



NYCO



SEMACO
ENVIRONNEMENT

Chemical and toxicological mapping of PFAS

19/06/2025

Nyco is a world leader in aeronautic lubricants.

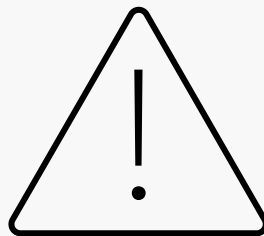


Our problem – During the last 60 years **toxic additives** were used in aviation oil.

For ten years we have worked to replace these compounds for **safer ones**, facing numerous challenges:



*Hundreds of molecules
to assess*



*The diversity of toxicity, the lack of
toxicological information*



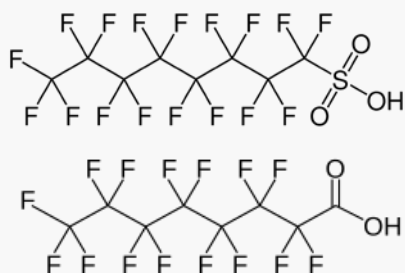
Safety By Design, a
software to successfully
find safer additives

Semaco – A need for a PFAS Tox Map

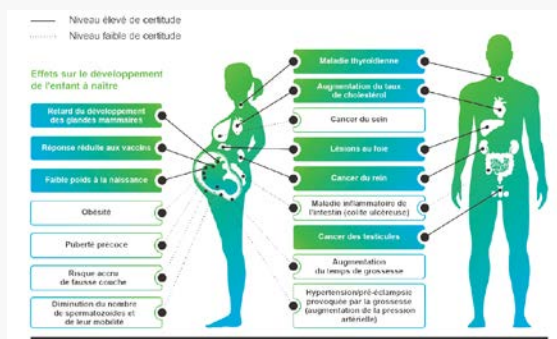
SEMACO is an independent consulting firm established in 1999, specializing in complex issues in the field of environmental management.

Certified NFX 31-620 by LNE, SEMACO maintains regular collaborations with the University of Lorraine and has contributed to the development of the software.

The challenges facing PFAS toxicity assessment :



