. These measures were chosen to preserve the majority of imidacloprid pest management utility, while also including at least some meager risk reduction for bees and other pollinators. Although most of these proposed mitigation measures will likely reduce some exposures, **in no case will the resulting expected exposures be reduced below levels of concern that will eliminate deleterious effects to pollinator communities as well as aquatic communities.**

Overall, EPA is proposing addressing risk posed by current registered uses of imidacloprid uses through the following risk mitigation measures:

- Cancel residential spray applications to turf, on-farm seed treatment (of canola, millet, and wheat), and use on bulb vegetables;
- Require additional PPE;
- Reduce maximum application rates or restrict applications during pre-bloom and/or bloom, targeting certain uses with potentially higher pollinator risks and lower benefits;
- Preserve the current restrictions for application at-bloom;
- Require advisory language for residential ornamental uses;
- Apply targeted application rate reductions for higher risk uses;
- Require additional spray drift and runoff reduction label language; and,

[22] Mikolić, A. and Karačonji, I.B., 2018. Imidacloprid as reproductive toxicant and endocrine disruptor: investigations in laboratory animals. *Archives of Industrial Hygiene and Toxicology*, *69*(2), pp.103-108.

- Promote voluntary stewardship efforts to encourage employment of best management practices, education, and outreach to applicators and beekeepers.

The agency did not propose risk mitigation on several imidacloprid uses, including citrus and grapes. For citrus crops, imidacloprid and other neonicotinoids are a key element in programs to control the Asian citrus psyllid (ACP), an invasive pest that transmits HLB, a devastating and incurable disease. In grapes, the neonicotinoids are used similarly to combat sharpshooters which vector Pierce's Disease, a fatal bacterial disease for grapes that can result in 100% yield loss. For other uses where mitigation was proposed, the mitigation does not completely eliminate all risks of concern from the use of imidacloprid, however overall risk and/or exposure is partially reduced. The agency finds the remaining risks to be reasonable under FIFRA given the benefits of the use of imidacloprid, even though many non-neonicotinoid alternatives exist, as discussed below.

Except for the Endocrine Disruptor Screening Program (EDSP), the Endangered Species Act (ESA) components of this case, the agency has made the following PID for imidacloprid: (1) no additional data are required at this time; and (2) changes to the affected registrations or their labeling are required. The agency is making no human health or environmental safety findings associated with the EDSP screening of imidacloprid, nor is it making a complete endangered species finding. However, we identify below several uncertainties and data gaps that the agency did not adequately address and, in summation, we recommend cancellation of all imidacloprid uses due to unreasonable risks posed to the environment and human health.

Clothianidin (EPA-HQ-OPP-2011-0865) and Thiamethoxam (EPA-HQ-OPP-2011-0581)

Clothianidin and thiamethoxam risks and their PIDs were combined because clothianidin is a major degradate/metabolite of thiamethoxam, so environmental exposures to either product are essentially clothianidin. Pollinator risk assessments for clothianidin, as with imidacloprid and the other neonicotinoids, use honey bees as an appropriate surrogate for assessing individual level risks to other species of bees. Tier I conclusions for honey bees are therefore also used to represent risks to solitary bees. One notable exception relates to differences in attractiveness of crops. For example, many of the fruiting vegetables are not attractive to honey bees but are attractive other species of bees (e.g., *Bombus sp*.). Therefore, additional crops in the fruiting vegetables group that were considered low risk to honey bees may pose a risk to non-Apis bees.

However, the agency has identified ecological risks of concern for clothianidin, particularly to pollinators and aquatic invertebrates, as a result of many of the same attributes that make the neonicotinoids effective pest control chemicals. Minimal risk mitigation measures are being proposed to address ecological risks of concern identified for pollinators, birds, mammals, and to aquatic invertebrates; and human health risks of concern to occupational handlers from certain clothianidin and thiamethoxam uses.

Overall, EPA is proposing to address potential risks posed by current registered uses of clothianidin and/or thiamethoxam through the following risk mitigation measures:

- Cancelling certain clothianidin uses;
- Restricting certain thiamethoxam uses;
- Requiring additional PPE;
- Reducing maximum application rates or restricting applications during pre-bloom and/or bloom, targeting certain uses with potentially higher pollinator risks and lower benefits;
- Preserving the current restrictions for application at-bloom;
- Requiring additional label language reducing use by homeowners;
- Applying targeted rate reductions for higher risk uses;
- Requiring additional spray drift and runoff reduction label language; and,
- Promoting voluntary stewardship efforts to encourage the use of best management practices, education, and outreach to applicators and beekeepers.

