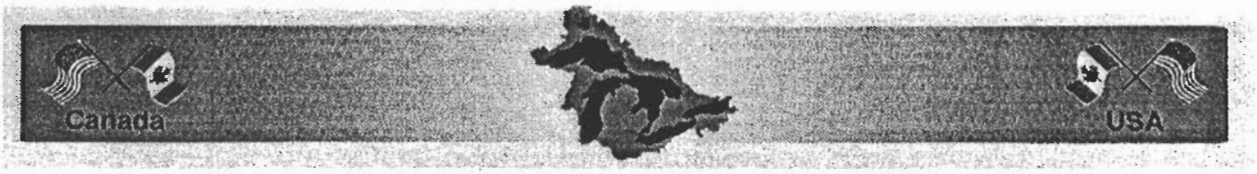

S.O.L.E.C.

1994 State of the Lakes Ecosystem Conference Background Paper

Effects of Great Lakes Basin Contaminants on Human Health

August 1995

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State of the Great Lakes Ecosystem Conference

Background Paper

EFFECTS OF GREAT LAKES BASIN ENVIRONMENTAL CONTAMINANTS ON HUMAN HEALTH

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NOTICE TO READER

These Background Papers are intended to provide a concise overview of the status of conditions in the Great Lakes. The information they present has been selected as representative of the much greater volume of data. They therefore do not present all research or monitoring information available. The Papers were prepared with input from many individuals representing diverse sectors of society.

The Background Papers were first released as Working Papers to provide the basis for discussions at the first State of the Lakes Ecosystem Conference (SOLEC) in October, 1994. Information provided by SOLEC discussants was incorporated into the these final SOLEC background papers. SOLEC was intended to provide key information required by managers to make better environmental decisions.

EXECUTIVE SUMMARY

This discussion paper examines the potential human health effects of exposure to certain Great Lakes Basin environmental contaminants from the following six groups: persistent organochlorine pesticides; chlorinated aromatic hydrocarbons (e.g., PCBs, dioxins, furans); heavy metals; airborne pollutants; radionuclides; and microbial contaminants.

Sources and Routes of Exposure: These contaminants of concern in the Basin have a variety of industrial, agricultural, municipal, and domestic sources. The major route of human exposure to PCBs, dioxins, furans, organochlorine pesticides and methylmercury is food consumption, particularly contaminated fish. Ingestion of untreated drinking water is a second route of human exposure to organochlorines, some heavy metals, and microbial contaminants. Breathing contaminated air is the obvious route of exposure to airborne pollutants. For those people using the Lakes for occupational or recreational purposes, dermal exposure to waterborne chemicals and microbes is relevant. Finally, all four routes of exposure are relevant in the case of radionuclides.

Exposure Trends: Research on trends in exposure to ***waterborne chemical contaminants*** reveals that: 1) there is no conclusive evidence that populations in the Basin are exposed to higher levels of toxic chemicals than are other populations in the world; 2) the few studies that have been done comparing measurable body burdens have produced varying, and sometimes conflicting, results; and 3) at present, researchers who have studied Great Lakes fish-eaters and compared body burdens of priority contaminants over time and with those in other populations have various explanations for current body burdens. Any measurable reduction in body burdens may be due to: a) reduced contamination in the ambient environment and in fish tissues and/or b) reduced fish consumption rates, especially in high-risk populations that are heeding fish consumption advisories.

Regarding ***airborne contaminants***, southern Ontario clearly has had the greatest number of days on which the Canadian air quality objective for ground-level ozone was exceeded. Average levels in several southern Ontario cities in the Basin have not changed significantly over the last ten years. Similarly, there has been little change in annual average levels of total suspended airborne particles (TSP) over the last 10 years. Areas in the southern Basin have had the highest sulphate levels (which correlate with actual acid aerosol levels), though other areas across Canada, such as the Maritimes, may experience comparable acid levels. Sulphate levels have declined slightly in Ontario over the last ten years. In the United States, the USEPA has estimated that on the U.S. side of the Basin 7.2 million people and 4.7 million people are exposed to levels of toxic air pollutants which are greater than health reference levels for acute and chronic effects, respectively.

Health Effects: This review focuses on hazard identification (not integrated exposure/health risk assessments), i.e., delineating the various *potential* adverse health effects.

Reproductive effects: Although there are inadequate data on exposure of Basin populations to trace concentrations of environmental contaminants and potential reproductive effects, the fetus

and neonate are thought to be at risk due to potential exposure *in utero* and via breast milk. Limited epidemiological evidence (based on the same cohort observed in different ways over time) suggest that *in utero* exposure to PCBs via maternal consumption of Great Lakes fish has resulted in lower birthweight, reduced gestational age, and smaller head circumference compared to controls. Increased susceptibility to infectious illness in the first four months of life has also been observed. More recently there has been speculation about a possible link between exposure to organochlorines and an increased incidence of breast cancer in women; and of abnormal sperm quality, density, motility, and testicular morphology in males. Further research is required to determine whether or not such links exist.

Neurological effects: As in the case of reproductive effects, the developing organism is more sensitive to neurotoxic effects than is the adult. There is epidemiological evidence and data from laboratory animal studies showing that low-level *in utero* exposure to PCBs via maternal consumption of contaminated Great Lakes fish results in adverse effects on cognitive, motor and behavioral development of infants, including deficiencies in cognitive ability to visually discriminate between objects, and in short-term memory scanning capabilities in infants. It is unclear whether body burdens of MeHg (methylmercury) in fish-eating Basin populations are associated with adverse neurological/behavioral effects. Exposure to lead *in utero* and/or during childhood at body burdens that are currently typical of humans in industrialized countries has resulted in deficits in IQ, and in distractibility, hyperactivity, inattention, increased reaction time, and other behavioral problems; and in developmental deficits in cognitive performance, abstract thinking, sustained attention, and psychomotor development.

Immunological effects: The immunotoxic potential of PCBs, dioxins, organochlorine pesticides (HCB, mirex, dieldrin and DDT), and the heavy metals cadmium, mercury and lead, raises concerns about subsequent effects on human health. Limited human epidemiological data and data from wildlife and laboratory animal studies indicate that certain human populations (e.g., those who consume large amounts of Great Lakes fish) might be vulnerable to adverse immunomodulating effects of these pollutants, which may be expressed either as immunosuppression or immunoenhancement. The former may be manifested either as decreased resistance to opportunistic viral, bacterial, fungal and other agents or increased susceptibility to cancer. Immunoenhancement, on the other hand, may either increase the risk of autoimmune reactions or result in allergic reactions.

Cancer: There is only limited human epidemiological evidence and case-control data to indicate that some drinking water sources with Great Lakes origin may be associated with increases in the incidence of several types of cancer in humans (e.g, bladder cancer). Some of these drinking water sources currently have elevated levels of certain contaminants represented by alpha-hexachlorocyclohexane (α-HCH), nickel, and trihalomethanes. However, the epidemiological evidence is not of sufficient strength to link exposure to these compounds with the elevated cancer incidences. In terms of risk estimates, according to USEPA the estimated number of potential excess cancer cases expected from ingesting contaminated Great Lakes drinking water is roughly 66 over a 70-year period; while that expected from consumption of Great Lakes fish is 30,000 over a 70 -year span, due mostly to PCB exposure, which accounts for an estimated

85% of human cancer risks associated with Basin contaminants. Finally, as mentioned earlier, there is recent speculation about a possible link between exposure to organochlorine pollutants such as PCBs and DDT, and the incidence of breast cancer.

Respiratory effects: The effects of air pollution on respiratory health can range from severe (aggravation of respiratory disease, death) to moderate (reduced lung function with or without symptoms) to minor (eye, nose and throat symptoms). Certain effects, such as mild inflammation in the lungs without symptoms, may or may not have any significance. Research which demonstrates increased death rates and rates of hospital admission due to air pollution could reflect a very large overall burden of illness in the population. There is strongly suggestive evidence from the Basin linking ozone, airborne particles and acid aerosols to significant respiratory health effects, including death and illness requiring hospital admission. There is also evidence from the Basin that these pollutants cause reduced lung function in children. This evidence is consistent with data from elsewhere in North America and Europe.

Radionuclide-related health effects: Using a no-threshold dose model for radiation effects, risk estimates for fatal cancer for the current Basin population of 36 million from exposure to natural background radiation are on the order of 5000 cases per year. The total estimated number of fatalities to the year 2000 from fallout radionuclides in the Basin is on the order of 4000. In contrast, estimates of risk for the nuclear fuel cycle (from exposures mainly to tritium and carbon-14 releases) based on environmental models are on the order of 10 cases per year. These numbers should be taken as upper limits, and show that the impact from current man-made sources is small compared to the effects of normal background radiation. With respect to drinking water, the total average effective doses of radionuclides for Great Lakes drinking water would result in two additional fatalities per year (also an upper limit) based on the maximum effective dose to the entire Basin population.

Microbe-Related Health Effects: Microbial (e.g., bacterial, viral, protozoan) contamination of Great Lakes water by human and animal sewage has been documented at numerous sites in the region. Those drinking the water at these locations run the risk of developing giardiasis, cryptosporidiosis, or gastrointestinal illness. A Canadian prospective study of swimming-related illness showed that swimmers experienced respiratory ailments most frequently, followed by gastrointestinal, eye, ear, and skin symptoms. Data on gastrointestinal illness rates among swimmers in this study revealed an excess of 13.3 cases per 1,000 compared to non-swimmers.

Knowledge Gaps and Directions for Future Research: There is a need for further research on exposure-response relationships (i.e., quantifying the level of exposure required to observe a specific adverse effect), contaminant exposure levels in Basin populations compared to those in other populations worldwide, the effects of chemical mixtures, and the use of biomarkers (i.e., to develop biomarkers of exposure and effect that are more sensitive and specific to particular chemical exposures). There is also a need to broaden the range of health effect endpoints studied and to gather additional epidemiological data, particularly on subpopulations at special risk.

Conclusions: It is clear that occupational or accidental exposure to high levels of certain environmental contaminants discussed in this paper (particularly PCBs, dioxins, organochlorine pesticides, lead, and methylmercury) pose a risk to human health. While the exact nature and the extent of health risk from exposure to environmental levels of these contaminants are unclear and require further study, recent research has contributed to a shift towards the "weight of evidence" approach in identifying and measuring potential adverse health effects. In addition to data from laboratory animal studies and (limited) human epidemiological studies, adverse metabolic, developmental, reproductive, behavioral, and immunological effects have been observed across a range of wildlife species exposed to mixtures of persistent toxic chemicals present in the Great Lakes ecosystem.

Furthermore, traditional health outcomes such as cancer and birth defects, which are relatively severe and well recorded, may be insensitive health indicators of the effects of low-level exposure to environmental chemicals. There is a need for further study of the less severe, more subtle effects due to long-term, low-level exposures to mixtures of toxic chemicals, including effects on reproduction, the immune system, the respiratory and circulatory systems, and development in children, and to identify any possible long-term adverse health effects.

Based on our knowledge thus far, it would appear that the health of some groups within the Basin population could be at greater risk than the general population. These include children, the elderly, those in ill health, the fetus and newborn child could have greater sensitivity to toxic chemicals; and sportsmen and Native peoples who consume contaminated fish and wildlife.

Finally, exploring directions for future research ranging from integrated exposure assessments to body burdens to potential health outcomes, should be a priority to help reduce the uncertainties in our knowledge of the potential short- and long-term adverse health effects from exposure to toxic chemicals in the Great Lakes Basin.

1.0 Introduction

The purpose of this paper is to review and summarize the state of the Great Lakes in terms of the human health impacts of exposure to environmental contaminants in the Great Lakes ecosystem. Most of the concern over health effects has focused on the presence of toxic chemical contaminants throughout the Great Lakes ecosystem, particularly those chemicals that have been shown to cause harm to the fish and wildlife which inhabit the Lakes. Extensive reviews of the effects of the chemicals of concern in the Great Lakes have led scientists and government agencies to focus their attention on reproductive, developmental and metabolic processes and how certain chemicals can disrupt these processes. This is a shift in recent years away from the almost exclusive regulatory focus on protecting people from substances which cause cancer or structural birth defects. This new focus highlights the effects that some chemicals can have even at minute exposures, including effects that are passed down from parents to their offspring. The result of this recasting of the human health question has been, ironically, to raise public concerns about environmental exposure to toxic substances when significant progress has been made in reducing the amount of toxic chemicals present in the Great Lakes. This paper will explore the state of current scientific knowledge on the human health impact of toxic chemical contamination of Great Lakes waters, and will also review the effects of air pollutants, radionuclides, and microbial contaminants in the Great Lakes Basin.

The many reports of harmful effects on wildlife from toxic chemicals in the Great Lakes environment have stimulated and maintained a high level of interest in environmental toxicology (Gilman *et al.*, 1991). As a result, the wildlife of the Lakes are among the most intensely studied of any in the world. In addition to the wildlife studies, thousands of toxicological experiments have been carried out on laboratory animals which demonstrate a range of toxic effects for some of the Great Lakes chemicals of concern even at extremely low levels of exposure. A variety of health effects have been described and documented in the scientific literature and repeated in many papers and reports. The results have been summarized in many documents while analysis of past data and new discoveries continue at an accelerated pace. For many people, the information is startling and raises obvious questions about health effects in human beings. When mink fed Great Lakes fish fail to reproduce, and when birth defects, sexual maldevelopment, and other developmental effects are reported by biologists studying wildlife in varying locations throughout the Great Lakes, it is natural for the public to ask if they or their children are similarly affected. Current research is aimed at addressing the question: if there are known causal relationships between toxic contaminants and consequent effects in wildlife, what are these toxic contaminants doing to human populations?

The International Joint Commission's Fifth Biennial Report on Great Lakes Water Quality (1989) summed it up with the conclusion that:

> *" ...the Commission must conclude that there is a threat to the health of our children emanating from our exposure to persistent toxic substances, even at very low ambient levels."*

Obligations under the Great Lakes Water Quality Agreement

The Canadian and United States federal governments, as Parties to the Great Lakes Water Quality Agreement, are committed to work in cooperation with state and provincial governments to develop and implement programs to fulfil the purpose of the Agreement. The goals outlined in the Agreement relating to human health are found in Annex 12 (IJC, 1978a) and include: 1) the establishment of monitoring and research programs to identify the impact of persistent toxic substances on the health of humans and the quality and health of living aquatic systems...2) development of the use of reproductive, physiological and biochemical measures in wildlife, fish and humans as health effects indicators and the establishment of a data base for storage, retrieval, and interpretation of the data...and 3) conducting research to determine the significance of effects of persistent toxic substances on human health and aquatic life. Furthermore, Annex 17 2(1) (IJC, 1978b) states that both parties shall "develop approaches to population-based studies to determine the long-term, low-level effects of toxic substances on human health."

The Science Advisory Board of the International Joint Commission recommends that the Parties consider policy objectives that reflect a preventive approach to protecting human health. Thus, recognizing the limits to scientific inquiry in determining cause and effect linkages of exposure to toxic chemicals, the IJC has recommended that the United States and Canada consider data from a variety of sources: laboratory animal studies, studies of acute human exposure, and studies of more subtle effects on humans from chronic low-level exposures; and using the "weight of evidence" of these data to determine the potential for adverse effects on human health (Great Lakes Science Advisory Board, 1991). Both the U.S. and Canada have instituted programs to review and continue research on possible effects on human health.

We will focus on the most recent results of human health studies undertaken in the United States and Canada, many of them preliminary and ongoing, specifically addressing issues of human exposures in the Great Lakes region and potential effects. There is no benchmark with which to compare the current status of human health in the Great Lakes region. The human health problems that are documented in research are not unique to the populations residing in the Great Lakes. However, the Great Lakes Basin is a unique ecosystem where many diverse stakeholders debate the focus and direction of human health research. The two federal governments have responded to public concerns by initiating research projects that are designed to address some of the most pressing concerns.

2.1 Priority Contaminants

Hundreds of chemicals have been identified in the Great Lakes ecosystem. The International Joint Commission on Great Lakes Water Quality has designated a number of these as critical pollutants, or priority contaminants, based on factors which determine the processes by which they appear in the environment and the level of concern and attention given to a particular compound: 1) presence and ambient concentration in the Great Lakes environment; 2) degree of toxicity; 3) persistence in the environment; 4) bioavailability; and 5) potential to bioconcentrate and bioaccumulate.

Presence in the environment: Using various screening techniques, 362 contaminants have been confirmed as being present in measurable concentrations in either the water or sediments or in the tissue of fish, wildlife or humans. This list includes 126 substances for which evidence exists of toxic effects on various life processes.

Toxicity: A toxic substance is defined by the GLWQA as a "substance which can cause death, disease, behavioral abnormalities, physiological or reproductive malfunctions or physical deformities in any organism or its offspring, or which can become poisonous after concentration in the food chain or in combination with other substances" (1978 Great Lakes Water Quality Agreement, Article I(v)) (IJC, 1978c). Substances vary widely in the concentrations at which they produce adverse effects. Toxicity can also be species-specific in that concentrations that are harmful or even lethal to one kind of organism may be harmless to another. Some substances are harmless in the condition in which they are released, but processes in the environment may change their chemical characteristics so that the resulting compounds are far more toxic than the original chemicals.

Persistence: Persistence is a measure of how successfully a chemical resists degradation and therefore how long it remains in the environment. Persistence increases the chances of a substance causing harm over time. In the Great Lakes Water Quality Agreement, a persistent toxic chemical is defined as "any toxic substance with a half-life in water greater than eight weeks." "Half life" refers to "the time required for the concentration of a substance to diminish to one-half of its original value in a lake or water body." However, half-life measurements will vary extensively depending on physical, chemical and biological conditions of the receiving waters. More generally applicable definitions of persistence are being developed based on the various processes by which a substance disappears in the environment.

Bioavailability refers to the extent to which, and at what relative rate, a substance is absorbed or assimilated by living organisms. Bioavailability is affected by a number of factors such as the physical state in which the substance is released, chemical characteristics of the water body, and characteristics of the substances with which the toxic compound is associated. A compound may bind to sediments and then be taken up by bottom-dwelling organisms. Thus, an organism's exposure to a chemical is determined by its bioavailability.

Potential to Bioconcentrate and Bioaccumulate: Bioconcentration refers to the tendency of a compound to concentrate in living organisms. Bioconcentration results from the direct uptake of pollutants by an organism, and the inability of an organism to eliminate the chemical as fast as it enters the body. It does not include pollutants accumulated through the intake of food. ***Bioaccumulation*** refers to the biological processes by which a substance is assimilated into an organism through eating another organism (plant or animal). Depending on the substance, it may be passed through the body fairly quickly, or it may accumulate in certain organs or tissues, thus enabling the chemical to concentrate in body tissues. In food webs such as those that exist in the Great Lakes ecosystem, organisms bioaccumulate toxic substances and pass them along to the next higher level all the way up to the top predators. As this process is repeated through the food web, persistent toxic substances become increasingly concentrated or ***biomagnified***. This is especially critical to the Great Lakes environment because top predators such as gulls, eagles and sport fish may, over their lifetime, accumulate large amounts of toxic pollutants through their consumption of fish that in turn have consumed large quantities of plankton; each organism in turn bioconcentrating and biomagnifying the persistent toxic chemicals available in the environment. As top predators, humans and wildlife that consume Great Lakes fish are thus exposing themselves to concentrated levels of toxic chemicals from the Great Lakes environment.

Among the hundreds of chemicals in the Great Lakes environment, certain ones are of greater concern than others. Consistent with the factors described above, these contaminants are chemicals that are found in parts or all of the Great Lakes, are known to cause harm to living organisms, are present in forms that are available to aquatic life, and have a tendency to accumulate to relatively high concentrations in the upper food chain. Obviously, a substance that is persistent and highly neurotoxic, such as lead or mercury, or highly carcinogenic such as benzo(a)pyrene will be of great concern if it is widely present, even if it does not bioaccumulate to a great degree.

Based on the above factors and considerations, the International Joint Commission's Great Lakes Water Quality Board has identified eleven chemicals as priority contaminants *(indicated below by *).* In addition to those designated by the IJC, there are several other substances (also listed below) that are worthy of consideration in the context of potential harm to the ecosystem and to human health.

Organochlorines

- polychlorinated biphenyls (PCBs) *
- dioxins (i.e., PCDDS; e.g., 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), *
- furans (i.e., PCDFs; e.g., 2,3,7,8-tetrachlorodibenzofuran, (TCDF) *
- certain pesticides:
  - DDT and metabolites (e.g., DDE) *
  - mirex *
  - toxaphene *
  - hexachlorocyclohexanes (HCHs; e.g., Lindane)

- hexachlorobenzene (HCB) *
- aldrin/dieldrin *
- chlordane and metabolites
- heptachlor and heptachlor epoxide

Airborne Contaminants

- ground-level ozone
- polycyclic aromatic hydrocarbons (PAHs) (e.g., benzo(a)pyrene, or B(a)P) *
- particulates
- acid aerosols
- nitrogen oxides and sulphur dioxides
- volatile organic chemicals (VOCs) (e.g., trihalomethanes, tetrachloroethylene)

Toxic Heavy Metals

- alkylated lead *
- methyl mercury *
- cadmium

Radionuclides

Examples:

- strontium
- cesium
- radon gas

Microbial Contaminants

Examples:

- bacterial pathogens (e.g., *Escherichia coli*)
- viral pathogens (e.g., Enterovirus)
- protozoa (e.g., *Cryptosporidium, Giardia*)

2.2 Sources of Priority Contaminants and Routes of Human Exposure

There are a number of pathways by which humans can be exposed to toxic contaminants in the Great Lakes Basin. The two major routes of human exposure are the consumption of food, primarily fish, and the ingestion of drinking water.

