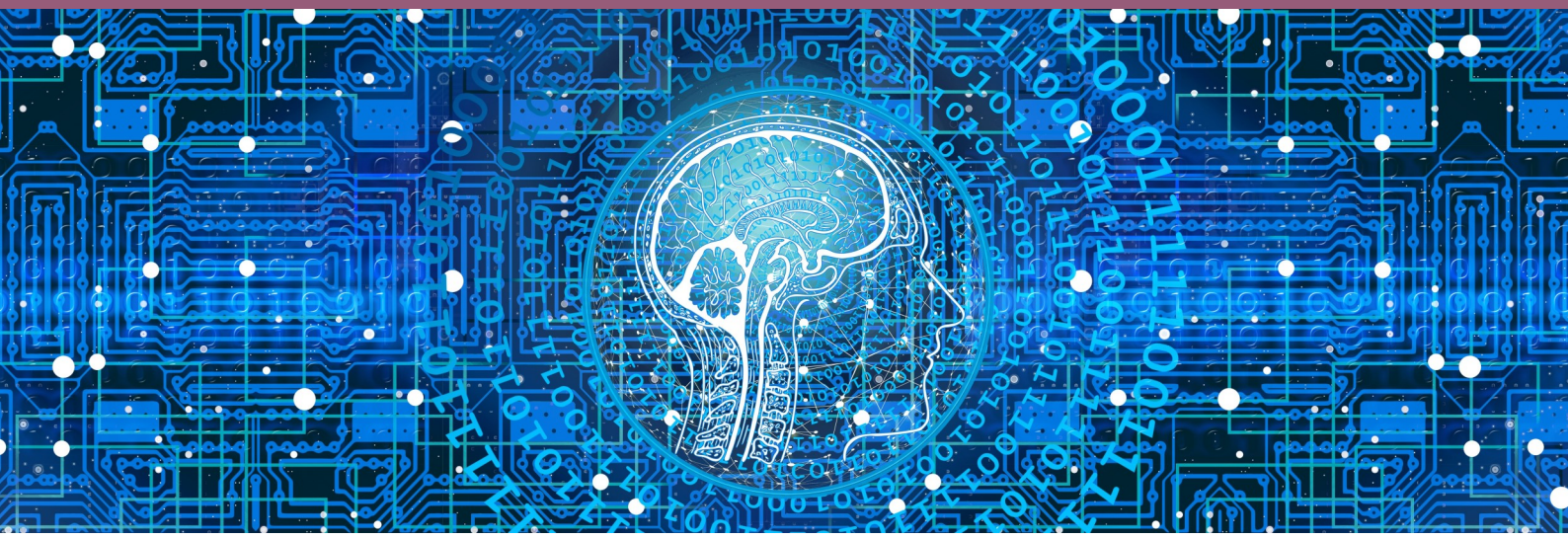
In silico Endocrine Disruptor Screening



ToxNavigation provides an in silico screening for endocrine disruption potential based on **153 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.

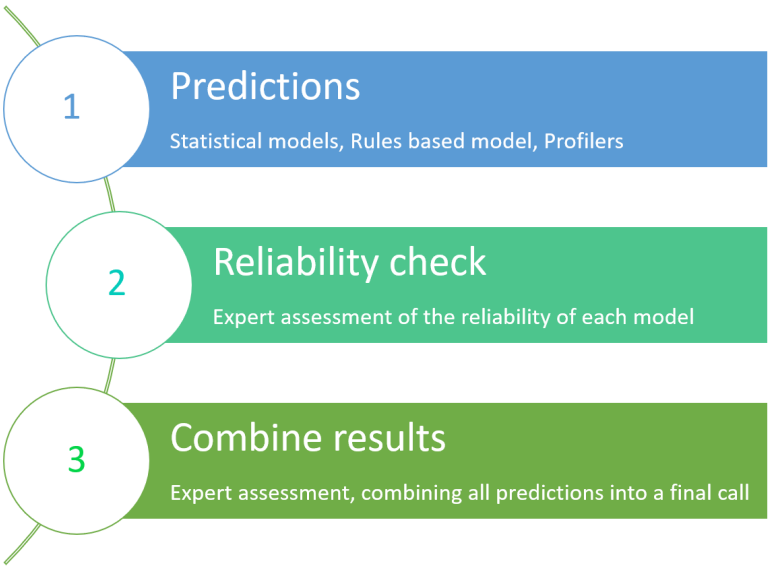
A **free of cost feasibility study** is conducted to ensure your compound is within the applicability domain of most models before accepting any contract.