The proposed mitigation does not eliminate all potential risks of concern from the use of clothianidin or thiamethoxam, however, the proposed mitigation reduces the overall potential of risk and/or exposure. The agency finds these remaining risks to be reasonable under FIFRA, given the benefits of using clothianidin and thiamethoxam even though many non-neonicotinoid alternatives to clothianidin and thiamethoxam exist, as discussed below.

Except for the Endocrine Disruptor Screening Program (EDSP), the Endangered Species Act (ESA) components of this case, the agency has made the following PID for clothianidin and thiamethoxam: (1) no additional data are required at this time; and (2) changes to the affected registrations or their labeling are required. The agency is making no human health or environmental safety findings associated with the EDSP screening of clothianidin and thiamethoxam, nor is it making a complete endangered species finding. However, we identify below several uncertainties and data gaps that the agency did not adequately address and, in summation, we recommend cancellation of all clothianidin and thiamethoxam uses due to unreasonable risks posed to the environment and human health.

Acetamiprid (EPA-HQ-OPP-2012-0329)

EPA has identified risks of concern to occupational handlers applying acetamiprid liquid and wettable powder formulations as basal bark treatments using backpacks. EPA has also identified risks to mammals and birds that consume treated seeds, to birds from foliar applications, to terrestrial invertebrates from foliar applications, to aquatic invertebrates from foliar applications, and to terrestrial plants. To mitigate the risks to occupational handlers, EPA proposes updating personnel protective equipment (PPE) standards for certain applications of acetamiprid. To mitigate risks to birds, invertebrates and terrestrial plants, EPA proposes spray drift mitigation and buffer zones to limit the movement of acetamiprid. To mitigate risks to birds and mammals, EPA proposes standards for handling acetamiprid-treated seeds. The agency is also proposing updated gloves statements, insecticide resistance management language, an environmental hazard statement for pollinators, and best practices language for water soluble packaging.

Except for the Endocrine Disruptor Screening Program (EDSP), and the Endangered Species Act (ESA), the agency has made the following Proposed Interim Registration Review Decision for acetamiprid: (1) no additional data are required at this time; and (2) changes to the affected registrations and their labeling are required. In this acetamiprid PID, the agency is making no human health or environmental safety findings associated with the EDSP screening of acetamiprid, nor is it making a complete endangered species finding. However, we identify below several uncertainties and data gaps that the agency did not adequately address and, in summation, we recommend cancellation of all acetamiprid uses due to unreasonable risks posed to the environment and human health.

Dinotefuran (EPA-HQ-OPP-2011-0920)

Overall, EPA is proposing addressing risk posed by current registered uses of dinotefuran uses through the following risk mitigation measures:

- Cancel use on bulb vegetables;
- Reduce maximum application rates or restricting applications during pre-bloom and/or bloom, targeting certain uses with potentially higher pollinator risks and lower benefits;
- Preserve the current restrictions for application at-bloom;
- Require advisory language for residential ornamental uses;
- Apply targeted application rate reductions for higher risk uses;
- Require additional spray drift and runoff reduction label language; and,
- Promote voluntary stewardship efforts to encourage employment of best management practices, education, and outreach to applicators and beekeepers.

Except for the Endocrine Disruptor Screening Program (EDSP) and the Endangered Species Act (ESA) components of this case, the agency has made the following PID for dinotefuran: (1) no additional data are required at this time; and (2) changes to the affected registrations or their labeling are required. The agency is making no human health or environmental safety findings associated with the EDSP screening of dinotefuran, nor is it making a complete endangered species finding. However, we identify below several uncertainties and data gaps that the agency did not adequately address and, in summation, we recommend cancellation of all dinotefuran uses due to unreasonable risks posed to the environment and human health.

