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Using experimental animal data from ToxValDB to derive points of departure for application in LCIA and comparative risk screening

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Life cycle impact assessment (LCIA) and comparative risk screening rely on chemical-specific points of departure (PODs) from regulatory toxicity data sources to evaluate toxicological impacts on human health from chemical exposures. However, regulatory PODs are not available for the majority of chemicals to which humans can be exposed. We thus aim to broaden the coverage of chemicals by using available *in vivo* data to estimate PODs that most closely mimic one that would be selected in a regulatory assessment context. As a starting point, we extracted and curated experimental animal data available from the US EPA ToxValDB, focusing on oral repeated-dose studies and three non-cancer effect-level types: lowest observed adverse effect level (LOAEL), no-observed adverse effect level (NOAEL) and benchmark dose lower bound (BMDL). The curation process included harmonization of units into mg/kg-d followed by extrapolations from subchronic or subacute studies to chronic, from different effect-level types to benchmark dose (BMD) and from tested animal species to humans. After curation, in the case of data-rich chemicals with at least 10 data points, we fit the resulting data to a lognormal distribution. For data-poor chemicals with less than 10 data points, we fit the distribution while applying a fixed standard deviation of $\log_{10}$=0.55, based on the average standard deviation across data-rich chemicals in our curated dataset. PODs were then derived for 9037 chemicals based on the 5th%-ile of the fitted lognormal distribution. The resulting POD values ranged by orders of magnitude from 1e-7 mg/kg-d to 1e4 mg/kg-d across the considered substances, with a median POD=7 mg/kg-d. For the 746 chemicals with available regulatory PODs, we observed a good correlation with our derived 5th%-ile PODs (R^2=0.70 and RMSE=0.64 of the $\log_{10}$-transformed values). These results suggest that the proposed method is able to derive PODs consistent with regulatory values in a high-throughput approach, thus substantially increasing the coverage of chemical substances for application in LCIA and risk screening. Next steps include using this curated dataset to train a machine-learning-based prediction model to estimate PODs for an even wider range of substances without any experimental animal data available. *This abstract does not necessarily reflect US EPA policy.*