TESTING FOR ENDOCRINE DISRUPTION

ACS POSITION

Endocrine hormones act as control agents that regulate homeostasis, development and many other bodily functions. They are secreted directly into the blood by the endocrine glands (pineal, hypothalamus, pituitary, thyroid, parathyroids, thymus, adrenals, pancreas, and ovaries or testes). The disruption of the endocrine system by chemicals, both natural and synthetic, in both experimental systems and humans is an area of toxicology that has received focused international attention since 1991 and is highly relevant to the American Chemical Society (ACS).

Endocrine disruption is the alteration of the endocrine system that causes adverse health effects in an intact organism, or its progeny, or (sub)populations. Endocrine hormones naturally act at ultra-low concentrations and certain chemicals are suspected of altering endocrine function at similarly low concentrations, which sometime occur in the environment. A large and growing body of environmental health literature shows that endocrine disrupting substances have complicated dose-response curves that do not fit the central tenet of regulatory toxicology, namely, that the 'dose makes the poison.' Like the hormones whose actions they disrupt, endocrine disrupting chemicals can follow what endocrinologists call bi-phasic, or non-monotonic, dose response curves. This makes it impossible to predict the effects of low-dose exposures based upon high-dose experiments. The effects can be not only different, but opposite. While well established in medical endocrinology, such responses have been less well understood in traditional toxicology.

Recommendations

The American Chemical Society strongly endorses expanded endocrine disruptor education and research and the development of more effective science-based decision-making tools and methods for reducing and eliminating exposures of humans and the environment. Specifically, ACS encourages expansion of funding for the following:

- Improvements in testing for endocrine disruption with emphasis on
  - *in vitro* and *in vivo* laboratory studies and human epidemiological investigations,
  - mechanisms of action with emphasis on understanding non-monotonic dose-response behaviors
  - improvement of early identification of endocrine active chemicals and chemical classes,
  - identification of exposure pathways, uptake mechanisms, and trends in human exposures and impacts, and
  - design of epidemiological research to reflect biological mechanisms.
- More rapid advancement of the congressionally-mandated effort by the EPA, called the Endocrine Disruptor Screening Program (EDSP), and its extension to other appropriate agencies to acknowledge that non-monotonic dose-response behaviors are standard features of endocrinology and to require that particular attention be paid to the very low dose experiments that are most relevant to human body burdens and environmental concentrations. EDSP site: http://www.epa.gov/scipoly/oscpendo/index.htm

- Updating of both the test protocols and the protocols by which federal agencies determine the legitimacy of scientific data related to non-monotonic dose-response behavior, with laboratory experiments conducted at biologically realistic levels.
- Development and application of a broad range of *in vivo*, *in vitro* and *in silico* assays that can serve as screening tests to potentially model endocrine disrupting activity.
- Expansion of education regarding endocrine disruption within the scientific community, especially for chemists through the approach of green chemistry, and throughout the formal education structures in universities and schools as well as for the public.
- Green chemistry research aimed at identifying and developing functional alternatives that do not have endocrine disrupting activity.