Fish consumption is a major exposure route because toxic substances such as dioxins, furans, DDT/DDE, hexachlorobenzene, mirex, mercury, PCBs, toxaphene, chlordane, and lindane found in the Great Lakes bioaccumulate in fish tissue (Colborn *et al.*, 1990). Many of these chemicals (e.g., PCBs, mercury, and DDE) have been found in the tissues of human populations that consume Great Lakes fish. A study of Wisconsin anglers revealed that there were significant correlations between sport-caught fish meals and PCB and DDE blood/serum levels, and between kilograms of fish caught and PCB blood/serum levels (Fiore *et al.*, 1989).

With respect to consumption of drinking water, a second route of exposure, the cumulative effect of long-term, low-dose exposure to chemicals in drinking water cannot be ignored due to the large population dependent on Great Lakes surface water. The USEPA has estimated that approximately 12,700,000 people drink about 2 liters of contaminated water per person per day from surface water supplied systems within the Great Lakes counties (USEPA Great Lakes National Program Office, 1992). Ingestion of contaminated drinking water or recreational water is also a route of exposure to microbial contaminants.

A third, less prominent, exposure pathway is inhalation of polluted air. The Great Lakes do not act as a barrier to air pollution. Long range atmospheric transport carries air pollutants across international boundaries, from their origin in the industrial centers (e.g., the Ohio River Valley) of the U.S. to the Great Lakes Basin, particularly southwestern Ontario. The air pollutants currently of greatest concern are ground-level ozone, airborne particles and acid aerosols (Stieb and Burnett, 1993). While inhalation of toxic substances resulting from atmospheric deposition is considered a minor toxic chemical exposure route when compared with ingestion of food (primarily fish), a recent study conducted by the International Joint Commission on the risks of hazardous air pollutants in the Detroit-Windsor/Port Huron-Sarnia region concluded that there is, in fact, a significant public health concern due to elevated levels of a number of compounds known as "air toxics" (e.g., benzene, trichloroethylene) in this region. Although insufficient information is available to define the extent to which excess disease or death rates in this particular area are attributable to exposure to these airborne toxic chemicals, the researchers recommend that air emission abatement programs be implemented and preventive measures be pursued (International Joint Commission, 1992).

Lastly, dermal exposure to waterborne contaminants has only recently been considered a notable exposure route, and deserves some mention here. People who use the Great Lakes for occupational or recreational purposes (e.g., swimmers) that involve skin contact with lakewater may be dermally exposed to low levels of a wide variety of chemical and microbial water

contaminants, including organochlorines, PAHs, heavy metals, volatile organic compounds, bacteria, viruses, protozoa, and parasitic worms. It is possible that these contaminants will be absorbed through or penetrate breaks in the skin to some degree and hence become bioavailable (Moody and Chu, 1994). In particular, lipophilic chemicals may be bound to the organic components of suspended sediments (which act as a "carrier" for transdermal delivery of the compounds) and would also tend to concentrate in the thin layer of oil, or surface slick, that is present over all natural bodies of water (Platford *et al.*, 1982; Moody *et al.*, 1987). Although dermal exposure is the least prominent route of human exposure to environmental chemicals in the Great Lakes, and the degree of dermal absorption may be low, it is possible that after prolonged exposure of a large body-surface area to lakewater -- especially under conditions that may enhance skin permeability, such as peeling of the stratum corneum following sunburn -- toxicologically significant amounts of certain chemicals could be absorbed via the dermal route (Wester, 1987). It is unlikely, however, with the possible exception of the marathon swimmer, that a large risk would result from such exposure.

Table 1 lists the sources and routes of exposure of the identified contaminants of concern in the Great Lakes Basin. In summary, the major route of human exposure to PCBs, dioxins, furans, organochlorine pesticides, and certain heavy metals (e.g., mercury) for residents of the Basin is food consumption, particularly contaminated fish. The relative exposure routes vary by chemical, but food is believed to contribute from 40% to nearly 100% for many of these toxic substances (Parfett *et al.*, 1994). Exposure via ingestion of untreated drinking water is a second route of human exposure to organochlorines, heavy metals, and microbial contaminants. Regarding airborne pollutants, obviously breathing contaminated air is the key route of exposure to these contaminants. Dermal exposure, though a minor route of exposure to waterborne chemicals, is more significant in the case of microbial contaminants, and is particularly relevant to those people using the Lakes for occupational or recreational purposes. Finally, with respect to radionuclides, inhalation of atmospheric radioactivity and consumption of contaminated food and water are routes of internal exposure, while external exposure can occur from irradiation by radionuclides in the air or deposited on the ground, and is dependent on the proximity of the source.

TABLE 1
SOURCES OF PRIORITY CONTAMINANTS AND ROUTES OF EXPOSURE

CONTAMINANT	SOURCES	ROUTES OF HUMAN EXPOSURE
Polychlorinated Biphenyls (PCBs)	Used in electrical transformers and capacitors, and in hydraulic equipment; also as lubricants and heat-transfer fluids. Released to environment primarily via equipment in use and by waste site leakage.	Consumption of contaminated foods, particularly fish, meat, and dairy products.
Polychlorinated dibenzo-p-dioxins (PCDDs) (esp. 2,3,7,8-TCDD) and polychlorinated dibenzofurans (PCDFs)	Formed as impurities during the synthesis of various chlorinated compounds (e.g., certain pesticides and herbicides); released through pulp and paper bleaching and solid waste incineration; found in exhaust from vehicles using fossil fuels; and can also result from the combustion of any chlorinated organic material.	Consumption of contaminated foods, particularly fish, meat, and dairy products, although it has been estimated that up to 99.9% of the total environmental burden exists in soils and sediments.
DDT and its degradation products (e.g., DDE)	An insecticide now banned in Canada and the U.S.A. Sources are leakage from waste sites and atmospheric transport and deposition.	Consumption of contaminated foods, especially fish and dairy products.
Mirex	A fire retardant and contact insecticide once used in Canada and the U.S. now banned in both countries. Extremely persistent; may reach the GLB via surface run-off from contaminated soils or by leaching from hazardous waste sites.	Consumption of contaminated foods.
Toxaphene	An insecticide used on cotton fields. Its use is restricted in Canada and the U.S. Sources include contaminated soils, hazardous waste sites, and air transport.	Consumption of contaminated foods.
Aldrin and Dieldrin (i.e., chlorinated cyclodienes. Other examples are chlordane and its metabolites, heptachlor and heptachlor epoxide)	Aldrin and dieldrin are insecticides used for control of soil insects and mosquitos. Dieldrin is also produced from the metabolic oxidation of aldrin. Their use is restricted.	Consumption of contaminated foods, especially fish.
Hexachlorobenzene (HCB)	A fungicide no longer used in Canada or U.S.; also generated as a by-product of fuel combustion and the production of some pesticides.	Consumption of contaminated foods, especially fish.
Hexachlorocyclohexanes (HCHs) (e.g., lindane)	An insecticide, lindane (γ-HCH) is one of 8 HCH isomers. β-HCH is the key isomer found in human tissue, accumulating in body fat; γ-HCH does not. No longer produced in U.S., but still used (imported). Registered for use in Alberta.	Consumption of contaminated foods. Can be transported by water and air.
Microbial Contaminants (e.g., bacteria, viruses, protozoa)	Found in poorly treated sewage discharge, agricultural run-off and urban run-off which promote algae and weed growth; also storm water run-off, animal feces.	Consumption of contaminated drinking water or recreational water; absorption through the skin.
Radionuclides	Arise from a variety of natural and man-made sources. Natural radiation comes from the sun and from various radioactive isotopes in the earth, while anthropogenic sources include nuclear weapons test fallout and emissions from nuclear power facilities.	Inhalation of contaminated air and consumption of contaminated food and water (internal dosing); and exposure by direct irradiation (external dosing).

TABLE 1 (cont'd)
SOURCES OF PRIORITY CONTAMINANTS AND ROUTES OF EXPOSURE

CONTAMINANT	SOURCES	ROUTES OF HUMAN EXPOSURE
Methyl Mercury (MeHg)	Synthesis as result of atmospheric deposition of elemental mercury from natural oceanic output (30-40% of annual Hg emissions to atmosphere); released from inundated vegetation. Inorganic Hg also occurs naturally in soils and as a by-product of chlor-alkali, paint, and electrical equipment manufacturing processes. MeHg bioconcentrates in fish.	Consumption of contaminated fish and marine products.
Cadmium	Atmospheric deposition, fertilizers, sewage sludge, solid wastes, cadmium mining/refining operations, soil, plant-life.	Consumption of contaminated foods, esp. organ meats (liver, kidney), seafood (shellfish, crustaceans), and cereals (e.g., wild rice); tobacco use; consumption of drinking water (minor).
Lead	Combustion of leaded gasoline, metal smelters, automotive batteries, contaminated soil and dust, lead-based paints, drinking water in contact with lead-soldered pipes, atmospheric deposition.	In the absence of a point source of contamination, consumption of contaminated foods and drinking water; inhalation of contaminated air.
Ground-level Ozone	Formed from the interaction of nitrogen oxides and hydrocarbons in the atmosphere in presence of high temperatures and sunlight. Can be transported long distances.	Inhalation of contaminated air.
Acid Aerosols	Formed when pollutants such as sulphur dioxide and nitric oxide are transformed in the atmosphere in presence of sunlight; may be transported long distances from the original source in the form of rain, snow, vapour, fine particles and gases; can be both air and water pollutants.	Inhalation of contaminated air.
Airborne particles	Very small pieces of solid or liquid matter that vary in size, chemical composition and source. Can be coarse or fine. Fine particles arise mainly from man-made sources such as combustion of fuels, and include sulphates and nitrates as well as metals. Coarse particles consist largely of naturally occurring substances, particularly soil.	Inhalation of contaminated air.
Polycyclic Aromatic Hydrocarbons (PAHs) (e.g., benzo[a]pyrene)	Incomplete combustion of fossil fuels, organic matter, and solid waste; combustion activities associated with industry (e.g., coke production, metal smelting, oil refining). Non-commercial sources include wood-burning fireplaces, cigarette smoke, vehicle exhaust; and smoked, grilled, fried, or barbecued meat and fish.	Inhalation of contaminated air and consumption of certain foods.
Volatile Organic Chemicals (VOCs) (e.g., trihalomethanes, benzene, trichloroethylene)	Formed from natural or industrial sources by the interaction of chlorine with organic materials; also found in dry-cleaning solvents; both an airborne and drinking water contaminant.	Inhalation of contaminated air during exposure to treated tap water (showering, bathing) or dry-cleaning solvents; and consumption of drinking water.

Source: Great Lakes Health Effects Program, Health Canada, 1993.

2.3 Populations at Greatest Risk

Due to the persistent nature of some of these contaminants and their biomagnification and accumulation in the food chain, Great Lakes residents who consume larger amounts of contaminated fish and wildlife than the general population are at greatest risk of exposure to toxic pollutants, and are at greatest risk of health effects. These subpopulations include sport anglers, their families, Native Americans and certain other communities that rely on Great Lakes fish for sustenance. In the United States approximately 11% of the population in the Great Lakes Basin are licensed anglers (USEPA, 1992), whereas in Canada roughly 8% of the Ontario population are fishing license-holders (Kearney, 1992; SPR Associates, 1991). (This latter figure includes both GLB and non-GLB residents; a reliable figure on the percentage of licensed anglers in the GLB Canadian population alone is unavailable). Surveys of the U.S. population have found that the average rate of fish consumption in the Great Lakes region is greater than the national average. Recent studies, however, indicate that some high-risk groups are reducing their fish consumption and fish preparation habits in response to health advisories. A survey of 8,000 licensed sport anglers from all of the U.S. Great Lakes states found that 36% of the respondents had made changes in their fish consumption behaviors in response to state health advisories. Modifying fish-cleaning and preparation methods was the most common change (59%), followed by eating less Great Lakes fish (Connelly and Knuth, 1993). In addition, Fitzgerald *et al.* (1993) found that pregnant women of the Mohawk nation had reduced their fish consumption substantially.

A notable Canadian initiative concerning Native communities at risk of exposure to environmental contaminants in the Great Lakes basin is the EAGLE (Effects on Aboriginals from the GreatLakes Environment) Project, which was established as a First Nations/Health Canada partnership and is linked to the latter's Great Lakes Health Effects Program under the Canadian government's Great Lakes Action Plan. EAGLE is a community-based epidemiologic project involving the study of the effects of environment contaminants on the health of the approximately 100,000 First Nations people living in 63 aboriginal communities in the Great Lakes Basin -- i.e., the program targets one of the specific "at risk" groups (Assembly of First Nations, 1993). It is based on the recognition that aboriginal people, because of their high consumption of fish and wildlife, are likely to be more exposed to bioaccumulating contaminants in the environment than is the general population. As a consequence, they may be at higher risk of adverse health effects.

The goal of the EAGLE project is to assess the extent of exposure of the Native people living in the Great Lakes Basin to bioaccumulating environmental contaminants and the associated risk to their health and wel-being. The project builds on earlier direct cause-and-effects studies by taking a holistic approach which includes examining exposures in both adults and children, socio-economic effects, and the impact on traditional ways of life, culture and values. These and other "indirect" health impacts of exposure to environmental contaminants in aboriginal communities are frequently more important than the direct effects of exposure to environmental contaminants.

The EAGLE project emphasizes strong community involvement that fosters a real sense of ownership among the residents of the 63 aboriginal communities in the Great Lakes Basin. The

community-based study has a solid scientific basis with innovative elements in its design, which blends scientific knowledge and the needs of the aboriginal communities, with each component carrying equal weight. This is reflected in the managment and administration of the project. The Assembly of First Nations (AFN), a native aboriginal organization representing First Nations across Canada, is responsible for the day-to-day operations of the project.

Among the study components of the EAGLE project are the following:

- an Eating Patterns survey which was initiated in 1993 following the results of a successful pilot study;
- a pilot exposure study being initiated in the First Nation community of Walpole Island;
- an analysis of morbidity and mortality data on aboriginal people in the Great Lakes region; and
- implementation of a geographic information system (GIS) to consolidate all data on a geo-reference basis relating to Great Lakes Native communities.

The EAGLE project was initiated in September 1990, and is targeted for completion by the end of 1996/97 fiscal year. The partnership approach to the project has already proven to be a very positive experience for all concerned. The holistic conceptual framework will enable the project to use the traditional ecological knowledge of the First nations to more clearly understand the effects of bioaccumulating contaminants on aboriginal health. Data on levels of these contaminants in fish and from the Eating Survey are being used to assess exposure in Native communities in the Great Lakes region. Measurements of the levels of organochlorine contaminants in the blood of individuals are being conducted at the request of the Native communities themselves.

Although data from the EAGLE project are still being analyzed and detailed results are not yet available, a preliminary analysis of the inital findings has confirmed longstanding assumptions that First Nations people do indeed eat considerably more fish and game and have significantly higher averages consumption levels than the majority of the Canadian general population (Wheatley, personal communication, 1994).

Several U.S. studies have also focused on Native communities that have traditionally depended on fish and wildlife as a major source of food in their diets. In New York State the Mohawks living along the St. Lawrence River consume an average of 25g/day (1/2 lb per week) of locally caught fish. This is two to six times higher than the average rates of consumption of sport-caught fish by recreational anglers, and two to four times higher than the average rate cited by the USEPA in its National Study of Chemical Residues in Fish (1993). Furthermore, the greater importance of locally caught fish is consistent with the traditional dependence of the Mohawks on fish and other local food sources (Forti *et al.*, 1993). Generally, the average rates of fish consumption in Native communities are higher than the average consumption rates for Wisconsin recreational anglers (11 g/day of sport-caught fish), Lake Ontario recreational anglers (4.3 g/day of Lake Ontario fish), and the general U.S. population (6.5 g/day of freshwater fish) (Fiore *et al.*, 1989; Connelly *et al.*, 1990; USEPA, 1993). (It should be noted that the amounts

of fish reported eaten by recreational anglers per day are for licensed anglers only; it is likely that some anglers are not license-holders). These data are also consistent with initial findings of the Canadian Department of Health's EAGLE project, which confirms longstanding assumptions that First Nations people do indeed eat considerably more fish and have significantly higher average consumption levels than the majority of Canadians (Wheatley, 1994).

However, it is evident from another U.S. study conducted on the same Mohawk population that certain high-risk groups such as pregnant women have changed their behavior to avoid exposure to contaminants. In 1992, Fitzgerald *et al* investigated the levels of PCBs, p,p'-DDE, mirex, and HCB in the breast milk of fifty-three Mohawk women from Akwesasne who gave birth from 1988-1990. Data from an assessment done between 1986-1989 on the Mohawk women showed a positive association between lifetime exposure to PCBs from the consumption of local contaminated fish and their breast milk PCB concentrations. In contrast, Fitzgerald's study concluded that this correlation was no longer apparent among women who participated in 1990 because their fish consumption rates were so low. Indeed, local fish consumption has decreased over time among the Mohawk women, from two meals to less than one-half of a meal per month during pregnancy. The researchers attribute this to the success of fish advisories issued by Mohawk, state, and federal agencies against the eating of fish from the local area by women of child-bearing age (Fitzgerald *et al.*, 1992).

In 1993, Dellinger *et al.* reached similar conclusions. They studied 89 Ojibwa from the Northern Wisconsin Chippewa Tribe to determine fish consumption habits and body burdens of mercury and PCBs. They concluded that there were no significant body burdens of contaminants that could be related to any known health risks. As with the Mohawk women, the researchers concluded that the majority of the sample populations in the Chippewa Tribe are aware of and heed Wisconsin fish consumption advisories (Dellinger *et al.*, 1993). Again, in another study of members of the Chippewa Tribe in northern Minnesota, researchers found fish consumption levels to be lower than expected (ATSDR, 1994).

Although certain populations may be changing their behavior, it is difficult to make generalizations about the whole Great Lakes fish-eating community from the studies cited above. For example, the figure of 36% in the Connelly and Knuth (1993) survey regarding the proportion of sport anglers who had changed their fish consumption behaviors in response to state health advisories appears to be lower than expected. Indeed, researchers in Michigan conducted a survey in 1989 of fishing license-holders and found that the average sport-fish consumption rate for sport fishermen and their families was approximately 18.3 g/person/day. For minority fishing license-holders the figure is 21.7g/day (West *et al.*, 1990).

The U.S. Environmental Protection Agency (USEPA) recently published a study on the health risks associated with chemical residues in fish from 338 sites nationwide. Two contaminants, specifically PCBs and dieldrin, were found at levels with an estimated upper-bound cancer risk equal to or greater than one in ten thousand for the average fish-eating population (assuming a fish consumption rate of 6.5 g per person per day) (USEPA, 1993). Of a total of 46 sites where these chemical residues are indicative of cancer risks, almost one third (13 sites) are in the Great

Lakes Basin (see **Table 2**).

Table 2

U.S. Sites on the Great Lakes with Estimated Cancer Risk Greater than 10^{-4} (1 in 10,000)

Waterbody	City
Lake Ontario	Olcott, NY
Grass River	Massena, NY
Lake Ontario	Rochester, NY
Niagara River	N. Tonawanda, NY
Eighteen Mile Creek	Olcott, NY
Oswego Harbor	Oswego, NY
Niagara River Delta	Porter, NY
Lake Michigan	Waukegan, IL
Kalamazoo River	Saugatuck, MI
Rouge River	River Rouge, MI
Muskegon Lake	Muskegon, MI
Milwaukee River	Milwaukee, WI

Source: Adapted from EPA National Study of Chemical Residues in Fish Fact Sheet, Nov. 1992

Table 3

National Human Adipose Tissue Survey in the United States

Contaminant	Regional Rankings								
	NE	MA+	SA	EN*	ES	WN	WS	MO	PA
Pesticides	6	3.5	3.5	8	1	5	2	7	9
PCBs	8	5	2	6	1	3	4	7	9
Semi-volatiles	7	5	3	1	4	6	2	8	9
Volatiles	5	6	1	3	7	9	2	4	8
PCDDs and PCDFs	9	2	4	1	3	7	8	5	6
Total Ranking @	35	21.5	13.5	19	16	30	18	31	41

Source: Adapted from Phillips et al., 1991
+MA = Mid-Atlantic states, including New York and Pennsylvania.
**EN = East North Central states, including Indiana, Ohio, Illinois, Michigan, and Wisconsin.*
@ = Regions which rank high for a particular contaminant category are indicated by low numerical scores.