A large dataset up to 20 000 compounds



*Multiple toxicity endpoint **

Only a couple of PFAS have extensive toxicological information

Lack of toxicological information

1. Gathering data :



**Scientific
data**



**Reglementary
data**

2. Predict :

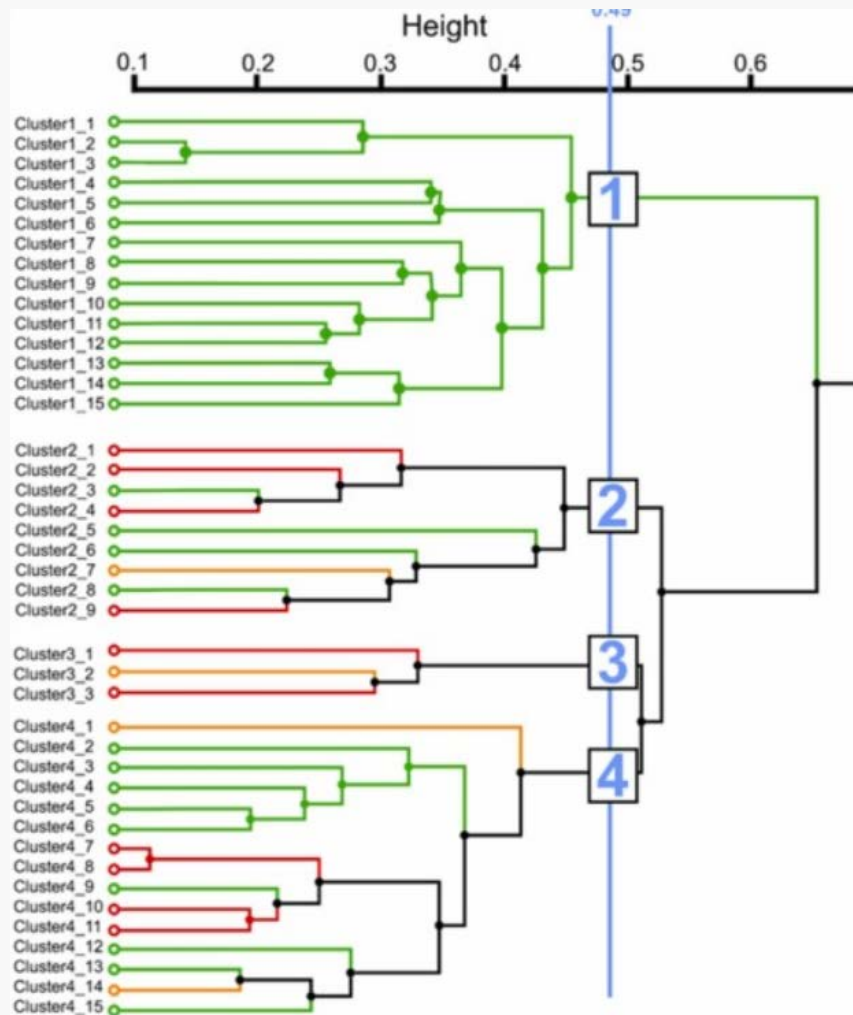


Toxicological
databases



**Artificial
intelligence
(QSAR)**

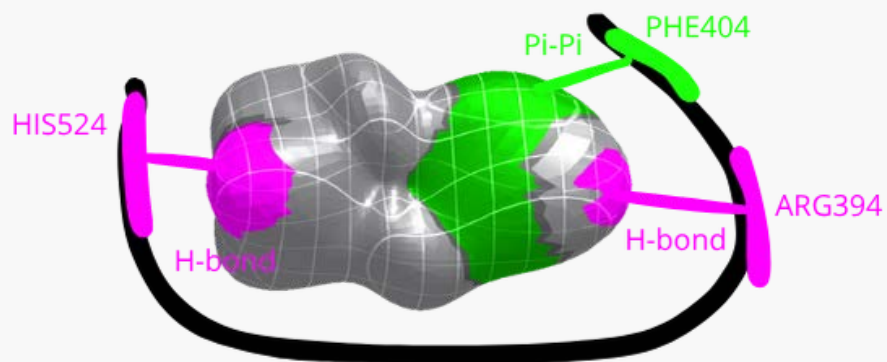
3D similarity map (neurotoxicity)



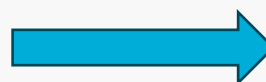
3. Map

Why do we use 3D molecular shape ?

The **three-dimensional shape** and chemical properties of a molecule determine its ability to interact with and activate specific protein binding pockets. This molecular recognition can trigger a biological response, which may be intended (drugs) or unintended, leading to adverse or toxic effects.

