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Mr. Chairman and Members of the Committee: I am pleased to present the President's Fiscal Year (FY) 2017 budget request for the National Institute of Environmental Health Sciences (NIEHS) of the National Institutes of Health (NIH).

UNDERSTANDING OUR EXPOSURES

An oil rig explodes in the Gulf of Mexico impacting an entire region's way of life. A manufacturing plant spills thousands of gallons of toxic chemicals into a river in West Virginia creating unknown risks to nearby residents. A combination of aging pipes and corrosive water leaches lead into drinking water in Flint, Michigan, posing irreversible harm to the city's children. These recent events bring into stark relief the critical need for strong exposure science – the first step in responding to an environmental health emergency is to understand the nature of the threat. But as prominent, tragic, and increasingly common as such occurrences are, they represent only a small part of the thousands of potentially harmful chemicals, metals, and other environmental pollutants our nation's people are faced with on a daily basis.

Protecting people's health from the consequences of such encounters requires knowledge, not only of the nature of the hazard itself, but just as importantly, of the means, amount, and effects of exposure to it. And further complicating our ability to determine our risk is the combination of human response variability and disparate exposures to environmental health threats. But such knowledge must be obtained if we are not only to respond to exposures after they occur, but be successful in the larger goal of avoiding harmful exposures, and thereby preventing illness and disease from ever occurring. The recognition of this fundamental scientific need is the basis of the work of NIEHS and the reason why our Institute has prioritized exposure science in its Strategic Plan. Although the issue of exposures is integrated throughout the plan, specific goals call for NIEHS to "Transform exposure science by enabling consideration of the totality of human exposures and links to biological pathways, and create a blueprint for incorporating exposure science into human health studies," and to "Understand how combined environmental exposures affect disease pathogenesis." I will describe just some of the ways in which NIEHS has made significant progress toward these goals and toward ensuring the health of the American people.

CONNECTING EXPOSURES TO OUTCOMES

Five years after the Deepwater Horizon (DWH) oil rig explosion, which caused the largest oil spill in U.S. history, NIEHS-supported researchers continue work in three related areas – a health effects study of oil spill cleanup workers called the GuLF Study, research partnerships between Gulf-area universities and community organizations, and an NIH disaster research response effort. The research team developed a job-exposure matrix that enabled scientists to characterize exposures of workers participating in the

GuLF Study and assess possible links between reported health symptoms and the chemicals each worker was exposed to, and preliminary results are being analyzed. University-community partnerships are focusing on health concerns identified by communities after the oil spill, including pregnancy and birth outcomes, general physical and mental health of coastal residents, and seafood safety. A study of 2,126 adult women residing in Southern Louisiana enrolled in the Women and Their Children's Health (WaTCH) study showed that both physical/environmental and economic exposure to the oil spill was associated with an increase in self-reported physical health outcomes. On a positive note, a risk assessment of exposure to polycyclic aromatic hydrocarbons of Vietnamese-Americans, a large shrimp-consuming population in the area, showed no acute health risks or excess cancers, reducing concerns about shrimp consumption following the DWH spill.

Following the spill of 10,000 gallons of the chemical 4-Methylcyclohexanemethanol (MCHM) into the Elk River upstream of the municipal water intake of Charleston, West Virginia, NIEHS researchers were able to help allay the fears of the community and state officials through a timely assessment that combined exposure data with a suite of health effect prediction studies, including computer modeling and laboratory toxicity studies. Findings of these investigators provided additional support for the adequacy of the drinking water advisory set by the Centers for Disease Control and Prevention at the time of the spill as being protective of health.

In response to the latest public health disaster, the exposure of the population of Flint, Michigan, to lead in contaminated drinking water, NIEHS staff and grantees are leading efforts to understand residents' – especially children's – lead exposures to inform the public health response, both immediately and over the long-term. A long and continuing history of support of research on lead enables such efforts. Recent research by NIEHS grantees in Michigan demonstrated, for the first time, that lead exposure of pregnant mothers can affect DNA methylation patterns in their grandchildren, suggesting that a much longer-term perspective may be needed when considering measures to protect environmental health in the future. Also, NIEHS-funded research of lead-poisoned children in China recently established that measurement of lead in bone (through X-ray fluorescence) is a useful biomarker of lead exposure in children. Such research illustrates the kind of knowledge that might be applied to situations like the one in Flint. It is this kind of useful knowledge that NIEHS hopes to enable researchers to obtain through its recently established Children's Health and Exposure Assessment Resource (CHEAR), which will provide a laboratory network, data repository, and an analysis center to leverage the public investments of NIH-funded scientists to better understand environmental exposures and human health.

Public health disasters such as chemical releases, hurricanes, infectious disease outbreaks, and others comprise unique exposure scenarios that can offer insights into environmental exposures encountered, not only by the affected communities and responders, but also by a broader range of the population. NIEHS, in collaboration with the National Library of Medicine, has developed the Disaster Research Response (DR2) program to further our national ability to gather time-critical exposure and health

information to reduce adverse health effects and improve response, recovery, and preparedness for future events. At the same time, this program will facilitate discovery research and generate novel hypotheses that will add to the body of knowledge underlying exposure related conditions such as cancer, neurological, and immune diseases and disorders.

