

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

A.C. Gore*, J. Balthazart, D. Bikle, D.O. Carpenter, D. Crews, P. Czernichow, E. Diamanti-Kandarakis, R.M. Dores, D. Grattan, P.R. Hof, A.N. Hollenberg, C. Lange, A.V. Lee, J.E. Levine, R.P. Millar, R.J. Nelson, M. Porta, M. Poth, D.M. Power, G.S. Prins, E.C. Ridgway, E.F. Rissman, J.A. Romijn, P.E. Sawchenko, P.D. Sly, O. Söder, H.S. Taylor, M. Tena-Sempere, H. Vaudry, K. Wallen, Z. Wang, L. Wartofsky, and C.S. Watson

Gustavus & Louise Pfeiffer Professor of Pharmacology & Toxicology, The University of Texas, Austin, TX (A.C.G.); University of Liege, GIGA Neurosciences, Belgium (J.B.); VA Medical Center and University of California, San Francisco, CA (D.B.); Institute for Health and the Environment, University at Albany, State University of New York, Albany, NY (D.O.C.); Section of Integrative Biology, University of Texas, Austin, TX (D.C.); Professor Emeritus of Pediatrics, University of Paris, Paris, France (P.C.); Medical School University of Athens, Sotiria Hospital, Athens, Greece (E.D.-K.); Department of Biological Sciences, University of Denver, Denver, CO (R.M.D.); Department of Anatomy, University of Otago, Otago, New Zealand (D.G.); Icahn School of Medicine at Mt Sinai, NY, New York (P.R.H.); Harvard Medical School, Boston, MA (A.N.H.); University of Minnesota Masonic Cancer Center, Minneapolis, MN (C.D.); University of Pittsburgh Cancer Institute and Magee Women's Research Institute, Pittsburgh, PA (A.V.L.); Wisconsin National Primate Research Center, Madison, WI (J.E.L.); UCT/MRC Receptor Biology Unit, University of Cape Town, Cape Town, S Africa (R.P.M.); Department of Neuroscience, The Ohio State University Wexner Medical Center, Columbus, OH (R.J.N.); Hospital del Mar Institute of Medical Research (IMIM) and School of Medicine, Universitat Autònoma de Barcelona, Barcelona, Spain (M.Porta); Uniformed Services University of the Health Sciences, Bethesda, MD (M.Poth); Department of Biosciences, Universidade do Algarve, Faro, Portugal (D.M.P.); Department of Physiology and Biophysics, University of Illinois, Chicago; Illinois (G.S.P.); Department of Medicine, University of Colorado School of Medicine, Denver, CO (E.C.R.); Department of Biochemistry and Molecular Genetics, School of Medicine, University of Virginia, Charlottesville, VA (E.F.R.); Division of Medicine, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands (J.A.R.); Laboratory of Neuronal Structure and Function The Salk Institute, La Jolla, CA (P.E.S.); Queensland Children's Medical Institute, University of Queensland, Royal Children's Hospital, Brisbane, Australia (P.D.S.); Karolinska Institutet at Karolinska University Hospital Solna, Stockholm, Sweden (O.S.); Department of Obstetrics, Gynecology & Reproductive Sciences, Yale School of Medicine, New Haven, CT (H.S.T.); Department of Cell Biology and Physiology, University of Cordoba, Cordoba, Spain (M.T.-S.); INSERM U982, University of Rouen, Rouen, France (H.V.); Department of Psychology and Yerkes National Primate Research Center, Emory University, Atlanta, GA (K.W.); Department of Psychology and Neuroscience, FL State University, Tallahassee, FL (Z.W.); Department of Medicine; Washington Hospital Center, WA, DC; Department of Biochemistry and Molecular Biology, University of Texas Medical Branch, Galveston, TX (C.S.W.)

We 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 the complete list of Signatories, Journal Associate Editors, Additional Signatories, including edi-

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torial board memberships, and Disclosures and Conflict of Interest Statements, see Appendix 1).

Thousands of published studies have revealed 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 also misrepresent the state of science on thresholds (6), stating that the evidence “clearly demonstrates the presence of a threshold for nongenotoxic compounds including EDCs.” Dietrich and colleagues 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 upon *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 U.S. National Academy of Sciences has concluded that because of the range of susceptibility to environmental chemicals across the population, such as from age, pre-existing conditions, and genetic variation, and because there are documented exposures to multiple chemicals, including EDCs, in the population, that 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 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 upon science, not assumptions based upon 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.

Signatories

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25. Frederick vom Saal, Ph.D., *Endocrine Disruptors*
26. Zuoxin Wang, Ph.D., *Hormones and Behavior*
27. Wade V. Welshons, Ph.D., *Endocrine Disruptors*
28. R. Thomas Zoeller, Ph.D., *Endocrine Disruptors*

Additional Signatories

1. Benson T Akingbemi, Ph.D.
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3. Scott M. Belcher, PhD
4. Dr. Fiorella Belpoggi, Ph.D.
5. Carl-Gustaf Bornehag, Ph.D.
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50. Laura Vandenberg, Ph.D.
51. Catherine VandeVoort, Ph.D.
52. Martin Wagner, Ph.D.
53. Hong-Sheng Wang, Ph.D.
54. Bernard Weiss, Ph.D.
55. Teresa Woodruff, Ph.D.
56. Tracey Woodruff, Ph.D.

Acknowledgments

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

Address all correspondence and requests for reprints to: * Andrea C. Gore, Ph.D., Editor-in-Chief, *Endocrinology*, Gustavus, Louise Pfeiffer Professor of Pharmacology, Toxicology, The

University of Texas at Austin, Austin, TX, 78712. Email: andrea.gore@austin.utexas.edu.

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