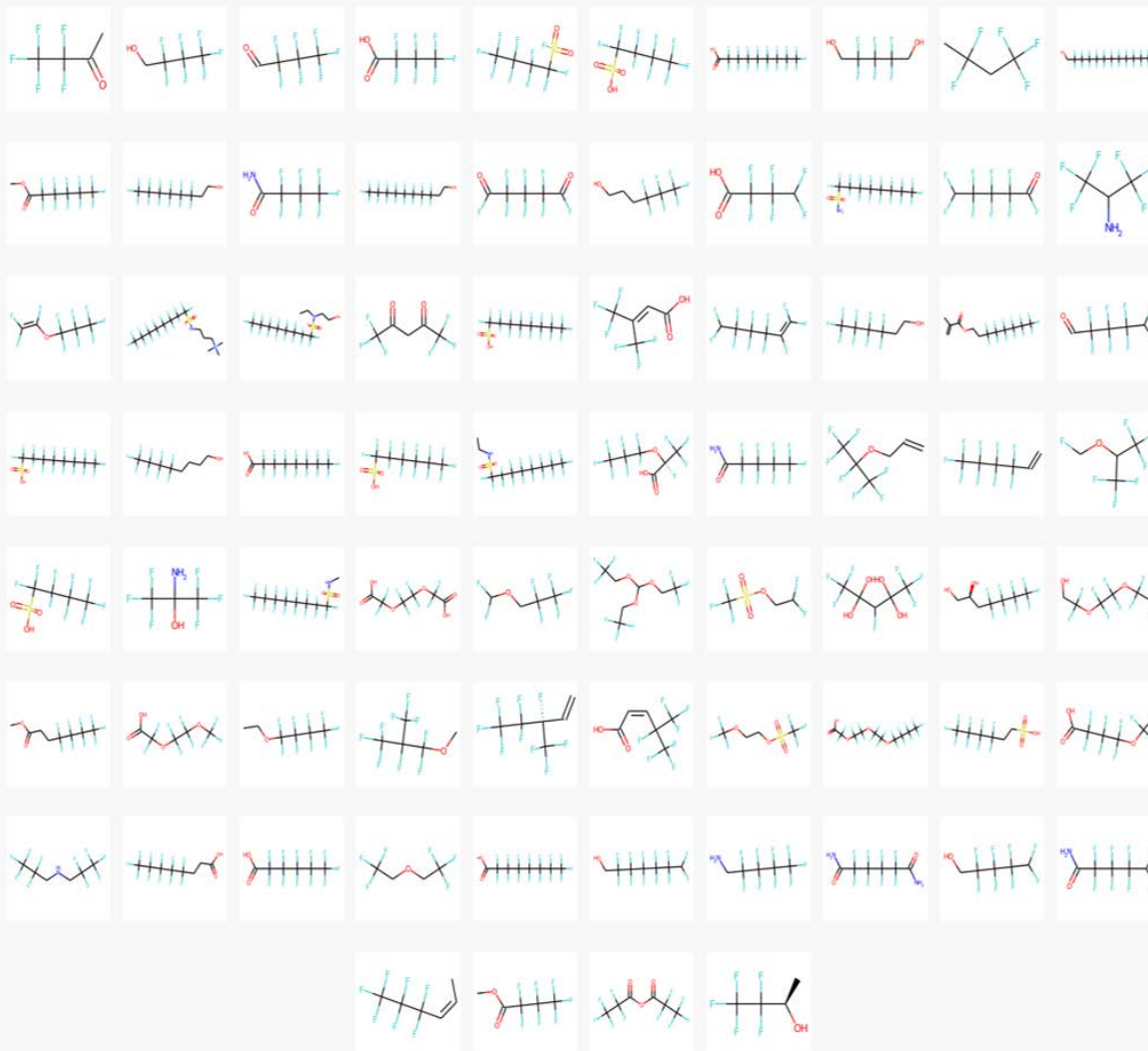


*Estradiol interaction with Eralpha binding pocket
 (Spherical Harmonic representation)*