International Recognition of Extensive Risks

EPA's Canadian counterpart, Pest Management Regulatory Agency (PMRA), in its reevaluation of imidacloprid, notes that further mitigation of risks would be unrealistic, unsustainable, and inadequate to protect sensitive aquatic species.[23] Current neonicotinoid uses are not sustainable, and knowing the environmental burden they pose to aquatic systems, uses that pose risks to these systems must be cancelled. PMRA notes that despite current label statements, levels of imidacloprid in waterbodies pose risks to aquatic insects. Based on this

[23] PMRA. 2016. Proposed Re-evaluation Decision PRVD2016-20, Imidacloprid. Health Canada. Ottawa, Ontario.

imidacloprid assessment, the agency believes that "effective risk mitigation through a use-reduction strategy would be difficult to achieve…" Specifically, the agency states, "[I]t would be difficult to identify the specific uses that are causing the elevated levels in water, given that much of the water monitoring data were from mixed-use areas of agriculture. In addition, it is not possible to accurately predict how much use reduction would be necessary to achieve acceptable levels of imidacloprid in the environment and, therefore, any use-reduction strategy would require extensive and comprehensive water monitoring information to confirm that risk reduction targets are being achieved."[24]

Similarly, the European Food Safety Authority (EFSA) found risks to aquatic organisms are unacceptable and beyond effective mitigation.[25] As a result, EFSA determined that neonicotinoid risks to bees are excessive and was unable to find a way to adequately avert risks to pollinators and recommended termination of these pesticide uses.[26]

Flawed Benefits Assessment

FIFRA requires the agency to take into account the benefits of a pesticide's use in risk management decision-making, however it does require that alleged benefits outweigh risks in its assessment. The agency considered the benefits of the various uses of imidacloprid, clothianidin, thiamethoxam, acetamiprid, and dinotefuran to determine whether the many risks identified present **unreasonable** (emphasis added) adverse effects. The agency asserts for many uses that the benefits are indeed very high for the neonicotinoid insecticides, specifically that they:

- can control a variety of piercing and sucking pests including those that vector plant diseases such as aphids and whitefly;
- each show certain benefits for the control of particular pests;
- offer both immediate, contact control and systemic, residual control of pests over an extended period of time; and,
- are comparatively less expensive and more effective than some alternatives.

In contrast, serious environmental and health risks of concern were also noted by the agency, but noticeably downplayed, while benefits were often overstated. There are cases where the agency is not proposing any risk mitigation, although risk quotients and levels of concern are greatly exceeded due to the agency's assertion that restricting use or imposing mitigation measures in these cases may impact a growers' ability to manage certain critical pest issues irrespective of the disproportionate risks of concern identified. We emphatically disagree that such flawed risk/benefit balance can make clearly demonstrated risks of serious environmental

[24] PMRA (Pest Management Regulatory Agency, Health Canada). 2016. Proposed Re-evaluation Decision PRVD2016-20, Imidacloprid. Health Canada. Ottawa, Ontario.
[25] EFSA (European Food Safety Authority), 2014. Conclusion on the peer review of the pesticide risk assessment for aquatic organisms for the active substance imidacloprid. EFSA Journal 2014;12(10):3835, 49 pp.
[26] EFSA (European Food Safety Authority), 2018. Evaluation of the data on clothianidin, imidacloprid and thiamethoxam for the updated risk assessment to bees for seed treatments and granules in the EU. EFSA supporting publication 2018:EN-1378. 31pp.

and adverse effects somehow reasonable or consistent with FIFRA's mandate to protect human health and the environment. If such risks cannot be mitigated, the agency has a statutory obligation to suspend or cancel all such uses, especially where alternative means are available to effectively manage such critical pest issues. In many such instances, the agency fails to fully consider or reconcile the available alternatives or negative externalities that diminish the emphasized benefits.

An example of a crop in which the benefits are overly weighted against overarching risks and alternative control strategies not fully considered is the citrus crops, where neonicotinoids are a key element in programs to control the Asian citrus psyllid (ACP), an invasive pest that transmits Huánglóngbìng (HLB) or citrus greening disease, a devastating and incurable disease. Intensive chemical control of ACP is the primary management tool currently being used to reduce ACP populations, but this strategy is costly, and increasingly ineffective.[27] Even intensive pesticide programs have little effect on the spread of HLB, and populations of ACP in Florida are becoming less susceptible to insecticides, including neonicotinoids.[28] The decreasing susceptibility of ACP to neonicotinoids illustrates the need for more sustainable tools and the reduced benefit offered by these chemicals. Nonchemical alternatives exist, such as *Tamarixia radiata*, a natural parasitoid of the Asian citrus psyllid. *Tamarixia radiata* attacks and kills ACP, and has no negative impact on any organism other than psyllids.[29] Improved micronutrient nutrition from soil amendments, such as rock powders, can be a key part of combating HLB, as research has found that providing a constant elevated supply of micronutrients can help restore root function, tree health, and productivity.[30] Use of inorganic kaolin clay and calcium carbonate have also proved effective at reducing ACP populations.[31] Unfortunately, biological control by predators and parasitoids usually is not compatible with chemical control nor considered an acceptable management option once a grove is infected by HLB.[32] Therefore, it is unlikely that traditional biological control will provide a solution to HLB, at least in Florida where HLB is prevalent while chemical control with neonicotinoids is predominant. Environmental conditions in other citrus areas in the US, such as California or Texas, are more favorable for biological control of ACP as long as chemical control practices are abated.

