



December 2013

KEY SCIENTIFIC STATEMENTS ON ENDOCRINE DISRUPTING CHEMICALS (EDCs)

NB: A separate CHEM Trust document, entitled “EU milestones on endocrine disrupting chemicals (EDCs): Official commitments and legislative action on EDCs in the EU” covers official meetings and documents orchestrated by the European Commission (EC) to underpin decision making in the EU. Therefore, for example, the Weybridge report and the Kortenkamp et al. report on the “State of the Art of the Assessment of Endocrine Disruptors”, both of which were orchestrated by the EC, are not covered in this document.

July 1991: Wingspread 1 - Consensus Statement on EDCs

The first Wingspread consensus statement, published in a book entitled “*Chemically-induced alterations in sexual development: the wildlife/human connection*”, started the alarm bells ringing about chemicals with endocrine disrupting (ED) properties. A group of concerned scientists got together to formulate a consensus statement outlining what they were certain about; what they estimated with confidence; what current models predicted; why there were uncertainties in their predictions; and their judgement.¹ Dr Theo Colborn was the inspirational person behind the Wingspread and Erice (see later) meetings, who sought to bring the science to the fore. This first Wingspread Consensus Statement is very insightful and still very relevant today.

For the full statement, see

<http://www.ourstolenfuture.org/consensus/wingspread1.htm>

December 1993: Wingspread 2 – “Environmentally Induced Alterations in Development: A Focus on Wildlife”

The scientists attending this meeting were certain of the following:

- *“Declines in a number of species and many taxa (including plants) are in progress on the North American continent. Some of these declines are related to exposure to man-made chemicals. Such declines are not solely a US or North American problem but are occurring on a global scale.*

- *There is a special cause for concern for long-lived species which may or may not (at this time) show overt signs of reproductive impairment. Examples of species that are near extirpation at the population level are those that are annually replenished by outside stock, not by intra-regional reproduction, such as Great Lakes lake trout and shoreline bald eagles, and Lake Apopka, FL alligators and turtles.*
- *Populations of many long-lived species are declining, some to the verge of extinction, without society's knowledge. The presence of breeding adults and even healthy young does not necessarily reflect a healthy population. Detailed population analysis is needed to determine whether offspring have the functional capacity to survive and reproduce.*
- *Wildlife is exposed to compounds that disrupt development of the reproductive, immune, nervous, and endocrine systems and thereby can lead to population instability. The pollutants of greatest concern affect cellular and molecular processes that regulate developmental, endocrine, and immunological functions. Hormones are natural substances that control normal development of all embryos and fetuses. Many of the contaminants mimic and/or interfere with female and male hormones, thereby modifying development and reproduction.*
- *The embryo is the most sensitive life stage of animals to the hazards posed by these chemicals.*
- *Current contamination in wildlife has reached levels in some regions at which there are known sub-lethal effects sufficient to impair populations. Unless the continuing release of man-made toxic chemicals is prohibited immediately in certain well-studied North American major aquatic systems, populations of important top predator species may become extirpated.²*

For the full statement, see

<http://www.ourstolenfuture.org/Consensus/wingspread2.htm>

February 1995: Wingspread 3 – “Chemically-induced Alterations in the Developing Immune System: The Wildlife/Human Connection”

This statement and the scientific research papers underpinning the conclusions of this third Wingspread meeting held in February 1995, were published in 1996 in Environmental Health Perspectives.³ The scientists involved in this meeting, who again included Dr Colborn, concluded amongst other things that:

- *“A competent immune system is essential for health.*
- *Experimental lab studies demonstrate that certain synthetic chemicals affect the immune system (e.g., aromatic hydrocarbons; carbamates; heavy metals; organohalogens; organophosphates; organotins; oxidant air pollutants, such as ozone and nitrogen dioxide; and polycyclic aromatic hydrocarbons). These effects are manifested as alterations in the immune system that may lead to a*

decreased quality of life. These alterations include immune modulation expressed as an increase or decrease in measured immune parameters, hypersensitivity, and autoimmunity.”

For the full statement, see

<http://www.ourstolenfuture.org/consensus/wingspreadimmune.htm>

July 1995: Wingspread 4 – “Chemically-Induced Alterations in Functional Development and Reproduction of Fishes”

This was published in 1997, but was drafted at a meeting held on 21-23 July 1995 at the Wingspread conference centre in Wisconsin.⁴ Dr Theo Colborn and her colleagues set down the state of the science on the effects of hormone disruption in fish.

