



# ToxGPS® In Silico Tools

## Versatile Tools to Support Chemical Safety Assessment

ToxGPS® In Silico Tools offer molecular and physico-chemical property calculations, QSAR models and rule-based predictions for toxicity endpoints, chemotype profiling to explore structural features, and a TTC workflow. ToxGPS® predictions employ a weight of evidence approach to combine mode-of-action models and rules to yield probabilistic outcomes. Projects at EFSA, US FDA, Health Canada, NIHS Japan, and at customer sites have helped to guide and validate this approach.



ChemTunes

### ChemTunes Database

#### Toxicity study data (experimental)

- Systemic/target organ
- Carcinogenicity
- Genetic toxicity
- Reproductive/developmental
- Acute toxicity
- Skin irritation/sensitization
- Neurotoxicity, immunotoxicity
- Absorption, distribution, elimination

#### Metabolism study data (experimental)

- Human *in vitro* hepatocytes
- Endogenous system pathways



ToxGPS

### ToxGPS In Silico Data

#### Chemotype profilers

- Reproductive/developmental
- Liver (steatosis, mitochondrial toxicity,...)
- Skin (permeability, irritation)
- Metabolic sites (liver, skin)

#### Regulatory models

- Genetic toxicity (Ames, *in vitro* chromosome aberration, *in vivo* micronucleus)
- Carcinogenicity (rat, mouse)
- Skin sensitization (LLNA hazard and potency)
- Developmental (cleft palate)
- Liver toxicity (human DILI)
- Acute toxicity (consumer products)

#### Calculated properties (34)

- Whole molecule (atoms, bonds, size, interfacial), shape, quantum mechanical energetics



Express

### Express In Silico Data

#### POD data (experimental)

- NOAEL (systemic/target organ, reproductive/developmental, neurotoxicity)
- EC3 (skin sensitization)

#### Toxicity (ML/AI QSAR)

- Skin irritation
- Preclinical liver toxicity (DILI)
- Clinical liver toxicity (DILI)

#### Bioavailability (ML/AI QSAR)

- Skin permeability
- Blood brain barrier
- Oral absorption
- Plasma protein binding
- Hepatic intrinsic clearance (OPERA)
- Caco-2 cell permeability (OPERA)

#### Physicochemical properties (OPERA)

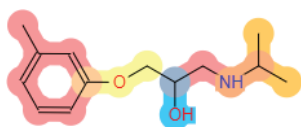
- pKa
- logD
- Water solubility
- Vapor pressure
- Melting point
- Henry's law constant,...

#### Environmental properties (OPERA)

- Biodegradation
- Ready biodegradability
- Soil absorption coefficient
- Fish bioconcentration factor

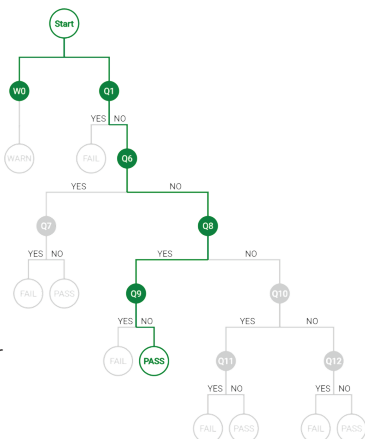
## Chemotype Profiles

- Profiling, grouping, and categorizing chemical compounds to assess their structural, biological, and metabolic similarity
- Extensive set of general, chemical reactivity, toxicity, and metabolism profilers such as DNA/protein binders, liver toxicity, or skin metabolism rules and alerts



## TTC Analysis

- Chemical domain and cohort of concern filters
- Different Cramer classification schemes
  - Toxtree implementation with original, extended, and revised Cramer classification
- Munro and cosmetics non-cancer EDI threshold values
- Interactive tree representation



## Molecular Properties

- Molecular and physiochemical properties – whole molecule properties (22) and shape descriptors (8)
- Quantum mechanical descriptors (4) – heat of formation, HOMO, LUMO, HOMO/LUMO gap
- Skyline profile to assess similarity in property space

