

**AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY  
WINGSPREAD '97 REVISITED – GREAT LAKES HUMAN HEALTH  
EFFECTS RESEARCH PROGRAM  
EXPERT PANEL MEETING**

**Marriott Century Center Hotel  
Atlanta, Georgia  
February 9–11, 2006**

## **Introduction**

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### **◆ Background**

The Division of Toxicology and Environmental Medicine at the Agency for Toxic Substances and Disease Registry (DTEM/ATSDR) is charged with preventing exposure, adverse human health effects, and diminished quality of life associated with exposure to hazardous substances from waste sites, unplanned releases, and other sources of pollution present in the environment. ATSDR also has a Congressionally-mandated Great Lakes Human Health Effects Research Program which is responsible for characterizing exposure to persistent toxic substances and the potential for short- and long-term adverse human health impacts from that exposure in vulnerable populations. In 1997, ATSDR held a workshop on policy implications of evidence regarding persistent toxic substances and human health (referred to as Wingspread '97).

### **◆ Rationale**

ATSDR has been at the forefront of this critical research program and hosted a 3-day conference to gather input from identified Great Lakes scientists. These experts in the fields of environmental health, environmental epidemiology, toxicology, analytical and biomarker research, and risk assessment met to discuss lessons learned from existing research and new and emerging issues for human health in the Great Lakes basin. An attendee list is provided in Attachment A.

### **◆ Purpose**

The purpose of this meeting was to identify recommendations to respond to the evidence that persistent toxic substances continue to adversely affect the health of humans, wildlife, and the aquatic ecosystem in the Great Lakes basin. The agenda is included in Attachment B.

### **◆ Future Directions/Recommendations**

In the area of conducting research in the Great Lakes the expert panel recommended the following is needed:

- Re-establish the ten cohorts of the Great Lakes program
- Establish a Web-based database management system (i.e., a “virtual institute”) to be a central repository for all the Great Lakes research being conducted
- Synthesize the current work and build on the strengths of the existing programs

- Bring the experts together to discuss the issues associated with combining the cohort data and establish a plan to address them
- Create a list of questions that could realistically be answered if one had access to data from all 10 studies
- Establish a centralized laboratory to quality control purposes
- Promote the virtual public health institute as a research tool for surveying population health

In the area of exposure assessment the expert panel recommended the following is needed:

- Focus on routes of exposure, and take a community-based approach to studying health effects
- Utilized the existing historic cohort data from the Great Lakes program
- Consider exposures through other pathways in addition to fish ingestion
- Conduct research on biologic markers for exposure in vulnerable populations
- Conduct research on mixtures of chemicals and their chemical interactions
- Relate wildlife effects and biomonitoring to human health effects

In the area of emerging chemicals the expert panel recommended the following is needed:

- Investigate potential health effects from exposure to emerging chemicals of concern such as: polybrominated diphenyl ethers (PBDEs); perfluorosulfonates (PFOS); chlorinated naphthalenes and perchlorates to assess their impact on human health
- Investigate mixtures of these chemicals and their potential impact on human health

In the area of human health effects the expert panel recommended that additional research is needed through out different life stages:

- Study the adverse health changes observed in exposed wildlife and relate them to effects being seen in the human population
- Conduct research of *in utero* exposures that potentially may cause adverse health impacts later in life
- Study multigenerational and transgenerational health effects, including reproductive status
- Investigate how childhood exposures might be related to diabetes and cardiovascular disease, and immune system dysfunction later in life
- Use the existing historic cohort data from the Great Lakes program
- Investigate less studied health effects in the historic Great Lakes cohort

In the area of surveillance the expert panel recommended that the following is needed:

- Conduct health surveillance activities on the established cohorts
- Create a Great Lakes Basin Registry to capture pertinent information about the exposed populations

- Conduct a syndromic surveillance study around the Areas of Concerns (AOCs) by correlating body burdens with environmental contaminant levels to discover potential health associations
- Continue to conduct hazard surveillance in the Great Lakes using the established cohort

In the area of health education and outreach activities the expert panel recommended the following is needed:

- Does the risk outweigh the benefits/balancing the benefits with the risks of eating fish
- Evaluate the effectiveness of fish advisories
- Develop fish advisories that are culturally appropriate for specific populations
- Revise conflicting/confusing advice
- Conduct risk communication research with affected populations
- Translate research to show its relevance to people
- Target specific populations with a simple, direct message concerning fish advisories through television and/or the print media

**Note:**

This summary is a general record of discussion and captures the main points and highlights of the meeting. It is not a complete record of all details discussed, nor does it embellish, interpret, or enlarge upon matters that were incomplete or unclear. The major topics of discussion are briefly summarized in Attachment C.

**Thursday, February 9, 2006**

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◆ **Wingspread '97 and Beyond**

Dr. Chris De Rosa began by welcoming everyone to the meeting and asking the experts to introduce themselves. He then explained that the foundation for biological plausibility for human health effects research encompasses toxicology, epidemiology, and wildlife biology. He stated that the Great Lakes are an unrecognized treasure and that the budget for Great Lakes research/preservation has been diminishing. The purpose of this meeting is to discuss implementing an action plan for informing decision makers about ongoing emerging public health issues, and the importance of Great Lakes Human Health Effects Research.

In his presentation, Dr. De Rosa reviewed the Wingspread Conference '97 recommendations. He also emphasized that the risk to vulnerable populations is real, even if it cannot be precisely determined. For the revision of the Great Lakes Water Quality Agreement, ATSDR recommended that human health be defined as a complete physical, mental, and social well being. He stressed the importance of continuing to study the long-term, low-level effects of toxic substances on human health. Dr. De Rosa summarized the conclusions from the 2005 Workgroup on the Ecosystem Health Conference, reaffirming, "that the evidence of harm to people and wildlife from current levels of contaminants is compelling. Without intervention, there will continue to be adverse health effects." (International Joint Commission, 10<sup>th</sup> Biennial Report, 2000).