For the full statement, see

<http://www.ourstolenfuture.org/Consensus/wingspreadfish.htm>

November 1995: Erice Statement

This consensus statement on "Environmental Endocrine-Disrupting Chemicals: Neural, Endocrine and Behavioral Effects"⁵ was produced under the auspices of the International School of Ethology at the Ettore Majorana Centre for Scientific Culture in Erice. Using the same format as the earlier Wingspread statements, this group of international scientists, gathered together by Dr Theo Colborn and colleagues, were certain, amongst other things, that:

- *“Endocrine-disrupting chemicals can undermine neurological and behavioral development and subsequent potential of individuals exposed in the womb or, in fish, amphibians, reptiles, and birds, the egg. This loss of potential in humans and wildlife is expressed as behavioral and physical abnormalities. It may be expressed as reduced intellectual capacity and social adaptability, as impaired responsiveness to environmental demands, or in a variety of other functional guises. Widespread loss of this in nature can change the character of human societies or destabilize wildlife populations. Because profound economic and social consequences emerge from small shifts in functional potential at the population level, it is imperative to monitor levels of contaminants in humans, animals, and the environment that are associated with disruption of the nervous and endocrine systems and reduce their production and release.”*

For the full statement, see <http://www.ourstolenfuture.org/Consensus/erice.htm>

1996: Publication of the book “Our Stolen Future” by Theo Colborn, Dianne Dumanoski and John Peterson Myers

Although not a scientific consensus statement, nor a declaration of scientists, “*Our Stolen Future*” is included in this list because it was a pivotal publication which raised awareness about the problems caused by EDCs. First published by Dutton, Penguin Books (NY) in 1996 it includes many references and has been published in 14 languages.⁶

August 1999: US National Research Council report, “Hormonally Active Agents in the Environment”

This report⁷ was commissioned in 1995 by the US Environmental Protection Agency (EPA) and the US Department of the Interior and Congress. The committee writing the report did not reach consensus on many points. However, because of its concerns about the potential risks, the committee concluded by recommending an ambitious, large-scale research program to resolve unanswered questions.

For the full report, see http://www.nap.edu/catalog.php?record_id=6029

December 1999: The Yokohama Consensus Statement

The Yokohama International Workshop on the effects of “Endocrine Disruptors in Living Things” was held following the 2nd International Symposium on Environmental Endocrine Disruptors in 1999, hosted in Kobe, Japan, by Japan's Environment Agency. It acknowledged that since the 1991 Wingspread Conference there had been several significant advances in scientific understanding of endocrine disruption. It was noted, amongst other things, that:

- *“Exposure is ubiquitous. All humans have been exposed to varying amounts.*
- *Laboratory experiments show that exposures have impacts at levels far lower than had been considered possible in traditional toxicology*
- *Many more hormone systems, perhaps all chemically-mediated message systems, are now known to be vulnerable to endocrine disruptors.”*

For the full report, see <http://www.ourstolenfuture.org/consensus/yokohama.htm>

June 2000: The UK Royal Society report, “Endocrine Disrupting Chemicals (EDCs)”

The UK Royal Society is a fellowship of many of the world's most distinguished scientists drawn from all areas of science, engineering, and medicine. The Royal Society's report⁸ acknowledged that some of the concerns about human impacts “*already have some foundation*” and stated that despite the uncertainty, it would be prudent to minimize exposure of humans, especially pregnant women, to EDCs. The

report further stated *"Regulations cannot be 'put on hold' until all the evidence has been collected."*

It also noted the need for improved test methods, and stated that, *"New tests which will detect the endocrine-disrupting activities of chemicals are necessary,"* particularly to deal with *"abnormalities of sexual differentiation/reproductive development where cause and consequence may be separated by a considerable period of time."*

Furthermore, this report highlighted the issue of multiple exposures. *"In reality, humans are exposed not to a single endocrine disrupter but to a 'cocktail' of such chemicals, and the possibility that such chemicals have additive or reinforcing effects (e.g., combination of an oestrogenic with an anti-androgenic compound) has to be considered seriously."*

For the full report, see

http://royalsociety.org/uploadedFiles/Royal_Society_Content/policy/publications/2000/10070.pdf

August 2001: The US National Toxicology Program's (NTP's) "Report of the Endocrine Disruptors Low-Dose Peer Review"

At the invitation of the US EPA, the NTP and the National Institute of Environmental Health Sciences (NIEHS) organized and conducted a scientific peer-review of data currently available on low dose effects of endocrine disrupting contaminants.⁹ The primary purpose of the review was to determine whether doses of chemicals in the dose range below doses typically tested for effects could produce effects. If low dose effects were agreed to be commonplace, this would throw regulatory toxicity testing into chaos, because most of the science that has guided regulatory standards has assumed they don't happen.

For this peer review, "low dose effects" referred to biological changes that occur in the range of human exposures or at doses that are lower than those typically used in the US EPA's standard testing paradigm for evaluating reproductive and developmental toxicity.

Studies on several compounds were examined, including bisphenol A (BPA), diethylstilbestrol, ethinyl estradiol, nonylphenol, octylphenol, genistein, methoxychlor, 17 β -estradiol, and vinclozolin. For BPA the conclusions were as follows:-

- *"there is credible evidence that low doses of BPA can cause effects on specific endpoints. However, due to the inability of other credible studies in several different laboratories to observe low dose effects of BPA, and the consistency of these negative studies, the Sub-panel is not persuaded that a low dose effect of BPA has been conclusively established as a general or reproducible finding."*

- *“Data are insufficient to establish the shape of the dose-response curve for bisphenol A in the low dose region, and the mechanism and biological relevance of reported low dose effects are unclear.”*

For the full report, see

<http://ntp.niehs.nih.gov/ntp/htdocs/liason/LowDosePeerFinalRpt.pdf>

2002: World Health Organisation (WHO) & UNEP report “Global Assessment of the State-of-the-Science of Endocrine Disruptors”

This assessment published by the WHO, was prepared by a large group of experts on behalf of the WHO, the International Labour Organisation, and the United Nations Environment Programme (UNEP).¹⁰

It contains a plethora of information on reported effects in humans and wildlife, and mechanisms of action of endocrine disruptors.

