



Proceedings

Endocrine Disruptors Program Progress Review Workshop

October 30, 2004
New Orleans, LA



Introduction

Despite considerable public interest and research activity, the scope and magnitude of the impact of putative endocrine disrupting chemicals (EDCs) on human health are largely unknown. Human exposures to these chemicals have been documented, and they are present in human tissues. Evidence is mounting from laboratory animal studies that exposure to some environmental toxicants alters hormone signaling pathways that can lead to toxic effects on reproduction and development, cancer, or other endocrine-related responses. Adverse effects have been associated with hormonally active chemicals in wildlife, but few studies have documented effects in humans exposed at levels encountered in the environment.

Research on endocrine disrupting chemicals is a high priority for the U.S. Environmental Protection Agency's (EPA) Office of Research and Development (ORD). The U.S. EPA chairs an interagency working group (IWG) under the Committee on the Environment and Natural Resources (CENR) of the Office of Science and Technology Policy. The IWG, with representatives from as many as 14 agencies, coordinates endocrine disruptors research on both the national and international level. Over the years, the CENR working group has: (1) developed a framework for federal research related to the human health and ecological effects of EDCs; (2) developed an inventory of ongoing federally funded research on EDCs; and (3) overlaid the framework with the inventory to identify high-priority research gaps in the federal portfolio. To begin addressing some of these gaps, the IWG has issued joint solicitations for research proposals.

ORD's National Center for Environmental Research (NCER) contributes to the endocrine disruption research program through its Science To Achieve Results (STAR) grants program. Since 1995, NCER has participated with the CENR IWG to support research to enhance our understanding about human and wildlife exposure and health effects, toxicokinetics and toxicodynamics, and biologic pathways. In 2000, the EPA, the National Institute for Occupational Safety and Health (NIOSH), the National Institute for Environmental Health Sciences (NIEHS), and the National Cancer Institute (NCI) announced a joint program to support research on exposure to endocrine disruptors and adverse health effects in humans, with a focus on epidemiologic approaches. Effects of interest included reduced fertility or altered reproductive function, pregnancy outcomes and developmental abnormalities of offspring of exposed women, hormonally mediated cancers among offspring exposed *in utero*, and endocrine-related malignancies. Study designs that clearly differentiated exposure categories and used quantitative exposure assessment methodologies were of special interest.

Twelve awards totaling almost \$19 million were provided for studies to be conducted over a period of 3 years. The epidemiology studies are investigating effects on reproduction and development and other health outcomes among exposed subjects or their offspring. Chemicals under study include dioxin compounds, polychlorinated and polybrominated biphenyls, heptachlor, DDT/DDE, and other polyhalogenated persistent pollutants, perfluorooctyl compounds, and phthalates. Investigative teams are using a variety of study designs and methods to measure and quantify exposure and to identify susceptibility, including biomarkers and the evaluation of gene-environment interaction. All of the studies will develop a quantitative estimate of risk of health effects associated with exposure.

This Proceedings document describes a workshop held to discuss the progress of the 12 epidemiologic studies funded as a result of the interagency collaboration. The workshop was held as a special symposium in conjunction with the e.hormone2004 Conference organized by the Center for Bioenvironmental Research at Tulane and Xavier Universities on October 30, 2004. The study investigators shared their research findings regarding the association of reproductive, developmental, cancer, and other endocrine effects with exposure to toxic hazards in the environment. The meeting culminated with a panel discussion on the "Translation of Research Into Public Health Practice and Policy." The panel discussion provided the opportunity to present and discuss different challenges in translating and applying the results of research to public health practice and policy. Panelists offered brief perspectives related to state and local regulatory decisions/practices, economic analyses, legal deliberations/actions, and public health promotions and interventions. This Proceedings in-

cludes the agenda for the symposium, summaries of the progress of the 12 epidemiology studies, responses to questions posed to the panelists before the workshop, a summary of the panel discussion, and biographical sketches for all of the presenters and panelists.

This interagency research effort represents the largest portfolio of coordinated federal funding looking at the impact of endocrine disruptors on humans. It is producing a body of work that will contribute significantly to the state of scientific understanding about human exposure and health responses to potential EDCs found in the environment. Policymakers and scientists will use the results of these studies to identify questions for future research, inform risk assessments, and inform decisions designed to protect public health.

The research described in this report has not been subjected to the Agency's required peer review and policy review, and does not necessarily reflect the views of the Agency. Therefore, no official endorsement should be inferred. Any opinions, findings, conclusions, or recommendations expressed in this report are those of the investigators who participated in the research or others participating in the Endocrine Disruptors Program Progress Review Workshop, and not necessarily those of EPA or the other federal agencies supporting the research.

For additional background information, go to the following Web site to read the Request for Applications (RFAs) that resulted in the award of the grants described in this report:

<http://es.epa.gov/ncer/rfa/archive/grants/01/endocrine00.html>

For more information on EPA's STAR program on endocrine disruption research, please contact Elaine Francis at 202-343-9696 (francis.elaine@epa.gov). For more information on all research areas in EPA's STAR program, please go to <http://www.epa.gov/ncer>.

U.S. EPA National Center for Environmental Research
Endocrine Disruptors Program Progress Review Workshop
Endocrine Disruptors: Epidemiologic Approaches

**Center for Bioenvironmental Research
Tulane and Xavier Universities
New Orleans, LA**

October 30, 2004

Agenda

9:00 a.m. – 12:00 noon	Part I
9:00 – 9:15 a.m.	Welcome and Opening Remarks Elaine Francis, Ph.D., U.S. Environmental Protection Agency, Office of Research and Development; Kumiko Iwamoto, M.D., Dr.P.H., Epidemiology and Genetics Research Program, National Cancer Institute
9:15 – 9:40 a.m.	<i>Phthalates in Pregnant Women and Children</i> Shanna H. Swan, Ph.D., University of Missouri—Columbia (Bio)
9:40 – 10:05 a.m.	<i>DDT, Endocrine Disruption, and Reproductive Outcomes</i> Xiaobin Wang, Sc.D., Children’s Memorial Hospital, Chicago (Bio)
10:05 – 10:30 a.m.	<i>Exposure to Endocrine Disruptors and Neurodevelopmental Outcomes in an Agricultural Community</i> Laura Fenster, Ph.D., California Department of Health Services (Bio)
10:30 – 10:55 a.m.	<i>Epidemiologic Evaluation of Perfluorooctyl Compounds as Endocrine Disruptors in Men</i> James H. Raymer, Ph.D., RTI International (Bio)
10:55 – 11:20 a.m.	<i>Serum PCBs, CYP1A1, GST Genetic Polymorphisms, and Breast Cancer in Connecticut Women</i> Tongzhang Zheng, M.D., Sc.D., Yale University (Bio)
11:20 – 11:45 a.m.	<i>Persistent Organic Pollutants and Endometriosis Risk</i> Victoria Holt, Ph.D., Fred Hutchinson Cancer Research Center (Bio)
11:45 a.m. – 12:00 noon	Questions and Discussions
12:00 noon – 1:00 p.m.	Lunch
1:00 – 4:40 p.m.	Part II
1:00 – 1:10 p.m.	Reconvene
1:10 – 1:30 p.m.	<i>Dioxins, Male Pubertal Development, and Testis Function</i> Russ Hauser, M.D., M.P.H., Sc.D., Harvard School of Public Health (Bio)

- 1:30 – 1:50 p.m. *Latent Effects of Gestational Exposure to Heptachlor*
Dean Baker, M.D., M.P.H., University of California (Bio)
- 1:50 – 2:10 p.m. *Early Childhood Development and PCB Exposures in Slovakia*
Irva Hertz-Picciotto, Ph.D., University of California (Bio)
- 2:10 – 2:30 p.m. *Endocrine Disrupting Chemicals and Thyroid Outcome Study: The Great Lakes Fish Consumption Study*
Pamela Imm, M.S., Wisconsin Department of Health and Family Services (Bio)
- 2:30 – 2:50 p.m. *Persistent Organochlorine Compounds, Genetic Susceptibility, and Testicular Cancer Risk*
Stephen M. Schwartz, M.D., Fred Hutchinson Cancer Research Center (Bio)

2:50 – 3:10 p.m.

Break

3:10 – 4:40 p.m.

Panel Discussion: Translation of Research Into Public Health Practice and Policy

Confirmed Panelists:

Harold Zenick, National Health and Environmental Effects Research Laboratory, U.S. EPA (moderator) (Bio)

R. DeLon Hull, Ph.D., National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention (Bio)

LuAnn White, Ph.D., DABT Center for Applied Environmental Public Health, Tulane University (Bio)

Mark Dickie, Ph.D., University of Central Florida (Bio)

Dan Greenbaum, Health Effects Institute (Bio)

This 90-minute panel discussion will explore the interface between basic and applied health research and its application to risk prevention and reduction and the promotion of health. The panel represents a broad spectrum of perspectives in this area, including policymakers, regulators, researchers, medical practitioners, economists, and environmental public health advocates.

4:45 p.m.

Evaluations and Adjournment

Meeting Abstracts

Phthalates in Pregnant Women and Children

Shanna H. Swan

University of Missouri—Columbia, Columbia, MO

Scientific Question

In this study, we are examining current levels of phthalates in the environment in relation to human reproductive health. We also are examining phthalate levels in relation to personal product use and other factors, including geographic location.

Methods

We are following children born to subjects recruited in our Study for Future Families (SFF), a pregnancy cohort study conducted in four U.S. cities. In addition to assaying urine samples from the babies and mothers (both pre- and postnatally) for metabolite levels of nine phthalates, pediatric physicians are conducting standardized genital and anthropometric examinations on the babies, and the mothers are providing detailed information on their use of personal care products. We expect that by December 2005, we will have complete data on 500 families. We are examining mothers' self-reported use of phthalate-containing products (soaps, cosmetics, teething rings, nipples, and other plastics) at the time of urine collection in relation to measured phthalate metabolite levels. Levels of phthalate metabolites in the mothers' prenatal urine are being examined in relation to infant growth and development. Data from maternal questionnaires are being modeled to identify factors (including geographic location) that predict phthalate metabolite levels. Here we report on results from prenatal samples from 214 women in Columbia, MO (MO), Minneapolis, MN (MN) and Los Angeles, CA (CA).

Results

Of the nine phthalates assayed, all were found above the LOD in at least 50 percent of prenatal samples, and five metabolites were found in almost all (over 90%) of the women (see Table 1). We saw a wide range for most metabolites at levels consistent with prior reports. Surprisingly, we found considerable geographic variability, with higher levels for eight of nine metabolites in women living in mid-Missouri (MO) compared with those in MN. Because we previously found poor semen quality in men living in MO compared with men living in MN, we hypothesized that elevated phthalate levels in MO women reflected household exposure that was shared by their partners and that adversely affected semen quality. In fact, in general linear models, we found that metabolite levels in women's samples of three butyl phthalates, but not other phthalates, were significantly and negatively associated with their partners' semen quality (see Table 2).

Conclusions

Our study is the first to obtain urinary phthalate metabolites in samples from mothers (pre- and postnatally) and infants. The finding of higher levels of eight of nine phthalates in pregnant women in mid-Missouri compared with urban Minneapolis is unexpected but would be consistent with the use of phthalates as inert compounds in pesticides commonly used in mid-Missouri. Our preliminary finding that mothers' levels of three butyl phthalates are inversely related to fathers' semen quality is novel and surprising, suggesting that mothers' levels may reflect a household exposure. We will measure phthalates in the men's urine and correlate these with the mothers' and babies' levels to test this hypothesis. Two human and several animal studies have found butyl phthalates to be related to decreased semen quality, consistent with our findings.

