Chapter Five

HUMAN HEALTH

THE COMMISSION'S PRIORITY

New risk factors to human health from waterborne pathogens, such as newly identified sensitive populations, global transportation, antibiotic resistance, and wastewater treatment efficiency, have created a heightened awareness of the importance of new scientific knowledge in managing these risks. In addition, several new or relatively unknown classes of chemicals are emerging as potential water pollutants in the Great Lakes basin. These include polybrominated diphenyl ethers (such as fire retardants), various pharmaceuticals and personal care products, and approximately 20 currently used pesticides that are a potential concern for human and ecosystem health.

The Commission's scientific assessment identifies priorities for future research and data needs. It also considers the policy implications of establishing action levels to protect human health based on multi-media exposure and the interactive effects of toxic substances including PCBs, mercury, and the substances noted above. Where information is unknown or incomplete, the relevance of the precautionary principle must be considered.

Chapter Five presents advice and insight from the Great Lakes Science Advisory Board to the Commission regarding human health.

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HUMAN HEALTH

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Waterborne Microbial Pathogens in the Great Lakes

5.1 Summary

Waterborne diseases still pose a threat to human health in the Great Lakes basin. Infection outbreaks and deaths in Milwaukee, Wisconsin in 1993 and Walkerton, Ontario in 2000 illustrate the threat from contaminated drinking water. Microbial pathogens can adversely impact contact recreation, such as swimming, and represent a continuing human health and economic threat. Untreated or partially treated sewage discharged to waterways is the most obvious route of potential exposure, but nonpoint source pollution is also a vehicle for microbial contamination. Pathogens from livestock, wildlife, and humans can be carried by agricultural and urban runoff. A comprehensive management approach is needed to address and minimize the risks from waterborne pathogens. The Hazard Analysis and Critical Control Point (HACCP) system is widely used as a food and water safety management tool. An Environmental Pathogens Strategy modeled on the Binational Toxics Strategy is proposed for adoption in the Great Lakes basin.

5.2 Introduction

The Work Group on Ecosystem Health reviewed scientific knowledge on waterborne microbial pathogens in the Great Lakes region. The Work Group prepared background reports and invited expert papers that discussed societal influences on microbial pathogens, monitoring of pathogens, and management tools.

Diseases such as typhoid and cholera are no longer major problems in the Great Lakes basin. However, outbreaks and deaths in Milwaukee, Wisconsin in 1993 and Walkerton, Ontario in 2000 illustrate that waterborne microbial pathogens still pose a threat to human health. These pathogens are generally transmitted by the fecal-to-oral route in which people are exposed when they ingest or come into contact with water contaminated with human or animal feces. Although attention and management efforts have focused on treating water and wastewater to prevent microbial contamination, human activities continue to contribute directly and indirectly to contamination of surface and groundwater. For example, contaminated water used for irrigating crops can contribute to human illness following ingestion of raw unwashed foodstuffs such as lettuce and other vegetables. Irrigation increases agricultural production, but the water returned to aquatic systems is often contaminated with nutrients and pathogens.

To manage microbial contamination, pathogens must be monitored in the environment and their transport and fate understood. In the early 1900s, the Commission undertook a bacteriological monitoring study that examined cross-boundary pollution. That study was revolutionary in its day, and remains relevant to current monitoring programs. New technologies and approaches can determine the presence of pathogens and provide information on their fate in the environment. The Global Ocean Observation System (GOOS), which tracks harmful algal blooms, can be used as a model for tracking waterborne pathogens in the Great Lakes. It could provide managers with accurate, real-time information on microbial contamination and help to determine if beach advisories should be issued. HACCP planning could provide a framework for a comprehensive plan to manage microbial contamination in the Great Lakes basin.

Despite the increase in the number of disease outbreaks due to waterborne pathogens since the late 1990s, many people drink and recreate in Great Lakes basin water without any thought of microbial pathogens. In the U.S., the Centers for Disease Control and Prevention (CDC) estimates that waterborne pathogens cause 300,000 infections per year. The largest event in U.S. history occurred in Milwaukee, Wisconsin in 1993, when 400,000 people became ill and 100 died due to *Cryptosporidium* contamination of the drinking water supply. Outbreaks have also occurred in Canada, most notably in Walkerton, Ontario in 2000 when seven people died as a result of drinking water supply contamination.

Microbial pathogens also pose a risk for contact recreation. In 1996, beaches in Great Lakes states were closed 3,700 times. Globally, the cost of human disease caused by sewage pollution of coastal waters is estimated at four million lost "man-years" annually, which is roughly equivalent to an annual economic loss of approximately $16 billion U.S. For one Lake Michigan

beach, net economic losses due to beach closures were estimated to range from about $1,200 to $37,000 per day, depending on value assumptions (Rabinovici *et al.* 2004).

Greater awareness of microbial pathogen issues is occurring because of the increase in size of sensitive populations, the existence of global transportation networks that spread pathogens worldwide, antibiotic resistance, and zoonotic transmission. New findings suggest that pathogens may be linked to diseases such as hardening of the arteries (Ismail *et al.* 1999). Chemical and microbial contamination may interact to exacerbate effects. Improved estimates of land-based inputs and models of water-circulation patterns and water quality are needed to reduce risks of human exposure, provide data and information for more effective control of anthropogenic inputs, and maximize recreational income (Cheves 2003).

5.3 Microbial Pathogens

Human activities have introduced many microbial pathogens that are not native to water bodies (National Research Council 2004). Few studies exist on the ecology and evolution of microbial pathogens in comparison to research investigating pathogenicity. In order to gain a real understanding of the pathogens' abundance, distribution, and fate in the environment, it is vital to understand their autecology and indicators.

The National Research Council (2004) identified five critical questions for studying pathogens:

1. What is the distribution and abundance of pathogens? Are the reservoirs for the pathogen biotic or abiotic?
2. What are the fates of freshwater pathogens in coastal or marine waters?
3. Is the residence time of a pathogen sufficient to allow genetic exchange or change to occur?
4. What biotic and abiotic factors influence the viability and survivability of waterborne pathogens? Are there environmental conditions that promote genetic exchange or the acquisition of genetic elements that confer selective advantage under clinical conditions?
5. What effect do sampling and environmental variations have on the efficacy of indicators?

Pathogens of concern include bacteria, toxic algae, protozoa, and viruses, which are briefly described below.

5.3.1 Waterborne Microbial Pathogens

Bacterial pathogens such as *Escherichia coli* (*E. coli*), *Campylobacter*, *Salmonella sp*., and *Shigella sp*. can be divided into two groups: native and introduced (National Research Council 2004). In aquatic systems, pathogenic bacteria are a small component of a diverse microbial community. Some can form endospores, specialized cells with no metabolic activity that can survive extended periods of time in harsh conditions. Other bacteria are found exclusively in humans, such as *Shigella*, whereas still others have multiple animal hosts. Bacteria with multiple hosts can transmit from one host to another. For example, *Campylobacter* is found in a wide range of mammalian and avian hosts and is a major cause of bacterial diarrheal illness in developing countries. It was also present in the drinking water during the Walkerton outbreak.

Campylobacter caused 16 cases of illness on South Bass Island, Ohio where from July 23 to September 12, 2004 a total of 1,450 cases of gastrointestinal illness were reported (Ohio Department of Health 2005). During the outbreak, nine cases of illness due to norovirus, three due to *Giardia* species, and one due to *Salmonella typhimurium* were also reported. The main source of pathogens was widespread contamination of groundwater, and several water supplies remain closed.

Campylobacter cells have a variety of hosts and are viable for months. Outbreaks have been associated with treated and untreated water sources. Other bacteria that have large environmental reservoirs include *Aeromonas*, *Salmonella*, and *E. coli*. Bacterial pathogens that are also widespread in aquatic systems are *Pseudomonas*, *Enterobacter*, *Acinetobacter*, *Klebsiella*, and *Stenotrophomonas*. These pathogens commonly cause outbreaks in hospitals and recreational settings, and are of particular concern because many are now resistant to antibiotics. Bacteria can share genetic information in several ways, which allows them to rapidly respond to environmental change.

Toxic algae, commonly cyanobacteria or blue-green algae, produce several toxins harmful to humans and wildlife. The most well-known is Microcystis. Concerns about harmful algal blooms (HABs) have increased over the last decade largely because of the perceived increase in the number and duration of events (Malone and Rockwell 2005). The toxins produced by these species cause finfish and shellfish poisoning, a variety of human pathologies that can lead to death, and mass mortalities of marine organisms including fish, mammals, and birds. A

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HAB outbreak in 1987-88 closed shellfishing on more than 400 kilometers of North Carolina coastline during the peak harvesting season with economic losses estimated at $25 million (Malone and Rockwell 2005).

Protozoans are single-celled eukaryotes, some of which are obligate parasites that cause disease in humans. These pathogenic protozoans are often transmitted via the fecal-to-oral route (National Research Council 2004). The enteric protozoans of concern are *Giardia lamblia*, *Cryptosporidium parvum*, *Toxoplasma*, and *Microsporidia*. Because animals and humans are hosts to these enteric protozoans, they may be transmitted between humans and other animals (zoonotic transmission). Populations of protozoans are influenced by both density-dependent and density-independent factors (National Research Council 2004). Density-dependent factors include the population dynamics of the host, and survival and reproductive success of the parasite. Density-independent factors include abiotic ones such as temperature and climate. Parasitic protozoans form cysts or oocytes that for enteric protozoa are the only form of the parasite that can survive outside its host. *Giardia*, one of the more common enteric protozoans, is an obligate parasite that causes diarrhea and abdominal pain in infected humans. Approximately 2.8 million people are infected with *Giardia* each year worldwide in developed and developing countries (Ali and Hill 2003).

Microsporidia, which form spores rather than cysts, infect all animals and therefore have a large biotic reservoir. Thirteen species of Microsporidia are known to infect humans and two are associated with gastrointestinal disease (National Research Council 2004). Very little is known about their sources and there are minimal data on occurrence in surface waters (National Research Council 2004).

Cryptosporidium and *Toxoplasma* are obligate parasites that require a host to reproduce. *Cryptosporidium* is an intestinal parasite and *Toxoplasma* is a tissue parasite. Cryptosporidium infections are ubiquitous and up to 30 to 50 percent of the U.S. population has antibodies to *C. parvum* (Frost *et al.* 2002; Isaac-Renton *et al.* 1999). The primary host for *Toxoplasma gondii* is the domestic cat. However, oocytes have been found in fresh waters and coastal waters. Aside from humans, sea otters and marine mammals reportedly have become infected.

In addition to these protozoan obligate parasites, two free-living protozoans common in aquatic ecosystems can also cause illness: *Naegleria* is found in stagnant bodies of fresh water while *Acanthamoeba* is found in more types of aquatic environments, including ocean sediments. The mode of infection for both is introduction to the nasal passages via swimming rather than the anal-to-oral route. *Naegleria* infections can be serious and involve the central nervous system rather than the gastrointestinal system.

Viruses are obligate intracellular parasites and several are among the emerging microbial pathogens receiving increased attention. The viruses of concern as waterborne pathogens include enteroviruses, norovirus, hepatitis A and E, parvovirus, and adenoviruses. Many human viruses infect the gastrointestinal or respiratory systems. Viruses persist in the environment, are readily transmitted by water, and can persist ten years or more in groundwater. The most common indicators for microbial pathogens, fecal coliform bacteria, are generally not a good measure of risk from viral pathogens (Payment and Rose 2005).

5.3.2 Sources

Pathogens are introduced to water systems from a variety of sources, although most are related to discharge of human or animal waste into surface or groundwater. The most obvious route is the direct discharge of untreated sewage into waterways. This may result from combined sewer overflows, sanitary sewer overflows, or failing septic systems. Nonpoint sources also contribute to contamination, carrying pathogens from wildlife, livestock, or humans to water bodies via agricultural or urban runoff. Domestic cattle and sewage discharges are the primary sources of *Cryptosporidium* and *Giardia* (National Research Council 2004). Birds and their droppings and wildlife also contribute to the contamination of aquatic environments. Tile drainage and irrigation systems can have major impacts on receiving water quality. Pharmaceuticals are a growing concern in institutional septic systems, and raw septage (hauled sewage) is commonly spread on farmland that may be tile drained. Ballast water and holding tank releases are also a source of pathogens.

5.3.3 Methods of Detection and Monitoring

Indicators, rather than the pathogens themselves, are commonly used to monitor for microbial pathogens because they are easier and less costly to sample and, in many cases, standard methods have been developed for their measurement. Important biological characteristics of indicator organisms have been identified (National Research Council 2004):

- Correlated to health risk
- Similar (or greater) survival to pathogens
- Similar (or greater) transport to pathogens
- Present in greater numbers than pathogens
- Specific to a fecal source or identifiable as to source of origin.

Coliforms are the most common type of indicator. Many communities use fecal coliforms, or *E. coli,* as an indicator of human fecal contamination. *Enterococci* are also used because they are of fecal origin and have been strongly correlated with gastrointestinal illness from contact recreation (National Research Council 2004). *Clostridium*, a spore-forming bacterium, is a potential indicator for protozoan parasites such as *Giardia* and *Cryptosporidium* because the spores of *Clostridium* may behave similar to oocytes or cysts of the protozoans

(National Research Council 2004). Bacteriophages—viruses that infect bacteria—are used as indicators of viral pathogens.

The use of indicators is complex. The relationship between the indicator organisms used and health risks is poorly developed. The indicator's use assumes that these occur at a constant ratio with the pathogens, but this is not always valid (National Research Council 2004). Indicators and pathogens also vary in space and time, complicating sampling and detection of the organisms. Payment and Rose (2005) illustrate the difficulties with indicators with the example of *Helicobacter pylori*. Studies in Pennsylvania have shown that *H. pylori* were found in wells that were free of the indicator, coliform bacteria. Therefore, fecal coliforms are a questionable indicator for *H. pylori*. More research on pathogens and indicator organisms is required to improve detection of pathogens and understand their ecology.

Several emerging techniques and approaches are improving the ability to detect and track pathogens. Polymerase chain reaction (PCR) techniques enable researchers to identify the actual pathogens. PCR techniques can be time consuming and expensive, although new techniques such as real-time PCR have reduced the time necessary to process samples. Also, micro-arrays have been developed using genomics technology. The micro-arrays, or biochips, can immobilize up to thousands of DNA probes for waterborne pathogens. Thus there is potential to identify a variety of microbes in a water sample. However, these tools are still being developed and need to be evaluated.

5.4 Social Factors Affecting Pathogens

Sattar and Tetro (2005) discuss how social factors, such as advancements in technology, have consequences on water quality. For example, drinking-water treatment and disinfection practices drastically reduce the number of illnesses of common waterborne infections (Sargeant 2005). Other advancements discussed by Sattar and Tetro (2005) include the development of antibiotics, agricultural uses, and municipal uses.

5.4.1 Pharmaceuticals and Antibiotic Resistance

Increasingly, antibiotics are found in freshwater systems (Halling-Sorensen 1998). Until recently, nearly one in three Americans was prescribed antibiotics even though there was no valid medical reason to do so (Nyquist *et al.* 1998). Antibiotics pass through wastewater treatment facilities and are discharged to receiving waters. The presence of pharmaceuticals in these waters further promotes antibiotic resistance. Hagedorn *et al.* (1999) found bacteria resistant to antibiotics in waters that received feces from nonpoint sources. In addition, the widespread use of antimicrobial disinfectants may contribute to the problem. For example, laboratory studies with triclosan (a common active ingredient in antibiotic and antimicrobial soaps) show that bacteria that become resistant to triclosan also show resistance to antibiotics that rely on the same site of action to kill pathogens (Levy *et al.* 1999).

5.4.2 Agriculture

Agricultural runoff is a long-recognized source of pollutants to waterways; however, much attention has focused on nutrient loads into aquatic systems. Agricultural runoff also has a high microbial load, including bacteria and parasites. Sheep and cattle harbor *Campylobacter,* and the application of manure is a known source of environmental contamination (Stanley and Jones 2003). Sischo *et al.* (2000) demonstrated that water contamination with *Cryptosporidium* was positively correlated with spreading manure. A public inquiry in Canada suggested that runoff contaminated by manure may have been the cause of the North Battleford outbreak, which infected up to 7,000 people (Saskatchewan Justice 2002). Contaminated runoff was also the likely cause of the Milwaukee incident.