For the full report, see

http://www.who.int/ipcs/publications/new_issues/endocrine_disruptors/en/

May 2005: The Prague Declaration on Endocrine Disruptors

This Declaration was initiated in Prague on 10-12 May 2005, when international experts gathered for a workshop on endocrine disruptors. It has now been signed by hundreds of scientists worldwide. It sets out many points, and starts as follows:

- *“There is serious concern about the high prevalence of reproductive disorders in European boys and young men and about the rise in cancers of reproductive organs, such as breast and testis. Lifestyle, diet and environmental contamination play a role in the observed regional differences of these disorders and their changes with time.*
- *Hormone action is important in the origin or progression of the aforementioned disorders. Therefore it is plausible that exposure to endocrine disruptors may be involved, but there are inherent difficulties in establishing such causal links in humans.*
- *There is a serious gap of knowledge regarding the effects of endocrine disruptive compounds on other serious human diseases such as obesity, neuronal disorders, stress etc.*
- *Causality is well established for detrimental effects in wildlife as a direct consequence of exposure to endocrine disruptors. In some instances the severity of effects is likely to lead to population level impacts. Wildlife provides early warnings of effects produced by endocrine disruptors which may as yet be unobserved in humans.”*

The Declaration was published in Environmental Health Perspectives.¹¹

For the full Declaration, also see
<http://www.ourstolenfuture.org/Consensus/2005-0620praguedeclaration.htm>

November 2006: Helsinki Consensus Statement “Is endocrine disruption within REACH?”

This statement by EU scientists working on endocrine disrupters expressed concern at the phrasing of the proposed regulation of EDCs in the REACH legislation. They noted that it would be “prudent to reduce exposures to certain substances with endocrine disrupting properties, in order to protect future generations”. Furthermore, “given endocrine disrupting substances can act in an additive manner, precautionary action needs to be taken, even though, in isolation, such a substance may be judged unlikely to cause serious effects at current exposure levels. Therefore, we consider that where scientific evidence shows a substance to have endocrine disrupting properties, there should not be a need to show that serious effects are probable, before this substance is subject to the REACH authorisation procedure.”

For the full Statement, see
<http://www.env-health.org/resources/references/article/helsinki-statement-is-endocrine-607>

November 2006: Chapel Hill Consensus Statement on BPA

The “*Chapel Hill Bisphenol A Expert Panel Consensus Statement: Integration of Mechanisms, Effects in Animals and Potential to Impact Human Health at Current Levels of Exposure*” published in 2007, was written by almost forty eminent scientists. This statement was the outcome of a meeting held in Chapel Hill, North Carolina in November 2006. It concluded that;

“the wide range of adverse effects of low doses of BPA in laboratory animals exposed both during development and in adulthood is a great cause for concern with regard to the potential for similar adverse effects in humans. Recent trends in human diseases relate to adverse effects observed in experimental animals exposed to low doses of BPA. Specific examples include: the increase in prostate and breast cancer, uro-genital abnormalities in male babies, a decline in semen quality in men, early onset of puberty in girls, metabolic disorders including insulin resistant (type 2) diabetes and obesity, and neurobehavioral problems such as attention deficit hyperactivity disorder (ADHD).”¹²

For the full Statement, see
www.ncbi.nlm.nih.gov/pubmed/17768031 or
<http://www.environmentalhealthnews.org/newscience/2007/2007-0801bpaconsensus.pdf>

May 2007: Prenatal Programming and Toxicity (PPTox1). “The Faroese Statement: Human Health Effects of Developmental Exposure to Chemicals in Our Environment”

The Faroese Statement¹³ highlighted that the periods of embryonic, foetal and infant development are remarkably susceptible to environmental hazards. It noted that the timing of exposure to potentially harmful chemicals was critical and highlighted the possibility of effects being seen in the children of those exposed in the womb. For example, it stated that *“chemical exposures during prenatal and early postnatal life can bring about important effects on gene expression, which may predispose to disease during adolescence and adult life. Some environmental chemicals can alter gene expression by DNA methylation and chromatin re-modeling. These epigenetic changes can cause lasting functional changes in specific organs and tissues and increased susceptibility to disease that may even affect successive generations.”* It highlighted that rodent experiments have shown that developmental exposure to endocrine disruptors *“may increase the incidence of reproductive abnormalities, metabolic disorders such as diabetes, and cancer presumably through epigenetic mechanisms that do not involve changes to DNA sequences but which may, nevertheless be heritable.”*

The Faroese Statement also highlighted that *“the brain is particularly sensitive to toxic exposures during development, which involves a complex series of steps that must be completed in the right sequence and at the right time. Slight decrements in brain function may have serious implications for social functioning and economic activities, even in the absence of mental retardation or obvious disease.”*

Furthermore, *“the immune system also undergoes important development both before and after birth. New evidence suggests that a number of persistent and non-persistent environmental pollutants may alter the development of the immune system.”* ... *“While the research on developmental toxic effects has, to date, emphasised maternal exposures and the infant environment, the possibility exists that paternal exposures may also affect the child’s development.”*