Table 4

Mean Concentration of PCBs in Breast Milk Throughout the U.S. & St. Lawrence

Area/Yr	N of Samples	% Positive	Mean+ (ppm)	Range (ppm)
Michigan ('76)	95	100	0.82(med)*	0.1-3.3
Michigan (77-78)	1,057	100	1.50	0.3-5.1
Hawaii (79-80)	50	100	0.78	0.02-1.8
Hawaii (79-80)	54	100	0.80	0.13-2.2
U.S. (79)	50	2	<1(med)*	<1-3
U.S. (79-80)	102	100	0.97	0.08-4.4
Michigan (82)	138	100	0.74(med)*	
N. Carolina (78-84)	617	94	1.50(med)*	0.3-14.8
Binghampton, NY (85-87)	7	pooled	0.15	
St. Lawrence, NY (90)	57		0.405	0.25->1.0

Source: Adapted from Fitzgerald, 1992
+Arithmetic mean
**med = median*

3.0 Exposure Trends

The following discussion of trends in exposure to organochlorine contaminants reveals that:

1) there is no conclusive evidence that populations in the Great Lakes region are exposed to higher levels of toxic chemicals than are other populations in the world;

2) the few studies that have been done comparing measurable body burdens have produced varying, and sometimes conflicting, results; and

3) at present, the researchers who have studied Great Lakes fish-eaters and compared body burdens of priority contaminants over time with those in other populations have various theories to explain current body burdens. The reasons given for any reduction in body burdens are: a) decreased contamination in the ambient environment and in fish tissues and/or b) reduced fish consumption rates, especially in high-risk populations that are aware of and are heeding fish consumption advisories.

3.1 Organochlorines

The question remains as to whether populations in the Great Lakes Basin are more highly exposed to toxic pollutants than populations elsewhere. There are relatively few studies that have measured the body burdens of people in the Great Lakes region and compared them to those in the general population. It is difficult to answer this question because some studies have shown that populations in the Great Lakes region may have higher levels of chemicals in their tissues than populations in other regions of the world, while others show no difference. This is attributable to the differences in analytical methods used by various researchers which make it difficult to compare the data from different studies.

The U.S. National Human Adipose Tissue Survey (NHATS) produced data that were used to test the hypothesis that individuals in different regions of the U.S. are subject to varying degrees of toxic chemical exposure. The objective of NHATS was to detect and quantify the prevalences of toxic compounds in the general population (Phillips *et al.*, 1991). The concentrations of 54 compounds reported by NHATS were used in this study to examine regional variations in human toxic chemical exposure. These compounds were chosen because of their persistence in the environment and included many of the critical pollutants, such as PCBs, PCDDS, and pesticides. The region with the highest mean concentration was ranked number 1, while the region with the lowest mean concentration was ranked number 9. Thus, high rankings were indicated by low numerical scores.

The East North Central region was identified as encompassing the states of Ohio, Indiana, Illinois, Michigan and Wisconsin, all of which are in the Great Lakes region. The researchers

concluded that individuals residing in the East North Central states may be exposed to greater amounts of toxic substances than people in other regions of the country. The East North Central region was ranked third among the nine regions for total toxic substances surveyed for all age groups, and fourth out of nine for grand total rankings which were re-calculated for each region and age category by summing the total rankings for each category and adjusting for bias (see **Table 3**).

Phillips *et al* further studied the hypothesis that there is a greater potential for human toxic chemical exposure in the Great Lakes region than in other geographic regions of the U.S., using the Environmental Protection Agency's STORET database which maintains water quality data in the U.S. (Phillips *et al.*, 1990). The researchers tested the potential for exposure to toxic chemicals by using the levels of toxic substances in fish tissue and sediment as surrogates for human exposure. For the toxic chemicals surveyed, the results showed that the Great Lakes region is not the highest ranked in the country. In fact, the researchers claim, if one were to use the levels of toxic chemicals found in fish and sediment in the Great Lakes as surrogates for human exposure, the extent of indirect human exposure occurring in this region may be less than that in other regions of the country. The authors point out that in order to address the total exposure one would have to account for local rates of fish consumption. As we have noted, studies on fish consumption rates throughout the Great lakes region vary in their conclusions.

Some studies have tried to compare levels of contamination in Great Lakes fish-eaters with those of other populations. For example, Fitzgerald *et al.* (1992) point out that the levels of PCBs in the breast milk samples taken from Mohawk women at the St. Regis Reservation in St. Lawrence were equal to or lower than the levels reported for other populations, including those with no unusual exposure to chemical contaminants (see **Table 4**).

It is difficult to determine whether the body burdens of environmental contaminants observed in human populations in the Great Lakes Basin studied over a relatively short period of time (5-10 years) are correlated with decreasing body burdens seen in fish and other species in the Basin that have been monitored for over two decades. Studies of Great Lakes fish and wildlife confirm that the levels of PCBs, dieldrin, DDT, mercury and chlordane have declined since the mid-1970's (Borgmann and Whittle, 1991; Miller *et al.*, 1992a). In order to examine trends in human populations Hovinga *et al.* (1992) conducted a longitudinal study of a cohort of Great Lakes fish-eaters from Michigan (mostly licensed sports anglers). The researchers found that between 1982 and 1989, mean serum DDT levels decreased substantially in 115 of the fish-eaters and in 95 of the non-fisheater controls, while mean serum PCB levels decreased only slightly. While there was no correlation between changes in DDT and PCB body burden levels and fish consumption rates, the authors concluded that decreases in DDT levels can be attributed to the banning of DDT, which has reduced the overall levels of this contaminant in the environment (Hovinga *et al.*, 1992).

One would think that subsequent levels of these priority contaminants in humans would also decline. It is known that for certain contaminants such as mercury, dietary intake levels in the U.S. have dropped significantly in the past 15 years (Nieboer and Fletcher, 1993). In Canada, the

current levels of PCBs observed in human milk, serum, and adipose tissue are comparable to those observed in other developed countries. Lebel *et al.* (1991) and Williams and Lebel (1991) have studied the concentrations of polychlorinated dibenzodioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) as well as a few PCB congeners in human tissue samples from five Canadian municipalities within the Great Lakes Basin (Lebel *et al.*, 1991; Williams and Lebel, 1991). Their results show that concentrations of PCDD/PCDF are within the range of levels reported in other studies conducted throughout the world. Results are similar for PCB concentrations, although the data from comparison studies were limited and levels were still higher in the Canadian samples as compared to samples from studies conducted in other North American regions.

Even though the priority contaminant levels in the Great Lakes biota have generally decreased over time, Hovinga's (1992) longitudinal follow-up study of Great Lakes fish-eaters and controls showed that PCB levels did not change substantially during the seven-year period from 1982 to 1989. According to the authors, there may be a number of reasons for the static PCB levels in the fish-eater population studied: 1) restrictions on PCB production alone may not ensure decreasing levels of PCB exposure in human populations; 2) other sources of PCB contamination such as atmospheric deposition and waste site leakages may be major sources of exposure; or 3) because of the persistent nature of PCBs, seven years may not be a long enough time to see a decrease in body burdens of PCBs in human populations. Consequently, although there are documented decreases in the levels of toxic chemicals in wildlife populations in the Great Lakes region, there are not enough historical data to draw the same conclusions about humans in the Great Lakes Basin.

3.2 Airborne Contaminants

A recent Health Canada study (Stieb and Burnett, 1993) of the respiratory health effects of airborne pollutants in the Great Lakes Basin includes some useful data on the levels of three priority contaminants: ground-level ozone, airborne particles, and acid aerosols.

Ground-level ozone is a gas which is formed when oxides of nitrogen and hydrocarbons interact in the atmosphere in the presence of high temperatures and sunlight. It can be transported long distances, and levels can actually be lower in urban areas, where oxides of nitrogen can act as ozone "scavengers". Ozone levels are highest during the daytime in the summer months, and are typically monitored continuously at fixed site monitoring stations, which tend to be in medium-size to large cities. Between 1980 and 1991, the highest average daily ozone levels (8 a.m. to 8 p.m., May to August) among selected Canadian cities were recorded in London and Windsor, Ontario (both at 39 ppb), while two other Great Lakes Basin cities, Hamilton and Toronto, had levels (31 and 29 ppb respectively) comparable to those observed elsewhere in Canada. Average levels for these four Great Lakes cities have not changed significantly over the last ten years. Average one-hour maximum levels, which more closely represent the highest potential exposures, followed a similar geographic pattern, with the highest average levels observed in Simcoe (63.2 ppb) and Long Point (70.0 ppb) on the North shore of Lake Erie, as well as Windsor (60.2 ppb).

In these locations, some levels exceeded 118 ppb (Burnett *et al.*, 1993). **Figure 1** summarizes data on exceedance of the Canadian air quality objective for ground-level ozone for locations across Canada between 1982 and 1986. Southern Ontario clearly had the greatest number of days on which the air quality objective was exceeded during this period.

Airborne particles are very small pieces of solid or liquid matter, which vary in size, chemical composition, and source. Due to the wide variety of these contaminants, they also vary in their effects on respiratory health (Stieb and Burnett, 1993). Because only "fine" particles (i.e., those less than 10 μm in diameter, or "PM_{10}") are capable of penetrating deeply into the lungs, they are of most interest from the point of view of respiratory health. Fine particles tend to arise from man-made sources, particularly combustion of fuels, and include sulphates and nitrates as well as metals. Coarse particles consist largely of naturally occurring substances, particularly soil. In Ontario, total suspended particles ("TSP" - all sizes, coarse and fine) have traditionally been measured at a large number of sites, while PM_{10} monitoring has only recently begun at selected locations. There has been little change in annual average TSP levels over the last 10 years. In 1991, the highest levels in Ontario were in Hamilton (65 $\mu g/m^3$) and the Metropolitan Toronto area (42-58 $\mu g/m^3$). The highest daily TSP levels were recorded in Sault St. Marie (393 $\mu g/m^3$), Toronto (379 $\mu g/m^3$) and Hamilton (211 $\mu g/m^3$). Annual average PM_{10} levels were also highest in Hamilton (33 $\mu g/m^3$). The highest daily PM_{10} level was recorded in Sault St. Marie (160 $\mu g/m^3$), although levels of 120 and 100 $\mu g/m^3$ were recorded in Toronto and Hamilton respectively (see **Table 5 and Figure 2**) (Ontario Ministry of Environment, 1992). At present there are no Canadian air quality standards for respirable particles (PM_{10}).

TABLE 5
PM_{10} Concentrations at 9 Urban Sites in Ontario, 1991

CITY (see Figure 2 for location of site)	PM_{10} CONCENTRATION ($\mu g/m^3$)	
	Annual Average	Maximum
Hamilton	26-33 (3 sites)	70-100
Thorold	32	100
Sault St. Marie	19-29 (2 sites)	65-160
Etobicoke	26	81
Toronto	25	120
Windsor	25	60-69 (2 sites)
Scarborough	24	75
London	19	55
Thunder Bay	17	46

Source: Ontario Ministry of Environment, 1992.

TABLE 6
Sulphate Concentrations at Selected Sites in Ontario, 1983-1988

CITY (see Figure 3 for location of site)	SULPHATE CONCENTRATION ($\mu g/m^3$)	
	Average (May-August, 1983-88)	95% of measurements below:
Windsor	8.2	21.1
Longwoods	6.8	21.5
Toronto	6.7	20.1
Courtright	5.8	14.4
Charleston Lake	5.4	17.3
Pickering	4.5	14.9
Dorset	4.2	14.9
Chalk River	3.4	12.1
Algoma	3.1	11.7

Source: Burnett *et al.*, 1993.

Acid aerosols are essentially particles which contain acid, and are formed when sulphur dioxide and other gases are chemically transformed in the atmosphere in the presence of sunlight. They may be found at long distances from the original sources of the gases from which they are formed. As is the case with ozone, they are primarily a summer problem, but have not traditionally been monitored on a routine basis to the same extent as other air pollutants such as ozone. However, routine measurements have been made of sulphate levels, which correlate to some degree with actual acid measurements. According to data on sulphate levels for various locations in Ontario between 1983 and 1988, areas in the southern Great Lakes Basin, such as Windsor, Longwoods (near London) and Toronto had the highest levels (8.2, 6.8 and 6.7 $\mu g/m^3$ respectively) compared to other sites (range of 3.1 to 5.8 $\mu g/m^3$; see **Table 6 and Figure 3**) (Burnett *et al.*, 1993). Sulphate levels have declined slightly in Ontario over the last ten years (Ontario Ministry of Environment, 1991). Recent measurements carried out across Canada suggest that although sulphate levels are highest in Southern Ontario, other areas such as the Maritimes may experience comparable acid levels. Canadian air quality standards do not currently exist for acid aerosols (Stieb and Burnett, 1993).

Other noteworthy air pollutants include sulphur dioxide, oxides of nitrogen, hydrocarbons, and other "***air toxics***". Since the 1970s, when more stringent emission controls were introduced, ambient levels of sulphur dioxide have declined considerably, and interest in sulphur dioxide now relates to its role in the production of acid aerosols. There has been little change in levels of nitrogen oxides over the years, and interest in these gases continues in relation to their role in the production of ozone and acid aerosols. It is difficult to generalize about trends in emissions of hydrocarbons over the years because of the wide range of different hydrocarbon compounds. As a group of pollutants, they are of interest because of their role in the production of ozone.

Similarly, "air toxics" refers to a broad range of substances ranging from metals such as arsenic, chromium and nickel, to organic compounds such as benzene, formaldehyde and trichloroethylene. These contaminants are not generally measured on a routine basis, and there is no standard measure or mixture agreed upon as "benchmark". However, a review of air quality data in the Detroit-Windsor, Port Huron-Sarnia region indicated that a number of these substances, some of which are known carcinogens, were present at elevated levels in this area (International Joint Commission, 1992).

In the United States, the Environmental Protection Agency (USEPA), using the Toxics Release Inventory, has estimated that air toxic emissions on the U.S. side of the Basin amount to approximately 2,420,000,000 pounds per year. Nationally, approximately 58 million people are exposed to levels of airborne pollutants that are greater than health reference levels for acute effects, and 38 million people for chronic effects. Using these national data, the USEPA estimates that in the Basin 7.2 million people and 4.7 million people are exposed to levels of pollutants which are greater than health reference levels for acute and chronic effects, respectively (USEPA Risk Characterization Study, 1992). In a prospective cohort study conducted in six U.S. cities, researchers found that daily mortality rates were associated with daily particulate air pollution rates. What was significant about this study was that the researchers found this association even after adjusting for cigarette smoking and other lifestyle factors which represent health risks (Dockery *et al*, 1993).

4.0 Linking Contaminant Exposure to Human Health Effects

4.1 The Use of Biomarkers

Biomarkers have an important role to play in establishing whether an organism has been exposed to an environmental chemical(s), whether it has been biologically affected, and/or whether it is susceptible to an increased response to exposure. Three subclasses of biomarkers, or biological indicators, have been suggested (Schulte, 1992):

- **biomarkers of exposure**: these indicate whether exposure has occurred and consist of measurements of chemicals (including metabolites) in body fluids, tissues, cells, or the interaction products between the chemicals and an endogenous substance (**Figures 4 and 5**).

- **biomarkers of effect**: these are morphological, physiological, or biochemical changes which have occurred as a result of exposure to xenobiotics (i.e., substances foreign to living organisms).

- **biomarkers of susceptibility**: any factors, usually intrinsic or genetic, which may result in an increased response to exposure. Susceptibility biomarkers can be used to explain inter-individual variations seen throughout the exposure-effect continuum.

A detailed summary of these three types of biomarkers as applied to a variety of Great Lakes contaminants can be found in **Table 7**. Although data on quantitative exposure assessments for the Great Lakes population are not available at present, the biomarkers of effect can be associated with data on specific exposure levels obtained from studies of occupational or accidental exposures to environmental chemicals. These data can be found in the background paper from which the summary is drawn (*Biomarkers*, M. Feeley, 1994). It should also be noted that the majority of biomarkers of effect and susceptibility are currently limited in their use because they are non-specific and can apply to a variety of environmental contaminants. There is a need to develop biomarkers that are more sensitive and specific to particular chemical exposures.

TABLE 7 -- SUMMARY OF BIOMARKERS

Contaminant	Biomarkers of		
	Exposure	**Effect**	**Susceptibility**
PCBs	Concentration in adipose tissue, blood, breast milk.	Serum PCB concentrations positively correlated with plasma triglyceride and cholesterol levels, and with AST (aspartate aminotransferase) and GGT (gamma-glutamyl transferase) (both liver enzymes) activity. Based on epidemiological studies, AST and GGT appear to be the most sensitive indicators of PCB exposure in humans. Reduction in antipyrene half-lives. Increased caffeine metabolism rates in exposed groups (indicative of hepatic CYP1A2 activity). Changes in the urinary excretion of porphyrin congeners, indicating enzymatic stimulation/inhibition of the hepatic heme biosynthetic pathway. Reproductive effects -- alterations in birth weight, gestational age and fetal development (physical and neurological)). Dermatological effects (at high levels of exposure) -- chloracne, hyperpigmentation, hyperkeratosis, conjunctivitis. Increased incidences of chromosomal aberrations and sister chromatid exchanges detected in peripheral blood lymphocytes.	From epidemiological investigations, it appears that the developing fetus is at greatest risk from PCB exposure. *In utero* exposure may be more important than later exposure.
PCDDs and PCDFs	Concentration in adipose tissue, blood, breast milk.	Chloracne and related dermatological effects. Increased GGT (gamma-glutamyl transferase, a liver enzyme) activity. Higher incidence of upper gastrointestinal tract ulcer. Higher incidence of neurological abnormalities (e.g., peripheral sensory neuropathy, decreased libido, depression, insomnia). Higher incidence of self-reported non-cognitive complaints (e.g., emotional instability, irritability). Possible immunological effects (e.g., increased levels of non-T peripheral lymphocytes, abnormal T_4/T_8 ratios, thymic atrophy) and endocrine alterations. Increased urinary D-glucaric acid excretion.	Induction of EROD/AHH (ethoxyresorufin-o-deethylase and aryl hydrocarbon hydroxylase) enzyme activity mediated through the Ah (aromatic hydrocarbon) receptor. Induction of EROD/AHH activity in human lymphocytes has been associated with increased susceptibility to lung cancer. *In utero* and lactational exposure to PCDDS/PCDFs may be capable of affecting the hypothalamic-pituitary-thyroid regulatory system in human infants.

	urine. As pyrene is a major constituent of PAHs, the monitoring of 1-hydroxypyrene in urine can be considered representative of exposure and internal dose, whether by inhalation, absorption or ingestion. Biomarkers of exposure are limited due to the extensive metabolism and excretion of PAHs.		metabolic phenotypes of humans and associate this with increased risk for PAH carcinogenicity. The vast interindividual genetic differences would have to be considered when applying biomarkers for PAHs.

TABLE 7 -- SUMMARY OF BIOMARKERS (Cont'd)

Contaminant	Biomarkers of		
	Exposure	**Effect**	**Susceptibility**
Organochlorine Pesticides: DDT DDE Chlordane Dieldrin HCB γ-HCH Heptachlor/HE Mirex Toxaphene ß-HCH	Concentrations in blood, adipose tissue, breast milk, and urine.	Increased plasma concentrations of the liver enzymes AST (aspartate aminotransferase), ALT (alanine aminotransferase), GGT (gamma-glutamyl transferase), LDH (lactate dehydrogenase), and AP (alkaline phosphatase); and of vitamin A and retinol. Occupational /epidemiological studies suggest that the nervous system and the liver are the most sensitive effect parameters for OC pesticides in humans. The nervous system effects include parathesia, repetitive tremors, and EEG pattern changes. Apart from accidental or occupational exposures, the low pesticide residues generally encountered in foods compared to the estimated adverse effect levels suggest that harmful effects are unlikely.	
Cadmium	Concentrations in blood, urine, feces, and body organs (e.g., kidney, liver).	Metallothionein (Mt) and consequences of nephrotoxicity (Cd-Mt in urine). Renal dysfunction as indicated by α_1-microglobulin, N-acetyl-ß-D-glucosaminidase, $ß_2$-microglobulin, and retinol binding protein (all indicative of microproteinuria).	Induction of metallothionein in human peripheral blood leukocytes appears to be partly under genetic control. In non-smoking adults, there is a 10-39-fold variation in Mt-mRNA induction which may explain the interindividual differences seen in the development of renal damage following cadmium exposure.
Mercury	For both inorganic and organic mercury: concentrations in blood, hair, kidney, placenta, breast milk, urine, and brain.	The central nervous system (CNS) is the critical target for methylmercury (MeHg) toxicity in both infants and adults. Prenatal exposure to MeHg results in biomarkers of effect ranging from psychomotor retardation to severe cerebral palsy. Mercury-induced porphyria is an additional biomarker of effect in both infants and adults.	

	teeth, kidney, liver, breast milk, placenta, brain.	acid synthetase) and inhibits ALAD (delta-aminolevulinic acid dehydrase) in erythrocytes, resulting in increased levels of ALA (delta-aminolevulinic acid) in blood and urine. Lead also inhibits ferrochelatase; consequently, protoporphyrin IX and coproporphyrin accumulate. Increased blood porphyrin. Decreased blood hemoglobin. Neurological deficits, including delayed neurological development, reduced IQ, and behavioral maturation deficits.	

Source: Adapted from Feeley, 1993

4.2 Factors in Establishing Links Between Great Lakes Environmental Contaminants and Human Health Effects

The biomarkers of effect cited above point to potential health effects that may appear as a result of exposure to chemical contaminants. However, any actual effects observed in Great Lakes populations may be due to a variety of factors, including exposure to environmental contaminants in the Lakes. A major consideration in conducting human health effects research is that people are exposed to an enormous number and variety of environmental and lifestyle factors that can affect health outcomes, but whose respective effects are difficult to isolate and measure (Jordan-Simpson *et al.*, 1994). Data on health effects of contaminants in the Great Lakes Basin have usually been obtained from animal laboratory studies and epidemiological studies describing the adverse effects of occupational or accidental exposure to high concentrations of chemicals.

