1. Background

Since the 1990's, numerous scientific studies have focused on a wide range of chemicals that are known or suspected to be disrupting the endocrine systems of humans and wildlife. A variety of natural and synthetic chemicals have been found to interfere with the endocrine systems of animals in laboratory studies, and extensive field evidence indicates that endocrine systems of certain fish and other wildlife have been affected by certain chemical contaminants, resulting in developmental and reproductive problems.

Suspected endocrine disrupting chemicals (EDCs) are now starting to be evaluated by several regulatory authorities, and a debate is in progress about whether or not EDCs can be safely assessed by taking the usual approach involving identification of intrinsic hazards, prediction of exposure and consequent calculation of risk.

The United States (US) Congress passed the Food Quality Protection Act and the Safe Drinking Water Act Amendments in 1996 requiring that the Environmental Protection Agency (EPA) screen pesticide chemicals for their potential to produce effects similar to those produced by the female hormones (estrogens) in humans, and giving EPA the authority to screen certain other chemicals and to include other endocrine effects. Based on recommendations from an Advisory Committee, EPA has expanded the Endocrine Disruptor Screening Program (EDSP) to include male hormones (androgens) and the thyroid system, and also to include effects on fish and other wildlife. The EPA will use a two-tiered screening and testing process. Through Tier 1, EPA aims to identify chemicals that have the potential to interact with the endocrine system. Through Tier 2, EPA will determine the endocrine-related effects caused by chemicals identified in Tier 1 and obtain information about effects at various doses (hazard assessment), which will ultimately be used for environmental risk assessment (for further information, see http://www.epa.gov/endo/). It is expected that similar risk assessment approaches will be followed in Japan and elsewhere.

In the European Union (EU), substantial developments regarding the regulation of endocrine disrupting chemicals (EDCs) are also taking place. Implementation of new regulations is awaiting the finalization of regulatory criteria for EDCs which will then be applied to most chemical types ranging from plant protection products, through biocides to industrial chemicals. A major difference from the US approach is that some in the EU consider a risk assessment approach for EDCs as potentially unreliable for a number of reasons, including the proposed lack of toxicity thresholds and presence of low-dose effects, the existence of non-monotonic dose-response relationships, the additive effects of low concentrations of EDCs with the same mode of action, and the difficulty of predicting long-term effects from short-term exposures. Despite these concerns, the European Food Safety Authority (EFSA) has recently stated that risk assessment of EDCs is the most appropriate approach. However, current legislation in the EU (i.e. the Plant Protection Product Regulation and Biocides Regulation) will regulate these substances primarily on the basis of their hazard, although it is not yet clear whether the European regulatory definition of an EDC will include some elements of the risk
assessement approach (e.g. a consideration of potency). For further information see http://ec.europa.eu/environment/chemicals/endocrine/index_en.htm.

There are also major developments taking place globally on this topic, such as the recent adoption by the World Health Organization/United Nations Environment Programme (WHO/UNEP) Strategic Approach to International Chemicals Management (SAICM-ICCM3) of endocrine disruption as a global ‘emerging issue’. Moreover, the Organisation for Economic Cooperation and Development (OECD) is working to develop new and revised Test Guidelines (TG) to detect developmental and reproductive health effects of chemicals (including endocrine disrupters). This is to address the international concern that current TGs are not yet fully sufficient to identify the potential mechanisms or modes of action and adverse effects of EDCs in all economically and ecologically important taxa. This issue was given very high priority for Test Guideline development by the OECD Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology. In terms of hazard assessment, the OECD work includes the development of TGs for both human health and the environment. Recently, several new OECD TGs have been validated and adopted for mammals, amphibians and fish, while ongoing activities include development of TGs for birds and aquatic invertebrates. In terms of exposure assessment, there is also extensive scientific activity on the diverse environmental inputs of potential EDCs entering the aquatic and terrestrial environments, together with numerous exposure assessment studies.

Importantly, now that mammalian and non-mammalian TGs have been adopted by the OECD, and the US EDSP is generating significant data, the key challenge remains the integration of scientific evidence to support the hazard and risk assessment of endocrine disrupters. Environmental risk assessment needs to take due account of both exposure and hazard information pertinent to ecological protection. In Europe, there is a need to provide scientific and regulatory advice on hazard assessment of endocrine disrupters under the new Biocides Products Regulation and Plant Protection Products Regulation, with wider implications for the REACH Regulation, Marine Strategy Framework Directive and the Water Framework Directive. Similar issues are being addressed in Japan and other OECD member countries in the Asia-Pacific region. The SETAC Endocrine Disrupter Testing and Risk Assessment (EDTRA) Advisory Group believes that both hazard and risk assessment procedures for EDCs are possible and appropriate in particular cases, and scientifically robust case studies are urgently needed to highlight optimal scientific approaches and any knowledge gaps pertinent to these procedures.

