

April 30, 2020
Re: EPA-HQ-OPP-2012-0329; 2011-0865;
2011-0920; 2008-0844; 2011-0581

Mary Reaves
Acting Director, Pesticide Re-Evaluation Division
Office of Pesticide Programs
United States Environmental Protection Agency
1200 Pennsylvania Avenue, N.W
Washington DC, 20004

Dear Acting Director Reaves,

The Endocrine Society appreciates the opportunity to comment on the Proposed Interim Decisions for the neonicotinoid pesticides acetamiprid, clothianidin/thiamethoxam, dinotefuran and imidacloprid. Founded in 1916, the Endocrine Society is the world's oldest, largest, and most active organization dedicated to the understanding of hormone systems and the clinical care of patients with endocrine diseases and disorders. Our membership of nearly 18,000 includes researchers who are advancing our understanding of the effects of exposures to chemicals that interfere with hormone systems, also known as endocrine-disrupting chemicals (EDCs). We are concerned about the endocrine effects of the neonicotinoid pesticides under review, particularly on the developing thyroid gland; **we ask that these pesticides be reviewed together as a cumulative assessment group.**

There is a substantial and increasing body of literature linking exposure to neonicotinoid pesticides and developmental thyroid toxicity in wildlife^{1,2,3} and in EPA's own laboratory assessments⁴. Consistent with current scientific understanding of the properties of hormones and the endocrine system, these chemicals may have effects at extremely low doses and display non-monotonic dose-responses (NMDR)⁵. Consequently, there may in fact be no 'safe' level for these chemicals. Because these pesticides as a class display similar features and effects on the thyroid during

¹ Berheim EH, et al., Effects of Neonicotinoid Insecticides on Physiology and Reproductive Characteristics of Captive Female and Fawn White-tailed Deer. *Sci. Rep.* 2019 Mar; 14;9(1):4534, available at <https://go.nature.com/2Q119Zf>.

² Wang Y, et al., Unraveling the toxic effects of neonicotinoid insecticides on the thyroid endocrine system of lizards. *Environ Pollut.* 2020 Mar;258:113731. doi: 10.1016/j.envpol.2019.113731

³ Pandey SP, Mohanty B. The neonicotinoid pesticide imidacloprid and the dithiocarbamate fungicide mancozeb disrupt the pituitary-thyroid axis of a wildlife bird. *Chemosphere.* 2015 Mar;122:227-234. doi: 10.1016/j.chemosphere.2014.11.061.

⁴ EPA 2002. Imidacloprid - Report of the Hazard Identification Assessment Review Committee. October 31, 2002. TXR#0051292

⁵ Caron-Beaudoin, E., et al., Effects of Neonicotinoids on Promoter-Specific Expression and Activity of Aromatase (CYP19) in Human Adrenocortical Carcinoma (H295R) and Primary Umbilical Vein Endothelial (HUVEC) Cells. *Toxicol Sci.* 2016 Jan;149(1):134-44. doi: 10.1093/toxsci/kfv220.



development, EPA should consider these chemicals together as a cumulative assessment group. This would also enable EPA to more effectively incorporate the peer-reviewed scientific literature across this class of chemicals.

While we appreciate that EPA will screen these chemicals for effects through the Endocrine Disruptors Screening Program (EDSP), we note that the current EDSP testing battery does not evaluate potential adverse effects of thyroid disruption. EPA must therefore include a thorough assessment of the peer-reviewed scientific literature on the toxic effects of these chemicals consistent with established principles of endocrine science, including the potential for NMDR and the possibility that no threshold for safety exists.

In summary, the data linking early-life neonicotinoid exposure to thyroid disruption is very concerning and EPA should conduct their review of these chemicals, incorporating the latest peer-reviewed science, as a cumulative assessment group. Thank you for considering our comments, if we can be of any further assistance please contact Joseph Laakso, PhD, Director of Science Policy at jlaakso@endocrine.org.

Sincerely,

Gary D. Hammer, MD, PhD
President
Endocrine Society