NATIONAL TOXICOLOGY PROGRAM
VISION
Headquartered at the National Institute of Environmental Health Sciences • NIH • DHHS

Toxicology in the 21st Century: The Role of the National Toxicology Program

The National Toxicology Program (NTP) was established in 1978 to coordinate toxicological testing programs within the Department of Health and Human Services, develop and validate improved testing methods, develop approaches and generate data to strengthen scientific knowledge about potentially hazardous substances and communicate with stakeholders. In its 25 years of existence, NTP has become a world leader in providing scientific information that improves our nation's ability to evaluate potential human health effects from chemical and physical exposures. The NTP has maintained a number of complex, interrelated research and testing programs that provide unique and critical information needed by health regulatory and research agencies to protect public health.

The last decade of the 20th century and the turn of the 21st century have produced dramatic technological advances in molecular biology and computer science. The NTP is again ready to evaluate its key activities and in a focused and concerted effort determine how best to incorporate these new scientific technologies into its research and testing strategies and broaden scientific knowledge on the linkage between mechanism and disease. The NTP Vision for the 21st Century is to move toxicology from a predominantly observational science at the level of disease-specific models to a predominantly predictive science focused upon a broad inclusion of target-specific, mechanism-based, biological observations. The stimulus for the NTP Vision is to develop a framework that will promote the further development/advancement of toxicology and refine its traditional role as a predominantly observational science. Over the next year, the NTP intends to develop a roadmap for implementation of its vision that will strategically position the program at the forefront for providing scientific data and the interpretation of those data for public health decision-making.

The NTP invites all interested stakeholders to read and comment on its vision and to provide input to a roadmap for its implementation. In developing its roadmap and milestones for tasks and changes to achieve the vision, the NTP seeks input on the issues raised by the following questions:

1. What scientific information should the NTP be producing and what technical capabilities should the NTP have by 2008? By 2013?
2. How do you envision that the refinement/replacement of classical toxicological studies with mechanism-based assays will impact on the evaluation of public health hazards?
3. How can we best structure the NTP to provide this information and to ensure its optimal utilization in the protection of public health?
4. What resources will be needed to realize this vision and how long will it take?

February 24, 2004

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The NTP Vision for the 21st Century:

To move toxicology from a predominantly observational science at the level of disease-specific models to a predominantly predictive science focused upon a broad inclusion of target-specific, mechanism-based, biological observations

Since its inception in 1978, the NTP has been a leader in toxicological testing and research within the United States and contributed significantly to the scientific knowledge upon which public health decision are based. In 1995, the National Toxicology Program (NTP) initiated a program to use mechanism-based toxicology to develop, evaluate and validate better toxicological test methods. This effort has led to major changes in toxicology at the national and international level. In recent years, mechanism-based toxicology has led to some changes in the scientific basis for public-health decisions; however, it has not dramatically reduced the need for the classical tests developed in the 1970s and 80s that were the basis for many decisions related to product safety, evaluation of environmental and occupational hazards and prioritization of chemicals for further testing. It is now time to focus on changing the scientific basis for decision-making and work toward improving or replacing older classical tests with faster, mechanism-based assays.

Two activities must occur simultaneously if this change is to occur. One, we need to aggressively incorporate new laboratory methods into the NTP testing program and insure that the data produced meet the high quality standards of the NTP. Two, we need to develop strategies for the integration of new types of scientific data into the decision-making process. As a leader in toxicology, the NTP is ready to seize this challenge for improving the scientific basis for public health decision-making.

A core element of the NTP is the design, conduct, evaluation and communication of toxicological tests in a broad number of areas of concern ranging from neurotoxicity to carcinogenesis. Through the testing program, the NTP has been a leader in developing and implementing experimental designs that not only address data gaps for the agent being tested, but contribute to our fundamental understanding of toxicity in the broader context. This strength of the testing program needs to be further developed to insure that every evaluation done contributes to knowledge-based safety evaluations that use the broadest possible range of scientific evidence in reaching a decision. As new methods are developed and gain greater acceptance in developing public health decisions, our dependence on the classical testing paradigms should diminish. During this time of transition, scientific quality and clarity must be preserved to insure that decisions based solely upon new methods do not endanger the health of the public or introduce greater scientific uncertainty than the approaches used in the last century.

