I. Persistent Toxic Substances (PTSs)

A. Findings in Humans

There is no evidence over the past five years of dramatic shifts in levels or types of bioaccumulating contaminants in tissues of residents of the Great Lakes basin. However, the levels of such contaminants in the tissues of people eating large amounts of Great Lakes fish continue to be several fold higher than in people who do not eat such fish. SOLEC 1996

Exposure

- At-risk populations continue to be exposed to PTSs. Some highly exposed groups have body burden levels 3-4 times higher than the background level (e.g., data from Schantz and coworkers on DDE, Hg, and PCBs).
- Fish consumption remains the major pathway for exposure to PTS in fish eaters. Levels of some contaminants in Great Lakes fish exceed state and federal guidelines. Contaminated sediments are also of concern.
- Sport fish eaters consume 2 to 3 times more fish than is estimated for the general population - FDA estimate is 6.5 grams/person-day (e.g., Schantz and coworkers report that high-fish eaters consume over 32 lbs/yr; Anderson and coworkers indicate that fish eaters on average consume 55 meals/yr with some consuming twice this amount; Kearney and coworkers found Lake Ontario fish eaters in Canada consumed approximately 21 g/day).
- The biological significance of these increases is uncertain. Preliminary evidence in humans of neurobehavioural effects has been reported by Jacobson et.al. and very recently by Mergler.

Demographics

- 4.7 million people consumed Great Lakes sport fish in 1994 / Fish is an essential component of diets of minority populations and Native Americans.
- Men consume more fish than women; men and women eat Great Lakes fish during most of their reproductive years.

Health Effects

- Reproductive function (e.g., delay in time to pregnancy and shortened menstrual cycles) may be disrupted by exposure to PTSs.
- Neurobehavioral and developmental deficits occur in newborns and continue through school-age children from in utero exposure to PTSs.
- Other systemic effects, e.g., self-reported liver disease and diabetes may be associated with elevated serum levels of PCBs.
**Other Conclusions:**

- Weight of evidence can be used in lieu of causality.
- Data are compelling: People are continuing to be exposed, and there are health consequences associated with these exposures.
- There is an immediate need to put science to service in implementing health intervention / health promotion strategies where necessary.
- All strategies should recognize the importance and benefits of fish consumption to particular populations. Risk and benefit analysis is essential for meaningful strategies.


**B. Environmental Trends**

- Concentrations of some persistent toxic substances in the Great Lakes in air, water, and biota appear to have leveled off, or declined only slightly, in recent years.
- 100 % of the Great Lakes waters continue to be under fishing advisories. PCBs are most commonly the focus of advisories issued in the basin, followed by dioxins, chlordane and mercury.
- The 1993 TRI data (USEPA Toxics Release Inventory data released in 1995) showed that all of the Great Lakes Basin states and counties had shown a decrease in releases of targeted chemicals between 1988 and 1993.
- USEPA's 33/50 Program was a nationwide voluntary effort aimed at reducing the releases and transfers of 17 targeted chemicals (including PCBs, Hg, Pb, and other heavy metals and organics) tracked under TRI, with a goal of 50% reduction by the end of 1995. The Program was successful, exhibiting 55.6% decrease from 1988, which is equivalent to a reduction of over 664 million lbs. In three areas of the basin (SE Chicago, NW Indiana, and SE Michigan), an average reduction of 62% was achieved.
- Up to 1997, Canada has reported substantial decreases in alkyl-lead (85%), octachloro-styrene (18%),
dioxins and furans (66%), and B(a)P (20%) primarily as a result of the ARET Program in the Great Lakes Basin.

**Focus on Mercury**

- Consumption advisories for human health have been issued in 38 states and Ontario and Quebec.
- 82% decline in mercury use in the USA from 1980-1995 due to bans in paints and pesticides, phaseouts in batteries, and reductions in industrial uses.
- Mercury emissions curtailed under the US federal Clean Air Act amendments.
- Eight Great Lake states have implemented numerous programs to reduce mercury.
- In 1996, the US chlor-alkali sector voluntarily committed to reduce emissions and use of mercury by 50% during the next decade.

**Focus on PCBs**

- Although banned or tightly restricted, all 5 Great Lakes, as well as numerous inland lakes and rivers, have fish consumption advisories as a result of PCB contamination.
- 12 major utility companies in the USA have accelerated their voluntary phasedown of electric equipment which contain PCBs.
- USEPA and many states are working to remove sediments contaminated with PCBs from Great Lakes rivers and embayments.
- In Ontario, 46% of high level PCBs have been decommissioned in Ontario. 30% of high level PCB wastes and 20% of low level PCB wastes have been destroyed.
- Measurable levels of PCBs can be found in the tissues of all residents of the Great Lakes Basin (majority of monitoring is in blood and breast milk).

**Focus on Pesticides.**

- In US Great Lakes basin counties, the overall use of pesticides has decreased by almost 10 million lbs from 1994-1995. Annual pesticide usage now stands at 57 million lbs.
- There is increasing concern about possible endocrine disrupting properties associated with some pesticides.
- Canada and Ontario confirmed in 1996, zero use and availability of five priority substances (aldrin/dieldrin, chlordane, DDT, toxaphene, and mirex).