Another example can be found in grape vineyards. A healthy population of beneficial insects is the single most effective way to control glassy winged sharpshooters that vector

[27] Grafton-Cardwell, E.E., Stelinski, L.L. and Stansly, P.A., 2013. Biology and management of Asian citrus psyllid, vector of the huanglongbing pathogens. *Annual Review of Entomology*, *58*, pp.413-432.
[28] Tiwari S, Mann RS, Rogers ME & Stelinski LL (2011) Insecticide resistance in field populations of Asian citrus psyllid in Florida. Pest Management Science 67: 1258–1268.
[29] Hoddle, M.S. and Hoddle, C.D., 2013. Classical biological control of Asian citrus psyllid with Tamarixia radiata in urban Southern California. *Citrograph*, *4*(2), pp.52-58.
[30] Cochrane, E.F. and Shade, J.B., 2019. Combatting Huanglongbing in Organic Systems. *International journal of Horticulture, Agriculture and Food science*, *3*(1).
[31] Ramírez-Godoy, A., Puentes-Peréz, G. and Restrepo-Díaz, H., 2018. Evaluation of the effect of foliar application of kaolin clay and calcium carbonate on populations of Diaphorina citri (Hemiptera: Liviidae) in Tahiti lime. *Crop Protection*, *109*, pp.62-71.
[32] Halbert SE & Manjunath KL (2004) Asian citrus psyllids (Sternorrhyncha: Psyllidae) and greening disease of citrus: a literature review and assessment of risk in Florida. Florida Entomologist 87: 330–353.

Pierce's Disease, a fatal bacterial disease for grapes. One of the most effective is a small wasp that feeds on the pest's egg masses.[33] Praying mantis, assassin bugs, lacewings and even kaolin clay are also extremely beneficial at managing sharpshooters in grapes.[34]

In fact, more examples of effective alternatives exist[35] that are neglected in the agency's benefits assessment and which contradict agency assertions that neonicotinoid use outweighs the considerable environmental harm posed. Thus, available alternatives nullify the supposed benefits and elevate risks to unreasonable, and actually it can be argued that the cessation of neonicotinoid use would facilitate more biocontrol methods and more sustainable pest management.

Another example where EPA's risk/benefit consideration is flawed is in the tree injection uses. The agency concludes that tree injections of neonicotinoids show significant risk extending into the following growing season. However, due to the low amount of overall usage and perceived benefits of the tree injection use, the agency is not proposing any risk mitigation. In effect, EPA implies that if a use is small, any risk, no matter how large, is exceeded by supposed benefits of the minor use.

The agency's benefits assessment is also inadequate for not fully factoring in the many negative externalities that should be considered as costs which diminish or even nullify many of the benefits advanced. These negative externalities include:

- Economic loss of pollinators and pollination services;[36,37,38]
- Economic loss of bee products (honey, beeswax, propolis, royal jelly);
- Loss of beneficial insects, compromised biocontrol, and reduced crop yields;[39]
- Increase in new crop pests due to loss of beneficials and biocontrol;[40]
- Increased pest resistance and cost of increased pesticide use;
- Increased human health issues; and,