The concentration of animals into a small area can also adversely impact water quality (Kirkhorn 2002). A concentrated animal feeding operation (CAFO) maintains a specified number of animals within a confined area. More than 238,000 CAFOs existed in the United States in 2002, which produced 500 million tons (454 million tonnes) of manure annually. This is approximately three times greater than the waste generated by the entire U.S. population (U.S. EPA 2003). Several pathogens have been identified from the manure of CAFO animals (Guan and Holley 2003) including *Helicobacter pylori*, *Streptococcus suis*, *Brucella suis*, *Campylobacter* sp., *Yersinia enterocolitica*, *Salmonella* sp., *Listeria monocytogenes*, *Cryptosporidium parvum*, and *E. coli.*

Another pathogen that has increased in prevalence in the developed world and is linked to swine farming is the hepatitis E virus (HEV) (Clemente-Casares *et al.* 2003). HEV causes acute, self-limited, icteric hepatitis in humans and is classified as a zoonotic infection (Smith 2001) with swine acting as the main animal reservoir. HEV was once endemic only in developing countries, but it has now been identified in the sewage of many industrialized countries including Spain, France, and the United States (Kasorndorkbua *et al.* 2004).

5.4.3 Municipalities

Municipal and other human activities account for less than 15 percent of all freshwater withdrawals in the U.S. and Canada (Sattar and Tetro 2005). Through technological advancements over the last century, local governments now provide water and wastewater treatment for communities that put clean water into nearly all homes and had built a sense of confidence in the water's safety (Hrudey and Hrudey 2004). The public perception of safe water may be declining, as reflected in the increasing sales of point-of-use devices and bottled water.

As water flows from a drinking water treatment plant to the tap, the residual disinfectant levels are depleted. Biofilms, which grow within the distribution system, incorporate various opportunistic bacteria that may cause disease in susceptible individuals. *Mycobacterium avium* represents a major threat to immuno-compromised individuals (Aronson *et al.* 1999). Other potential biofilm-based bacteria include *Pseudomonas* (associated with hospital-acquired infections), *Moraxella* (ocular and respiratory infections), *Aeromonas* (urinary tract disorders), and *Legionella* (pneumonia) (Rusin *et al.* 1997; Pryor *et al.* 2004).

Three areas of waste disposal are relevant for management of pathogens: wastewater, sludge, and solid waste. Most large cities now have some form of wastewater treatment to reduce the discharge of microbial or chemical contaminants into receiving waters. For those facilities that do not use tertiary treatment, chemical pollutants that are not removed as solids are released into the environment, albeit at lower concentrations. Among the chemicals that escape treatment systems are pharmaceuticals and microbiocides.

The second waste category is sludge produced at municipal wastewater treatment plants. The use and safety of sludge is controversial because about 150 enteric pathogens may exist and thrive in sludge (Gerba and Smith 2005). Various chemical pollutants such as antimicrobials, disinfectants, and heavy metals are also present and may pose an environmental risk. Depending on the process by which sludge is converted into biosolids, microbial and organic chemical loads may decline. However, there is always a risk for heavy metal and residual contamination through either leaching or runoff. Furthermore, this risk may be heightened due to potential interactions of pathogens and irritant chemicals (Lewis *et al.* 2002). Many communities now have pretreatment programs to prevent potentially harmful chemicals from entering the municipal waste stream, thus reducing contaminant loadings to soils and receiving waters.

The third waste category is solid waste and the threat to water quality from landfills. In terms of microbial hazards from landfills, enteric viruses are unlikely to withstand the environmental conditions of a landfill (Sobsey 1978).

5.5 Monitoring Microbial Pathogens in the Great Lakes

Given their threat to aquatic ecosystems and human health, information on the presence, distribution, fate, and transport of pathogens is critical. Monitoring is essential to gain this information. The International Joint Commission (IJC) conducted a comprehensive bacteriological study in 1913-1914. That effort, although overlooked for some time, is still relevant today. By combining lessons learned from the past with current monitoring programs, traditional and new approaches can be used to increase the knowledge base required to manage microbial pathogens in the Great Lakes. The Agreement contains scarce mention of microbial pathogens.

5.5.1 Historical Monitoring: A Lesson from the Past

In the early 1900s, the IJC commissioned a landmark study to examine the extent of cross-boundary pollution in the Great Lakes. The study was limited to those areas where pollution on one side of the U.S.-Canadian border was thought to affect waters on the other (IJC 1914). Assistance was given by the U.S. Public Health Service, the Ontario and Quebec boards of health, the Michigan State Board of Health, and the New York State Department of Health. Also, many municipalities cooperated by providing information about their water and wastewater treatment practices. The study cost about $42,000, which was divided equally between the U.S. and Canada.

The study examined more than 2,000 miles of sampling transects and collected over 19,000 water samples. The study involved 17 laboratories, each of which was installed, equipped, and staffed by the IJC. A total of 1,447 locations were sampled across the Great Lakes during the summer of 1913. Investigators used methods for detecting and culturing bacteria that correspond to current techniques to determine total coliform bacteria. In addition to the bacteriological analyses, meteorological data were recorded at the sampling sites. For all the municipalities, the area, population, source of water supply, amount of water pumped, and an estimate of sewage discharge were recorded. Each municipality also reported the number of deaths due to typhoid per 100,000 people. For some cities, bacteriological analyses of domestic tap water were also conducted.

The results of the study showed extensive cross-boundary pollution in the Detroit River, Niagara River, Rainy River, St. Clair River, St. John River, lower Lake Erie, and lower Lake Ontario (IJC 1914). The major cause of this pollution was the discharge of untreated human sewage by municipalities and vessels into Great Lakes waters. The IJC recommended that "all sewage should, before being discharged into boundary waters, receive some purification treatment, and the degree of such treatment is to be determined in a large measure by the limits of safe loading of a water-purification plant." The IJC

also recommended that the requirement for treatment balance concerns of public health and economics. Current treatment mirrors the approach outlined by the IJC in 1918, namely primary (mechanical) and secondary (biological) treatment of sewage (IJC 1918). The recommendations were not immediately adopted, and the scientific value of the study was limited because it was not published in the scientific literature.

Several lessons can be learned from this IJC study. One reason the study was so advanced is that it involved scientists, engineers, and public health officials across the basin. An expert panel gave serious review of the study methods and the adequacy of the research questions posed to the IJC by Canada and the U.S. The advisors promoted the use of the most technologically advanced methods. For example, bacteria samples were often grown in gel rather than agar (Durfee and Bagley 1997). Also, interested parties were given a chance to comment on the study at public hearings. The study's design and successful completion shows how input from experts and stakeholders can help to produce high-quality research. The study also shows the need to communicate findings and continue engagement with the governments to support implementation efforts.

5.5.2 Current Monitoring Efforts

The Great Lakes region has not completed another study as comprehensive as the 1913-1914 IJC assessment (Durfee and Bagley 1997). Various government agencies at all levels monitor bacteria in the basin. However, a recent complete investigation into the extent of bacterial contamination has not been conducted. Current monitoring includes drinking water and wastewater treatment facilities, and recreational beaches.

The U.S. Environmental Protection Agency (EPA) has set health goals and legal limits for total coliform levels in drinking water (EPA 2001). The total coliform rule also details the required monitoring protocol for water treatment plants, including the frequency and number of samples to collect. Wastewater treatment plants (WWTPs) or publicly owned treatment works also monitor fecal coliform. Beach monitoring programs are commonly conducted by local government health departments. These monitoring programs have the potential to provide important information regarding trends in nearshore bacterial contamination.

Bacterial contamination of public Great Lakes beaches in Canada is regularly assessed during the swimming season by public-health authorities. The authorities determine the numbers of *E. coli* or similar (fecal coliform) bacterial indicators in the waters, but their sampling and testing procedures have not been standardized (Edsall and Charlton 1997). Thus, long-term trends in bacterial indicators are difficult to identify because of inconsistencies in monitoring methods and incomplete reporting over time.

Many water quality monitoring programs in the Great Lakes basin do not include bacterial analyses. The U.S. Geological Survey's National Water Quality Assessment Program recently conducted a comprehensive study of water quality in Lake Erie and the St. Clair River (Myers *et al.* 2000), but fecal coliform bacteria were not monitored. University research programs, such as the University of Wisconsin-Milwaukee WATERbase program (UWM 2003), monitor bacterial levels, but focus on free-living bacteria and bacterial production, not pathogens. As human illness in the Great Lakes region due to waterborne contaminants became rare in the 20th century (Health Canada 1995a, 1995b, 1995c; Health and Welfare Canada 1980), management and monitoring efforts shifted to other environmental problems such as invasive species, eutrophication, and toxic sediments. Use of ecosystem-level indicators has become more popular in the Great Lakes following the start of the State of the Lakes Ecosystem Conference (SOLEC) program in 1994. In 2004 the IJC recommended that new methods to detect the actual pathogens be used rather than rely on indicators such as total coliform or *E. coli* (IJC 2004).

Water quality data are currently gathered at county and state levels, but a consistent methodology or comprehensive database does not exist, and the data are fragmented in time and space. Thus, knowledge of the extent of bacterial contamination in the Great Lakes largely is limited by a lack of consistency in monitoring, assessment, and basin-scale planning. Future efforts can learn from past and present successes and failures that show the importance of stakeholder engagement, long-term commitment, and communication in developing a successful strategy for managing bacterial pollution in the Great Lakes.

5.5.3 The Global Ocean Observation System (GOOS): A Model Monitoring Program

GOOS is a global network that collects and disseminates data and information on marine and ocean variables (Malone and Rockwell 2005). At the United Nations Conference on Environment and Development member nations ratified the Framework Convention on Climate Change and the Program of Action for Sustainable Development, which called for the creation of GOOS to enable effective management of marine systems. GOOS is based on the data and information requirements of groups that depend on oceans, thus it is a multi-user (*e.g.,* scientists, managers) and multidisciplinary (*e.g.,* chemistry, biology, oceanography) approach.

GOOS is designed to deliver relevant information to users quickly to achieve management goals and make informed decisions. GOOS is composed of:

- A monitoring network of *in situ* and remote sensing measurements;
- A data assimilation and analysis component that includes conceptual, statistical, and numerical models as well as geographic information systems (GIS); and

- A data communications component to provide rapid access to gathered information.

The Gulf of Mexico Harmful Algal Blooms Observing System (HABSOS) illustrates how such a system works (Malone and Rockwell 2005). The ultimate goal of HABSOS is to predict the probability of when and where harmful algal blooms will occur and will impact humans and fisheries. The ability to make this prediction requires, *inter alia*, information on the algal species, factors that influence blooms, and water currents. Based on observations of the forcing functions of blooms (*e.g.,* wind, flow, nutrients) and ecosystem properties, models can be developed to predict blooms based on environmental conditions.

An observing system such as GOOS could be used to monitor pathogens in the Great Lakes and to manage public beaches (Malone and Rockwell 2005). Given the current time lag between collecting a sample and laboratory analysis, a beach may stay open while it is actually unsafe, or closed after the fact. Thus, the ability to monitor and predict exposure to pathogens at beaches could improve management efforts and be more protective of threats to human health.

Such a Great Lakes observing system could use the GOOS/HABSOS model in the following way. First, basic information about the pathogens is needed to characterize their transport and fate in the environment. For example, pathogens introduced via stormwater runoff are concentrated in plumes that can be detected by remote sensing. With the new tracking techniques that are available, the movement of the plume, combined with information on the pathogens, can be used to predict the risk to bathing beaches. A regional system is being developed for southern Lake Michigan beaches (Whitman 2005).

To develop an effective Great Lakes observing system, three capabilities must be developed: more rapid detection of pathogens; timely predictions of where and when public health risks are unacceptable; and timely forecasts of trajectories and contaminated water masses in space and time. To accomplish this, more investment must be made in monitoring (*in situ* and remote sensing) and in research on pathogens. Also, the system must be sustained permanently to provide continuity and to capture the variability that characterizes the aquatic environment and the organisms inhabiting it.

5.6 Management of Microbial Pathogens

5.6.1 Current Programs

U.S. EPA has set the health goal for total coliform in drinking water at zero (EPA 2001). Water systems with coliform in more than five percent of collected samples each month fail to meet the total coliform standard, and water system operators must report the violation to the state. Positive fecal coliform tests may indicate that the system's treatment technologies are not performing properly, and actions may be needed to avoid or eliminate contamination. This may include repairing the disinfection/filtration equipment, flushing or upgrading the distribution system, and/or enacting source-water protection programs (EPA 2001). The only limit on coliform bacteria in ambient water is found in the exception to the *Surface Water Treatment Rule* (EPA 1989) to avoid filtration of surface waters, which states that total coliform bacteria should be less than 100 colony-forming units (CFU)/100 milliliters (ml) or fecal coliform should be less than 20 CFU/100 ml in 90 percent of the samples collected.

In the U.S., fecal coliform is considered a conventional pollutant under the Clean Water Act, so it is controlled through technology standards. Wastewater treatment plants must use the best available technology to minimize fecal coliform in effluent discharged to receiving waters.

Long-term trends in beach closings are difficult to interpret because of inconsistencies in monitoring methods and incomplete reporting over time. Another complicating factor is the use of varying guidelines for what triggers a beach closing. The U.S. Beach Act of 2000 requires states to adopt bacteria limits that are protective of human health as a part of their state water quality standards. U.S. EPA (2004) recently published the final rule for coastal and Great Lakes waters, which sets federal standards for ambient bacteria levels. U.S. EPA recommended a criterion of 126 /100 ml for *E. coli*, but states are allowed to use a more stringent standard. Michigan and Ohio have adopted standards as protective as the U.S. EPA criterion, and the other Great Lake states are in the process of adopting similar standards.

Ontario uses a standard of 100/100 ml whereas the national standard recommended by Environment Canada is 200/100 ml (Edsall and Charlton 1997).

5.6.2 A New Management Tool: The HACCP Approach

The Hazardous Analysis and Critical Control Point (HACCP) system is widely used in the management of food and water quality and safety (Martel *et al.* in preparation). The purpose of creating a HACCP plan is to:

- Document the major sources of risk to the end point of concern;
- Identify and implement the major means of controlling those risks in practice;
- Monitor to provide early warning of the failure of those control processes; and
- Implement corrective actions when control processes fail (Deere and Davidson 2005).

There are six basic steps in developing a HACCP plan (Deere and Davidson 2005):

- All involved in creating the HACCP must commit resources for development. Once committed, the scoping phase can begin.
- The selection of a representative to serve on the HACCP team. This calls for the identification of all users, uses, and requirements.
- Development of a conceptual model of the sources of risks and identification of possible control strategies.
- Completion of a risk assessment, including identifying the risk of water quality that is unacceptable for uses or to users, the causes (events) and hazards (contaminants), and control measures to reduce risk.
- Management planning is undertaken that identifies control loops. The loops identify the controls, monitor their effectiveness, and attempt to correct any failures based on monitoring.
- The final step is validation and verification of the HACCP. Validation determines if the scientific and technological underpinnings of the plan are valid. Verification determines if the plan is being implemented and requirements met.

Once completed and implemented, the HACCP plan provides confidence that the major risks have been identified and that ongoing, operational controls are in place to manage the risks to water quality and give early warning if water quality is likely to become impaired. The plan can be improved over time using adaptive management, as well as through expansion of its scope and the rigor of its implementation.

5.6.3 A Proposed Management Technique: An Environmental Pathogens Strategy

The Binational Toxics Strategy provides an effective mechanism to work toward the goal of virtual elimination of persistent toxic substances to protect and ensure the health and integrity of the Great Lakes basin ecosystem. A similar mechanism could provide an efficient method to address microbial contamination in the Great Lakes basin. Key components of an Environmental Pathogens Strategy include:

- Establishment of a consistent monitoring framework for pathogens across the basin;
- Promotion of the application of new technology and approaches to detect, monitor, and control microbial contamination;
- Increased employment of GIS mapping to strengthen evidence of waterborne infections;
- Investment in the creation of a water quality information database that includes microbial pathogens for the Great Lakes;
- Development and use of novel techniques, including simulation modeling, to better define the risk to human health from waterborne microbial contamination;
- Establishment of a Microbial Water Quality Network to foster collaboration among groups conducting water quality monitoring in the basin; and
- Adoption of a collaborative process by which Environment Canada and U.S. EPA—in consultation with other federal departments and agencies, Great Lakes states, the Province of Ontario, tribes, and First Nations—work in cooperation with their public and private partners to further the goals of the strategy.

5.7 Conclusions and Recommendations

The common themes among the pathogens discussed above identify research and management needs for the Great Lakes basin. Firstly, there is a need to understand the natural history and ecology of pathogens and indicators in order to better detect and manage risks to human health. Secondly, a comprehensive strategy to monitor waterborne microbial pathogens is required. This strategy should use the latest technologies and consistent methods across the basin, be maintained so that long-term data are collected, and be readily accessible. GOOS is a model for how a monitoring program or observation system can serve a variety of users and goals. Lastly, a comprehensive management approach is needed to address the risks from waterborne pathogens. HACCP provides a step-by-step approach to implement a management plan based on risk assessment. The adoption of an Environmental Pathogens Strategy for the Great Lakes basin could provide an effective mechanism to address long-standing microbial contamination issues that currently impact human health.

