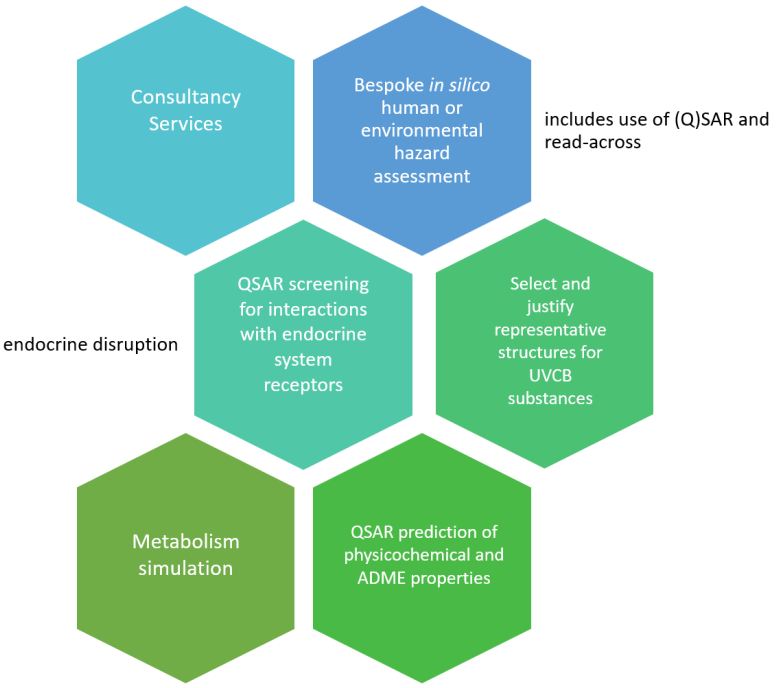
ToxNavigation: training and consultancy for *in silico* toxicology

Consultancy for *in silico* toxicology to incorporate data generated *in silico* with either freely available or commercial tools into your safety or hazard assessment.

Training for *in silico* toxicology to build or to enhance your skills in predicting chemical toxicity performing a read-across or a (Q)SAR analysis using freely available tools.

Consultancy for *in silico* toxicology



How we operate

initiation
- Project brief including overall purpose for the work
- The chemical structures of the target substances shared with ToxNavigation

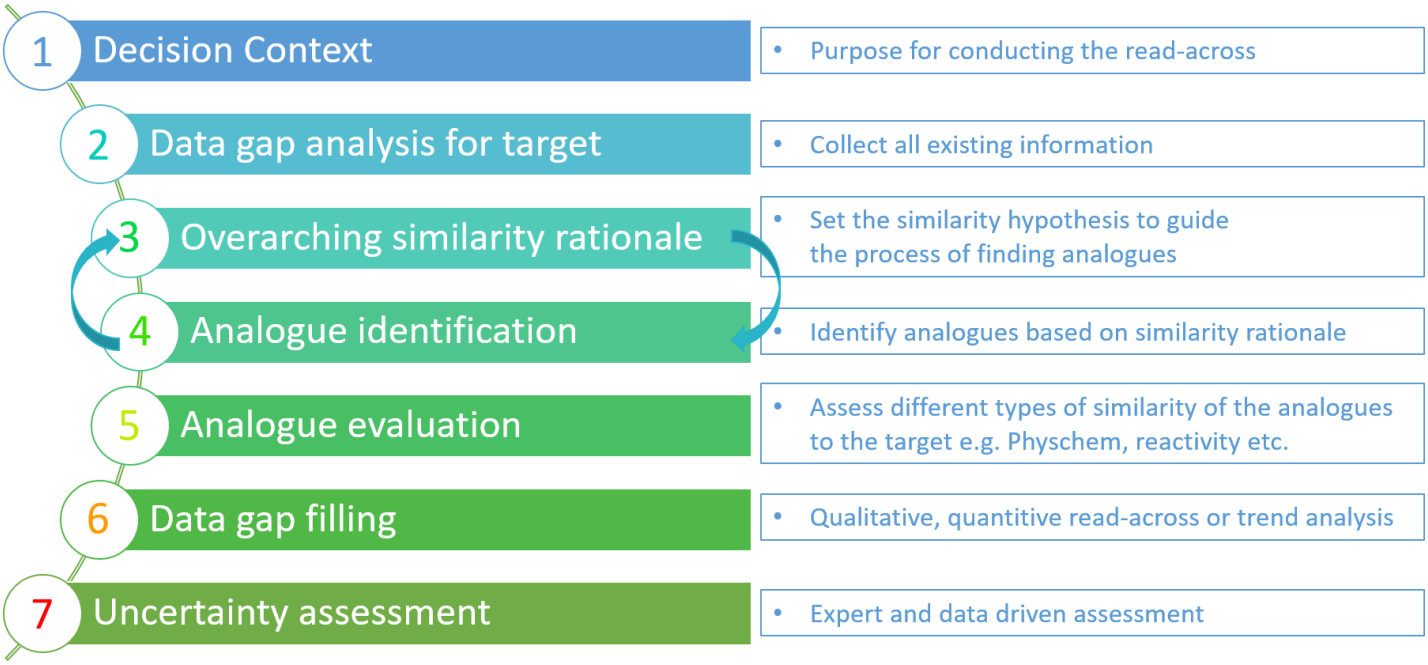
feasibility study
- Feasibility study is conducted to ascertain if *in silico* methods can be employed
- Proposal including scope of work, cost and estimated delivery

