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RISK21: Realizing the Future of Risk Assessment

Workshop Synopsis

Overview: On January 11, 2011 the ILSI HESI Risk Assessment in the 21st Century (RISK21) project held the first face-to-face meeting of its participants and hosted a day-long public session to hear commentary from those not yet directly involved with the program. Over 80 RISK21 participants and approximately 40 visitors were in attendance at the meeting, which was held at the Omni Shoreham Hotel in Washington DC. This workshop provided a unique opportunity for the participants to evaluate the project and offer suggestions on how the project should proceed.

The RISK21 project's multi-stakeholder team members aim to develop better methods to bring applicable, accurate, and resource appropriate approaches to the evolving world of human health risk assessment. RISK21 is not an implementation program for the NAS Toxicity Testing in the 21st Century Report *per se*, nor is it specifically tackling the use of "new technologies." RISK21 is creating a science-based approach for improving human health risk assessments, developing a viable mechanism for transitioning to novel approaches, as available and when appropriate. RISK21 does not aim to address regulatory policy. Instead, RISK21 will develop an integrated evaluation framework that targets the acquisition and interpretation of essential data to improve the efficiency of human health risk assessment for a large number and broad array of chemicals.

Perspectives: A series of seven highly knowledgeable speakers addressed the audience with academic, government, industrial, NGO, and legal viewpoints. These speakers highlighted the challenges that will be faced in the fields of toxicology, exposure science, and risk assessment over the next few years. Speakers included *Drs. Lynn Goldman* (George Washington University), *Gail Charnley* (HealthRisk Strategies), *Sue Leary* (Alternatives Research and Development Foundation), *Steve Bradbury* (USEPA Office of Pesticide Programs), *Corrado Galli* (University of Milan), *Paul Carmichael* (Unilever), *and Douglas Throckmorton* (USFDA Center for Drug Evaluation and Research). Some of the themes touched-upon by the speakers included the following:

- The field of risk assessment must move away from the current scenario where the totality of data is needed up-front and towards a more targeted, pathway-based approach.
- Specific risk assessment approaches that are currently in use, such as the threshold of toxicological concern (TTC), enable decisions to be reached in risk assessment even when only limited information is available. Such methods should be embraced and expanded upon as the field evolves.
- We must question our current toxicity testing approach that is based on standardized animal testing and the hazard evaluation paradigm embraced for many years by regulatory agencies around the world.
- Though not the direct goal of new method development, *in vitro* and pathway-based toxicity testing approaches may lead to a reduction or elimination of animal usage.
- In order to harness new methodologies, direct links must be made to adverse public health outcomes and validation is critical.
- Currently, *in vitro* methods are available for prediction of potential human adverse effects for acute events, such as eye or skin irritation, but additional research is still needed before *in vitro* tests will be able to accurately ascertain potential longer-term effects.
- Communication, cross-disciplinary coordination, and data sharing are key to the development and acceptance of new risk assessment approaches.

RISK21 Presentations: Overviews of the four RISK21 project areas (Exposure, Dose-Response, Cumulative Risk, and Integrated Evaluation Strategies[1]) were provided by the sub-team co-chairs. Following these presentations the audience broke into small discussion groups to share suggestions for the RISK21 project. Some of the themes that emerged included the following:

- RISK21 is a truly innovative project, providing a multi-stakeholder, multi-disciplinary forum to evolve the field of human health risk assessment by advancing scientific approaches.
- The ultimate goal of the RISK21 program should be to create a practical roadmap for a flexible, hypothesis-driven, integrated approach.
- Coordination amongst the four RISK21 project areas is critical, and additional effort should be made to broaden involvement of more countries and international agencies, as well as leverage work that is ongoing in related initiatives.
- A concerted effort should be made to include epidemiology and the use of human data more generally within the project.
- The age of animal testing is not yet over. Rather, there is increased focus on improving the science to create better models.
- Attention should be given to issues surrounding validation of assays and approaches, and incorporation of uncertainty.
- Communication is key. This concept involves open and transparent dialog with the public as well as training new scientists and regulators on new approaches.

Specific issues raised during the discussion will be carefully considered by each of the RISK21 sub-teams and integrated, as appropriate, into their future work plans.

The Panel: Six panel members discussed the imperatives of RISK21 and the realities of shifting to a new paradigm in risk assessment. Discussants included *Drs. Tina Bahadori* (American Chemistry Council), *Peter Chan* (Health Canada), *Vincent Cogliano* (USEPA's Integrated Risk Information System), *Michael Dourson* (Toxicology Excellence for Risk Assessment), *Yvonne Dragan* (AstraZeneca), and *Andrew Rowan* (Humane Society International).

Panelists expressed clear enthusiasm for RISK21 to move forward, to do so with public health in mind, and to consider the need to quickly evaluate tens of thousands of data-deficient chemicals with reliable, human-relevant tests. They emphasized that RISK21 should avoid reinventing the wheel and focus on strategy rather than tactics.

Summary: The participants at the RISK21 meeting clearly endorsed the project and offered many valuable insights to help RISK21 succeed. There was recognition that there are major social, political, and scientific drivers that necessitate an evolution of our current risk assessment approach. Classic toxicology continues to play an important role, but the field needs to continue to search for ways to improve the generation and interpretation of toxicological and exposure data. The charter for RISK21 lies within the realm of taking advantage of these new approaches coupled with time-tested classical methods with the primary objective of improving accuracy and efficiency.

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[1] See http://www.hesiglobal.org/i4a/pages/index.cfm?pageid=3492 for PowerPoint presentations and other workshop information.