

## **Collaborative Modeling Project for Predicting Acute Oral Toxicity (CATMoS)**

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To fulfill the pressing need to accurately assess chemicals for acute oral toxicity potential, NICEATM and the ICCVAM Acute Toxicity Workgroup organized the Collaborative Acute Toxicity Modeling Suite (CATMoS) project to develop *in silico* models to predict LD50 and bridge data gaps. Participants from 35 international groups submitted 139 predictive models built using 11,992 chemicals split into training (75%) and evaluation sets (25%). Crowdsourced models were developed for five endpoints identified as relevant to regulatory decision frameworks: 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 submitted models were evaluated, then combined into consensus predictions based on a weight-of-evidence approach. The resulting CATMoS consensus model leverages the strengths and overcomes the limitations of individual modeling approaches. The consensus predictions are fully reproducible and performed as well as independent replicate *in vivo* acute oral toxicity assays. The CATMoS consensus model can be applied to any new chemical via a k-nearest neighbors approach, and is available via the free and open-source tool OPERA (Open Structure-activity/property Relationship App). OPERA is a comprehensive standalone suite of QSAR models including chemical structure standardization workflow and molecular descriptor processing, in addition to applicability domain and accuracy assessments. CATMoS predictions processed by OPERA for the DSSTox ~850k chemical structures are publicly accessible via NTP's Integrated Chemical Environment and the EPA's CompTox Chemicals Dashboard. This project funded with federal funds from NIEHS, NIH under Contract No. HHSN273201500010C.