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[35] Furlan, L., Pozzebon, A., Duso, C., Simon-Delso, N., Sánchez-Bayo, F., Marchand, P.A., Codato, F., van Lexmond, M.B. and Bonmatin, J.M., 2018. An update of the Worldwide Integrated Assessment (WIA) on systemic insecticides. Part 3: alternatives to systemic insecticides. *Environmental Science and Pollution Research*, pp.1-23.
[36] Hanley, N., Breeze, T.D., Ellis, C. and Goulson, D., 2015. Measuring the economic value of pollination services: Principles, evidence and knowledge gaps. Ecosystem Services, 14, pp.124-132.
[37]Gill, R.A., 1990, August. The value of honeybee pollination to society. In *VI International Symposium on Pollination 288* (pp. 62-68).
[38] Nabhan, G.P. and Buchmann, S.L., 1997. Services provided by pollinators. *Nature's Services: societal dependence on natural ecosystems*, pp.133-150.
[39] Douglas, M.R., Rohr, J.R. and Tooker, J.F., 2015. 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), pp.250-260.
[40] Harper, C.R. and Zilberman, D., 1989. Pest externalities from agricultural inputs. *American Journal of Agricultural Economics*, *71*(3), pp.692-702.

- Market loss and reduced availability of "bee friendly" produce and products.[41]

The agency should consider the degree the asserted benefits in its assessment are diminished or negated by the many negative externalities.

Ineffective Mitigation Proposal

The agency acknowledges that the proposed mitigation measures, except for the proposed cancellations of certain uses, do not eliminate all potential risks of concern, but asserts that the proposed mitigation reduces the overall potential of risk and/or exposure without providing convincing evidence. Furthermore, in its assessments the agency fails to clarify that these reduced exposure and/or risks from what mitigation is imposed do not reduce exposure/risks below serious risk quotients of concern. The agency also admits that for several neonicotinoid use scenarios where serious risk concerns were identified, no mitigation is proposed at all. While other regulatory authorities such as PMRA (Canada) and EFSA (Europe) determined no mitigation would be effective in reducing adequately unacceptable risks and moved to prohibit continued use neonicotinoids, EPA, on the other hand, is willing to accept such limited mitigation. We urge the agency to reconsider and join with its international partners to cancel all neonicotinoid uses.

Uncertainties and Data Gaps

The agency has not considered the cumulative or combined toxicity of the prevalent and widespread use of neonicotinoid insecticides and the agency fails to recognize a common mechanism of action for these chemicals,[42,43,44,45,46] as required by law. However, neonicotinoids universally act as agonists at the nicotinic acetylcholine receptors (nAChRs) of insects and mammals (particularly the α4β2 subtype).[47] Neonicotinoid insecticides target insect nAChRs and exhibit strikingly diverse actions on their nAChR targets.[48] Neuronal nicotinic acetylcholine receptors (nAChRs) in human brains are involved in a number of physiological and behavioral processes and are additionally implicated in a number of pathological conditions including Alzheimer's disease, Parkinson's disease and schizophrenia.[49] EPA has acknowledged for one neonicotinoid, imidacloprid, "evidence of increased qualitative susceptibility in the rat developmental neurotoxicity study." The agency further concludes that maternal treatment

[41] Wollaeger, H.M., Getter, K.L. and Behe, B.K., 2015. Consumer preferences for traditional, neonicotinoid-free, bee-friendly, or biological control pest management practices on floriculture crops. *HortScience*, *50*(5), pp.721-732.
[42] Environmental Protection Agency. 2003. Acetamiprid; pesticide tolerance. Fed. Regist. 68:52343–53.
[43] Environmental Protection Agency. 2003. Clothianidin; pesticide tolerance. Fed. Regist. 68:32390–400.
[44] Environmental Protection Agency. 2003. Dinotefuran; notice of filing a pesticide petition to establish a tolerance for a certain pesticide chemical in or on food. Fed. Reg. 68:39547–54.
[45] Environmental Protection Agency. 2003. Imidacloprid; pesticide tolerances. Fed. Reg. 68:35303–15.
[46] Environmental Protection Agency. 2002. Thiamethoxam; pesticide tolerance. Fed. Reg. 67:66561–71.
[47] Tomizawa, M. and Casida, J.E., 2005. Neonicotinoid insecticide toxicology: mechanisms of selective action. *Annu. Rev. Pharmacol. Toxicol.*, *45*, pp.247-268.
[48] Matsuda, K., Kanaoka, S., Akamatsu, M. and Sattelle, D.B., 2009. Diverse actions and target-site selectivity of neonicotinoids: structural insights. *Molecular pharmacology*, *76*(1), pp.1-10.
[49] Paterson, D. and Nordberg, A., 2000. Neuronal nicotinic receptors in the human brain. *Progress in neurobiology*, *61*(1), pp.75-111.