For the full Statement, see

<http://onlinelibrary.wiley.com/doi/10.1111/j.1742-7843.2007.00114.x/pdf>

June 2009: Endocrine Society Scientific Statement “Endocrine Disrupting Chemicals”

The Endocrine Society is the world's oldest, largest, and most active organization devoted to research on hormones and the clinical practice of endocrinology. It works to foster a greater understanding of endocrinology. Their informed review included over 400 references. One of the key points they noted, was that the *“effects of endocrine disrupting chemicals may be transmitted to further generations through germ-line epigenetic modifications or from continued exposure of offspring to the environmental insult.”*¹⁴

For the full Statement, see

https://www.endocrine.org/~media/endosociety/Files/Publications/Scientific%20Statements/EDC_Scientific_Statement.pdf

November 2009: American Medical Association endorsed the regulation of endocrine disrupting chemicals

They noted that regulatory oversight of endocrine disrupting chemicals in the USA should be centralized and moreover, that policy should be based on comprehensive data covering both low-level and high-level exposures (p27).

For the full Resolution, see

<http://www.ama-assn.org/resources/doc/hod/i-09-resolutions.pdf>

November 2009: The American Public Health Association policy statement – “Opposition to the Use of Hormone Growth Promoters in Beef and Dairy Cattle Production”

This noted that since 1988, the use of steroid hormones in cattle production has been illegal in Europe. In contrast, the US government held the position that hormone residues in beef from adult cattle posed no threat to human health. The American Public Health Association challenged this assumption of safety, noting that it did not take account that hormones and hormonally active chemicals may exert their toxicity via epigenetic changes.

For the Policy Statement, see

<http://www.apha.org/advocacy/policy/policysearch/default.htm?id=1379>

December 2009: The second International Conference on Foetal Programming and Developmental Toxicity (PPToxII).

This conference in Miami, Florida further explored the “Developmental origins of non-communicable disease: Implications for research and public health.”

For the full report and list of signatories,¹⁵ see

<http://www.ehjournal.net/content/11/1/42/comments>

April 2010: The President’s Cancer Panel Annual Report 2008-2009: “Reducing Environmental Cancer Risk”

This US report from the prestigious President’s Cancer Panel highlights the role that chemicals in our environment may be playing in the increasing incidence of some cancers. Although not solely focussed on endocrine disrupting chemicals, it does address much of the evidence that these chemicals may be impacting on hormone related cancer rates.

For the full report, see

http://deainfo.nci.nih.gov/advisory/pcp/annualReports/pcp08-09rpt/PCP_Report_08-09_508.pdf

November 2010: The American Public Health Association policy statement: “A Precautionary Approach to Reducing American Exposure to Endocrine Disrupting Chemicals”

This urged support for the Endocrine Society and the American Medical Association in proclaiming that more needs to be done to protect the public from potential health risks of exposure to EDCs.

For the full Policy Statement see

<http://www.apha.org/advocacy/policy/policysearch/default.htm?id=1397>

June 2011: The American Medical Association policy on “BPA in baby bottles and infant cups”

The AMA recognized BPA as an endocrine-disrupting agent and urged that BPA-containing products with the potential for human exposure be clearly identified. The new policy also supported on-going industry actions to stop producing BPA-containing baby bottles and infant feeding cups and supported a ban on the sale of such products.

For the full Policy Statement, see

<http://www.ama-assn.org/ama/pub/news/news/2011-new-policies-adopted.page>

October 2011: A European Society for Paediatric Endocrinology and Paediatric Endocrine Society Call to Action Statement

This noted that studies in the US and EU show that human fluids and tissues contain small concentrations of a high number of EDCs. The boards of European Society for Paediatric Endocrinology and the Pediatric Endocrine Society urged their members to be alert to the possible significance of EDCs when assessing both clinical problems and research data about endocrine problems where disease etiologies are lacking.

For the full Statement, see <http://jcem.endojournals.org/content/96/10/3056.full>

September 2012: Berlin Low Dose meeting

This International Workshop on “Low Dose Effects and Non-Monotonic Dose Responses for Endocrine Active Chemicals: Science to Practice” set out the debate for low dose effects and non-monotonic dose responses in relation to endocrine active chemicals, with the goal of establishing whether there was a need to re-examine the ways in which chemicals are tested for endocrine disrupting properties and how risk to human health may be managed¹⁶.

The workshop was sponsored by NIEHS/ NIH and the Pew Trust in the US, the European Commission Joint Research Centre (JRC), the French Agency for Food, Occupational and Environmental Health (ANSES), the German Federal Environment Agency (UBA), the Danish Ministry of the Environment and National Food Institute from Denmark and Charité Medical University, Berlin.

For the workshop summary, see

<http://www.sciencedirect.com/science/article/pii/S0045653513008850>

May 2012: The European Environment Agency (EEA) Report - Weybridge + 15

This report from the EEA entitled “The impacts of endocrine disruptors on wildlife, people and their environments. The Weybridge+15 report (1996–2011)” is not a consensus statement as such, but it was written by numerous scientists active in the field. It presents a review of the state of the science, and identifies knowledge gaps and research priorities. The link to the original Weybridge report is not included in this document, as it is covered in the CHEM Trust document “*EU milestones on endocrine disrupting chemicals (EDCs): Official commitments and legislative action on EDCs in the EU*” because the 1996 Weybridge meeting was an initiative of the European Commission.