The Science Advisory Board recommends to the IJC that:

- **The Parties create an Environmental Pathogens Strategy, similar to the Binational Toxics Strategy, to establish an inventory of baseline data for the United States and Canada and to undertake a complete analysis of pollution reduction scenarios for key sources and determine their effectiveness in reducing microbial contamination of the waters of the Great Lakes basin.**
- **The Parties invest substantially in research and pilot studies for the removal of pathogens from wastewater treatment plant effluents, environmentally friendly sludge disposal, and strategically upgraded wastewater treatment infrastructure.**
- **The Parties create a waterborne disease registry for the Great Lakes basin.**

5.8 References

Waterborne Microbial Pathogens in the Great Lakes

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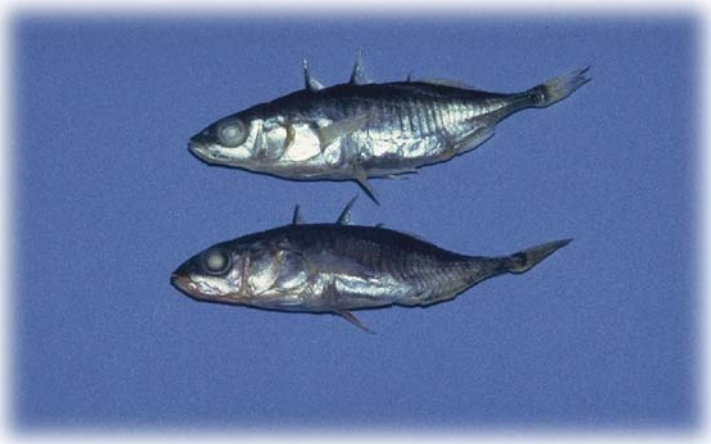
REPORT OF THE GREAT LAKES SCIENCE ADVISORY BOARD

Chemical Exposure and Effects in the Great Lakes Today

5.9 Introduction



As part of the Science Advisory Board's (SAB) activities to maintain current knowledge of health effects in the Great Lakes basin, the Work Group on Ecosystem Health invited a series of expert presentations and consultations during the 2003-2005 biennial cycle. The culmination of these activities was a conference held March 29-31, 2005 in Chicago entitled, Chemical Exposure and Effects in the Great Lakes Today. Twenty-two investigators considered the outcomes of the most current epidemiological and wildlife studies on chemical exposure and effects. A list of conference participants is in Chapter 6.4. The following summarizes the current state of knowledge on these topics.

Table 1. Concentrations of Persistent Toxic Substances in Great Lakes Sport Fish, 1999-2000.

Concentrations are expressed as ng/g (ppb) wet weight. Data supplied by Swackhamer.

LAKE	SPECIES	YEAR	Total PCBs	Total DDTs	Mercury	Dieldrin	Toxaphene	Total Chlordanes
Superior	Lake trout	1999	272	167	123	21	673	62
	Lake trout	2000	784	567	433	31	2493	321
Huron	Lake trout	1999	918	504	144	36	467	120
	Lake trout	2000	779	557	144	32	676	122
	Chinook salmon	2000	719	362	NA	16	395	94
Michigan	Lake trout	1999	1865	883	127	96	813	292
	Lake trout	2000	1614	1056	146	90	1123	303
	Coho salmon	2000	563	257	124	9	192	54
Erie	Walleye	1999	569	95	124	9	31	29
	Walleye	2000	1241	85	114	12	232	27
	Coho salmon	2000	473	52	127	6	107	23
Ontario	Lake trout	1999	1294	594	123	64	169	122
	Lake trout	2000	1174	864	115	45	521	120

Data for lake trout and walleye are means for ten composites, each containing five whole fish. Data for salmon are means for three composites, each containing skin-on fillets from five fish. The Lake Michigan data are the grand means for four sites. NA – not available.

5.10 Exposure

Despite decades of action to reduce toxic chemical discharges and clean up contaminated sediments, recent monitoring confirms that persistent "legacy" chemicals such as polychlorinated biphenyls (PCBs), dioxin, and methylmercury (MeHg) still pose hazards to fish and wildlife and, therefore, people in the Great Lakes region (Table 1). The concentrations of PCBs and total DDT and its metabolites in fish and wildlife tissues showed almost no decline between 1990 and 2000.

Much of the available monitoring data relate to contaminant concentrations in fish tissue. The U.S. Environmental Protection Agency's (EPA) Great Lakes Fish Monitoring Program consists of an open lake trends monitoring component and a game fish fillet component. Ontario's Sport Fish Contaminant Monitoring Program monitors the concentrations of selected contaminants in sport fish and posts regularly updated fish consumption advisories.

U.S. EPA's open lake trends monitoring component monitors contaminants in the open waters of all of the Great Lakes using predatory fish (lake trout in lakes Superior, Michigan, Huron, and Ontario and walleye in Lake Erie). Ten composites of five whole fish within the size range of 600-700 millimetres are analyzed. The PCB concentrations measured in 2000 represent decreases of 53 percent (Erie) to 93 percent (Michigan) from the highest recorded value. While PCBs and DDT declined rapidly in all the lakes immediately following regulatory actions in the early to mid-1970s, the rates of decline slowed for both compounds in lakes Superior, Huron, and Michigan beginning in the mid-1980s. In fact, there has been no statistically significant decrease in either chemical in Lake Superior, or for DDT in lakes Huron or Michigan since the mid-1980s. The current half-life for PCBs in lakes Huron and Michigan is 10-15 years, compared to four to six years in the 1970s.

PCB concentrations in fillets of some large lake trout from Lake Michigan exceed by 40 fold the level (0.05 ppm) which would allow unrestricted consumption. These large lake trout still exceed the 2 ppm tissue criterion for "do not eat" advice for all populations following the Great Lakes Protocol for a Uniform Sport Fish Consumption Advisory. PCB concentrations in popular Lake Michigan sport fish remain at levels that require fish consumption advice ranging from "1 meal per week" to "do not eat" depending on the fish species

and size (Schrank, personal communication). One of the progress goals of U.S. EPA's Great Lakes Strategy 2000 is a "25% decline in PCBs in whole lake trout and walleye samples between 2000-2007." A detailed analysis of the available data suggests that the probability of meeting this goal is negligible and, instead, predicts a decline of seven to nine percent (Stow *et al.* 2004). The rate of decline in lakes Erie and Ontario has not changed with time, and the half-lives of PCBs and DDT are nine to eighteen years (Swackhamer, personal communication).

U.S. EPA's game fish fillet monitoring component of the Great Lakes Fish Monitoring Program monitors potential human exposure to contaminants through consumption of popular sport fish (coho and chinook salmon, and steelhead trout in Lake Erie). Contaminants are measured in three composites, each containing skin-on fillets from five fish. The PCB concentrations in the fillets of all sport fish collected in 1999 and 2000 and all whole lake trout exceed the Great Lakes Water Quality Agreement objective for protection of fish-eating wildlife. Of the 19 fillet composites, PCB concentrations in only one were low enough to allow consumption of one meal per week, while concentrations in 14 composites would restrict consumption to one meal per month. Those in the remaining four would restrict consumption to six meals per year. The concentration of DDT in one lake trout composite exceeded the Agreement objective for protection of fish-eating wildlife. Toxaphene concentrations in eight samples exceed the lowest Ontario advisory action level of 235 ppb.

Although salmonids may be sought by sport fishers, subsistence fishers usually catch yellow perch, walleye, rock bass, white bass, smallmouth bass, and other species that can be harvested with low-tech gear from shore. Contaminant concentrations in these species are monitored by Ontario's Sport Fish Contaminant Monitoring Program, but not by U.S. EPA's game fish fillet monitoring component, and may differ greatly from those in sport-caught fish. According to the *Guide to Eating Ontario Sport Fish* (Ontario MOE 2005), several of these species should not be consumed by women of child-bearing age and children under 15 if caught in Areas of Concern (AOCs) in Lake Ontario. The mean concentration of PCBs in 22 white bass and 50 walleye caught by subsistence fishers in the Fox River were 2,200 and 1,400 ng/g (ppb), respectively (Schantz, presentation). On the basis of the *Guide to Eating Ontario Sport Fish*, white bass from the Fox River should not be eaten, and only six meals of walleye should be eaten per year. This highlights the dilemma of the subsistence fisher.

These findings are of concern given the State of the Lakes Ecosystem Conference's (SOLEC) desired outcome of fishability, which states, "There shall be no restrictions on the human consumption of fish in the waters of the Great Lakes basin ecosystem as a result of anthropogenic inputs of persistent toxic substances."

Available evidence suggests that the concentrations of polybrominated diphenyl ethers (PBDEs) and perfluorooctane sulfonate (PFOS), two emerging contaminants (Table 2), are doubling every three and ten years, respectively. ***If present rates of change continue, total PBDE concentrations could surpass PCB concentrations in lake trout tissues within a decade. Insufficient data are available to establish consumption guidelines for these toxic substances.***

Great Lakes sport and subsistence fishers consume considerably more fish than the general population and therefore have higher body burdens of persistent toxic substances (DeRosa, presentation). In the New York State Anglers cohort (Bloom, presentation) and in groups of fishers who consumed fish from lakes Erie, Huron, and Michigan (Anderson *et al.* 1998), serum polychlorinated dibenzo-para-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), and co-planar PCBs were markedly greater than for the general population. PCB and DDE levels were significantly associated with age and fish consumption histories (Hanrahan *et al.* 1999), and years of sport-caught fish consumption was the most robust predictor of serum PCBs. Mercury levels were significantly associated with levels of fish consumption in Lake Ontario sport and subsistence fishers (Cole *et al.* 2004). In a study of pregnant women residing along the upper St. Lawrence River, serum PCBs increased with age (Mergler, presentation).

While the concentrations of most persistent and bioaccumulative "legacy" contaminants have decreased substantially in the last 30 years due to source regulation, mercury concentrations have not decreased or have increased due to emissions from coal-fired power plants and other sources. Elemental and inorganic mercury, deposited in water bodies, can be methylated to form MeHg by microorganisms in sediment. MeHg bioaccumulates through the food chain and can cause decrements in neurobehavioral function in children. MeHg is the leading cause of sport fish consumption advisories in the U.S. and Canada (Wood and Trip, 2001, U.S. EPA, 2001a, U.S. EPA Office of Water, 2002).

Table 2. Concentrations of Polybrominated Diphenyl Ethers, Perfluorooctane Sulfonate, Nonylphenol, and Nonylphenol Ethoxylate in the Great Lakes

CHEMICAL	YEAR	SPECIES OR MEDIUM	LAKE OR LOCATION	CONCENTRATION in parts per billion unless indicated	CITATIONS
Total PBDEs	1997	Lake trout	L. Michigan	126 (5)[a]	Stapleton & Baker 2003
	1997	Smelt	L. Michigan	11 (5)	
	1997	Alewife	L. Michigan	36 (5)	
	1997	Sculpin	L. Michigan	3 (5)	
	1997	*Diaporea*	L. Michigan	2 (5)	
	1997	*Mysis*	L. Michigan	1 (5)	
	2000	Lake trout	L. Superior	180 (6)	Swackhamer (personal communication)
	2000	Lake trout	L. Huron	94 (6)	
	2000	Lake trout	L. Michigan	355 (6)	
	2000	Walleye	L. Erie	51 (6)	
	2000	Lake trout	L. Ontario	227 (6)	
	2003	Snapping turtle eggs	Hamilton Harbour	107 (9)	Fernie & Letcher (personal communication)
	2000	Herring gull eggs	13 colonies around GLs basin	200-1400 (7)	Norstrom *et al.* 2002
	97-99	Beluga blubber	St. Lawrence Estuary	156-935 (10)	Lebeuf *et al.* 2004
Total PFOS	2000	Lake trout	Lakes Superior Michigan, Ontario	13-35	Swackhamer (personal communication)
	2001	Lake trout	L. Ontario	186	Martin *et al.* 2004
	2001	Smelt	L. Ontario	182	
	2001	Alewife	L. Ontario	50	
	2001	Sculpin	L. Ontario	600	
	2001	*Diporea*	L. Ontario	460	
	2001	*Mysis*	L. Ontario	143	
	91-93	Bald eagle nestling plasma	GLs shorelines	330 <1-2220	Kannan *et al.* 2001a
	95-96	Mink liver	Fox River, Wisconsin	5140	Kannan *et al.* 2002
	2003	Water	L. Erie and Ont.	31 and 54 ppt	Boulanger *et al.* 2004
	02-04	Surficial sediments	Lakes Superior Michigan, Huron, Erie	1.0 – 4.0 ng/g	Song *et al.* 2005, Zhu & Hites 2005
NP + NPEO[b]	98-00	Carp	Cuyahoga & Detroit R.	32 -920	Rice *et al.* 2003, Schmitz-Afonso *et al.* 2003
	98-99	Carp and walleye	Near WWTP outlet	4750	Schmitz-Afonso *et al.* 2003
	1999	7 fish species	Kalamazoo R.	< 3- 29	Keith *et al.* 2001
		Herring gull liver	Lower Great Lakes	225-464	Grasman *et al.* in preparation.
	1998	Sediments	Cuyahoga R.	250-1020	Rice *et al.* 2003
	1998	Sediments	Detroit and Rouge R.	<10-60000	Kannan *et al.* 2001b
	1998	Water	Cuyahoga R.	0.13 -5.1	Rice *et al.* 2003

[a] Number in parenthesis is number of PBDE congeners measured [b.] NP - nonylphenol, NPEO – nonylphenol ethoxylate

5.11 Effects

In the 1960s and 1970s, numerous studies documented reproductive failures in lake trout, mink, and fish-eating birds; gross deformities in fish-eating birds; and tumours and other deformities in bottom-dwelling fish. These findings pointed to the presence of significant quantities of unidentified toxicants in the Great Lakes capable of affecting the health and well-being of animals that eat fish, drink, and swim in the Great Lakes. Although there were few investigations of health effects or chemical exposure at that time, these concerns were reflected in the 1978 Agreement.

A 1991 basinwide assessment of the health of herring gulls nesting in 11 colonies representing all five Great Lakes, relative to two reference colonies outside of the basin, revealed widespread DNA damage (Fox *et al*. 2005) and chronic periportal hepatitis (inflammation of the liver) and interstitial nephritis (inflammation of the kidney). These effects were more severe in highly contaminated colonies. There was evidence of decreased biosynthetic activity and intermediary metabolism in the liver and altered glucose and mineral homeostasis. Great Lakes gulls suffered from hypothyroidism and had enlarged hyperplastic thyroid glands. These toxipathic responses were most frequently associated with PCBs. Studies of pre-fledgling herring gulls in 1994-1999 in lakes Huron, Erie, and Ontario revealed marked suppression of T-cell-mediated immune function and altered antibody production (Grasman *et al*. 1996). Studies of herring gulls in colonies in the Detroit River, western Lake Erie and Lake Ontario 2001-2004 revealed that biochemical, thyroid, and immune effects still persist. In addition, there were effects on corticosterone secretion and, at some sites, the plasma of males contained vitellogenin, suggesting they were exposed to biologically significant concentrations of estrogens. Similar biochemical effects were seen in male snapping turtles, and thyroid effects were seen in snapping turtles and fish. Vitellogenin was also found in the plasma of male fish and snapping turtles. The surveys revealed decreased embryo viability in herring gull eggs and decreased hatching success in snapping turtles at some AOCs. Detailed studies revealed altered reproductive steroid levels and production in fish at some sites. The livers of 57 percent of mink collected from 1999-2002 from western Lake Erie tributaries and marshes contained PCB concentrations greater than the lowest-observable-effect level for reproductive impairment (Fox, presentation).

Recent research revealed significant negative associations between mercury concentrations in the cerebrum and the numbers of cholinergic and dopaminergic receptors in the cerebral cortex of river otters and mink trapped in Ontario, Nova Scotia, and Yukon Territory, suggesting that environmentally relevant concentrations of mercury may exert sub-clinical neurotoxic effects on fish-eating mammals (Basu *et al.* 2005a, 2005b). Gonzalez *et al.* (2005) monitored the expression of 13 genes associated with responses to chemical stressors in the brains, muscles, and livers of zebra fish exposed to environmentally relevant concentrations of MeHg for nine weeks. They observed altered expression of multiple genes in the muscles and liver, but no response in the brains, despite the brains having accumulated the highest concentration of MeHg. This may suggest that the brain has no inherent ability to demethylate MeHg and deal with its toxicity. When Hammerschmidt *et al.* (2002) fed juvenile fathead minnows diets containing concentrations of MeHg present in some aquatic food webs through to their sexual maturity, they found no overt toxicity. However, gonadal development of females was reduced leading to delayed spawning and reduced spawning success. The offspring of adult killifish fed environmentally relevant concentrations of MeHg had altered sex ratios and lowered reproductive success in adults with whole body concentrations of 440 to 1200 ng/g (ppb) (Matta *et al.* 2001).