◆ **Burden Levels and Associated Health Effects in Vulnerable Populations**

Dr. Heraline Hicks reviewed the history of the Great Lakes Human Health Effects Research Program, and stated that the program is currently in the impact assessment stage. Ten grants were given to academic institutions, state health departments, and tribal governments to study human health endpoints in vulnerable populations. The research showed a significant trend of increasing body burdens with increased fish consumption. Several studies showed an increase in adverse reproductive and developmental effects with increased fish consumption. Additional studies showed neurodevelopmental delays with increased exposure to highly chlorinated polychlorinated biphenyls (PCBs). Endocrine effects and impairments in memory and learning were also correlated with exposure to PCBs.

The current focus of the Great Lakes Human Health Effects Research Program is prevention and impact assessment. Dr. Hicks said that an abundance of data indicates that the current ("low") levels of exposure are continuing to cause harmful health effects. She pointed out that both minorities and women were less informed about the hazards of eating polluted fish.

In response to questions, Dr. John Vena clarified the fish consumption habits of the Lake Ontario cohort, and noted that dioxin and mirex are the contaminants of most concern in Lake Ontario. The expert panel members pointed out the difference in consumption between subsistence and sport fishers. They also emphasized the importance of keeping the sensitive populations safe, and noted that early *in utero* exposure could put individuals at risk for developing diseases later in life. The expert panel also indicated that there is a strong relationship between adults eating fish and their children eating fish, even if the advisory warns children to avoid eating fish. The panel

also noted the difference between voluntary exposures (such as eating fish) and involuntary exposures (such as drinking contaminated groundwater). The expert panel also emphasizes that it is unreasonable to assume exposure to a single chemical and that additivity of multiple chemicals is a default, conservative assumption.

The experts briefly discussed the criticism that causality between Great Lakes exposures and adverse health effects has not been established. Dr. Fox noted, however, that the weight-of-evidence is “heavy.” Dr. De Rosa wondered how much “weight” is needed to affect the decisions and pointed out that good health is generally economically beneficial as well.

### ◆ **Health of Wildlife of the Great Lakes, Past and Present**

Dr. Glen Fox presented the following findings:

- Lake trout are the most sensitive species to dioxin-like substances and Ah receptor-mediated early life stage toxicity was sufficient to eliminate reproduction in Lake Ontario, 1940–1980, and was still sufficiently high to reduce reproductive performance in the 1990s.
- The cormorant population has rebounded due to decreasing DDE levels.
- There is widespread DNA damage and reduced immune function in herring gulls studied at contaminated sites.
- There is a negative correlation between plasma PCB levels and T-lymphocyte function in Caspian terns.
- Embryo viability in herring gull eggs is decreased in most of the study sites.
- Artificially incubated snapping turtle eggs from Wheatley show very low hatching success.
- Mink is a sensitive species and contained PCB liver levels greater than the lowest-observed-effect level (LOEL) for reproductive impairment.
- Productivity of eagles nesting in some areas is poor.
- Brown bullheads from Wheatley show altered steroid hormone levels.
- Significant changes in the herring gull and snapping turtle thyroid are compelling. There are strong correlations between exposure and effect.
- There are significant negative relationships between PCB/dioxin levels in herring gull embryos and stress response.
- There are across-species effects on reproduction and other endocrine effects from exposure.
- “It is still not a healthy place to live and more clean-up is necessary!”

Dr. Fox noted that for across-location comparisons, fish should be sampled—even though snapping turtles and gulls provide good data, they are not present everywhere. He also suggested conducting research to investigate potential environmental causes for decreased bone density.

After Dr. Fox’s presentation, some of the experts hypothesized about the reaction wildlife managers and the public will have to this research. The panel discussed the challenge of determining a threshold level of contamination and speculated that due to the contamination could there be changes to the overall genotypic profile of the population i.e., favoring the less vulnerable genetic polymorphisms. The panel agreed that it would be beneficial to document

generational effects in humans. Dr. Annette Ashizawa commented that she recently collaborated on an article that demonstrated a decline in serum PCB levels in Great Lakes study subjects as the level of PCB in the environment declined. The environmental decline was shown in the indicator species (Great Lakes lake trout) that the U.S. Environmental Protection Agency periodically tests. The documentation also indicates that the more contaminated Great Lakes fish is consumed the more likely that the serum PCB level will reflect the increased consumption.

***The panel experts recommended that the following is needed:***

- Sample fish for across-location comparisons.
- Conduct research to investigate potential environmental causes for decreased bone density.
- Document generational effects in humans.

### ◆ **Chemical Exposures**

Dr. Elizabeth Guillette conducted a longitudinal study of children exposed to pesticides in the Yaqui Valley, Sonora, Mexico. She explained that there were two separate groups of Yaqui Indians—children living in the valley, who are exposed to pesticides and children living in the foothills, who are not exposed to pesticides. She noted the following:

- The exposed children had body function and mental deficits.
- The exposed children could not reproduce designs nor recognize their errors.
- The non-exposed children made more complete pictures of a person, with more details of body parts and gender.
- The non-exposed children were sick less often with the exposed having more infections and displaying autoimmune symptoms.
- Seven exposed girls had breast development, but no mammary tissue. Because of the recent long-term drought, there is some indication that these girls were exposed to pesticides *in utero*.
- Exposed girls demonstrated the mental changes accompanying puberty earlier.
- Physicians noted that there is an increase in pre-puberty obesity with the development of mammary glands in boys exposed to pesticides.