For the full report, see

<http://www.eea.europa.eu/publications/the-impacts-of-endocrine-disrupters>

May 2012: PPTOX3 – “Environmental Stressors in the Developmental Origins of Disease: Evidence and Mechanisms”

The report and consensus statement from this Paris conference was published in *Toxicological Sciences*¹⁷ (Schug et al.,2012).

For the full report, see

<http://toxsci.oxfordjournals.org/content/early/2012/09/05/toxsci.kfs267.abstract>

October 2012: WHO report “Endocrine disruptors and child health. Possible developmental early effects of endocrine disruptors on child health”

This document, written by several experts in the field, provides a summary of the current knowledge of the effects of endocrine disruptors on child health.¹⁸ “The main focus is on congenital disorders, cryptorchidism and hypospadias, which have an endocrine connection, on thyroid hormone-related problems, and on puberty. There is ample evidence of endocrine disruption in wildlife, and the mechanisms of action of endocrine disruptors have been elucidated in experimental animals, but there is limited knowledge of the association of human disorders with exposure to endocrine disruptors. Accumulating data suggest that many adult diseases have fetal origins, but the causes have remained unexplained. Improving fetal and child health will influence the whole life of an individual and improve the wellbeing of our society.”

For the full report, see

http://apps.who.int/iris/bitstream/10665/75342/1/9789241503761_eng.pdf

February 2013: WHO & UNEP report “State of the Science of Endocrine Disrupting Chemicals-2012”

This authoritative update of the state of the science was written by experts in the field and published by the WHO in Geneva. A full report is available, which includes an update of the state of the science, and in addition, there is a useful summary for policy makers. Both highlight the need for better test methods to identify EDCs and for such tests to be implemented in regulations.

For the full report, see <http://www.who.int/ceh/publications/endocrine/en/>

May 2013: The Berlaymont Declaration

This initiative started with the international scientists who attended the June 2012 European Commission convened conference on endocrine disruptors. The scientists welcomed the Commission’s activities on EDCs and noted that as the first major economic area to target endocrine disrupters, the EU has the opportunity to put in place standards that will be exemplary for health and environmental protection policies in other regions of the world. The Declaration summarised the evidence and their concerns and called for the European Commission to implement regulatory measures that are in line with the best available science. The first 10 points are shown below.

1. *“We are concerned that the prevalence of endocrine-related diseases is higher than it has ever been. The disease burden continues to increase in the EU and globally.*
2. *Evidence is strengthening that environmental factors, including chemical exposures, play a role in these phenomena.*
3. *European wildlife is also affected and some effects are widespread.*
4. *Animal experiments and some human health studies have shown that exposure to endocrine disrupters during developmental periods can cause irreversible harm that becomes apparent long after these exposures took place. Etc*
5. *Internationally agreed test methods currently capture only some of these effects and are inadequate for revealing the full range of the effects of EDCs.*
6. *Existing EU chemicals regulations are entirely inadequate for identifying EDCs, and internationally validated test methods that have been available for years have not been implemented.*
7. *Some proposals for regulating EDCs from EU Member States are not sufficiently protective, do not follow the best available science, and place commercial interests above the protection of human and wildlife health.*
8. *Certain EDCs have toxicological properties that preclude the definition of thresholds below which exposures can be deemed safe.*
9. *There is the plausibility that EDCs cause serious, irreversible harm, but more data are needed for better risk assessment. This tension can only be resolved by developing a targeted research strategy for endocrine disrupters as part of Horizon 2020 which should aim at better exposure assessment, assay development and human health studies.*
10. *We call on the European Commission to implement a regulatory regime for EDCs that is based on sound scientific principles. Although uncertainties in*

risk assessment remain, European Commission-funded research has greatly contributed to substantiating the plausibility of serious, irreversible harm from endocrine disruptors. Scientific uncertainty should not delay regulatory action and commercial interests must not take precedent over concerns about risks associated with endocrine disruptors.”

For the full Declaration, see

http://www.brunel.ac.uk/__data/assets/pdf_file/0005/300200/The_Berlaymont_Declaration_on_Endocrine_Disrupters.pdf

June 2013: Collegium Ramazzini Statement, “Endocrine Disrupting Chemicals in the European Union”

This statement called for stringent hazard based criteria, and the authorisation of an EDC only if it is shown that socio-economic benefits outweigh the risk to human health or the environment arising from the use of the substance and if there are no suitable alternative substances or technologies. They noted that EDCs are causing health effects in the European population and recommended improved test protocols and testing requirements to identify EDCs. Furthermore, they noted that academic studies which are not GLP must be taken into account in any risk assessments.