2. Introduction to SETAC’s Activities in the Field of Endocrine Disruption

The Society of Environmental Toxicology & Chemistry (SETAC; www.setac.org) is a non-profit professional society founded to promote the use of multi-disciplinary approaches in the study of environmental issues, and it draws its membership from academia, government and industry. Reflecting the gaining momentum in the field of EDCs, in 2011 SETAC launched the EDTRA Advisory Group which covers all fields pertinent to conducting effective environmental hazard and risk assessments of known or suspected endocrine disrupters, such as transport, fate, exposure, effect, and impact analysis. A highly successful SETAC Europe Scientific Symposium on Endocrine Disrupter Testing and Evaluation was organized in Brussels, Belgium in October 2012. An equally successful follow-on SETAC Focused Topic Meeting on Endocrine Disrupting Chemical Testing and Risk Assessment was held in Raleigh, North Carolina on 5-6th February 2014.
3. Proposed SETAC Pellston Workshop on the Environmental Hazard & Risk Assessment of Endocrine Disrupters

It is widely, but not universally, recognized that there is a need to evaluate effects data on some EDCs within the context of relevant routes of exposure (e.g. via food, sediments, soil and water). Decision makers in many countries are seeking to use scientifically rigorous methods for the environmental hazard and risk assessment of an increasingly diverse range of EDCs (including environmental transformation products that may show endocrine disrupter activity). However, it will also be important to develop scientific methods which will help to identify and prioritise EDCs for which risk assessment is inappropriate, and where the only practical or conservative approach is to regulate them on the basis of their intrinsic hazards. In this context, scientific information which needs to be considered for relevant chemicals includes factors such as high persistence and bioaccumulation, lack of a monotonic dose-response and lack of an apparent adverse effects threshold.

An important step to support this global need is to develop scientific case studies of both environmental hazard and risk assessment approaches applied to EDCs. The advantages of these case studies are that they will use real-world data to evaluate different assessment methods, and when conducted rigorously by global experts on EDCs, they will give rise to authoritative guidance to regulators in this novel field.

It is therefore proposed to organize a SETAC Pellston workshop to develop six EDC case studies including:

(1) a chemical or group of chemicals currently regulated under the Stockholm Convention on Persistent Organic Pollutants or ‘POPs’ (e.g. PCBs or other chemicals listed at http://chm.pops.int/TheConvention/ThePOPs/ListingofPOPs/tabid/2509/Default.aspx);
(2) an agrochemical (e.g. prochloraz or vinclozolin);
(3) a biocide (e.g. tributyltin);
(4) an industrial chemical (e.g. 4-tert octylphenol);
(5) a natural chemical (e.g. β-sitosterol or zearalenone); and
(6) a pharmaceutical (e.g. 17α-ethinylestradiol or tamoxifen).

The examples of named substances are solely for illustrative purposes and alternative suggestions would be welcome. However, it will be essential to choose substances for which abundant, good quality data are available, ideally including information on known environmental impacts against which laboratory data can be compared.

4. Tentative Workshop Schedule

It is proposed to aim for a workshop in January or February 2016, possibly to be held in Florida. Based on previous SETAC workshops using a case studies model, the draft schedule could be: day 1 (from 1300-1800), day 2 (from 0900-1800) and day 3 (from 0900-1500). Draft case study documents would be prepared and circulated one month in advance to allow the workshop attendees to refine the
case studies and highlight key gaps for future work (including a set of manuscripts for a SETAC journal and identification of critical gaps in the current suite of OECD test guidelines).

5. Proposed Participation

Internationally-recognized scientists will be invited from academia, government and industry and will be expected to employ their expert knowledge of the use of ecotoxicity test guidelines and complementary data in environmental exposure and effects assessment (both aquatic and terrestrial). Specialist skills in EDC screening and testing will also be of central importance. It is envisaged there will be five to seven scientists in each case study group (total 30 to 42 persons), plus participation from UNEP and other relevant international organizations such as OECD, the WHO International Programme on Chemical Safety (IPCS), and the Endocrine Society1. Consideration is still being given to the Endocrine Society as a potential workshop partner.

6. Expected Workshop Outcomes

The key benefits and outcomes we envisage are:

1) The development of a transparent, science-based approach to the environmental hazard and risk assessment of EDCs illustrated through scientific case studies;
2) The preparation of scientific guidance for regulators to help in the identification of EDCs for which risk assessments may be unreliable and regulation by hazard therefore appropriate;
3) Publication of the case studies plus an overview of the key recommendations from the workshop in a SETAC journal (e.g. Integrated Environmental Assessment & Management);
4) Identification of gaps in the currently available assessment tools for potentially important environmental exposure scenarios (e.g. sediments) or in taxonomic groups or critical life stages (e.g. embryo-larvae).

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1 Founded in 1916, the Endocrine Society is the world's oldest, largest, and most active organization devoted to research on hormones and the clinical practice of endocrinology. The Society works to foster a greater understanding of endocrinology among the general public and practitioners of complementary medical disciplines, and to promote the interests of all endocrinologists at the international and national scientific research and health policy levels of government (www.endocrine.org).