Another key factor which affects the interpretation of the results from studies examining the association between environmental contaminants and its effect on human health relates to the methodologic problems associated with quantitatively assessing hazards and risk. In human populations it is often very difficult to characterize the exposure, and to separate potential confounding factors from the factor of interest. This also makes it difficult to choose an appropriate comparison group. There are a number of difficulties associated with studies carried out in free-living populations, and inevitably differences will exist between exposed and unexposed individuals that may allow alternative explanations for any effects observed (Constable and Hatch, 1983, cited in Jordan-Simpson *et al.*, 1994). As well, participation and recall bias may seriously compromise the validity of a study (Jordan-Simpson *et al.*, 1994).

Comprehensive health risk assessment is a complex multi-step procedure. Human health risk assessment as practised by the United States Environmental Protection Agency is derived from the paradigm established by the National Academy of Sciences. This paradigm sets out four steps in the risk assessment process: i) hazard identification (what does the chemical do); ii) dose-response evaluation (how much of the chemical is needed to observe an adverse health effect); iii) exposure assessment (who is exposed and to what degree); and iv) risk characterization -- the full characterization of hazard identification, dose-response evaluation and exposure assessment, along with the uncertainty and assumptions that entered into the assessment. The risk characterization is the product of the risk assessment, and feeds into the risk management process along with technological considerations and non-risk analyses to determine a risk management option.

By comparison, the risk assessment model used by Canada's Department of Health involves: i) risk analysis, which consists of (a) hazard identification, and (b) risk estimation involving dose-response evaluation, exposure estimation, and risk characterization; and ii) option evaluation, comprised of (a) option development and (b) option analysis. The subsequent steps in the risk management process would include the decision-making leading to a chosen option, implementation, monitoring and evaluation, and ongoing review (Health Protection Branch, Health Canada, 1989, 1990). A closer inspection of both the USEPA's and Health Canada's risk

assessment models shows that they are very similar, with steps (ii), (iii) and (iv) of the USEPA model subsumed in the risk estimation step of the Canadian model.

As indicated above, risk assessment at present is based on data from toxicological investigations carried out in the laboratory (both *in vitro* toxicity studies and *in vivo* animal studies) combined with data from epidemiological studies of human populations. Traditionally, investigations include evaluation of acute and chronic toxicity in animal species, studies of the metabolism of chemical substances, short-term tests for genetic alterations, special studies such as teratology (the study of malformations), reproduction, and long-term tests for carcinogenic effects (Bernier *et al.*, 1994).

Foster and Rousseaux (1994) have itemized a number of factors which make it difficult to establish a link between environmental contaminants and adverse reproductive effects in humans in the Great Lakes Basin. These factors can also apply more generally to other categories of health effects, and are listed below:

- the continuous nature of exposure over many years to low levels of chemicals;
- exposure to mixtures rather than individual compounds;
- hazard definition and identification (i.e., the large number and in some instances the poor definition of health effect endpoints to be examined, and the difficulty in measuring some effects);
- experimental design (for example, inability in some cases to obtain adequate sample sizes for evaluations with measurements that are suitably sensitive and specific to detect changes);
- dose-response questions;
- accurate exposure assessment; and
- confounding variables that may hinder research studies.

These and other factors in the study of adverse human health effects associated with environmental contamination have contributed to the adoption of the "weight of evidence" approach that allows for the consideration of supplementary data that may shed some light on *potential* effects in humans. These supplementary data -- derived from wildlife studies, toxicological research on laboratory animals, *in vitro* cellular studies, and human epidemiological investigations of accidental or occupational exposures to high levels of specific contaminants -- help to expand our knowledge of the actual and potential health effects of environmental contamination on living organisms, including humans, and to point the way to new research directions in this area.

5.0 HEALTH EFFECTS OF EXPOSURE TO ENVIRONMENTAL CONTAMINANTS IN THE GREAT LAKES BASIN

In view of the limitations cited above, this review of the health effects of exposure to environmental contaminants in the Great Lakes Basin focuses for the most part on hazard identification, i.e., delineating the various **potential** adverse health effects, most of which have been observed at relatively high exposure levels in occupational settings or as the result of accidental exposures. In some cases, information on exposure assessment and suggestions concerning future directions in research and accurate risk assessment are also presented. It should also be noted that the exposure data necessary to carry out *integrated exposure assessments* (i.e., an assessment based on all routes of exposure and specific exposure levels for a particular health effect) are unavailable and beyond the scope of this paper. Consequently, the discussion of reproductive, neurological, immunological and carcinogenic endpoints relates for the most part to food (primarily fish) consumption as a major route of exposure, and water consumption as a secondary route (particulary in the case of cancer endpoints and infectious diseases). Respiratory effects are discussed separately, since inhalation is the obvious route of exposure for airborne contaminants.

In general, it is important to recognize that although health effects associated with environmental contamination may be correlated with multiple exposure routes, those related to one exposure route cannot always be extrapolated to another, and identifying the specific exposure route(s) and levels of exposure associated with particular categories of health effects cited in various studies would be essential when undertaking integrated exposure assessments.

As well, in reviewing the health effects of the various classes of Great Lakes contaminants, radionuclides and microbial contaminants will each be discussed separately from the "chemical" pollutants, due to their fundamentally different natures and the effects they have on human health. In the case of radionuclides, the essential difference is that they are elements that emit high-energy radiation called ionising radiation, large doses of which can kill cells directly, or cause genetic or other changes in the body that may lead to cancer. Microbial contaminants are living organisms that can cause a variety of infections and diseases.

5.1 Reproductive Toxicology

As indicated above, data on the reproductive effects of exposure to environmental contaminants have usually been obtained from wildlife studies (see Fox, 1992 for review; also Flint and Vena,

1991), animal laboratory experiments, and from epidemiological studies describing occupational exposure to high concentrations of chemicals (Whorton *et al.*, 1977; 1979; Hemminki *et al.*, 1983, 1985; Olshan *et al.*, 1990; Rowland *et al.*, 1992). Although serious effects on reproduction in animals and a potential hazard to human reproduction have been shown in these studies, it is difficult to estimate the adverse reproductive effects in humans of chronic and low-level exposure to environmental contaminants in the Great Lakes Basin due to the factors listed in the preceding section. Furthermore, among the additional confounding variables in reproductive toxicology are lifestyle factors such as alcohol consumption and smoking, which have been linked to an increased risk of stillbirth (Prager *et al.*, 1984) and congenital anomalies (Savitz *et al.*, 1991). Failure to account for these and other confounding factors in epidemiological studies makes it difficult to establish cause-effect relationships.

Developmental Effects of Environmental Contaminants

The developing fetus and neonate are considered to be at particular risk as there is great potential for exposure to environmental contaminants *in utero* and through breast milk. The developing fetus is captive within its mother's environment and is not completely protected by the placenta, animal experiments having shown that the placenta is an ineffective barrier to heavy metals and chlorinated hydrocarbons (Buchet *et al.*, 1978; Ando *et al.*, 1985). As well, the transport of persistent environmental contaminants in breast milk has been well documented (cited in Foster and Rousseaux, 1994 and reviewed by Sim and McNeil, 1992). The developmental consequences of exposure to high concentrations of chemical contaminants and certain drugs include intrauterine growth retardation (IUGR), shortened or prolonged gestational lengths, low birthweight, congenital malformations, and spontaneous abortion (Foster and Rousseaux, 1994; Jordan-Simpson *et al.*, 1994). Examples of reproductive toxicants present in the Great Lakes and known to induce such developmental effects include lead, methylmercury, DDT/DDE, PCDFs, PCBs, and polybrominated biphenyls (PBBs) (Foster and Rousseaux, 1994 and Jordan-Simpson *et al.*, 1994). Developmental toxicity in humans following occupational exposure to high levels of chemical contaminants such as heavy metals, pesticides, PCBs, dioxins and organic solvents has also been well documented (cited in Foster and Rousseaux, 1994 and reviewed by Rosenberg *et al.*, 1987; Taskinen, 1990; and Thomas and Ballantyne, 1990). However, there is a dearth of data on low-level exposure and exposure to mixtures.

It is important to emphasize that the increased risk to the developing fetus and neonate is also due to the nature of those stages in the life cycle. For example, in the fetus there are physiological systems that have not yet differentiated into their mature, final form and function. Damage at an early stage can thus affect whole organ systems, whereas in the adult organism the same insult from exposure to an environmental contaminant may result in only limited, reversible damage (Tong and Gorsky, 1994). Parental exposure to lead, a priority Great Lakes contaminant, underscores the significance of prior contaminant exposure on reproductive outcomes. Roughly 90% of ingested lead is deposited and stored in bone, from which it is mobilized during pregnancy (Shannon *et al.*, 1988b; Silbergeld *et al.*, 1988; Markowitz and Weinberger, 1990; Silbergeld, 1990). Exposure of the fetus to lead ingested and/or mobilized from bone at critical developmental periods has been shown to adversely affect neurodevelopment

(Sierra and Tiffany-Castiglioni, 1992), delay sexual maturation (Der *et al.*, 1974; Kimmel *et al.*, 1980), and has been associated with an increased incidence of spontaneous abortions (Fahim *et al.*, 1976; Odenbro and Kihlstrom, 1977; Nordstrom *et al.*, 1978; McMichael *et al.*, 1986). Lead is also mobilized from bone during lactation, thereby posing a continuing risk to the developing infant.

Effects of Environmental Contaminants on Fertility

Occupational exposures to high concentrations of environmental contaminants and animal experiments involving chronic exposure have shown the potential for adverse reproductive effects on human fecundity and fertility. Known toxicants affecting female reproductive processes include the heavy metals lead, methylmercury, and cadmium; the organochlorines hexachlorobenzene (HCB), DDT, DDE, and PCBs; as well as alcohol and tobacco smoke (Foster and Rousseaux, 1994).

Animal studies on ***female reproductive endpoints*** have shown altered menstrual function in laboratory animals exposed to lead (Vermande-Van Eck and Meigs, 1960; Hilderbrand *et al.*, 1973; Laughlin *et al.*, 1987; Franks *et al.*, 1989), and suppression of circulating luteinizing hormone (LH), follicle stimulating hormone (FSH), and estrogen (E_2) levels during the follicular phase of the menstrual cycle in the monkey (Foster, 1992). These results raise concerns regarding the health of the developing follicle and ovum. In addition, primordial follicle numbers in the ovary have been shown to be significantly reduced following exposure to reproductive toxicants such as 7,12-dimethylbenz(a)anthracene, benzo(a)pyrene and hexachlorobenzene (Iatropoulos *et al.*, 1976; Siracusa *et al.*, 1992; Miller *et al.*, 1992b; Weitzman *et al.*, 1992; Jarrell *et al.*, 1993). Overall, the effects of environmental pollutants on female reproductive endpoints such as oocyte (egg) maturation and quality, ovarian follicle development, ovarian function and uterine receptivity require further study in order to elucidate the potential link between environmental chemicals and adverse reproductive effects.

While considerable research attention has been directed to both developmental and female reproductive toxicity, there has been comparatively little research on the effects of chemical contaminants on ***male reproductive endpoints*** (for review see Colie, 1993). The majority of data regarding the effects of chemicals on male reproductive processes have been derived from rodent studies (Sullivan and Barlow, 1985; Working, 1989; Hess, 1990; Linder *et al.*, 1992; Vachhrajani *et al.*, 1992), in which moderate to severe sperm damage has been detected in rodents following acute exposure to suspected reproductive toxicants. In a broader context, other biomarkers of male reproductive toxicity include fecundity; circulating concentrations of the hormones LH, FSH, prolactin (PRL), inhibin, testosterone and dihydrotestosterone; semen quality and testicular histomorphology (for review see Ewing and Mattison, 1987 and Mattison, 1991).

Regarding human males, the importance of male-mediated effects has been demonstrated in the case of increased prevalence of congenital malformations in the offspring born to wives of fire-fighters (Olshan *et al.*, 1990). In addition, reduced fertility has been observed in men working in pesticide manufacturing plants (Whorton *et al.*, 1977). In a recent report (Carlsen *et al.*, 1992)

a decline in semen quality was described on the basis of published reports on semen quality appearing in the literature over the preceding 50 years. It was suggested that the decline was more likely the consequence of environmental than genetic factors although no direct evidence to support this claim was presented. A decline in sperm quality, however, may also be related to increased incidence of sexually transmitted disease, metabolic disorders such as diabetes, and sample selection, among other factors. Nevertheless, sperm density has previously been negatively correlated with tissue levels of persistent environmental contaminants (Lantz *et al.*, 1981; Szymczynski and Waliszewski, 1981; Takahashi *et al.*, 1981; Abdel-Rahman *et al.*, 1982; Couri *et al.*, 1982; Mann and Lutwak-Mann, 1982; Jockenhövel *et al.*, 1990). As well, reduced sperm quality and impaired fertility have been associated with men occupationally exposed to lead (Jockenhövel *et al.*, 1990), although many other reports fail to demonstrate a relationship between lead exposure and alterations in fertility, which may be due to study design and various confounding factors.

Alterations in male reproductive endpoints other than sperm quality have also been demonstrated with lead treatment in experimental animals. For example, lead exposure has been associated with altered hypothalamic-pituitary function (Sandstead *et al.*, 1970; Braunstein *et al.*, 1978; Petrusz *et al.*, 1979; McGivern and Sokol, 1990; Foster *et al.*, 1993a) and testicular function (Braunstein *et al.*, 1978; Foster *et al.*, 1993b). In addition, histopathological (i.e., structural) alterations have been shown in lead-exposed rodents (Timm and Schulz, 1966; Hilderbrand *et al.*, 1973), primates (Foster *et al.*, 1993b) and occupationally exposed men (Lancranjan *et al.*, 1975). Altered sperm count (Golubovich *et al.*, 1968), decreased sperm motility (Hilderbrand *et al.*, 1973) and increased abnormal sperm (Eyden *et al.*, 1978) have all been reported in rodents treated with varying concentrations of lead. However, weight loss in treated rats makes it difficult to interpret these results as altered sperm counts, morphology, and motility could all be explained by indirect effects of lead on other metabolic systems.

Hormone Disruption

A number of xenobiotics have the potential to disrupt the activities of certain naturally occurring hormones in an organism. This disruption can be manifested in a number of ways, including the mimicing of a hormone or the blocking of its activity. For example, TCDD (a dioxin) may block the activity of estrogens, the female sex hormones which play an important role in the development of the sexual organs and sexual behaviour. Under certain conditions dioxins can also lower the levels of androgens and can affect the thyroid hormone levels in the body (Birnbaum, 1994).

The best-studied of the xenobiotics that have been shown to alter hormone systems are environmental estrogens, i.e., compounds which effects similar to those of estrogens (hence the term *hormone mimicry*). These substances may either be man-made or occur naturally in the environment. Of the former, certain persistent environmental contaminants such as PCBs (Korach *et al*, 1988), 3,9-dihydrobenz[a]anthracene, kepone, DDE, and o,p-DDT (McLachlan et al, 1987) have been found to have weak estrogenic abilities. Concern exists regarding the potential of both the natural and man-made estrogenic compounds to interact with the estrogen

receptor and possibly induce adverse reproductive effects. Potential adverse consequences of exposure to compounds with estrogenic activity include feminization of the male and premature female sexual maturation (Foster and Rousseaux, 1994). For example, precocious puberty in young boys and girls eating meat contaminated with diethylstilbestrol (DES), a synthetic hormone, has been reported (New, 1985), and exposure to DES has also been shown to infrequently induce vaginal adenocarcinoma in women whose mothers were given DES during pregnancy to prevent miscarriage (Herbst *et al.*, 1971; Greenwald *et al.*, 1971).

Although there have not been any reports of adverse effects following exposure to environmental levels of estrogenic compounds in the human population, estrogenic effects of environmental pollutants have been implicated in developmental abnormalities in wildlife species (Fox, 1992). The presence of estrogenic contaminants in human tissues, and demonstration of effects in animal species, have promoted speculation that effects in humans such as increased incidence of breast cancer may occur among women exposed to organochlorines (Manz *et al.*, 1991; Falck *et al.*, 1992; Wolff *et al.*, 1993). However, the majority of these compounds have been shown to be very weak estrogens (Soto *et al.*, 1992) with few apparent biological effects. At present the link between exposure to estrogenic compounds, such as PCBs, DDE and DDT, and breast cancer cannot be established with confidence, and comprises a priority area for future research.

With respect to males, recent work suggests that chemicals with an estrogenic effect pose an increased reproductive risk by decreasing semen quality (Carlsen *et al.*, 1992). Further research will be needed to confirm whether trace amounts of chemicals with an estrogenic effect do have an effect on male reproduction.

5.2 Epidemiological Studies of the Effects of Environmental Contaminants on Reproductive Outcomes in Great Lakes Populations

Because fish consumption is considered one of the major routes by which humans are exposed to environmental contaminants present in the Great Lakes, a number of studies have looked at the association between maternal consumption of Great Lakes fish and the health of offspring. Results from some of these studies indicate a relationship between PCB exposure *in utero* and alterations in both neonatal health and health in early infancy (Swain, 1991). During the 1980s, the Michigan Maternal/Infant Cohort study evaluated the impacts of consumption of contaminated fish on the offspring of mothers who had consumed at least 11.8 kg of contaminated Lake Michigan fish over a 6-year period. The study consisted of 313 infants of mothers who consumed moderate to high amounts of Lake Michigan fish, and 71 infants whose mothers ate no Lake Michigan fish. Effects were seen in the offspring of mothers in the former group, and were attributed to intrauterine exposure to PCBs. These effects included lower birthweight, reduced gestational age, and smaller head circumference compared to controls (Fein *et al.*, 1984b). In later studies on the children at 4 years of age, researchers found that weight gain was still lower compared to controls, indicating that the adverse effects may extend beyond infancy

(Jacobson *et al.*, 1990a).

A second study, the Wisconsin Maternal/Infant Cohort study, consisted of mothers who ate fish from Lake Michigan or the Sheboygan River for at least three years prior to the date of birth (1980-81) of their offspring. The research showed that maternal PCB levels were associated with increased incidence of infectious diseases suffered by the infants. The author concluded that PCB exposure *in utero* resulted in the increased susceptibility to infectious illness in the first four months of life (Smith, 1984).

Other research results are less alarming. In another study of mothers who consumed fish from the Great Lakes, researchers examined prenatal exposure to PCBs and reproductive outcomes in a population of 1112 women during 1987-1989 in the Green Bay area. Following the pregnancy period, reproductive outcomes were measured, including fetal wastage, stillbirths, birthweight, birth length, and head circumference. The researchers expected to find that, as in the Michigan cohort study, there would be a decrease in birthweight associated with an increase in PCB exposure. However, the opposite was true: birthweights were often higher for infants of those mothers who claimed to eat more Lake Michigan fish prior to pregnancy. The researchers noted, however, that the amounts of fish these women consumed were much lower than in the Michigan maternal cohort study, and speculated that the relatively low estimated exposure to PCBs experienced by the Green Bay cohort did not appear to have an effect on birth outcomes. Perhaps, the researchers concluded, there is a threshold exposure level below which there are no observable negative effects (Dar *et al.*, 1992).

Likewise, in a recent study of a cohort of New York anglers, researchers examined the relationship between consumption of PCB-contaminated fish from Lake Ontario and birthweight of newborns. The New York cohort consisted of 11,717 people. Using a sample of recent births (1986-91) from parents in this study, birthweight, gestational age, and other birth parameters were abstracted from birth certificates. Preliminary results have shown no differences in mean birthweights across estimated cumulative lifetime exposure to PCBs from contaminated fish (Buck *et al.*, 1993). An additional study was carried out on 1,820 women from the same cohort to assess the relationship between PCB exposure due to consumption of contaminated Lake Ontario sport fish and spontaneous fetal death (SFD). An analysis of fish consumption and reproductive history data indicates that exposure to PCBs in contaminated sport fish does not increase the risk of SFD (Mendola *et al.*, 1994).

In conclusion, there is no doubt that accidental or occupational exposure to high concentrations of certain chemicals presents an increased risk to human reproductive health. Although it is not possible to state conclusively that exposure to environmental contaminants in the trace concentrations currently reported in human tissues is or is not associated with adverse reproductive effects, evidence from wildlife studies (Fox, 1992; Flint and Vena, 1991) and epidemiological investigations of occupational exposures to various chemicals indicates that environmental pollutants might be able to alter human reproduction. Epidemiological studies that have addressed adverse pregnancy outcomes in populations in the Great Lakes have shown some potential effects of concern, while other studies have shown little or no effects. Due to the

current difficulties in estimating reproductive risk to the human population, and incompleteness of the data base concerning reproductive effects of environmental contaminants, the real risk to people residing within the Great Lakes region or elsewhere cannot be determined at present.

5.3 Neurotoxicity of Lead, Methylmercury, and Polychlorinated Biphenyls (PCBs)

There are a number of contaminants in the Great Lakes that are neurotoxic or potentially so. There is a large data base from animal and human epidemiological studies on two of these: lead and methylmercury. The data base is less complete for a third class of contaminants, PCBs. While it is reasonably certain that some PCBs are neurotoxic, particularly in developing organisms, there are fewer human studies upon which to determine a "no observed adverse effect level (NOAEL)" or "lowest observed adverse effect level (LOAEL)" than for lead or methylmercury. For most other Great Lakes contaminants, there are no or scant data regarding neurotoxicity, or the levels to which the general population is exposed via the Great Lakes Basin are not cause for concern. For example, there is reason to be concerned about such substances as toxaphene, HCB and HCHs based on their chemical structure, but neurotoxicity data based on observations of humans are almost nonexistent. Other agents known to be neurotoxic, such as organotin compounds and various pesticides, are found in the Great Lakes Basin at levels which are orders of magnitude lower than those that have been tested in animals or at which neurotoxicity has occurred in humans. Therefore, this discussion of neurotoxicity is restricted to PCBs, methylmercury and lead.

