EDITORIAL

Policy decisions on endocrine disruptors should be based on science across disciplines: a response to Dietrich et al.


1Division of Pharmacology and Toxicology, The University of Texas, Austin, Texas 78712, USA, 2GIGA Neurosciences, University of Liege, B–4000 Liege, Belgium, 3VA Medical Center, University of California, San Francisco, California 94143, USA, 4Institute for Health and the Environment, University at Albany, State University of New York, Albany, New York 12222, USA, 5Section of Integrative Biology, University of Texas, Austin, Texas 78712, USA, 6Professor Emeritus of Pediatrics, University of Paris, 75006 Paris, France, 7Medical School, Sotiria Hospital, University of Athens, Athens 115 27, Greece, 8Department of Biological Sciences, University of Denver, Denver, Colorado 80208, USA, 9Department of Anatomy, University of Otago, North Dunedin 9016, New Zealand, 10Kehan School of Medicine of Mount Sinai, New York, New York 10029, USA, 11Harvard Medical School, Beth Israel Deaconess Medical Center, Boston, Massachusetts 02115, USA, 12Masovic Cancer Center, University of Minnesota, Minneapolis, Minnesota 55455, USA, 13Cancer Institute and Magee Women’s Research Institute, University of Pittsburgh, Pittsburgh, Pennsylvania 15213, USA, 14Wisconsin National Primate Research Center, Madison, Wisconsin 53715, USA, 15UCT/MRC Receptor Biology Unit, University of Cape Town, Cape Town, South Africa, 16Department of Neuroscience, Wexner Medical Center, The Ohio State University, Columbus, Ohio 43210, USA, 17School of Medicine, Hospital del Mar Institute of Medical Research (IMIM), Universitat Autònoma de Barcelona, 08004 Barcelona, Spain, 18Uniformed Services University of the Health Sciences, Bethesda, Maryland 20814, USA, 19Department of Biosciences, Universidade do Algarve, 8005-139 Faro, Portugal, 20Department of Physiology and Biophysics, University of Illinois, Chicago, Illinois 60612, USA, 21Department of Medicine, School of Medicine, University of Colorado, Denver, Colorado 80208, USA, 22Department of Biochemistry and Molecular Genetics, School of Medicine, University of Virginia, Charlottesville, Virginia 22906, USA, 23Division of Medicine, Academic Medical Center, University of Amsterdam, 1012 WX Amsterdam, The Netherlands, 24Laboratory of Neuronal Structure and Function, The Salk Institute, La Jolla, California 92037, USA, 25Queensland Children’s Medical Institute, Royal Children’s Hospital, University of Queensland, Brisbane, Queensland 4000, Australia, 26Karolinska Institutet, Karolinska University Hospital, 171 76 Solna, Stockholm, Sweden, 27Department of Obstetrics, Gynecology and Reproductive Sciences, Yale School of Medicine, New Haven, Connecticut 06510, USA, 28Department of Cell Biology and Physiology, University of Córdoba, 14071 Córdoba, Spain, 29Institut National de la Sante et de la Recherche Medicale U982, University of Rouen, 76821 Rouen, France, 30Department of Psychology, Yerkes National Primate Research Center, Emory University, Atlanta, Georgia 30322, USA, 31Department of Psychology and Neuroscience, Florida State University, Tallahassee, Florida 32306, USA, 32Department of Medicine, Washington Hospital Center, Washington, District of Columbia 20010, USA and 33Department of Biochemistry and Molecular Biology, University of Texas Medical Branch, Galveston, Texas 77555, USA

(Correspondence should be addressed to A C Gore; Email: andrea.gore@austin.utexas.edu)

European Journal of Endocrinology 169 E1–E4

We are writing as scientists, editors and leaders of 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 Supplementary Table 1, see section on supplementary data given at the end of this article published on The Endocrine Society’s Journals Online web site (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, 3, 4, 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, 5, 6, 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, 12, 13, 14, 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 (e.g. references (16, 17, 18, 19, 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 not represent ‘common sense’.

Further, the USA 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.

**Signatories**

**Journal Editors-in-Chief**

1. Jacques Balthazart, PhD, Frontiers in Neuroendocrinology
2. David O Carpenter, MD, Reviews on Environmental Health.
4. Donald B DeFranco, PhD, Molecular Endocrinology
5. Robert M Dores, PhD, General and Comparative Endocrinology
6. Andrea C Gore, PhD, Endocrinology
7. Peter D Sly, MBBS, FRACP, MD, DSc, Reviews on Environmental Health.
8. Jon E Levine, PhD, Frontiers in Neuroendocrinology
9. Deborah M Power, PhD, General and Comparative Endocrinology
10. Carol Lange, PhD, Hormones and Cancer.
11. E Chester Ridgway, MD, MACP, Endocrine Reviews.
12. Robert P Millar, PhD, FRSE, Endocrine Science
13. Hubert Vaudry, PhD, Dr Sci, Frontiers in Neuroendocrine Science; also Senior Editor, Journal of Neuroendocrinology; Associate Editor, Hormone and Metabolic Research; Associate Editor, General and Comparative Endocrinology; and Associate Editor, Peptides.
14. Cheryl S Watson, PhD, Endocrine Disruptors.
Journal Associate Editors