Pesticides are an ongoing concern, just as they were in the 1960s. Although atrazine has been banned by the European Union, it is still in use in the U.S. and Canada. It is, however, under regulatory review in both countries. Although controversy surrounds the studies undertaken to clarify its safety to amphibian development, the weight of evidence suggests that it is toxic to amphibians at or near concentrations currently measured in aquatic environments (Hayes 2004).

5.12 Special Consultation on Mercury

During the priority cycle, the Work Group on Ecosystem Health closely followed published reports regarding human-health effects due to exposure to MeHg, and consulted with mercury experts. Numerous reports have raised concerns regarding MeHg in sport fish and adverse health risks, particularly to the developing child (National Research Council 2000, Great Lakes Science Advisory Board 2003, Gilbertson and Carpenter 2004). For example, the National Research Council (NRC) concluded that "the population at highest risk is the children of women who consumed large amounts of fish and seafood during pregnancy." Its report concluded that the risks to that population are likely to result in an increase in the number of children who have to struggle to keep up in school, and who might require remedial classes or special education. Subsequent information continues to indicate public health concerns, including potential cardiovascular effects, as do national fish consumption advisories issued by the U.S. Food and Drug Administration and U.S. EPA (U.S. FDA and EPA 2004). Current research focuses on three main questions:

- What are the most appropriate human-health measures to assess mercury impacts in adults and children?
- What is the nature of mercury-related human-health impacts?

- Is there a threshold blood-mercury level below which impacts on cognition are not seen?

Dr. Allen Stern was a member of a panel of scientists charged by the NRC to evaluate MeHg health effects. In its report, the NRC supported U.S. EPA's methodology to derive a reference dose (RfD) for acceptable chronic exposures to MeHg. The RfD of 0.1 microgram (ug) MeHg per kilogram of body weight (kg-bw) per day, a maternal dose, was based on developmental effects of mercury assessed in children who have been exposed to mercury *in utero* through the maternal diet (U.S. EPA 2001b, Rice 2004, Stern 2005a). The RfD was derived from MeHg in fetal-cord blood to a reconstruction of the maternal dose that gives rise to blood levels in the fetus. Using data from three epidemiological studies conducted in New Zealand, the Faroe Islands, and Seychelles Islands, the NRC determined that a fetal-cord blood of 58 micrograms per liter (ug/L) was associated with twice the probability of adverse neurological effects in children (National Research Council 2000, Rice 2004, Stern 2005a).

Following recommendations from the NRC committee and U.S. EPA peer reviewers, U.S. EPA applied an uncertainty factor of ten to derive a concentration of 5.8 ug/L in fetal-cord blood from which to calculate an RfD without a significant increased risk of adverse neurological effects in children (Rice 2004, Stern 2005a). The factor of ten included a factor of three for variation in maternal elimination of MeHg (pharacokinetic variability) and a factor of three for pharmacodynamic variability (Rice 2004, Stern 2005a, U.S. EPA 2001b).

Stern's published work supports the appropriateness of directly estimating the percentile of maternal dose corresponding with fetal-cord blood levels (Stern 2005a). While U.S. EPA based the RfD on the assumption of a 1:1 ratio of mercury in fetal cord to maternal blood, more recent evidence found the ratio to be 1.7:1.0. This lowers the maternal dose at which adverse effects may occur in the fetus (Mahaffey *et al.* 2004, Rice 2004, Stern 2005a, Morrissette *et al*. 2004). Stern's analyses indicated that U.S. EPA's determination of the RfD would agree within a factor of two based upon his work. Using his findings, a benchmark RfD based on the first percentile maternal dose corresponding to a cord-blood concentration of 58 ug/L and incorporating an uncertainty factor of three would be 0.07 ug MeHg/kg-bw/day.

These findings suggest that future fish-consumption advisories in the Great Lakes region, which are largely issued to protect women of child-bearing age and children, may need to be extended to other segments of the population (such as adult males, etc.).

There is no evidence to date that a threshold blood-mercury concentration exists where effects on cognition are not seen. The NRC (2000) concluded that the likelihood of neurobehavioral deficits increased as cord-blood concentrations increased from 5 to 58 ug/L (the U.S. EPA benchmark dose). Trasande *et al.* (2005) used 5.8 ug/L in cord blood, the lowest concentration at which adverse neurodevelopmental effects were demonstrated in cohort studies (Grandjean *et al.* 1997, Kjellstrom *et al.* 1986, 1989) and applied the cord blood: maternal blood ratios of 1.3:1.0 (Budtz-Jorgensen *et al.* 2002) and 1.7:1.0 (Stern 2005a) to derive a range of maternal blood mercury concentrations above which neurobehavioral deficits would be expected. These values are 3.4 to 4.5 ug/L. Based on blood-mercury concentrations obtained for the 1999-2000 National Health and Nutrition Examination Survey, Mahaffey *et al.* (2004) calculated 9.7 and 15.7 percent of American women 16 to 49 years would have blood-mercury concentrations of ≥5.0 ug/L and ≥3.5 ug/L, respectively. The geometric mean blood-mercury concentration for a sample of Asian-Canadian subsistence fishers who fished in five Great Lakes AOCs was 7.9 ug/L (Cole *et al.* 2004). Anderson *et al.* (1998) found geometric mean blood total mercury concentrations in samples of high sport-fish consumers from lakes Michigan, Huron, and Erie ranged from 3.2 ug/L (Erie) to 4.7 ug/L (Michigan).

Stern reviewed information available since publication of the NRC report regarding MeHg exposure via fish consumption suggesting an association with heart attacks, ischemic heart disease, hypertension, and heart-rate variability. He provided an overview to the SAB based on a recently published literature review (Stern 2005b). In his view, the current evidence suggests an association between rates of MeHg exposure from fish consumption with heart disease, particularly myocardial infarction. The causal mechanism may be an antagonistic interaction between MeHg and fatty acids, which provide health protection from heart disease. A study of 1,871 men in a Finnish cohort (Virtanen *et al*. 2005) provides the strongest basis for a formal quantitative risk assessment of the cardiovascular effects of MeHg, although a quantitative relationship between exposure and effects has yet to be developed.

Dr. Ellen Silbergeld of Johns Hopkins Medical School also presented her research that suggests that mercury is an immunotoxin that, in the appropriate rodent model, triggers autoimmunity and autoimmune myocarditis. The immunotoxic effects of mercury in rodents occur at significantly lower doses than other effects.

These findings suggest that future fish-consumption advisories in the Great Lakes region, which are largely issued to protect women of child-bearing age and children, may need to be extended to other segments of the population (such as adult males, etc.).

5.13 Health Effects of Toxic Contaminants

In the late 1980s, Health Canada and the U.S. Agency for Toxic Substances and Disease Registry (ATSDR) initiated Great Lakes health effects programs that provided funding for investigations of human exposure to toxic contaminants and establishment of human cohorts for cross-sectional and prospective epidemiological studies. Numerous epidemiological studies have documented effects on human reproduction and development, metabolism, endocrine and immune function associated with Lake Ontario, Lake Michigan, and the St. Lawrence River (Johnson *et al*. 1998). Adverse health effects are evident even in those individuals that consume relatively small amounts of certain Great Lakes fish. Relatively few health-effects data exist for subsistence fishers who consume larger amounts of more contaminated fish. Several well-designed studies are in progress.

The following summarizes current research on the health effects of toxic contaminants in the Great Lakes basin.

5.13.1 Reproductive Success

Scientists from the University of Buffalo investigated various reproductive outcomes in members of the New York State Angler Cohort. They found associations between maternal sport-fish consumption and a delay in the probability of conception (Buck *et al.* 2000). There was also an association between sport-fish consumption by males and reduced probability of fathering a male child (Travers *et al.* 2000). However, studies of Lake Michigan anglers showed a higher proportion of males in offspring of fathers with serum PCB concentrations greater than 8.1 ug/L (Karmaus *et al.* 2002).

Investigators from the University of Quebec at Montreal found an association between cord blood-serum PCBs and birth weight in a cohort of 159 pregnant women living along the upper St. Lawrence River (Lafond and Mergler, 2005). This is consistent with earlier studies of effects of maternal consumption of Lake Michigan fish (Fein *et al.* 1984). In a more recent study of Lake Michigan sport fishers, there was an association between maternal serum DDE, but not PCBs. Concentrations and birth weight effects associated with Great Lakes sport-fish consumption have decreased over time (Weisskopf *et al.* 2005). Investigators from the Institute for Health and the Environment at the University of Albany found a significant association between lower birth weight and parental residence near a PCB-contaminated site in more than 900,000 births in New York State (Baibergenova *et al.* 2003).

In a study of 159 women who resided near the upper St. Lawrence River, a negative association existed between their blood-lead concentration and the rate of calcium uptake by their placental syncytiotrophoblasts - the layer of placental cells that regulates the flow of nutrients between mother and fetus (Lafond *et al.* 2004).

Scientists from the Institute for Health and the Environment have conducted studies of Mohawk youth at the Akwesasne Reserve which is just south of Cornwall, Ontario. Their analysis of multi-chemical exposure among adolescent Mohawk girls suggested that the age of attainment of menarche may be sensitive to relatively low levels of lead and certain PCB congeners (Denham *et al.* 2005).

Among the 2,237 infants born to female members of the New York State Angler Cohort between 1986 and 1991, there was an increased probability of a major malformation (including hypospadias, cleft palate, and musculoskeletal defects) in males but not females, whose mothers consumed two or more sport fish meals per month during pregnancy (Mendola *et al.* 2005).

5.13.2 Neurobehavioral Effects

Researchers are discovering an increasing suite of behavioral abnormalities in infants and children and in laboratory rodents prenatally exposed to environmentally relevant concentrations of PCBs or mercury. Numerous papers have documented persistent effects on neurobehavioral development associated with maternal consumption of Lake Michigan fish (the Jacobsons and colleagues 1986, 1990, 1992, 1996). These findings have been substantially duplicated by investigators from the Center for Neurobehavioral Effects of Environmental Toxics, SUNY Oswego for a cohort of children whose mothers consumed Lake Ontario fish. In this longitudinal study, prenatal PCB exposure was consistently predictive of cognitive and behavioral deficits in children from birth to age five (Stewart *et al.* 2000b, Stewart *et al.* 2003b).

The most robust associations were between measures of attention and impulse control and highly chlorinated PCB congeners. These findings also have been confirmed with laboratory animals (Stewart *et al.* 2000a). In a subset of these children, the risk of abnormal performance increased markedly in those individuals with a smaller splenium, suggesting that contaminants may have a much larger impact in some children than in others (Stewart *et al.* 2003a). Scientists from the University of Buffalo investigated gender-associated behaviors in more than 1,000 children born to members of the New York State Angler Cohort. They found an exposure-associated increase in masculine behavior in young males (Sandberg *et al.* 2003).

Investigators at the University of Illinois at Urbana-Champaign assessed the impact of PCBs and other fish-borne contaminants on intellectual function in older members of the Lake Michigan sport-fisher cohort. They found that PCB exposure during adulthood was associated with impairments in memory and learning, but not executive or visual-spatial function (Schantz *et al.* 2001). These investigators are now studying the combined exposure to PCBs and MeHg, two of the most widespread chemical contaminants that are responsible for almost all Great Lakes fish-consumption advisories. Since both are developmental neurotoxicants, there is potential for

interactive effects on the nervous system. The investigators are characterizing the cognitive, motor, and sensory effects of developmental exposure to these toxicants in animals, and will use their findings to guide selection of outcome measures for infants and children. Both PCBs and MeHg caused deficits in working memory, but there was no additivity (Widholm *et al.* 2004). Neither chemical caused significant effects on balance or coordination when administered alone, but combined exposure caused a deficit (Roegge *et al.* 2003). PCBs, but not MeHg, caused deficits in auditory function, and there was no additivity (Lasky *et al.* 2002).

5.13.3 Other Effects

In pregnant women who resided on the shores of the upper St. Lawrence River, there was an inverse association between plasma concentrations of total triiodothyronine and three non-coplanar, highly persistent PCB congeners, DDE, and hexachlorobenzene (HCB) (Takser *et al.* 2005). In Mohawk youth from Akwesasne, also located on the St. Lawrence River, concentrations of thyroid-stimulating hormone were increased, and decreases were found in thyroxine and free thyroxine associated with some PCB congeners and lead (Schell, presentation). In studies of 66 males from the New York State Angler Cohort, there was a negative relationship between thyroxine and HCB (Bloom, presentation). In a grouping of high sport-fish/wildlife consumers and non-consumers, free thyroxine with the lipid-adjusted concentrations of total dioxins was significantly decreased (Bloom *et al.* in press). Among a subset of 178 men and 51 women studied by the Great Lakes Consortium, a relationship was found between fish consumption and serum PCB concentration and serum thyroxine (Persky *et al.* 2001). There was also an association between both PCBs and fish consumption, and sex hormone-binding globulin-bound testosterone in the males (Persky *et al.* 2001).

A recently published study of adult Mohawks from Akwesasne has shown associations between plasma PCB concentrations and induction of cytochrome P450 1A2, an enzyme involved in sex steroid hormone synthesis. The study also showed metabolic activation by a number of toxicants and carcinogens (Fitzgerald *et al.* 2005).

McElroy *et al.* (2004) found an increased relative risk of developing breast cancer of 70 percent in pre-menopausal Wisconsin women who recently consumed Great Lakes sport-caught fish.

Michigan investigators found a significantly increased relative risk for inner ear infections for the combined effect of DDE + PCBs or DDE + HCBs (Karmaus *et al.* 2001). They also found significantly higher relative risk for asthma and increased immunoglobulin E concentrations with DDE exposure, suggesting impacts on immune function.

The half-life of a particular contaminant is of considerable importance in determining its relevance to society. The half-life of MeHg in the human body is about 70 days, whereas the half-life for organohalogen compounds can be as long as ten years. This difference has great significance for reducing the danger of neurobehavioral decrements to the fetus. If a young woman stops eating MeHg-contaminated fish a year prior to getting pregnant, she can clear her body of most of the MeHg. However, if she waits until she's ready to get pregnant to stop eating organohalogen-contaminated fish, it will be too late to reduce her levels of these contaminants. Her body burdens will reflect her previous exposure.

5.13.4 Health Effects of Living in Areas of Concern

In 1998, Health Canada reported on retrospective epidemiological evidence for each of the 17 Canadian AOCs (Elliot *et al.* 2001). They used mortality, hospital admissions/separations, and cancer data for 1986-1992 to calculate morbidity, mortality, and incidence rates. The data suggested that there was increased morbidity and mortality for a variety of health effects associated with residence in these AOCs relative to the Province of Ontario as a whole. Also, residence in a particular location was found to adversely affect health independent of whether Great Lakes fish is consumed.

The Health Canada studies for the various Canadian AOCs found increased incidence of genital-tract disorders, thyroid disease, diabetes, ischemic heart disease, chronic obstructive pulmonary disease, and asthma. These findings led investigators at the Institute for Health and the Environment at the University of Albany to test a series of hypotheses based on the assumption that these health end points are associated with place of residence. Using a variety of available health data collected in the 1990s, they tested these hypotheses for individuals living near the nearly 900 contaminated sites identified in New York state, including AOCs. They found convincing evidence that a number of chronic and acute diseases occur more commonly in patients who reside near hazardous waste sites and AOCs containing priority pollutants, especially persistent organic pollutants such as PCBs (Carpenter presentation). The elevated incidence is not accounted for by socio-economic status or lifestyle factors such as smoking, diet, or exercise. These findings imply that inhalation is a major route of exposure (Sergeev and Carpenter 2005, Baibergenova *et al.* 2003). Effects documented include adverse impacts on reproduction and development, metabolism, and endocrine and immune functions. In addition, studies suggest that increased risks of heart disease, chronic obstructive pulmonary disease, and diabetes are associated with residence near AOCs and hazardous waste sites (Carpenter presentation). A recently published study has also shown a strong association between ambient air pollution and respiratory hospitalization in the Windsor AOC (Luginaag *et al.* 2005).