PCBs

High doses of PCBs result in reproductive toxicity in humans (Rogan *et al*, 1988; Lione, 1988; Safe, 1987). Less is known about the effects of PCBs on human neurobehaviour. However, in laboratory monkeys behavioral deficits have been observed as a result of developmental exposure to PCBs (Schantz *et al.*, 1989, 1991). Research on other laboratory animals also links PCBs and other toxic contaminants in the Great Lakes to adverse neurobehavioral effects. For example, rats fed Lake Ontario salmon contaminated with PCBs, mercury and lead showed an increased reactivity to aversive events (Daly, 1991).

It is clear from both the animal literature and epidemiological studies on humans that the developing organism is more sensitive to behavioral deficits resulting from PCB exposure than is the adult. Two well-designed prospective epidemiological studies in humans provide evidence of behavioral deficits associated with low-level *in utero* exposure to PCBs. In one study, exposure was via contaminated Great Lakes fish (Fein *et al.*, 1984a, 1984b; Jacobson *et al.*, 1984, 1985, 1989, 1990a, 1990b; Schwartz *et al.*, 1983), while in the other, a North Carolina study, there was no identified source of exposure (Gladen *et al.*, 1988; Gladen and Rogan, 1991; Rogan *et al.*, 1986). Regarding the former, in a series of follow-up studies conducted over ten years, the Jacobsons have tracked and evaluated the development of children born to mothers who had

consumed at least 11.8 kg of contaminated Lake Michigan fish over a 6-year period. Data were collected on the mothers' fish consumption habits, the PCB levels in their breast milk and in the blood serum of both the mothers and their infants. Their research has shown that the cognitive, motor and behavioral development of the infants were adversely affected by the mothers' consumption of contaminated fish from Lake Michigan. The authors concluded that prenatal exposure to PCBs was associated with deficiencies in the infants' cognitive ability to visually discriminate between objects, and in their short-term memory scanning capabilities. In a follow-up study of these children at age 4, the Jacobsons evaluated their processing efficiency (short-term memory and visual discrimination) and sustained attention span. Processing efficiency was measured because of its link to reading ability and the ability to master quantitative operations, two dimensions of cognitive functioning fundamental to learning. The authors concluded that prenatal exposure to PCBs was associated with less efficient visual discrimination processing and more errors in short-term memory, but not with changes in sustained attention (Jacobson *et al.*, 1992).

A possible limitation of these studies is the failure to assess and control for other potential neurotoxicants possibly correlated with PCB levels, such as methylmercury. However, the congruence between the laboratory monkey and human data suggests that the behavioral deficits observed in the human studies are associated with developmental exposure to PCBs (Rice, 1994).

The most significant route of exposure to PCBs from the Great Lakes is the consumption of contaminated fish. Estimates of PCB levels in Great Lakes fish tissue can vary by several orders of magnitude among species and Lakes. One estimate of the present average PCB level in recreational fish, taken from the Great Lakes is 0.037 μg/g (.04 ppm) (Rice, 1994), while the Great Lakes Water Quality Board estimates the approximate PCB concentration to be 1.32 ppm, which represents an average for all the Great Lakes (USEPA 1992, 1993). These figures suggest that PCB levels in Great Lakes fish may present a potential hazard to offspring of women consuming large quantities of fish, based on the behavioral data from human epidemiological studies. Further studies, including prospective studies, should serve to define levels at which toxicity is known to occur.

Methylmercury

Methylmercury was recognized as a neurotoxic agent following outbreaks of human poisoning in Japan in the 1950s and 1960s through consumption of contaminated fish (Japan Environment Agency, 1975). A later episode of human poisoning in Iraq following consumption of grain treated with methylmercury fungicide resulted in neurotoxic effects, and provided detailed estimates of thresholds for various health endpoints (WHO, 1976, 1989, 1990). It became evident that the developing fetus is much more sensitive than is the adult. There also exists a reasonably good animal data base replicating effects observed in humans.

Consumption of contaminated fish represents the main exposure route for methylmercury in the Great Lakes Basin. The most sensitive endpoints affected by MeHg are developmental delays in children exposed *in utero* (Amin-Zaki *et al.*, 1980; Marsh, 1987; Chang, 1977; Harada, 1968).

There have been few epidemiological studies of Great Lakes populations in this regard. In one recent study of mercury levels in the Chippewa Tribe at the Red Cliff Reservation on Lake Superior (the least polluted of the Great Lakes), researchers at the University of Wisconsin found no obvious adverse behavioral effects that could be related to consumption of Lake Superior fish, as there were no significant methylmercury body burdens found in the study (Dellinger *et al.*, 1993). It is unclear whether the body burdens of MeHg in subpopulations who consume fish from the other Great Lakes are associated with adverse behavioral effects.

Lead

Lead has been known to be neurotoxic since ancient times (Cantarow and Trumper, 1944; Oliver, 1914). The present body burden of lead in the general population is 2-3 orders of magnitude above historical background levels, as a result of human activity (NAS, 1980). In the last decade and a half, it has become clear that exposure to lead *in utero* and/or during childhood at body burdens that are presently typical of humans in industrialized countries results in deficits in IQ, and in distractibility, inattention and other behavioral problems (Needleman *et al.*, 1979). Approximately 20 epidemiological studies, both prospective and retrospective, provide extremely strong and consistent evidence (Rice, 1994). The retrospective studies have been extensively reviewed (see Rutter and Russell Jones, 1983; Mahaffey, 1985; Mushak *et al.*, 1989), and the most recent ones have utilized populations with lower body burdens of lead than the children assessed by Needleman. Effects of lead on intellectual and behavioral functions in children in these studies include intellectual deficit, hyperactivity, inattention, and increased reaction time.

Prospective studies also provide convincing data regarding developmental deficits produced by low-level lead exposure (for review see Mushak *et al.*, 1989; Hammond and Dietrich, 1990), including deficits in cognitive performance, abstract thinking, sustained attention, and psychomotor development. There is also a large body of animal data that indicates that lead produces behavioral impairment consistent with the types of impairment observed in lead-exposed children and the blood levels at which they occur (for review see Cory-Slechta, 1984; Rice, 1992, 1993). Among other findings is the association between an elevated maternal blood lead level and abnormal reflexes, poor muscle tone, and neurological soft signs such as jitteriness, hypersensitivity, and abnormal cry in the infant following exposure *in utero* (Ernhart *et al.*, 1985, 1986).

It is also becoming increasingly clear that there is no apparent threshold for these effects at present day body burdens. An important unanswered question is the contribution of total maternal body burden, rather than blood level, to the risk to the infant. Bone contains over 90% of body lead stores, and it is established that lead increases in bone throughout the life-span of humans (Barry, 1975). Women currently at reproductive age have been exposed to the most lead since ancient times, and thus will generally have a significantly higher total body burden of lead than previous generations and will provide a significant source of both *in utero* and neonatal exposure via mobilization of lead from bone stores during pregnancy and lactation, long after exposure has ceased (Thompson *et al.*, 1985).

The most significant sources of lead exposure are food (indirectly from environmental fallout) and drinking water via lead or lead-soldered plumbing, or environmental contamination. The Great Lakes Basin does not present a particular hazard with regard to lead exposure. However, as there is no apparent threshold for intellectual impairment produced by lead in the developing organism, every reasonable effort should be made to minimize point sources of lead contamination in the Great Lakes Basin (Rice, 1994).

5.4 Immunotoxicology of Heavy Metals, PCBs, Dioxins and Organochlorine Pesticides

The immune system plays a crucial role in maintaining health. However, accumulating evidence indicates that this system can be the target for immunotoxic effects caused by a variety of chemicals, including environmental pollutants such as PCBs and chlorinated dibenzo-p-dioxins; the pesticides HCB, mirex, dieldrin and DDT; and the heavy metals cadmium, mercury and lead. Their immunotoxic potential raises concerns regarding subsequent effects on human health. Limited human epidemiological data and data derived from studies using experimental animal models and *in vitro* cell culture systems indicate that certain human populations might be vulnerable to the immunomodulating effects of these pollutants (Tryphonas, 1994; Bernier *et al.*, 1994; Thomas, 1994; Kerkvliet, 1994). Adverse immunomodulation may be expressed either as immunosuppression or immunoenhancement. The former may be manifested either as decreased resistance to opportunistic viral, bacterial, fungal and other agents or increased susceptibility to cancer. Immunoenhancement, on the other hand, may either increase the risk of autoimmune reactions or result in allergic reactions (Bradley and Morahan, 1982; Koller and Exon, 1983; Koller *et al.*, 1983; Munson *et al.*, 1982; Vos, 1977). Following is a description of the current status of knowledge on the immunomodulatory effects of selected groups of contaminants present in the Great Lakes.

Heavy Metals

The existing limited data on humans exposed to heavy metals accidentally or occupationally and data derived from experimental animal models and *in vitro* studies reveal that such metals are among the most potent immunotoxic inorganic chemicals. Frequently, these chemicals exert their adverse effects on the immune system at doses much lower than those required for overt toxicologic effects (Exon, 1984). The adverse immunomodulating effects of mercury, lead and cadmium on the immune system have been the subject of numerous studies, and have been reviewed by Bernier *et al.* (1994) in a background paper prepared for Health Canada, highlights from which are presented below.

Cadmium-induced immunosuppression is suspected to cause decreased resistance to infections by adversely affecting the activity of various important components of the immune system, including reduced macrophage phagocytosis and natural killer cell activity. However, the role of cadmium in reducing host resistance to experimental infections is not conclusive. With respect

to cancer, the carcinogenic potential of cadmium in man is questionable. Yet, animal studies show a strong association between cadmium exposure and tumorigenesis. Overall, the mechanism of cadmium-induced immunotoxicity remains elusive and further mechanistic studies are required.

Inorganic and organic forms of ***mercury*** have definitive toxic effects on the immune system (e.g. altered levels of lymphocyte subsets in rodents). *In vitro* studies have shown increased DNA synthesis in lymphocytes at low mercury concentrations, whereas *in vivo* mercury exposure has resulted in decreased antibody response to certain antigens. Among other effects, mercury exposure can alter non-specific host defenses such as suppression of natural killer cell activity. In addition, it has been well documented that mercury has the potential to induce allergy and autoimmunity, phenomena possibly dependent upon genetic susceptibility.

Lead is immunotoxic, as it has been shown to depress the antibody response in mammals and to diminish host resistance to pathogens in experimental infections in laboratory animals. Lead can also moderately enhance certain immune responses such as B cell differentiation and mixed lymphocyte culture responses. These phenomena are probably mediated through an increase in activity of the T-helper cell. Regarding possible carcinogenic effects, there is no epidemiological evidence that implicates lead as a human carcinogen, although it has been shown to cause tumors in experimental animals.

Generally, the immunosuppressive effects of cadmium, mercury and lead have been shown to increase the susceptibility of laboratory animals to infectious agents (Bernier *et al.*, 1994). In addition, these three contaminants should be regarded as potential epigenetic carcinogens, acting possibly through interference with the immunosurveillance mechanisms (Exon, 1984).

PCBs

The results of *in vivo* and *in vitro* experimental animal studies indicate that commercially available PCB mixtures, known as Aroclors, alter several morphologic and functional aspects of the immune system (reviewed by Vos and Luster, 1989; see also Tryphonas, 1994). High but sublethal dermal and oral PCB exposure have resulted in (a) structural alterations of immune system organs (loss of thymic cortical lymphocytes, reduction of germinal center size, and reduction of leukocyte and T lymphocyte counts in peripheral blood) and (b) altered functional reactivity of the immune system, characterized by reduced antibody production against foreign antigens and reduced skin reactivity to specific antigens (delayed type hypersensitivity); functional defects in the mononuclear phagocytic cells and natural killer cell activity, both of which play primary roles in combating infection; and increased susceptibility to normally tolerated doses of bacterial and viral infections and parasitic infestations. Although the degree of immunotoxicity has been shown to vary across species with dose, duration of exposure and PCB mixture, the more highly chlorinated PCB mixtures (Aroclors 1260, 1254, and 1248) have been found to be more immunotoxic than the less chlorinated Aroclors 1232, 1016 and 1242.

Despite the evidence that PCB-induced immunosuppression impairs the immune surveillance,

Aroclor 1254 has been shown to protect mice and rats against certain kinds of experimentally induced tumours (reduced tumour growth and metastasis) (Keck, 1981; Koller, 1977; Kerkvliet and Kimedorf, 1977). This paradox points to the need for additional studies on PCBs and their relationship to tumour formation and growth.

While the degree of human sensitivity to PCBs relative to that observed in laboratory monkeys is not well characterized, the results of chronic immunotoxicity studies have revealed that monkeys with blood and fat PCB levels comparable to background levels of PCBs found in humans had significant immunotoxic manifestations. In one such study, reduced antibody levels to the T-dependent antigen sheep red blood cells were observed at levels as low as 0.005 mg/kg body weight/day (Tryphonas *et al.*, 1989, 1991a, 1991b). Furthermore, a no-effect dose was not identified in this study. The impact of these findings on the evaluation of the potential risk PCBs pose to humans is presently unclear.

Epidemiological studies (Smith, 1984 and Humphrey, 1988) suggest that PCBs in the Great Lakes may have an immunosuppressive effect in humans. Significant positive correlations were revealed (a) between the maternal serum PCB level during pregnancy and the number and type of bacterial infections suffered by the breast-fed infant during the first four months of life and (b) between the incidence of infections in the breast-fed infant and cumulative fish consumption by the mother (Swain, 1991). Limited data from recent studies on rodents fed fish diets from selected areas of Great Lakes suggest that the immune system may be affected. Further studies are needed to determine the risk that Great Lakes contaminants pose to the human immune system and consequently to human health.

With respect to the interactive effects of PCBs, the existing limited data suggest that under certain experimental conditions PCB congeners in mixtures may either have additive effects or antagonize the immunotoxic effects of other chemicals, including those of dioxin (Davis and Safe, 1989).

The mechanism of PCB-induced immunomodulation has not been adequately elucidated. Many of the immunotoxic effects of PCB congener mixtures depend on the presence of the aromatic hydrocarbon (Ah) receptor and on the ability of the PCBs to bind to this receptor. The molecular events following binding of certain PCBs to the receptor are believed to be similar to those of dioxin. It should be noted, however, that other PCB congeners do not share a common mechanism with dioxins, suggesting a different mechanism of action (Tryphonas, 1994).

Polychlorinated Dibenzo-p-dioxins (Kerkvliet, 1994)

Immunosuppression is a widely recognized toxic effect following exposure of animals of various species to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), expressed as lymphoid tissue depletion, especially in thymus and bone marrow, functional alteration in immune responsiveness, and increased susceptibility to infectious disease. Some studies suggest that prenatal exposure to TCDD is more immunosuppressive than comparable exposure in adults, which may be related to effects on the thymus. Since the thymus is critical for the development of T-cells that can

appropriately discriminate between self and non-self, prenatal exposure to TCDD has the potential to produce serious, long-term effects on immune function.

The immunotoxicity of TCDD depends on the aromatic hydrocarbon (Ah) receptor, and the expression of this receptor in different species or tissues is thus a very important factor determining the toxicity of dioxins and related compounds. Although the effects of TCDD exposure on immunity have been widely studied over the last 15 years, there is still no consensus regarding the target cells and functions that mediate TCDD immunotoxicity. There is a fair amount of conflicting data. In mice, the generation of a primary antibody response appears to be particularly sensitive to suppression when mature animals are exposed to TCDD. The effect on antibody production may result from effects on both T and B lymphocytes. Although most macrophage functions appear to be resistant to TCDD-induced alterations, recent studies indicate that macrophage production of inflammatory cytokines is enhanced following TCDD exposure. Natural killer cell cytotoxicity is not altered in mice exposed to relatively high doses of TCDD. Mitogen-induced blastogenesis of lymphocytes from adult mice is not altered by doses of TCDD that significantly suppress antibody production. Delayed type hypersensitivity (DTH) responses and T-cell mediated cytotoxic responses are suppressed by TCDD, but require higher doses than those capable of affecting antibody production.

The immunotoxicity of TCDD in humans has been the subject of a limited number of studies, primarily based on accidentally or occupationally exposed humans (e.g., in Italy and in Missouri). A decrease in the level of the thymus peptide, thymosin alpha-1, has been reported; however this change was not associated with changes in other immune system parameters nor with any increased incidence of clinically diagnosed immune suppression. The decrease in thymosin alpha-1 levels in humans contrasts with an increase of this peptide seen in PCB-exposed monkeys. The lack of clearly documented immunotoxic effects of TCDD in humans may relate to both the exposure status of the cohorts studied which may have been lower than the immunotoxic dose, as well as the assays chosen to assess immune function, which may have been insensitive to the effects of TCDD.

Organochlorine Pesticides (Thomas, 1994)

There are several pesticides in the Great Lakes Basin which are known to have immunomodulatory effects. These include hexachlorobenzene (HCB), mirex, dieldrin and DDT and its metabolites. At present there is no clear evidence that environmental exposure to these pesticides through consumption of contaminated fish or wildlife poses a threat of immune-mediated health effects in humans. However, laboratory animal studies have shown that these compounds are immunomodulatory (albeit at exposure levels that are orders of magnitude higher than those reported for human exposure), with immunotoxic effects ranging from an increased severity of experimental infection, to specific effects on immune system structure (histopathology) and function.

In rodent studies, hexachlorobenzene (HCB) has been shown to be immunomodulatory based upon increased susceptibility to infection, increased sensitivity to endotoxin challenge and

histopathologic alterations, while altered immune responses suggestive of impaired host defense mechanisms have been observed in mice exposed to dieldrin. With respect to mirex, little is known about the potential immunotoxicity of this compound.

In contrast to the other priority pesticides found in the Great Lakes Basin, there have been numerous studies of the effect of DDT on the immune system of laboratory animals. The results included suggestions of immunosuppression. However, there is no evidence of any adverse long-term effects resulting from small daily doses of DDT, and no conclusive evidence that DDT is immunosuppressive in humans exposed through the food chain. There have been recent reports of an association between DDT exposure and appearance of breast cancer. However, the relationship of this observation to changes in tumour surveillance mechanisms remains unclear.

In summary, there is limited direct evidence that exposure to heavy metals, PCBs, dioxins, and pesticides induces significant immune dysfunction in humans. However, data derived from wildlife (Fox, 1993) and laboratory animal models including monkeys provide evidence of structural changes in tissues of the immune system and of functional deficits in both humoral and cell-mediated immunity. While more information is needed on the mechanism(s) underlining the immunomodulatory effects of these chemicals, the existing limited data suggest that these chemicals may have potential adverse immune-mediated effects in humans who consume large quantities of fish from the Great Lakes.

An important consideration regarding the potential immunotoxic effects of Great Lakes contaminants is that, unlike certain other health effects areas, adverse health effects related to immune dysfunction can be quite subtle yet significant following prolonged exposure. Research in this area is problematic due to a number of confounding factors, including the difficulty in assessing subclinical immunomodulation in a heterogeneous human population, and in quantifying associated health effects. Therefore, there is a strong need to establish a broad database of normal values for the clinical immunology endpoints that may be of use as biomarkers of immune function in immunotoxicity assessment in humans. To validate these biomarkers, there is a parallel need for animal research to identify sensitive immune endpoints that can also be measured in humans in order to establish correlative changes in the biomarker and immune function.

5.5 Carcinogenicity and Genotoxicity

While laboratory animal studies (Parfett *et al.*, 1994) and wildlife studies on Great Lakes fish populations and Beluga whales in the St. Lawrence River (Flint and Vena, 1991) provide evidence that a number of critical pollutants are potentially carcinogenic, there are few epidemiological data on human cancer incidence and mortality and their association with Great Lakes pollutants. In their review conducted for Health Canada, Parfett *et al.* (1994) examined selected persistent chlorinated organic chemicals, volatile organic chemicals, polyaromatic hydrocarbons (PAHs), metals, minerals, and nitrates known to contaminate Great Lakes drinking

water, and concluded that there is limited epidemiological evidence to indicate that some drinking water sources with Great Lakes origin may be associated with increases in the incidence of several types of cancer in humans. Some of these drinking water sources currently have elevated levels of certain contaminants represented by alpha-hexachlorocyclohexane (α-HCH), nickel, and trihalomethanes. However, the epidemiological evidence is not of sufficient strength to link the presence of these compounds with the elevated cancer incidences.

Case-control studies have also examined the association between Great Lakes pollutants and human cancer incidence and mortality. Vena *et al.* (1993) investigated the occurrence of bladder cancer in white males, and a possible association with overall fluid intake and the consumption of specific beverages. Their study involved 351 cases of confirmed transitional cell carcinoma and 855 controls selected from the Erie, Niagara, and Monroe counties of western New York state, all counties bordering the Great Lakes. For more than 95% of the cancer cases and controls in this study, the source of tap water was the public supply obtained from the surface waters of Lake Erie, the Niagara River, and Lake Ontario. After controlling for numerous potential confounding factors, total fluid consumption was found to be a strong risk factor for bladder cancer. More importantly, tap water was associated with an increased risk of bladder cancer, with a clear dose-response relationship (Vena *et al.*, 1993).