In response to questions, Dr. Guillette clarified that pesticide exposure was the only variable between the two Yaqui Indian tribes, the two tribes do not interact, and there is no buffer zone between the fields where pesticides are applied and their homes. The expert panel commented that this study reinforces the need to take a closer look at *in utero* exposures and endocrine disruptors.

Dr. Guillette also conducted a study in Bhopal, India, where a massive release of methyl isocyanate (MIC) caused thousands of deaths within 24 hours. People are still showing long-term health effects. In addition, because the water supply is contaminated, people are continually being exposed. Dr. Guillette found similar results to the Yaqui Indian study, in that children with parental exposure had poor self orientation, poor balance, and low energy levels. Children with parental exposure were also less mentally productive than the control population. Menarche

occurred later for girls with parental exposure to contaminated water or gas. Boys with parental exposure also developed the ability to reproduce later than boys in the control population.

Dr. Guillette pointed out the societal and political implications resulting from exposure to environmental contaminants, and stated that children should have the right to develop to their full innate potential. The future of any country is determined by the quality of its children.

***The panel experts recommended that the following is needed:***

- □ Conduct additional research on *in utero* exposures and endocrine disruptors.

#### ◆ **Discussion: What Have We Learned/Revisited?**

Dr. Hicks began the discussion by asking the experts what actions they think need to be taken to mitigate the effects being seen from low level exposures. The expert panel summarized some of the points conveyed during earlier panelist discussions: (1) there should be increased interest in thyroid and endocrine dysfunction, (2) the levels of PCBs are decreasing, and (3) there is a need to study *in utero* exposures potentially causing impacts later in life. The expert panel also stated that the benefits of eating fish had not been brought into any of the discussions. Do the benefits outweigh the risks? They also noted it would be interesting to focus on the routes of exposure, and take a community-based approach to studying effects.

The expert panel pointed out that the focus has been on 11 contaminants, and that it has been demonstrated that changes observed in exposed wildlife are also occurring in the human population (e.g., low level exposures affect pregnancy and birth weight). The expert panel also agreed and commented that human thyroid abnormalities also follow the same patterns as those seen in wildlife.

The expert panel indicated that multigenerational effects have not yet been studied, along with how childhood exposures might be related to diabetes and cardiovascular disease later in life. The expert panel agreed that transgenerational effects should be investigated, health surveillance is needed, and that cohort data provides invaluable information and studies should be conducted involving cognition in older people. Dr. DeRosa noted that ATSDR is leaning toward conducting a meta-like analysis on the cohort data. The expert panel members recommended that ATSDR retain the established cohorts for future study because the cohorts have great historic value.

The expert panel discussed the dose-response correlations, and that additional work is needed to sort out all the questions (e.g., is there a threshold for effects? Are effects additive or synergistic?).

The expert panel agreed that the case has already been made that the areas of concern (AOCs) require remediation. The expert panel expressed interested in learning about what other kinds of exposures are of concern, especially from the newly emerging chemicals. The panel experts expressed their concerned about potential effects from exposure to emerging chemicals.

The expert panel suggested bringing the individual groups working on the Great Lakes together to discuss what has been learned and let them collaborate on future work. Mr. Edwin Smith said

that the U.S. Environmental Protection Agency (EPA) is now using that kind of collaborative process in their grants program. Dr. DeRosa summarized that ATSDR would talk to their grants department about forming a consortium to identify logical next steps for the Great Lakes Human Health Effects Research Program.

***The panel experts recommended that the following is needed:***

- Study the changes observed in exposed wildlife and relate them to effects being seen in the human population.
- Perform additional research on thyroid and endocrine dysfunction.
- Study cognition in older people.
- Research *in utero* exposures potentially causing impacts later in life.
- Study multigenerational/transgenerational effects.
- Investigate how childhood exposures might be related to diabetes and cardiovascular disease later in life.
- Evaluate dose-response correlations to sort out several questions.
- Focus on the routes of exposure, and take a community-based approach to studying effects.
- Discuss whether the benefits of eating fish outweigh the risks.
- Conduct better health surveillance.
- Use the historic cohort data.
- Retain the established cohorts for future study.
- Investigate potential effects from exposure to emerging chemicals.
- Bring the individual groups working on the Great Lakes together to discuss what has been learned and let them collaborate on future work.

## **Friday, February 10, 2006**

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### **◆ Eight Great Lake States Consortium: Where Do We Go From Here?**

Dr. Anderson presented an ethnocentric view of the Great Lakes Fish Consumption Study from a state health department perspective. He said that the information gathered from the research does not tend to reach the general public. Further, the focus has been on the most susceptible populations (e.g., the developing fetus); however, health effects in the aging population (e.g., cardiovascular issues in older men) should also be considered. He also highlighted the difficulty in risk communication—i.e., balancing the benefits with the risks.

Dr. Anderson explained that fish is now a more important staple food than beef and poultry, and sport fishing is a substantial industry. He reviewed the original members of the consortium and the activities that occurred (e.g., developing a Protocol for a Uniform Great Lakes Sport Fish Consumption Advisory). However, politics have impeded the process and budgets have been reduced, leaving many states currently without the support they need.

Dr. Anderson presented the findings of the two basin-wide telephone surveys. He reported that there were no significant changes in consumption of Great Lakes fish, nor were there significant differences in awareness and compliance, despite the reduction in resources. Dr. Anderson also

presented the findings from the 1993–1994 and 2002–2003 Great Lakes sport fish consumer cohorts. He found that 5 percent of men and 5 percent of women ate more than 104 fish meals per year. Advisories that focus only on sport fish miss much of the fish-consuming population. Although people have continued to eat fish, a decline in PCB serum levels has occurred because the fish are less contaminated. Dr. Anderson presented two case studies in which the people had high mercury intakes even though the fish contained levels below EPA’s guidance.