This work was supported by the Environmental Protection Agency STAR Grant No. [R829436](#).

Table 1. Phthalate metabolite levels by center.

Metabolite	Statistics	MO	MN	CA
N		63	87	64
mBP	Mean	19.1	14.8	17.7
	Median	26.6	19.1	28.8
	% > LOD	95.2 %	95.4 %	98.4 %
mBZP	Mean	29.2	13.2	17.6
	Median	15.6	8.2	8.7
	% > LOD	95.2 %	93.1 %	95.3 %
mCPP	Mean	3.1	2.5	3.3
	Median	2.5	1.5	2.5
	% > LOD	77.8 %	65.5 %	70.3 %
mEHHP	Mean	61.7	21.0	24.5
	Median	14.6	9.7	11.1
	% > LOD	96.8 %	98.9 %	98.4 %
mEHP	Mean	15.7	7.7	6.0
	Median	5.9	4.1	2.6
	% > LOD	85.7 %	83.9 %	68.8 %
mEOHP	Mean	52.3	19.1	20.0
	Median	13.9	8.8	9.5
	% > LOD	95.2 %	95.4 %	95.3 %
mEP	Mean	876	358	1489
	Median	100	86	265
	% > LOD	96.8 %	100 %	100 %
mMP	Mean	2.0	2.9	2.4
	Median	2.0	1.3	1.3
	% > LOD	46.0 %	52.9 %	51.6 %
miBP	Mean	4.0	3.0	4.2
	Median	3.0	2.1	2.1
	% > LOD	82.5 %	69.0 %	70.3 %

Table 2. Woman's prenatal levels of butyl phthalates and partner's semen parameters.

Semen Parameter	Parameter	mBP	mBZP	miBP
Concentration ²	Correlation	-0.16	-0.07	-0.17
	p-value	(0.028)	(0.32)	(0.038)
	Beta coefficient ¹	-0.0018	-0.006	-0.113
	p-value	(0.025)	(0.32)	(0.05)
Total motile count ²	Correlation	-0.21	-0.14	-0.22
	p-value	(0.003)	(0.048)	(0.008)
	Beta coefficient ¹	-0.003	-0.0019	-0.019
	p-value	(0.0036)	(0.045)	(0.024)

¹ GLM models of log semen parameters in relationship to log phthalate metabolite level, controlling for abstinence time, season, and fertility problems.

² Using hemocytometer counts on first semen samples.

DDE, Endocrine Disruption, and Reproductive Outcomes

Xiaobin Wang
Children's Memorial Hospital, Chicago, IL

Scientific Question/Hypothesis

Dichlorodiphenyl trichloroethane (DDT) is a broad-spectrum synthetic insecticide that was used widely in agriculture and residential settings beginning in the 1940s. It was banned in the United States in 1972 and in China in the 1980s. Because of their chemical stability, lipophilic nature, and propensity to bioaccumulate, DDT and its primary metabolite, dichlorodiphenyl dichloroethene (DDE), remain ubiquitous contaminants of various environmental media, foods, and human adipose tissue despite bans on their use. DDE residues have been found in detectable amounts in all human populations monitored to date. DDT and DDE are similar structurally to various steroid hormones, including estrogens, and might interact with hormone functions, thereby raising concerns about their potential toxicity via endocrine disruption. Both animal and *in vitro* studies support the hypothesis that DDT, its metabolites, and related compounds are potentially important human reproductive toxins. However, the epidemiologic data associating DDT with human reproductive health are limited. The overall goal of this project, which is funded by the National Institute of Environmental Health Sciences, is to establish a dose-response relationship between exposure to DDE, endocrine dysfunction, and adverse reproductive outcomes in women.

Study Design

This prospective cohort study was conducted among women textile workers in China. The women were enrolled before conception. The information collected at baseline and through followup questionnaire interviews includes sociodemographic characteristics, medications, past medical and reproductive history, job history and occupational exposures, job-related stress, social support, physical activities, active and passive smoking, indoor air pollution, air conditioner use, consumption of tea, coffee, and alcohol, and dietary intake. The enrolled women were followed prospectively for reproductive endpoints. Each woman kept a diary of menstrual bleeding, premenstrual symptoms, use of medications, illness, sexual intercourse, contraceptive use, active and passive smoking, alcohol use, physical activity, stress, and any unusual events or accidents and job activities. Daily urine samples were collected from each woman for up to 1 year or until she became pregnant. Urine samples were analyzed for β -hCG to detect early pregnancy loss. Furthermore, preconception serum DDT and DDE concentrations and the urinary hormones pregnanediol-3-glucuronide (PdG) and estrogen conjugates (E_1C) were measured.

Research Results/Conclusions

This presentation will summarize the major findings obtained to date, including: (1) distributions and determinants of preconception serum DDT and its isomers; (2) DDT exposure, age at menarche, and length of menstrual cycle; (3) DDT exposure and early pregnancy loss; (4) DDT exposure and birth outcomes; and (5) DDT exposure and urinary hormone (PdG and E_1C) concentrations. Our data provide consistent evidence that DDT and DDE exposures affect reproductive hormones and a broad spectrum of reproductive outcomes in a dose-response fashion.

Methodological Contributions/Innovations

The availability of prospectively collected epidemiologic and clinical data as well as urine and plasma samples from a large homogeneous cohort of women, combined with a multidisciplinary approach and state-of-the-art laboratory analyses of plasma DDT/DDE and urinary reproductive hormones, provides an opportunity to investigate dose-response relationships between DDE exposure, hormone dysfunction, and adverse reproductive outcomes.

Biological Mechanisms

Our data support the hypothesis that DDT/DDE is a reproductive toxin and might act at least in part via an endocrine disruption mechanism.

Scientific Significance

The results from this study should improve our understanding of the scope, magnitude, and underlying biological mechanisms of DDT/DDE related to human reproductive health.

This work was supported by the National Institute of Environmental Health Sciences Grant No. 7 R01ES011682-04.

Exposure to Endocrine Disruptors and Neurodevelopmental Outcomes in an Agricultural Community

*Laura Fenster, California Department of Health Services, Emeryville, CA
(Brenda Eskenazi, Principal Investigator, University of California, Berkeley, CA)*

Agricultural pesticide use may be a significant source of environmental endocrine disruptor (ED) exposure in the United States. California, the leading agricultural state in the Nation, requires the reporting of all agricultural pesticide use. The Pesticide Use Reporting (PUR) data indicate that over 600,000 pounds of potentially ED pesticides are used annually in the Salinas Valley. Animal and human evidence suggests that prenatal exposure to EDs might result in adverse neurodevelopmental effects on children. The objectives of this study are to: (1) determine whether prenatal exposure to ED pesticides, including nonpersistent ED pesticides and organochlorine pesticides, is associated with adverse effects on fetal growth and neurobehavioral development of children, and (2) identify population correlates of exposure (e.g., occupation, season, PUR data) so that appropriate interventions can be developed in the future to reduce exposure. We are investigating this relationship in approximately 600 pregnant women and their children from low-income Latino families living in the Salinas Valley of Monterey County, CA. These children, whose mothers were enrolled during pregnancy, are participants in the Center for Health Analysis of Mothers and Children of Salinas (CHAMACOS), a study conducted by the Center for Children's Environmental Health Research at the University of California—Berkeley and funded by the National Institute of Environmental Health Sciences and EPA. CHAMACOS is investigating the relationship between environmental exposures and children's health.

We measured organochlorine pesticides and polychlorinated biphenyls (PCBs) in serum samples collected from the pregnant women at 26 weeks gestation, and nonpersistent ED pesticides or their metabolites in maternal urine samples collected at 13 and 26 weeks gestation. We are examining the association of these biomarkers with growth and neurodevelopment in newborns (Brazelton) and in 6-, 12-, and 24-month-old children. Data were collected about family sociodemographic characteristics, habits, housing, exposure, work, and medical history. Geographic coordinates for each home have been linked to the PUR data.

We found that organochlorine and several other pesticide metabolite levels in our population were higher than the U.S. averages reported by the Centers for Disease Control and Prevention (CDC) in the Second National Report on Human Exposure to Environmental Chemicals (2003). For example, we observed that pregnant women in the CHAMACOS cohort had median DDE levels on average more than threefold higher than Mexican-American women of reproductive age in the National Health and Nutrition Examination Survey study during the same time period (1,053 versus 331 ng/g lipid, respectively). Factors related to increased DDT/DDE levels included the mother's age and being born in Mexico versus the United States. Lower levels of DDT/DDE were associated with more years lived in the United States, having more than one child, and higher education. We have examined the relationship of these exposures to fetal growth and length of gestation and found few adverse associations. Increased DDE levels were associated with somewhat shorter infant body length ($\beta = -0.43$ centimeters, $p = 0.07$) and lower birthweight ($\beta = -69$ grams, $p = 0.12$) but were not related to gestational age, head circumference, or ponderal index. However, the sum of PCBs reported to induce CYP1A and CYP2B detoxifying enzymes was positively associated with neonatal thyroid-stimulating hormone (TSH) levels. Neonatal TSH levels have been shown to be related to infant neurodevelopment. Finally, CDC has developed new laboratory methods to test for ethylene thiourea (ETU) in urine. ETU is an endocrine disruptor and breakdown product of commonly used fungicides (maneb and mancozeb) in agriculture and forestry.

This study will provide key data on the exposure and health effects of persistent and nonpersistent ED pesticides on pregnant women and their children living in an agricultural community. This information is directly related to efforts by federal agencies, including the National Institute for Occupational Safety and Health and EPA, to understand and reduce occupational and take-home exposures to these pesticides.

This work was supported by the National Institute of Occupational Health and Safety Grant No. 1 R01OH007400-01.