The reliability of each prediction is assessed by an expert analysis and grouped by receptor to reach a consensus outcome. A detailed report is provided for a **highly competitive price** and can be used, as an example, under the Guidance for the identification of endocrine disruptors (ECHA and EFSA) in the context of the Biocidal Products Regulation (BPR, Regulation (EU) 528/2012).

Two tiers of services are provided:

- The **Screening Tier** is used to help set up a testing strategy or substance selection in product development.
- The **Regulatory Tier** is provided when the predictions are used as part of the weight of evidence for a regulatory submission and includes a more detailed analysis. This expert analysis is particularly important in cases where the predictions do not result in an obvious call.

(Q)SAR Models and Receptors



Receptor	n. of models
Arylhydrocarbon	8
Androgen Receptor	26
Human Aromatase	1
Constitutive Androstane Receptor	16
Cytochrome P450 3A4	4
Estrogen Receptor	39
Glucocorticoid Receptor	3
Liver X receptor	2
Mineralocorticoid Receptor	2
P-glycoprotein	3
Peroxisome proliferator-activated receptor	3
Progesterone Receptor	2
Pregnane X Receptor	16
Retinoic Acid Receptor	6
Retinoid X receptor alpha	1
Thyroperoxidase	8
Thyroid hormone receptor	12
Vitamin D Receptor	1