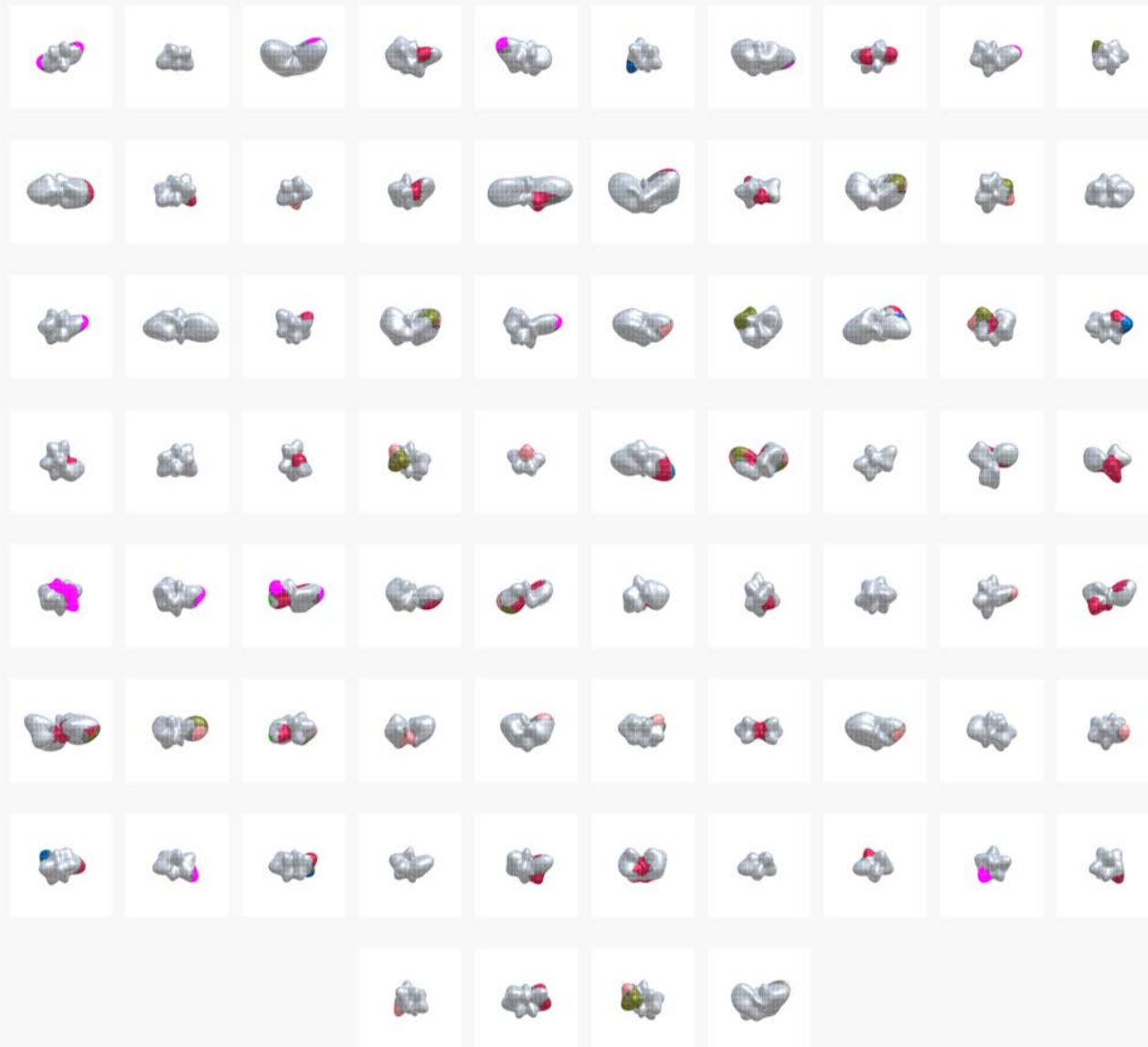


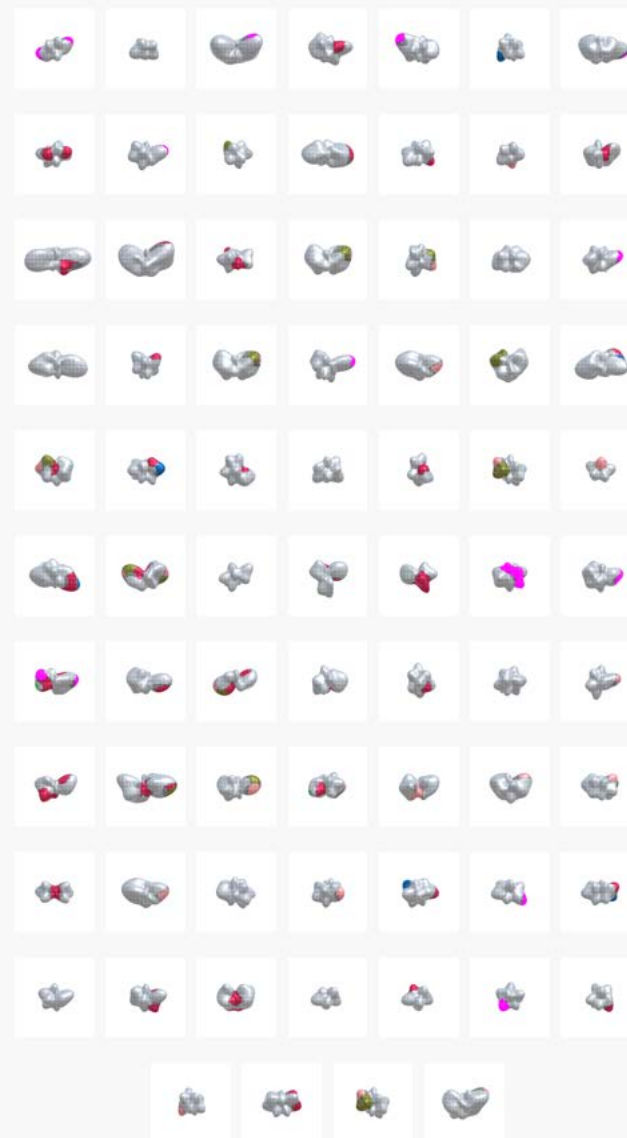