order placed
- Delivery confirmed and work commences

draft report
- Draft report submitted in Word format
- Optional video meeting

final report
- Final report delivered by email
- Report in Word and Adobe format

Read-across approach

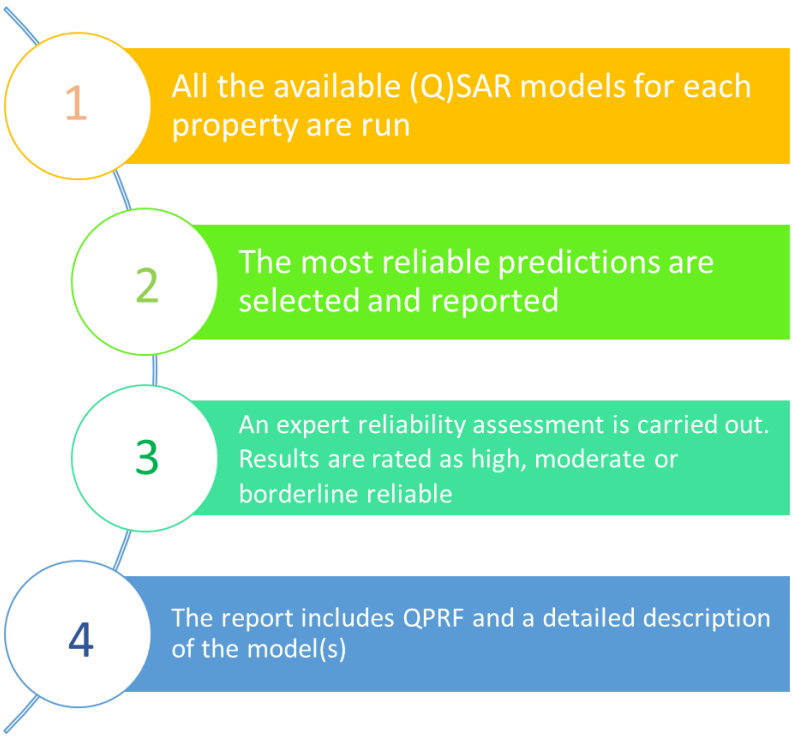


A video explaining the above workflow in more detail can be viewed: https://www.toxnavigation.com/read-across

The analogue evaluation includes the analysis of the similarity between your target and the analogues carried out in four steps: physicochemical, structural, toxicokinetic and mechanistic similarity analysis.

The standard report includes the read-across result, a prediction report for the target substance, the list of analogues, their evaluation and their experimental values used in assigning the final read-across prediction. The report is structured in line with the Read-Across Assessment Framework (RAAF). A more detailed analogue evaluation can be requested. For example: a review of a rejected read-across by a regulator can be strengthen by including a metabolic, a toxicokinetic or a toxicodynamic similarity analysis.

QSAR predictions of physicochemical and ADME properties



ADME endpoints (absorption, distribution, metabolism and excretion)

- Percentage bound to human plasma proteins (% PPB)
- Affinity constant to serum albumin (logKaHSA)
- Passive permeability across jejunal epithelium based on logP and pKa
- The extent of oral absorption (%HIA)
- The relative contributions of transcellular and paracellular routes to overall %HIA
- Absorption (ka),
- total body clearance (ke),
- solubility in the gastrointestinal tract (SolGI),
- volume of distribution (Vd), and
- presystemic metabolism in the gut and liver (first-pass clearance)

Phys-chem endpoints

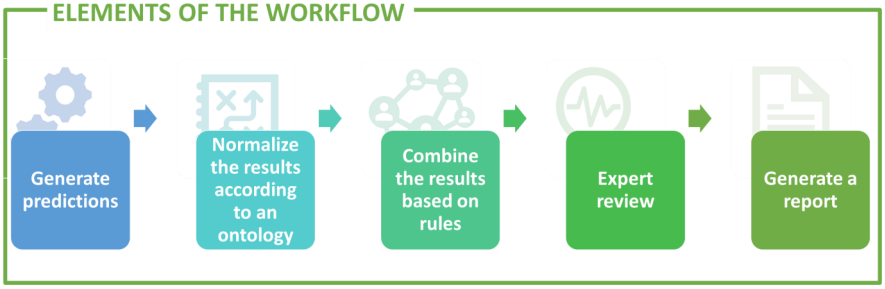
- Water solubility
- $logK_{ow}$ or logP
- Dissociation constant (pK_a)

