

A Strategy for Implementing the Vision for Toxicity Testing in the 21st Century

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Proposed Topic

A Strategy for Implementing the Vision for Toxicity Testing in the 21st Century

Problem Statement:

In 2007 the National Research Council (NRC) published the seminal report, *Toxicity Testing in the 21st Century: A Vision and a Strategy*, which envisioned using information derived from human-based assays and models to provide a more efficient, predictive, and less costly system for assessing the effects of xenobiotics on human health. Over the ensuing decade, significant investments in technology development and biomedical research have resulted in many transformative scientific breakthroughs necessary for implementing the NRC vision. However, these advances have yet to be met with a concomitant increase in our ability to more accurately predict the adverse human health effects caused by ubiquitous exposure to xenobiotic chemicals, whether alone or in mixtures. This limited translational impact is attributable, at least in part, to rapid scientific advancements outpacing the change in institutional standards required for their effective utilization. Specifically, legacy test methods and classification systems developed using animal models cannot always evaluate the nuances of human pathophysiology and genetic variability important for modern risk assessment. Ironically, however, the institutionalized use of animal-based methods may limit more human-predictive approaches from being developed and adopted by both government and industry stakeholders. Left unaddressed, this growing disparity between information gained from human-relevant approaches and reliance on animal data for safety and risk evaluations could impede our ability to capitalize on the remarkable knowledge and tools arising from projects such as ToxCast, Tox21, Human Tissue Chips, and the Precision Medicine Initiative.

Although the United States leads the world in biomedical research and technology development, we lag significantly behind almost all other “advanced economies” in developing a strategy and roadmap for implementing the use of 21st century science for assessing the impact of xenobiotics on human health and the environment. For example, the EU is now two years into its ambitious program, *Horizon 2020: Roadmap to Next Generation Safety Testing*¹, and *A non-animal technologies roadmap for the UK: Advancing predictive biology*² was published in 2015. These and other efforts recognize the important benefits to public health that can be achieved using more human-predictive/non-animal approaches. In addition, many of our international trading partners (e.g., EU, India, Brazil, South Korea, Canada, Australia, Russia) have already moved towards banning the sale or import of cosmetic products or ingredients which have been tested on animals, and a bill with the same intent has recently been introduced in the

U.S.³ Without validated non-animal alternatives in place, these testing bans could stifle innovation and also put the public, especially sensitive populations, at risk for exposure to insufficiently characterized chemicals.

In order to realize the full potential for improving and protecting human health offered by advances in science and technology, the U.S. must develop a strategy for the safe, effective, and timely implementation of human-based predictive approaches for toxicity testing. The recently enacted Frank R. Lautenberg Chemical Safety for the 21st Century Act, which calls for increased use of information from alternative test methods and strategies, and the Precision Medicine Initiative, a bold new research effort to revolutionize how we improve health and treat disease, both speak to the urgent need to develop a strategy for evaluating the impact of xenobiotics on human and environmental health. A pending report from the National Academy of Sciences (NAS) on Incorporating 21st Century Science into Risk-Based Evaluations will certainly help inform future efforts. However, developing a holistic approach for establishing confidence in these new approaches may require significant changes in policy, practice, and regulation; a challenge so complex and broad in scope that it cannot adequately be addressed by any single agency or existing government entity. Consequently, a discussion of the best path(s) forward to address this issue needs to be started.

References

1. Horizon 2020

<https://ec.europa.eu/programmes/horizon2020/>

2. UK Roadmap

http://nc3rs.org.uk/sites/default/files/documents/NonAnimalTechCO082_RYE_4_nrfinal2.pdf

3. HR2858: The Humane Cosmetics Act

<https://www.congress.gov/bill/114th-congress/house-bill/2858>