While this study links the ingestion of tap water and bladder cancer risk, it does not link exposure to specific contaminants in Great Lakes drinking water with elevated cancer incidences. However, the authors do note that surface waters from which drinking water is drawn have much higher levels of naturally occurring organic substances than does groundwater. The chlorine added to drinking water as a disinfectant reacts with these organic compounds during the chlorination process to form a variety of volatile organic compounds such as trihalomethanes, and a host of other chlorinated non-volatile compounds that have been found to be carcinogenic in laboratory rodents. Among recent research efforts in this area is a case-control study currently being conducted by the Ontario Cancer Treatment and Research Foundation (OCTRF). The OCTRF is examining the possible association between consumption of Great Lakes drinking water and the risk of cancers of the bladder, colon and rectum in residents of Ontario; however, no results are yet available. As well, a national study being initiated by Health Canada will investigate potential risks from Great Lakes water consumption and trihalomethanes based on historical residence. Cancer sites and types under study include liver, testes, brain, pancreas, prostate, stomach, leukaemia, kidney, non-Hodgkin's lymphoma and lung (Johnson, 1993).

It is important to consider that the potential risks associated with the ingestion of drinking water is much lower than the risks associated with other types of exposures. For example, the U.S. Environmental Protection Agency considers the risk of cancer posed by drinking water from the Great Lakes much lower than that for other exposure routes. According to USEPA estimates, the potential number of excess cancer cases related to the ingestion of drinking water across the Basin may total approximately 66 over a 70-year span. On the other hand, the estimated total number of potential excess cancer cases related to consumption of Great Lakes fish is 30,000 over a 70-year span -- several orders of magnitude higher (USEPA Great Lakes National Program Office, 1992). The USEPA based its estimate on the following assumptions: that the residents

of the Great Lakes Basin who derive their drinking water from surface water sources ingest 2.0 litres of contaminated water per person per day; an estimated duration of exposure of 70 years (lifetime) and an estimated average body weight of 70 kg; a Great Lakes population of 12,700,000 relying on drinking water from surface water supplied systems within the Great Lakes counties in the U.S.; and concentrations of lindane, α-BHC (a by-product of lindane), dieldrin, p'p-DDE, PCBs, and HCB for all of the Great Lakes as estimated by the International Joint Commission's (IJC) Water Quality Board (1989).

In addition, the USEPA's Great Lakes Basin Risk Characterization study has estimated cancer risks from multiple exposure to contaminants Basin-wide. The study results indicate that health risks related to Basin-wide exposure to contaminants in Great Lakes fisheries and ambient water are driven primarily by PCB exposure. With regard to Great Lakes fish consumption, chemical risk analyses suggest that PCB exposure accounts for 85% of human cancer risks. Indeed, there have been studies linking PCB levels in certain populations with breast cancer incidence. For example, recent studies conducted on cohorts from Connecticut and New York state provide some evidence linking organochlorine pollutants such as DDT and PCBs to breast cancer incidence (Falck *et al.*, 1992, Wolff *et al.*, 1993). These studies point to potential adverse effects that should be considered in health studies for the Great Lakes region. This is based on predictive modeling and assuming that 3.4 million people consume 19 grams of Great Lakes fish per day over a 70 year life time exposure, which is a conservative estimate. In addition, concentrations for fish contaminants were averaged for all the Great Lakes and based on figures from the IJC Great Lakes Water quality Board's Report on Water Quality for PCB, DDT, Dieldrin and mercury and assumes that contminant level would not decline.

Regarding mixtures of chemicals from the major groups discussed in this review, these have been linked to excess cancer mortality associated with occupational exposures. Consistent with exposure to qualitatively similar hazards, cancer sites implicated in these studies overlap with the cancer sites identified in Ontario drinking water studies. Occupational exposures to PAHs, TCDD, cadmium and nickel have been associated with increased lung cancers; pesticide exposures have been associated with lung cancer and non-Hodgkin's lymphoma; and various exposures to some volatile organic chemicals have been associated with oesophageal, cervical, and non-Hodgkin's lymphatic cancers (Parfett *et al.*, 1994).

With respect to relevant data from animal studies, most Great Lakes contaminants for which animal carcinogenicity data are available are classifiable as animal carcinogens at high doses. Consistent with exposure to qualitatively similar hazards, the listing of tumour sites obtained from positive animal studies overlap with human tumour sites associated with "contaminated" Great Lakes drinking water sources. However, no cause-effect relationships have been established regarding the very low concentrations of environmental contaminants. In laboratory animals, lung and kidney cancers have resulted from treatments with members of all groups of contaminants (PAHs; certain volatile, chlorinated organics; metals; pesticides; dibenzodioxins, dibenzofurans and PCBs). As well, thyroid tumours have resulted from treatments with individual volatile, halogenated alkanes and alkenes, pesticides, chlorinated dioxins and PCBs, while leukaemias were found in animals treated with some pesticides, and cadmium treatment

gave rise to lymphomas (Parfett *et al.*, 1994).

Evidence also indicates that TCDD is active in rodent and human systems at lower concentrations than any of the other contaminants discussed and identified as carcinogenic risks by Parfett *et al.* in their review. TCDD induces gene expression and transformation of human cells *in vitro* at concentrations similar to the background levels in the sera of the majority of North Americans. Levels and effects (e.g., likely cancer sites, gene inductions, etc.) of this persistent compound should receive special attention in populations receiving greatest exposure to Great Lakes contaminants (Parfett *et al.*, 1994).

In addition, available data further indicate that in human cells certain volatile, chlorinated alkanes and alkenes (trichloroethylene, tetrachloroethylene, chloroform) cause sister chromatid exchanges *in vivo*, and induced cell proliferation *in vitro* at concentrations only ten-fold higher than those in the guidelines established for drinking water contamination (Parfett *et al.*, 1994). (Note: levels in drinking water can be compared to levels in culture fluid used to incubate cells. They cannot be compared with levels *in vivo* (i.e., tissue fluids) because only 2 litres of water per day are consumed and most of the water is excreted. The tissue or blood levels are the result of a composite exposure through food consumption, inhalation, and dermal contact with water). Lastly, combinations of Great Lakes contaminants known to have carcinogenesis-related effects at low doses in human cells have received little or no attention with regard to effectiveness in chemical mixtures. This represents an important area for future research.

5.6 Respiratory Health Effects

The effects of air pollution on respiratory health can range from severe (aggravation of respiratory disease, death) to moderate (reduced lung function with or without symptoms) to minor (eye, nose and throat symptoms). Certain effects, such as mild inflammation in the lungs without symptoms, may or may not have any significance (American Thoracic Society, 1985). Some researchers have suggested that there is a logical "cascade" of these effects (Bates, 1992); in other words, if a few people die as a result of air pollution, then more should experience worsening of respiratory disease, even more should experience reduced lung function, and a very large number should experience eye, nose and throat symptoms, so that the total burden of illness could be very large. This means that research which demonstrates increased death rates and rates of hospital admission due to air pollution could reflect a very large overall burden of illness in the population.

Effects on Death Rates

Several studies have examined the relationship between air pollution and death rates, two of which were carried out in the Great Lakes Basin. A study in Hamilton, Ontario looked at the geographic distribution of lung cancer deaths between 1972 and 1976, comparing industrial and non-industrial areas of the city (Shannon *et al.*, 1988a). A 15% excess of lung cancer deaths was

observed in industrial areas, after taking into account different age and smoking patterns. Air pollution levels were not reported.

A second study in Detroit, Michigan examined parallels between daily death rates and air pollution levels (Schwarz, 1991). This study used statistics on all causes of death other than accidents between 1973 and 1982 and measured weather variables and levels of airborne particles, ozone, and sulphur dioxide. There was a clear relationship noted between increased death rates and increased levels of airborne particles and, to a lesser extent, sulphur dioxide, even when the effects of weather and other variables were taken into account. It was estimated that when daily levels of airborne particles increased from the low end to the high end of levels observed in the study (100 $\mu g/m^3$), the death rate increased by 6%. As described in the section on airborne particles, levels such as this are commonly observed in Great Lakes cities in Ontario.

Other studies have linked increased death rates with elevated levels of sulphur dioxide, sulphate and particles (Plagiannakos and Parker, 1988), as well as ozone (Kinney and Ozkaynak, 1991). In addition, increased death rates from asthma have been observed worldwide in recent years (Mao *et al.*, 1987), which may be partially attributable to exposure to air pollution.

Effects on Hospital Admission Rates

Three studies have examined the relationship between daily air pollutant levels and rates of hospital admission in Great Lakes cities. The first study, based on data for southern Ontario between 1974 and 1983, looked at the effect on hospital admissions of levels of ozone, nitrate, sulphur dioxide, airborne particles, and sulphate (Bates and Sizto, 1987). Increased temperature, ozone, sulphate and sulphur dioxide accounted for an increase in respiratory admissions of about 5%. These effects were observed within the range of pollutant levels described in the sections on ground-level ozone and acid aerosols.

The second study took a similar approach, using data for the years 1983-1988 for a larger number of Ontario communities, some of which were in the Great Lakes Basin (Burnett *et al.*, 1993). This study attributed 5% of respiratory admissions to ozone, and an additional 1% to sulphates. The largest impact appeared to be on children under 2 years of age, in whom 15% of hospital admissions were attributed to ozone and sulphate together. Again, these effects were observed within the range of pollutant levels described in the sections on ground-level ozone and acid aerosols.

The third study looked at hospital admissions in Toronto during July and August 1986-1988 (Thurston, 1993). This study found significant associations between hospital admission rates and elevated temperature and pollutant levels, including ozone and acid aerosols.

With regard to the health impact of exposure to air pollutants on the U.S. side of the Great Lakes Basin, the U.S. Environmental Protection Agency has conducted a risk assessment of populations in the Basin and estimated that exposure to toxic air pollutants results in 148 premature deaths and approximately 470 hospital admissions annually. In addition, the USEPA estimates that over

33,000 children and nearly 110,000 adults in the Basin experience respiratory symptoms as a result of exposure to sulphates. Consequently, the costs arising from the 148 predicted premature deaths and the 470 hospital admissions are $11 million and $2.1 million, respectively (USEPA Risk Characterization Study, 1992).

Effects on Lung Function

A number of studies have examined the relationship between levels of various pollutants and decreases in lung function, particularly in children. A study conducted in Hamilton between 1978 and 1982 measured exposure to suspended particles and sulphur dioxide, and correlated these with symptoms and lung function measurements in children aged 6 to 11 years (Pengelly *et al.*, 1986). Children living in the most industrial areas of the city, who had the greatest exposure to small particles, had poorer lung function, although the effect was smaller than that of maternal smoking.

A second study was conducted in a girls' camp on the north shore of Lake Erie in the summer of 1986 (Raizenne *et al.*, 1989). This study examined the relationship between ozone, acid and sulphate levels (measured on site) and lung function in girls aged 8-14. Small (up to 5-10 %) decreases in lung function were observed on days when pollutant levels were high. The highest ozone, acid and sulphate levels were 143 ppb, 550 nmol/m^3 and 83 μg/m^3, respectively, which are much higher than average levels observed in southern Ontario, but are typical of air pollution episodes in this area.

A more recent study in 24 North American communities related measurements of acid aerosols, small particles ($PM_{2.1}$;<2.1 μm), larger particles (PM_{10};<10 μm), and sulphate, to lung function measurement in children. Two of these communities (Dunnville - near Hamilton, and Leamington - near Windsor) were in the Great Lakes Basin area and experienced pollutant levels which were intermediate compared to other communities. Children exposed to the highest acid aerosol levels were 2.5 times as likely to have lung function below 85% of that predicted for healthy children based on sex, height, weight and other factors.

In conclusion, there is strongly suggestive evidence from the Great Lakes Basin linking ozone, airborne particles and acid aerosols to significant respiratory health effects including death and illness requiring hospital admission. There is also evidence from the Great Lakes Basin that these pollutants cause reduced lung function in children. This evidence is consistent with data from elsewhere in North America and Europe.

5.7 Health Effects Associated with Radionuclides

The Great Lakes Basin is an area of radiological concern as a result of the large population that may be exposed to actual or potential sources of ionizing radiation arising from both natural and artificial sources. Exposure to ionizing radiation can affect the various organs and tissues of the body, and may result from rediation originating in deep space, or emitted by the decay of

radioactive elements found in the environment. These radioactive elements, or radionuclides, are unstable nuclides of a particular atomic species that return to stability by emitting ioning radiation. Specific radionuclides of interest in the Basin arising from natural and artificial sources include tritium (^{3}H), carbon-14 (^{14}C), strontium-90 (^{90}Sr), radioiodine (^{129}I, ^{131}I), cesium-137 (^{137}Cs), radon-222 (^{222}Rn), radium-226 (^{226}Ra), uranium isotopes (^{235}U, ^{238}U),and plutonium isotopes (e.g., ^{239}Pu, ^{240}Pu, ^{241}Pu).

By far, the greatest contribution to the average public radiation exposure is the natural background radiation that comes from radioactive elements in the earth's crust and from cosmic radiation originating in deep space. Natural sources contribut on average more than 98% of the human radiation dose, excluding medical exposures. The global average dose from natural sources as estimated by the United Nations Scientic Committee on the Effects of Atomic Radiation (UNSCEAR, 1993) is about 2.4 milliSieverts (mSv -- a unit of effective dose) per year, which can be compared with the national Council on Radiation Protection and Measurments estimate of 2.6 mSv a^{-1} for Canada (NCRP, 1987a). this dose results mainly from internal and external exposure to radioactive potassium (^{40}K), and from the inhalation and accumulation in the respiratory system of the short-lived radon decay products (the rapidly decaying radionuclides formed as a result of successive decays of ^{222}Rn). The natural radiation dose provides a measure by which contributions from human activities can be evaluated.

Global fallout of radionuclides produced during atmospheric nuclear weapons tests has resulted in the largest total input of anthropogenic radioactivity into the Lakes (**Table 8**), although the 1963 moratorium on atmospheric detonations of nuclear weapons has resulted in declining radiation levels since the mid-1960s. The total committed dose (the average total dose resulting from radionuclides accumulated in the body) to the year 2050 to each individual in the Basin from weapons tests conducted between 1945-1980 has been estimated to be about 1.9 mSv (UNSCEAR, 1993), Most of which has already been received. This truncated dose provides a measure of the radiation hazard presented to those living during the period of intensive testing prior to 1963, and is equvalent to slightly less than one extra year of exposure to natural background radiation.

Increases in local exposure above background levels may result from radionuclides released during the various stages of the nuclear fuel cycle. Nearly all components of the nuclear fuel cycle are found within the Basin, the main elements of which are uranium mining, fuel preparation, power generation, and waste management (see Figure 6). Normal fuel cycle operations result in controlled and regulated release of radionuclides into the atmosphere and aquatic environments (**Table 8**), adding to the radiation exposure from both natural sources and radioactive fallout from atmospheric nuclear weapons tests (see **Table 9**).

The doses from these three sources can be compared in terms of the total collective doses to the Basin population from 50 years of exposure at current levels, or to the year 2050 in the case of nuclear weapons fallout. These doses are obtained by multiplying the average annual individual exposure by the number of people exposed and the number of years considered (**Table 9**). The collective dose to the Basin population from 50 years of expsoure to natural background radiation

is therefore of the order of 4.7 x 10^6 man-sievert (man-Sv). The collective dose from 50 years of fuel cycle operation in the Basin based on actual radionuclide emmissions from 1985-1989 (UNSCEAR, 1993) has been estimated to be about 2.8 x 10^3 man-Sv, or about 3 orders of magnitude less than the exposure due to natural background radiation. Although currently very low, the dose from fuel cycle activities can be expected to increase if there is continued growth of the nuclear industry.

TABLE 8
INVENTORY OF RADIONUCLIDES IN THE GREAT LAKES FROM FALLOUT TO 1983 AND NUCLEAR FACILITY RELEASES, AND 1989 INVENTORIES STORED AT THE FACILITIES

	ESTIMATED RADIONUCLIDE INPUTS AND INVENTORIES BY LAKE (TBq)				
SOURCE	Superior	Michigan	Huron	Erie	Ontario
Tritium (^{3}H):					
Fallout*	7 x 10^4	6 x 10^4	7 x 10^4	4 x 10^4	3 x 10^4
Nuclear Facilities	-----	2 x 10^3	1.5 x 10^4	2 x 10^2	5 x 10^2
Strontium-90:					
Fallout*	123	98	98	45	33
Nuclear Facilities	-----	0.015	0.11	1.5	0.15
Stored at Facilities	-----	5 x 10^6	3.5 x 10^6	6 x 10^5	4 x 10^6
Cesium-137:					
Fallout*	200	159	159	74	54
Nuclear Facilities	-----	9	0.12	0.2	25
Stored at Facilities	-----	8 x 10^6	5 x 10^6	7 x 10^5	7 x 10^6

* Input from fallout calculated using deposition flux at mid-basin location for each Lake using New York City data, adjusted for latitude.

Source: Joshi, 1991 (cited in Ahier and Tracy, 1994)

Radiological Effects and Health Implications of Human Exposure to Radionuclides

In their review of radionuclides in the Great Lakes Basin, Ahier and Tracy (1994) present an informative discussion of the radiological and health effects of exposure to radionuclides, on which the following summary is based. In essence, the decay of a radionuclide results in the emission of ionising alpha, beta, and gamma radiation, which can disrupt cells in the human body as energy is transferred from the radiation to the tissue. A measure of this disruption is the *absorbed dose*, defined as the amount of energy imparted by ionising radiation to a unit mass of tissue. The term *effective dose* is introduced to account for the difference in effectiveness of the type of radiation and the different susceptibilities of bodily organs. Generally, the effective dose can be considered a broad indicator of the risk to health from any exposure irrespective of the type and energy of the radiation, or of the organ or organs exposed.

Exposure to ionising radiation, whether natural or man-made, can cause two kinds of health effects. Effects for which the severity of the damage caused is proportional to the dose, and for which a threshold exists below which the effect does not occur, are called *deterministic effects*. These are generally manifested in the individual within a few days or weeks following exposure. Deterministic effects have not been observed at exposures below 0.5 Sv. Under normal conditions, doses received from natural radioactivity and routine exposures from regulated practices are well below the threshold levels. Effects for which the probability of occurrence, rather than the severity, is proportional to dose are known as *stochastic effects*, and it is assumed that there is no threshold below which they do not occur. Stochastic effects are the most important consequence of environmental levels of radiation.

Stochastic effects can be either hereditary or somatic in nature. *Hereditary effects* appear in future generations as a result of radiation-induced changes in the reproductive cells of an exposed individual. Although studies have been conducted on the hereditary damage induced in experimental animals, no conclusive evidence for hereditary effects attributable to exposure from either natural or artificial radiation has been found in human offspring.

The stochastic effects of concern are late *somatic effects*, mainly cancer, which follow a variable latent period of up to several decades. These effects result primarily from relatively low exposures received over an extended period of time, although they can result from massive doses that have caused immediate effects (e.g., atomic bomb survivors). The main somatic hazards from environmental radiation are the development of leukaemia and other cancers, particularly in the bone, thyroid, lung, or breast.

The primary sources of epidemiological information on radiation effects have come from studies of individuals or groups who have received high or intermediate levels of exposure. As it is impossible to obtain dose-effect relationships in humans at low levels of exposure, a linear, no-threshold model is assumed, extrapolated from the epidemiological studies of the effects of high dose and dose-rate exposures. Thus, health effects are generally assumed to be proportional to

the dose received, without a dose threshold (i.e., there is no dose, however small, that may in principle be considered without risk). The no-threshold hypothesis is believed to be conservative, and estimates of risk based on this model are upper limits. One consequence of the no-threshold approach is that even when the risk to an individual is small, a finite number of theoretically attributable radiation-induced cancers is predicted if a sufficiently large population is exposed. Based on the epidemiological data, the International Commission on Radiological Protection (ICRP, 1991) has established a risk of 5×10^{-5} per mSv for the induction of fatal cancer after low dose, low dose-rate whole body irradiation of a member of the general population. The ICRP has alsorecognized that not all cancers are fatal, and that this, in addition to the possibilty of hereditary effects, should be considered. Therefore, the ICRP has estimated the risk of incidence of non-fatal cancers, weighted for severity, and of hereditary effects. The total risk coefficient for fatal and weighted non-fatal cancers, and hereditary effects, based on all epidemiologic data, has been estimated to be 7.3×10^{-5} per mSv (ICRP, 1991).

Radiological Risk Assessment in the Great Lakes Basin

Risk assessments of exposures in the Great Lakes Basin require estimates of total effective dose for both local and regional populations, as well as for the maximally exposed individual or group living in the vicinity of a nuclear facility (see **Table 9**). Assuming a no-threshold model for radiation effects, the ICRP risk estimate for fatal cancer can be applied to the total effective dose for the relevant population. Estimates of collective dose and risk committed by 50 years of exposure have been derived by Ahier and Tracy (1994) for the current Basin population of 36 million. The total number of predicted fatalities over the lifetime of the current Basin population that could be theoretically attributed to a 50-year exposure to natural background radiation is of the order of 2.4×10^{5}. By comparison, the total number of predicted fatalities theoretically attributable to radioactive fallout from all weapons tests to date would be of the order of 3,400. Estimates of theoretically attributable fatalities due to 50 years of exposure to current nuclear fuel cycle effluent (from exposures mainly to ^{3}H and ^{14}C releases) based on environmental models and actual radionuclide emission rates (UNSCEAR, 1993) are on the order of 140. These numbers are hypothetical values based on conservative exposure models, rather than predictions of actual effects from either natural or artificial sources. These numbers should be taken as upper limits, and show that the inpact from man-made sources is small compared to the effects of normal background radiation.

