National Institute of Environmental Health Sciences
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FY 2012 NIEHS Director's Statement

Department of Health and Human Services

National Institutes of Health

FY 2012 Budget Request

Witness appearing before the Senate Subcommittee on Labor-HHS-Education Appropriations
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National Institute of Environmental Health Sciences
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Mr. Chairman and Members of the Committee:

I am pleased to present the President's Fiscal Year (FY) 2012 Budget request for the National Institute of Environmental Health Sciences (NIEHS) of the National Institutes of Health (NIH). The FY 2012 budget includes $700,537,000; an increase of $17,400,000 over the comparable FY 2011 enacted level of $683,137,000, comparable for transfers proposed in the President's request.

Introduction

Good health is vitally important for all Americans, and it depends on a clean and safe environment. Currently, our health care system expends huge resources controlling a variety of diseases and dysfunctions that are known to be at least partially connected with environmental exposures: asthma, cancer, developmental disabilities, neurological/cognitive deficits, heart attack, and many others. Preventing these diseases through prevention of adverse environmental exposures could make an enormous difference in reducing health care costs. At NIEHS, and through NIEHS-funded projects in research institutions across the United States, we are bringing all the tools of biomedical science to bear on the fundamental questions of the effects of environmental exposures to toxic substances on biological systems. Environmental health science is advancing at a tremendous rate and new tools – genetics, genomics, proteomics, metabolomics, informatics, and computational biology, just to name some of these new disciplines – give us new insights on how environmental effects happen in our bodies. They also point the way toward technologies and testing procedures to provide better and more timely

information for the use of our agency partners who are responsible for policy decisions and regulations.

Advances in Toxicology and Exposure Assessment

With our rapidly increasing understanding of the subtleties of biological effects of environmental exposures, we are moving toward a new kind of toxicological testing that is less expensive and time-consuming than our current methods, and also gives us an improved understanding of the actual effects on humans. Toxicology is becoming a more powerful predictive science focused on making target-specific, mechanism-based, biological observations. Alternative assays are targeting the key pathways, molecular events, and processes linked to disease or injury and incorporating them into a research and testing framework. Our National Toxicology Program (NTP) at NIEHS is laying the foundation for this new testing paradigm in partnership with the National Human Genome Research Institute, the Environmental Protection Agency, and the Food and Drug Administration. We are using quantitative high-throughput screening assays to test a large number of chemicals. The resulting data are being deposited into publicly accessible relational databases. Analyses of these results will set the stage for a new framework for toxicity testing.

The NIEHS-led Exposure Biology Program (EBP), part of the NIH Genes, Environment and Health Initiative, has resulted in the development of dozens of new technological advances for personalized measurement of environmental exposures. At a recent workshop, EBP investigators presented their prototypes: miniaturized personal monitors for black carbon and other air pollutants; a wearable nanosensor array for real-time monitoring of exposure to diesel and gasoline exhaust; a personal aerosol sensor platform to link children's exposures to asthma severity; personal exposure assessment systems for chemical toxicants; gene expression biomarkers of airway response to tobacco exposure; and biomarkers of organophosphate-linked proteins. One prototype of a continuously operating wearable badge that provides real-time measurements of chemical toxicants has attracted subsequent R&D funding from the Department of Defense to develop this model for use by military personnel. Others are being moved into validation studies as a next step towards their deployment in environmental health research.

Epigenetics, Endocrine Disrupters, and Environmental Health

Our understanding of chemical toxicity has been challenged by the new science of epigenetics, which is the study of changes to the packaging of the DNA molecules that

influence the expression of genes, and hence the risks of diseases and altered development. Studies indicate that exposures that cause epigenetic changes can affect several generations.[1] This new understanding heightens the need to protect people at critical times in their development when they are most vulnerable. NIEHS is making key investments in understanding basic epigenetic processes and how they are influenced by environmental factors. Recently, some of this work has provided a critical resource for understanding and characterizing properties of human induced pluripotent stem cells.[2] The development of pluripotent stem cells shows promise for research and clinical applications in lieu of embryonic stem cells, but many questions remain to be answered about their structure, utility, and safety. NIEHS-funded investigators have established genome-wide reference maps of DNA methylation (an epigenetic marker) and gene expression in previously derived human embryonic cell lines and human iPS cell lines, to assess their epigenetic and transcriptional similarity and predict their differentiation efficiency. A separate report by another NIEHS-funded group reported "hotspots" of aberrant epigenomic reprogramming in human iPS cells.[3] There are still many questions about the role of these important epigenetic processes which will need to be answered before iPS cells can be confidently used in research and therapy.

