Meeting Report:
FutureTox II: Contemporary Concepts in Toxicology
"Pathways to Prediction: *In Vitro* and *In Silico* Models for Predictive Toxicology"

Susan A. Elmore[1], Anne M. Ryan[2], Charles E. Wood[3], Torrie A. Crabbs[4], and Robert C. Sills[1]

[1]National Toxicology Program, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA
[2]Pfizer Inc., Pfizer Global R&D, Groton, Connecticut, USA
[3]US Environmental Protection Agency, Research Triangle Park, North Carolina, USA
[4]Experimental Pathology Laboratories, Inc., Research Triangle Park, North Carolina, USA

The Society of Toxicology (SOT) held a very successful FutureTox II Contemporary Concepts in Toxicology (CCT) Conference in Chapel Hill, North Carolina, on January 16th and 17th, 2014. There were over 291 attendees representing industry, government and academia; the sessions were also telecast to 9 locations, including Health Canada, US FDA/National Center for Toxicologic Research, the US EPA and the California EPA Office of Environmental Health Hazard Assessment. The conference also included more than 50 posters as well as several vendor exhibits.

The theme of the meeting was "Pathways to Prediction: *In Vitro* and *In Silico* Models for Predictive Toxicology." This conference was the product of the Scientific Liaison Coalition (SLC), which is a partnership of 16 societies, including the Society of Toxicologic Pathology, with the aim to increase the awareness and impact of toxicology on human health and disease prevention. The focus of this FutureTox II meeting was integration of current and developing *in vitro* methodologies and computational modeling approaches with advances in systems biology to facilitate human risk assessment. The overarching theme in each session was to articulate the current strengths and limitations of these newer approaches and their utility in prioritizing chemicals for safety testing.

The meeting co-chairs Thomas B. Knudsen (US EPA, RTP, NC, USA) and Douglas A. Keller (Sanofi US, Bridgewater, NJ, USA), along with the organizing committee, divided the two-day conference into 3 session themes: (I) current and future biological systems, (II) science of predictive models, and (III) regulatory integration and communication. Over the course of the conference, attendees heard 20 presentations across these 3 themes. The last session consisted of 4 interactive breakout sessions (regulatory toxicology, hepatotoxicity, developmental/reproductive toxicity, and cancer), each given the task of identifying the next steps in the refinement and application of these technologies to hazard identification and risk assessment.

Platform and poster presentations covered a diverse range of current research. Prominent topics included:

- Application of high-throughput screening (HTS) data from large-scale *in vitro* platforms (e.g. ToxCast/Tox21) and *in silico* models for risk assessment.
- Application of pluripotent stem cells to *in vitro* screening paradigms.
- Developments in three-dimensional cell/tissue models as screening tools.
- The use of zebrafish as high(er) throughput phenotypic screens for chemical toxicity.
- The development of adverse outcome pathway (AOP) maps and a molecular initiating event atlas for specific toxicities.
- The use of *in vitro* data to differentiate adverse from non-adverse and adaptive effects.
- Development of next-generation quantitative structure-activity relationship (QSAR) models.

The conference organizers plan to publish the conference proceedings as a special supplement to the journal *Reproductive Toxicology* (http://www.journals.elsevier.com/reproductive-toxicology/). The meeting overview and agenda are available at http://www.toxicology.org/ai/meet/cct_futureToxII.asp.

The general premise of this meeting was based on a 2007 report by the U.S. National Research Council titled "Toxicity Testing in the 21st century: A Vision and a Strategy" (NRC 2007). This concept was initiated by the US EPA in collaboration with the National Toxicology Program/National Institute of Environmental Health Sciences and the US National Institutes of Health. The proposed paradigm, now often referred to simply as "Tox21," called for a shift in safety assessment away from traditional animal-based endpoints and towards *in vitro* and other HTS assays, alternative models in lower organisms, and computational systems. The objectives of this effort are to transform toxicology from a largely observational science to a more predictive one and, ultimately, to better align future toxicity testing and assessment programs with regulatory needs (Collins et al., 2008).

In a parallel initiative, the European Union (EU) has begun several programs to promote more efficient safety assessment of chemicals and reduce or eliminate unnecessary animal testing. At FutureTox II, keynote speaker Maurice Whelan, from the Institute of Health and Consumer Protection of the European Commission, summarized recently enacted EU legislative directives that have resulted in more stringent restrictions on the use of animals for scientific purposes. For example, the EU Cosmetics Regulation has banned, after March 2013, the marketing of new cosmetics products in Europe that contain any ingredient that has been tested on animals. Other initiatives to replace animal use in repeat-dose toxicity testing were also noted for Europe (see www.seurat-1.eu). Dr. Whelan also noted that scientific communities around the world have increasingly been focused on the 3 Rs: replacement, refinement, and reduction in animals in research. Conference speakers