For the full Statement, see

http://www.collegiumramazzini.org/download/EDCs_Recommendations%282013%29.pdf

June 2013: The Royal College of Obstetricians & Gynaecologists (RCOG) (Scientific Impact Paper 37) “Chemical Exposures During Pregnancy: Dealing With Potential, But Unproven, Risks to Child Health”

The RCOG has about 12,500 fellows and members worldwide of whom nearly half are based outside Britain. Their report, written by experts in the field, highlighted that although there was a lack of proof that in-utero exposure to hormone disrupting chemicals were causing many of the health effects with which they had been associated, pregnant women might be best advised to reduce their exposure to such chemicals. The paper therefore suggests that the best approach for pregnant women is a ‘safety first’ approach, which is to assume there is risk present even when it may be minimal or eventually unfounded. Recommendations made in the paper include: using fresh food whenever possible by reducing foods in cans/plastic containers, minimising the use of personal care products, avoiding paint fumes and use of all pesticides, and only taking over-the-counter medicines when necessary.

For the full Scientific Impact Paper, see

<http://www.rcog.org.uk/womens-health/clinical-guidance/chemical-exposures-during-pregnancy-scientific-impact-paper-37>

June 2013: Dietrich et al. consensus statement – “Scientifically Unfounded Precaution Drives European Commission’s Recommendations on EDC Regulation, While Defying Common Sense, Well-Established Science and Risk Assessment Principles”

This commentary¹⁹ and open letter to Anne Glover, the chief scientific advisor to the President of the European Commission, signed by 18 editors of ‘prominent’ journals of pharmacology and toxicology, aimed to draw attention to the imminent decisions by the European Commission to enforce a regulatory framework for EDCs.

Dietrich et al attacked the proposed EU regulatory framework for EDCs and maintained that the *“currently drafted framework is based on virtually complete ignorance of all well-established and taught principles of pharmacology and toxicology, of opinions raised by the European Commission’s own competent expert authority (European Food Safety Authority (EFSA, 2013)), and of critical statements made by member countries, while avoiding asking for support from the European Commission’s own scientific expert committees.”* This group of scientists were condemnatory of a hazard based approach (based solely on the intrinsic properties of the substance) to identifying EDCs, and vociferously argued for a risk based approach, where potency and exposure would play an important part in determining whether a substance was an EDC. Thus, they highlighted *“What is even more disturbing is that, where a scientific advisory body such as EFSA has been consulted, critical elements of this body’s opinion are ignored. For example, in assessment of chemicals with endocrine activity, EFSA supported a substance specific risk assessment approach integrating exposure and adverse effects instead of developing horizontal criteria for defining whether a substance is an “endocrine disruptor”. Development of horizontal lists ignores the long-standing principle that an assessment of a substance should be based on data obtained from toxicity testing on this specific substance and derived information on potency.”*

They went on to assert that EDCs have thresholds for adverse effects and that it would be tantamount to rewriting the rules and accepted practices of toxicology if a substance could be identified as an EDC from non-animal test methods and without it being shown to have adverse effects in an experiment on an intact organism. Moreover, these scientists attacked the Commission’s proposal that *“Relevance of the data to humans should be assumed in the absence of appropriate data demonstrating non-relevance”* because they maintained that *“as all scientists should know, it is biologically and statistically impossible to demonstrate “absence of effect” and thus “absence of relevance””*.

This commentary and letter, with Daniel Dietrich as the lead author, were published in several journals including:- Alternatives to Animal Experimentation (ALTEX); Chemico Biological Interactions; Regulatory Pharmacology and Toxicology; Toxicology in Vitro and Food and Chemical Toxicology.

For the full Comment and Open Letter see
http://www.altex.ch/resources/open_letter.pdf

However, two comprehensive rebuttals (see below) were published that effectively dealt with these criticisms. These rebuttals were signed by many prestigious world class scientists working in the area of endocrine disruption, and moreover, were signed by many heavy weight editors of other journals active in the field. They are referenced below but are worth reading in full.

August 2013: Bergman et al. consensus statement – “Science and Policy on Endocrine Disruptors Must Not Be Mixed: A Reply to a ‘Common Sense’ Intervention by Toxicology Journal Editors”

This rebuttal was signed by dozens of scientists, including many who had contributed to the 2013 WHO review.²⁰ It was published in Environmental Health along with an editorial commentary by Grandjean and Ozonoff.²¹ With regard to Dietrich and colleagues’ criticism of the proposed wording on relevance to humans, it was noted that Dietrich et al *“conflate the statistical impossibility of demonstrating the absence of effects (and thresholds) with the issue of demonstrating human relevance of toxicity data derived from testing on animals. In doing so they reveal ignorance of important risk assessment principles elaborated in an IPCS Framework document for assessing the human relevance of non-cancer endpoints. The default assumption under that framework is of human relevance, unless there is evidence of toxicodynamic or toxicokinetic differences between the animal test species and humans that shows that the effect seen in animals is not expected to occur in humans. The applicability of that default assumption was tested through a number of case studies. The alternative a priori assumption (that effects seen in animals are not relevant for humans) would be unworkable and would undermine the sense of conducting toxicological testing in animals at all.”*

For the full Critique by Ake Bergman et al. see

<http://www.ehjournal.net/content/pdf/1476-069X-12-69.pdf>

For the editorial by Philippe Grandjean and David Ozonoff see

<http://www.ehjournal.net/content/pdf/1476-069X-12-70.pdf>

September 2013. Gore et al consensus statement - “Policy Decisions on Endocrine Disruptors Should be Based on Science Across Disciplines: A Response to Dietrich et al”