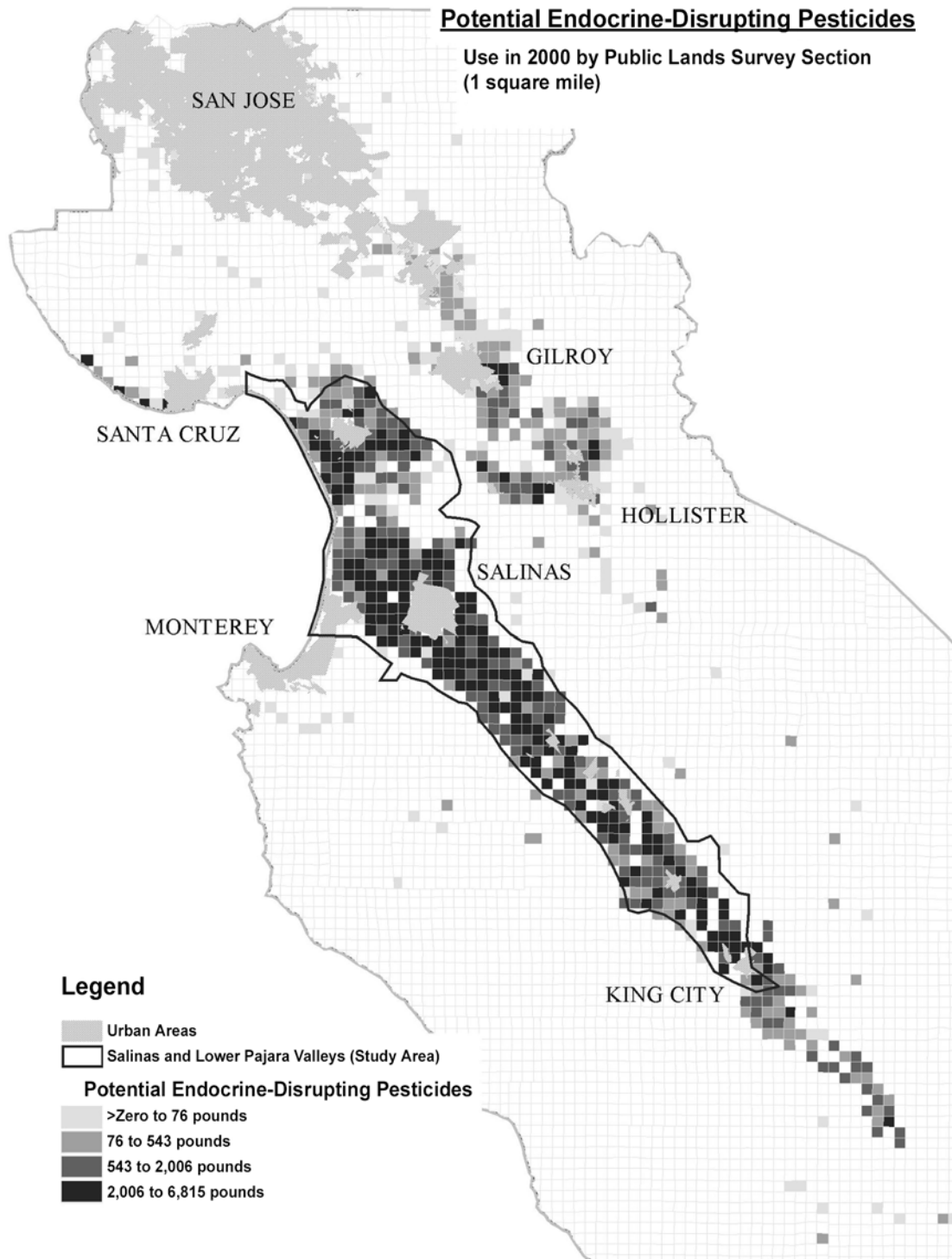


Figure 1. Potential endocrine-disrupting pesticides.
Source: 2000 Pesticide Use Reports.

Epidemiologic Evaluation of Perfluorooctyl Compounds as Endocrine Disruptors in Men

James H. Raymer

RTI International, Research Triangle Park, NC

Products containing perfluorinated chemicals, including perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA), have been largely withdrawn from the market by a major manufacturer amid concerns of persistence, toxicity, and widespread population exposures. Additional concerns have been raised recently about PFOA from cookware. This study is focused on the possible relationships of PFOS/PFOA concentrations in plasma and semen with semen quality and endocrine status of a potentially susceptible subpopulation (i.e., men of couples who present at a fertility clinic). Study participants are expected to represent a range of exposures to PFOA and PFOS (linear and branched), as well as a range of semen quality. Concentrations in these biological media will reflect the multiroute exposures to these chemicals experienced by virtually all people in our society. Semen quality is being assessed using both routine measures (sperm concentration, motility) and a test designed to more accurately and reproducibly assess normal, motile, and fertile sperm (swim-up). Measurements of follicle-stimulating hormone, luteinizing hormone, prolactin, estradiol, and free and total testosterone reflect the hormonal status of the males and will provide evidence of perturbed endocrine function. In 108 semen samples analyzed to date, the mean sperm concentration was $63 \times 10^6/\text{mL}$ (0–432 $\times 10^6/\text{mL}$), the average motility was 53 percent (0–89%), and the average swim-up total motile was $1.4 \times 10^6/\text{mL}$ (0–4.5 $\times 10^6/\text{mL}$). These results will be viewed in conjunction with concentrations of PFOS isomers/ PFOA in plasma and semen, circulating hormones, and potential sources of exposure reported by participants.

This work was supported by the National Institute of Environmental Health Sciences Grant No. 1 R01ES011683-01.

Serum PCBs, CYP1A1, GST Genetic Polymorphisms, and Breast Cancer in Connecticut Women

*Tongzhang Zheng, Y. Zhang, T.R. Holford, J.P. Wise, F. Ali-Osman, P. Boyle, and S.H. Zahm
Yale School of Public Health, New Haven, CT*

This case-control study evaluated the potential gene-environment interaction between *CYP1A1*, glutathione S-transferase (GST), and polychlorinated biphenyl (PCB) on the risk of breast cancer among Caucasian women in Connecticut. A total of 374 histologically confirmed breast cancer cases and 406 noncancerous controls were included in this study. Compared with those who had the homozygous wild-type *CYP1A1 m2* genotype, a significantly increased risk of breast cancer was found for postmenopausal women who had the *CYP1A1 m2* variant genotype (OR = 2.4, 95% CI: 1.1,5.0). The risk was highest for postmenopausal women with higher levels of serum PCBs (OR = 3.8, 95% CI: 1.2,12.1). *CYP1A1 m1* and *m4* genotypes were not associated with breast cancer risk independently or in combination with PCB exposures in this study. *GSTM1* and *GSTP1* genotypes were not associated with breast cancer risk. Among postmenopausal women, *GSTT1* null genotype was associated with a 70 percent increased risk of breast cancer (OR = 1.7, 95% CI: 1.0,2.8), and a nonsignificant twofold increased risk (OR = 2.2, 95% CI: 0.9,5.2) was observed for those who also had higher serum levels of PCBs. In summary, the *CYP1A1 m2* and *GSTT1* genetic polymorphism was associated with an increased risk of female breast cancer and may modify the relationship between PCB exposure and breast cancer risk.

This work was supported by the National Cancer Institute Grant No. 5 R01CA095788-02.

Persistent Organic Pollutants and Endometriosis Risk

Victoria L. Holt¹, Stephen M. Schwartz¹, and Dana B. Barr²

¹University of Washington and the Fred Hutchinson Cancer Research Center, Seattle, WA;

²Centers for Disease Control and Prevention, Atlanta, GA

Endometriosis, a chronic disease affecting approximately 5 percent of U.S. reproductive-aged women, causes chronic pelvic pain, dysmenorrhea, and infertility. Endometriosis has been linked in epidemiologic studies to exposures indicating high circulating estrogen levels. There has been recent public and scientific concern that endocrine-disrupting chemicals in the environment may have estrogenic effects in the body and therefore increase endometriosis risk, but results of the few epidemiologic studies of this issue have been mixed. Thus, we undertook this study to examine the relationship between endometriosis and exposure to organochlorine compounds and polychlorinated biphenyls in a large health maintenance organization (HMO) population. An additional question of interest was whether these associations are modified by polymorphisms in genes involved in estrogen metabolism.

The current study is an ancillary investigation to a National Institute of Child Health and Human Development-funded case-control study of risk factors for endometriosis that was conducted within a large Washington State HMO, providing extensive interview data on a variety of characteristics, including occupational and nonoccupational chemical exposures. Results of laboratory analyses of two polymorphic genes (*GSTM1* and *COMT*) involved in detoxification and estrogen metabolism are available for 295 cases and 581 controls from that study, and the current study determined genotypes of two polymorphic cytochrome p450 genes (*IA1* and *IA2*) in these subjects as well. Initial results from the interview data on pesticide exposures indicate no association between self-reported exposure to all pesticides combined and endometriosis risk (OR 0.96, 95% CI 0.70-1.33); however, exposure to herbicides and fungicides appeared to increase disease risk. Specifically, any exposure (occupational and nonoccupational exposures combined) to herbicides was associated with a significant increase in endometriosis risk (OR 1.65, 95% CI 1.03-2.64), and a stronger risk elevation was seen when considering occupational herbicide exposure separately (OR 2.87, 95% CI 0.98-8.40). Similarly, any self-reported exposure to fungicides was associated with more than a doubling of risk of endometriosis (OR 2.15, 95% CI 0.99-4.70), and there was a stronger risk elevation with occupational fungicide exposure (OR 2.80, 95% CI 0.95-8.23). There was little apparent modification of these risks by genetic polymorphisms.

We are currently in the process of determining serum levels of total polychlorinated biphenyls (PCBs), PCB congeners, hexachlorobenzene, β -hexachlorocyclohexane (β -HCH), λ -HCH, aldrin, heptachlor epoxide, oxychlorane, transnonachlor, p,p'-dichlorodiphenyl dichloroethylene (p,p'-DDE), o,p'-DDE, dieldrin, endrin, o,p'-dichlorodiphenyl trichloroethane (o,p'-DDT), p,p'-DDT, and mirex residues for 283 cases and 581 controls. In addition, 450 urine samples (150 cases and 300 controls) will be tested for levels of the methoxychlor metabolite 2,2-bis-(p-hydroxyphenyl)-1,1,1-trichloroethane (HPTE).

This work was supported by the Environmental Protection Agency STAR Grant No. [R829438](#).

Dioxins, Male Pubertal Development, and Testis Function

Russ Hauser

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Puberty is the transition from the prepubertal state to sexual maturity and the attainment of reproductive capacity. There is currently scientific and public debate regarding the potential effects of environmental chemicals on pubertal development. Specific concern centers on whether exposure to environmental toxins causes an earlier onset of puberty and alters the progression of pubertal development and the attainment of sexual maturation. Chemicals of concern include dioxins, a family of highly toxic environmental contaminants. Although the general U.S. population has background exposure to dioxins through diet and air, there are special populations with high dioxin exposure. Studies within these special populations are more powerful than general population studies with a narrower range of exposure. Therefore, in the proposed study, we targeted a population in Chapaevsk, Russia, with documented high exposure to dioxins. The source of contamination is a large chemical-industrial complex built during World War II to manufacture chlorine-containing compounds, including chemical warfare agents.

We are conducting a prospective cohort study designed to determine the association between dioxins and physical growth and the timing of pubertal development in boys from Chapaevsk. Between May 2003 and January 2005, we will recruit a cohort of 500 boys ages 8 and 9 years. At recruitment, baseline examinations focus on physical and physiologic markers of growth and pubertal development. Physical markers include careful measurement of anthropometric factors and determination of secondary sexual characteristics and gonadal maturation assessed by Tanner staging for genital and pubic hair development and measurement of testicular volume. Physiological markers consist of biochemical measures assessed by increased levels of reproductive hormones, such as follicle-stimulating hormone, luteinizing hormone, testosterone, prolactin, inhibin-B, and mullerian-inhibiting substance. Blood samples will be collected and analyzed for dioxins.

The specific aims of the project are to: (1) investigate the relationship between exposure to dioxins and dioxin-like compounds with somatic growth, weight gain, and body mass index; (2) explore the relationship between serum levels of dioxins and dioxin-like compounds and the timing and tempo of pubertal development; and (3) investigate the biological processes underlying the effects of dioxins and dioxin-like compounds on growth and pubertal maturation.

This work was supported by the Environmental Protection Agency STAR Grant No. [R829437](#).

Latent Effects of Gestational Exposure to Heptachlor

Dean Baker¹, Haiou Yang¹, Ulrike Luderer¹, Satry Gollapudi¹, and James Kesner²
¹University of California—Irvine, Irvine, CA; ²National Institute for Occupational Safety and Health, Washington, DC

Scientific Question

Does gestational exposure to the chlorinated cyclodiene pesticide heptachlor result in latent effects on neurobehavioral, reproductive, or immunologic function?