1. Åke Bergman, PhD, Archives of Environmental Contamination and Toxicology; Environmental Science and Pollution Research.
2. Daniel Bikle, MD, PhD, Endocrinology.
3. Barbara A Cohn, PhD, Endocrine Disruptors.
4. David Crews, PhD, Endocrine Disruptors; Journal of Experimental Zoology; Ecological Genetics and Physiology; Sexual Development; Epigenetics.
5. Peter L DeFur, PhD, Endocrine Disruptors.
6. Evanthia Diamanti-Kandarakis, MD, PhD, European Journal of Endocrinology.
7. Anthony N Hollenberg, MD, Endocrinology.
8. Susan Jobling, PhD, Endocrine Disruptors.
9. Jun Kanno, MD, PhD, Environmental Health Perspectives.
10. Carolyn Klinge, PhD, Endocrine Disruptors.
11. B Paige Lawrence, PhD, Endocrine Disruptors.
12. Adrian V Lee, PhD, Endocrinology.
13. J P Myers, PhD, Endocrine Disruptors.
14. Randy J Nelson, PhD, Endocrine Disruptors.
15. Miquel Porta, MD, MPH, PhD, Journal of Epidemiology and Community Health; European Journal of Clinical Investigation; European Journal of Epidemiology.
17. Gail S Prins PhD, Endocrinology; Andrology.
18. Emilie F Rissman, PhD, Endocrinology.
19. Paul E Sawchenko, PhD, Journal of Comparative Neurology.
20. Olle Söder, MD, PhD, Hormone Research in Pediatrics.
22. Shanna Swan, PhD, Endocrine Disruptors.
24. Manuel Tena-Sempere, MD, PhD, Endocrinology.
25. Frederick vom Saal, PhD, Endocrine Disruptors.
26. Zuoxin Wang, PhD, Hormones and Behavior.
27. Wade VWelshons, PhD, Endocrine Disruptors.
28. R Thomas Zoeller, PhD, Endocrine Disruptors.

Additional Signatories

1. Benson T Akingbemi, PhD.
2. Koji Arizono, PhD.
3. Scott M Belcher, PhD.
4. Fiorella Belpoggi, PhD.
5. Carl-Gustaf Bornemag, PhD.
6. Jean-Pierre Bourguignon, MD, PhD.
7. Terry R Brown, PhD.
8. Ernesto Burgio, MD.
9. Terrence J Collins, PhD.
10. D Andrew Crain, PhD.
11. Barbara Demeneix, PhD.
12. Rodney R Dietert, PhD.
13. Loretta Doan, PhD.
14. Thea M Edwards, PhD.
15. Mariana F Fernandez, PhD.
16. R William Field, PhD, MS.
17. Linda C Giudice, MD, PhD.
18. Louis J Guillette, PhD.
19. Y Leon Guo, MD, PhD, MPH.
20. Tyrone Hayes, PhD.
21. Andrea Hinwood, PhD.
22. C Vyvyan Howard, MB, ChB, PhD, FRC Path.
23. Eric R Hugo, PhD.
24. Patricia Hunt, PhD.
25. Taisen Iguchi, PhD.
26. Richard J Jackson, MD, MPH, AIA (Hon), ASLA (Hon).
27. Patricia Joseph-Bravo, PhD.
28. Hans Laufer, PhD.
29. Duk-Hee Lee, MD, PhD.
30. Rachel Morello-Frosch, PhD, MPH.
31. Jane Muncke, PhD.
32. Angel Nadal, PhD.
33. David O Norris, PhD.
34. Jörg Oehlmann, PhD.
35. Nicolas Olea, MD, PhD.
36. Edward F Orlando, PhD.
37. Vasantha Padmanabhan, PhD.
38. Paola Palanza, PhD.
39. Stefano Parmigiani, PhD.
40. Donald W Pfaff, PhD.
41. Beverly S Rubin, PhD.
42. Joan V Ruderman, PhD.
43. Arnold Schecter, MD, MPH.
44. Toshi Shioda, MD, PhD.
45. Martin Scheringer, PhD.
46. Niels E Skakkebaek, MD.
47. Howard M Snyder III, MD.
48. Carlos Sönnenschein, MD.
49. Richard W Stahlhut, MD, MPH.
50. Laura Vandenberg, PhD.
51. Catherine VandeVoort, PhD.
52. Martin Wagner, PhD.
53. Hong-Sheng Wang, PhD.
54. Bernard Weiss, PhD.
55. Teresa Woodruff, PhD.
56. Tracey Woodruff, PhD.

Supplementary data
This is linked to the online version of the paper at http://dx.doi.org/10.1530/EJE-13-0763.

Acknowledgments
The following is the list of signatories. The complete list of their affiliations and disclosure information is provided in Supplemental Table 1 (see section on supplementary data given at the end of this article).

References
1 American Society of Human Genetics, American Society for Reproductive Medicine, Endocrine Society, Genetics Society of America, Society for Developmental Biology, Society for Pediatric


8 Birnbaum LS. Environmental chemicals: evaluating low-dose effects. *Environmental Health Perspectives* 2012 **120** A143–A144. (doi:10.1289/ehp.1205179)

9 Phoenix CH, Goy RW, Gerall AA & Young WC. Organizing action of prenatally administered testosterone propionate on the tissues mediating mating behavior in the female guinea pig. *Endocrinology* 1959 **65** 369–382. (doi:10.1210/endo-65-3-369)


15 Romberg LR & Goodman JE. Low-dose effects and nonmonotonic dose–responses of endocrine disrupting chemicals: has the case been made? *Regulatory Toxicology and Pharmacology* 2012 **64** 130–133. (doi:10.1016/j.yrtph.2012.06.015)