Inhalation can be a major route of exposure. The health of large numbers of people in many communities in the Great Lakes basin may be compromised by multi-media exposure to the contaminants in their environment. A much greater focus on place

of residence and multi-media exposure is needed, in addition to fish consumption, if the health impacts of contaminated sites and other contaminant sources on communities and populations in the basin are to be understood.

Preliminary analyses of data and statistics for the hospitalization rates of males for cerebral palsy in the 17 Canadian AOCs indicate a possible geographic association with locations with elevated mercury from natural or industrial sources (Gilbertson 2003). It should be noted that the amount of mercury released from cloralkali plants in Sarnia and Cornwall (Trip and Thorleifson 1998) exceeds the estimated amounts released into Minimata Bay by a factor of four and two times, respectively (Gilbertson 2003).

The costs of learning and behavioral problems, low birth weight, immune system disorders, and other effects are real and are borne by individuals, families, and communities. Grosse *et al.* (2002) have estimated that the economic benefit resulting from improved cognitive ability (IQ points) associated with reductions in children's exposure to lead in the United States ranges from $110 billion to $319 billion annually. Using similar methodologies, Trasande *et al*. (2005) have estimated the U.S. cost of loss of intelligence in children born each year with deficit-associated cord-blood mercury levels, an effect that persists throughout the life of each individual. An estimated $7.8 billion (ranging from $2.2 to $44 billion) is lost annually through the associated loss in productivity. Of this, $1.3 billion is attributable to mercury emissions from American power plants.

These findings emphasize the individual and community impacts of toxic chemical pollution. Future research on the health effects of contaminants in the Great Lakes basin will therefore be most effective if it is community-based and participatory. In collaboration with the Children's Environmental Health Centers, Schantz and others are using such an approach to conduct a prospective cohort study of children born to Hmong immigrants who eat contaminated fish from the Fox River.

5.14 Managing Chemicals to Protect Human Health and the Environment

In the Great Lakes basin, three approaches have been used to manage chemicals in the environment: fish consumption advisories; mitigation of existing sources; and prevention/control at source. Underpinning all three efforts is a requirement for adequate monitoring systems to track not only concentrations (exposures), but also human health and ecosystem effects. New or newly detected chemicals in the environment must also be identified. The following summarizes current research in these areas.

5.14.1 Fish Consumption Advisories

Fish consumption is one of the main routes by which toxic substances enter the human body. Fish-consumption advisories were created almost 30 years ago to protect those who consume sport fish. While advisories provide excellent advice, they have limited effectiveness, in part because they focus on sport fishing. Subsistence fishers who depend on Great Lakes fish to feed their families often eat species that are not covered by advisories. In addition, the current emphasis on sport fishing tends to target male sport fishers rather than subsistence fishers, many of whom are women and minorities. These latter groups are largely unaware of the dangers of contaminated fish. One-size-fits-all advisories therefore are less effective than originally intended. The most vulnerable populations of fishers need to be identified and specifically targeted with clear advisories that address ethno-cultural, nutritional, and economic concerns.

The goals of Great Lakes sport-fish consumption advisories are to maintain the health benefit of fish consumption while minimizing toxic chemical exposure, and thus present information in a way that maximizes voluntary compliance. However, in trying to simplify language for the consumer, many advisories introduce unintended confusion and provide little detail as to their basis. In some systems, a single pollutant such as mercury may be responsible for most of the fish-consumption advisories; in others, multiple pollutants may be of concern.

The Ontario Sport Fish Contaminant Monitoring Program covers the most common species of sport fish for 1,700 locations across the province. Boneless, skinless fillets of dorsal muscle are tested. A variety of species and locations are selected based on:

- Their popularity;
- Suspected sources of pollution;
- Importance as a source of food for the local community;
- Recreational development; or
- Long-term monitoring sites.

The *Guide to Eating Ontario Sport Fish (2005-2006 edition)* (Ontario MOE 2005) provides location-specific contaminant data and excellent information aimed at anglers (and their families) who consume moderate amounts of fish. The *Guide* provides separate advice for "the sensitive population of women of child-bearing age and children less than 15 years of age" and explains the basis for this precaution. It also suggests that these individuals should further reduce their consumption if they regularly eat processed fish. The *Guide* is written in English and French, and two-page summary brochures are available in 16 other languages covering the majority of subsistence fishers. The notice of their availability, however, is only in English. The notice would be more accessible if written on the back cover in all 16 languages. The brochure's focus is proper use of the *Guide,* but does emphasize the separate advice for women of child-bearing age and children. Another educational brochure for women of child-bearing age is available in English only, on request. One brochure, containing the essence of both and available in all 16 languages, would be an improvement.

According to the *Guide,* the overall percentage of fish consumption advice that results in some level of restriction for the general population ranges from 37 percent (Lake Superior) to 57 percent (Lake Ontario). PCBs are responsible for 25 percent (Lake Superior) to 79 percent (Lake Ontario) of the advisories. Mercury is responsible for two percent (Lake Erie) to 32 percent (Lake St. Clair, the St. Clair and Detroit Rivers) of the advisories. Dioxins are responsible for 17 percent (Lake St. Clair, the St. Clair and Detroit Rivers) to 65 percent (Lake Superior) of the advisories. No single advisory describes both lipid-soluble contaminants such as PCBs or dioxins as well as MeHg, which is confusing to fish consumers.

An important question is the effectiveness of current advisories. The Consortium for the Health Assessment of Great Lakes Sport Fish Consumption conducted approximately 1,000 telephone interviews in each of seven Great Lakes states in 1994, prior to the introduction of the Uniform Great Lakes Sport Fish Consumption Advisory and about 500 interviews in each state in 2001. The results suggest that the numbers of individuals consuming fish and the amount of Great Lakes sport fish consumed had not decreased. Awareness of the advisories had increased by five to ten percent in higher-consumption categories and in males, but had decreased in females and non-white fishers. Compliance had increased most for cooking/cleaning and fishing locations, but had not changed for consumption frequency (Anderson, presentation).

In a 12-state initiative to evaluate awareness of sport-fishing advisories for mercury among women of child-bearing age, more than 66 percent of the women who consumed sport fish were not aware that such guidelines even existed (Knobeloch 2005). In a population-based telephone survey of adults residing in the eight Great Lakes states, seven percent of respondents, of an estimated 4.2 million adults, reported consuming fish caught from the Great Lakes. Consumption of Great Lakes-caught sport fish was greatest among residents of Michigan and Ohio (Imm *et al.* 2005). Awareness of advisories varied by gender and race, and was lowest among women (30 percent) and African-American residents (15 percent). However, 70 percent of those who consumed Great Lakes-caught sport fish twice a month or more were aware of the advisories.

In a recent study of pregnant women in southwest Quebec, consumption of St. Lawrence fish decreased and that of commercial fish increased during pregnancy, compared with consumption prior to pregnancy (Mergler, presentation).

Arquette and colleagues (2002) from the Akwesasne Task Force on the Environment note that *"In the case of Akwesasne, it has been found that the traditional cultural practices that express and reaffirm identity and culture increase exposure of community members to toxic substances. Adverse health effects have resulted when Mohawk people are forced to abandon traditional cultural practices in order to protect their health and the health of future generations."*

Ethno-cultural groups who consume Great Lakes fish identified to date include immigrants from a variety of European countries; Asians from Laos, Vietnam, and Bangladesh; African-Americans; and various aboriginal tribes. Investigators collected fish-consumption, health, and contaminant data from fishers on the shorelines of five AOCs: Toronto, Hamilton Harbour, Niagara River, Detroit River, and St. Clair River (Sheeshka, presentation). They surveyed 4,595 participants over five years, 38 percent of whom ate some or all of their catch. From this group, 27 percent ate more than 26 meals per year. Two ethno-cultural groups predominated, Asian Canadians and European Canadians. A sample of 91 high-fish consumers ate 26 to 501 Great Lakes fish meals/year, with a median of 88. Males consumed more often than females and Asians more often than Europeans (Sheeshka, presentation). Although some of these individuals were aware of consumption advisories, the language, culture, economic circumstances, and personal and community experience affected advisory effectiveness. For these fish consumers, perceived benefits outweighed perceived harm.

Fish consumption advisories can only be regarded as a limited and temporary solution for public health protection. The advisories externalize the economic costs to individuals and society by permitting the exposure of fish consumers to toxic chemicals. Advisories must be accompanied by systematic and effective programs to reduce or eliminate discharges of toxic chemicals to the Great Lakes basin.

Rather than "one-size-fits-all," to be effective advice needs to be targeted for specific ethnic communities written clearly in their language, and perceived as personally relevant, practical, and culturally sensitive. Voluntary restriction of one's consumption of contaminated fish requires sufficient knowledge and economic flexibility to make informed choices. The majority of subsistence fishers currently have neither. The goal of fish advisories is to encourage each consumer to eat a varied and nutritious

diet, including fish as desired, and to select fish that are lower in contaminants. Providing fishers with comparative risk information that focuses on different foods or protein sources would enable consumers to make appropriate decisions based on fish size, species, location, or food type (Knuth *et al.* 2003). Fish consumers could better make appropriate choices if provided with comparative risk information such as size, species, fishing location, or food type that have, on balance, greater benefits than risks.

Great Lakes sediments contaminated with "legacy" pollutants remain an ongoing source of contaminants. Elimination or reduction of health effects in wildlife and humans in the Great Lakes basin requires removal or capping of contaminated sediment, a technically challenging and expensive process (Clark, presentation). For example, the effort to remove 90 percent of the PCBs from the Fox River, Wisconsin will take at least five years and cost at least $500 million. Some consider this an imperfect solution since residual PCBs will remain in the system for years (Foran, presentation). The relative costs and benefits of such cleanup are hotly debated, in part because most assessments ignore the costs of the environmentally contaminated fish to the health of wildlife and human populations at risk, and the costs associated with lost economic activity.

5.14.2 Detecting and Managing Emerging Chemicals

Within five years of the initial flagging of environmental concerns about PBDEs and PFOs, chemists mapped their global distribution, measured their concentrations in the tissues of humans and numerous other species, determined changes in their compositional pattern, and established temporal trends over periods of 10 to 30 years. This was possible because of tissue archives and the small, dedicated cadre of scientists who systematically collect and properly preserve tissues for just such purposes. Coupled with appropriate analytical chemistry, such archives allow problems to be identified and quantified and thus provide early warning. This "exposure" monitoring is essential to assessments of whether we are moving closer or further away from achieving virtual elimination of toxic chemicals and protecting public health.

While current long-term monitoring programs are adequate to document trends in the *concentration* of contaminants in the Great Lakes environment, there is no formal program in either country to monitor trends in the incidence of *effects* due to the presence of these contaminants. Well-planned monitoring assists scientists in anticipating surprises. Without monitoring of both ambient conditions and the impact on Great Lakes organisms, decision makers are poorly equipped to identify appropriate policy responses or even areas of uncertainty. Such knowledge is also fundamental to developing cost-effective and appropriate research questions.

Effective monitoring programs are complicated by the need for continuously updated analytical methods. Monitoring the vast array and low concentrations of chemicals in the environment is a daunting challenge. In the 1970s and 1980s, gas chromatography/mass spectrometry (GC-MS) was the instrumentation of choice. In the 1990s, the availability of the combination of high-volume sampling, solid-phase extraction, and liquid chromatography/mass spectrometry (LC-MS) allowed the development of more sensitive methods capable of measuring a wide array of chemicals in a single environmental sample.

With increasingly efficient instrumentation and improved sample-preparation protocols, chemists are discovering more persistent or biologically active compounds in water and tissue samples from the Great Lakes environment. The results show increasing numbers and concentrations of chemicals that have been in use for decades that were not previously detected, and for which there are only minimal and/or disturbing health data. Chemicals from pharmaceuticals, personal-care products, and household-cleaning compounds are now found regularly in rivers and lakes receiving municipal effluents. These "emerging" chemicals are found in addition to the widely dispersed persistent, bioaccumulative "legacy" chemicals. Municipal wastewater treatment plant effluents are a major source of many of these "emerging" contaminants to surface waters and biota.

Comprehensive congener-specific, multi-analyte analysis of plasma or serum using a combination of GC-MS and LC-MS is also providing considerable insight into the metabolism and storage of contaminants. Blood plasma bathes all tissues. Frequently, much tighter associations are found between specific metabolites and effects measures, rather than with the parent compounds. Careful examination of congener profiles, using pattern recognition techniques and polytopic vector analysis, can reveal information on sources and subject-dependent factors such as biotransformation enzyme polymorphisms. Such polymorphisms may be very important in determining individual susceptibility (DeCaprio, presentation).

Unfortunately, the instrumentation required for effective monitoring is expensive, the availability of experienced analytical chemists limited, and the financial security of environmental-monitoring programs constantly in question. Therefore, in a May 2004 consultation, the SAB asked for expert advice on how to identify, prioritize, and indeed anticipate "emerging" contaminants of concern.

Derek Muir (presentation) described his search strategy to identify potential chemicals of concern among the approximately 100,000 chemicals in commerce, approximately 70,000 of which are on the Toxic Substances Control Act list created in 1976, and 5,200 that exceed a production volume of 1,000 tonnes/year according to the Organization for Economic Cooperation and Development. Of these 5,200 chemicals, 43 percent had no toxicity data available as of 2004.

A predictive approach that addresses the paucity of available data uses structural, chemical, and physical properties of the chemicals coupled with quantitative structure-activity

relationships (QSARs) to identify substances of concern. Due to analytical limitations, only a very low proportion of the large number of potentially troublesome compounds identified as likely present in the Great Lakes environment are currently analyzed in Great Lakes monitoring programs. Of greatest concern are those chemicals used in large quantities and in environmental concentrations similar to, or approaching, those known to cause adverse effects.

Another strategy focuses on chemicals present in environmental media and tissues that are not persistent or bioaccumulative, but are chronically discharged into the aquatic environment. With the exception of pesticides, most of these chemicals are not acutely toxic, but are pharmacologically or hormonally active at very low concentrations. When they contaminate the environment and are consumed unknowingly by humans and species for which they were not intended, they can be toxic. Using new, sophisticated instrumentation and improved sample preparation protocols, chemists today are identifying an increasing suite of these "new" chemicals or groups of chemicals whose concentrations are increasing in water and tissue.

As a result of the May 2004 consultation, the following groups or classes of chemicals are considered "emerging" contaminants of concern in the Great Lakes (see also Table 2):

- Brominated fire retardants (BFRs), PBDEs and tetrabromo bisphenol-A;
- Perfluorinated compounds or PFCs (PFOS, perfluorooctanoic acid, N-ethyl perflourooctane sulfonamidoethanol);
- Phthalates (a large class of plastic additives);
- Pharmaceuticals and chemicals found in personal care and household products (PPCPs);
- Estrogenic and hormonally active compounds (birth control agents, natural estrogens, alkylphenol ethoxylates, bisphenol-A, Trenbolone); and
- Some currently used pesticides (Atrazine).

These chemicals and their uses are described in more detail in Chapter 5.17 (Appendix).

Pharmaceuticals and personal-care products are persistent by virtue of their ongoing release into the environment in human and animal excreta. However, health professionals, agricultural producers, and society are unlikely to forego access to the benefits of these products. Therefore their virtual elimination will require further restrictions on their disposal and release into the environment.

5.14.3 Chemical Mixtures

In addition to awareness of "emerging" chemicals, there is a growing awareness of a larger range of developmental and functional health impacts associated with exposure to mixtures of chemicals, including the persistent "legacy" contaminants and the "emerging" chemicals. It is now clear that a single chemical can have an impact on multiple-organ systems via several exposure pathways and a number of modes of action, and that those impacts can be expressed in multiple ways. Many "emerging" chemicals affect the same target organs and/or systems as the "legacy" chemicals associated with trans-generational impairment.

It is known that the combined effects of a mixture of dioxin-like compounds are additive when adjusted for potency. This has been shown for end points such as various manifestations of reproductive toxicity and for CYP1A induction, which were used to derive the toxic equivalency factors for each chemical. This has now been extended to the assessment of their cancer risk (Walker *et al.* 2004). Recently, investigators discovered that the same holds true for estrogenic chemicals (Brian *et al.* 2005). Crofton *et al.* (2005) dosed young rats with a mixture of two dioxins, four dibenzofurans and twelve PCBs. The mixture was formulated to reflect typical concentrations measured in breast milk, and in fish and other foods. None of the concentrations in any of the doses exceeded the LOELs for the constituent chemicals. The mixture reduced serum thyroxine levels at concentrations that were at least an order of magnitude below their LOELs. The effects on thyroxine were cumulative (additive) at low doses and synergistic at higher doses. The activity of both estrogens and dioxin-like compounds is mediated through specific nuclear receptors. ATSDR has begun to develop interaction profiles, based on *in vivo* and *in vitro* laboratory studies, for some of the most common contaminants of concern in AOCs and contaminated sites, using a weight-of-evidence approach (DeRosa, presentation). *They recommend that mixtures be evaluated using a component-based approach that assumes additive joint toxic action*. A hazard index is calculated as the sum of individual hazard indices (exposure concentration ÷ toxicity threshold) for each component.