Background

The study is based on a well-characterized episode in which the commercial milk supply on the Hawaiian island of Oahu was contaminated with heptachlor epoxide (HE) during a 15-month period (1981–1982), resulting in gestational exposure to offspring of women who drank cow's milk during that period. The overall study has had three phases. First, we conducted two statewide population-based surveys to measure HE concentrations in human milk and sera. These surveys verified that HE concentrations in the biological specimens were significantly higher in the Oahu population than on the unexposed neighbor islands. These surveys also demonstrated a significant association between HE concentrations and reported cow's milk consumption during 1981 and 1982. Second, we conducted an islandwide survey of 20,408 high school students to identify 1,891 young adults who were born during 1981 and 1982 and lived on Oahu for at least 15 years. Using this sampling frame, we selected 332 Oahu-born participants and 113 participants not born on Oahu to assess neurobehavioral function and academic achievement using standard test instruments and school records. Analyses controlling for many confounding factors indicated that consumption of cow's milk by mothers during pregnancy was associated with lower neurobehavioral performance and more reported behavioral problems. There were no apparent associations for school-based performance measures.

Study Design

For the current study of reproductive and immune function, we are using the same sampling frame to recruit 400 Oahu-born young adults and 200 comparison participants who were not born on Oahu, matched by age and ethnicity. Indicators of reproductive function include serum testosterone in males; estradiol and progesterone in females; luteinizing hormone and follicle-stimulating hormone in both sexes; semen samples; and daily first morning urine specimens in females for one menstrual cycle to measure luteinizing hormone, estrone-3-glucuronide, and pregnanediol 3-alpha-glucuronide. Indicators of immune function include skin tests for standard recall antigens; antibody titer response to immunization with tetanus and pneumococcal vaccine; Th1 and Th2 type CD4+ cell subsets in peripheral blood; and susceptibility of peripheral blood T cells to activation-induced cell death using *in vitro* analysis of Fas (CD95) and its ligand (CD95L) expression.

Results

The study has initiated followup of one-half of the sampling frame and enrolled 250 participants, including 238 participants with substantially complete data collection. Of these participants, 209 were born on Oahu and 29 were born elsewhere. Initial analysis of the reproductive and immune function parameters has indicated no clear associations with place of birth or, among Oahu-born participants, mothers' reported cow's milk consumption during pregnancy.

Discussion

The findings indicate that gestational exposure to HE may be associated with subtle latent effects on neurobehavioral performance. It is relevant to evaluate whether gestational HE exposure also is associated with latent effects on reproductive and immune function. Further data collection will be needed to achieve sufficient statistical power to address the hypotheses. This study is funded by the U.S. Environmental Protection Agency.

This work was supported by the Environmental Protection Agency STAR Grant No. [R829439](#).

PCB Exposures in Eastern Slovakia in a Birth Cohort

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Contamination from a polychlorinated biphenyl (PCB) manufacturing plant in eastern Slovakia is widespread in the environment, and a cohort of births in two districts is being assembled to determine early life developmental effects from exposures. PCBs are being analyzed in maternal serum collected at delivery by gas chromatography with an electron capture detector (GC-ECD) and will be related to a number of immunologic and neurodevelopmental outcomes during the first few years of life. We report on exposure levels measured in maternal serum as $\mu\text{g}/\text{dL}$ on a wet weight basis, and on the individual-level predictors of these body burdens. A measure of total PCBs was obtained by summing the following 15 PCB congeners: 28, 52, 101, 105, 114, 118, 123 and 149, 138, 153, 156 and 171, 157, 167, 170, 180, and 189. Preliminary data from several hundred births indicate that the exposure levels are lower than those reported in the late 1990s, but are still high relative to most other populations currently under investigation. From these data, we obtained a mean of $0.689 \mu\text{g}/\text{dL}$, with an interquartile range from 0.282 to $0.776 \mu\text{g}/\text{dL}$ and a median of $0.441 \mu\text{g}/\text{dL}$. Descriptive data from the first few hundred births show that more than one-half of the families grow their own fruits and vegetables, about one-third raise their own chickens, and about one-third raise their own pigs. Total PCB concentration was associated with increasing age of the mother, decreasing parity, increasing duration of pregnancy, having a relative who worked at the Chemko manufacturing plant, district of residence, and consumption of eggs from locally raised chickens. The association with age likely represents duration of exposure, whereas the inverse relationship with parity reflects unloading during previous pregnancies and/or lactation. The gestation result probably is due to the rise in lipids during late pregnancy. The higher body burdens among those consuming local eggs raises concerns about environmental cleanup.

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Endocrine Disrupting Chemicals and Thyroid Outcome Study: The Great Lakes Fish Consumption Study

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(Henry Anderson, Principal Investigator, Wisconsin Department of Health
and Family Services, Madison, WI)*

The Wisconsin Department of Health and Family Services began survey data collection for the Endocrine Disrupting Chemicals and Thyroid Outcome Study in the spring of 2004. The overall goal of the study is to assess the impact of fish consumption and other dietary and occupational exposure to polybrominated diphenyl ether (PBDE), polychlorinated biphenyl (PCB), and other environmental contaminants on thyroid and reproductive health status.

The study sample consists of charter boat captains, anglers, and infrequent fish consumers who participated in a 1993–94 reproductive outcome study. A screener questionnaire was mailed to over 3,600 respondents and focused on fish consumption and medical history. Respondents who agreed to participate in the followup study provided contact information.

The followup study will characterize serum thyroid parameters, reproductive hormone levels, and PCB and PBDE levels of over 500 study participants. These participants also will complete another questionnaire asking for a more detailed medical history, medication use, and occupational exposure to chemicals. Specimen collection has just begun and will continue through 2005. Based on the preliminary analysis of 223 participants in an Agency for Toxic Substances and Disease Registry repeat biomarker study in 2003, we anticipate dichlorodiphenyl dichloroethene and PCB levels to continue to decrease. (Biomarker data were compared with 1992 laboratory results.)

This work was supported by the Environmental Protection Agency STAR Grant No. [R830254](#).

Persistent Organochlorine Compounds, Genetic Susceptibility, and Testicular Cancer Risk

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Background

The incidence of testicular germ cell carcinoma (TGCC), the most common malignancy in young men, has increased several-fold since the 1950s. Experimental and observational studies in animal systems have raised concern that the increasing rates are due in part to populationwide, persistent exposure to endocrine-disrupting compounds from industrial and agricultural applications. Many such compounds appear to impair the synthesis or function of testosterone in vertebrates, and a reduced testosterone (e.g., as manifested by the testicular dysgenesis syndrome) may be an important cause of TGCC in humans. Whether human exposure to such chemicals is associated with TGCC risk has not been directly studied.

Objectives

We will determine whether the risk of TGCC is related to serum levels of persistent organochlorines, focusing on p,p'-DDE, polychlorinated biphenyls (PCBs), and other compounds (e.g., dieldrin, hexachlorocyclohexane, hexachlorobenzene). We also will examine whether the risk of TGCC associated with these compounds varies according to whether a person carries versions of genes that are likely to be involved in how these compounds affect TGCC risk. Specifically, we will determine whether TGCC risk is related to interactions between: (1) elevated serum p,p'-DDE and polyglutamine repeat tract polymorphisms in the androgen receptor (*AR*) gene, and (2) elevated serum PCB levels and genetic polymorphisms in oxidative stress defense enzyme genes (e.g., glutathione *S*-transferases and superoxide dismutases).

Approach

A population-based series of TGCC cases (~250) and controls (~750), all of whom resided in the Seattle metropolitan area between 1999 and 2003, are being recruited into a protocol that includes: (1) a detailed in-person interview; (2) a blood draw; (3) analyses of genetic variation in androgen synthesis, metabolism, and signaling genes; and (4) analysis of serum levels of organochlorine compounds. Results relating to available organochlorine compound data and genetic polymorphism data will be presented for approximately 560 and 775 participants, respectively. The results should add significant new information to our understanding of the role, if any, of environmental contaminants in the pathogenesis of TGCC.

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The Effects of Perinatal Endocrine Disruption in Children

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Scientific Question/Hypothesis

The extended followup of this cohort, located in the Faroe Islands, will be used primarily to examine whether biomarkers of exposure to endocrine disruptors are associated with development and neurobehavioral function in boys and/or girls at prepuberty ages, and whether effects of organochlorine compounds, such as polychlorinated biphenyls (PCBs), can be differentiated from those caused by exposures, such as methylmercury.

Study Design

This study is based on consecutive singleton births at the National Hospital, Torshavn, Faroe Islands, during a 12-month period in 1994–1995. In this community, excess exposures to persistent organic pollutants, including PCBs and p,p'-DDE, occur because of the traditional habit of eating pilot whale, including the blubber. The subjects also were exposed prenatally to elevated concentrations of methylmercury. The exposures cover a range of up to 1,000-fold, and postnatal exposure data also have been obtained. Detailed clinical examinations were carried out at ages 7.5 and 10 years. Both examinations focus on neurobehavioral functions, especially sex-dimorphic functions, and general development, and the tests included are comparable. Blood samples are included for exposure assessment.

Research Results/Conclusions

At age 7 years, 165 of the 184 cohort members were examined. The attrition was due mainly to families that had moved abroad. In the spring of 2004, the examinations at age 10 were initiated. All of the first 50 children invited for the 10-year examinations accepted, and all but two consented to have a blood sample taken.

Preliminary analysis of the 7-year data suggests that the results are comparable to those of the first Faroese cohort, also examined at age 7 years, and a neurotoxic effect of mercury exposure has been confirmed. However, detailed analysis of the data is awaiting the completion of advanced exposure measures (as well as the examinations at age 10 years). We are using stored maternal pregnancy serum to determine the integrated estrogen activity (after removal of endogenous hormones), as well as the dioxin-like effect on the Ah receptor. This work will be completed later this fall.

Methodological Contributions/Innovations in the Areas of Recruitment/Enrollment, Exposure Assessment, Health Effects Assessment, FollowUp, or Analytic Models

The Faroe Islands constitute a highly useful setting for this type of research. Because some Faroese eat substantial amounts of whale blubber and others eat little or none, a wide variety of exposures occur, and exposures are independent of major confounders. The highest exposures greatly exceed those reported in Western societies, whereas the lowest exposures overlap with U.S. levels and therefore comprise a built-in control group.

Biological Mechanisms Suggested by Research Results

Research data have not yet been analyzed because we are still in the process of seeing subjects. We anticipate that the receptor-activation results will provide integrated measures of the exposure levels and that they might affect sex-dimorphic functions.

Scientific Significance

Environmental exposures to persistent pollutants include compounds that might cause disruption of endocrine functions. Prenatal exposures to endocrine disruptors (EDs) have been linked to developmental abnormalities and neurobehavioral deficits, but causal links to specific compounds as well as purported dose-response relationships are unclear. This study includes advanced assessment of prenatal ED exposures and objective assessment of important clinical outcomes assumed to be sensitive effects. The present study will shed new light on these questions.

This work was supported by the National Institute of Environmental Health Sciences Grant No. 7 R01ES011681-03.

U.S. EPA National Center for Environmental Research
Endocrine Disruptors Program Progress Review Workshop
Endocrine Disruptors: Epidemiologic Approaches

**Center for Bioenvironmental Research
Tulane and Xavier Universities
New Orleans, LA**

October 30, 2004

Panel Discussion Summary

Dr. Harold Zenick, Associate Director for Health, National Health and Environmental Effects Research Laboratory (NHEERL), was the moderator of the panel discussion. He introduced each of the panel members. These included: Mr. Dan Greenbaum from the Health Effects Institute, Boston, MA; Dr. R. DeLon Hull, National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention, Cincinnati, OH; Dr. LuAnn White, Director of the Center for Applied Environmental Public Health (CAEPH), Tulane University, New Orleans, LA; and Dr. Mark Dickie, Professor of Economics, University of Central Florida, Orlando, FL.

