Testimony
Before the Subcommittee on Superfund, Toxics and Environmental Health
Committee on Environment and Public Works
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Statement for hearing entitled, "Current Science on Public Exposures to Toxic Chemicals"

Statement of

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Mr. Chairman and distinguished members of the Subcommittee, I am pleased to appear before you today to present testimony on recent science related to exposure assessment.

Since human disease sometimes results from the interactions of our genetic susceptibilities and our environmental exposures,[1] having reliable data on exposure is essential to planning for and carrying out research on how environmental exposures initiate or promote disease.

From the days when one outdoor monitor in a city would be used to measure air pollution for a study to backpack monitors to badges pinned on a shirt, our ability to measure exposure continues to improve significantly.

In this statement, I shall describe some examples of research where exposure in the U.S. population or a vulnerable subgroup drove or changed the research agenda, some studies exploring the initiation or promotion of disease related to environmental exposures and the efforts made by researchers to use the best possible exposure data, and some of the technologies to assess exposures under development by the National Institute of Environmental Health Sciences (NIEHS), which is part of the National Institutes of Health, an agency of the U.S. Department of Health and Human Services (HHS).

The importance of biomonitoring cannot be underestimated. It can tell us three things: whether exposure to humans is actually occurring; at what levels; and how widespread the exposure is in the population. Sometimes the information is new; other times it confirms something we already suspected based on what we know about how a manmade or naturally occurring compound is used and where it is found in the environment. And occasionally, we are surprised by the results.

Findings from biomonitoring studies often trigger new research, either toxicology or population-based studies to investigate potential adverse health outcomes. One example is the surprising finding by HHS's Centers for Disease Control and Prevention (CDC) in 2002 of high levels of tungsten in urine of residents of Churchill County, Nevada, the site of a childhood leukemia cluster. Since we do not know enough about tungsten to understand whether this is a health risk, this discovery prompted the National Toxicology Program (NTP) to initiate studies on tungsten. More recently, CDC national blood and urine data showing widespread U.S. population exposure to parabens, triclosan and oxybenzone were an important factor in the decision to conduct additional toxicology studies for these compounds. What biomonitoring cannot tell us is the source of the exposure. For example, bisphenol A exposure is widespread in the population as evidenced by urinary levels in biomonitoring studies. We suspect that much of the bisphenol A exposure is coming from food and beverage containers. The findings from a small CDC study that premature infants in neonatal intensive care units (NICUs) had substantial levels of bisphenol A in urine indicated other sources of exposure. In a recently published study, the authors suspect the source was the presence of bisphenol A in polyvinyl chloride-containing medical devices used in NICUs.[2] Since premature infants represent a uniquely sensitive

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[1] The World Health Organization defines exposure as the contact between an agent and a target. The target may be an individual or a population; it can be an organ, a tissue, or a cell. The agent of exposure can be a biological, physical, or psychosocial stressor.

[2] Exposure to Bisphenol A and Other Phenols in Neonatal Intensive Care Unit Premature Infants. Environ Health Perspect 117:639–644 (2009).

subpopulation, additional research is being carried out to understand the health risks of such exposures. Many if not all of the substances in CDC's biomonitoring program are included because of evidence that they pose potential human health hazards. For example, DEHP and other phthalates were included in CDC's first National Exposure Report because of known adverse developmental and reproductive effects in rodents, as identified in NTP and other toxicological studies. The same is true for heavy metals, certain pesticides, polycyclic aromatic hydrocarbons (PAHs), etc. As new hazards are identified from toxicological research, these compounds become good candidates for inclusion in national biomonitoring studies, e.g., brominated flame retardants. Once biomonitoring studies show us the range and nature of exposures occurring in the general U.S. population, the cycle continues as additional toxicological and epidemiological research is triggered to increase our knowledge on specific adverse health risks.

The Agricultural Health Study is a cohort study of 57,000 licensed pesticide applicators and 32,000 of their spouses in Iowa and North Carolina. NIEHS scientists, in collaboration with colleagues from NIH's National Cancer Institute (NCI), the Environmental Protection Agency (EPA) and CDC's National Institute for Occupational Safety and Health (NIOSH), have carried out biomonitoring studies of subgroups of pesticide applicators using specific chemicals and have used these data to validate and refine their questionnaire-based exposure algorithms for the much larger study population. In other studies conducted within the cohort, researchers have collected house/farm dust and biological samples to assess exposure to pesticides, endotoxins, and metals as well as gene variants that may affect risk of specific health outcomes.

