***In Silico* Prediction of Acute Oral Rat Toxicity**

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Assessing the acute toxic potential of a substance is necessary to determine the potential effects of accidental or deliberate short-term exposure. There are no accepted in vitro approaches available and few in silico models to predict acute toxicity. Until recently, a paucity of experimental in vivo acute toxicity data was available for model development and evaluation. Here a large dataset of acute oral toxicity was compiled from different sources including the Hazardous Substances Databank (HSDB). Many of the studies were limit tests which report a LD50 as above a threshold, typically 2000 mg/kg or 5000 mg/kg. These data present challenges for model development because they give us less information than a LD50 value. To overcome this limitation, a two-step approach was used to model acute oral toxicity. In the first step, a random forest model was built to predict which substances would be above and below a LD50 of 5000 mg/kg. This model was constructed with a training set of 5931 substances with experimental LD50 values and ToxCast/Tox21 activities as descriptors. On a test set of 1482 substances, the balanced accuracy of the model was 76% and its negative predictive value was 84%. In the second step, a ridge regression model was derived using a training set of 4164 substances with experimental LD50 values and ToxCast/Tox21 activities as descriptors. For a test set of 1387 substances, 85% of the predictions made were within 1 log unit of their experimentally reported LD50 value. These models show considerable promise in predicting acute oral toxicity.

This abstract does not reflect EPA policy.