Only through a concerted effort focused on the linkage between mechanism and disease will toxicology achieve sufficient predictability to refine or replace disease-specific testing models with mechanism-based assays that are more informative, faster and closely linked to disease incidence and progression. This vision should enable the program to continue its leadership in toxicology and provide the scientific data and knowledge necessary for making appropriate decisions that protect (and improve) public health and the environment.

February 24, 2004

NTP Roadmap

During 2004, the NTP is seeking input for development of a roadmap to implement the vision. The NTP is inviting input to the roadmap from numerous groups, including its federal partners, its advisory committees and the public. The NTP has formed three working groups: the NTP Board of Scientific Counselors Working Group, the NIEHS Working Group, and the NTP Interagency Working Group. Each of these groups will prepare a report on elements and milestones important for the NTP to consider in the roadmap. The NTP will also seek input on the vision and roadmap at several public meetings. The NTP held a public meeting on January 29, 2004, at the Lister Hill Center Auditorium, National Library of Medicine, National Institutes of Health in Bethesda, Maryland. Additional opportunities for public comment include upcoming meetings of the Scientific Advisory Committee on Alternative Toxicological Methods (March 10 – 11) and the NTP Board of Scientific Counselors (June 29). The NTP plans to have a draft roadmap developed by the end of summer 2004 for release in the fall.

In developing the framework for implementing the NTP Vision for the 21st Century, the NTP will examine its current activities, examine opportunities for modifying those activities to include recent scientific advances, identify specific activities that need to be accomplished to implement the vision and develop a framework targeted towards achieving the intent of this vision and including the necessary components for implementation, management and communication of changes in NTP activities. In developing this framework, the NTP will 1) identify the tools and technical capabilities needed to utilize new methods, models and approaches within the program; 2) develop strategies for the generation, evaluation and integration of new types of scientific data into the decision-making process; and 3) identify the resources needed to achieve both the short-term and long-term goals for the vision. The NTP will examine each mechanism through which it currently operates and evaluate its functionality toward addressing the vision. Some of the changes and directions in the roadmap will be specific to the NTP, its operations and its personnel, while others will apply to the broader field of toxicology as it is currently practiced. It is envisioned that the acceptance and implementation of this vision in addressing public health priorities will result in better science and ultimately better decisions.

NTP Mission and Goals

The mission of the NTP is to evaluate agents of public health concern by developing and applying tools of modern toxicology and molecular biology. The elements of this mission are to provide toxicological evaluations on substances of public health concern, develop and validate improved (sensitive, specific, rapid) testing methods, develop approaches and generate data to strengthen the science base for risk assessment and to communicate with stakeholders (government, public, industry, academia, environmental community) involved in the application and use of scientific data in making decisions about the safety of agents routinely encountered by humans. The overall goal of the NTP, encompassed by these mission elements, is to provide the best science possible for preventing disease due to human exposures. Unfortunately, the changing nature of biological science is such that this goal can never really be attained; however, it is a goal that requires constant diligence to insure that the tools of modern biological science are used appropriately and efficiently.

In its current manifestation, the NTP accomplishes its mission for toxicological testing through several mechanisms:

- Contract laboratories that conduct studies designed by NTP staff and contracts administered by the National Institute of Environmental Health Sciences (NIEHS)
- Collaboration and cooperation with multiple federal agencies, including toxicological research and testing at the National Center for Toxicological Research (NCTR) of the Food and Drug Administration
- Human exposure and toxicity research at the National Institute for Occupational Safety and Health (NIOSH) of the Centers for Disease Control and Prevention
- Biological, toxicological, clinical and epidemiological research in the intramural laboratories of the Division of Intramural Research (DIR) at the NIEHS
- Research grants, contracts and interagency agreements supported through the NIEHS Division of Extramural Research and Training (DERT)
- NTP Centers, including the Report on Carcinogens, the Interagency Center for the Evaluation of Alternative Toxicological Methods, the Center for the Evaluation of Risks to Human Reproduction, and the Phototoxicology Center at the NCTR, and the NIEHS National Center for Toxicogenomics
- Collaboration and support of research with other national and international toxicology and public health agencies
- Review and evaluation of data gaps in our understanding of environmentally induced diseases through the NTP Office of Nominations
- Focused conferences and symposia, and communications to a broad spectrum of stakeholders through public meetings, electronic media and print media managed by the NTP Liaison and Scientific Review Office