Dr. Zenick noted that the seating arrangement was meant to encourage a dialog between the panel members and the audience. Members of the panel were chosen for their wide variety of research throughout their careers. Prior to the panel discussion, each of the panel members was asked to respond to a set of five questions; their written responses were included in the workshop's handout. Dr. Zenick posed each question. The panel members provided verbal responses and then the audience was given an opportunity to comment.

Question 1: Do you have the opportunity to identify and use the most relevant research in carrying out your professional obligations? If so, how can you document the value/impact of such research? Do current systems/processes work to provide the needed information? What new approaches should be considered?

Dr. Zenick posed Question One and commented that among the written responses from the panelists, one thing that was consistently addressed was the issue of doing research for a specific purpose, as opposed to doing research for the sake of it. He indicated that in his office, he works closely with the client. He asked the panelists to describe how to create a dialog between researchers and end users.

Dr. White drew upon her experience with state health departments and practitioners in the field. She noted that end users have some specific research needs, but that in her experience the research community has been relatively unresponsive to end users of data. There is often a "disconnect" between the practitioners in the field and the university researcher. Practitioners need information in a form that is readily available and understandable. Dr. White posed the question—How do we create a system in which information cascades down from the basic researcher to the community based researchers to the practitioners in the field?

Dr. Dickie responded that he brings two perspectives to this question. The first is that of the social scientist. The social scientist tries to determine how environmental health affects peoples' lives and the quality of their lives; what are the limitations on activities that they might experience, and what are the risks of illness that can be determined. From the scientific perspective of the epidemiologist or toxicologist, interested in reliable and precise measurements of subtle change in physiological function or indicator symptoms, there needs to be a translation to peoples' understanding of how their lives are affected. Economists, as end users of health research data, try to bridge the gap between those precise measurements of health researchers and the individual's perception and understanding of how these numbers will affect his life. Dr. Dickie elaborated that one

can measure blood pressure and cholesterol levels, but that these are just numbers. Most people want to know what is the link to long-term health risks and the activities that they can sustain. As an economist, he would like to see a mapping between what epidemiologists can measure and what “ordinary” people experience and understand as it pertains to them.

Mr. Greenbaum noted a difference between what the “policy world” needs and what the “science world” provides. He discussed the incentives and the system, currently in place, for the publishing of scientific information. He noted that research findings such as hazards and effects are likely to be published, but that a more integrated approach would be beneficial for most policy analysts. He referred to air pollution studies that have been underway for more than 35 years. A mechanism for integrating the various types of sciences has evolved. He noted that endocrine disruptors (ED) studies have not been underway for nearly as long as the air pollution studies, but that an integrated approach would be of value to policymakers.

Dr. Hull noted that researchers do a great job disseminating information to the research community, but that they rarely take the next step that results in a stronger impact. Researchers need to know how their research is to be used. Also, researchers need other pieces in their “research toolbox” to design relevant research.

A participant commented that ED studies have been ongoing for quite some time, although they appeared to be in the early stages during the presentations. The audience member gave the example of Rachel Carson’s animal studies that were carried out quite some time ago, and noted that wildlife scientists are ahead of epidemiologists in studying ED-related questions. She noted that this opens up a number of questions about the relevance of animal-human studies and extrapolations that have yet to be resolved.

It was agreed that scientists need to know more about the information policymakers require to make decisions. Agencies are being held accountable for the kinds of impact their funded research will have in the long term. Dr. White described a typical grant cycle as 3 or 5 years in duration. As such, the long-term impacts of the research findings cannot be ascertained. At best, experiments may be completed. It is important to determine what will be the short-term measures of impact to determine if research is beneficial. It is necessary to determine how information moves across fields, and whether somebody else will take up the research at the completion of a grant cycle.

Mr. Greenbaum described what he calls a tension between efforts that rely on the scientific community’s creativity to address a range of problems, and the desire to have more closely overseen and managed research that answers specific questions.

A participant commented that it is the scientist’s job to define risk, and not to identify the acceptable risk. Dr. Dickie agreed that there is a lot to be gained from a division of labor and that scientists are especially equipped to do science, but perhaps there needs to be an intermediate step that translates science into what is amenable to policy and social analysts. Mr. Greenbaum added that although differences need to be preserved, this translation moves us closer and closer to policy relevance. He described how studies pertaining to particulate matter drove policy discussion with respect to air quality standards, which subsequently led to additional health effects studies. As research evolves, it becomes more usable to the policymaker. The scientific findings help to form actions.

A participant took exception to the artificial separation between science and the rest of the world. He noted that individuals are motivated by different things. Some scientists are more involved with social and political factors, others want to “solve the puzzle” or answer questions. He asked if perhaps there was a way to motivate mechanistic researchers to areas of publicly relevant research. NIH’s approach to research, which includes a community outreach component, is clearly evolving. There are attempts to link research to outcomes, however, there needs to be clarification in the evaluation of proposals as to what constitutes significance.

Question 2: What roles have emerging information technologies (e.g., wide access to the Internet with its massive volume of data and information) played to facilitate or complicate your ability to access and use the research information?

Dr. Zenick made the observation that from the written responses provided by the panel, Information Technology is revolutionizing the ability to get information. He then moved on to the next question.

Question 3: What responsibilities should accompany publicly funded research? Is publication in peer-reviewed journals enough?

Dr. Zenick asked the audience if they were familiar with the recently published NIH proposal to ensure that publicly funded research findings move quickly and readily to the public domain. The proposal is an attempt to “change the playing field” and has generated intense dialog and discussion. He noted that a number of institutional traditions are violated by going this route.

Dr. White was asked to respond. She noted that her organization acts somewhat in the role of translator, as data are conveyed to the public. One of the challenges her office faces is to provide translation, to distill, and to disseminate information to decisionmakers who often lack the necessary scientific knowledge. She stated that it is important to distinguish between summaries of pertinent findings and collections of research, many of which conflict with one another.

Mr. Greenbaum noted that in addition to the NIH proposal, there is a law that requires that data used in the justification of a significant policy decision be made available to the public. He suggested that volumes of data may be necessary for the scientific community, but that in the policy arena much of it is over the heads of policy analysts. He recognized the rights of the researchers to publish and get the benefits from their data, but held that from the standpoint of the policy analyst, if a researcher was unwilling to share data, then there must be something to hide. Dr. Dickie said that the flip side to this issue was that if data were shared, it increased the credibility of the researcher. In his personal experience, there was no such thing as “bad publicity.” He described a controversial study in which his methods and results were criticized, but noted that because other researchers were able to recreate identical results using his methods, his credibility was increased.

Dr. Hull noted that scientists can be very possessive of their data, but that sharing of data is the thing to do. It saves a lot of time and effort. There may be some practical issues to be resolved in getting language into grants to ensure that data are available.

A participant suggested that there is a need for infrastructure to support the translation of information. She added that the process is expensive. Web sites are expensive and cannot be considered just a spin-off of research. Additional funding should be included in proposals and grants to support the effort. Actually, raw data may not be the right form for decisionmakers. Different target audiences may require different formats.

A participant stated that information was not passed along to the front line physicians. She stated that there needs to be a forum to get the word out to medical schools and “into the trenches.”

Question 4: What can academic researchers do to communicate and interpret the result of their research to public health practitioners and policymakers at the local, state, and federal levels?

Dr. Zenick asked Mr. Greenbaum to discuss communicating scientific materials to audiences with different levels of understanding. Mr. Greenbaum stated there is no gold standard, but that knowing your audience is of paramount importance. He noted that his group makes a conscientious effort to communicate to different target audiences through a system of tiered writings. Summaries approximately two pages in length are prepared for decisionmakers, while multi-page documents with detailed information are prepared for the scientific community. He noted that the degree to which information is cited in peer-reviewed literature is one measure of the impact work is having in the policy process. He also commented that his group has begun to track citations in regulatory documents.

Dr. White acknowledged that knowing the target audience is imperative to getting the right message to the right people. She noted that making data available and assessing how to make it accessible are challenging issues. She stated that there needs to be an underlying infrastructure to aid the process. She recognized that some public data lacks quality control.

Dr. Hull offered that research is needed on how to get the right message to the right people to effect behavioral changes. He suggested that, not only should the target audience be correctly identified, but also that the audience needs to be part of the process to effect the greatest impact. He gave the example of lead studies in which lead workers were bringing home contaminated clothing. Individuals were given a simple card with information to slip into the pocket of their lead-contaminated clothing. These cards subsequently were removed at the time the clothing was laundered, and the health information was passed on. He noted that the goal of research is to have impact, and that the best way to ensure a change in the behavior of people is to bring them into the process of change, rather than depend on regulations.

Question 5: How can institutions that support environmental health research facilitate the communication of research results to public health practitioners and policymakers? Are there instructive examples that you can provide?

The audience was asked to provide their input on investigative burden, the costs of doing business, and training concerns. From the audience, comments were made regarding involving other disciplines more formally in one's research (e.g., risk communicators, social scientists, and other qualitative researchers). It was stated that the peer review process generally does not merit or acknowledge the time that it takes to engage other groups. Writing and translating science findings is a very time-consuming, ongoing process.

One participant commented that epidemiological research is in a "dire" condition. She noted that with telemarketing, one used to expect a 70-80 percent response rate. Today, it is more likely to be in the 25-30 percent range. She stated that only well-educated and interested parties, those not likely to be Type A personalities, provided any type of response. She also indicated that the response rate in control groups was even worse. She feared enormous amounts of time were going to be spent on studies without representative samples. She also expressed her frustration with trying to do research with respect to the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule.

Another concern of researchers is that the public may not be aware of the quality of information posted on various Web sites. The average person may view a very polished Web site and take it for granted that the data are reputable, but another individual from the audience encouraged others not to underestimate the power of the Web to inform individual decisionmakers. She noted that a number of individuals have requested citations to pass along to their health care providers.

There was a consensus that the communication of scientific findings is time-consuming and costly, and that the burden of these factors must be considered in the grant-giving process.

Panelists' Responses to Questions

R. DeLon Hull, Ph.D., National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Cincinnati, OH

- 1. Do you have the opportunity to identify and use the most relevant research in carrying out your professional obligations? If so, how can you subsequently document the value/impact of such research? Do current systems/processes work to provide the needed information? What new approaches should be considered?**

Information on how to translate scientific research into public health practice would be very helpful. It also would be helpful to have information available that would help researchers better understand the needs of the potential users of their research results.

- 2. What roles have emerging information technologies (e.g., wide access to the Internet with its massive volume of data and information) played to facilitate or complicate your ability to access and use the research information?**

The Internet makes a tremendous volume of information available, but sorting through it all to identify the most relevant information can be a burden. It does facilitate data collection with activities such as Web-based surveys. It also allows researchers to more readily locate information about potential users of their research findings if the users are in an organization that has a Web site (e.g., trade associations, worker unions, etc.).

- 3. What responsibilities should accompany publicly funded research? Is publication in peer-reviewed journals enough?**

Publication in peer-reviewed journals is an effective way of communicating research results to other researchers, but is often not the best way to put the research results into practice that prevents injury or illness. The needs of the audience the research is addressing must be understood to translate the research findings into prevention practice.

- 4. What can academic researchers do to communicate and interpret the results of their research to public health practitioners and policymakers at the local, state, and federal levels?**

The key is in understanding the needs of the audience you are trying to address. Potential users, stakeholders, and decisionmakers (policy implementers) should be involved during the early research planning phase so that their needs are well understood early in the research process. This group also should be involved through the research process so that communication products and translation activities address their needs.