with imidacloprid produced persistent changes in offspring brain structures and poor performance on some behavioral tests. Animal studies report neurobehavioral impairments in rodents that were exposed to imidacloprid prenatally.[50] It is scientifically reasonable and prudent to presume that there may be no safe level of exposure during early life development for these neurotoxic agents. Nonetheless the agency still does not consider children to be uniquely sensitive, so it has not applied the Food Quality Protection Act (FQPA) 10X safety factor to any of the five EPA approved neonicotinoid risk assessments. By ignoring the cumulative exposure to all neonicotinoid chemicals and not imposing the statutorily required FQPA safety factor, much higher exposure limits result, which will almost certainly fail to protect vulnerable populations, including pregnant women and children. We implore the agency to address the cumulative impacts of the neonicotinoids as a group, as required by the FQPA and include the 10X safety factor in its health assessments as required by the FQPA to protect sensitive populations, including pregnant women, infants and children.

In its pollinator risk assessment, the agency lays out several uncertainties that contribute to pesticide risks posed to bees and other pollinators. These include: pesticides with sublethal and chronic toxicity, including neonicotinoids and other systemic pesticides, the impact of chemical mixtures, and other pesticide types, such as insect growth regulators, fungicides, and microbial pesticides. These various pesticide substances can adversely impact bees and can have cumulative, synergistic, and additive effects on long-term pollinator health. EPA has published new data requirements for assessing risks to pollinators[51] and states that these new and clarified requirements would be applied across all pesticide ecological assessments, yet the agency concludes for one of the subject neonicotinoids, acetamiprid, that such higher tier pollinator data are not needed. Potential synergistic impacts of combined chemical mixture exposures have not been assessed. Chemical mixture exposures occur from multiple active ingredient formulations, tank mixes, and overlapping treatments. With neonicotinoids being systemic and persistent, the likelihood of overlapping exposures occurring on field or from adjacent fields is increased.

The ecological risk assessments for all five neonicotinoids used fish early life stage (ELS) tests to estimate chronic fish toxicity. This is inappropriate. The fish ELS is a subchronic test of sensitive life stages and may be predictive of chronic fish toxicity in some cases, it is not a universally suitable chronic test. It does not adequately address potential adverse effects on reproduction or transfer of a mobile and persistent test chemical to eggs/offspring from parental exposure. Only a complete life-cycle test can satisfy the requirements of a chronic

[50] Abou-Donia, Mohamed B., Larry B. Goldstein, Sarah Bullman, T. Tu, Wasi A. Khan, Ankelika M. Dechkovskaia, and Ali A. Abdel-Rahman. "Imidacloprid induces neurobehavioral deficits and increases expression of glial fibrillary acidic protein in the motor cortex and hippocampus in offspring rats following in utero exposure." *Journal of Toxicology and Environmental Health, Part A* 71, no. 2 (2008): 119-130.
[51] USEPA. 2014. Guidance for Assessing Pesticide Risks to Bees. Office of Pesticide Programs. Washington DC.

toxicity test, an early life-stage test cannot be correctly substituted.[52,53,54] FIFRA regulations (40 CFR § 158.630) require a fish life cycle test (freshwater and/or saltwater fish) if data from other organisms indicate that the reproductive physiology of fish may be affected such as is documented for neonicotinoids in birds and mammals. A full life cycle test with fathead minnow (freshwater) (OSCPP 850.1500) or medaka extended one-generation test (OSCPP 890.2200) would be needed to fulfill a requirement for reproduction and chronic toxicity for freshwater fish. For saltwater fish, a sheepshead minnow life cycle test (OCSPP 850.1500) or sheepshead minnow multi-generation test[55] would be recommended.

The agency is making no human health or environmental safety findings associated with the potential for endocrine disruption, or identifying additional data needs to satisfy Endocrine Disruptor Screening Program requirements in the PIDs. Under FFDCA § 408(p), the agency must screen all pesticide chemicals for potential endocrine activity. In 2009 and 2010, EPA issued test orders/data call-ins for the first list of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. The agency has reviewed all of the assay data received for the List 1 chemicals and the conclusions of those reviews are available in the chemical-specific public dockets. A second list of chemicals identified for EDSP screening was published in 2013 and includes some pesticides scheduled for Registration Review and chemicals found in water. Erroneously, the agency states "Imidacloprid is not on either list" on page 73 of the imidacloprid PID.[56] However, imidacloprid was included in List 1 and all Tier 1 EDSP called-in data were submitted. The agency completed review of all Tier 1 data for imidacloprid (June 29, 2015) and concluded: "Overall, there was no convincing evidence to indicate a potential to interact with the thyroid hormone pathway. Based on weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for imidacloprid since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways."[57] However, these conclusions should be revisited as emerging data and other scientifically relevant information have reported evidence of endocrine disrupting activity for imidacloprid.[58,59,60]