Wisconsin and Maine formed a consortium for improving the effectiveness of fish consumption advisories for mercury-contaminated sport fish. They conducted a 12-state mercury awareness survey in which they found that minorities and sport fishers ate more fish, women did not seem to be aware of the advisories, and television newscasts are the vehicles through which most people learned of the advisories. Dr. Anderson presented the results of the mercury hair analysis component of this effort and concluded that approximately 12 percent of Wisconsin adults are likely to exceed the exposure guideline for methylmercury. Dr. Anderson ended his presentation by highlighting additional projects being conducted by the state of Wisconsin, and said the new priorities should be surveillance, additional hazards, and health outcomes of the aging population.

#### ◆ **Discussion: What Do We Need to Know?**

The expert panel discussed the ineffectiveness of fish advisories, especially for minorities and women and that part of the problem is the lack of a universal advisory. The expert panel provided suggestions to improve the effectiveness of fish advisories: (1) develop a unified campaign that would be more successful, and develop fish advisories for targeted populations; (2) recommend researching new educational methods, such as teaching children in an effort to reach the adults, (3) stress the importance of cultural considerations when conveying an effective message, (4) and conveying that message through the “gatekeepers” of the communities which has proven to be very effective, (5) better coordination between the federal and state agencies, (6) and conducting research on the most effective communication strategies. The expert panel members indicated that sport fishers have a choice about eating the fish, whereas subsistence populations should be given viable alternatives if told not to eat the fish. The expert panel members agreed and also noted one positive item—that the levels of PCBs in people have decreased, even though people are still eating the fish.

The expert panel expressed their support for studying the effects of organochlorine exposure in older adults. The panel indicated that most people do not associate cardiovascular disease with environmental exposures. The expert panel members agreed that more information is needed to address potential long-term effects such as cardiovascular disease, neurological disorders, and diabetes. The panel experts suggested two areas of study (1) effects from exposure to the current levels and (2) long-term health impact from past *in utero* exposure. The expert panel members indicated that (1) it would be challenging to determine whether the effects are from an *in utero* exposure that is now manifesting itself in older adults or from a cumulative exposure, (2) expressed concern about potential, unknown transgenerational effects associated with exposure to PCBs, but however agreed (3) that continued hazard surveillance is extremely important. The expert panel also suggested establishing a cohort approach across all eight Great Lakes states and Canada to quantify baseline exposures and follow their health. In addition, it was suggested that a Great Lakes Basin Registry be established to capture pertinent information

about the exposed populations. The expert panel member noted that if the goal is to measure diseases, then additional exposures other than through fish consumption need to be considered.

Ms. Fisher asked whether it would be reasonable to have questions regarding potential mercury exposure be part of a woman's prenatal exam. The expert panel members discussed how each state determines whether to mandate that kind of testing (e.g., lead screening in children). The expert panel also indicated it would be relatively inexpensive (about \$30/sample) to test a woman's hair at her first prenatal visit.

The expert panel lamented the conflicting messages from nutritionists and environmental communities concerning the benefits and risks of eating fish. Ms. Fisher noted that a group of dietitians are working on this issue. The panel members reported that one group of researchers tested 50 different fish oil products and found that only one product contained PCBs. This same group preliminarily research found that excessive amounts of fish oil can be harmful (e.g., rapid cell death was observed at high doses).

The expert panel expressed concern over emerging pollutants, specifically toxins from algal blooms and suggested looking at emergency room statistics during algal blooms. Mr. Smith said that EPA is developing a systematic approach for determining and analyzing emerging pollutants (e.g., pharmaceuticals). The expert panel discussed the current state of environmental policy and the importance of preventing additional contamination from entering the environment and that with a show of support from other agencies, they can enhance the awareness of the people who make the policy decisions.

The expert panel also discussed the idea of focusing a syndromic surveillance study around the AOCs. The expert panel suggested correlating body burdens with environmental contaminant levels in an area to discover any associations. The expert panel members discussed the pros and cons of this type of study and would it be beneficial, especially since the AOCs are being remediated. The expert panel indicated that the AOCs have different contaminants, there is not a tight connection between the AOCs and fish consumption. The expert panel indicated that a recently conducted study suggests that fish consumption is not the main exposure factor—living near an AOC was the largest factor. The expert panel also noted the difficulty in selecting control populations.

Because of the substantial resource the Great Lakes provide, the expert panel members urged increased vigilance concerning pollution. The expert panel indicated that it is clear that pollution has caused subtle human and ecosystem health effects. The expert panel discussed (1) the importance of developing remediation methods to remove the contamination from the environment, which is the only way to reduce exposure of certain populations (such as those not heeding the fish advisories) and (2) applying the precautionary principle to reduce the amount of contamination released to the environment. The expert panel members stated that a recent report cited in a newspaper article circulated at the meeting indicated the skepticism that the pollution burdens are decreasing. Dr. Ed Murray asked whether the dynamics of the ecosystem is adding to the problem, and whether it would be beneficial to look into ways to mitigate phosphorous loading for example.

The expert panel members noted that with limited funds, it would be prudent to determine how the money can be best spent to make the most impact. Several suggestions were made (1) establishing a consortium of multiple partners and expanding the research beyond sport fish, (2) establishing a unified program among the federal agencies would be ideal, (3) stressing the fact that the Great Lakes are a sentinel ecosystem, and (4) highlighting the positive impacts of the Great Lakes program.