Related to the field of epigenetics is the key concept of "windows of susceptibility." Research shows that the developmental processes that occur at fetal and early life stages are especially vulnerable to disruption from relatively low doses of certain chemicals.[4,5,6] We first saw this in the case of lead and other metals, such as mercury and arsenic, which we learned decades ago could harm neurological development as a result of fetal and childhood exposures. This concept also applies to hormonally active agents which disrupt the endocrine system. This is an active area of our research program. For example, NIEHS and NTP are funding important studies to fill the gaps in our knowledge about bisphenol A (BPA), a widely distributed compound used in plastics, can linings, thermal paper, and more. NTP's Center for Evaluation of Risks to Human Reproduction determined that there was "some concern" about effects to the brain, behavior, and prostate gland in fetuses, infants, and children exposed to BPA.[7] NIEHS is now supporting an aggressive research effort to fill the research gaps in this area, especially concerning BPA effects on behavior, obesity, diabetes, reproductive disorders, development of prostate, breast and uterine cancer, asthma, cardiovascular diseases and transgenerational or epigenetic effects.

Any consideration of important public health issues in the United States. has to include obesity. Environmental exposures are beginning to be implicated in the obesity epidemic.[8,9] NIEHS is supporting research on the developmental origins of obesity and the theory that environmental exposures during development play an important role in the

current epidemic of obesity, diabetes, and metabolic syndrome. There are data showing weight gain in adult rats and mice following developmental exposure to a number of different chemicals, such as tributyltin compounds,[10] which have been termed "obesogens" by some researchers. A groundbreaking workshop on environmental factors in obesity and diabetes was sponsored by NIEHS in January 2011. Many research gaps still need to be filled, but if these early research results are confirmed, we may find it more useful to expand our approach to fighting obesity to include not just educating about diet and lifestyle but also reducing early life exposure to these "obesogenic" chemicals that might be setting the stage for us to gain weight later in life.

Planning for the Future

NIEHS recently began work on the development of a new Strategic Plan to set goals for guiding our research investments over the next five years. Our process is designed to bring in information and perspectives from a wide variety of sources: community members, advocacy groups, agency partners, and scientists from all disciplines.

In summary, understanding the connection between our health and our environment, with its mixture of chemicals, diet and lifestyle stressors, is a complex and intricate scientific endeavor. At NIEHS, we remain committed to leading the evolution of the field of environmental health sciences to meet emerging public health challenges.

Linda S. Birnbaum, Ph.D., D.A.B.T., A.T.S

Linda S. Birnbaum, Ph.D., is the director of the National Institute of Environmental Health Sciences (NIEHS), part of the National Institutes of Health, and the National Toxicology Program (NTP). As NIEHS and NTP director, Birnbaum funds biomedical research to discover how the environment influences human health and disease. The Institute also supports training, education, technology transfer, and community outreach.

A board certified toxicologist, Birnbaum has served as a federal scientist for 31 years. Prior to her appointment as NIEHS and NTP director, she spent 19 years at the Environmental Protection Agency where she directed the largest division focusing on environmental health research. Birnbaum started her federal career with 10 years at the NIEHS — first as a senior staff fellow in the National Toxicology Program, then as a principal investigator and research microbiologist, and finally as a group leader for the Institute's Chemical Disposition Group.

Birnbaum has received many awards and recognitions. In October 2010, she was elected to the Institute of Medicine of the National Academies, one of the highest honors in the

fields of medicine and health. She was elected to the Collegium Ramazzini, and received an honorary Doctor of Science from the University of Rochester and Distinguished Alumna Award from the University of Illinois. Her awards include the Women in Toxicology Elsevier Mentoring Award, the Society of Toxicology Public Communications Award, EPA's Health Science Achievement Award and Diversity Leadership Award, and 12 Science and Technology Achievement Awards, which reflect the recommendations of EPA's external Science Advisory Board for specific publications. Birnbaum is also an active member of the scientific community. She was vice president of the International Union of Toxicology, the umbrella organization for toxicology societies in more than 50 countries; 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, abstracts, and reports. Birnbaum's own research focuses on the pharmacokinetic behavior of environmental chemicals, mechanisms of action of toxicants including endocrine disruptors, and linking of real-world exposures to health effects. She is also an adjunct professor in the Gillings School of Global Public Health, the Curriculum in Toxicology, and the Department of Environmental Sciences and Engineering at the University of North Carolina at Chapel Hill, as well as in the Integrated Toxicology Program at Duke University. A native of New Jersey, Birnbaum received her M.S. and Ph.D. in microbiology from the University of Illinois at Urbana-Champaign.

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