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[52] Woltering, D. M. (1984). The growth response in fish chronic and early life stage toxicity tests: a critical review. *Aquatic Toxicology*, *5*(1), 1-21.
[53] Suter, G. W., Rosen, A. E., Linder, E., & Parkhurst, D. F. (1987). Endpoints for responses of fish to chronic toxic exposures. *Environmental Toxicology and Chemistry*, *6*(10), 793-809.
[54] Nagel R., Isberner K. (1998) Testing of chemicals with fish — a critical evaluation of tests with special regard to zebrafish. In: Braunbeck T., Hinton D.E., Streit B. (eds) Fish Ecotoxicology. EXS, vol 86. Birkhäuser, Basel
[55] Cripe, G.M., Hemmer, B.L., Goodman, L.R. and Vennari, J.C., 2009. Development of a methodology for successful multigeneration life-cycle testing of the estuarine sheepshead minnow, Cyprinodon variegatus. *Archives of environmental contamination and toxicology*, *56*(3), pp.500-508.
[56] EPA-HQ-OPP-2008-0844-1619.
[57] EPA-HQ-OPP-2008-0844-0137.
[58] Yuan, X., Shen, J., Zhang, X., Tu, W., Fu, Z. and Jin, Y., 2020. Imidacloprid disrupts the endocrine system by interacting with androgen receptor in male mice. *Science of The Total Environment*, *708*, p.135163.
[59] Mikolić, A. and Karačonji, I.B., 2018. Imidacloprid as reproductive toxicant and endocrine disruptor: investigations in laboratory animals. *Archives of Industrial Hygiene and Toxicology*, *69*(2), pp.103-108.
[60] Pandey, S.P. and Mohanty, B., 2015. The neonicotinoid pesticide imidacloprid and the dithiocarbamate fungicide mancozeb disrupt the pituitary–thyroid axis of a wildlife bird. *Chemosphere*, *122*, pp.227-234.

The other four neonicotinoids have not completed EDSP Tier 1 testing and the agency states it will not complete its registration review of these chemicals until the agency completes its EDSP FFDCA § 408(p) determination. It is important for the agency to include all other scientifically relevant information along with the full EDSP Tier 1 testing in its final determinations.

Conclusions

EPA has determined unequivocally that neonicotinoids pose risks to the environment that cannot be acceptably mitigated in any long-term, sustainable way. The agency in its proposed interim decisions for these chemicals identifies several uses for imidacloprid, clothianidin, and dinotefuran that are necessary to be cancelled. However, other uses for these neonicotinoids and for thiamethoxam and acetamiprid, the agency is only proposing limited mitigation measures or even no mitigation. The agency's benefits assessment does not adequately consider the many negative externalities, such as loss of pollinators and ecosystem services from impaired habitats, increased insect resistance and crop loss, loss of beneficials and compromised biocontrol, and diminished benefits because of ample availability of alternatives. Given the frequency of detection in U.S. waterways, soil, and plants the acute and recognized chronic risks posed to pollinators, aquatic invertebrates, vertebrate wildlife, and human health, this is pitifully insufficient and we urge EPA to quickly cancel all remaining neonicotinoid uses. Additional data to address existing uncertainties and gaps will not alter nor lessen the environmental and health risks already unmistakably recognized.

Respectfully,

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Beyond Pesticides
City of Boulder, Colorado
Central Maryland Beekeepers Association
Farmworker Association of Florida
Friends of the Earth
Hawaii Alliance for Progressive Action
Herbicide-Free Campus
Kansas Rural Center
LEAD for Pollinators
Maryland Pesticide Education Network
National Latino Farmers & Ranchers Trade Association
Northeast Organic Farming Association - Massachusetts Chapter
Northwest Center for Alternatives to Pesticides
Organic Consumers Association
People and Pollinators Action Network
Toxic Free NC