***The panel experts recommended that the following is needed:***

- Create a universal fish advisory, with better coordination between the federal and state agencies (i.e., a unified campaign).
- Develop fish advisories for targeted populations.
- Research new educational methods and communication strategies for conveying fish advisory messages.
- Ask the “gatekeepers” to spread the fish advisory recommendations.
- Investigate the potential long-term effects of organochlorine exposure in older adults.
- Evaluate the long-term health impact from past *in utero* exposure.
- Study transgenerational effects associated with exposure to PCBs.
- Continue to conduct hazard surveillance.
- Establish a cohort across all eight Great Lakes states and Canada to quantify baseline exposures and follow their health.
- Create a Great Lakes Basin Registry to capture pertinent information about the exposed population.
- Consider exposures routes other than fish consumption.
- Ask pregnant women about potential mercury exposures during prenatal exams and consider hair analysis.
- Look at emergency room statistics during algal blooms to address the concern over emerging algal pollutants.
- Prevent additional contamination from entering the environment by increasing vigilance and applying the precautionary principle.
- Enhance the awareness of the people who make the policy decisions.
- Focus a syndromic surveillance study around the AOCs by correlating body burdens with environmental contaminant levels to discover associations.
- Develop remediation methods to remove the contamination from the environment.
- Investigate ways to mitigate phosphorous loading in the ecosystem.
- Establish a consortium of multiple partners and expand the research beyond sport fish.
- Establish a unified program among the federal agencies.
- Stress the fact that the Great Lakes are a sentinel ecosystem.
- Highlight the positive impacts of the Great Lakes program.

**◆ Potential Human Health Effects in U.S. Areas of Concern: Update**

Dr. De Rosa and Dr. Ashizawa presented the results of ATSDR’s assessment of health implications associated with the 26 AOCs, as requested by the International Joint Commission (IJC). About 50 percent of the ATSDR sites located in AOCs have a completed exposure pathway, and 70 percent of these sites have two or more chemicals of concern. ATSDR found over 15,000 instances where contaminants exceeded health-based screening levels in a variety of

media. Dr. Ashizawa explained the data contained within several geographic information system (GIS) maps, calling attention to the highly populated areas within each AOC.

Syndromic surveillance uses data from site exposure, toxicology, and epidemiology to identify diseases which may have an environmental link. Using this approach, ATSDR looked at the potential association of chemicals with health outcomes, and reported the following:

- ☐ Lung cancer at AOCs with benzo(a)pyrene, arsenic, and chromium
- ☐ Stroke at AOCs with lead and mercury
- ☐ Bladder cancer at an AOC with benzidine
- ☐ Low birth weight at AOCs with PCBs

Dr. Ashizawa indicated that no causal inferences were being drawn from these observations (e.g., low birth weight and the presence of PCB) since any actual exposure, lifestyle, and other risk factors for low birth weight were unavailable for this report. The bladder cancer data, detected in residents residing near a facility (located in a Michigan AOC site) that produced benzidine (known bladder carcinogen) and 3, 3'-dichlorobenzidine (probable carcinogen), were evaluated for the period from 1985 to 1993. The bladder cancer incidence in 1993 was statistically significantly higher than the state-wide incidence in 1993. In addition, the National Institute of Occupational Safety and Health conducted a study in 1985 among workers at this same facility and found 10 cases of bladder cancer in facility employees. This data had been presented in summary form and did not reveal if statistical analysis of the data had been done.

Dr. Ashizawa acknowledged some of the evaluation's shortcomings, including a lack of chemical mixtures data to determine potential health effects from exposure to mixtures. Dr. De Rosa presented information about ATSDR's mixtures risk assessment strategy and announced that the Agency has released and/or revised several interaction profiles for volatile organic compounds, metals, and pesticides, as well as for persistent chemicals found in breast milk and fish. These interaction profiles are available at ATSDR's Web site: <http://www.atsdr.cdc.gov/iphome.html>. As a conservative measure, the interaction profiles assume additivity.

Dr. De Rosa concluded by citing the IJC's conclusion, "Without interventions, future exposures will continue to harm human health."

The expert panel members were concerned that the public might be unduly alarmed about possible health outcomes when they read ATSDR's AOC report because they will not fully understand it. Dr. Ashizawa replied that the report contains language that emphasizes that the AOC evaluation is only making comparisons and is not establishing causal relationships. Two panel members cautioned ATSDR against overstating the results. They recommended presenting the strongest, most reasonable information only, and none of the marginal results.

The expert panel supported ATSDR's effort to determine human disease outcomes from exposure to contaminants at AOCs, however, pointed out the difficulty in removing confounding factors. The expert panel also suggested that the analysis could be further refined

for certain states that contain data at the zip code level, and thought that the data could be aggregated better.

The panel of experts also recommended (1) looking at morbidity data over mortality data, and (2) asking the Great Lakes state partners to participate in the AOC evaluation. The expert panel indicated that it would have been advantageous to talk to the health assessors, rather than extract the information from the public health assessments. The expert panel members indicated that EPA provided comments on the draft report, and strongly recommended that the states also be allowed to review the report. Dr. De Rosa agreed that ATSDR's approach would be in full coordination with the states; and that the states will be provided a draft for review.

Dr. Ashizawa clarified that ATSDR is mandated by law to conduct public health assessments at sites on the National Priorities List. These public health assessments are done in cooperation with the state governments and EPA. The IJC agreed that the public health assessments were a good source of information for the study. She stressed that ATSDR does not work in isolation and asked people to please e-mail her any further comments.

The expert panel members asked what ATSDR wants to accomplish with the information from the AOC report. Dr. De Rosa replied that the hope is to "galvanize the will to do additional work." The expert panel members thought it was a positive sign that the IJC requested this kind of evaluation.