This rebuttal to Dietrich et al was signed by many scientists and editors of leading peer-reviewed journals with a track record of publishing important contributions in the study of EDCs.²² It was signed by 18 editors in chief and 24 associate and senior editors of endocrine, neuroendocrine, and environmental journals. They noted that 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. They also stressed that EDCs pose a global health threat. These scientists were particularly concerned that the recent editorial (Dietrich et al.2013) which was signed by a number of editors of other toxicology journals, argued for the status quo in the regulation of EDCs, despite the large volume of evidence indicating that current regulations are ineffective in protecting human health. In contradiction of the arguments put forward by Dietrich, Gore and colleagues highlighted that in their view a regulatory approach which includes an assumption of no thresholds for EDCs is supported by the science. Gore et al underlined that when public health is at stake, policies “should be based on scientific evidence obtained from the world’s leading researchers, and should derive from a more evolved, modern understanding of science rather than on older, outdated concepts and data taught in classrooms 20 or

more years ago.” They concluded that the attacks in Dietrich et al. do nothing to advance science or protect public health – and furthermore noted that the Bergman et al and the Grandjean and Ozonoff editorials support their viewpoint.

For the editorial by Professor Gore and other journal editors, see <http://endo.endojournals.org/content/early/2013/09/18/en.2013-1854.short?rss=1>

In a separate editorial, written just by Professor Gore by herself, as the editor in chief of the journal *Endocrinology*,²³ it was noted that “while the science behind EDC health effects is unequivocal, there continues to be unrelenting pressure from individuals and corporations with stakes in the status quo to keep doubt alive.” She noted that this production of uncertainty had also in the past been the strategy of individuals and corporations seeking to de-fang regulatory policy worldwide.

For the editorial by Professor Gore entitled “The International Scientific Community Speaks on Endocrine-Disrupting Chemicals” see <http://endo.endojournals.org/content/early/2013/09/18/en.2013-1853.short?rss=1>

Conflicts of interest

It is also pertinent to note that 17 of the 18 scientists (including Daniel Dietrich) who wrote the original June 2013 criticism of the Commission entitled “*Scientifically Unfounded Precaution Drives European Commission’s Recommendations on EDC Regulation, While Defying Common Sense, Well-Established Science and Risk Assessment Principles*” were subsequently found to have undeclared conflicts of interest. This investigative research outlining how these scientists, who were so critical of the Commission’s proposals to regulate EDCs, had ties to industry was undertaken by Stéphane Horel and Brian Bienkowski and published on Environmental Health News. It is also interesting to note that previously when asked about potential conflicts of interest by reporters at Chemical Watch, Professor Dietrich had erroneously replied that “there is no conflict of interest.” (25th July 2013)

For the full article by Stéphane Horel and Brian Bienkowski see:- <http://www.environmentalhealthnews.org/ehs/news/2013/eu-conflict>

Intervention by Anne Glover, chief scientific advisor to EU President Barroso

In order to try to resolve the important differences of opinion between the Dietrich et al scientists (with industry connections) and the other independent scientists in Bergman’s group, Anne Glover invited them for a meeting on 24th October 2013. The minutes and some agreed conclusions of this meeting are now publicly available on her web site shown below. These documents show that Dekant and colleagues from the Dietrich camp have had to back down from their earlier published position that “the weight of scientific evidence...clearly demonstrates the presence of a threshold for non-genotoxic compounds including EDCs” as they have now agreed that “it is possible that thresholds do not exist; the reason of the uncertainty is the limitation of the experimental constraints and the understanding of the biology.” http://ec.europa.eu/commission_2010-2014/president/chief-scientific-adviser/documents/minutes_endocrine_disruptors_meeting_241013_final.pdf

September 2013: The American College of Obstetricians and Gynecologists Committee Opinion on “Exposure to toxic environmental agents”

This was a committee opinion from the American College of Obstetricians and Gynecologists Committee on Health Care for Underserved Women, the American Society for Reproductive Medicine Practice Committee and the University of California, San Francisco Program on Reproductive Health and the Environment. It noted that “the evidence that links exposure to toxic environmental agents and adverse reproductive and developmental health outcomes is sufficiently robust. It called for timely action to identify and reduce exposure to toxic environmental agents while addressing the consequences of such exposure. Furthermore, it particularly referred to endocrine disrupting chemicals stating that “a group of chemicals called endocrine disrupting chemicals has been shown to interfere with the role of certain hormones, homeostasis, and developmental processes.”