Report

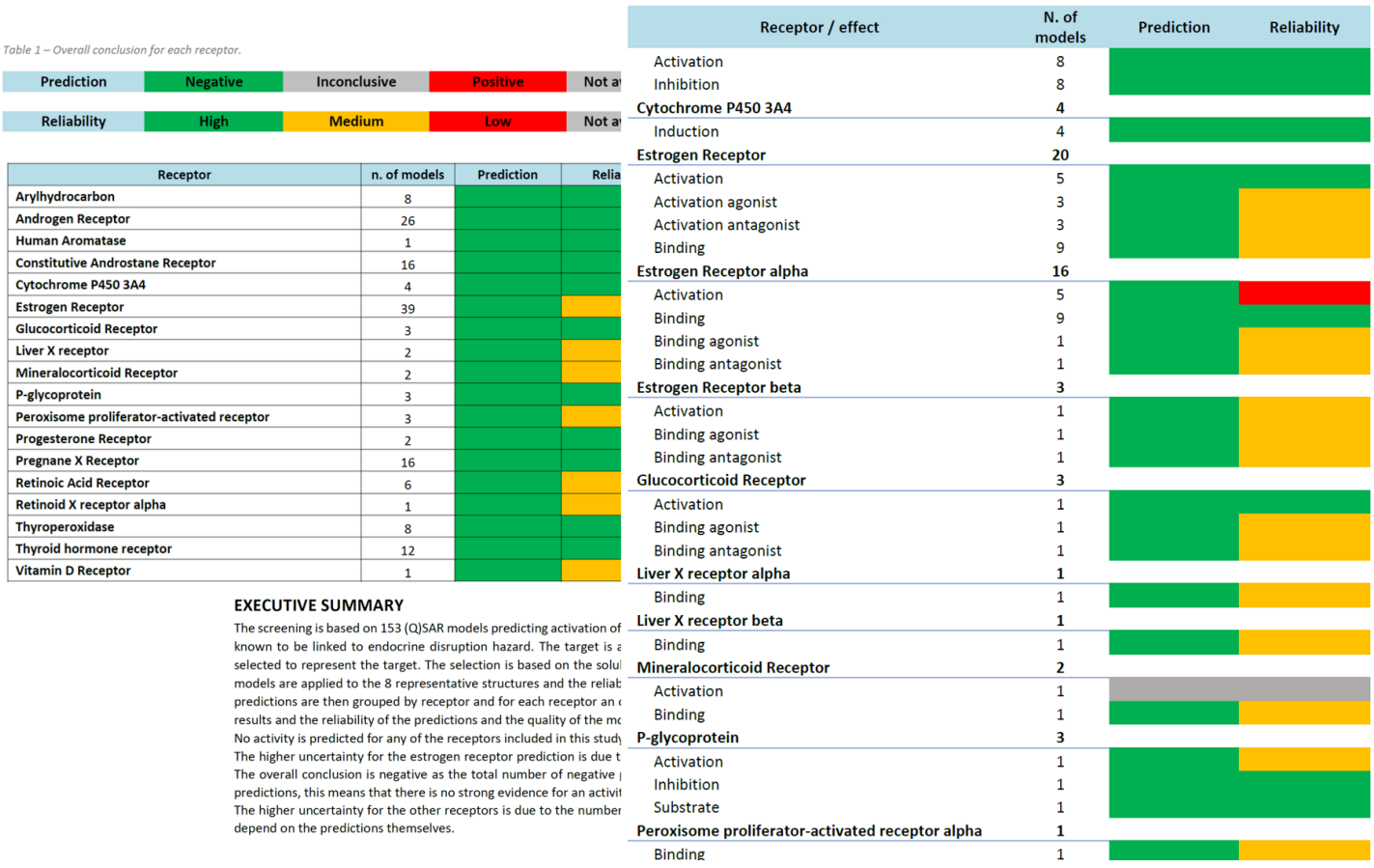


Table 1 – Overall conclusion for each receptor.

Prediction	Negative	Inconclusive	Positive	Not a

Reliability	High	Medium	Low	Not a

Receptor	n. of models	Prediction	Relia
Arylhydrocarbon	8		
Androgen Receptor	26		
Human Aromatase	1		
Constitutive Androstane Receptor	16		
Cytochrome P450 3A4	4		
Estrogen Receptor	39		
Glucocorticoid Receptor	3		
Liver X receptor	2		
Mineralocorticoid Receptor	2		
P-glycoprotein	3		
Peroxisome proliferator-activated receptor	3		
Progesterone Receptor	2		
Pregnane X Receptor	16		
Retinoic Acid Receptor	6		
Retinoid X receptor alpha	1		
Thyroperoxidase	8		
Thyroid hormone receptor	12		
Vitamin D Receptor	1		

EXECUTIVE SUMMARY

The screening is based on 153 (Q)SAR models predicting activation of
known to be linked to endocrine disruption hazard. The target is a
selected to represent the target. The selection is based on the solu
models are applied to the 8 representative structures and the reliab
predictions are then grouped by receptor and for each receptor an
results and the reliability of the predictions and the quality of the mo
No activity is predicted for any of the receptors included in this study
The higher uncertainty for the estrogen receptor prediction is due t
The overall conclusion is negative as the total number of negative
predictions, this means that there is no strong evidence for an activit
The higher uncertainty for the other receptors is due to the number
depend on the predictions themselves.

Receptor / effect	N. of models	Prediction	Reliability
Activation	8		
Inhibition	8		
Cytochrome P450 3A4	**4**		
Induction	4		
Estrogen Receptor	**20**		
Activation	5		
Activation agonist	3		
Activation antagonist	3		
Binding	9		
Estrogen Receptor alpha	**16**		
Activation	5		
Binding	9		
Binding agonist	1		
Binding antagonist	1		
Estrogen Receptor beta	**3**		
Activation	1		
Binding agonist	1		
Binding antagonist	1		
Glucocorticoid Receptor	**3**		
Activation	1		
Binding agonist	1		
Binding antagonist	1		
Liver X receptor alpha	**1**		
Binding	1		
Liver X receptor beta	**1**		
Binding	1		
Mineralocorticoid Receptor	**2**		
Activation	1		
Binding	1		
P-glycoprotein	**3**		
Activation	1		
Inhibition	1		
Substrate	1		
Peroxisome proliferator-activated receptor alpha	**1**		
Binding	1		

A visual colour-coded report is provided. An executive summary details the reasoning behind the expert opinion.

EXPERIENCE

- 25 years of experience with *in silico* modelling
- Multiple relevant models are used to increase confidence in the derived toxicity estimates
- Expert selection of tools and methods in agreement with the official guidelines
- *In silico* results complementary to *in vitro* results

COST EFFECTIVE & FLEXIBLE

- Free feasibility study
- *In silico* methods - lower cost compared to *in vitro* methods
- Rapid access to several free and commercial tools
- Service tailored to your needs (e.g. internal decision making or safety evaluation)

DELIVERY & CUSTOMER SUPPORT

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

The scientists at ToxNavigation have more than 25 years of experience in *in silico* modelling to predict the effects of chemicals on humans and in the environment and can generate **reliable safety data *in silico*** by combining results from **(Q)SAR** models, **chemical categories**, **grouping** and **read-across**.

CONTACT US

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