Chapter 8: General Conclusions and Research Needs

This assessment summarized the current state of the scientific knowledge regarding the potential effects of exposure to EDCs in humans and wildlife. Predominantly, the information was gathered from North American and European studies, which limits drawing conclusions on a worldwide basis. The potential risks to humans and wildlife posed by EDCs in many other areas of the world (particularly in developing countries) have not been addressed adequately to date. Although it is clear that certain environmental chemicals can interfere with normal hormonal processes, there is weak evidence that human health has been adversely affected by exposure to endocrine-active chemicals. However, there is sufficient evidence to conclude that adverse endocrine-mediated effects have occurred in some wildlife species. Laboratory studies support these conclusions.

Generally, studies examining EDC-induced effects in humans have yielded inconsistent and inconclusive results, which is responsible for the overall data being classified as "weak." This classification is not meant to downplay the potential effects of EDCs; rather, it highlights the need for more rigorous studies. This document has identified a number of inherent challenges and confounding factors that contribute to the difficulties in understanding the risks that EDCs pose to human health. The only evidence showing that humans are susceptible to EDCs is currently provided by studies of high exposure levels. Our understanding of the effects of chronic, low levels of EDCs are much more obscure. In particular, the relationship between early-life exposures to EDCs in humans and functioning in adult life is poorly understood. This is a concern because laboratory animal studies have indicated that early life stages may be especially sensitive to the effects of EDCs. Only recently have human epidemiological studies been conducted with the necessary rigor to sufficiently address potential cause-and-effect relationships in regards to EDC exposures.

Compared with humans, the evidence that wildlife have been affected adversely by exposures to EDCs is extensive. In part, this may reflect the fact that many studies on wildlife have been conducted in areas where it is known that the levels of environmental chemicals are high (e.g., point source discharges, the Great Lakes, the Baltic Sea area). These studies have focused predominantly on animals inhabiting aquatic ecosystems, which bioaccumulate certain EDCs and represent one of the largest sinks of environmental chemicals that may act as EDCs. Progress in establishing cause-and-effect relationships in wildlife has been aided by the ability to experiment with the species of concern under both laboratory and field conditions. Many of the challenges encountered in assessing the risks of EDCs to human health are also relevant to wildlife species. However, there are unique challenges to determining the potential effects of EDCs on wildlife compared with humans, including the large number of potential target species, varied life history strategies, differences in physiological mechanisms, and lack of basic understanding of endocrine regulation for many species.

List of Abbreviations

EDCs Endocrine-disrupting chemicals
NRC National Research Council

This assessment has clearly identified that there is little information on linkages between exposures to putative EDCs and health outcomes in both humans and wildlife. Progress has been made in the identification and quantification of a wide array of chemicals with endocrine-active properties. Predominantly, research efforts have focused on compounds that persist and bioaccumulate in organisms and their environment. Only recently have efforts been directed at exposure studies of less persistent compounds and in the development of biologically based assays, which would enable more direct assessments of endocrine-active compounds. Given the dynamic nature of the endocrine system, future efforts in the study of EDCs need more focus on the timing, frequency, and duration of exposure to these chemicals.

This assessment has clearly demonstrated that further research is necessary to address the uncertainties that remain in this field of study. Some specific research recommendations are cited in the preceding chapters of this document and have also been the subject of a number of international workshops (Kavlock et al., 1996; EC, 1996; Ankley et al., 1998; Kendall et al., 1998; NRC, 1999; Vos et al., 2000). Strengthening international collaborative efforts in the following broad research areas will help resolve uncertainties and should be considered of high priority:

1) **Biology underlying endocrine-mediated effects**
- Expand basic knowledge about endocrine systems in humans and wildlife.
- Elucidate the range of mechanisms by which endocrine disruption may interfere with reproductive/population success, immune function, neurobehavior, and development of cancer, at all levels of biological organization and at key stages of life cycles.

2) **Methodology**
- Develop improved methodologies for assessing dose–response relationships at environmentally relevant concentrations.
- Develop more specific and sensitive biomarkers for detecting endocrine-mediated effects in individuals and populations.

3) **Monitoring**
- Increase long-term monitoring of "sentinel" wildlife species to provide baseline data on population status.
- Improve international collaboration and cooperative research to assess the exposure and effects of EDCs on wildlife populations on a more global basis.
- Extend monitoring of trends in relevant human health outcomes to provide information that is comparable across regions and over time.

4) **Identifying endocrine disruptors**
- Continue to identify chemicals (persistent and nonpersistent, naturally occurring and anthropogenic) that are the most likely candidates for high-impact effects in populations at environmentally relevant concentrations.

- Identify "hot spots" for exposure or effects that warrant particular concern.
- Focus work on populations/subgroups most likely to be susceptible to endocrine disruptors.
- Assess the role of endocrine disruptors relative to other environmental stressors on the fitness of populations.

5) **Database development**

- Develop better global data, especially in countries outside North America and Europe, on status and trends of environmental contamination, exposure, and health outcomes.
- Improve international coordination for sharing of information on effects caused by endocrine disruption.

This state-of-the-science assessment has revealed that our current understanding of the effects posed by EDCs to wildlife and humans is incomplete. The evidence that high-level exposure may impact both humans and wildlife indicates that this potential mechanism of toxicity warrants our attention. Uncertainty over the possible effects of chronic, low-level exposures to a number of chemicals with endocrine-disrupting potential and the fundamental roles played by the endocrine system in maintaining homeostasis make understanding the potential effects posed by exposure to these chemicals an obvious international priority. There is a need to identify life stages and species that are more vulnerable to the effects of EDCs and to understand how this mechanism of toxicity may affect individual populations and communities.