Glossary

ADME	The four key processes describing a chemical's journey through the body: Absorption, Distribution, Metabolism, and Excretion.
Adverse outcome	The final, detrimental biological effect at the individual or population level (e.g., organ toxicity, impaired reproduction) that results from progression through the key events of an AOP.
Adverse Outcome Pathway (AOP)	A structured representation of biological events leading to an adverse effect, starting from a Molecular Initiating Event (MIE), through Key Events (KEs), to an Adverse Outcome (AO).
Applicability domain	The chemical, biological, and parameter space within which a predictive model (e.g., QSAR, PBPK, ML) is scientifically valid and reliable.
Artificial Intelligence (AI)	The broad discipline of creating computer systems capable of performing tasks that typically require human intelligence, such as interpreting chemical structures or predicting toxicological endpoints.
Chemical analogue	A chemical that is structurally similar to a target chemical and is used to predict the target's toxicity, physicochemical properties, or biological activity when direct data for the target is limited or unavailable.
Classification model	A modeling task where the goal is to predict a categorical label for a chemical (e.g., "Toxic" or "Non-Toxic").
Context of use	A precise description of how a method, model, or dataset is intended to support a regulatory or scientific decision, defining acceptable performance and limitations.
Deep Learning	A specialized subset of ML using multi-layered artificial neural networks (ANNs) capable of learning complex, non-linear patterns from high-dimensional toxicological data (e.g., predicting toxicity directly from molecular graphs).
ex vivo	Experiments conducted using tissues, organs, or cells taken from an organism and maintained outside the body, preserving physiological structure while enabling controlled testing.

External Validation	The process of assessing the reliability and relevance of a model, ensuring it performs accurately on chemicals it was not trained on.
in chemico	Experimental methods performed in a controlled chemical system without cells or living tissue, often used to measure direct chemical reactivity relevant to toxicity pathways.
in silico	Computational or computer-based methods used to model, predict, or simulate chemical, biological, or toxicological behavior without physical testing.
in vitro	Experiments performed in controlled laboratory environments using cells, cell lines, tissues, or biochemical systems outside a living organism.
In Vitro to In Vivo Extrapolation (IVIVE)	Analysis methods used to translate concentrations active in *in vitro* assays (e.g., cell cultures) into estimates of equivalent *in vivo* doses (e.g., oral mg/kg/day) expected to cause effects in humans or animals.
Internal Validation	Statistical test that uses the same dataset used to build the model (often by splitting it temporarily) to confirm the model's consistency and statistical robustness.
Key event	A measurable, essential biological change that occurs between the molecular initiating event and the adverse outcome within an AOP framework.
Key event relationship	The scientifically supported causal and quantitative linkage between two key events, describing how a change in one event leads to a change in the next.
Machine Learning (ML)	A subset of AI where algorithms learn patterns from chemical and biological data (training sets) to make predictions on new chemicals without being explicitly programmed for specific rules.
Molecular Descriptor	A numerical representation of a chemical’s properties (e.g., molecular weight, logP, presence of specific substructures) used as the input "features" for mathematical models.
Molecular initiating event (MIE)	The first point of chemical interaction at the molecular level that begins a toxicity pathway, such as receptor binding, covalent attachment, or enzyme inhibition.
New Approach Methodology (NAM)	A broad term (often synonymous with Non-Animal Method) referring to any technology, including *in silico* models and *in*

	vitro assays, used to assess chemical hazard without using intact animals.
Physiologically-Based Pharmacokinetic (PBPK), Physiologically-Based Toxicokinetic (PBTK)	A mathematical modeling technique that predicts the absorption, distribution, metabolism, and excretion (ADME) of a chemical by simulating the body as a set of interconnected physiological compartments (e.g., liver, kidney, blood).
Parameter optimization, Parameter estimation	The process of finding the best set of parameters for a model, algorithm, or system to achieve optimal performance according to a defined objective or metric.
Quantitative Adverse Outcome Pathway (qAOP)	An AOP that includes mathematical relationships (response-response functions) between key events, allowing for the prediction of the magnitude or timing of the adverse outcome based on the intensity of the initiating event.
Quantitative Structure-Activity Relationship (QSAR)	A computational method that models the relationship between the chemical structure of a molecule (represented by descriptors) and its biological activity or toxicity using statistical or machine learning techniques.
Read-across	A data-gap filling technique where toxicity data from a "source" chemical (with known data) is used to predict the toxicity of a similar "target" chemical (with missing data), based on structural or biological similarity. Such similar chemicals are called analogues.
Regression model	Modeling task that predicts a chemical's activity as a continuous numerical value, such as a precise potency (AC_{50} or LD_{50} value).
Reverse toxicokinetics, Reverse dosimetry, Dose reconstruction	Using biomonitoring data (e.g., chemical concentration in urine or blood) and PBPK modeling to estimate the external dose (exposure) the individual likely received.