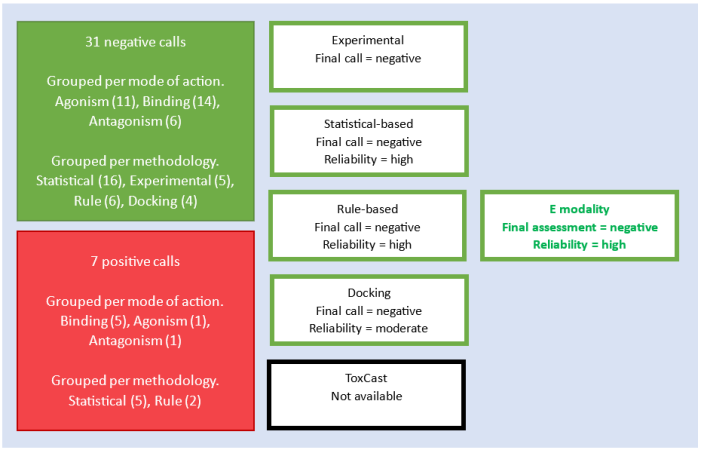
QSAR screening for interactions with endocrine system receptors

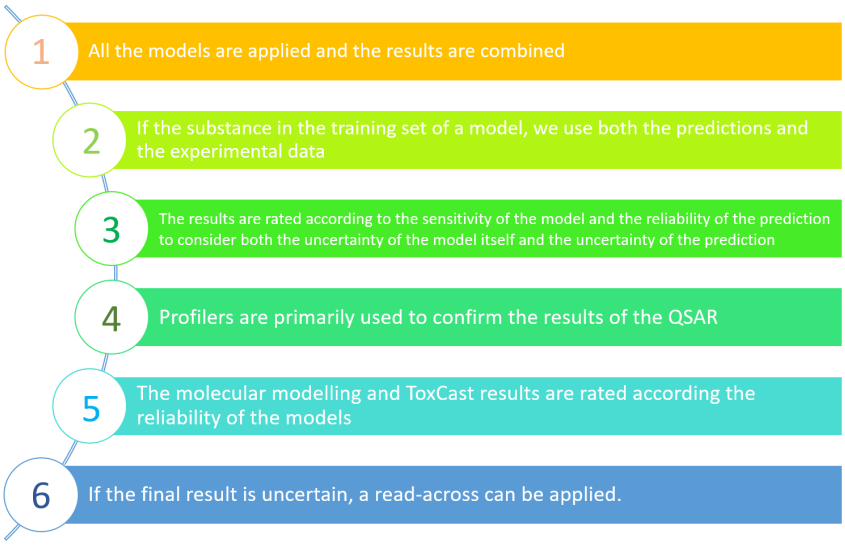
ToxNavigation provides an *in silico* screening for endocrine system receptors based on over 100 models covering 18 receptors linked to the endocrine system.

The models that we employ include statistical-based and rule-based (Q)SAR as well as predictions based on docking to the 3D structure of the receptor. A wide selection of commercial and open source models are applied and all models are valid according to the OECD principles.

Number of models		Modalities				
		E	A	T	S	O
MoA	Agonism	9	5	--	1	6
	Antagonism	5	5	--	1	--
	Binding	19	9	20	1	20
	Multiple	2	1	2	2	5
Methods	Docking	4	2	2	2	6
	Profilers	5	2	2	2	6
	QSAR	23	13	18	1	19
	ToxCast	3	3	--	--	--