*USEPA Great Lakes Program Report on the Great Lakes Water Quality Agreement (December 1997).*

*USEPA Deposition of Air Pollutants to the Great Waters. Second Report to Congress (June 1977).*


**II. Endocrine Disruptors**

**Background:** A major issue in toxicology today is potential endocrine disruption. The current view is that a number of environmental chemicals and/or natural products may mimic, block, or alter hormonal activity in offspring and thus pose a hazard to normal development. Canada and the US have both initiated action to address scientific and regulatory issues related to endocrine disruptors.

**US Activities:** As a result of growing concerns regarding the presence of endocrine disruptors in food, water, and the environment, and the 1996 passage of the Food Quality Protection Act (FQPA) and the amendments to the Safe Drinking Water Act, USEPA was required to develop a screening and testing program.
Specifically, EPA was required to:

- develop a screening program and testing program by August, 1998,
- implement the program by August, 1999, and;
- report to Congress on the program's progress by August 2000.

To implement this plan, USEPA formed the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) in 1996 and charged this committee with providing advice on how to design an appropriate screening and testing program. The EDSTAC was composed of scientists and representatives from USEPA, other federal agencies, state agencies, industry, water providers, worker protection and labor organizations, national environmental groups, environmental justice groups, public health groups, and research scientists. The committee was organized into work groups, and as of July 16, 1998, the draft document developed by the EDSTAC committee had been accepted by the full committee and delivered to USEPA on September 1.

Summary of recommendations:

1. The universe of chemicals (+ 87,000) considered for screening and testing should include:
   - all chemicals currently listed on the TSCA inventory (~75,500).
   - all active ingredients (approximately 900) and approximately 2,500 inert ingredients used to formulate over 20,000 pesticide products.
   - approximately 8,000 chemicals regulated by the FDA, including 5,000 ingredients in cosmetics and 3,000 food additives.
   - naturally occurring non-steroidal estrogens (NONEs) and other naturally occurring or environmentally degraded chemicals.
   - nutritional supplements (currently not regulated therefore difficult to estimate the number).

2. The screening and testing program should be implemented in a phased manner. This means the chemicals which are determined to be a high priority should be screened and, if necessary, tested prior to those which are determined to be a lower priority.

The proposed 2-tier battery follows.

Tier 1 was designed to detect chemical substances or mixtures capable of interacting with estrogen, androgen, or thyroid hormone systems. The recommended battery includes three **in vitro** assays, three **in vivo** mammalian assays, and two **in vivo** nonmammalian assays.

**In Vitro**

- Estrogen Receptor (ER) Binding/Transcriptional Activation Assay
- Androgen Receptor (AR) Binding/Transcriptional Activation Assay
- Steroidogenesis Assay with Minced Testis

**In Vivo**

- Rodent 3-day Uterotrophic Assay (Subcutaneous)
- Rodent 20-day Pubertal Female Assay with Thyroid
- Rodent 5-7-day Hershberger Assay
- Frog Metamorphosis Assay
- Fish Gonadal Recrudescence Assay

Alternate assays for possible inclusion:
In Vitro

- Placental Aromatase Assay

In Vivo

- Modified Rodent 3-day Uterotrophic Assay (Intraperitoneal)
- Rodent 14-day Intact Adult Male Assay With Thyroid
- Rodent 20-day Thyroid/Pubertal Male Assay

Tier 2 was designed to characterize the nature, likelihood, and dose-response relationship of endocrine disruption of estrogen, androgen, and thyroid in humans and wildlife. These tests are longer term studies designed to encompass critical life stages and processes, a broad range of doses, and administration by a relevant route of exposure, so a more comprehensive profile of biological consequences of chemical exposure can be identified and related to the dose of exposure which caused them. Tests will usually encompass 2 generations since effects associated with endocrine disruption may be latent and not manifested until later in life or may not appear until the reproductive period is reached.

Mammalian Tests

- Two-generation Mammalian Reproductive Toxicity Study; or
- A Less Comprehensive Test (when appropriate):
  - Alternative Mammalian Reproductive Test; or
  - One-Generation Test

Multigeneration Tests in Other Taxa

- Avian Reproduction (with bobwhite quail and mallard)
- Fish Life Cycle (fathead minnow)
- Mysid Life Cycle (Americamysis)
- Amphibian Development and Reproduction (Xenopus)

Canadian Activities: Health Canada works with Environment Canada on an inter-departmental committee on endocrine disruptors. The committee coordinates research activities and provides support for policy initiatives required to address endocrine disrupting substances currently in the environment, found in food, consumer products or drugs, or as pesticides, or those that may enter into commerce in the future.

Health Canada has an endocrine disruptor committee that addresses research, regulatory and policy issues. A draft annual report is attached.

Health Canada also participates in international activities under the OECD Working Group on Endocrine Disruptor Testing and Assessment and the WHO/IPCS Steering Committee for the Global Assessment of Endocrine Disruptors.

An increase in research funding will be directed to endocrine disruptors and their implications for health and the environment in 1999.