

July 18, 2018

EDC science has advanced rapidly in the years following the 1999 European strategy. As described in the Endocrine Society's new Scientific Statement on EDCs, we have much stronger knowledge about how EDCs contribute to a range of diseases<sup>1</sup>. Certain substances from groups like bisphenols and phthalates have been shown to alter gene-environment interactions via physiological, cellular, molecular, and epigenetic changes, thereby producing effects in exposed individuals as well as their descendants. Causal links between exposure and manifestation of disease are substantiated by experimental animal models and are consistent with correlative epidemiological data in humans. There are also ecological concerns from endocrine disruption that should be considered. For instance, EDCs can cause depletion of fish populations, potentially affecting local economies<sup>2</sup>. These discoveries make the development of an updated European strategy crucial.

We are concerned that the roadmap refers to “scientific uncertainty” as a cause of potential concern and confusion among stakeholders and the public. This assessment would be mistaken; open questions are a feature of every field of research, yet there is a scientific consensus among endocrinologists and other researchers in the field that EDCs pose health risks. Citizens are right to be concerned about harms from EDCs; public interest is amplified not by scientific uncertainty over effects, but rather the steady increase in scientific knowledge and education from public health groups and medical/scientific organizations. Recent reports released by the United Nations Environment Programme identified dozens of EDCs and hundreds more potential EDCs, illustrating the scope of the problem and the urgent need for further action<sup>3</sup>. Further, the contribution of EDCs to disease burden is increasingly measured and understood quantitatively<sup>4</sup>. Other EDCs or potential EDCs are likely to exist and may be included in future communications.

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<sup>1</sup> A. C. Gore, et al.; EDC-2: The Endocrine Society's Second Scientific Statement on Endocrine-Disrupting Chemicals, *Endocrine Reviews*, Volume 36, Issue 6, 1 December 2015, Pages E1–E150, <https://doi.org/10.1210/er.2015-1010>

<sup>2</sup> United States Geological Survey, Toxic Substances Hydrology Program. “Tackling Fish Endocrine Disruption” at [https://toxics.usgs.gov/highlights/fish\\_endocrine\\_disruption.html](https://toxics.usgs.gov/highlights/fish_endocrine_disruption.html) Accessed July 17, 2018.

<sup>3</sup> United Nations Environment Programme “Scientific knowledge of endocrine disrupting chemicals” at <https://www.unenvironment.org/explore-topics/chemicals-waste/what-we-do/emerging-issues/scientific-knowledge-endocrine-disrupting> Accessed July 17, 2018.

<sup>4</sup> Leonardo Trasande et al.; Estimating Burden and Disease Costs of Exposure to Endocrine-Disrupting Chemicals in the European Union, *The Journal of Clinical Endocrinology & Metabolism*, Volume 100, Issue 4, 1 April 2015, Pages 1245–1255, <https://doi.org/10.1210/jc.2014-4324>



The Roadmap refers to a “demand for clear and comprehensive information [EU citizens] can rely on”. A comprehensive approach to EDCs should account for gaps in public health protection, and ensure that EDCs in food packaging materials, personal care products, and other consumer goods are substituted with safer alternatives<sup>5</sup>. This should also include consideration for vulnerable/susceptible populations such as pregnant women, adolescents, and workers with elevated exposures. A goal of “comprehensive and clear information” cannot be a substitute for taking the necessary regulatory actions justified by scientific knowledge and a precautionary approach.

As with all scientific fields, EDC issues are complex, but issues like low-dose effects, non-monotonic dose-response, developmental origins of disease, and other features of EDCs are recognized and characterized for some individual chemicals. These areas are missing from the Roadmap and should be included as areas of study. Research will be necessary to better understand mixture and synergistic effects, and better scientific understanding of EDC effects will help accelerate regulatory decision making, but we know enough about chemicals and classes to take action now. Agencies can use systematic review frameworks to make transparent, clear, and reproducible decisions based on existing scientific literature or identify specific data needs that can inform testing efforts. A detailed understanding of mechanisms and pathways is not necessary and a lack of comprehensive details should not preclude regulatory activity to protect the public where there is evidence of adversity occurring with endocrine-mediated action.

Current regulatory practice, where restrictions may be different, or exemptions may exist depending on category of use, is not sufficiently coherent, as health impacts occur regardless of the source of exposure. Incoherent regulations may result in secondary exposures, as may have occurred for fipronil on eggs in the Netherlands<sup>6</sup>. We also recommend that the roadmap address:

- Specific measures for how legal gaps will be closed, including an approach for EDCs that includes cosmetics, food packaging materials, and other consumer products;
- Ambitious targets for identifying EDCs (consistent with some national strategies in the EU) and adoption of safer alternatives;
- Better test methods, biomonitoring, and screening - including testing requirements for sensitive endpoints that capture interference with endocrine systems and allow regulators to make informed decisions;

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<sup>5</sup> AM Andersson et al., (2016), Endocrine disruptors: we need research, biomonitoring and action. *Andrology*, 4: 556-560. doi:10.1111/andr.12244

<sup>6</sup> BBC News, “Germany recalls contaminated Dutch eggs in fipronil scare” June 12, 2018. <https://www.bbc.com/news/world-europe-44452399> Accessed July 17, 2018.



- Recognition of the need to evaluate groups of chemicals with similar properties for potential regulation to prevent regrettable substitutions, without which regulators will always remain a step behind;
- Additional scientific research to address gaps in knowledge noted above.

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

Sincerely,

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