The expert panel supported and were interested in ATSDR's effort to develop guidance for conducting mixtures risk assessments. Dr. De Rosa noted that the guidance was developed in cooperation with EPA and that the method has been adopted by the Health Council in the Netherlands and by the World Health Organization (WHO).

***The panel experts recommended that the following is needed:***

- ☐ Present the strongest, most reasonable information only.
- ☐ Further refine the analysis for certain states that contain data at the zip code level.
- ☐ Aggregate the data better.
- ☐ Look at morbidity data instead of mortality data.
- ☐ Ask the state partners to participate in the AOC evaluation.
- ☐ Allow the state partners to review the AOC report.
- ☐ Continue to develop guidance for conducting mixtures risk assessments.

**◆ Discussion: What Further Action/Research Needs to be Done?**

The expert panel members began the discussion by suggesting that the focus be on emerging chemicals. The experts reiterated that EPA is trying to set up a monitoring program to determine whether there are potential health impacts from these emerging chemicals.

The expert panel indicated that the following areas need additional research:

- ☐ Emerging chemicals
- ☐ Mixtures

- Chronic disease outcomes
- Relationship between effects seen in wildlife and humans
- Remediation technologies for residual contaminants

The expert panel agreed that better, faster remediation technologies should be developed, and the observations of health outcomes in wildlife which act as sentinels for human health. The expert panel members suggested focusing research on the aging population and as the burden of disease goes up, so will the associated health care system costs. The expert panel discussed the importance of studying the following areas of human health effects research:

- Delayed onset of disease
- Heart disease
- Diabetes
- Hypertension
- Immune system effects
- Endocrine system effects
- Reproduction system effects, including adult reproductive failure

The expert panel members also suggested (1) applying an information mapping strategy to the advisories to enhance risk communication, (2) target specific populations with a simple, direct message through television and/or the print media, and (3) conducting research on effective risk communication strategies (e.g., instant messaging to reach teenagers).

Dr. De Rosa confirmed that ATSDR's Great Lakes Human Health Effects Research Program has a financial commitment of \$1 million. The expert panel members discussed the most efficient use of the available money. The panel members agreed that the focus should be on the Great Lakes. The expert panel indicated that it might be beneficial to open participation to other agencies, which they then may be able to contribute additional money to the program. The panel members also indicated that even without additional funds, collaboratively bringing the cohorts together might be as valuable as continuing the program.

The expert panel indicated that exposure routes other than fish consumption also should be evaluated. Dr. Hicks responded that individual diet information was collected from all of the cohorts and that fish consumption was determined to be the main source of exposure to persistent toxic substances in the Great Lakes populations.

The expert panel also suggested a study designed to look at hospitalization rates of people living within 5 miles of the lake shore. However, the panel members indicated that most of the Great Lakes states do not have this information available at the zip code level. The expert panel inquired whether drug prescriptions could be used as another index or form of morbidity.

***The panel experts recommended that the following is needed:***

- Focus additional research on emerging chemicals, mixtures, chronic disease outcomes, relationship between effects seen in wildlife and human health outcomes, and remediation technologies for residual contaminants.

- Study the following areas of human health effects research: delayed onset of disease, heart disease, diabetes, hypertension, immune system effects, endocrine system effects, and reproduction system effects.
- Apply an information mapping strategy to the fish advisories to enhance risk communication.
- Target specific populations with a simple, direct message concerning fish advisories through television and/or the print media.
- Conduct research on effective risk communication strategies.
- Consider opening participation in ATSDR's Great Lakes Human Health Effects Research Program to other agencies.
- Bring the cohorts together.
- Evaluate exposure routes other than fish consumption.
- Design a study to look at hospitalization rates of people living within 5 miles of the lake shore.
- Consider using drug prescriptions as another index of morbidity.

#### ◆ **Discussion: Cohorts**

The expert panel members suggested synthesizing the current work and building on the strengths of the existing programs. The expert panel stressed the importance of continuing to follow up with the cohorts and suggested establishing a Behavioral Risk Factor Surveillance System (BRFSS) for all eight Great Lakes states. The panel members agreed that tracking the people in the cohorts could provide valuable information and present a unique opportunity to potentially answer specific questions, such as those related to transgenerational effects. Dr. Hicks stated that there are roughly 30,000 people in the Great Lakes cohorts, who have been tracked for a number of years. Dr. Fox reminded the experts of the substantial number of archived samples. The expert panel also suggested creating a Web-based database management system to be a central repository for all the research being conducted.

Dr. De Rosa agreed that a consortium of Great Lakes research would be beneficial. This type of system would allow for a researcher to aggregate the data and conduct a meta-like analysis. The expert panel agreed that health effects observed in one cohort might also be seen in another cohort, which would provide corroborating evidence. The expert panel members referred to this system as a "virtual institute." The expert panel did indicate that it would be logistically difficult to use the data maximally, given the different non-standardized sources.

The expert panel members suggested that (1) the grantees meet to discuss the issues (such as combining the data) and establish a plan to address the issues, (2) creating a list of questions that could realistically be answered if one had access to data from multiple studies, and (3) establishing a centralized laboratory for quality control purposes. The expert panel discussed several funding aspects and various funding strategies and the advantages and disadvantages of having a non-competitive, collaborative effort. The expert panel agreed that cooperation across states is usually viewed positively.

#### ***The panel experts recommended that the following is needed:***

- Synthesize the current work and build on the strengths of the existing programs.

- Establish a BRFSS for all eight Great Lakes states.
- Continue to track the people in the cohorts.
- Create a Web-based database management system (i.e., a “virtual institute”) to be a central repository for all the Great Lakes research being conducted.
- Bring the experts together to discuss the issues associated with combining the cohort data and establish a plan to address them.
- Create a list of questions that could realistically be answered if one had access to data from multiple studies.
- Establish a centralized laboratory for quality control purposes.

