

Collaborative Modeling Project for Predicting Acute Oral Toxicity

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With an increasing number of chemicals to assess for acute systemic toxicity potential and a lack of available *in vitro* approaches, *in silico* models provide an alternative to predict acute oral toxicity and bridge data gaps. NICEATM and the ICCVAM Acute Toxicity Workgroup organized an international collaborative project to develop *in silico* models for predicting acute oral toxicity. In total, 35 groups participated, submitting 139 predictive models built using a dataset of 11,992 chemicals. Models were developed for five endpoints: LD50 value, EPA hazard categories, GHS hazard categories, very toxic (LD50 < 50 mg/kg), and non-toxic (LD50 > 2000 mg/kg). Predictions within the applicability domains of the submitted models were evaluated using external validation sets, then combined into consensus predictions for each endpoint, forming the Collaborative Acute Toxicity Modeling Suite (CATMoS). The resulting consensus models leverage the strengths and overcome the limitations of individual modeling approaches. The consensus predictions performed at least as well as the *in vivo* acute oral toxicity assay in terms of accuracy and reproducibility. CATMoS consensus models are available as free and open-source tools via the OPERA predictive tool (<https://github.com/NIEHS/OPERA>), which provides applicability domain assessments and accuracy estimates. CATMoS predictions for the ~850k chemical structures in DSSTox will ultimately be publicly accessible via NTP's Integrated Chemical Environment (ice.ntp.niehs.nih.gov) and the EPA's CompTox Chemicals Dashboard (comptox.epa.gov/dashboard). *This project was funded with federal funds from NIEHS under Contract No. HHSN273201500010C. This abstract does not necessarily reflect EPA policy.*