TABLE 9

MAXIMUM INDIVIDUAL AND COLLECTIVE EFFECTIVE DOSES AND RISKS FROM RADIATION SOURCES IN THE GREAT LAKES BASIN

SOURCES	ANNUAL DOSES		50 YEAR DOSE AND RISK		
	Individual ($mSv\ a^{-1}$)	Collective ($man\text{-}Sv\ a^{-1}$)	Collective (man-Sv)	Risk (fatalities)	
Natural	2.6	94,00	4.7×10^6	2.4×10^5	
Fallout	1.9 (mSv to 2050)		6.8×10^4	3.4×10^3	
Nuclear Fuel Cycle					
Mining, milling[1]		0.65	15		
Conversion[2]		0.044	0.1		
Reactor operation[3]		0.01 - 0.04	40		
Low-level waste			<0.1		
Total Fuel Cycle			55	2.8×10^3	140

50-Year Collective Risk to Basin Population	
Natural	2.4×10^5
Weapons Fallout	3.4×10^3 (to year 2050)
Nuclear Fuel Cycle	140

Collective doses and risk for natural and fuel cycle exposures integrated over 50 years based on current dose rates; integrated to the year 2050 for weapons fallout exposure.
Collective doses for nuclear fuel cycle based on doses per unit release, and measured emissions for Basin facilities, 1985 -1989 (UNSCEAR, 1993).

1 maximum individual dose from mining activities from (NCRP 1987)
2 maximum dose from Health Canada Port Hope study (Ahier and Tracy, 1993)
3 maximum dose for reactors based on Ontario Hydro estimates (Ontario Hydro, 1994)

Source: (Ahier and Tracy, 1994)

Concentrations of important radionuclides in Great Lakes water that would result in a 50-year committed effective dose equal to the ICRP (1991, 1991a) public exposure limit of 1 mSv from a single year of consumption of drinking water (550 l per year) are shown in **Table 10**. These are compared with actual measured concentrations, which are well below the maximum derived concentrations. The effective doses for drinking water for each lake are shown in **Table 11**. The total average dose for Great Lakes water is estimated to be about 1.0 μSv for Lakes Ontario, Erie, and Huron, and 0.7 μSv for Lake Michigan (Ahier and Tracy, 1994). These are well below the ICRP exposure limit, and would result in two additional fatalities per year based on the maximum effective dose to the entire Basin population. As with other estimates of risk, this estimate is an upper limit based on the conservative assumption of a no-threshold dose model.

TABLE 10

COMPARISON OF PROPOSED CANADIAN FEDERAL GUIDELINE CONCENTRATIONS FOR RADIONUCLIDES IN WATER, AND ACTUAL CONCENTRATIONS IN THE GREAT LAKES

RADIONUCLIDE	GUIDELINE CONCENTRATION	OBSERVED CONCENTRATION (Bq L^{-1})				
		Superior	Michigan	Huron	Erie	Ontario
^{3}H	7,000	5.4	6.6	9.1	12	8.7
^{90}Sr	4	1.5×10^{-2}	1.9×10^{-2}	2.7×10^{-2}	2.3×10^{-2}	2.9×10^{-2}
^{137}Cs	7	1.7×10^{-3}	1.4×10^{-3}	1.1×10^{-3}	0.6×10^{-3}	1.0×10^{-3}
^{226}Ra	0.6	--	----	0.7×10^{-3}	----	1.2×10^{-3}
$^{239,240}Pu$	0.3	--	4.4×10^{-7}	4.8×10^{-7}	1.8×10^{-7}	1.7×10^{-7}
U ($\mu g\ L^{-1}$)*	200	0.08	0.38	0.39	0.59	0 .42

Maximum allowable concentrations in water based on an annual exposure limit of 0.1 mSv and an annual water consumption of 730 L. Water contrations from IJC (1983) and Joshi (1991.

*Uranium concentration given in units of $\mu g\ L^{-1}$; guideline concentration corresponds to approximately 6 Bq/L.
The limit based on chemical toxicity 100 $\mu g\ L^{-1}$.

Source: Ahier and Tracy, 1994.

TABLE 11
50 YEAR COMMITTED EFFECTIVE DOSE FROM THE INGESTION OF GREAT LAKES WATER FOR ONE YEAR

RADIONUCLIDE	50 YEAR COMMITTED EFFECTIVE DOSE (μSv)				
	Superior	Michigan	Huron	Erie	Ontario
^{3}H	0.08	0.09	0.1	0.2	0.1
^{90}Sr	0.4	0.5	0.7	0.6	0.7
^{137}Cs	0.02	0.02	0.02	0.01	0.01
^{226}Ra	0.2	0.2	0.2	0.2	0.2
U (natural)	0.04	0.2	0.2	0.3	0.2
TOTAL (μSv)	0.7	1.0	1.2	1.3	1.2

Average Risk: 2 theorectically attributable fatalities per year from consumption of Great Lakes waters

Does based on concentrations from Table 10, except for ^{226} Ra, for which a concentration of 1 mBq L^{-1} is assumed. Average basin risk based on a committed effective dose of 1.2 μSv for a population of 36 million.

Source: Ahier and Tracy, 1994

In spite of strict regulations concerning the design and operation of nuclear power facilities, the potential exists for a serious nuclear accident as a result of the large inventories of radionuclides contained in the reactor core and spent fuel bays. Although the probability of occurrence is small, the release into the environment of a significant fraction of this inventory could lead to many deaths and other health effects, and would have severe social and economic consequences. Long-range atmospheric transport and dispersion of radioactive plumes could result in the exposure of many people to marginally or significantly elevated levels of radiation. In a similar fashion, serious accidents outside of the Basin could also affect local ecosystems. Additional future deaths due to cancer could occur as a result of increased collective doses. With the engineered safeguards of North American reactors, the risks associated with a severe accident are orders of magnitude less than risks from other natural and man-made hazards.

An area of priority over the next few decades will be the management of the substantial amounts of high-level and low-level wastes generated by the nuclear facilities in the Basin. Current and historic low-level waste sites are situated in the Basin. Proposed methods for permanent disposal of high-level wastes include the deep-geological disposal concept, which is currently under environmental review in both Canada and the United States. It is conceivable that a Canadian facility could be located within the Basin. Due to the presence of long-lived radionuclides in the spent fuel, the technical requirements of any disposal method are momentous. Considerable effort is being expended to ensure that the impact on any environment in which a repository is sited will be negligible to the far future.

5.8 Health Effects Associated with Microbial Contaminants

Water in the Great Lakes Basin is used for drinking and recreational purposes by an estimated 40 million people. Microbial contamination of the water by human and animal sewage has been documented at numerous sites in the region. Those drinking the water at these locations run the risk of developing giardiasis, cryptosporidiosis, or gastrointestinal illness (Xu *et al.*, 1994). The largest documented waterborne outbreak in the United States history occurred in Milwaukee, Wisconsin during March and April of 1993. Cryptosporidium was the etiologic agent. As a result, 880,000 customers served by the Milwaukee Water Works were advised to boil their water (Gradus, 1994). During March and April, before and after the advisory, an estimated 370,000 city residents (roughly one quarter of those living in the metropolitan area) experienced severe diarrhea, nausea, and stomach cramps (Edwards, 1993). There are a number of possible causes of the outbreak of the parasite cryptosporidia in Milwaukee: 1) a combination of spring water runoff, which overstressed the treatment system and most likely brought the parasite into the city, 2) a substitute coagulant used to settle particulates prior to sand filtration which did not filter out the parasite, and 3) chlorination, a standard procedure in water treatment, is not effective in killing the parasite hence making the other physical treatment procedures all the more important. Among bathers, higher rates of gastrointestinal, respiratory, eye, ear, and skin infections have been noted. A Canadian prospective study of swimming-related illness showed that swimmers

experienced respiratory ailments most frequently followed by gastrointestinal, eye, ear, and skin symptoms (Seyfried *et al.*, 1985a, 1985b). A second Canadian prospective study in 1989 reported similar results (Lightfoot, 1989). A similar survey in New Jersey showed that the beachgoers had red itchy eyes and sore throat most commonly, followed by skin rash, gastrointestinal illness and ear infections (New Jersey Department of Health, 1990). The New Jersey researchers suggested that the illnesses may have resulted from person to person transmission of viruses rather than sewage contamination. The difference between gastrointestinal illness rates among swimmers and nonswimmers in the 1985 Canadian epidemiological study was similar to those observed by Cabelli (1982, 1983) and the New Jersey survey, i.e. an excess of 13.3 cases per 1000 in Canada compared with excesses of 4.0 to 16.0 cases per 1000 in Cabelli's studies and an excess of 12.2 cases per 1000 in the New Jersey survey.

The bacteria used as water quality indicators in the epidemiological surveys are not the etiological agents of the illnesses which they index. For this reason it has been difficult to demonstrate a relationship between the bacteriological quality of the water and adverse health effects. A number of new water quality indicators, such as the F2 bacteriophage to assess viral survival in receiving waters, have been proposed but are still under investigation (Xu *et al.*, 1994).

Future studies on the relationship between health effects and water quality in the Great Lakes Basin should include other bacteria and viruses, in addition to the usual fecal indicator bacteria. Furthermore, water sampling and microbial monitoring should be carried out as frequently as possible during the survey. Finally, clinical investigations could be included in the determination of illness rates in order to minimize the effects caused by respondents and interviewers.

6.0 Knowledge Gaps and Directions for Future Research

Recent research into the human health effects of exposure to Great Lakes contaminants, including risk assessment methodologies, has focused on the potential for pollutants to cause cancer, birth defects and related readily observable health outcomes. This traditional evaluation of the significance of environmental pollution in terms of adverse health effects pervades both health policy and regulatory policy. The focus on cancer as a health effect endpoint of environmental contamination reflects a valid scientific and public concern. However, an important point arising from the Great Lakes research community is that the public health implications of toxic pollution go well beyond cancer to other health effects priorities. Great Lakes researchers have revealed evidence that some health effects of toxic pollutants may be more subtle and far-reaching than previously thought. Accordingly, a more holistic approach to evaluating human health effects requires identifying, assessing and monitoring potential noncancer endpoints in order to develop and implement effective remedial action strategies. The Great Lakes research community is currently breaking new ground in its research into potential human health impacts in a number of areas, such as immunotoxicity, reproductive outcomes additional to birth defects, neurotoxicity and developmental effects, respiratory health effects, and newer concerns such as multiple chemical sensitivity (MCS) (Bell, 1994; Miller, 1994). As a result, the Great Lakes research agenda provides a fitting model for such environmental health effects research worldwide. However, researchers have identified a number of gaps in our knowledge of the actual and potential human health effects of chronic, low-level exposure to Great Lakes contaminants. Consequently, there are several potential research areas that decision-makers might consider in efforts to expand our knowledge in this field:

♦ ***Exposure***: Further research is required to improve exposure data (including expanded routine monitoring of priority air pollutants) so that quantitative exposure-response relationships can be determined -- i.e., linking tissue contaminant levels with health effects endpoints, including noncancer endpoints (e.g., immunological, neurological, reproductive).

♦ There is also a need to monitor Great Lakes populations exposed to persistent toxic substances to evaluate whether or not they are accumulating body burdens at higher rates than the national average, and to identify highly exposed groups. Monitoring could include long-term surveillance to determine trends in contamination.

♦ As well, further study of pathways of exposure other than fish consumption is required, and related risks assessed -- e.g., for ingestion of drinking water, inhalation of polluted air, and consumption of contaminated locally grown meat and dairy products. Research is also needed to examine the potential for dermal absorption of Basin water contaminants during bathing at home or in Great Lakes waters. PAHs from Basin sludge located near the lakeshores in contaminated areas needs special attention.

♦ ***Chemical Mixtures***: Additional research is required to better define the potential interactions among the many Great Lakes contaminants to determine the net effect of exposure to mixtures of environmental pollutants, i.e., a more holistic evaluation of the risk these chemicals pose to human health. Research is also required to develop better technologies for measuring exposure to multiple chemicals and subtle related effects on health.

♦ ***Range of Endpoints***: There is a need to identify the most sensitive and reliable health effect endpoints and to broaden the range beyond cancer and birth defects in order to better assess the risks to human health associated with chronic low-level exposure to Great Lakes contaminants. The endpoints monitored should include neurological, endocrinological, immunological, respiratory, cancer and reproductive effects -- including those of growing public concern, such as breast cancer and multiple chemical sensitivity.

♦ In addition, the majority of biomarkers of effect and susceptibility are currently limited in their use because they are non-specific and can apply to a variety of environmental contaminants. There is a need to develop biomarkers that are more sensitive and specific to particular chemical exposures.

♦ ***Epidemiological studies***: Baseline data from epidemiological studies are required to quantify the health effects of exposure to low environmental concentrations of specific contaminants, including air pollutants, in a way that accounts for them apart from the many other known risk factors (e.g., socio-economic and lifestyle factors, biological and occupational exposures); and to determine whether the incidence of adverse health effects for individuals living within the Great Lakes Basin differs from that observed in other areas of Canada and the United States.

♦ In the design of epidemiological studies, identification and verification of high-risk, high-exposure cohorts, consideration of past exposure histories and other risk factors for adverse health effects are critical.

♦ There is a further need for information on the long-term health effects on children exposed *in utero* and in early childhood to low levels of persistent environmental Great Lakes toxicants. Indications are that such health effects as might exist are not necessarily expressed as classical physical disease. Rather, the endpoints may be psychosocial in nature and require long-term neurobehavioral and biochemical assessments to detect what might be subtle effects. For example, there have been calls for more studies of behavioral, developmental, and immune system characteristics as well as of stages of sexual development in growing children (Colborn *et al.*, 1990, cited in Jordan-Simpson *et al.*, 1994). There is also a need to study delayed effects that may occur after puberty, such as endometriosis and premature reproductive senescence.

♦ ***Subpopulations at special risk***: With regard to relative risks, future public research efforts should be focused on those subpopulations which have the highest potential for exposure, such as people who eat large amounts of contaminated fish or wildlife from the Great Lakes, and those who live near hazardous waste sites. Of particular concern are people whose immune systems are already suppressed either through medication or certain disease states; developing fetuses and

infants; the oldest population groups, and others who are especially vulnerable to adverse health effects.

7.0 Conclusions

1) It is clear that occupational or accidental exposure to high levels of certain contaminants discussed in this paper -- ***PCBs, dioxins, organochlorine pesticides, lead, and methylmercury*** -- pose a risk to human health. While the exact nature and extent of the health risk from exposure to environmental levels of these chemicals in the Great Lakes ecosystem are unclear and require further study.

2) Because of the limitations inherent in human health effects research, the study of potential effects and their use as a gauge for "State of the Lakes" water quality are problematic, and thus the ***"weight of evidence"*** approach includes a substantial amount of data from laboratory animal and wildlife studies. In addition to data from (limited) epidemiologic studies, adverse reproductive, developmental, behavioural, endocrine, and immunologic effects have been observed in laboratory animal studies and across a range of wildlife species exposed to mixtures of these persistent toxic chemicals present in the Great Lakes Basin. While differences exist between humans and animal life, these findings are indicators of a potential risk to human health at certain levels of exposure, and warrant further study.

   Furthermore, traditional health outcomes such as cancer and birth defects, which are relatively severe and well recorded, may be comparatively insensitive indicators of the effects of low-level exposure to environmental contaminants. There is a need for further study of the less severe, more subtle adverse health effects of long-term, low-level exposures to mixtures of chemicals, including effects on human reproduction (additional to birth defects), the immune, endocrine, respiratory and circulatory systems; and on neurobehaviour, development in children, and psycho-social health status.

3) The uncertainty as to whether these chemicals (PCBs, dioxins, organochlorine pesticides, lead, and methylmercury) have long-term adverse health effects on humans is predominantly in the quantification of the ***dose-response relationship***; i.e., what level of exposure is required to observe an adverse effect.

   Comprehensive data on contaminant ***exposure levels*** in Great Lakes populations compared to those in other populations worldwide are lacking. With regard to fish consumption as a major route of exposure, there is some evidence that the contaminant levels seen in people who live in the Basin and consume fish are no greater than levels in populations elsewhere. Whether or not this is attributable to lower levels of toxic chemicals in fish is uncertain. However, recent evidence suggests that certain subpopulations that are traditionally large fish-eaters (i.e., sports anglers and Native people) have changed their fish consumption habits, either by consuming less fish or by modifying their fish-cleaning and preparation methods in response to health advisories.

4) While it is clear that fish consumption is a major route of human exposure to persistent chemicals in the Great Lakes, those other than Native people who consume large amounts of fish make up a minority of the Great Lakes population. When measuring total exposure to Great Lakes contaminants as part of an integrated exposure assessment, other ***exposure routes*** -- i.e., ingestion of drinking water, inhalation of polluted air, consumption of contaminated meat or dairy products and, to a much lesser degree, dermal exposure to water contaminants -- must also be considered.

5) With respect to the other groups of environmental contaminants discussed in this paper, there is strongly suggestive evidence from the Great Lakes Basin linking ***ground-level ozone, airborne particles and acid aerosols*** to significant respiratory health effects, including illness requiring hospital admission, and death. There is also evidence from the Basin that these pollutants cause reduced lung function in children. This evidence is consistent with data from elsewhere in North America and Europe.

Available data show that the health impact of exposure to ***radionuclides*** from man-made sources appears to be small compared to the effects of normal background radiation.

Health effects of ***microbial contaminants*** have not been adequately studied, but there are indications of increased incidences of short-term infections in users of recreational waters and in consumers of treated drinking water.

7) Based on our knowledge thus far, it would appear that ***some subpopulations in the Great Lakes Basin may have greater sensitivity*** to low levels of environmental contaminants, and could be at higher risk than is the general population. These would include the fetus and newborn infant, children, the elderly, and those in ill health. Sportsmen and Native people who consume large amounts of contaminated fish and wildlife may also be at higher risk because of their increased exposure to persistent toxic chemicals.

8) Finally, identifying ***research data gaps*** (as outlined in the preceding section) and exploring directions for future essential research -- ranging from integrated exposure assessments, to body burden estimates, to a broader spectrum of health effect endpoints -- should be a priority to help reduce the uncertainties in our knowledge of the potential short- and long-term adverse human health effects of exposure to environmental contaminants in the Great Lakes Basin.

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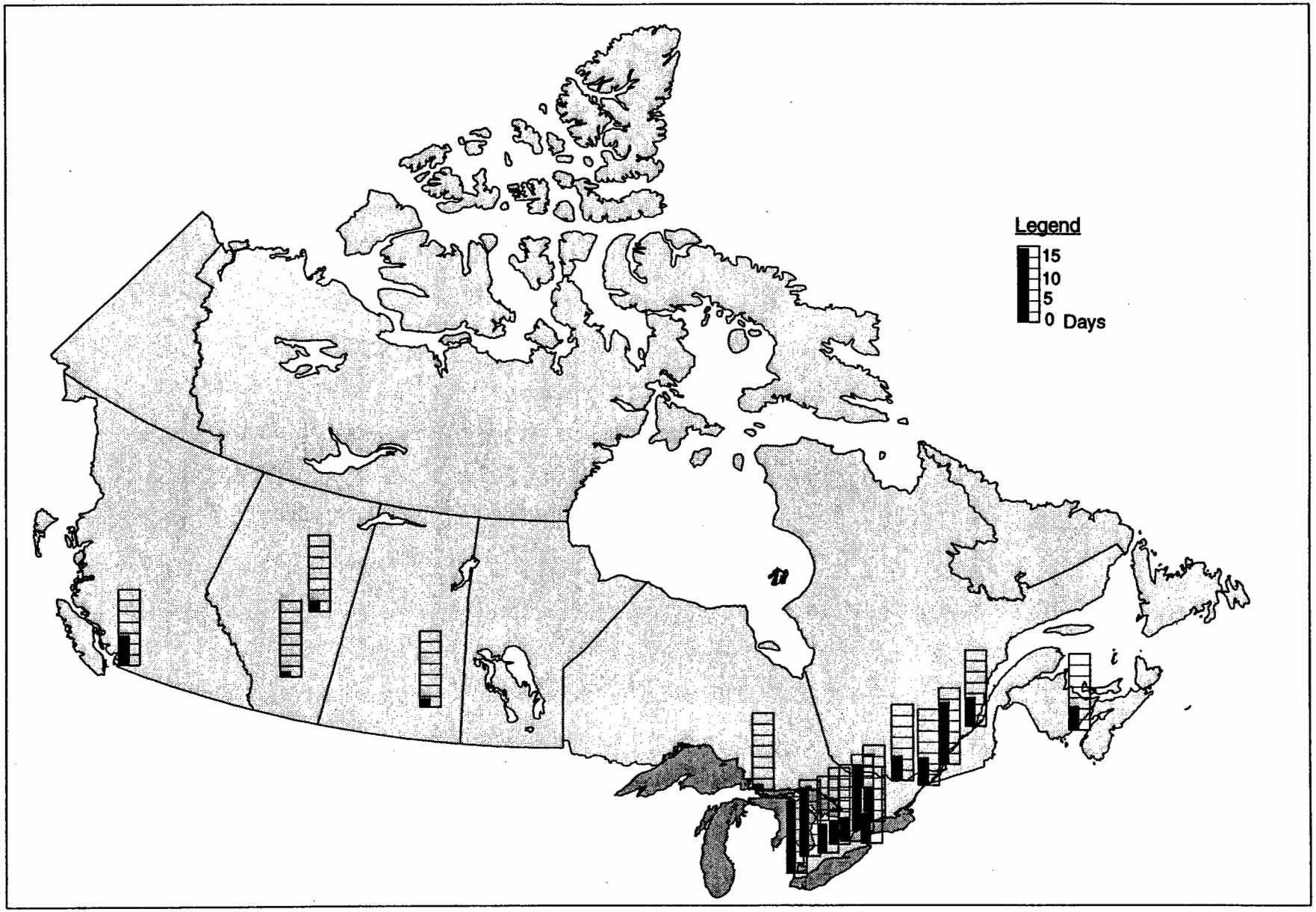

Figure 1. Number of days per year with ozone levels in excess of the one-hour air quality objective of 82 ppb.