## **Saturday, February 11, 2006**

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### **◆ Discussion: Virtual Public Health Institute**

Dr. De Rosa continued the discussion from yesterday about establishing a virtual public health institute to study human health effects, focusing on ATSDR’s goals to deal with life stages—children, adolescents, and the elderly. Dr. De Rosa explained that transgenerational refers to effects from parental exposures in not only the F1 generation, but also the F2 generation. The expert panel again stressed the importance of looking for health effects in the elderly in addition to the children.

The expert panel indicated that (1) the virtual institute could build partnerships and provide access to core databases, (2) there is value in preserving the cohorts and establishing cooperation among the different agencies, (3) how a virtual public health infrastructure could respond to world-wide emergency situations, especially since the Great Lakes are an important migratory path for birds, which can carry the bird flu, and (4) if the virtual institute had a public health tracking program (i.e., obtaining geographic distribution and frequency information), it could deal with epidemics of any sort. The expert panel also identified the need to work out the inherent confidentiality issues.

The expert panel members also cautioned that the core management infrastructure could cost a substantial amount of the allotted budget because individual tracking was beyond the current capabilities. The expert panel also suggested that the virtual institute should go beyond public health tracking and promote it as a research tool for surveying population health. The panel indicated that there are some barriers to using environmental data to identify hot spots and the difficulty of tracking individual’s medications and of documenting potential interactions—i.e., preventative health can interfere with being able to study effects from exposure.

The expert panel members wondered whether the individual states communicate with each other. The expert panel indicated (1) if ATSDR were the lead agency, there would be better interaction, (2) it would be important for the states to maintain their separate identities, (3) suggested discussing the idea of a virtual institute at the next ATSDR partners meeting, (4) recommended talking to the current grant awardees about whether they would be interested in participating in a project like this and willing to share their data.

The experts panel discussed the current projects being conducted with the existing cohorts, and decided that it would be beneficial to get the agencies managing Great Lakes cohorts together to inventory the projects and fully determine the availability and compatibility.

***The panel experts recommended that the following is needed:***

- Establish a virtual public health institute to study human health effects in both the elders and the children.
- Preserve the cohorts.
- Work out the inherent confidentiality issues associated with the cohort data.
- Promote the virtual public health institute as a research tool for surveying population health.
- Discuss the idea of a virtual public health institute at the next ATSDR partners meeting.
- Talk to the current grant awardees about whether they would be interested in participating and willing to share their data.
- Get the agencies managing Great Lakes cohorts together to inventory the projects and fully determine the availability and compatibility.

#### ◆ **Discussion: Additional Human Health Effects Research**

The expert panel members suggested a strategy for connecting the health effects seen in wildlife with the mainstream human health literature (i.e., use wildlife as sentinel species). For the following reasons: (1) health effects documented for the wildlife population, reproductive and endocrine effects are being evaluated in the human population, (2) that there might be a correlation between bone density loss in women and environmental exposures to endocrine disruptors, since the wildlife results report fragile eggshells and bone density loss, and (3) wildlife research proves that more human health effects research needs to be conducted. The experts emphasized the following areas of additional research:

- *In utero* exposures potentially causing effects later in life
- Multigenerational/transgenerational effects, including reproductive fertility
- Life stage issues
- Effects in populations other than the vulnerable population, such as older men
- Less studied effects such as cardiovascular disease, diabetes, and immune system dysfunction
- Endocrine and metabolic dysfunction
- Developmental effects, including cognitive effects through life (e.g., memory dysfunction in older adults)
- Neurological effects
- Genetically susceptible individuals

The expert panel members also indicated that all the listed areas can be pursued with the existing cohorts. The expert panel member suggested using PCBs as the marker for halogenated aromatic compounds (noted that for many compounds the harmful effects are due to a hydroxyl metabolite), (2) wondered whether one of the metabolites could be used as the predictor instead of using total body burdens (though useful, that kind of analysis requires expensive analytical chemistry).

The expert panel members inquired whether there are tissue samples that could be used to determine genetic susceptibility. Most samples are serum, not tissue. Other experts also thought that genetics may be an important variable for susceptibility to diseases.

The expert panel discussed the possibility of obtaining health tracking information from a national exposure report, such as the National Health and Nutrition Examination Survey (NHANES).

The expert panel also suggested (1) adding targeted questions to address issues specific to the Great Lakes, (2) pointed out some options for obtaining additional tracking information from the cohorts, (3) that there is biological data already collected that could be further evaluated, (4) suggested obtaining and analyzing outdated blood bank serum to identify new chemicals of concern.

The expert panel members commented that (1) fish consumption advice is conflicting, (2) wondering whether an additional research project should be to “separate fact from fiction” and communicating the results, and (3) that the fish advisories are not being viewed as relevant to older men and women.

***The panel experts recommended that the following is needed:***

- Use wildlife as sentinel species for human health effects.
- Conduct additional human health effects research, specifically in the following areas: *in utero* exposures causing effects later in life, multigenerational/transgenerational effects, life stage issues, effects in populations other than the vulnerable population, less studied effects, endocrine and metabolic dysfunction, developmental effects, neurological effects, and genetically susceptible individuals.
- Use the existing cohorts to pursue these research areas.
- Use PCBs or one of the hydroxyl metabolites as the marker for exposure.
- Investigate whether genetics is an important variable for susceptibility to diseases.
- Look into obtaining health tracking information from a national exposure report.
- Add targeted questions to a national exposure report to address issues specific to the Great Lakes.
- Evaluate the biological data already collected.
- Obtain and analyze outdated blood bank serum to identify new chemicals of concern.
- Separate fact from fiction concerning the fish consumption advice and communicate the results.