Disasters are compelling for both public and research attention, and deservedly so. But NIEHS efforts to elucidate the broad range of environmental exposures are far more proactive than responsive, and consistently generate findings that increase our ability to protect and improve people's health. For example, an ongoing project is using a matrix biomarker of tooth development to reconstruct the exposome – the compilation of multiple chemical exposures – over different life stages. A better understanding of how and when specific exposures occur will improve our ability to target interventions, particularly during critical windows of development. NIEHS-funded investigators also are working at the cutting edge of research on the microbiome, investigating interactions between the gut microbiome and exposure to arsenic, a known human carcinogen, and uncovering the relationship between obesity and exposure to ozone.

TRANSLATING SCIENCE INTO ACTION

NIEHS efforts are directly supportive of major health initiatives in the United States including Big Data to Knowledge (BD2K), the National Cancer Moonshot, and the Precision Medicine Initiative.

NIH's BD2K initiative is focused on developing new strategies to analyze and leverage the explosion of increasingly complex biomedical data sets. NIEHS is leading the program's Training and Workforce Development efforts. These awards support current and future generations of researchers to specialize in data science fields and in the use or generation of Big Data. A current awardee is working to establish new integrative and data-driven methods for building systems neuroscience models of executive functioning during childhood, reporting recent advances in improving the specificity of magnetic resonance imaging (MRI) scans.

The recently announced National Cancer Moonshot aims to bring about a decade's worth of advances in five years, in part by improving our ability to prevent cancer and detect it at an early stage. Cancer, like most other non-communicable diseases, is a result of a person's genetics, age, and environment (including lifestyle), and the World Health Organization estimates that nearly 20 percent of cancers may result from toxic chemical exposures. NIEHS-supported researchers continue to make groundbreaking advances in our understanding of the complex interactions between these three factors, leading to knowledge to inform cancer detection and prevention strategies, as well as treatments and therapies. For example, polycyclic aromatic hydrocarbons (PAHs) are probable carcinogens found in coal tar, diesel exhaust, and wildfire, cookstove, and cigarette smoke. People are primarily exposed to PAHs in mixtures, though current risk assessments focus on individual components. An NIEHS grantee and

colleagues have developed a faster, more accurate method to assess cancer risk from mixtures of PAHs by evaluating bioactivity after short-term exposure.

An example of NIEHS contributions to potential cancer therapy lies in treatment of ovarian cancer. The recurrence rate of ovarian cancer exceeds 75 percent, and the success of subsequent chemotherapy is limited because of the progressive development of drug resistance. New NIEHS findings suggest that a novel mechanism, combined activation of an early growth factor (EGR1) and microRNA (MIR152), may provide a useful therapeutic strategy to overcome resistance to the chemotherapy drug cisplatin, and improve outcomes in ovarian cancer.

NIEHS research spans the spectrum of scientific inquiry from basic mechanisms to exposure science to clinical research aimed toward intervention and treatment. Precision medicine is an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person. Advances by NIEHS scientists are poised to make great contributions to the promise of precision medicine. These contributions range from identifying factors including autoantibodies, clinical factors, and environmental exposures at illness onset associated with the disease course of juvenile myositis, a group of rare and life-threatening autoimmune diseases in children, to developing a method for isolating certain rare cells of metastatic breast cancers in blood and profiling their gene expression to provide real-time warnings of emerging chemotherapy resistance.

CONCLUSION

To conclude, NIEHS continues to be at the forefront of environmental health: identifying emerging health threats, developing and implementing new technologies to characterize and analyze our exposure to the world around us, and leading the generation of knowledge of how our environment interacts with our genetics to cause illness and disease. And consistent with our mission, we will continue to lead these efforts in support of the nation’s initiatives to improve and ensure the health of the American people.

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Linda S. Birnbaum is the Director of the National Institute of Environmental Health Sciences (NIEHS) at the National Institutes of Health (NIH), and Director of the National Toxicology Program. A board certified toxicologist, Birnbaum has served as a Federal scientist for over 36 years. Dr. Birnbaum has received many awards and recognitions, including the Women in Toxicology Elsevier Mentoring Award, the Society of Toxicology Public Communications Award, EPA's Health Science Achievement Award and Diversity Leadership Award, the National Center for Women's 2012 Health Policy Hero Award, Breast Cancer Fund Heroes Award, and 14 Science and Technology Achievement Awards, which reflect the recommendations of EPA's external Science Advisory Board, for specific publications. Dr. Birnbaum was also elected to the National Academy of Medicine of the National Academies, and has received honorary degrees from the University of Rochester and Ben-Gurion University in Israel.

Dr. Birnbaum is a former president of the Society of Toxicology, the largest professional organization of toxicologists in the world; former chair of the Division of Toxicology at the American Society of Pharmacology and Therapeutics; and former vice president of the American Aging Association. She is the author of more than 700 peer-reviewed publications, book chapters, and reports. She also is an adjunct professor at the University of North Carolina at Chapel Hill and at Duke University. A native of New Jersey, Dr. Birnbaum received her M.S. and Ph.D. in microbiology from the University of Illinois at Urbana-Champaign.