Due to analytical limitations, only a very low proportion of the large number of potentially troublesome compounds identified as likely present in the Great Lakes environment are currently analyzed in Great Lakes monitoring programs. Of greatest concern are those chemicals used in large quantities and in environmental concentrations similar to, or approaching, those known to cause adverse effects.

When investigators dosed sexually mature male rats with a complex mixture of organochlorines and metals for 70 days (one full cycle of spermatogenesis), they induced effects on liver physiology and T-cell function at low-to-moderate doses. Effects were also seen on liver, kidney, and general metabolism at high doses, but there was no apparent effect on reproductive physiology (Wade *et al.* 2002a). The mixture consisted of 12 organochlorines and two metals frequently detected in human tissues and were administered at 1, 10, 100, and 1,000 times the tolerable daily intakes (TDIs) for the individual substances. Thyroid-hormone physiology was affected at the lowest concentration that is currently accepted as the TDI (Wade *et al.* 2002b). This is consistent with the findings of Crofton *et al*. (2005). Given that individuals are exposed to chemical mixtures similar to those used by Crofton *et al*. and Wade *et al*., the current TDIs may not be sufficiently protective of thyroid homeostasis or the liver.

5.14.4 Prevention at Source

The "emerging" chemicals highlighted in this chapter illustrate the inadequacy of the current approach to chemical regulation to protect public health and the environment. The question could be asked, "Have we learned anything from the past regarding persistent, bioaccumulative, and lipophilic compounds?" In an editorial entitled, "A Sluggish Response to a Smoldering Problem," Reddy (2005) asks why PBDEs are used despite all of the data and scientific knowledge that has been available for decades. If persistence and bioaccumulation were used to screen for potential hazards, then the size and seriousness of future "surprises" could be reduced. However, less than 10 percent of high-volume industrial chemicals have been evaluated regarding their bioaccumulation, environmental fate, and toxicity.

A much more precautionary, responsive, and democratic approach is clearly required. Thornton (2000) identified several reasons why the current risk paradigm is inappropriate for the regulation of chemicals—particularly persistent, bioaccumulative chemicals—on a global scale (Table 3).

Table 3.
Limitations of Current Risk Paradigm for Chemical Regulation

Risk Assessor's World	The Great Lakes
Assumes a well-characterized, linear system where probabilities of individual events can be added or multiplied to yield the probability of an overall outcome, and where uncertainties can be defined and quantified.	Living organisms and ecosystems are complex, unpredictable, interconnected, and hierarchical. Characterized by multifactorial causality, redundancy, multiple functions, and critical periods of high sensitivity. Scale effects are common in living systems. These systems are not well understood or characterized. There is much uncertainty and even greater ignorance. Reliable predictions are therefore impossible and illusionary.
Assumes impacts are local and immediate.	Chemicals enter water, atmosphere, and biota, and are very mobile. Therefore a "local scenario" is inadequate. The effects of chemicals may not be immediate, but depend on bioaccumulation or a particular combination of stresses. Effects may be transgenerational.
Assumes that living things can absorb and eliminate synthetic chemicals.	Individual organisms and the Great Lakes ecosystem have limited capacity to cope. Chemicals accumulate in media and often bioaccumulate in organisms.
Assumes exposure to one chemical at a time.	Organisms and ecosystems are chronically exposed to a complex and variable cocktail of synthetic chemicals, which is usually poorly characterized.
Requires adequate and appropriate data.	Adequate data are lacking for the majority of chemicals in commerce. Industry's capacity to invent and produce new chemicals has overwhelmed both their ability to produce adequate data for the regulatory system to assess, and the regulatory system's capacity to assess it.
Frequently recommends "end-of-pipe" approaches of control and disposal.	These approaches at best reduce contamination. They transfer substances from one form to another and from one location to another. Little is actually eliminated.

Human-health effects associated with contaminants in fish include a range of serious health consequences involving neurodevelopmental, reproductive, carcinogenic, respiratory, behavioural, and circulatory systems.

It is difficult for decision makers to make wise decisions when environmental or health impacts may occur far into the future. The costs of impact-averting decisions are large and immediate. Prevention usually requires acting before there is strong proof of harm, particularly if the harm may be delayed and irreversible. This protective approach to scientific evidence and policy making is part of the Precautionary Principle. One task of the European Environmental Agency (EEA) is to provide information to improve decision-making and public participation in regard to toxic compounds and their use in commerce. The EEA gathers information on the hazards of human activities and uses it to propose actions to better protect the environment and the health of species and ecosystems that are dependent on it. The process provides information in situations of scientific uncertainty.

The issues associated with "legacy" and "emerging" contaminants of concern and the contaminant-associated health effects described in this chapter are, to varying degrees, surprises, in that they highlight the short-sightedness of our profit-driven approach to innovation, and the inadequacy of our hazard-based regulatory system. They illustrate that having sufficient information and acting wisely for the wide range of environmental and health issues are a daunting task. The interconnections among issues, the pace of technological change, our limited understanding of effects, and the "time to harm and then to heal" ecological and biological systems affected over decades by our technologies present an unforgiving context (Beltran in EEA 2001). They also present immense and exciting challenges, and opportunities to understand the system and meet human needs while greatly reducing ecological and health costs. Other jurisdictions widely apply the Precautionary Principle to stimulate innovation and science, and provide good governance.

In trying to reduce current risks and future surprises, the lessons of history have rarely been used. The EEA's publication, *Late Lessons from Early Warnings: The Precautionary Principle 1896-2000* (EEA 2001) is an exception. Fourteen case studies are presented representing a variety of well-known hazards to workers, the public, and the environment, where sufficient information is now known about their impacts to enable conclusions to be drawn about how well they were dealt with by governments and civil society. The cases include collapsing fisheries, mad-cow disease, radiation, a variety of chemicals and drugs, growth promoters, and chemical contamination of the Great Lakes. The cases consider "false negatives," agents or activities that were regarded at one time as harmless by governments and others at prevailing levels of exposure, and "control," until evidence about harmful effects emerged. From the cases, 12 lessons were distilled (Table 4).

Table 4.
Twelve Lessons to Guide Sound and Effective Policies to Minimize Future "Surprises"

- Respond to ignorance as well as uncertainty
- Research and monitor for "early warnings"
- Search out and address "blind spots" and gaps in scientific knowledge
- Identify and reduce interdisciplinary obstacles to learning
- Ensure that real-world conditions are fully accounted for
- Systematically scrutinize and justify the claimed "pros" and "cons"
- Evaluate alternatives and promote more robust, diverse, and adaptable solutions
- Use "lay" and local knowledge as well as all relevant specialist expertise
- Take account of wider social interests and values
- Maintain regulatory independence from economic and political special interests
- Identify and reduce institutional obstacles to learning and action
- Avoid "paralysis by analysis" by acting to reduce potential harm when there are reasonable grounds for concern

A new approach to chemical regulation is required that incorporates these lessons. Thornton (2000) proposed an ecological paradigm to prevent global chemical pollution built around four principles:

- Zero discharge;
- Reverse onus (one could add Responsible Care and Product Stewardship);
- Emphasis on classes of compounds; and
- Clean production.

5.15 Conclusions

A number of strategies have been identified to address concerns related to new and emerging contaminants. They include:

- Work with industry to develop and implement cost-effective strategies that reduce ongoing releases to the environment from consumer products that enter waste streams;
- Require a basic information package that includes the octanol/water partition coefficient and that persistence data be made available for all compounds;
- Systematically monitor concentrations in human blood and breast milk, sport fish, and fish-eating birds;
- Support research on the health effects of these chemicals in fish, fish-eating wildlife, and humans at environmentally relevant concentrations, singly and in mixtures;
- Formalize and adequately fund programs that monitor health effects in humans, fish, and wildlife;
- Provide appropriate funding to investigate the effects of pharmacologically and hormonally active chemicals in fish and fish-eating wildlife at environmentally relevant concentrations;
- Develop cost-effective strategies for collecting and destroying unused or expired medications, and for reducing and treating waste streams from hospitals;
- Introduce labeling programs for PPCPs that enable consumers to make environmentally friendly choices concerning use and disposal; and
- Assess the impact of contaminants in biosolid and liquid-manure applications to agricultural lands in terms of exposure and effects on terrestrial wildlife.

There are a wide variety of transport pathways by which "emerging" chemicals enter and persist in surface waters. Some compounds, such as pesticides, are intentionally released in measured applications. Others, such as industrial by-products, are released through regulated and unregulated industrial discharges to water and air. Some are deposited in precipitation. Household chemicals, pharmaceuticals, and other consumables as well as biogenic hormones are released directly to the environment after passing through wastewater treatment plants or domestic septic systems, which often are not designed to remove them from the effluent. Veterinary pharmaceuticals and growth-promoting hormones used in animal feeding operations may be released to the environment with animal wastes through surface runoff, overflow, or releases from storage structures or land application.

Municipal wastewater treatment plants discharge much of the PFOS, PPCPs, synthetic estrogens, and estrogenic alkylphenols entering the Great Lakes. Most removal of these chemicals from wastewater occurs during advanced treatment. To be more effective, medium- and larger-sized sewage plants must be upgraded to incorporate secondary biological treatment with retention times of greater than 15 hours, as well as nitrification combined with denitrification. Tertiary treatment processes such as activated carbon filtration, ozonation, and membrane filtration will further reduce—but not eliminate—the loads of these "emerging" chemicals into the lakes.

Great Lakes success in environmental management to date is largely based on regulation and control programs. The concentrations of targeted chemicals such as PCBs have decreased markedly since regulations were introduced, but current rates of decrease are very low because regulation does not address the legacy sources—contaminated sediments. To eliminate the need for fish consumption advisories, cleanup of PCB-contaminated sediments and a 90 percent reduction of mercury emissions from U.S. coal-fired power plants within the next 10 years are required.

Meanwhile, concentrations of new classes of persistent toxic contaminants such as BFRs and PFCs are increasing rapidly in tissues of humans, wildlife, and fish. Laboratory studies suggest some "emerging" contaminants have toxicities and modes of action similar to "legacy" contaminants. Precautionary regulatory actions effectively reduce exposure to "emerging" chemicals. For example, concentrations of brominated diphenyl ether 47 are now declining in breast milk in Sweden (Bergman, presentation at Brominated Flame Retardants 2004). Germany's precautionary actions to reduce exposure to alkylphenols are already reflected in declining concentrations in fish (Wenzel *et al.* 2004). Kirby *et al.* (2004) have shown a striking relationship between the introduction of secondary treatment at the Howden sewage-treatment plant on the River Tyne with the reduction of mean estrogenic potency of the effluent from 80 to 0.4 ng/L and the reduction in plasma vitellogenin in male flounder caught near the outfall.

Since consumption of many "emerging" chemicals is expected to increase as populations grow and age, a proactive, precautionary, cost-effective control strategy must focus on reduction, minimization, and elimination at the source. This includes:

- Separate and appropriate treatment for hospital and industrial wastewater, and treatment of effluents from concentrated animal-feeding operations;
- Regulations to ensure that unused, expired pharmaceuticals are collected and appropriately destroyed under controlled conditions; and
- Environmental labeling introduced in cooperation with industry.

In this biennial cycle it became clear that our understanding of health hazards associated with "legacy" contaminants has increased much more rapidly than their levels are currently decreasing. PCB and mercury levels in fish are many times greater than values protective of human health. PCB concentrations in fillets of some large lake trout from Lake Michigan exceed by 40 fold the level which would allow unrestricted consumption. Despite consumption advisories, many individuals are exposed unnecessarily, and often unconsciously, to toxic contaminants through their diet. We have also learned that air transport is an important pathway of exposure and that living near highly contaminated areas increases one's exposure. In addition, we have become aware of "emerging" chemicals that were not previously detected. There is also a growing awareness of a larger range of developmental and functional health impacts associated with exposure to mixtures of chemicals, including the persistent "legacy" contaminants and the "emerging" chemicals. It is now clear that a single chemical can have an impact on multiple-organ systems via several exposure pathways and a number of modes of action, and that those impacts can be expressed in multiple ways. Many "emerging" chemicals affect the same target organs and/or systems as the "legacy" chemicals and will contribute to the cumulative toxicity. What evidence of human-health effects will be sufficient to create the political will to clean up the areas that continue to make major contributions to system contamination?

If sufficient resources to support remediation and required protection efforts are to be committed, Great Lakes citizens must understand the risks and demand accountability under the Agreement for long-term progress and implementation strategies that are protective of human and wildlife health and 20% of the world's fresh surface water.

The need for improving overall coordination of Great Lakes, coastal, and ocean activities has been emphasized repeatedly in recent years ...

5.16 Recommendations

The Science Advisory Board recommends to the IJC that:

- **The Parties target brominated flame retardants, perfluorinated alkylsulfonates (and their salts), and alkylphenols as Level 1 substances under the Binational Toxics Strategy in order to achieve their policy of virtual elimination of the discharge of persistent toxic substances.**
- **The Parties invest in strategies to detect and mitigate the environmental effects of new and emerging contaminants.**
- **The Parties' Binational Executive Committee adopt a binational approach to the use of the precautionary principle in the management of chemicals in the Great Lakes basin.**
- **The Parties accelerate the removal of severely contaminated sediment from Areas of Concern.**
- **The Parties modify their fish consumption advice to address overall fish consumption to focus on:**
  - **Developing a single advisory that addresses both lipid-soluble contaminants such as PCBs, dioxins, and pesticides as well as methylmercury;**
  - **Providing readily accessible information that is linguistically, culturally, and economically appropriate;**
  - **Reaching the most vulnerable populations;**
  - **Promoting special precautions for pregnant women including effects on the fetus, women of child-bearing age, and children under 15, and advocating that this group adopt the additional prudence of not eating Great Lakes fish as an option; and**
  - **Providing information on nutritionally equivalent alternatives to fish.**
- **The Parties conduct a thorough and transparent benefit-cost analysis of mercury emissions to the Great Lakes environment, including impacts on the health of humans and wildlife, lost economic activity to sport and commercial fishing, as well as the costs of controlling emissions from coal-fired power plants, chloralkali plants, and other sources and remediating mercury contamination.**
- **The Parties undertake human health-effects research focusing on multi-media exposure due to place of residence, with consideration of non-cancer effects such as heart and respiratory disease, diabetes, and endocrine, reproductive, and neurological disorders.**

5.17 Appendix – Emerging Contaminants of Concern

5.17 1 Brominated Flame Retardants

Name

Polybrominated diphenyl ethers (PBDEs), hexabromocyclodecane (HBCD), tetrabromo bisphenol A (TBBPA), bis(2,4,6-tribromophenoxy)ethane (BTBPE)

Use and Sources

PBDEs are manufactured in three mixtures. The penta-BDE mixture is used almost entirely on polyurethane foam in upholstered furniture. The octa-BDE mixture is used exclusively in plastic resins for electronic housings. Deca-BDE is primarily used in thermoplastics for electronic equipment housings (TVs and computers), and smaller amounts are used to flame retard upholstery textiles. PBDEs are "additive" flame retardants and are blended with, rather than covalently bonded into, the product. They can comprise as much as 50 percent by weight of foam cushions. Global demand for PBDEs in 1999 reached 67,125 tonnes, near the PCB production maximum in 1970.

HBCD is the most widely used brominated fire retardant (BFR), at around 16,000 tons per year. HBCD is added to polystyrene foams that are used as thermal insulation in the building industry. Lesser amounts are used in upholstery textiles for furniture and transportation seating, and in draperies and wall coverings. It is considered a replacement for PBDEs.

TBBPA is another high-volume BFR widely used in paper products, clothing, upholstery, carpets, and other household materials. It is also found in resins, polycarbonates, and other plastics used to make computers, the housing for other electronics such as telephones, appliances, circuit boards, and many other consumer products. Worldwide, this is the most used BFR.

BTBPE is used in high-temperature plastics.

BFRs slowly volatilize into the environment during the treated product's lifetime. Concentrations in indoor air are much greater than outdoor air (Wilford *et al.* 2004). The large amounts in residential-use products suggest that the home environment is a significant source of human exposure. High concentrations of PBDEs have been measured in house dust and clothes dryer lint (Stapleton *et al.* 2005), particularly of congeners associated with the penta- and deca-BDE mixtures.