**◆ Final Comments**

Dr. De Rosa thanked the experts for their participation, hard work, perseverance, and patience. He said that the discussions from this meeting will be shared with the IJC and others. ATSDR is planning to create and circulate a briefing document with the recommendations discussed at this meeting, which can also be used when approaching other agencies about participating in the program. An expert member suggested that when presenting the proposal, ATSDR should first list all of the achievements of the Great Lakes program to justify the existing work, and then highlight the fact that this proposal is a continuation of the existing work.

## Attachment A. Attendee List

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Henry Anderson, M.D.  
Chief Medical Officer  
Wisconsin Division of Public Health  
One W. Wilson Street, Room 150  
Madison, WI 53703  
608-266-1253  
[anderha@dhfs.state.wi.us](mailto:anderha@dhfs.state.wi.us)

Annette Ashizawa, Ph.D.  
Epidemiologist  
ATSDR  
Atlanta, GA 30341  
770-488-3338  
[annette.ashizawa@cdc.hhs.gov](mailto:annette.ashizawa@cdc.hhs.gov)

David Carpenter, M.D.  
Institute for Health and the Environment  
University of Albany, East Campus A-217  
One University Place  
Rensselaer, NY 12144-3456  
518-525-2660  
[carpent@uamail.albany.edu](mailto:carpent@uamail.albany.edu)

Christopher DeRosa, Ph.D.  
Director, Division of Toxicology  
And Environmental Medicine  
ATSDR, Atlanta, GA 30341  
770-488-3301  
[christopher.derose@cdc.hhs.gov](mailto:christopher.derose@cdc.hhs.gov)

Jacqueline Fisher  
U.S.EPA – GLNPO  
77 W. Jackson Blvd. (G-17J)  
Chicago, IL 60604-3507  
312-353-1481  
[Fisher.Jacqueline@epa.gov](mailto:Fisher.Jacqueline@epa.gov)

Glen Fox, Ph.D.  
Retired Wildlife Biologist  
877 Ridley Boulevard  
Ottawa, Ontario K2A 3P4 Canada  
613-729-1185  
[glen.Afox@gmail.com](mailto:glen.Afox@gmail.com)

Elizabeth Guillette, Ph.D.  
Assistant Research Scientist  
University of Florida  
Department of Anthropology  
Gainesville, FL 32611-7305  
352-375-5929  
[eguillet@anthro.ufl.edu](mailto:eguillet@anthro.ufl.edu)

Heraline Hicks, Ph.D.  
Senior Environmental Health Scientist  
ATSDR, Great Lakes Program Manager  
Atlanta, GA 30341  
770-488-3347  
[heraline.hicks@cdc.hhs.gov](mailto:heraline.hicks@cdc.hhs.gov)

Edward Murray, Ph.D.  
Chief, Applied Toxicology Branch  
ATSDR  
Atlanta, GA 30341  
770-488-3317  
[emurray@cdc.gov](mailto:emurray@cdc.gov)

Edwin Smith  
U.S. EPA – GLNPO  
77 W. Jackson Blvd. (G-17J)  
Chicago, IL 60604-3507  
312-353-6571  
[Smith.Edwin@epa.gov](mailto:Smith.Edwin@epa.gov)

John Vena, Ph.D.  
Professor and Chair  
Department of Epidemiology and  
Biostatistics  
Norman J. Arnold School of Public Health  
University of South Carolina  
800 Sumter Street  
Columbia, SC 29208  
803-777-7333  
[jvena@sc.edu](mailto:jvena@sc.edu)

## **Attachment B. Agenda**

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### **Thursday – February 9, 2006**

1:30 p.m. - 2:00 p.m. Arrival of Attendees

2:00 p.m. - 2:15 p.m. Opening/Dr. De Rosa

2:15 p.m. - 3:00 p.m. Presentation/Dr. Hicks

“Burden Levels and Associated Health Effects in  
Vulnerable Populations in the Great Lakes: What We Have Learned”

3:00 p.m. - 3:30 p.m. Presentation/Dr. Fox

“Toxic Effects in Wildlife”

3:30 p.m. - 3:45 p.m. Break

3:45 p.m. - 4:15 p.m. Presentation/Dr. Guillette

“Changes in Childhood Development From Chemical Exposures”

4:15 p.m. - 5:30 p.m. Discussion Moderator/Dr. Anderson

“What Have We Learned/Revisited”

5:30 p.m. Adjourn

### **Friday – February 10, 2006**

8:30 a.m. Continental Breakfast

9:00 a.m. - 9:30 a.m. Presentation/Dr. Anderson

“Great Lakes Consortium – Where Do We Go From Here?”

9:30 a.m. - 10:30 a.m. Discussion Moderator/Dr. Vena

“What Do We Need to Know?”

10:30 a.m. - 10:45 a.m. Break

10:45 a.m. - 11:45 a.m.	Discussion Moderator/Dr. Carpenter
	“What Further Research Needs to be Done?”
11:45 a.m. - 1:00 p.m.	Lunch
1:00 p.m. - 3:00 p.m.	Recommendations
3:00 p.m. - 3:15 p.m.	Break
3:15 p.m. - 5:30 p.m.	Recommendations
5:30 p.m.	Adjourn
Dinner	

**Saturday – February 11, 2006**

8:30 a.m.	Continental Breakfast
9:00 a.m. - 10:30 a.m.	Review Draft Report
	Continuation – Developing Recommendations
10:30 a.m. - 10:45 a.m.	Break
10:45 a.m. - 11:45 a.m.	Action Plan
11:45 a.m. - 12 noon	Closing Remarks/Dr. De Rosa
12 noon	Adjourn

