IN SILICO TOOLS FOR PREDICTING REPEAT-DOSE SYSTEMIC TOXICITY

Repeat-dose systemic toxicity involves multifactorial interactions across organ systems, and as such, it can be useful to use a combination of *in vitro* and *in silico* tools for filling data gaps and supporting weight of evidence assessments under regulatory frameworks, such as REACH and the EU Cosmetics Regulation.

The primary computational strategy for evaluating these complex systemic effects is Quantitative Structure-Activity Relationship (QSAR) models, which are used to predict distinct adverse outcomes such as hepatotoxicity, nephrotoxicity, and cardiotoxicity, often using structural alerts to flag potential organ-specific damage.

Ultimately, integrating these *in silico* predictions with *in vitro* and exposure data within Integrated Approaches to Testing and Assessment (IATA) enables a robust, mechanistically grounded evaluation of long-term health risks.

A non-exhaustive list of *in silico* tools for predicting repeat-dose systemic toxicity is provided below. Please contact Kyle Martin at kmartin@thepsci.eu to include additional resources on this list or with any questions.

TOOL	DEVELOPER	METHOD/APPROACH	AVAILABILITY
ACD/Percepta	ACD/Labs	Statistical	Commercial
ADMET Predictor	Simulations Plus	Statistical	Commercial
CASEUltra	MultiCase	Statistical	Commercial
Derek Nexus	Lhasa Limited	Expert rules-based	Commercial
iSafeRat	KREATiS	Statistical	Commercial
OECD QSAR Toolbox	OECD/ Laboratory of Mathematical Chemistry	Statistical (read-across/QSAR)	Open-source
VEGA QSAR	VEGAHub	Statistical	Open-source