In Silico NAMs Quick Reference Sheet

Method	Main Purpose	Typical Inputs / Data Needs	Typical Outputs
Artificial Intelligence (AI)	Broad category encompassing ML, DL, and rule-based approaches	Rule sets, training data, models, simulations	Any combination of predictions, simulations, optimizations, or decision support outputs
Deep Learning (DL)	Learn hierarchical features from complex data for prediction or mechanistic insight	High-dimensional data: images, molecular graphs, omics, time series, labeled endpoints	Predictions, learned embeddings, automated feature extraction, explainability metrics
In vitro to in vivo extrapolation (IVIVE)	Convert in vitro bioactivity or clearance data to in vivo dose/PoD	In vitro effect concentration (AC50, BMC), clearance, scaling factors, optional PBPK	Estimated human equivalent dose (HED), screening PoD
Machine Learning (ML)	Learn patterns from structured/semi-structured data to predict toxicity or properties	Chemical descriptors, assay matrices, omics, TK time series, labeled endpoints	Toxicity/property predictions, parameter calibration, feature importance, embeddings
Molecular Modeling	Characterize chemical interactions with biological targets (MIE/MOA)	2D/3D chemical structures, conformers, protein structures, simulation parameters	Binding affinities/scores, interaction maps, mechanistic hypotheses
Physiologically-based pharmacokinetic (PBPK) modeling	Simulate ADME to estimate tissue/plasma concentration-time profiles	Chemical physicochemical properties, clearance, partitioning, physiology parameters, exposure scenario	Tissue/plasma concentration-time curves, HED, variability estimates

Method	Main Purpose	Typical Inputs / Data Needs	Typical Outputs
Quantitative AOPs (qAOPs)	Model causal key-event pathways from MIE to adverse outcome	MIE dose-response, KE dose-response, KE→KE link functions, optional TK/PBPK	Pathway PoD, KE sensitivity, AO probability/severity, uncertainty bounds
Quantitative structure activity relationship (QSAR)	Predict toxicity or physicochemical properties from chemical structure	Chemical structure (SMILES, InChI), molecular descriptors, fingerprints, training data	Predicted toxicity values/categories, applicability domain, uncertainty metrics
Read-Across	Fill data gaps using experimental data from similar analogs	Target chemical structure, analog structures, experimental study data, similarity justification	Hazard class, numeric endpoint (PoD), justification report

Tips for Quick Reference

- **QSAR** and **ML/DL** are predictive; **Read-Across** is evidence-based
- **PBPK** and **IVIVE** link external dose to internal concentration and PoD.
- **qAOPs** quantify mechanistic pathways, useful for integrating multiple key events.
- Always report **uncertainty**, **applicability**, and **confidence** in regulatory context
- **DL** is preferred for high-dimensional data like images, graphs, or omics; traditional **ML** is fine for tabular descriptor data.