- 5. How can institutions that support environmental health research facilitate the communication of research results to public health practitioners and policymakers? Are there instructive examples that you can provide?**

Research should be relevant, high quality, and lead to an illness or injury prevention impact. Translating research findings to products, interventions, or policies that have an impact is somewhat unique for each research effort. We need to foster an environment in which researchers include appropriate translation of research findings into their research plans. Some examples can be found on the National Institute for Occupational Safety and Health (NIOSH) Web Site (www.cdc.gov/niosh) through the Research to Practice (r2p) link or through NIOSH eNews, which includes an r2p example in each newsletter. Subscribe to NIOSH eNews through the NIOSH Web Site.

LuAnn White, Ph.D., Center for Applied Environmental Public Health, Tulane University, New Orleans, LA

- 1. Do you have the opportunity to identify and use the most relevant research in carrying out your professional obligations? If so, how can you subsequently document the value/impact of such research? Do current systems /processes work to provide the needed information? What new approaches should be considered?**

Currently, scientific journals are the prime means of dissemination for most research. The reward system for promotion and tenure in academia values only publication in scientific journals. Most researchers target other scientists for communication and dissemination. The traditional system overlooks major groups who could use and are in the position to act on the research findings.

Other modes of dissemination are more difficult to document in terms of impact. In journals, citations are one monitor of impact. In public health practice, seldom is one research finding the basis for action or policy; rather, the body of evidence is the driving factor, which is difficult to trace back to one researcher or to one funded project. Furthermore, the impact might not be observed for years. Identifying more proximate indicators of use of data is needed, but not easy.

- 2. What roles have emerging information technologies (e.g., wide access to the Internet with its massive volume of data and information) played to facilitate or complicate your ability to access and use the research information?**

The Internet has opened access to information exponentially. Information that was once difficult to find is now readily available from the desktop. Electronic journals have expanded access and reduced the time needed to find information. Data and information can be disseminated widely, very quickly, and less expensively than printed material. However, caution is necessary. Much of the historical literature is not in an electronic format. Just because something is posted on the Internet does not make it true. This situation can cause problems with the lay audience, who might lack the knowledge to discern what is fact, what is opinion, and what is blatantly not true.

- 3. What responsibilities should accompany publicly funded research? Is publication in peer-reviewed journals enough?**

Receiving public funds brings the responsibility to disseminate the findings to multiple target audiences, not just other scientists. Most of the time, scientists think of publication only in scientific journals. The scientific community is only one of many target audiences for dissemination; others include the general public, policymakers, and professional organizations. Each audience receives information through different media. There also is the responsibility to put the findings into language that the various target audiences can understand and use. Many public health practitioners do not read scientific journals because specific findings do not relate directly to their problems. Other modes of dissemination include white papers and summaries targeting specific users, training and education, toolkits for using the findings, and news media.

- 4. What can academic researchers do to communicate and interpret the results of their research to public health practitioners and policymakers at the local, state, and federal levels?**

The type and maturity of research determines how and to whom it might be communicated. Generally, there needs to be a body of basic research that provides a basis for policy. Individual findings,

unless a profound breakthrough, are not usually directly translatable to policy. Thinking of the path that research takes to become useful might guide the communication of research to appropriate target audiences.

Partnerships and interactions among those who conduct basic research, applied research, and community-based research and practitioners can serve as a means for two-way communication—the dissemination of findings to those who use them and then communication back to researchers on research questions needed to answer the problems faced in practice.

5. How can institutions that support environmental health research facilitate the communication of research results to public health practitioners and policymakers? Are there instructive examples that you can provide?

Communication with practitioners depends on ongoing dialog, not sporadic pronouncement from the Ivory Tower. In many of our projects at the Tulane Center for Applied Environmental Health, we have advisory boards that include researchers, community members, governmental agency personnel, and other policymakers. Regular meetings provide a means of communicating with public health practitioners, policymakers, and the community. Regular exchanges of ideas and information set up a two-way communication channel that helps to make research more relevant to practitioners.

Making data understandable to policymakers is essential in communication. In one project, we used GIS mapping to show the prevalence of childhood lead poisoning in the city of New Orleans. The graphic showed the areas of the city with the highest rates and identified the risk factors geographically. The graphic was used in the news media and in summary reports. This data served as the basis of a city ordinance banning the dry sanding of leaded paint. The use of GIS provided an easy-to-see graphic; the same policymakers would not have read a report with the same data in tables or charts.

Mark Dickie, Ph.D., University of Central Florida, Orlando, FL

- 1. Do you have the opportunity to identify and use the most relevant research in carrying out your professional obligations? If so, how can you document the value/impact of such research? Do current systems/processes work to provide the needed information? What new approaches should be considered?**

Research in environmental epidemiology and environmental toxicology is an important input in conducting economic analysis of environmental policies and regulations. The U.S. Environmental Protection Agency and other federal agencies are directed by executive orders, as well as some statutory requirements, to conduct various types of economic analysis of regulations with significant economic impact. These analyses range from assessments of impacts on specific groups, such as small businesses or minority populations, to estimates of benefits and costs throughout society. (Although use of benefit-cost analysis in policy decisions is controversial, as a method of analysis rather than decisionmaking, benefit-cost can be one useful way of highlighting the tradeoffs involved in any decision.) Economic analysis is rarely decisive in policy decisions, but it does provide information that policymakers can use, along with other information, in examining options and setting priorities. Consequently, economic analysis provides one avenue through which epidemiologic and toxicologic research can enter the process of analyzing and setting environmental policies. For example, epidemiologic research relating particulate air pollution to premature mortality has provided the basis for establishing the enormous economic benefits of air quality improvements under the Clean Air Act. However, epidemiologic and toxicologic research often does not provide the information necessary to conduct economic analysis.

The ideal information to support an economic analysis is a best estimate of a dose-response or concentration-response function relating changes in a hazard to changes in the frequency, severity, or risk of an adverse health effect that is meaningful to people, accounting for statistical uncertainty and for any behavioral adjustments that people make to avoid exposure to the hazard. For three reasons, it can be difficult or impossible in some cases to glean this information from epidemiologic or toxicologic research.

Epidemiologists often measure somewhat subtle changes in physiologic or neurologic function, such as decreased lung function associated with air pollution exposure. However, economic impacts arise partly from avoiding, or from reducing the risk of, health effects that ordinary people recognize as adverse. People may not recognize a decrease in lung function as adverse without additional information about how lung function affects their daily activities, symptoms, or long-term health status. As a result, economists have no way to estimate the economic impacts of avoiding reduced lung function and thus might understate the beneficial effects of reducing air pollution. Similarly, increased finger-tapping associated with manganese emissions, or heart rate variability, or changes in body chemistry cannot be assessed economically without a mapping from these measures into effects that are meaningful to people.

Research in the health sciences often does not account for behavioral adjustments people sometimes make to avoid exposure to hazards. For example, some research indicates that symptomatic individuals restrict outdoor activities on days of elevated ozone concentrations. To the extent that behavioral adjustments like this are effective in reducing adverse health effects, ignoring the responses could lead to an underestimation of the true effect of a hazard, which in turn could lead to understatement of the beneficial economic impacts of regulation. Of course, there are many situations in which behavioral adjustments are unimportant, perhaps because people do not know they are exposed or have no practical way of reducing exposure. However, the issue of behavioral adjustments may increase in importance if warnings such as smog alerts or fish consumption advisories effectively encourage individuals to take the burden of protection on themselves.

Epidemiologic and toxicologic research often does not provide enough information about the best estimate of a dose-response or concentration-response function, information that would include estimates of slope and curvature and an assessment of any thresholds, rather than simply the statistical significance of an effect. This problem is particularly difficult to overcome when economists try to use information from the risk assessments, more often based on toxicologic studies of animals than on epidemiology, that summarize what is known about risks posed by hazardous substances. A key problem is the inherent conservatism in risk assessment, driven by an overall philosophy of avoiding understatement of risk. Although this philosophy is perfectly understandable from the standpoint of protecting public health, it is not conducive to economic analysis because it does not yield a best estimate of the central tendency of the relationship between risk and exposure to a hazard. Furthermore, risk assessments of noncancer health effects do not provide a measure of risk but only a threshold type of measure, such as a reference dose or reference concentration. This situation makes it difficult or impossible for an economist to work out a dose-response function that would be needed to estimate the economic impacts of controlling a hazard.

2. What roles have emerging information technologies (e.g., wide access to the Internet with its massive volume of data and information) played to facilitate or complicate your ability to access and use the research information?

Emerging information technologies, such as wide access to the Internet, have facilitated economists' access to research in the health sciences.

3. What responsibilities should accompany publicly funded research? Is publication in peer-reviewed journals enough?

One element of this question is whether publicly funded researchers have a responsibility to share their data with others, and opinions differ on this point. I am not sure whether the government can resolve this issue to anyone's satisfaction. An often neglected point is that it can be in the self-interest of researchers to make their data available, at least after they have had some time to make exclusive use of the data themselves. For example, independent replication of a researcher's results enhances the researcher's credibility.

4. What can academic researchers do to communicate and interpret the results of their research to public health practitioners and policymakers at the local, state, and federal levels?

An important step in communicating research results to policymakers would be making clear the implications of all key assumptions affecting the derivation of results or interpretation of conclusions. In addition, the following steps would better communicate research results to economic analysts. First, if effects measured in research studies represent changes in body chemistry or function, researchers could provide a mapping of these effects to health effects meaningful to people, such as changes in symptoms, ability to perform daily activities, or changes in risks of morbidity or premature mortality. Second, researchers could characterize key features of the best estimate of central tendency of dose-response or concentration-response functions, along with associated measures of statistical uncertainty. Third, researchers could give more attention to the behavioral adjustments that people make to protect themselves against environmental or other hazards, and how these adjustments may affect the estimated association between ambient concentrations or emissions and health effects. Fourth, researchers could provide some guidance as to what, if anything, relationships measured for a special subpopulation, such as children aged 8 to 12 years, might imply for the broader population.

5. How can institutions that support environmental health research facilitate the communication of research results to public health practitioners and policymakers? Are there instructive examples that you can provide?

If there were interest in incorporating behavioral adjustments into epidemiologic estimation of health effects, funding agencies might encourage more communication and cooperation between environ-

mental epidemiologists and researchers who specialize in studying human behavior, such as psychologists, decision analysts, and possibly even the occasional economist. Interdisciplinary research sometimes looks better on paper than in actual practice, but the strategy might be worth testing.

Dan Greenbaum, Health Effects Institute, Boston, MA

- 1. Do you have the opportunity to identify and use the most relevant research in carrying out your professional obligations? If so, how can you subsequently document the value/impact of such research? Do current systems/processes work to provide the needed information? What new approaches should be considered?**

Both in my role as Commissioner of Environmental Protection in Massachusetts and at the Health Effects Institute (HEI), I have had to frequently identify, from a wide range of sources and disciplines, the key findings for informing policy and public health decisions, ranging from the cleanup standards for Superfund sites to the most relevant data for setting ambient air quality standards. To inform such decisions in often controversial settings, it is essential that the science be of the highest quality, that is, drawn from studies relevant to the exposures and effects at issue, based on syntheses of the full literature (rather than individual studies), and integrating results from a variety of disciplines (e.g., epidemiology, toxicology, exposure). Science can provide this information, but it is usefully incorporated into the decision process only if it is designed initially to answer key policy questions (e.g., by providing dose-response information rather than just hazard assessment at high doses) and there is a transparent multidisciplinary expert process to ensure its thoughtful integration into decisions. (One example has been, at times, EPA's Clean Air Scientific Advisory Committee.)

