EDC Criteria and next steps: A scientific perspective

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Outline

• The Endocrine Society – Who we are and how we are involved
  • My research and background

• The Guidance Document for Implementing the EDC criteria – What does the science say and what are the gaps?

• What Is Needed:
  • A revised EU strategy for EDCs
  • Additional investment in research
The Endocrine Society

- Over 18,000 members from over 120 countries
- Basic researchers, clinical scientists, clinicians in practice
- We unite, lead, and grow the endocrine community to accelerate scientific breakthroughs and improve health worldwide
- Involved in EU EDC Criteria process since 2013
EDCs are not like other chemicals

- Low dose effects, no threshold
- Windows of vulnerability - foetus & children
- Developmental origin of adult disease
- Mixtures: on average every baby born is exposed to over 100 potential EDCs
EDCs have been linked by epidemiology and experiment to multiple non-infectious diseases

- EDC Science has advanced rapidly in recent years
- [www.endocrine.org/edc](http://www.endocrine.org/edc)
- Better regulation needed to protect public health
My own focus: Thyroid EDCs & Brain Development

- Since 2001 - asked to represent France on OECD chemical testing committees
- Co-founded Watchfrog 2005
- Published many papers on thyroid disruption and brain development
- Major review in 2018

REVIEW
Thyroid disrupting chemicals and brain development: an update
Bilal B Mughal, Jean-Baptiste Fini and Barbara Demeneix
My knowledge and concern led to:

- My writing two single author books
- The CNRS medal for innovation in 2014
EDCs present in maternal blood are also found in amniotic fluid and affect thyroid hormone signaling. A mixture of 15 common chemicals at levels found in human amniotic fluid alter:

- Thyroid hormone signaling in an animal model
- Brain gene expression
- Behaviour
EU EDC Criteria and Guidance Document

- Gaps and uncertainties remain and need to be addressed:
  - Potential for false-negatives is high
  - Need to apply criteria to other chemicals and other endocrine systems (besides androgen, estrogen and thyroid)
  - Certain categories require **better test methods** - hence H2020 call for **screening**
  - Focus on thyroid, neurodevelopment, metabolism, female reprod, non-genomic carcinogens

• Scope of guidance is too limited
  • EDCs can act on a wide variety of receptors and pathways beyond what is covered in guidance—must eventually cover other hormone pathways involved in for example metabolism, body weight, and insulin action/secretion.

• Required level of proof too high to protect health
  • *If an adverse effect is observed and endocrine-mediated action observed, this should be sufficient to support the definition of an EDC.*
  • In this case detailed study of ED action and mechanisms should not be required and would delay precautionary action.
We Need Better Public Health Protection

• New scientific information has been developed since the original 1999 European Strategy on EDCs
• EDCs are ubiquitous, and many potential sources of exposure are not covered in biocides and pesticides law.
• Still have gaps in cosmetics legislation and food packaging regulations
A New Strategy is Required

- Therefore, the EU Strategy on EDCs should be rapidly updated and revised,
  - Prioritize new scientific information developed in recent years
  - Aim to minimize exposure to hazardous EDCs throughout the environment and in consumer products
- The European Commission and agencies should support further research into EDCs
  - See: Hormone disrupting chemicals: slow progress to regulation  BMJ 2018; 361
    - [https://doi.org/10.1136/bmj.k1876](https://doi.org/10.1136/bmj.k1876) (Published 30 April 2018)
Additional Research is Necessary

Example research opportunities:

• Evaluation of EDC exposures and outcomes at different life stages
• Research on genetic susceptibility and population-based differences in exposures and outcomes
• Chemical mixtures, synergistic effects of chemicals, steady-state and cumulative exposures
• Storage of EDCs in the body and effects of exercise and weight loss on EDC storage
• Longitudinal and multigenerational studies on animals and humans
• Epigenetics and endocrine-disruption crosstalk
Regulatory implications of endocrine science

- EDC effects are complex:
  - Chemicals may have different effects on different organs, or through different mechanisms, and may have different effects (e.g., sex-specific, genetics)
  - Timing of exposure matters (e.g., fetal development, adolescence)
  - Hormones act at very low concentrations
- Regulatory agencies need to address:
  Sensitivity of single endpoints; susceptible populations and vulnerability at different developmental stages; low-dose and non-monotonic dose response
Scientific Evidence for EDC Effects

- EDC Science has advanced rapidly in recent years.
- Increasing evidence links EDC exposure to a variety of adverse health outcomes, including obesity and diabetes, reproductive disorders, hormone-sensitive cancers, and neurodevelopmental disease.

www.endocrine.org/edc