

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

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

Tiered Evaluation Strategies: An Animal Protection Perspective, Martin Stephens  
(Humane Society of the United States)

- Talk to focus on tiered evaluation strategies from the perspective of an animal welfare organization, the Humane Society of the United States (HSUS). HSUS is a NGO that is not affiliated with local humane societies, is funded by private donations, and addresses the full array of animal protection issues.
- HSUS's view of animal use and the 3Rs is that they would like to see the day when no animals are used in harmful testing. They are aware that day is far away; however, implementation of the 3Rs will hasten progress and reduce animal suffering.
- In tiered evaluation strategies, existing information makes up the bottom tiers, screening tests are in the middle, and apical animal tests are at the top. Various triggers move a chemical on to the next testing tier and outcomes result from all tiers. Animal use typically increases with increasing tiers. The HSUS would like to see animal testing, when deemed necessary, restricted to the top level.
- Tiered evaluation strategies are part of the reduction approach to animal use on a macroscopic level. They can be used in short- (limit animal use to medium and high tiers), medium- (limit use to top tier only for confirmation), and long-term (zero animal use).
- In a larger context, tiered evaluation strategies are a form of intelligent testing strategies (ITS) to reduce the use of the checkbox approach. Intelligent testing strategies are tailored to risk management contexts, chemical properties, and available tests and data, to decrease animal use. These types of strategies help to address the compromises that often arise in testing programs, over issues such as cost, duration, animal welfare, and the depth (vs. the scope) of testing.
- Key animal welfare principles that HSUS would like to see incorporated into testing programs include: multi-stakeholder involvement, transparency, data sharing, international collaboration, ITS application, use of the precautionary principle, and outcomes that need limited animal testing (little or no animal testing in early tiers, implementation of triggers that screen chemicals out of the testing program, and making negatives definitive).
- The use of tiered evaluation strategies and intelligent testing were not initially incorporated to the HPV program, partially because animal protection groups were excluded from the formulation of the program. It was originally designed as a battery to fill data gaps in SIDS with existing data. Stakeholder workshops held after the program was designed allowed animal protection groups to convince the government to incorporate some intelligent testing strategies in the HPV program. Review of proposed testing programs showed that compliance with these strategies was disappointing, largely because it was voluntary. Additionally, companies justify the use of animal testing based on the potential requirements of other programs. Animal protection groups heavily criticized the proposed test plans, with some company responsiveness.

- The REACH program does propose the use of tiered evaluation and intelligent testing approaches along with a partnership with ECVAM. Many European animal protection groups have weighed in and provided details of various tiered evaluation strategies so that they may be implemented from the beginning.
- In the US, a two-tiered testing strategy has been developed for endocrine disruption. However, Tier 1 employs animal-intensive tests that are improperly labeled as ‘screens.’ The HSUS would like to see those tests used in higher tiers after non-animal screening methods have been used.
- The inherent innovation of the ILSI/HESI approach is appreciated by animal protectionists.
- Barriers and challenges to tiered evaluation strategies include: over-confidence in animal methods, variability in animal data, black-box nature of animal tests, under-confidence in non-animal methods, institutional inertia, low empathy factor for rodents, limited animal protection stakeholder access and influence, limited exposure data, limited data sharing, limited human data, statutory / regulatory / public pressure to move forward, lack of data on mechanism and systems biology, translating the latest biological techniques into test methods, limited funding for translational research on methods, translating industry’s in-house methods into regulatory toxicology, and risk managers’ reliance on the built-in redundancy of tests.