

## Policy Decisions on Endocrine Disruptors Should Be Based on Science Across Disciplines: A Response to Dietrich *et al.*

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Abbreviations: EDC, endocrine disrupting chemical; UNEP, United Nations Environment Programme; WHO, World Health Organization.

**W**e are writing as scientists and editors of leading peer-reviewed journals that have published important contributions in the study of endocrine disrupting chemicals (EDCs). By signing this editorial, we affirm that regulatory decisions on EDCs should be made based on the best available science and expertise that involves, among others, reproductive biology, endocrinology, medicine, genetics, behavior, developmental biology, and toxicology (1). (For a complete list of Signatories and their Disclosures, see Supplemental Table 1 published on The Endocrine Society's Journals Online web site at <http://end.endojournals.org>.)

Thousands of published studies have revealed the health effects of EDCs on wildlife and laboratory animals and, moreover, have shown associations of EDCs with effects in humans. Many of these studies have been reviewed recently by The Endocrine Society, the United Nations Environment Programme (UNEP) and World Health Organization (WHO), and other independent scientists (2–5). The conclusions presented in each of these documents are extraordinarily consistent: like hormones, EDCs are active at very low doses and can induce a range of adverse health outcomes, many of which are not examined in traditional toxicology assays (1). In sum, these reports point to the conclusion that EDCs pose a global health threat.

A recent editorial signed by a number of editors of toxicology journals argues for the status quo in the regulation of EDCs (6), despite the large volume of evidence indicating that current regulations are ineffective in protecting human populations from these chemicals (4–7). As the UNEP/WHO report notes, the incidence of chronic disease is now greater than that of communicable disease; many of these diseases have an endocrine basis. Both experimental animal and epidemiology studies provide plausible causal links between EDCs and many of these diseases; for some, the data are sufficiently robust (8).

The dismissive approach to endocrine disruption science put forth by Dietrich et al (6) is unfounded, as it is neither based on the fundamental principles of how the endocrine system works and how chemicals can interfere with its normal function, nor does it consider the consequences of that interference. Their letter also ignores a growing and rigorous body of literature on both endogenous hormonal and exogenous EDC effects.

Basic scientists, clinical investigators, and physicians understand that the endocrine system's functions and responses change remarkably across the life cycle. Of particular concern is incontrovertible evidence, published more than a half century ago (9, 10), that there are critical life stages, especially during early development, when hormones dictate the differentiation and development of tissues. Any perturbation of the delicate hormonal balance,

whether due to the absence of natural hormones or the presence of exogenous hormones, can have irreversible effects on endocrine-sensitive organs. EDCs are known to upset this delicate balance.

Dietrich et al (6) also misrepresent the state of science on thresholds, stating that the evidence “clearly demonstrates the presence of a threshold for nongenotoxic compounds including EDCs.” Dietrich et al assert that their position constitutes “common sense” and that the European Commission's approach departs from common sense. They do not, however, provide scientific support for this position. Instead, they list several references (11–15) that, upon examination, do not contain data supporting their assumption but rather simply assert that the assumption is true. They also fail to address the considerable literature that speaks against that assumption (eg, Refs 16–20). Finally, they argue that structuring regulation upon the assumption of no threshold “will set an unforeseen precedence [sic].” This is simply and demonstrably not true. The assumption of no threshold has been widely used, for many years, in the regulation of genotoxic carcinogens, often based on *in vitro* data. We believe extending this precedent to EDCs is supported by the science (19).

Furthermore, we hold that common sense dictates that policies, particularly those in which public health is at stake, should be based on scientific evidence obtained from the world's leading researchers and should derive from a more evolved, modern understanding of the science, rather than on older, outdated concepts and data taught in classrooms 20 or more years ago. The European Commission policy, by that standard, does represent “common sense.”

Further, the US National Academy of Sciences has concluded that because of the range of susceptibility to environmental chemicals across the population, such as that from age, preexisting conditions, and genetic variation, and because there are documented exposures to multiple chemicals, including EDCs, in the population, it is more appropriate to consider lack of thresholds at a population level (16).

Many toxicologists have developed rigorous research programs on EDCs that incorporate endocrinological principles, including two former presidents of the Society of Toxicology, Cheryl Walker and Linda Birnbaum. They and many other toxicologists do work in this area and report results that have contributed to the breadth and depth of concern about EDCs as a global public health threat. The *ad hominem* attacks in Dietrich et al (6) do nothing to advance science or opportunities to protect public health; we refer readers to two additional responses to their editorial that support this point of view (21, 22). We need the fields of toxicology, endocrinology and other stakeholders to work together to address these issues, not engage in recriminations.

Policymakers in Europe and elsewhere should base their decisions on science, not on assumptions based on principles that arose out of research on chemicals that are not EDCs. The letter by Dietrich et al does the European Commission, science, including the field of toxicology, and most importantly, public health, a profound disservice.

## Acknowledgments

The following is the list of signatories. The complete list of their affiliations and disclosure information is provided in Supplemental Table 1.

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