NIH collaborates with EPA to improve the safety testing of chemicals

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Testing the safety of chemicals ranging from pesticides to household cleaners will benefit from new technologies and a plan for collaboration, according to federal scientists from the National Institutes of Health (NIH) and the U.S. Environmental Protection Agency (EPA), who today announced a new toxicity testing agreement. The concept behind this agreement is highlighted in the Feb. 15, 2008 issue of the journal *Science*.

Two NIH institutes have formed a collaboration with the EPA to use the NIH Chemical Genomics Center's (NCGC) high-speed, automated screening robots to test suspected toxic compounds using cells and isolated molecular targets instead of laboratory animals. This new, trans-agency collaboration is anticipated to generate data more relevant to humans; expand the number of chemicals that are tested; and reduce the time, money and number of animals involved in testing. Full implementation of the hoped-for paradigm shift in toxicity testing will require validation of the new approaches, a substantial effort that could consume many years.

This collaboration is being made possible through a newly signed, five-year Memorandum of Understanding (MOU), which leverages the strengths of each organization. The MOU builds on the experimental toxicology expertise at the National Toxicology Program (NTP), headquartered at the National Institute of Environmental and Health Sciences (NIEHS), NIH; the high-throughput technology at NCGC, managed by the National Human Genome Research Institute (NHGRI),

NIH; and the computational toxicology capabilities at the EPA's recently formed National Center for Computational Toxicology (NCCT).

The MOU provides for sample and information sharing necessary to more rapidly and effectively identify chemicals that might pose possible risks to the health of humans and animals and to the environment. It addresses opportunities for coordination in four basic areas related to achieving the toxicant testing goals, including: identification of toxicity pathways; selection of chemicals for testing; analysis and interpretation of data; and outreach to scientific and regulatory communities. The collective budget is yet to be determined.

The MOU and the plans articulated in the *Science* article provide a framework to implement the long-range vision outlined in the 2007 National Research Council (NRC) report, Toxicity Testing in the 21st Century: A Vision and a Strategy, which calls for a collaborative effort across the toxicology community to rely less on animal studies and more on in vitro tests using human cells and cellular components to identify chemicals with toxic effects. Importantly, the strategy calls for improvements in dose-response research, which will help predict toxicity at exposures that humans may encounter.

The collaborative research program is outlined in the jointly authored *Science* paper.

The co-authors — Francis S. Collins, M.D., Ph.D., NHGRI director; George M. Gray, Ph.D., assistant administrator for EPA's Office of Research and Development which houses the NCCT; and John R. Bucher, Ph.D., NTP associate director — describe the possibility of shifting from reliance on animal testing to biochemical- and cell-based assays, as well as those using lower organisms, such as zebrafish and roundworms.

Data collection to determine chemical toxicity currently relies heavily on whole-animal tests. The growing number of new chemicals, high testing costs and public unease with animal testing led to the search for alternate toxicology testing methods. Quantitative high-throughput screening (qHTS), developed at NCGC, increases the rate at which chemicals are tested, and profiles compounds over a wide range of concentrations. These qualities make the new qHTS technology ideal for toxicology testing, with the potential for advancing the goal of more accurate and timely public health decisions.

“A central component of federal effort will explore the use of high-throughput screening assays in toxicology,” NHGRI’s Dr. Collins said. “Such assays allow for the testing of thousands to hundreds of thousands of chemicals a day to determine their possible toxic effect.” NCGC is part of a larger Molecular Libraries Imaging Program within the NIH Roadmap for Medical Research. It was designed to advance research on molecules from which most medicines marketed today are derived.

“We now are seeing tools newly available to us for chemical genomics research deployed for greater refinement, speed and capacity in chemical toxicity screening,” Dr. Collins said.

“The experimental and computational expertise required to transform toxicology is an enormous undertaking and too great for any of our existing organizations to accomplish alone,” said NTP’s Dr. Bucher. “This collaborative approach allows us to draw on our individual strengths and establishes a long-term, multiple U.S. federal agency commitment.” NTP will contribute thousands of compounds for testing. NTP’s animal toxicology expertise will be utilized, along with a large database of the chemicals’ effects on animals, with which the new cell-based data will be compared.

“As our detailed research strategy continues to develop, we will welcome

the participation of other federal partners, as well as interested public and private sector organizations, to make this vision of 21st century toxicology a reality" said EPA's Dr. Gray. The EPA's engagement in this collaboration is part of its ToxCast™ program—an initiative launched in 2007 to revolutionize the agency's chemical toxicity evaluation procedures. ToxCast™ will use advances in computers, genomics and cellular biology to speed up toxicity testing and enhance capacity to screen new compounds.

Source: National Human Genome Research Institute