

# Artificial Intelligence and AOP-based *in silico* models for safety assessments





**Statistical and artificial** 

intelligence modelling

Modelling by three statistical and artificial

intelligence algorithms: random forest model

(RF), k-nearestneighbors algorithm (k-NN) and

Deep Learning models, using a dataset

containing rigorously curated structures.

Altox Ltda is an alternative toxicology services company located in Brazil, with resources focused on toxicity assessment for regulatory purposes. Our team includes experts in software development, data science, predictive toxicology, safety assessment and regulatory toxicology.

Our team experts utilize advances in toxicology and in silico methodologies for assessment of new molecules, drug substances, biocides, cosmetics ingredients, food ingredients of contact-materials, degradation products, impurities, residue, and contaminants. The company now also provides advanced machine learning services for pharmaceutical, skin care, food, biocidal and fine chemistry companies.

## **Alert analysis**

Analysis of structural alerts rigorously curated by our team to prioritize multiple arguments for and against the toxicity of a chemical weighed up by the evidence.



Visual representation of the structure fragments predicted to contribute to toxicity (red) or non-toxicity (green) Model Prediction Mutager Random Fores Non-Mutar implemented with the 2D MACCS (75.5%) fingerprint kNN Non-Mutager k-nearest neighbors decision model (71.4%) implemented with the 2D Extended Connectivity Fingerprint Deep Learning 30 Deep Learning de Non-Mutager emented with the 3D conformer (91.0%) fingerprint like Extended Connectivity Finge

#### Supporting the expert workflow **STEP STEP** 2

**STEP** 

The interactive visualization tools help you to know when to apply to expert knowledge that could potentially refute a (Q)SAR prediction and how to do that for each step.

4

**STEP** 3

**Inspecting the Applicability** Domain (Within the Domain) Density

> 0.0 0.2 0.4 0.6 0.8 1.0 MACCS Dice Similarity

#### Applicability Domain (AD) inspection

Our visual AD Inspection® is used to establish the AD and limitations of the models, which are represented by a density plot of the average fingerprint-dice similarity for the k-nearest neighbors of each compound during the 5-Fold external model's validation.

### A standardized report is generated to ensure that results are transparent, complete, and consistently documented



Our tools and models: Expert workflow			What makes our tools special?		
~	Selection of the regulatory endpoints		~	Fulfills the requirements of the prediction methodologies under the validation principles set by the Organisation for Economic Co-operation and Development (OECD)	
$\checkmark$	Relevant data search and curation steps of the datasets			An overall <b>visual</b> assessment of the results from the two (Q)SAR methodologies, which individually generate positive, negative, or inconclusive predictions, provides an easy to understand, user-friendly interface	
~	Development of (Q)STR models using different approaches like rule-based, statistical and/or Machine Learning-based				
				The interactive viewalization tools halp you to know when to	
~	Validation of the models following the OECD Principles and reviews		~	apply expert knowledge that could potentially refute a (Q)SAR prediction and how to do that;	
				The workflow supports a rationale that may be considered for	
<ul> <li></li> </ul>	Reporting the (O)STR models employing the standard Reporting Format Files (QMRF) and document process Implementation of real-time interface with experts for each endpoint		$\checkmark$	use in a robust expert review	
			~	A standardized report is generated to ensure that results are consistently documented, transparent and complete;	
			~	You have direct support with our scientists and developers!	

## About our tools

	Genotox-iS <sup>™</sup>	Software for the prediction of mutagenicity by alerts, statistical and machine learning-based models.
	IrriTest <sup>™</sup>	Software for the prediction of skin corrosion and irritation by alerts, statistical and machine learning-based models with accumulative evidence from experimental data.
	AOP-Sens <sup>™</sup>	Software for the prediction of skin sensitization by alerts, statistical and machine learning-based models, in a logical adverse outcome pathway (AOP) framework that balances transparency, mechanistic interpretability, and predictivity.
0	iS-Ocular <sup>™</sup>	Software for the prediction of ocular corrosion and irritation by alerts, statistical and machine learning-based models.
	Acute-Tox <sup>™</sup>	Software for the prediction of acute toxicity by statistical and machine learning-based models.
	Pred-Oral <sup>™</sup>	Software for the prediction of oral bioavailability and permeability Caco-2 by statistical and machine learning-based models.
	Pred-CYP2D <sup>™</sup>	Software for the prediction of metabolites by statistical and machine learning- based models.
	iS-Liver <sup>™</sup>	Software for the prediction of the hepatotoxicity in vitro and in vivo of by statistical and machine learning-based models in a logical adverse outcome pathway (AOP) framework.
	DevTox-iS <sup>™</sup>	Software for the prediction of the developmental toxicity by statistical and machine learning-based models.
	Pred-Ecotox <sup>™</sup>	Software for the prediction of the acute and chronic aquatic toxicity by statistical and machine learning-based models.
	BCF-Test <sup>™</sup>	Software for the prediction of the bioconcentration factor (BCF) by statistical and machine learning-based models.

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