

Michael Goodis
Acting Director, Pesticide Re-Evaluation Division,
Office of Pesticide Programs.
United States Environmental Protection Agency
1200 Pennsylvania Ave NW
Washington, DC 20460

RE: EPA-HQ-OPP-2015-0794-000

October 03, 2016

Dear Dr. Goodis,

The Endocrine Society appreciates the opportunity to comment on the draft ecological risk assessments for the registration review of atrazine, simazine, and propazine. 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 over 18,000 includes researchers who are making significant contributions to the advancement of knowledge in toxicology, especially in the field of endocrine-disrupting chemicals (EDCs), a class of chemicals that includes chlorotriazine herbicides. Although we do not take a position on specific restrictions or regulatory decisions on the chemicals in question, scientific evidence has accumulated since the last re-registration that strongly implicates atrazine and other chlorotriazines in a range of human health impacts.

In summary, the most recent scientific studies have shown that:

- Atrazine is a known endocrine disruptor that can alter hormone levels in wildlife and in a variety of animal models of human health and disease;
- Atrazine can impact neurological function and reproductive health in animals;
- Reproductive effects in humans may include risk of preterm birth;
- The effects of atrazine and related chemicals may depend on timing of exposure; and
- Low-dose effects (e.g. those occurring below the doses that have been evaluated using traditional regulatory approaches including guideline assays) must be considered.

On September 28, 2015, the Endocrine Society released an update to the breakthrough 2009 Scientific Statement on EDCs. The updated statement (EDC-2) examined the state of scientific evidence on EDCs and risks posed to human health due to exposures to EDCs. EDC-2 focused on topic areas for which the evidence was strongest. This comprehensive assessment of the scientific literature concluded that recent research has led "to a much fuller understanding of the endocrine principles by which EDCs act, including nonmonotonic dose-responses, low-dose effects, and developmental vulnerability.¹" A copy of the full scientific statement will also be uploaded to the docket as a separate attachment.

¹ Gore, AC, et al., "EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals." *Endocr Rev.* 2015 Dec; 36(6): E1-E150.



In 2009, Atrazine was highlighted in the Endocrine Society's first scientific statement as an EDC that influenced estrogen levels by stimulating aromatase², an enzyme that affects the metabolism of estrogen. New research over the past decade presented in EDC-2 has confirmed these findings in several animal models and has shed additional light on the reproductive health consequences of atrazine and simazine exposure. For example, both atrazine and simazine can affect pubertal timing, and studies in humans show an association between atrazine exposure and menstrual irregularities and a potential association with preterm birth. Additionally, atrazine has been shown to adversely affect the function of the pituitary gland, and is associated with significant neurodevelopmental effects in mice.

As with other EDCs, principles of endocrinology need to be taken into account when assessing atrazine's effects. As described in EDC-2, the effects of atrazine and related chemicals depend on the timing of exposure and these chemicals may also have effects at extremely low doses. Regulatory decision-making processes will therefore need to take into account critical developmental windows and periods of heightened vulnerability to exposures. Regulations should be designed to protect the most vulnerable populations, including but not limited to fetuses, children, and pregnant women, from irreversible effects. Decisions should also be based on comprehensive data covering both low-level and high-level exposures, including cumulative and mixture effects. The default approach to assessing atrazine and related chemicals must include low-dose studies comparable with human exposures, doses well below those ranges used for traditional toxicity testing.

We ask that the EPA consider these and other relevant research findings in your registration review of atrazine, simazine, and propazine. We believe that considering the science presented in EDC-2 will help ensure that pesticide registrations are based on the most up to date scientific knowledge of the effects of pesticides on human and environmental health. Thank you for considering the Endocrine Society's comments. If we can be of further assistance, please contact Joseph Laakso, Associate Director of Science Policy, at jlaakso@endocrine.org.

Sincerely,

Henry Kronenberg, MD
President
Endocrine Society

² Diamanti-Kandarakis E, Bourguignon JP, Giudice LC, et al. "Endocrine-disrupting chemicals: an Endocrine Society Scientific Statement." *Endocr Rev.* 2009;30:293–342.