

Replacing Animals for Acute Systemic Toxicity Testing: A U.S. Strategy and Roadmap

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ICCVAM is contributing to a U.S. strategy and roadmap for implementing 21st century toxicity testing approaches by promoting alternative approaches for required acute systemic toxicity testing. Development and implementation of these approaches will involve four key steps: (1) defining testing needs, (2) identifying available alternatives, (3) developing integrated approaches to testing and assessment (IATA), and (4) addressing both scientific and non-scientific challenges. Each of these steps was considered in a 2015 workshop (<http://ntp.niehs.nih.gov/go/atwksp-2015>) which explored how to move alternative approaches for acute systemic toxicity testing from research to regulatory testing. Our review of U.S. and international testing needs highlighted that, while there are regional differences in specific testing requirements, all currently accepted guidelines for these tests share core principles. These include essential testing needs to be addressed by alternative approaches and opportunities for existing information to enable waivers of required testing. For example, guidance recently published by EPA on waiving the acute dermal toxicity test was based on a NICEATM analysis that demonstrated how sufficient hazard labeling was obtained with acute oral toxicity test information alone. While a variety of available alternative test methods can reliably identify potential cytotoxicants, none can single-handedly assess the multiple mechanisms of acute systemic toxicity following oral, dermal, or inhalation exposure. Accordingly, IATA will need to be developed to address the breadth of different mechanisms, ensure good coverage of the chemical landscape of interest and leverage the collective strengths of the most promising test and non-test methods. Finally, to ensure that the scientific and non-scientific considerations that could impede the adoption and implementation of such approaches are addressed, input will be needed from industrial sectors, academic disciplines, federal agencies, stakeholder organizations, and international partners. *This project was funded in whole or in part with Federal funds from the NIEHS, NIH under Contract No. HHSN273201500010C. This abstract does not necessarily represent U.S. EPA policy.*

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