For the full report, see

<http://www.acog.org/~media/Committee%20Opinions/Committee%20on%20Health%20Care%20for%20Underserved%20Women/co575.pdf?dmc=1&ts=20130926T0828386306>

Gwynne Lyons

Gwynne.lyons@chemtrust.org.uk

REFERENCES

- ¹ Colborn T & Clements C. 1992. Chemically-induced alterations in sexual and functional development: the wildlife/human connection. Princeton Scientific Pub. Co., Princeton, N.J. (USA) http://www.endocrinedisruption.com/files/wingspread_consensus_statement.pdf
- ² Bantle J, Bowerman WW IV, Carey C, Colborn T, Deguise S, Dodson S, Facemire CF, Fox G, Fry M, Gilbertson M, Grasman K, Gross T, Guillette L Jr., Henny C, Henshel DS, Hose JE, Klein PA, Kubiak TJ, Lahvis G, Palmer B, Peterson C, Ramsay M, White D (May 1995). "Statement from the Work Session on Environmentally induced Alterations in Development: A Focus on Wildlife". *Environ. Health Perspect.* 103 (Suppl 4): 3–5. doi:10.2307/3432404.
- ³ Holladay, S. D., and M. Luster. Chemically-Induced Alterations in the Developing Immune System: The Wildlife/Human Connection. *Environmental Health Perspectives* 104 (Supplement 4): 809- 814. 1996.
- ⁴ Rolland RM, Gilbertson M and Peterson RE (editors). 1997. Chemically induced alterations in functional development and reproduction of fishes. Proceedings from a session at the 1995 Wingspread Conference. ISBN. 1-880611-19-8. SETAC Press, USA.
- ⁵ Alleva E, Brock J, Brouwer A, Colborn T, Fossi MC, Gray E, Guillette L, Hauser P, Leatherland J, MacLusky N, Mutti A, Palanza P, Parmigiani S, Porterfield, Santi R, Stein SA, vom Saal F (1998). "Statement from the work session on environmental endocrine-disrupting chemicals: neural, endocrine, and behavioral effects". *Toxicol Ind Health* 14 (1–2): 1–8.
- ⁶ Colborn, Theo; Dumanoski, Dianne; Myers, John Peterson (1996). *Our Stolen Future: Are We Threatening Our Fertility, Intelligence, and Survival? A Scientific Detective Story*. Dutton. ISBN 0-525-93982-2.
- ⁷ Committee on Hormonally Active Agents in the Environment, US National Research Council. 1999. *Hormonally Active Agents in the Environment*, National Academies Press. ISBN 978-0-309-06419-4
- ⁸ The Royal Society. 2000. *Endocrine Disrupting Chemicals (EDCs)*. Document 06/00.
- ⁹ National Toxicology Program. 2001. *Report of the Endocrine Disruptors Low-Dose Peer Review*. Sponsored by the US EPA and the NIEHS.

-
- ¹⁰ Damstra T, Barlow S, Bergman A, Kavlock R and Van Der Kraak G (editors). 2002. Global Assessment of the State-of-the-Science of Endocrine Disruptors. International Programme On Chemical Safety.
- ¹¹ Kortenkamp A. 2007. Endocrine Disruptors— Exposure Assessment, Novel End Points, and Low-Dose and Mixture Effects; Environmental Health Perspectives, Volume 115, Number S-1.
- ¹² Chapel Hill Bisphenol A Expert Panel Consensus Statement (2007). Integration of Mechanisms, Effects in Animals and Potential to Impact Human Health at current levels of exposure. *Reproductive Toxicology* 24(2): 131-8.
- ¹³ Grandjean P et al. 2007. The Faroes Statement: Human Health Effects of Developmental Exposure to Chemicals in Our Environment. *Basic & Clinical Pharmacology & Toxicology*, 102, 73-75.
- ¹⁴ Diamanti-Kandarakis E et al. 2009. Endocrine-Disrupting Chemicals: An Endocrine Society Scientific Statement. *Endocrine Reviews* 30(4):293-342.
- ¹⁵ Barouki R, Gluckman PD, Grandjean P, Hanson M and Heindel JJ. 2012. Developmental origins of non-communicable disease: Implications for research and public health. *Environmental Health* 11:42.
- ¹⁶ Beausoleil C et al. 2013. Low dose effects and non-monotonic dose responses for endocrine active chemicals: Science to practice workshop: Workshop summary. *Chemosphere*. Available online 9 August 2013.
- ¹⁷ Schug T T et al. 2013. PPTOX III: Environmental Stressors in the Developmental Origins of Disease: Evidence and Mechanisms. *Toxicological Sciences*.
- ¹⁸ Toppari et al., 2012. Endocrine disruptors and child health. Possible developmental early effects of endocrine disruptors on child health. ISBN 978 92 4 150376 1. Public Health & Environment Department (PHE), WHO. Geneva.
- ¹⁹ Dietrich D R et al. 2013. Scientifically unfounded precaution drives European Commission's recommendations on EDC regulation, while defying common sense, well-established science and risk assessment principles. *ALTEX*, 30. 3/13. P381-385.
- ²⁰ Bergman A et al. 2013. Science and policy on endocrine disruptors must not be mixed: a reply to a "common sense" intervention by toxicology journal editors. *Environmental Health*, 12:69.
- ²¹ Grandjean P & Ozonoff D. 2013. Transparency and translation of science in a modern world. *Environmental Health*, 12:69.
- ²² Gore AC et al. 2013. Policy Decisions on Endocrine Disruptors Should be Based on Science Across Disciplines: A Response to Dietrich et al. *Endocrinology*. September.
- ²³ Gore AC. 2013. The International Scientific Community Speaks on Endocrine-Disrupting Chemicals. *Endocrinology*, September.