In preparation for studies to assess health-related risks to mothers and their offspring, NIEHS researchers are assessing the validity of using blood and urine samples at a single time during pregnancy. They are assessing the agreement between measures from samples taken at three points during pregnancy to determine if a single sample is reliable enough to assess risk related to phthalates, pesticides, bisphenol A, and perfluorooctanoic acid (PFOA).

An example of biomonitoring where surprising results triggered additional research occurred in one of the NIEHS/NCI Breast Cancer and Environment Centers studies. Researchers found unexpectedly high levels of PFOA in girls in one school district. The source of the exposure could not be determined. The researchers worked with their community partners who had been involved in the program from the beginning to survey families about how they wanted to receive study results. In response to the survey, the researchers and the community partners produced a newsletter to provide updates to the families. The researchers have since received a second grant to identify possible sources and health effects of PFOA.

Sometimes an event changes an exposure in a population allowing a "before" and "after" comparison. In a study of infants born before the EPA's regulatory actions to phase out residential use of chlorpyrifos and diazinon, the association between birth weight and length and cord blood levels of these insecticides was highly significant. Among infants born after January

2001, exposure levels were substantially lower and no association with fetal growth was apparent.[3]

Concern about widespread exposure in the U.S. population often guides the NIEHS research agenda. In 1974, NIEHS launched a classic study in six cities to explore the associations between air pollution produced by fossil fuels and respiratory health in large cohorts of adults and children which provided a wealth of information. Collaboration with EPA led to expansion of this study to include more cities and confirmed the negative effects of air pollution on human health. In 1978, the NTP tested yellow paint on pencils; there was no evidence of carcinogenicity in rats or mice.[4] In a 2009 study of the effects of PAHs on children's IQ in New York City (Washington Heights, Harlem, and the South Bronx), the mothers' exposure as measured during their pregnancies by wearing backpack monitors was associated with a decrease in IQ among the more exposed children. The extent of this effect was similar to that of low-level lead exposure.[5]

By 2015, the use of engineered nanomaterials (ENMs) and nano-enabled devices is expected to exceed $3 trillion, resulting in exposures with possible unknown consequences to health and the environment. A key first step in understanding risk is to develop ways to measure exposures. NIEHS is supporting studies with funding from the American Recovery and Reinvestment Act of 2009 (ARRA) to conduct real-time, on-site measurement of exposures with a suite of instruments to characterize ENMs during different phases of the production process. The next step is to understand their interactions with biological systems and the resulting health risks. Again using ARRA funding, NIEHS is supporting studies on ENM-induced inflammatory and oxidative stress responses in multiple cell culture systems with the goal of finding biomarkers of response. This information will provide cell-specific and ENM-specific toxicity profiles. Other studies are looking at the fundamental interactions of ENMs at the cellular and molecular levels. ARRA funding is also supporting studies using animals to determine organ specific health effects and to evaluate human health risks of ENMs. Studies planned include research on the following:

- The effect of inhaled ENMs on the respiratory tract, brain, liver, and other organs;
- Whether inhaled cadmium nanoparticles can cross the placenta and influence fetal stability and development; and
- Pulmonary effects of ENMs to understand whether they modify the effects of other agents (e.g., drugs, vaccines) while having minimal effects on their own, enhance allergen sensitization, or alter innate immunity.

NIEHS is also supporting research on nanotechnologies to improve environmental monitoring. Detection devices under development include:

- a microsensor for detecting formaldehyde in air
- nanobiosensors for probing chemical exposures and their effects on individual cells

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[3] Prenatal insecticide exposures and birth weight and length among an urban minority cohort. Environ Health Perspect 112:1125-1132 (2004).

[4] Bioassay of diarylanide yellow for possible carcinogenicity CAS No. 6358-85-6. National Cancer Institute Carcinogenesis Technical Report Series No. 30 (1978) http://ntp.niehs.nih.gov/ntp/htdocs/LT_rpts/tr030.pdf - 2234.3KB

[5] Prenatal airborne polycyclic aromatic hydrocarbon exposure and child IQ at age 5 years. Pediatrics 124:e195-e202 (2009).