- 2. What roles have emerging information technologies (e.g., wide access to the Internet with its massive volume of data and information) played to facilitate or complicate your ability to access and use the research information?**

There is no question that the Internet and enhanced computing power and data storage have provided the possibility for much greater access to current scientific information and have, in some instances, greatly enhanced the ability of decisionmakers to use the full range of information available (most notably through the growing practice among journals of providing access to extensive backup data for published articles). One particularly innovative approach to this practice has been the Internet Health and Air Pollution Surveillance System Web Site (IHAPSS), developed by Johns Hopkins University to place national health and air quality databases, along with the programs necessary to analyze them, on the Web (www.ihapss.jhsph.edu).

The plethora of information now available, however, has greatly increased the need for the kind of multidisciplinary synthesis and review processes mentioned above, as well as for new approaches to data screening and quantitative synthesis to sift through the voluminous (and not always peer-reviewed) information now available online.

- 3. What responsibilities should accompany publicly funded research? Is publication in peer-reviewed journals enough?**

I do not see a distinction between publicly and privately funded research. If research is being carried out in areas affecting public health and policy decisions, both types of research should be carried out in ways that maximize the utility for decisions, including being designed to answer policy-relevant questions and having transparency in the funding, design, and reporting of results (i.e., all negative as well as positive results). To meet these responsibilities, peer-reviewed publications—which often abstract positive findings from a broader and more important and diverse context of data and findings—are not sufficient, especially for studies that can be used for tasks such as quantitative risk assessment. To further ensure the credibility of either kind of research, it is important that other investi-

gators have access to data from important studies once the original investigators have had the opportunity to publish from their data.

4. What can academic researchers do to communicate and interpret the results of their research to public health practitioners and policymakers at the local, state, and federal levels?

They can identify and work with professionals and professional associations that have expertise in communicating complex scientific information in careful but understandable fashion to decisionmakers. They also can learn how to communicate effectively in public settings, such as workshops, with decisionmakers and how to testify before agency officials and legislators. These venues are challenging for many scientists, but scientists must increasingly realize that their communication work does not end, but rather begins, with the publication of results.

5. How can institutions that support environmental health research facilitate the communication of research results to public health practitioners and policymakers? Are there instructive examples that you can provide?

Institutions can facilitate the communication of research results in many ways, including the following:

- Creating understandable summaries to accompany publication of studies. (HEI, for example, publishes both a two-page “Statement” and a longer “Commentary” with each research report.)
- Convening workshops and meetings with targeted sessions that bring together scientists, science communicators, and public health and policy officials.
- Maintaining an accessible and easy-to-use Web site that quickly links users to different levels of information depending on their interest and skills. One example is the site maintained by the European group GreenFacts.org, which presents interlinked versions of complex reports (e.g., World Health Organization documents) at the executive summary, interpretive summary, and full report levels.

Biographical Sketches

Biographical Sketches

Shanna H. Swan, Ph.D., University of Missouri—Columbia, Columbia, MO

Dr. Shanna H. Swan is Research Professor in the Department of Family and Community Medicine, School of Medicine, and Adjunct Professor in Statistics at the University of Missouri—Columbia. She received an M.S. in Biostatistics from Columbia University and a Ph.D. in Statistics from the University of California—Berkeley. From 1981 to 1998, she served as Chief of the Reproductive Epidemiology Section at the California Department of Health Services. Dr. Swan is known for her work on the impact of environmental exposures on male and female reproductive health and has served on the National Academy of Science's Committee on Hormone-Related Toxicants. Since 1998 she has been Principal Investigator (PI) of the Study for Future Families, a multicenter pregnancy cohort study examining environmental causes of geographic variation in reproductive health endpoints in men, women, and children. Dr. Swan was elected Chair of the 2008 Gordon Research Conference on Environmental Endocrine Disruptors.

Xiaobin Wang, Sc.D., Children's Memorial Hospital, Chicago, IL

Dr. Xiaobin Wang received her M.D. degree from Beijing Medical University in 1983, her M.P.H. degree from Tulane University in 1987, and her Sc.D. degree from Johns Hopkins University in 1991. She received post-doctoral training in Environmental Epidemiology at the Harvard School of Public Health from 1991 to 1994 and pediatric residency training at Boston Medical Center from 1994 to 1998.

In the past 15 years, Dr. Wang's research has focused on children's growth and development, respiratory health, and molecular epidemiology of reproductive and birth outcomes. At present, Dr. Wang is the PI of three epidemiology projects funded by the National Institutes of Health and one epidemiology project funded by the March of Dimes Birth Defect Foundation. She leads a multidisciplinary research team that consists of representative(s) from each of the following disciplines: clinical medicine, epidemiology, molecular biology/genetics, biostatistics/bioinformatics, and environmental health sciences. The current research focus of her team is to investigate environmental factors and gene-environmental interactions in determining the risk of adverse reproductive outcomes and to integrate epidemiologic, clinical, and laboratory methods to better understand their pathogenic pathways and biological mechanisms.

Laura Fenster, Ph.D., California Department of Health Services, Emeryville, CA

Dr. Laura Fenster is a reproductive epidemiologist at the California Department of Health Services (CDHS), where she has worked since completing her Ph.D. in Epidemiology at the University of California—Berkeley. She has experience as a PI and co-investigator on a number of large collaborative multicenter studies of reproductive outcomes associated with *in utero* toxicant exposures; these studies have examined risk factors for spontaneous abortion and adverse fetal growth outcomes. She is currently the PI at the CDHS for the Endocrine Disruptors and Neurodevelopment Outcomes grant funded by the National Institute for Occupational Safety and Health (NIOSH). In addition she is a co-investigator, with the Center for the Health Assessment of Mothers and Children of Salinas, on a community-based participatory research project titled "A Longitudinal Birth Cohort Study of the Effects of Pre- and Postnatal Pesticide Exposure on Growth, Neurodevelopment, and Respiratory Health in Children Aged 3 to 7 Years in an Agricultural Community." She also has served as a co-investigator on studies of other reproductive endpoints, such as menstrual function and semen quality. For example, she was a co-investigator on the Women's Reproductive Health Study (WRHS) that involved daily collection of urine samples to measure hormone metabolites. The focus in the WRHS study was on the steroid hormones that were used to define several parameters of menstrual function, which were then examined in relation to exogenous exposures. Dr. Fenster had primary responsibility for the analyses of the semen quality of the male partners of women in the WRHS; semen quality was investigated in relation to a number of environmental and lifestyle factors.

James H. Raymer, Ph.D., RTI International, Research Triangle Park, NC

Dr. James H. Raymer of RTI International received a Ph.D. in Analytical Chemistry from Indiana University—Bloomington in 1984. His research interests have included the identification and quantitation of trace-level organic compounds in biological and environmental media using chromatographic, spectroscopic, and mass spectrometric methods. For the past 15 years, he has been heavily involved in human exposure analysis research for both adults and children and currently holds the position of Senior Program Director for the Health-Directed Exposure Research Program at RTI. Some of Dr. Raymer's current projects are focused on linking adverse health outcomes with environmental exposures to various chemical classes, including pesticides, water disinfection byproducts, endocrine disruptors, and persistent organic chemicals, including perfluorinated compounds.

Tongzhang Zheng, M.D., Sc.D., Yale University

Dr. Tongzhang Zheng is the Division Head for the Division of Environmental Health Sciences at Yale University School of Public Health. During the past 14 years, his research has been in the areas of environmental exposures and cancer risk, including breast cancer, non-Hodgkin's lymphoma, and Hodgkin's disease. He is especially interested in the relationship between environmental endocrine disruptors and human cancer risk.

Victoria Holt, Ph.D., M.P.H., Fred Hutchinson Cancer Research Center, Seattle, VA

Dr. Victoria Holt is Professor of Epidemiology at the University of Washington School of Public Health and Community Medicine and Member (Joint) at the Fred Hutchinson Cancer Research Center. She has more than 15 years of experience conducting epidemiologic studies of women's reproductive health issues, including most recently a case-control study of the etiology of endometriosis conducted in a large health maintenance organization in Washington State. Dr. Holt teaches a graduate-level course in Reproductive Epidemiology at the University of Washington.

Russ Hauser, M.D., M.P.H., Sc.D., Harvard School of Public Health, Boston, MA

Dr. Russ Hauser is an Associate Professor in the Department of Environmental Health at the Harvard School of Public Health. He obtained his M.D. from the Albert Einstein College of Medicine and his Sc.D. from the Harvard School of Public Health. His research interests are in the areas of reproductive health and childhood development. With funding provided by the U.S. EPA, he is conducting a large cohort study on the relationship between dioxin exposure and growth and development in adolescent boys in Chapaevsk, Russia. He also is conducting a study funded by the National Institute of Environmental Health Sciences on the relationship between PCBs, phthalates, and male reproductive health.

Dean B. Baker, M.D., M.P.H., University of California—Irvine, Irvine, CA

Dr. Dean Baker is Professor and Chief of the Division of Occupational and Environmental Medicine, Department of Medicine, and Director of the University of California—Irvine Center for Occupational and Environmental Health (COEH). He is an expert in occupational and environmental health. Dr. Baker received his medical degree from the University of California—San Diego and his M.P.H. degree in epidemiology from the University of California—Berkeley. He completed residency training in Family Medicine and Occupational Medicine prior to working as a medical officer for NIOSH. He was a faculty member of the UCLA School of Public Health and the Mount Sinai School of Medicine in New York before coming to the University of California—Irvine.

Dr. Baker's research emphasizes two areas. One area is the health effects of work environment and workplace psychosocial stressors. Dr. Baker is the co-author of a seminal article that was the first publication in the United States to demonstrate the association between high job strain (the combination of high work demands and low control) and increased risk of cardiovascular disease. During the past 20 years, the Job Strain Model

has become the predominate theoretical model of workplace stress, providing the foundation for a large body of research conducted by investigators throughout the world. Over the years, Dr. Baker has made substantial contributions to the medical literature in this area. Dr. Baker and colleagues at the University of California—Irvine will host an international conference on the Work Environment and Cardiovascular Disease next March in Southern California.

Another area of research is children's environmental health. Dr. Baker conducted a series of epidemiologic studies examining the health effects of gestational and early childhood exposure to heavy metals and organochlorine chemicals. For example, Dr. Baker completed a study of over 2,000 children in Tijuana, Mexico, to determine their blood lead levels and sources of lead exposure. He also conducted studies of families potentially exposed to DDT from a hazardous waste site in Southern California, and of high school students in Hawaii who had potential gestational exposure to the pesticide heptachlor. The research on the Hawaii cohort of children, who are now 21 years of age, addressed biological indicators of exposure, latent neurobehavioral effects, and current reproductive and immunologic function effects due to the gestational pesticide exposure. Because of this expertise, the UC Irvine COEH has been designated by the U.S. EPA as a regional Pediatric Environmental Health Specialty Unit. In both of these areas, Dr. Baker made contributions to the epidemiologic study design and methods. These contributions were recognized by the World Health Organization (WHO), which asked Dr. Baker to serve as the lead editor for the WHO's textbook on *Environmental Epidemiology* (1999). Dr. Baker also has been recognized by his peers, being elected twice as Secretary-Treasurer of the International Society for Environmental Epidemiology, the leading international professional society in his field of research. He also is strongly devoted to teaching occupational medicine and epidemiology. He was the director of the preventive medicine residency program and professor of epidemiology at the UCLA School of Public Health. He then directed an environmental epidemiology fellowship program at the Mount Sinai School of Medicine in New York. Since 1993, he has directed the UC Irvine occupational medicine residency program and taught in the graduate programs in epidemiology and toxicology at the university. His medical writings include multiple chapters in reference and teaching textbooks.

