International Regulatory Needs for Acute Toxicity Data

J. Strickland[1], A. Daniel[1], D. G. Allen[1], N. Kleinstreuer[2], E. Haugabrooks[3]

[1]ILS, RTP, NC, United States; [2]NIH/NIEHS/DNTP/NICEATM, RTP, NC, United States; [3]Physicians Committee for Responsible Medicine, Washington, DC, United States

Chemical regulatory authorities around the world consider acute systemic toxicity data to substantiate safety assessments, and for many regulations these data are required. Acute oral, dermal, and inhalation data are typically used to develop product hazard labels for consumer or worker protection and to assess risks from acute exposure to chemicals. Other uses include setting occupational exposure levels, dose-setting for longer term studies, and classifying mechanism of action. To identify opportunities for regulatory uses of non-animal replacements for acute systemic toxicity tests, we reviewed acute systemic toxicity testing requirements for Brazil, China, Canada, Japan, the European Union, South Korea, and the United States, which participate in the International Cooperation on Alternative Test Methods (ICATM). Our chemical sectors of interest for each jurisdiction were cosmetics and personal care products, consumer products, industrial chemicals, pharmaceuticals, medical devices, and pesticides. We found acute systemic toxicity data were most often required for hazard identification rather than risk assessment. Where animal methods were required, animal reduction methods were typically recommended. However, for many jurisdictions and chemical sectors, non-animal alternatives were not accepted. The most frequently acceptable non-animal approaches were test waivers. For example, guidance on medical device testing from the International Standards Organization and for pharmaceuticals from the International Conference on Harmonization both indicate that acute toxicity information can potentially be obtained from other studies. An understanding of international regulatory requirements for acute systemic toxicity testing will inform the development of ICATM's strategy for the development, acceptance, and implementation of non-animal alternatives to assess the health hazards and risks associated with acute toxicity. This project was funded by the Physicians Committee for Responsible Medicine and with federal funds from the NIEHS, NIH under Contract No. HHSN273201500010C.