

### **Session 3: Tiered Evaluation Strategies**

*Session Chairs: Jay Ansell (Yves Rocher North America, Inc.), Simon Webb (Procter & Gamble)*

#### Panel Discussion and Audience Dialogue

- When asked what the panel members learned from each other, most agreed they gained more in depth information on various testing programs. They acknowledged that intelligent testing strategies are being implemented more widely and that eventually there will be convergence in methodology, in part due to recognition of worldwide chemical exposure. The forward looking talks in this workshop have allowed all to see that there is a revolution in chemical testing out there that needs encouragement and short-term capitalization.
- Several audience members discussed the conundrum of ‘proving a negative.’ It was asked how one can fully demonstrate that there is no possibility of a chemical having an adverse effect through testing (including in vitro assays). The panel recognized that proving the negative is a big challenge needing to be addressed to replace animal testing with alternative methods and that recognition of the limitations of animal testing and implementation of the weight of evidence approach will help. An answer proposed was that batteries of mechanistic tests need to be developed that model living systems. A series of negative results from this battery could be sufficient to label a chemical as non-toxic.
- When asked why the number of chemicals on different lists for testing varies so greatly, the panel explained that several factors played a role in list development that differed between countries, such as, timeframe, tonnage, etc.
- Ann Blacker clarified that the ILSI/HESI project timeline did not provide enough time to make the database generated publicly available. She stated that several EPA representatives expressed interest in collaborating with Syngenta to populate the database further and to put it in the public domain.
- Some observations provided by an audience member that has been in the field of toxicology for 50 years included:
  - The frontiers of toxicological research are being pushed very rapidly, but in the real world, many excellent proposals for progress in science sit on the shelves of regulatory agencies.
  - A scientist must pay attention to all that is going on and present their research in context.
  - Risk analysis was mentioned very little in the workshop, however, this is where all the data will be applied.
  - Novel scientific methods will be understood and accepted by knowledgeable scientists in the regulatory agencies. The challenges include changing the regulatory framework and the law which can take years.
  - Scientists need to keep practicality in mind, i.e. methods begin as theoretical but must move to be practical and applied. Challenges to face will include regulatory legislative, and judicial.
- When asked their opinion on whether or not alternatives will be incorporated into all the new testing programs, Dr. Stephens replied that they will have to be due to

the sheer number of chemicals and scope of work to be done; alternatives provide the only plausible methods for screening tens of thousands of chemicals. Internal pressure to challenge agencies to incorporate alternative methods such as QSAR will also fuel research and method improvement. Also, fallout from other programs, such as REACH and the categorization of Canada's Domestic Substances List, has prompted talk in the United States of redoing TSCA, which would provide an opportunity for implementing some tiered testing strategies employing alternative methods.

- A request was made that all testing programs run a prediction component in parallel for further model development/improvement. Additionally all data generated should be put in the public domain, which is where most modelers go for data to use.
- An audience member suggested that three things are of concern regarding alternative testing methods: 1) all new in vitro technologies need to be validated for use in a high-throughput capacity, 2) there is a sizable education component, 3) alternative methods in toxicology need to be on the forefront, especially for academics as they are the ones instructing the toxicologists of the future.
- A statement was made that the United States has the tendency to throw money at problems, but that it is not targeted; however in the EU, the culture and law (i.e. prioritization) provides a framework for targeted funding. Dr. Owens responded that in the EU, the use of alternatives is not just theory, it is actively being legislated and put into use with animal protection at the forefront as can be seen in the Cosmetics Act to reduce and eliminate animal testing.