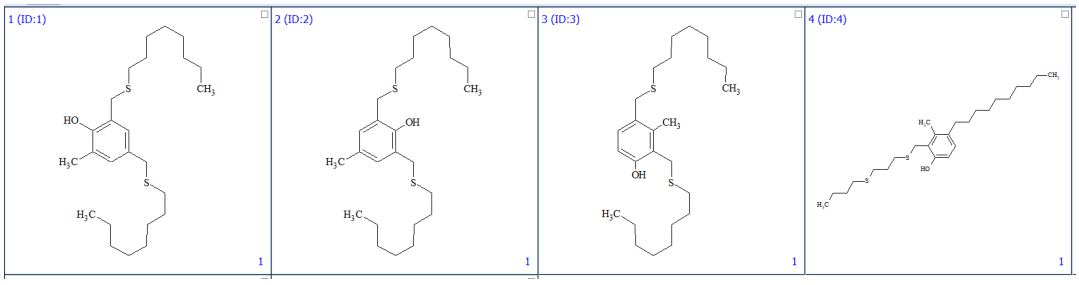






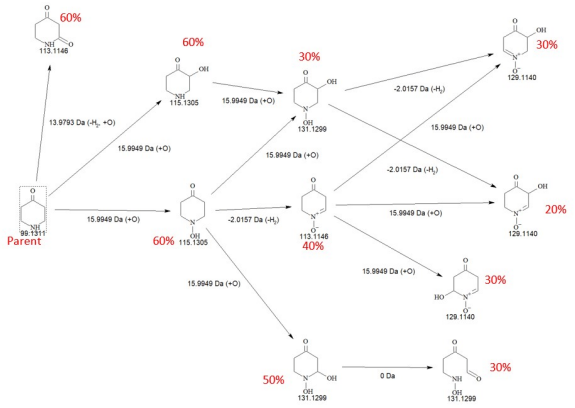
Select and justify representative structures for UVCB substances

For complex mixtures, polymeric substances or even UVCBs, ToxNavigation provides a service to enumerate justifiable representative structures of the substance by utilising cheminformatics. The purpose is to significantly reduce the number of different structures to a pragmatic and justifiable selection that represents the mixture from a toxicological, physiochemical or ADME perspective for either screening using QSAR or for a component based read-across.



If it is not possible to enumerate representative structures and a read-across is required, then a substance approach may be employed if suitable data is available.

Metabolite simulation



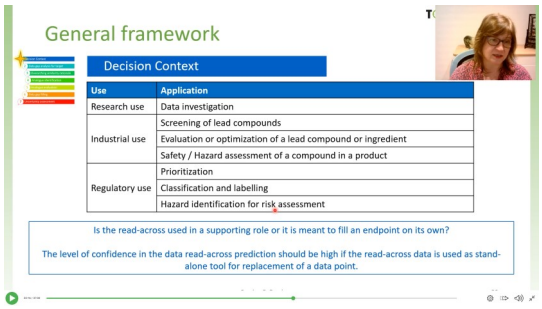
1. Apply commercial and freely available metabolite simulators to the parent
2. Compare the output from the various models
3. An expert assessment is carried out to identify the most likely metabolised structures
4. Option available for the rendering of a bio-transformation map

Training courses

ToxNavigation have been running training course for *in silico* toxicology since 2019. The course delivery has traditionally been either classroom based or video-streamed. Now we are also offering "tutor-assisted eLearning". This marries the convienence of studing when you are free, yet retaining the advantage of access to live tution. The courses follow a logical progression as knowledge is gained. For more details: toxnavigation.com/training. The courses are recognised by EUROTOX for Continued Professional Development.

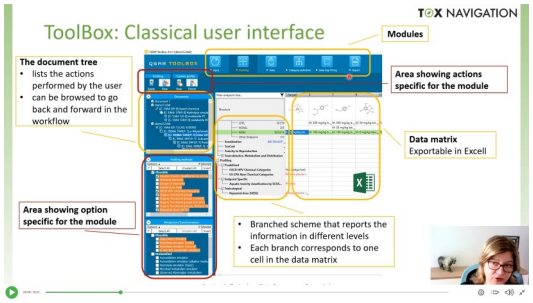
As this is a fast moving discipline, the courses are updated once a year to cover new tools, software updates and new research and new regulatory approaches

NAMs—use and application of QSAR and read-across



- **Background to build a justifable read-across and use of (Q)SAR for both screening and regulatory purposes**
- **Introduction and demonstrations of a wide variety of free software resources**
- **Recognised by EUROTOX for CPD**

Navigating the OECD QSAR Toolbox



- **Practical demonstrations and guides on how to use the modules in the OECD QSAR Toolbox**
- **Reporting**
- **Database building**

ToxNavigation also run special courses for companies and organisations. This can include live lectures and a bespoke agenda

About ToxNavigation

Experience

- More than 30 years of experience with *in silico* modelling
- Expert selection of tools and methods in agreement with the official guidelines
- Multiple relevant models and approaches are used to increase confidence in the derived toxicity estimates

Cost effective and flexible

- Free feasibility study
- *In silico* methods - lower cost and time compared to *in vitro / in vivo* methods
- Rapid access to several free and commercial tools
- Service fit-for-purpose (e.g. internal decision making or safety evaluation)

Delivery and customer support

- Feasibility study typically delivered in two days
- Study report typically delivered within two weeks
- Typically a 24 hour reactivity to client questions

Primary contact

Dr Elena Fioravanzo has 30 years experience in cheminformatics and the Managing Director of ToxNavigation - a consultancy utilising the latest methods of computational toxicology to facilitate the chemical risk assessment process. Elena has presented at many international conferences and has currently 36 papers and 85 posters published.

Contact us

TOX NAVIGATION

Training and consultancy for computational toxicology

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