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INNOVATIVE RESEARCH FOR A SUSTAINABLE FUTURE

ADVANCING THE NEXT GENERATION OF RISK ASSESSMENT

EPA'S NexGen PROGRAM

Background

The landscape of chemical risk assessment is rapidly changing as a result of phenomenal advances in molecular systems biology, greater understanding of gene-environment interactions, recent publication of important reports from the National Research Council and volumes of new test data from the United States and Europe.

In response, EPA has started the Next Generation Risk Assessment (NexGen) effort. NexGen aims to create a cheaper, faster and more robust system for chemical risk assessment by incorporating new chemical testing data (including high-throughput screening from EPA's ToxCast program and from Europe's REACH programs) and advances in molecular system biology.

The new effort involves the National Institutes of Environmental Health Sciences, the Centers for Disease Control and Prevention, Food and Drug Administration's National Center for Toxicological Research, the National Human Genome Research Institute, and California's Environmental Protection Agency.

NexGen is part of EPA's Chemical Safety for Sustainability research, which is integrating diverse scientific disciplines to: 1) develop new prediction techniques, 2) pioneer the use of innovative technologies for chemical toxicity testing, and 3) design tools to advance the management of chemical risks.

Goals & Objectives

Molecular systems biology is revealing the complexity of biological processes and variations that exist within the human population. This rapidly evolving body of knowledge helps to explain the multifaceted nature of susceptibility to disease and how disease actually occurs.

The goal of NexGen is to incorporate this new knowledge into risk assessment. Some applications, however, are now feasible, such as understanding how chemicals cause toxicity and the relative potency of these chemicals to cause effects.

The NexGen goals are to:

1. Implement a research action plan for risk-based decision making that includes characterization of risk management needs, identification of policy related questions and risk assessment implications, and a description of how stakeholders can be involved.

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2. Refine bioinformatics techniques, which are computer-assisted ways to find, organize and analyze new biologic information.

3. Develop prototype health assessments that are responsive to the risk context (see Box 1 for an example) and that can evolve as conversations with scientists, risk managers and stakeholders occur.

Box 1: Risk Context (National Research Council, 2008a)

- *Evaluation of new environmental agents*
- *Evaluation of existing environmental agents*
- *Evaluation of a site*
- *Evaluation of potential environmental contributors to a specific disease*
- *Evaluation of the relative risks posed by environmental agents*

Progress to Date

In November 2010, a group of experts from a variety of disciplines (e.g. microbiologists, computational biologists, clinicians, toxicologists, epidemiologists, bioinformaticians) convened at a workshop in Research Triangle Park, N.C. The goal of the gathering was to elicit input on several early-stage health effects assessments, or prototypes.

At a February 2011 public dialogue conference in Washington, DC, scientists from the government, industry, environmental groups, and the public were invited to comment on the NexGen process and offer recommendations on the effort.

At the conference, Paul Anastas, Assistant Administrator of EPA's Office of Research and Development, said that sustainability is the crux of the challenge facing NexGen. He encouraged people to be creative and visionary.

One example application of these new methods was in response to the massive oil spill from the Deepwater Horizon oil platform in the Gulf of Mexico. This oil spill led to the use of correspondingly large volumes of the oil dispersants to mitigate impacts of the spill, posing additional environmental concerns. The results from the rapid testing of several oil dispersants were used to rank the dispersants based on toxicity to cells and endocrine- related activity.

Batteries of receptor or transcription factor activation and quantitative high-throughput assays were used in the evaluation. This information was critical in supporting the Administrator's decision on the use of dispersants in response to the Gulf oil spill disaster (Judson et al, 2010).

Next Steps

A risk manager's workshop is scheduled for summer 2011. The goals of the manager's workshop are to help decision makers become more familiar with emerging methods and to gain insights from these decision makers into the potential utility of these new tools in various applications.

Materials from the February meeting will be posted on EPA's web site and can be accessed at:

www.epa.gov/risk/nexgen.

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