

July 06, 2020

Science Advisory Committee on Chemicals
U.S. Environmental Protection Agency
Office of Science Coordination and Policy (7201M)
1200 Pennsylvania Ave. NW.
Washington, DC 20460-0001

Re: EPA-HQ-OPPT-2019-0502

“Toxic Substances Control Act (TSCA) Science Advisory Committee on Chemicals Review of Risk Evaluation for Perchloroethylene”

Dear Members of the Science Advisory Committee on Chemicals,

On behalf of the Endocrine Society, thank you for the opportunity to comment on the draft risk evaluation for perchloroethylene (PCE). 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 our understanding of interference with hormonal systems by manufactured chemicals, called endocrine-disrupting chemicals (EDCs). In addition to the well-characterized hazards posed by PCE on various endpoints described in the draft risk assessment, new and emerging evidence demonstrates that PCE can act as an EDC by impacting gene networks and hormonal pathways. These findings support the determination that PCE poses an unreasonable risk to human health, and we urge EPA to carefully consider effects on endocrine systems during preparation of the final risk assessment for PCE and related chemicals.

While some harmful effects of PCE exposure have been documented for years, studies have only recently begun to examine the endocrine-disrupting effects of this chemical. A recent study (Alofe 2019) provided strong evidence that PCE can interact directly with the estrogen receptor and impact estrogen, progesterone, and glucocorticoid signaling pathways. Consistent with principles of endocrinology and the latest science on EDCs, the effects of PCE were seen at very low levels and with the ability to produce additive effects in combination with other chemical exposures. Furthermore, subsequent studies (Burman 2020) reinforce the fact that EDCs acting on these pathways can have widespread effects, which can differ depending on the cellular environment and genetic sex.

We are concerned that the draft risk assessment does not properly account for the entire range of health effects that could be caused by PCE due to endocrine disruption. We appreciate that



numerous studies have characterized neurological effects due to PCE exposure, supporting the determination of an unreasonable risk to human health; however, PCE has also been implicated in cancer and negative impacts on reproductive health due to chronic, long-term exposure. Given new evidence regarding PCE's ability to impact hormonal systems, EPA should pursue a more complete characterization of PCE with careful attention to endpoints that are relevant to endocrine systems and associated diseases. We note with concern that exposures to PCE continue after use and lead to groundwater and soil contamination, resulting in additional public exposure that should be captured by the risk assessment. Absent additional evidence demonstrating safety, EPA should pursue actions that minimize human exposure to PCE with careful attention to vulnerable populations, such as pregnant women and children.

In conclusion, recent evidence published after the initiation of the PCE risk assessment demonstrates that PCE is an endocrine-disrupting chemical with the potential for widespread effects on endocrine sensitive tissues. In addition to neurological effects, these findings and other evidence of harms support an aggressive approach by EPA in mitigating harms due to PCE exposure. Final decisions by EPA should add additional safety margins, acknowledging the potential for mixture effects where PCE and related chemicals can act synergistically on the same pathway to produce adverse effects.

Thank you for considering the Endocrine Society's comments. If we can be of further assistance, please contact Joseph Laakso, PhD, Director of Science Policy at jlaakso@endocrine.org.

Sincerely,

Gary D. Hammer, MD, PhD
President
Endocrine Society

APPENDIX: Additional references submitted to regulations.gov

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<https://doi.org/10.1016/j.envint.2019.104969>
- A. Burman, et al., *Hum Genomics* May 24;14(1):19 (2020)
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