Report 74: Integrated Assessment and Testing Approaches (IATA)

Convener: Robert Kavlock

Brief History: The topic was based on two assumptions: (1) it is a fundamental mission of NIEHS to provide information on the hazards and risks of environmental chemicals and (2) the current approach to hazard and risk determination is neither efficient nor effective as it needs to be. There are too many chemicals with too little data, and the data to reduce uncertainties in the risk assessment process even for data rich chemicals is less than optimal based upon recent experiences. The emerging transformation of toxicology is posed to change both the methods used in (1) and the approach used in (2). In order for this transformation to occur, it is necessary for a strategic plan by which the knowledge of human disease processes are discovered and how these discoveries can be applied in the conduct of chemical safety assessment studies

Discussion Highlights: The IATA approach has been proposed by a number of organizations (e.g., IPCS, the Canadian Council of Academies, EPAs Office of Pesticide Programs) as a way to intelligently integrate the information coming from various data domains (e.g., in silico models, computational chemistry, high content and high throughput bioassays, genomics (broadly defined), human exposure, pharmacokinetics, etc,) in order to better understand the likely biological targets of chemicals which in turn will inform the design of specific animal bioassays to define critical dose-response information. For example, screening results may point to a chemical to possess activities that suggest potential impacts on cardiovascular function, and animal bioassays would be specifically designed to explore this lead at a higher level of biological organization. Conversely, this chemical would be de-prioritized for effects on cancer because the screening results showed a low probability of cancer mechanisms being triggered.

To date, however, there has been no broad scale effort to bring all the components needed for IATA to occur and it remains largely a theoretical construct (although components of IATA are being employed in NIEHS and regulatory organizations across the globe). This is despite all the potential benefits that might occur by its full implementation and use. If successful, the IATA approach would allow for a transparent and uniform way to integrate the information flow from various sources, target animal use appropriately, and address the key uncertainties normally present in contemporary chemical risk assessments. For this to happen, it is important that the field not develop in a haphazard process, but be guided by strategic planning and implementation. The challenges to implement IATA are broad, and it will take a coordinated effort to realize the potential. NIEHS has the capabilities and capacity to be the leader in moving the IATA approach forward and bringing us closer to the vision of toxicology in the 21st century.

Recommendations:

- IATA could become a unifying concept by which research on chemical safety is conducted at NIEHS and should be guided in its development at the Institute level.

- NIEHS should become the institute that leads the transformation of development of the knowledge bases for human disease etiology caused by environmental chemicals (and other influences) and their application for disease prevention.

- NIEHS should become the leader in transforming the process of chemical safety assessment by developing broad scale proof-of-concept studies that show the potential of IATA in resolving key toxicological issues

- There are complementary roles for the DIR and DERT with the NTP in moving the science forward. Basic discovery of causes of diseases would be the responsibility of the DIR and DERT (and other NIH institutes) and this knowledge would be actively transferred to the NTP for application of proof of concept. Conversely, the NTP could advise the DIR and DERT about significant gaps present in the ability to characterize the broad spectrum of biological interactions of concern to guide basic biological discovery. NIEHS is uniquely positioned to foster this activity as a core part of its mission.

- There is also a role for broader cross-NIH interactions to mine the information on basic biology of disease pathways and to bring that information into the context of environmental health. The multi-disciplinary expertise available within the NIH is an extremely valuable resource to be tapped.

- Implementation of IATA will require a strong biomathematical/computational contribution for synthesizing the large volumes of various information flows. This will likely require development of both an intramural capacity, as well as support for the extramural scientific community. This is key component will need careful fostering to develop the appropriate capability and capacity.

- System model development inherent in IATA must develop in an iterative fashion between the computational/information scientists and the biologists developing the data. New approaches must be done in parallel with traditional approaches so that the added value is apparent.

Discussion Participants: Michael DeVito, Michael Holsapple, Claude Hughes, Christopher Kemp, Ed Levin, Cheryl Marks, James Putney, William Stokes, Tracey Woodruff