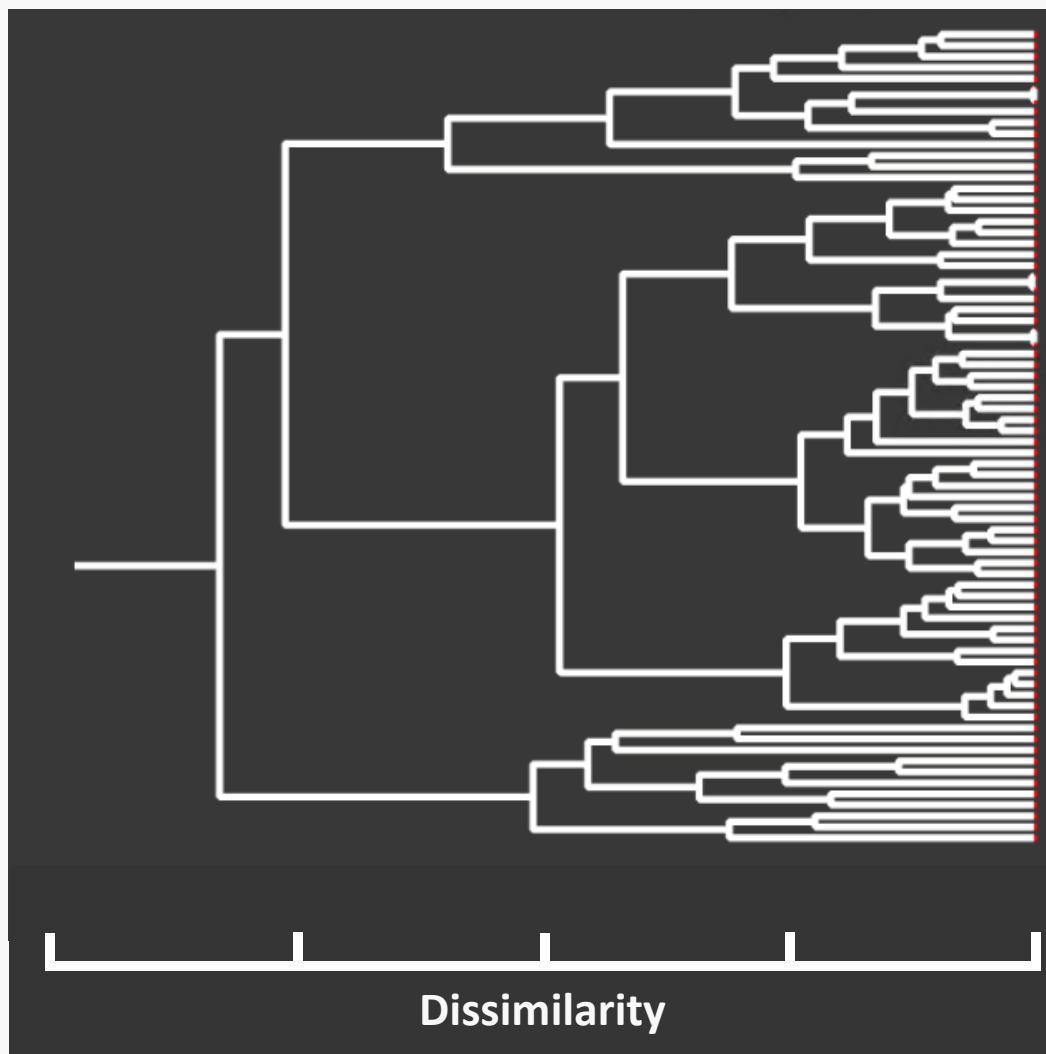
Biological Effect