Urban indoor air is a source to urban outdoor air, which is a source to the regional environment (Butt *et al.* 2004, Shoeib *et al.* 2004). Currently PBDE concentrations equal or exceed those of PCBs in rural Ontario air.

Thus, large reservoirs exist of the penta-BDE mixture and other BFRs in the form of treated products (cars, upholstered furniture, carpets, and electronics), which will serve as sources for years to come. Environmentally friendly methods of disposal of polyurethane foam, cars, upholstered furniture, carpets, TVs, and computers must be found and practiced.

History

PBDEs were introduced in 1972 to replace PCBs. By 1986, a voluntary phase-out was initiated in Germany, followed by legislation to restrict their use in 1993. Swedish chemists reported that PBDEs had doubled in human breast milk every five years since their introduction in 1972 (Darnerud *et al.* 1998, Noren and Meironyte 2000). Sweden proposed a phase-out by March 1999.

Penta-BDEs are being considered a "potential/candidate" under the United Nations Economic Commission for Europe's persistent organic pollutant convention. Great Lakes Chemical Company, the sole producer of penta-BDE in the U.S., chose to phase out production by the end of 2004. The European Union phased out the use of the penta- and octa-BDE mixtures in 2005 and California will do so in 2008.

The United Kingdom's Chemical Stakeholder's Forum determined that HBCD is persistent, bioaccumulative, and toxic, and poses a risk to the environment.

Properties

PBDEs are persistent, hydrophobic, lipophilic, bio-accumulative, and subject to long-range transport. They have a greater tendency than PCBs to adhere to particles that are washed out of the atmosphere by precipitation.

Current Concentrations

See Table 2. It is estimated that approximately 15 million people in the U.S. have lipid PBDE levels greater than 300 parts per billion.

Concerns

Residues of PBDEs are ubiquitous in the global environment. In North America, tissue concentrations are doubling every two to five years in fish, whales, birds, and humans (Hites 2004, Lebeuf 2004). The doubling time in human tissues in North America is shorter than in Europe and Japan, where tissue concentrations are less than one-tenth of those measured in North America. If present rates of change continue, total BDE concentrations will surpass those of PCBs in gull eggs and lake trout tissues within a decade. Norstrom *et al.* (2002) found that penta-BDE, which is mainly used in polyurethane foam, was responsible for the rapid increase in overall concentration in gull eggs. Dramatic increases in PBDE concentrations toward the surface of sediments are evident in Great Lakes sediment cores (Song *et al.* 2005).

In a study conducted in Indiana, the concentrations of PBDEs in maternal and fetal-blood samples were very similar (Mazdai *et al.* 2003), confirming that PBDEs cross the placenta. Structurally, PBDEs are similar to the thyroid hormone thyroxin. Like PCBs, each PBDE congener exhibits different potency and toxicity. Chronic administration of PBDE congeners during

lactation (neonatally) to rodents revealed thyroid and estrogenic effects similar to some PCBs (Zhou *et al.* 2002), and altered expression of estrogen-regulated genes in the prostate and the brain (Lichtensteiger *et al.* 2003). Rodent studies revealed altered spontaneous behavior (Eriksson *et al.* 2002), learning and memory difficulties that became worse with age (Viberg *et al.* 2003), as well as hearing loss, delayed puberty, and increased ventral prostate and seminal vesicle weight gains in males (Stoker *et al.* 2004), and delayed puberty in females (Laws *et al.* 2003). The additive effect of PBDEs with co-exposure to PCBs increases concerns about their impacts on development of the brain and reproductive system. The presence of PBDEs in household products makes indoor-air exposure a pathway of concern, especially for infants and small children.

When American kestrel eggs were injected with a mixture of penta-BDE congeners and the hatchlings fed a diet containing the same mixture at environmentally relevant concentrations, T-cell mediated immunity and relative bursal mass were inversely associated with BDE-47 (Fernie *et al.* 2005). There were also structural changes in the spleen, bursa, and thymus. These exposures also altered thyroxin and vitamin A homeostasis and induced oxidative stress (Fernie *et al.* in press). In *in vitro* assays using lake trout thymocytes, BDE-47 markedly reduced thymocyte viability, increased apoptosis and necrosis at 100 mg/L, whereas the effects of BDE-99 were minor at this concentration (Birchmeier *et al.* 2005).

HBCD is bioaccumulating and biomagnifying in the Lake Ontario food chain at a rate similar to DDE and PCBs (Tomy *et al.* 2004). Very little is known about its toxicity, and nothing is known about the toxicity of BTBPE, which is a modified diphenyl ether.

5.17.2 Perfluorinated Acids, Alcohols, and Salts

Name

The compounds of concern include N-ethyl perfluorooctane sulfonamidoethanol (N-EtFOSE), the acrylate polymer and parent compound of perfluorooctane sulfonate (PFOS, Scotchgard®), and aqueous film-forming foams such as Light Water Line®. N-EtFOSE eventually breaks down into two end products widely found in the environment, PFOS and perfluorooctanoic acid (PFOA). The fluorinated compounds also include polytetrafluoroethylene (PTFE or Teflon®).

Use and Sources

Approximately 14.3 million pounds of perfluoronated chemicals (PFCs) were produced in 2002. N-methyl perfluorooctane sulfonamidoethanol (N-MeFOSE, Scotchgard®) was used for surface treatments of apparel, leather, upholstery, carpet, and auto interiors, and on paper products such as plates, bags, food wraps, and masking paper. N-EtFOSE (Scotchban®) and PTFE are used in the production of industrial coating applications, fire-fighting foam, lubricants in aeronautical systems, industrial surfactants, floor polishes, photographic film, denture cleaners, shampoos, and floor finishes.

Environmental sources are largely uncharacterized. Direct sources are aqueous film-forming foams and indirect sources through abiotic or biotic degradation of products used in surface treatment applications. Concentrations in indoor air are significant and about 100 times those in outdoor air (Shoeib *et al.* 2004), suggesting that they originate in releases from products present in homes and businesses. Despite manufacturing phase-outs, these products will serve as a continuing source throughout their lifetimes, and exposure is greater in more urbanized areas than in more remote areas. Mass balance studies on Lake Ontario revealed that the greatest source of N-EtFOSE and PFOS was from municipal wastewater effluent discharges (Hornbuckle, presentation). PFOS in effluents comes directly from consumer products through sewage systems. PFOS was found in household vacuum cleaner dust at 3.7 ppm (Moriwaki *et al.* 2003). A survey of sewage sludges from wastewater treatment plants in the San Francisco Bay area revealed concentrations of 55 to 3370 ng/g for total PFOS-based chemicals (Higgins *et al.* 2005).

History

PFOS and related PFCs had been manufactured by 3M Company since 1948. Due to concerns about biopersistence and widespread exposure to wildlife and humans, 3M announced in 2000 that it would voluntarily cease production of PFOS-based chemicals as of December of that year. The U.S. Environmental Protection Agency (EPA) immediately proposed legislation that would regulate new uses of PFOS and related chemicals. In 2001, Kannan *et al.* confirmed widespread contamination in humans and wildlife over large geographic areas. In 2004, Environment Canada released a Draft Screening Assessment that concluded PFOS, its salts, and its precursors are "toxic" under Paragraph 64(a) of the 1999 Canadian Environmental Protection Act (CEPA), and recommended that they be considered for virtual elimination under subsection 65(3). Sweden proposed a ban to eliminate PFOS under the Stockholm Convention.

Properties

PFCs have unique physical, chemical, and biological properties. They are both lipophobic and hydrophobic. They do not accumulate in lipid-rich tissues, but bind to proteins and accumulate in the liver and blood. Their high-energy, carbon-fluorine bond renders them resistant to all known forms of abiotic and biotic degradation. In laboratory tests, bioconcentration of PFCs increases with carbon-chain length. In mink that were fed Saginaw Bay carp containing a mean of 120 ng/g, the mean biomagnification factor was 18, similar to that of PCBs in the same study (Kannan *et al.* 2002). However, a bioconcentration factor range of 6,300 to 125,000 was calculated for PFOS based on concentrations in fish liver and surface water following an accidental spill of perfluorinated surfactant-containing fire retardant foam (Moody *et al.* 2002).

Current Concentrations

See Table 2. In humans, 645 adult donor serum samples from six American Red Cross blood-collection centers had a geometric mean PFOS concentration of 35 ng/ml (4 to 1,656), somewhat higher in males than females, but no substantial difference with age (Olsen *et al.* 2003).

Concerns

Organofluorine residues in wildlife tissues suggest they are globally distributed (Giesy and Kannan 2002). PFOS concentrations doubled every twelve years between 1980 and 2001 in archived lake-trout tissue from Lake Ontario (Martin *et al.* 2004). Boulanger *et al.* (2005) highlight the need for monitoring studies to identify wastewater treatment plants with unusually high concentrations of PFCs in their effluent so that remedial actions can be taken.

Related fluorochemicals have been shown to affect cell-to-cell communication, membrane transport, and the process of energy generation. PFOS and PFOA exhibit multi-system, low-dose toxicity, driven by several mechanisms including mitochondrial activity, peroxisome proliferation, inhibition of thyroid hormones, and increased serum estradiol as a result of liver aromatase induction (Thayer, presentation).

Exposure of rats and mice to PFOS during pregnancy at concentrations of 1 to 20 mg/kg resulted in maternal (weight loss, decreased thyroxine, reduced triglycerides) and developmental toxicity (birth defects) in both species (Thibodeaux *et al.* 2003), compromised neonatal survival, and caused delays in growth and development that were accompanied by hypothyroxinemia in the surviving rat pups (Lau *et al.* 2003). U.S. EPA has raised concerns about the long residence time of PFOS in humans, high blood concentrations, and the possibility of developmental risk to fetuses and children. Little is known about the toxicity of PFOS in wildlife.

5.17.3 Phthalates

Name

Diethylhexylphthalate (DEHP), butylbenzylphthalate (DBP), and di-n-butylphthalate

Use and Sources

Phthalates are produced in extremely large volumes and their use is increasing. Production of DEHP, the most widely used phthalate, amounts to 400,000 to 500,000 tons per annum in Europe alone. Phthalates are found in soft plastics and packaging, cosmetics (up to 50 percent by weight), insecticide sprays and repellants, carpeting, wood finishes and paints, coating on time-release capsules, vinyl flooring, adhesives, sealants, car-care products, inks, and medical equipment. Since phthalates are not covalently linked to the plastic polymer, they leach out into the environment. It has been estimated that one percent of phthalates used are eventually lost to the environment (ECPI 1996).

History

Phthalates have been used in plastic and other products for a long time.

Current Concentrations

Phthalates are ubiquitous. However, for decades analytical challenges prevented an accurate assessment of their concentrations. Today, modern instrumentation and "clean" laboratory procedures permit their measurement, but few data are available.

In a nationwide survey of phthalates in stream-bed sediments (Lopes and Furlong 2001), the western Lake Michigan drainage was among those sites with the highest concentrations (sum approximately 850 ppm). High concentrations were found in urban and industrialized regions and in large metropolitan areas. DEHP, DBP, and di-n-butlyphthalate were the most frequently found in environmental samples.

Eight phthalates were detected in dust from 86 to 100 percent of households with maximum concentrations ranging from 31,000 ng/g (DBP) to 7,700,000 ng/g (DEHP) (Rudel *et al.* 2003). These same phthalates were detected in air samples from 15 to 100 percent of the same households, with median DEHP (530 ng/m^3, 130 to 4300) and DBP (220 ng/m^3, 52 to 1100) concentrations being the highest. These data suggest indoor air is an important exposure vector.

Concerns

Phthalates are of concern because they accumulate in the environment and human blood, have numerous exposure vectors, and act as endocrine disruptors in rodents. Some, including DBP and DEHP, are weakly estrogenic *in vitro* (Harris *et al.* 1997). They are testicular toxins (Gray and Gangolli 1986), reproductive teratogens (Barlow and Foster 2003) and embryo toxins, and anti-androgens (Mylchreest *et al.* 2000, Fisher 2004). Among the phthalates, DEHP is the most potent anti-androgen (Gray *et al.* 2000).

In a multigenerational reproductive toxicity study, Wine *et al.* (1997) found that several reproductive parameters were adversely affected by exposure to DBP in food, and that the second generation appeared more adversely affected than the first in that most of the F1 males were infertile. Prenatal phthalate exposure has been associated with shortened anogenital distance in boys (Swan *et al.* 2005). Anogenital distance was correlated with penile volume and the proportion of boys with incomplete testicular descent. These associations between male genital development and phthalate exposure are consistent with the phthalate-induced incomplete virilization observed in prenatally exposed rodents (Gray and Foster 2003).

Monoethylphthalate (MEP) was found 100 percent of the time in the urine of 2,540 human subjects at a geometric

mean concentration of 179 ppb (Silva *et al.* 2004). MEP in human urine has been associated with alterations and increased DNA damage in sperm (Duty *et al.* 2003a, b). Exposure to monobutylphthalate is associated with reduced sperm motility and velocity (Swann *et al.* 2005).

5.17.4 Pharmaceuticals, Personal Care, and Household Products

Low levels of reproductive hormones, steroids, antibiotics, pain killers, contraceptives, beta-blockers, lipid regulators, tranquilizers, anti-epileptics, serotonin re-uptake inhibitors, and numerous other prescription and non-prescription drugs, as well as some of their metabolites, have been detected in surface waters. Along with pharmaceuticals, products used in everyday life such as detergents, disinfectants, fragrances, insect repellents, fire retardants, and plasticizers are turning up in the aquatic environment. Effluents from concentrated animal feeding operations contain antibiotics and growth-promoting hormones. Little is known about the toxicity of these "emerging" contaminants at low levels and on non-target organisms, particularly hormonally active chemicals, pesticides, and pharmaceuticals that are designed to stimulate a response in humans, animals, and plants. It is difficult to predict what health effects they may have on humans and aquatic systems (Erickson 2002), and they always occur in a complex mixture.

Exposure

During and after treatment, humans and animals excrete a combination of intact and metabolized pharmaceuticals in the form of bioactive metabolites. Personal care products do not have to pass through the human body, but enter wastewater directly after their use. Wastewater treatment plants are likely to be the most significant conduit of human medications to surface waters, while application of contaminated livestock manure may also contribute a high load of veterinary drugs to the aqueous phase of runoff events. Sewage is a continuous point source, while runoff from agriculture is diffuse and concentrations are dependent on the application rate and runoff parameters.

Pharmaceuticals were reported in Lake Ontario and Lake Erie surface waters in 2000 and in final effluents from wastewater treatment plants on the Detroit and Niagara Rivers in 2001. They included Carbamazepine (an anti-epileptic) at 0.65 ug/L, naproxen and ibuprofen (anti-inflammatories), and several lipid-regulating drugs found below three wastewater treatment plants. Concentrations remained constant as far as 100 metres downstream. Fluoxitine (Prozac®) was found in the final effluent at three out of four locations as high as 0.099 ug/L, and in downstream surface water (Metcalfe, presentation).

Koplin *et al.* (2002) measured 95 organic wastewater contaminants in water from 139 streams across 30 states in 1999 to 2000; 82 were found at least once, and 80 percent of the streams contained two or more. As many as 38 contaminants were measured in a single sample, with a median of seven. The most frequently encountered were diethyltoluamide (an insect repellent), caffeine (a stimulant), triclosan (antimicrobial disinfectant), tri (2-chloroethyl) phosphate (a fire retardant), and nonylphenol (NP) (non-ionic detergent metabolite). Three classes of compounds—the detergent metabolites, plasticizers, and steroids—had the highest concentrations.

Synthetic musks, used as fragrances in a variety of personal care products, are consistently found in municipal wastewater discharges (Simonich *et al.* 2002). More than one million pounds of one such compound, HHCB (Galaxolide), is produced or imported into the U.S. annually. It was estimated that 3,470 kilograms enters Lake Michigan in wastewater effluents each year (Peck and Hornbuckle 2004). Simonich *et al.* (2002) found a mean of 1,640 ng/L in 12 U.S. wastewater treatment plant effluents.

Concerns

For the most part these substances are not bioaccumulative, but their continual input into the environment ensures their persistence. By design, pharmaceuticals and pesticides are biologically active at the cellular-receptor level. Therefore, very low concentrations may be biologically significant. Potential concerns about the environmental presence and chronic low-level exposure to these compounds include abnormal physiological processes, reproductive impairment, teratogenicity, altered behavior, increased incidences of cancer, development of antibiotic-resistant microorganisms, and potentially increased toxicity and interactions of complex chemical mixtures and effects. In addition, the pharmacological target of a drug in mammals may be markedly different in fish and other organisms. For example, Propranolol is a potent inhibitor of photosynthesis by algae (Escher *et al.* 2005). Preliminary studies suggest prostaglandin-inhibiting analgesics frequently found in water are capable of altering reproductive function and behavior in fish (Miller *et al.* 1999, Stacey 1976), blood-lipid regulators alter their intermediary metabolism (Donohue *et al.* 1993, Haasch *et al.* 1998), and serotonin re-uptake inhibitors induce developmental abnormalities, increase plasma estradiol, and alter their migration behaviors (Brooks *et al.* 2003). Inui *et al.* (2003) found three common ultra-violet screens to be estrogenic to male Japanese medaka, a fish commonly used in toxicity testing. There is almost no information about the effects of mixtures of this vast array of compounds at environmentally relevant concentrations.