Irva Hertz-Picciotto, Ph.D., University of California

Dr. Irva Hertz-Picciotto, Professor, received her B.A. in mathematics, M.A. in biostatistics, and Ph.D./M.P.H. in epidemiology from the University of California (UC)—Berkeley. After 12 years on the faculty at the University of North Carolina (UNC)—Chapel Hill, she returned to California to join the UC Davis Department of Public Health Sciences (formerly the Department of Epidemiology and Preventive Medicine). Her research interests are in environmental exposures (metals, pesticides, polychlorinated biphenyls, air pollution), pregnancy outcomes (spontaneous abortion, fetal growth, early child development), and epidemiologic methods (left truncation in survival analysis, the "healthy worker survivor bias," timing issues, and use of epidemiologic data in quantitative risk assessment). Dr. Hertz-Picciotto authored the chapter "Environmental Epidemiology" in the textbook *Modern Epidemiology* by Rothman and Greenland, and she currently serves on editorial boards for the *American Journal of Epidemiology*, *Environmental Health Perspectives*, and *Epidemiology*, as well as on scientific advisory boards for the State of California, EPA, the National Toxicology Program of the National Institute of Environmental Health Sciences, and the National Institute for Occupational Safety and Health. In 2000 and 2002, Dr. Hertz-Picciotto chaired the U.S. Institute of Medicine/National Academy of Sciences Committee on the Health Effects in Vietnam Veterans of Exposure to Agent Orange and Other Herbicides. She directed the program in Reproductive Epidemiology at UNC Chapel Hill and is the Deputy Director of the Children's Center for Environmental Health at UC Davis, focused on autism and other neurodevelopmental disorders. Dr. Hertz-Picciotto has taught courses on 4 continents; was dissertation advisor for 17 doctoral students, 4 of whom won prizes for work conducted as doctoral students; and mentored 3 dozen other Ph.D. students.

**Pamela Imm, M.S., Wisconsin Department of Health and Family Services,
Madison, WI**

Ms. Pamela Imm is currently the Research Program Manager/Epidemiologist for the Great Lakes Sport Fish (GLSF) Consortium Program with the Wisconsin Department of Health and Family Services, Bureau of Environmental Health. She joined the Bureau in January 2003 as an epidemiologist for the vermiculite/mesothelioma grant funded by the Agency for Toxic Substances and Disease Registry before becoming the manager of the GLSF Consortium. Ms. Imm has worked for the Department for the past 10 years as a research and policy analyst as well. She has managed two statewide health surveys, including the Behavioral Risk Factor Survey, sponsored by the Centers for Disease Control and Prevention, and the Wisconsin Family Health Survey. She also has managed Medicaid programs as a policy analyst in the Wisconsin Division of Health Care Financing.

**Stephen M. Schwartz, M.D., Fred Hutchinson Cancer Research Center,
Seattle, WA**

Dr. Stephen M. Schwartz currently is appointed as a Member in the Division of Public Health Sciences at the Fred Hutchinson Cancer Research Center, where he directs molecular epidemiologic studies of testicular cancer, HPV-related anogenital cancers, and oral cancer. He also serves as co-PI of the Cancer Surveillance System of western Washington and is a participant in the Surveillance, Epidemiology, and End Results (SEER) program of population-based cancer registries funded by the National Cancer Institute. In addition, he is a Full Professor in the Department of Epidemiology, School of Public Health and Community Medicine, University of Washington, where he serves as Graduate Program Director and teaches courses on the integration of laboratory methods in population studies.

**Philippe Grandjean, M.D., Ph.D., Occupational Health Program, Harvard School
of Public Health, Boston, MA**

Dr. Philippe Grandjean has been an Adjunct Professor of Environmental Health at the Harvard School of Public Health since January 2003. Prior to this, he spent 8 years as an Adjunct Professor of Environmental Health and Neurology at Boston University. Concurrently, Dr. Grandjean serves as Professor and Chair of Environmental Medicine at the University of Southern Denmark, Odense, Denmark, and he has been appointed Consultant at the National Board of Health, Denmark. He is editor-in-chief (with Dr. David Ozonoff) of the Web-based journal *Environmental Health* and is a member of the editorial boards of 10 other scientific journals. He has served on or chaired committees under the auspices of WHO, the International Agency for Research on Cancer, the European Commission, the International Union of Pure and Applied Chemistry, and the U.S. EPA, and he is a member of the newly founded Panel on Food Contaminants of the European Food Safety Authority. The research on marine contaminants and their effects on child development in the Faroe Islands was initiated in the mid-1980s, and the prospective birth cohort studies have led to an international collaborative project that inspired downward revisions of methylmercury exposure limits worldwide. Dr. Grandjean was the founding Director of the Department of Occupational Medicine at the Danish NIOSH and since then has never left occupational health research. His main research efforts relate to metal toxicology, biomarker development and validation, endocrine disruption (especially estrogenicity caused by organochlorine exposures and their possible role as risk factors for breast cancer), and the carcinogenicity of fluoride, metals, and mineral fibers. In addition, Dr. Grandjean is a leader in the effort to introduce the precautionary principle into standards-setting in occupational and environmental health and research. Of his more than 300 scientific publications, half are in international journals with peer review.

PANELISTS

Harold Zenick, Ph.D.

Dr. Harold Zenick is the Associate Director for Health, National Health and Environmental Effects Research Laboratory (NHEERL) in the Office of Research and Development in the U.S. Environmental Protection Agency (EPA). Dr. Zenick earned a Ph.D. in Physiological Psychology from the University of Missouri (Columbia). He also completed a Postdoctoral Fellowship in Toxicology at the University of Cincinnati. Prior to joining NHEERL, he was a Branch Chief in EPA's Office of Health and Environmental Assessment, Office of Research and Development. Before coming to EPA, Dr. Zenick spent 13 years in academia with the Department of Environmental Health in the University of Cincinnati Medical School preceded by an appointment at New Mexico Highlands University. Dr. Zenick serves as EPA's liaison to the National Institute of Environmental Health Sciences (NIEHS), the National Toxicology Program (NTP), and the National Center for Environmental Health/Centers for Disease Control and Prevention (NCEH/CDC) Advisory Councils/Boards.

Currently, Dr. Zenick serves as a U.S. Co-Chair of the Environmental Health Workgroup under the binational U.S.-Mexico Border 2012 Program. Within the Agency, he is Chair of the Agency's Health Effects Institute Advisory Board and is ORD's senior executive lead for environmental justice matters. He has received numerous Agency awards, including the prestigious Presidential Meritorious Executive Rank Award and the ORD Statesmanship award. Recently, he has had a leading role in several emerging programs at EPA, including efforts to develop better indicators of public health impact of environmental decisions. In this capacity, he has participated on a number of prominent National and Federal projects. Dr. Zenick also has the lead for the Office of Research and Development for several cross-EPA/cross-Federal Agency initiatives, including the impact of the environment on the rapidly growing, aging population and the Futures of Toxicity Testing.

Dr. Zenick has more than 100 publications. His current interests are in integrating human health and ecological risk assessment, strengthening the linkages between environmental and public health agendas and agencies, and the application of emerging computational and molecular sciences in improving risk assessment practices.

R. DeLon Hull, Ph.D., National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Cincinnati, OH

Dr. R. DeLon Hull is Director of NIOSH's Office of Research and Technology Transfer and leads the Research to Practice (r2p) initiative. Research to Practice is an initiative directed at enhancing the relevance and impact of NIOSH-funded research. Dr. Hull joined NIOSH in 1976 and has held a number of scientific and managerial positions throughout the Institute. Prior to his current assignment, Dr. Hull served as the Acting Deputy Director of NIOSH and Acting Director of NIOSH's field research division, which conducts health hazard evaluations; epidemiologic and industrial hygiene evaluations and research; and hazard, illness, and medical surveillance. He was involved in developing the National Occupational Research Agenda, was lead author of the NIOSH Alert on Latex Allergy, and has authored numerous research publications and NIOSH analytical methods.

LuAnn White, Ph.D., DABT, Center for Applied Environmental Public Health, Tulane University, New Orleans, LA

Dr. LuAnn White, a toxicologist, serves as the Director of the Center for Applied Environmental Public Health (CAEPH) at Tulane University School of Public Health and Tropical Medicine (SPHTM). She received a B.S. degree in chemistry from St. Mary's Dominican College and a Ph.D. in Pharmacology and Toxicology from Tulane University Medical Center. She is a Diplomate of the American Board of Toxicology.

Dr. White directs the Center of Excellence in Environmental Public Health Tracking and is co-director of the Tulane Prevention Research Center. Both of these Centers are funded by the Centers for Disease Control and Prevention and reside within CAEPH.

Dr. White's research focuses on the prevention of health effects in humans from environmental and occupational agents. She has developed methods to combine environmental health science with epidemiologic methods to identify and assess the effects of environmental and occupational agents on human health. Dr. White has conducted community-based health studies that encompass both emergency response situations and long-term exposures at hazardous waste sites. Her research also focuses on the prevention of childhood lead poisoning as well as environmental and occupational exposures. Dr. White has developed methods for developing risk communication messages for communities based on hazard, exposure, and health outcome data.

A leader in developing models for environmental health training and education programs, Dr. White has developed a skills-based approach for designing curricula for environmental health practice professionals. She also established the master's programs in environmental toxicology and risk assessment and in occupational health in the Department of Environmental Health Sciences at Tulane. Dr. White also has pioneered the development of distance learning at SPHTM. She launched the distance learning programs leading to the M.P.H. in Occupational Health and Safety Management, and Occupational Health, and the M.S.P.H. in Industrial Hygiene using interactive Internet technologies.

Mark Dickie, Ph.D., University of Central Florida, Orlando, FL

Dr. Mark Dickie is Professor of Economics at the University of Central Florida in Orlando, Florida. His research involves estimating the economic benefits of reducing adverse environmental health effects, understanding the determinants of individuals' perceptions of health risks from environmental hazards, and examining individuals' behavioral reactions to environmental health hazards. His current research examines these issues in the context of children's environmental health, focusing on asthma, acute symptoms of air pollution exposure, and skin cancer. Dr. Dickie's work is funded by the U.S. Environmental Protection Agency. He also serves on EPA's Children's Health Protection Advisory Committee.

Dan Greenbaum, Health Effects Institute, Boston, MA

Mr. Dan Greenbaum is the President and Chief Executive Officer of the Health Effects Institute (HEI), an independent nonprofit research institute supported jointly by the U.S. EPA and industry to provide public and private decisionmakers with high-quality, impartial, relevant, and credible science about the health effects of air pollution. Mr. Greenbaum has chaired a number of national panels on air pollution and health for EPA and the National Research Council (NRC). Most recently, he served as vice chair of the NRC's Committee for Air Quality Management in the United States. He regularly presents the results of HEI's scientific work to U.S., international, and state audiences; the U.S. Congress; the Asian Development Bank; and the European Parliament.

Mr. Greenbaum has three decades of government and nongovernment experience in environmental health. Prior to coming to HEI, he served as Commissioner of the Massachusetts Department of Environmental Protection from 1988 to 1994.

U.S. EPA National Center for Environmental Research
Endocrine Disruptors Program Progress Review Workshop
Endocrine Disruptors: Epidemiologic Approaches

**Center for Bioenvironmental Research
Tulane and Xavier Universities
New Orleans, LA**

October 30, 2004

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