Data Source: Hilborn, J. and Still, M., 1990. *A State of the Environment Report: Canadian Perspectives on Air Pollution.* Ministry of the Environment

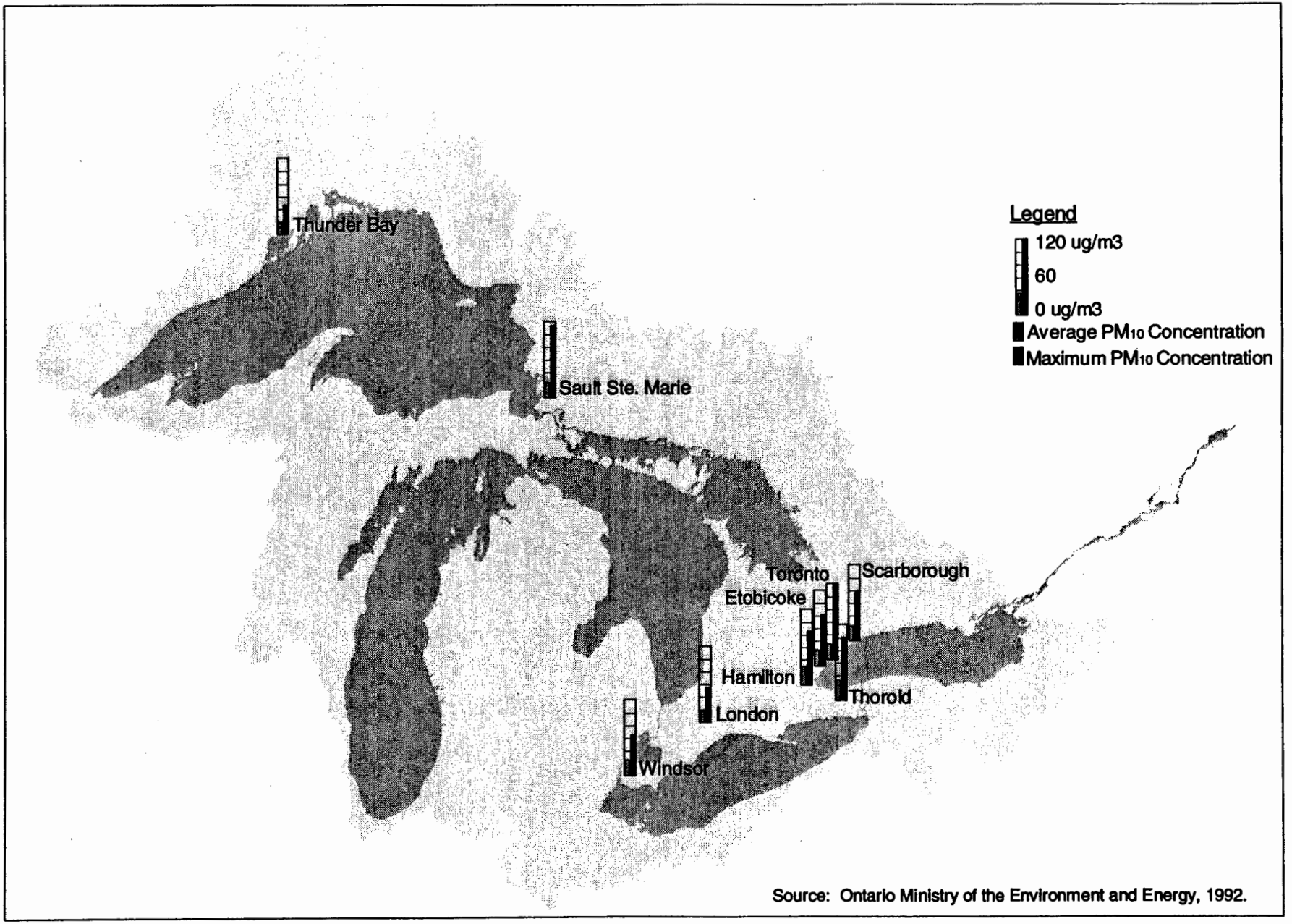

Figure 2. PM_{10} Concentrations at 9 Urban Sites in Ontario, 1991.

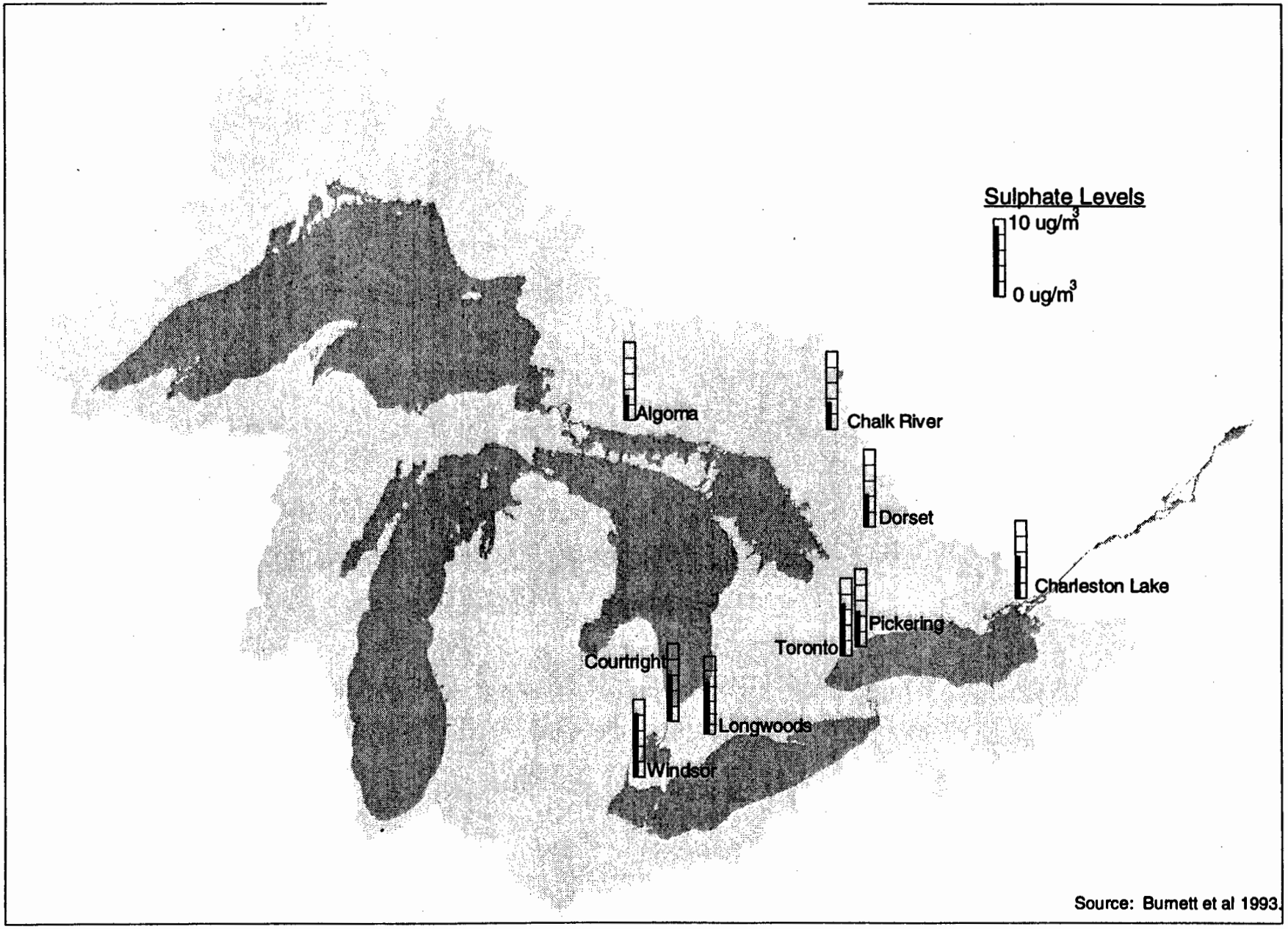

Figure 3. Sulphate Concentrations at Selected Sites in Ontario, 1983 - 1988.

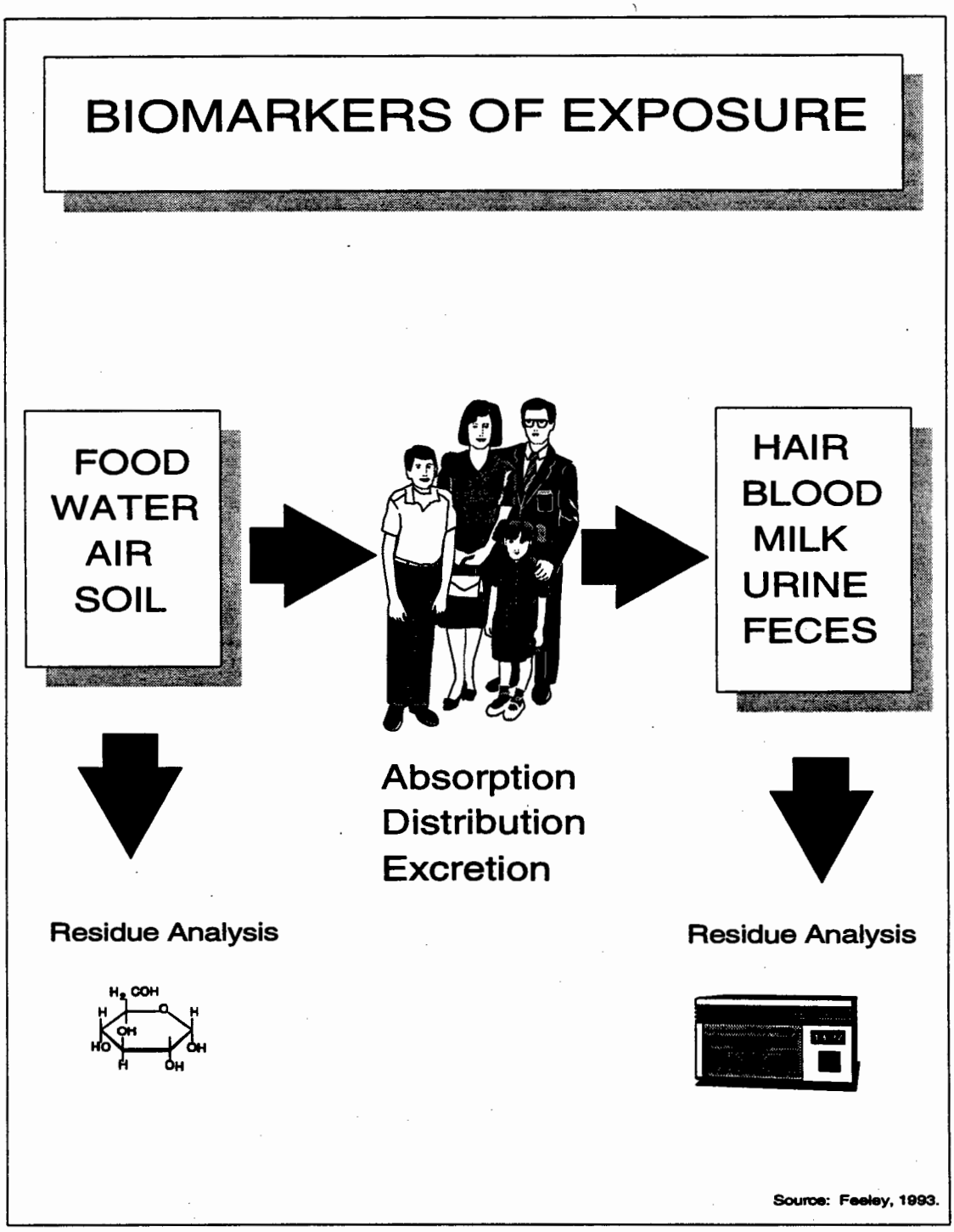
BIOMARKERS OF EXPOSURE
FOOD
WATER
AIR
SOIL
HAIR
BLOOD
MILK
URINE
FECES
Absorption
Distribution
Excretion
Residue Analysis
Residue Analysis
Source: Feeley, 1993.

Figure 4.

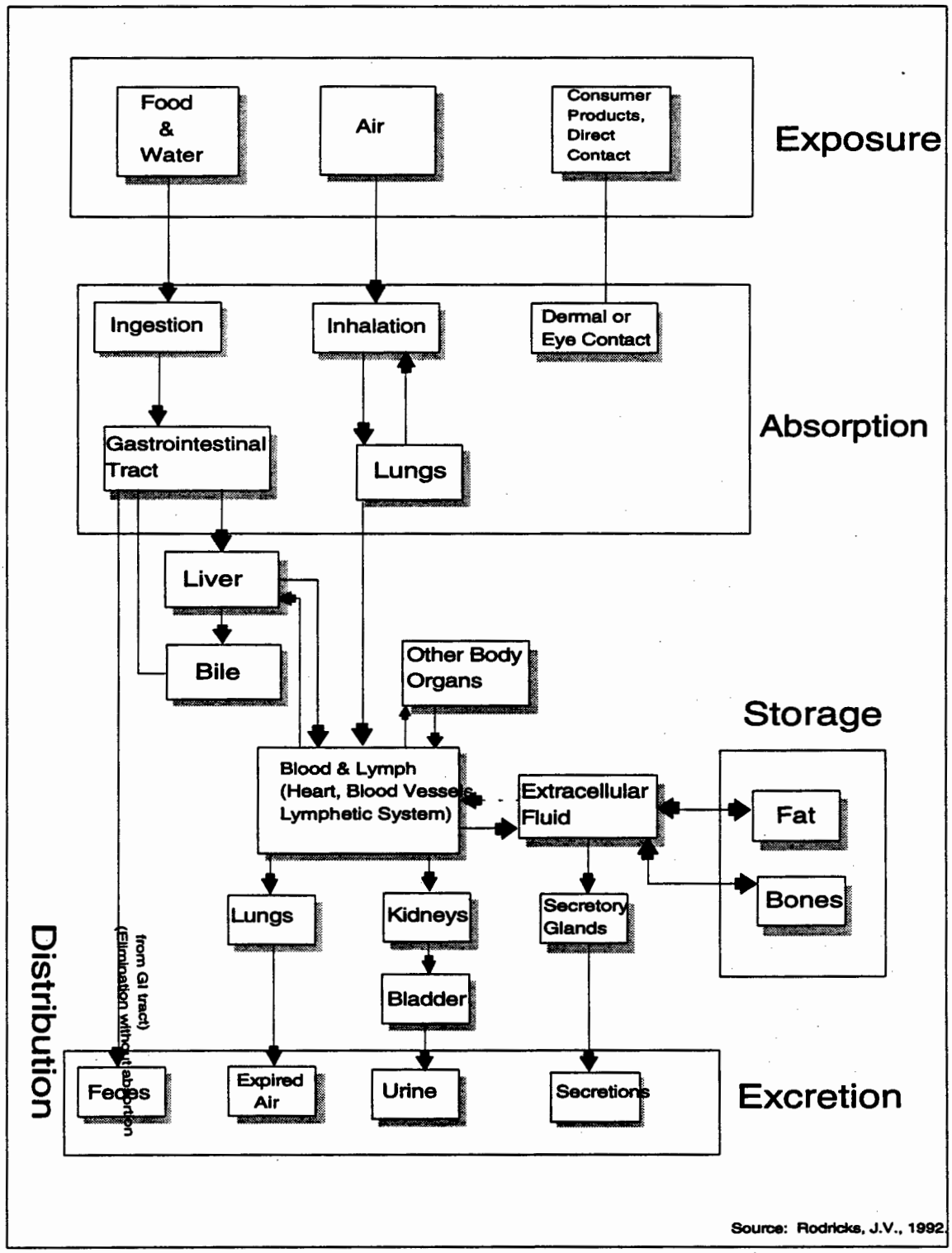
Food & Water
Air
Consumer Products, Direct Contact
Exposure
Ingestion
Inhalation
Dermal or Eye Contact
Gastrointestinal Tract
Lungs
Absorption
Liver
Bile
Other Body Organs
Storage
Blood & Lymph (Heart, Blood Vessels, Lymphetic System)
Extracellular Fluid
Fat
Bones
Lungs
Kidneys
Secretory Glands
Bladder
Distribution
from GI tract
(Elimination without absorption)
Feces
Expired Air
Urine
Secretions
Excretion
Source: Rodricks, J.V., 1992.

Figure 5.

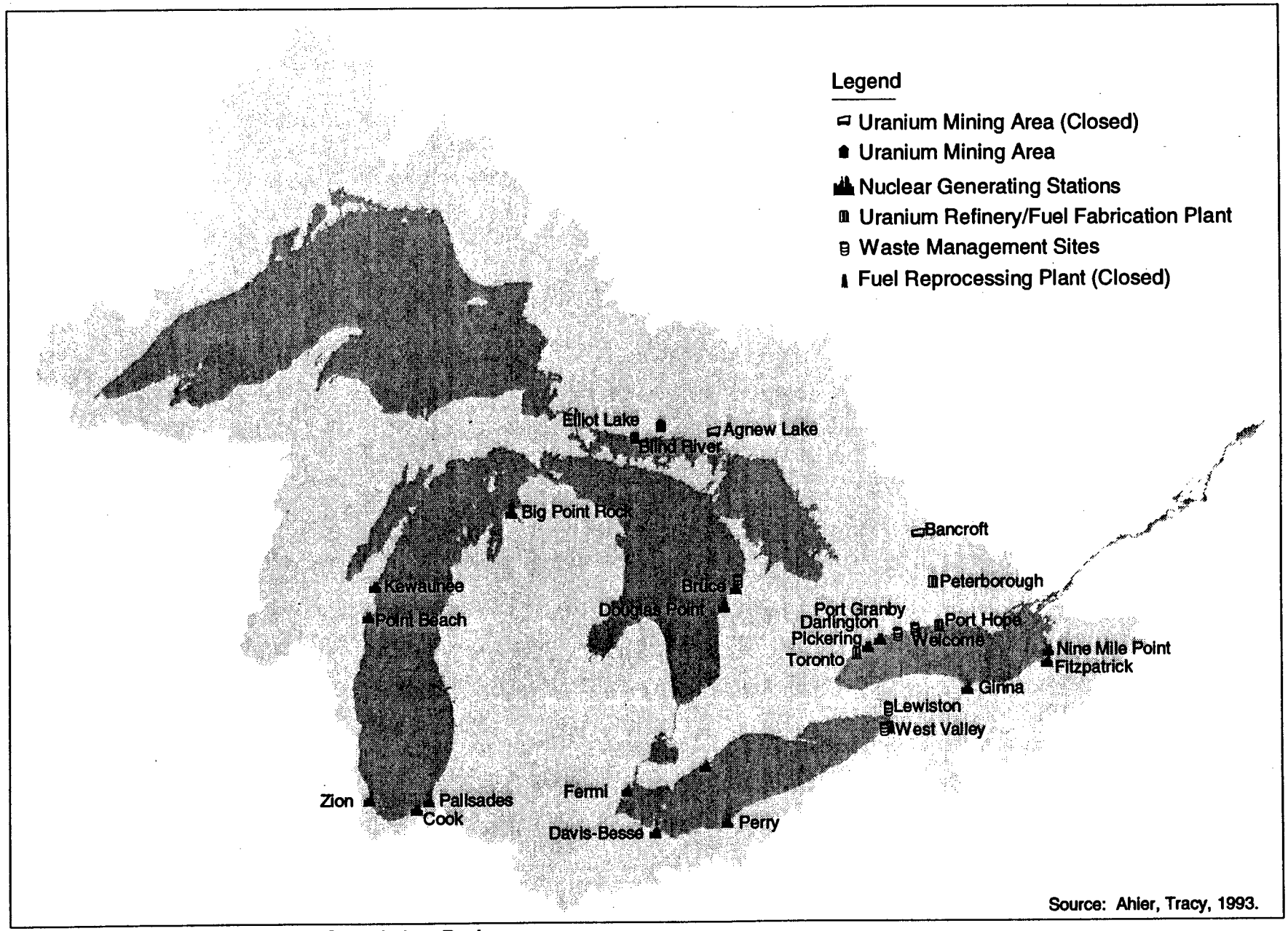

Figure 6. Nuclear facilities in the Great Lakes Basin.