Triclosan exhibits antibacterial, antifungal, and antiviral properties and is therefore a very useful disinfectant. Its incorporation into toys, kitchen tiles, athletic clothing, and other products, coupled with its occurrence in surface water and wastewater treatment plant effluent, have raised concerns that they might promote microbial resistance.

Synthetic musks, including HHCB, bioaccumulate and have been found in top predators in marine food chains (Nakata

2005). In marine mammals there is evidence of transplacental transfer. Synthetic musks test positive in *in vitro* assays for estrogenic activity (Bitsch *et al.* 2002, Scheurs *et al.* 2004). Elevated levels of musks in women's blood have been associated with ovulation and premenstrual symptoms and in a dose-response manner with miscarriage (Eisenhardt *et al.* 2001).

5.17.5 Estrogenic, Androgenic, and Other Hormonally Active Compounds

Name

These compounds are called ethinyl estradiol, bisphenol A (BPA), Trenbolone, and alkylphenol ethoxylates (treated separately in the next section).

Use and Sources

Ethinyl estradiol, the potent synthetic estrogen present in birth-control pills, and 17-beta estradiol, the naturally produced female estrogenic hormone, are excreted in feces and urine and enter open waters via municipal sewage effluents. BPA is a building block in polycarbonate and other plastic resins and is used to line food containers, make baby bottles, high-impact sporting equipment, dental sealants, and shatterproof glass. It is also used in detergents to reduce re-deposition of dirt and has been found in wastewater from commercial laundries. Its production in the U.S. alone exceeds 800 million kilograms a year. The concentrations of 17-beta estradiol— the hormone normally excreted by premenopausal women— found in the environment can have disruptive effects on key steroidogenic enzyme pathways that control sexual development in fish (Halm *et al.* 2002).

Trenbolone and melengestrol are licensed to promote the growth of livestock in North America. The anabolic effect of Trenbolone is eight to ten times stronger than testosterone, while melengestrol is 125 times more potent than progesterone (Neumann 1976).

Concerns

Exogenous hormones modulate a system that is physiologically active, potentially above any response threshold that might exist. Ethinyl estradiol was found in surface waters across the U.S. in a recent survey (Koplin *et al.* 2002).

BPA has been found in raw sewage, sewage sludge, and final effluents across the continent. The median concentration in sewage sludge in 35 samples from across Canada was 0.45 ug/kg, with a maximum of 5 ug/kg (Environment Canada 2001). However, it has been found in the Mississippi River as high as 113 ppb and in storm-water channels at 158 ppb. BPA was detected in dust samples from 86 percent of 118 homes at a median concentration of 821 ng/g (range from less than 200 to 17,600 ng/g) (Rudel *et al.* 2003).

Trenbolone had a half-life in liquid manure of more than 260 days (Schiffer *et al.* 2001). Effluents from concentrated cattle feeding operations contain significant amounts of estrogenic and androgenic activity (Soto *et al.* 2004). Male fathead minnows were demasculinized and females defeminized in a stream receiving such effluent (Orlando *et al.* 2004). Laboratory exposures of fathead minnows to Trenbolone for 21 days altered female and male reproductive biology (Ankley *et al.* 2003). Fecundity was significantly reduced by exposure to concentrations greater than 27 ng/L.

The presence of estrogens in the aquatic environment has been intensively studied in the U.K., where they were associated with an elevated incidence of intersex in the gonads of fish (Jobling *et al.* 1998). Similar surveys in North America suggest that they are also present in biologically significant concentrations in surface waters (Koplin *et al.* 2002). Fish below sewage treatment outfalls have altered sex steroid ratios, abnormal reproductive organs and, upon prolonged exposure to the estrogens, the critical threshold of response is lowered (Jobling *et al.* 1998). Nichols *et al.* (1999) did not find any evidence of endocrine disruption in fathead minnows caged for 21 days near the outfalls of seven municipal WWTPs in central Michigan.

Metcalfe *et al.* (2001) used the Japanese medaka bioassay to determine the relative estrogenic potency of estrogen hormones, nonylphenol ethoxylate (NPEO) degradation products, BPA, and DEHP using the development of intersex gonads and altered sex ratio as end points. The lowest observed effect levels (LOELs) were 0.03 ng/L for ethinyl estradiol, 4 ng/L for estradiol, 8 ng/L for estrone, 31,000-47,000 ng/L for NPEO plus nonphenol diethoxylate, and 5,900 ng/L for BPA. The LOELs for the estrogen hormones and alkyphenol ethoxylates are within the range of concentrations reported for wastewater treatment plant effluents. Ethinyl estradiol induced vitellogenin in male rainbow trout at a concentration of 1.8 ng/L (Jobling *et al.* 1996). When zebra fish were exposed to an environmentally realistic concentration of ethinyl estradiol of 5 ng/L over multiple generations, there was a 57 percent reduction in fecundity in the F1 generation and complete population failure due to a lack of functional testes (Nash *et al.* 2004). Although these males lacked functional testes, they showed normal spawning behavior, a phenomenon that is likely to affect breeding dynamics and reproductive success of group-spawning fish (Nash *et al.* 2004).

In 2000, the prevalence of intersex gonads in white perch was 83 percent in fish from Cootes Paradise in Hamilton Harbour, 44 percent in fish from the Bay of Quinte, and 45 percent in fish from Lake St. Clair (Kavenagh *et al.* 2004), but was not observed in hatchery-reared white perch. Analysis of plasma of male white perch collected in Cootes Paradise in 2002 revealed high concentrations of vitellogenin (Kavanagh *et al.* 2004). Male snapping turtles from Cootes Paradise also show evidence of feminization (de Solla *et al.* 1998). In surveys conducted 2001-2003 in Canadian Areas of Concern on the lower Great

Lakes and the Detroit River, vitellogenin was detected in male fish, snapping turtles, and herring gulls at several locations (Fox, presentation).

When Japanese medaka were exposed from hatching to sexual maturity to an environmentally relevant concentration of 10 ng/L ethinyl estradiol, reproductive behavior and performance were suppressed and intersex gonads were induced in males (Balch *et al.* 2004). Male fish with intersex gonads were capable of reproductive behavior and fertilizing eggs. The adult fish also showed evidence of liver and kidney toxicity (both sexes) and testicular toxicity (Weber *et al.* 2004).

Significant estrogenic activity in the St. Lawrence River is associated with vitellogenin induction, delayed spermatogenesis, reduced sperm production and motility, and a high incidence of intersexuality in male spottail shiners (Aravindakshan *et al.* 2004a). When lactating female rats were gavaged with homogenates of spottail shiners from these affected populations, their male offspring had significantly decreased sperm production and motility, and other indicators of altered testicular function (Aravindakshan *et al.* 2004b). This is the first indication that xenoestrogenic contaminants may pass through the food chain and exert their effects on the male progeny of predators.

Humans and their developing fetuses are widely exposed to BPA (Ikezuki *et al.* 2002). There are more than 100 published studies showing adverse effects of low doses of BPA in a variety of experimental animals (Vom Saal and Hughes 2005). Exposure to low doses during fetal life accelerates post-natal growth and advances puberty (Howdeshell *et al.* 1999), stimulates mammary epithelium (Markey *et al* 2001), disrupts the development of the fetal prostate and urethra (Timms *et al*. 2005), alters maternal behavior in mice (Palanza *et al.* 2002), and causes an increase in serum thyroxine in rat pups and alters the expression of a thyroid hormone-responsive gene in their brains (Zoeller *et al.* 2005). Post-natal exposure to very low doses disrupts meiosis in mouse oocytes (Hunt *et al.* 2003) and an epidemiological study of Japanese women has shown a correlation between both polycystic ovarian disease and obesity with blood levels of BPA (Takeuchi *et al.* 2004).

5.17.6 Alkylphenols

Name

The alkylphenol ethoxylates most commonly found in the environment are nonylphenol ethoxylates (NPEOs) and octylphenol ethoxylates (OPEOs), and their parent structures nonylphenol (NP) and octylphenol (OP).

Use and Sources

The use of NP is greater than OP. NPEOs are high-volume chemicals used as detergents, emulsifiers, and wetting and dispersing agents in many sectors including textile processing, pulp and paper processing, steel manufacturing, oil and gas recovery, and power generation. They are also used in paints, resins and protective coatings, and pest control products, and are found in cosmetics and cleaning products, degreasers, and detergents used in institutional and domestic sectors (Environment Canada 2001).

NP and NPEOs enter the environment primarily via industrial effluents (textile mills and pulp and paper mills) and municipal wastewater treatment effluents (liquid and sludge). Mean concentrations of NP and OP of up to 37,800 and 23,700 ng/g, respectively, were detected in sediments near sewage treatment plants and industrial wastewater discharges in the Great Lakes region (Bennett and Metcalfe 1998). Alkylphenols can be accumulated by biota near sewage outfalls, but distribution is localized to areas close to the point of discharge (Bennett and Metcalfe 2000). Substantial concentrations of NP and lower-chain NPEOs are found in sludge from municipal wastewater treatment plants. The application of NP-containing sludge to agricultural land may result in potential exposure in terrestrial environments. In the biosolids (sludge) from ten of 11 municipal wastewater treatment plants in the U.S., NP concentrations ranged from 5.4 to 887 ug/g, with a mean of 491 ug/g (La Guardia *et al.* 2001). OP was detected in eight of 11 of the biosolids tested at concentrations ranging from less than 0.5 to 12.6 ug/g. NP concentrations ranged from 0.07 to 1,260 ug/g (dry weight) (30 sites), with a mean of 491 ug/g in sludge samples from municipal treatment plants from across Canada (Environment Canada 2001). NP and NPEOs were detected in the dust from 80 to 93 percent of the 118 households at maximum concentrations ranging from 8,680-49,300 ng/g (Rudel *et al.* 2003).

History

Environment Canada concluded that NP and its ethoxylates are "toxic" as defined in Section 64 of CEPA ("entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity"). Norway banned the production, import, use, and distribution of NPEOs and OPEOs as of January 1, 2002.

Properties

The available literature suggests that the ability of NP and NPEOs to bioaccumulate in aquatic biota is moderate. Liber *et al.* (1999) measured a bioaccumulation factor of 87 for NP in bluegill sunfish in a littoral enclosure in northeastern Minnesota over a 20-day period.

Current Concentrations

See Table 2.

Toxicity

Chronic toxicity values (no-observed-effects concentrations) for NP are as low as 6 ug/L in fish and 3.9 ug/L in invertebrates. There is an increase in the toxicity of NPEOs with decreasing ethoxylate chain length.

NP and NPEO have been reported to cause a number of estrogenic responses in a variety of aquatic organisms. Their potency, however, is 100,000 less than estradiol. NP and NPEOs are found as complex mixtures in effluents and their combined estrogenic effects on aquatic organisms should be considered together. Exposure of sexually mature fathead minnows to NP at 1,600 to 3,400 ng/L for 42 days resulted in statistically significant effects on gonadal histology of males (Miles-Richardson *et al.* 1999), while concentrations as low as 50 ng/L have been observed to elevate plasma estradiol concentrations five-fold over background levels in males and females (Giesy *et al.* 1998). The lowest observed effects concentration for induction of testis-ova in Japanese medaka was 50,000 ng/L (Gray and Metcalfe 1997). In male rainbow trout, the lowest concentration to induce a significant increase in vitellogenin was 20,300 ng/L, and 54,300 ng/L significantly decreased testicular growth (Jobling *et al.* 1996). OP induced a significant increase in vitellogenin at 4,800 ng/L, but no effect was seen on testicular growth.

U.S. EPA estimated that 60 percent of the 6.9 million tons of biosolids generated in 1998 was land-applied (U.S. EPA 1999). They predicted that biosolid use would increase by 40 percent by 2010. The implications in terms of exposure to terrestrial organisms and contamination of surface waters have not been investigated. Scottish investigators have reported that near-term male fetuses of sheep pastured on land treated repeatedly with sewage sludge suffered from a major attenuation of testicular development and hormonal function (Paul *et al.* 2005). The liquid sludge applications contained a mean of 146 mg/kg NP (dry matter), 0.27 mg/kg OP, and 96 mg/kg DEHP (Rhind *et al.* 2002).

5.17.7 Atrazine

Use and Sources

Atrazine is a pre-emergent herbicide used on corn. The annual use in the U.S. Great Lakes basin was estimated at 2,700 tonnes (U.S. General Accounting Office 1993).

History

Introduced in Canada in about 1960, it was subsequently found infrequently and at high concentrations in surface waters (Bodo 1991). Lower application rates were introduced in 1993.

Prevalence and Concentrations

In more than 490 surface water samples from 29 locations representing all five Great Lakes from 1990 to 1993, Schottler and Eisenreich (1994) detected Atrazine in all samples with mean concentrations, by lake, ranging from 3 to 110 ng/L. The highest concentrations were measured in Lake Erie, the lowest in Lake Superior. Between 1994 and 2000, Environment Canada measured 39 in-use pesticides in large-volume surface water samples collected at multiple stations in two or three years, in lakes Erie, Ontario, Huron, and Superior (Struger *et al.* 2004). The number of pesticides detected ranged from 32 in Lake Erie to four in Lake Superior. The maximum concentrations of all pesticides occurred in samples from Lake Erie. Atrazine occurred in 97 percent of the samples, with a maximum concentration of 1,039 ng/L. Recent surveys by Environment Canada found a maximum concentration of 4,900 ng/L in eight tributaries to Lake Erie, and 450 ng/L in eight tributaries to Lake Ontario (Struger, personal communication).

Concerns

Of the pesticides surveyed, Atrazine is the most prevalent and most concentrated. In the early 1990s, the estimated inventory of Atrazine in the waters of the Great Lakes was in excess of 600,000 kilograms with an estimated water column residence time in the order of years (Schottler and Eisenreich 1994).

Atrazine is an antiandrogen (Sanderson *et al.* 2001). The sex ratio of *Daphnia magna*, the water flea, shifts to males exposed to Atrazine at 0.5 ng/L (Dodson *et al.* 1999). Exposure during amphibian larval development induced hermaphroditism and abnormal gonadal development at 100 ng/L, and demasculinized the larynx of males at 1,000 ng/L by inducing aromatase, which converts testosterone to estrogens (Hayes *et al.* 2002). When leopard frog (*Rana pipiens*) larvae were exposed to 100 ng/L of Atrazine under controlled laboratory conditions, 36 percent suffered from gonadal dysgenesis and an additional 29 percent showed various degrees of sex reversal (Hayes *et al.*2003). In the field, sex reversal was encountered in males in all collections where Atrazine concentrations exceeded 200 ng/L (Hayes *et al.* 2003). Reeder *et al.* (1998) found an association between intersexuality and Atrazine exposure in wild cricket frogs (*Acris crepitans*) in Illinois. There is evidence that Atrazine potentiates parasitic trematode infections, which result in amphibian deformities (Kiesecker 2002). Atrazine has been associated with decreases in dissolved oxygen, pH, and phytoplankton, periphyton, and macrophytes, which are important food sources of larval amphibians and fish (Diana *et al.* 2000).

Applied as a pre-emergent herbicide, Atrazine contamination of water sources peaks with spring rains and coincides with amphibian breeding activities, as many amphibians reproduce during early spring rains. Atrazine concentrations in precipitation collected over the Great Lakes in May 1995 were greater than 1000 ng/L (Environment Canada 1996). Amphibians breed in a wide range of freshwater habitats including temporary pools, flooded fields, irrigation ditches, streams, rivers, lakes, and other permanent sources of water. Maximum concentrations in tributaries and precipitation occur from April to July, the peak period of larval development of amphibians in the Great Lakes basin. Given the proven sensitivity of amphibian larvae to Atrazine, and the evidence of widespread contamination at concentrations exceeding those known to cause sensitive developmental effects, it is highly probable that Atrazine is affecting amphibians in the vicinity of Lake Erie. Two of these species — Blancher's cricket frog (*Acris crepitans blanchardi*) and Fowler's toad (*Bufo fowleri*) — are currently considered at risk and listed under the Species at Risk Act.

5.18 References

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