A proposed framework for the systematic review and integrated assessment (SYRINA) of endocrine disrupting chemicals

**Background:** The issue of endocrine disrupting chemicals (EDCs) is receiving wide attention from both the scientific and regulatory communities. Recent analyses of the EDC literature have been criticized for failing to use transparent and objective approaches to draw conclusions about the strength of evidence linking EDC exposures to adverse health or environmental outcomes. Systematic review methodologies are ideal for addressing this issue as they provide transparent and consistent approaches to study selection and evaluation. Objective methods are needed for integrating the multiple streams of evidence (epidemiology, wildlife, laboratory animal, in vitro, and in silico data) that are relevant in assessing EDCs.

**Methods:** We have developed a framework for the systematic review and integrated assessment (SYRINA) of EDC studies. The framework was designed for use with the International Program on Chemical Safety (IPCS) and World Health Organization (WHO) definition of an EDC, which requires appraisal of evidence regarding 1) association between exposure and an adverse effect, 2) association between exposure and endocrine disrupting activity, and 3) a plausible link between the adverse effect and the endocrine disrupting activity.

**Results:** Building from existing methodologies for evaluating and synthesizing evidence, the SYRINA framework includes seven steps: 1) Formulate the problem; 2) Develop the review protocol; 3) Identify relevant evidence; 4) Evaluate evidence from individual studies; 5) Summarize and evaluate each stream of evidence; 6) Integrate evidence across all streams; 7) Draw conclusions, make recommendations, and evaluate uncertainties.

**Conclusions:** The proposed method is tailored to the IPCS/WHO definition of an EDC but offers flexibility for use in the context of other definitions of EDCs. When using the SYRINA framework, the overall objective is to provide the evidence base needed to support decision making, including any action to avoid/minimise potential adverse effects of exposures. This framework allows for the evaluation and synthesis of evidence from multiple evidence streams. Finally, a decision regarding regulatory action is not only dependent on the strength of evidence, but also the consequences of action/inaction, e.g. limited or weak evidence may be sufficient to justify action if consequences are serious or irreversible.