- wearable nanosensors (approximately 4”x4”) for real-time monitoring of diesel and gasoline exhaust
- Low-cost, portable sensors for measuring metals such as arsenic and mercury at hazardous waste sites.

Investigators studying the interplay of genetic and environmental factors in the risk for Parkinson’s disease have developed a new model to estimate residential exposure of individuals to pesticide drift from nearby farms. The exposure model uses a geographic information system that combines data on home addresses, land use, and pesticide applications. By measuring the proximity of residences to the fields where pesticides were applied, this model allows estimation of exposures that occur with drift from application sites and/or travel through soil to water wells. One of their studies showed that residential exposure to a combination of the herbicide paraquat and the fungicide maneb increases the risk of Parkinson’s disease.[6] Another study revealed that estimated pesticide exposures from drift and from well water contamination combined to increase risk of Parkinson’s disease.[7]

An investigator in California is using ARRA funding to improve exposure modeling in a study of birth outcomes related to exposure to pollution from traffic. Using real-time global positioning system (GPS) tracking and detailed activity questionnaires to determine locations more accurately, the model will assess pregnant women’s exposure to traffic-related air pollution with greater precision.

In the NIEHS Sister Study of 51,000 women whose sisters have breast cancer, researchers have collected urine, blood, toenail, and dust samples to provide a snapshot of environmental exposures at the time of enrollment in the study. The study will assess exposure to pesticides, other hormonally active compounds such as bisphenol A and phthalates, toxic metals, trace metals, vitamin D, specific micronutrients, and hormones. Samples will also be used to measure gene variants that may be related to disease risk. The study design will allow researchers to assess the associations between breast cancer and other diseases with these markers of exposure, nutrition and health status. Ultimately these data will be used in studies of gene-environment interactions. These data will also be used in conjunction with self-reported questionnaire data to develop questionnaire-based exposure measures and to validate both questionnaire-based methods and the use of single biological samples. Lastly, these data will support mechanistic studies of specific pathways leading to breast cancer risk and to develop markers for early detection or for predicting progression of disease.

Determining actual levels of exposure for use in research, risk assessment, and risk management is an ongoing challenge, and NIEHS is actively pursuing many research approaches to help solve this problem and thus promote more accurate science and better decision making. For example, the NIEHS is supporting development and testing of a robot called PIPER[8] capable of mimicking children’s floor activities while collecting better estimates of young children’s

[6] Parkinson’s Disease and residential exposure to maneb and paraquat from agricultural applications in the central valley of California. Am J Epidemio 169(8):919-926 (2009)
[7] Well-water consumption and Parkinson’s Disease in rural California. Environ Health Perspect 117:1912-1918 (2009).
[8] Pretoddler Inhalable Particulate Environmental Robotic

exposure to indoor air pollutants (particulate matter, pesticides, allergens, endotoxins and airborne fungi). A study of asthma and indoor environmental contaminants is currently underway to test PIPER in the homes of 200 children. The study will compare measurements of particulates obtained by PIPER with those from standard adult height monitoring stations and examine their association with asthma symptoms.

The NIEHS has the lead for the Exposure Biology Program of the trans-NIH Genes, Environment and Health Initiative. The Program is funding 32 projects focusing on the development of innovative technologies to measure environmental exposures, diet, physical activities, psychosocial stress, and others factors that contribute to disease development. In addition to developing new measures of exposure, the program also supports the development of markers of biological response and DNA damage, as well as the development of biosensors based on monitoring biological responses. A critical aspect is the integration of these technologies to enable a more accurate understanding of exposure. For example, the combination of physical activity measurements with particulate matter exposure allows for an improved estimate of individual dose. With the additional inclusion of GPS analysis, this information can potentially be used to identify the sources of these exposures and guide the development of interventions to improve public health.

In summary, understanding the connection between our health and our environment, with its mixture of chemicals, diet and lifestyle stressors, is no less complex than understanding the intricacies of the human genome. At NIEHS, we remain committed to helping the field of exposure science evolve to meet emerging public health challenges. We look forward to the increased contributions of exposure scientists as we work to understand the role of environment in the etiology of disease.

Mr. Chairman and members of the Subcommittee, I am pleased to present testimony on this important issue and would be happy to answer any questions.