

Poster: free communications

## **Non-animal approaches to inhalation toxicity assessment: a proposal for a way forward**

*Kristie Sullivan, Chad Sandusky*

Physicians Committee for Responsible Medicine (Washington) (US)

e-mail: ksullivan@pcrm.org

In the drive to develop alternatives for animal-based acute toxicity tests, the oral LD<sub>50</sub> has received considerable attention and investment compared to the development of alternatives for acute inhalation LC<sub>50</sub> testing. Concerted efforts at developing a strategic approach to *in vitro* acute oral toxicity testing have recently culminated in the European Union ACuTox project. Conversely, there are a plethora of respiratory-tissue specific cell or tissue models being used in individual laboratories for various environmental research purposes, and work has progressed towards surmounting air/liquid interface considerations are crucial that to correctly predicting respiratory toxicity. However, despite early efforts to develop a concerted strategy for replacement of *in vivo* acute inhalation toxicity testing, one has not emerged. In the alternatives field large amounts of resources are being invested into optimization and validation efforts to replace existing animal-based testing methods on a one-to-one basis. It has become clear that just as with acute oral toxicity, replacing acute inhalation testing in animals will require a more strategic, combinatorial approach versus this one-to-one replacement approach.

In order to identify a system-wide non-animal approach to respiratory toxicity, one must take into account potential respiratory insults that could occur (i.e. acute site-specific tissue damage, bronchial muscle effects, deep lung deposition and/or injury, respiratory sensitization, etc.), and also systemic effects as a result of the distribution and metabolism of a chemical should it be absorbed. Of course, one method may cover multiple insults; similarly, some insults may be covered by methods used in considering other exposure routes (i.e. oral exposure).

This presentation briefly summarises previous discussions and proposes several potential ways forward utilising the most promising current research methods. It provides a forward-looking analysis on the most efficient ways to move ahead, taking into account potential challenges as well as the explosion of recent work in cell and tissue models, computational toxicology, virtual lung and airway modelling, systems biology, and pathway analysis as it relates to inhalation toxicology.

*Keywords: in vitro, inhalation toxicity, testing strategy*