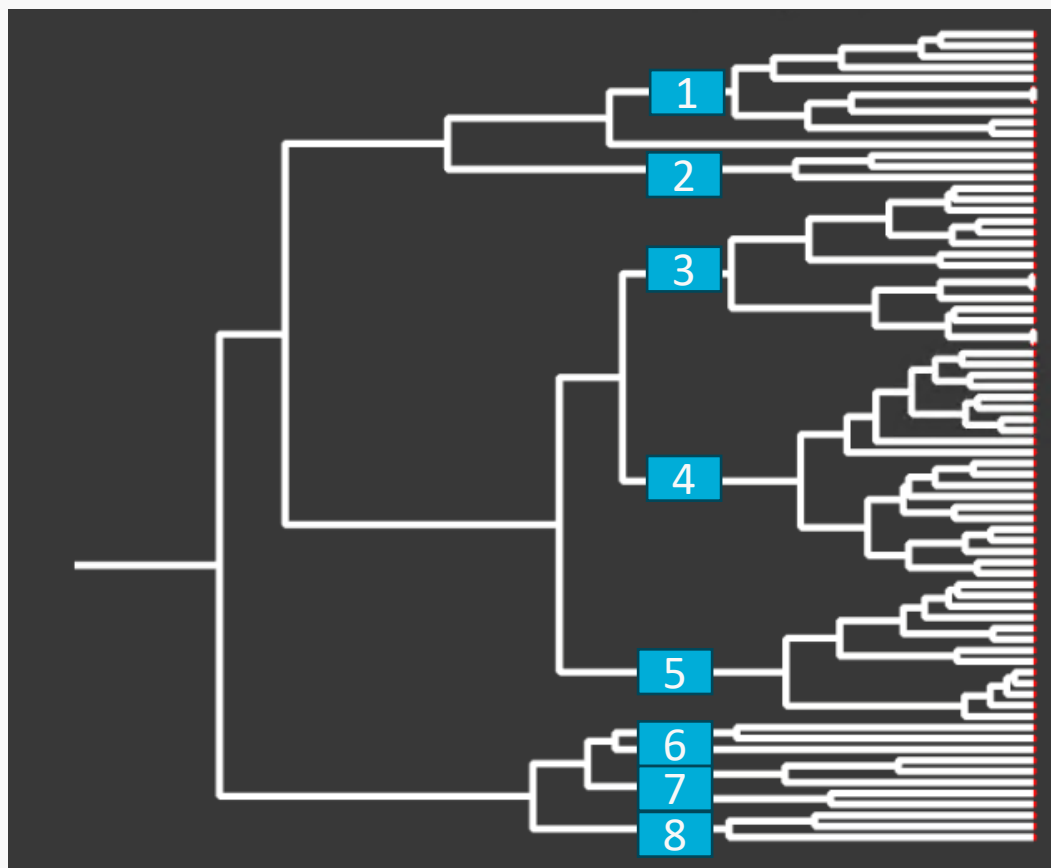
74 PFAS Priority list by EPA



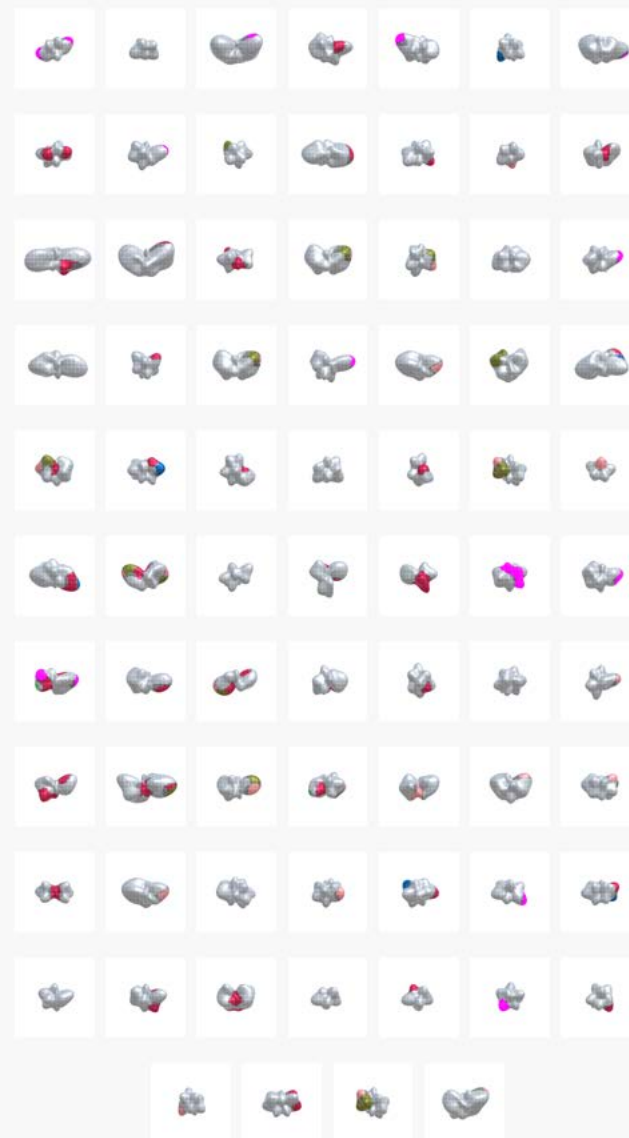
Spherical harmonics 3D representation



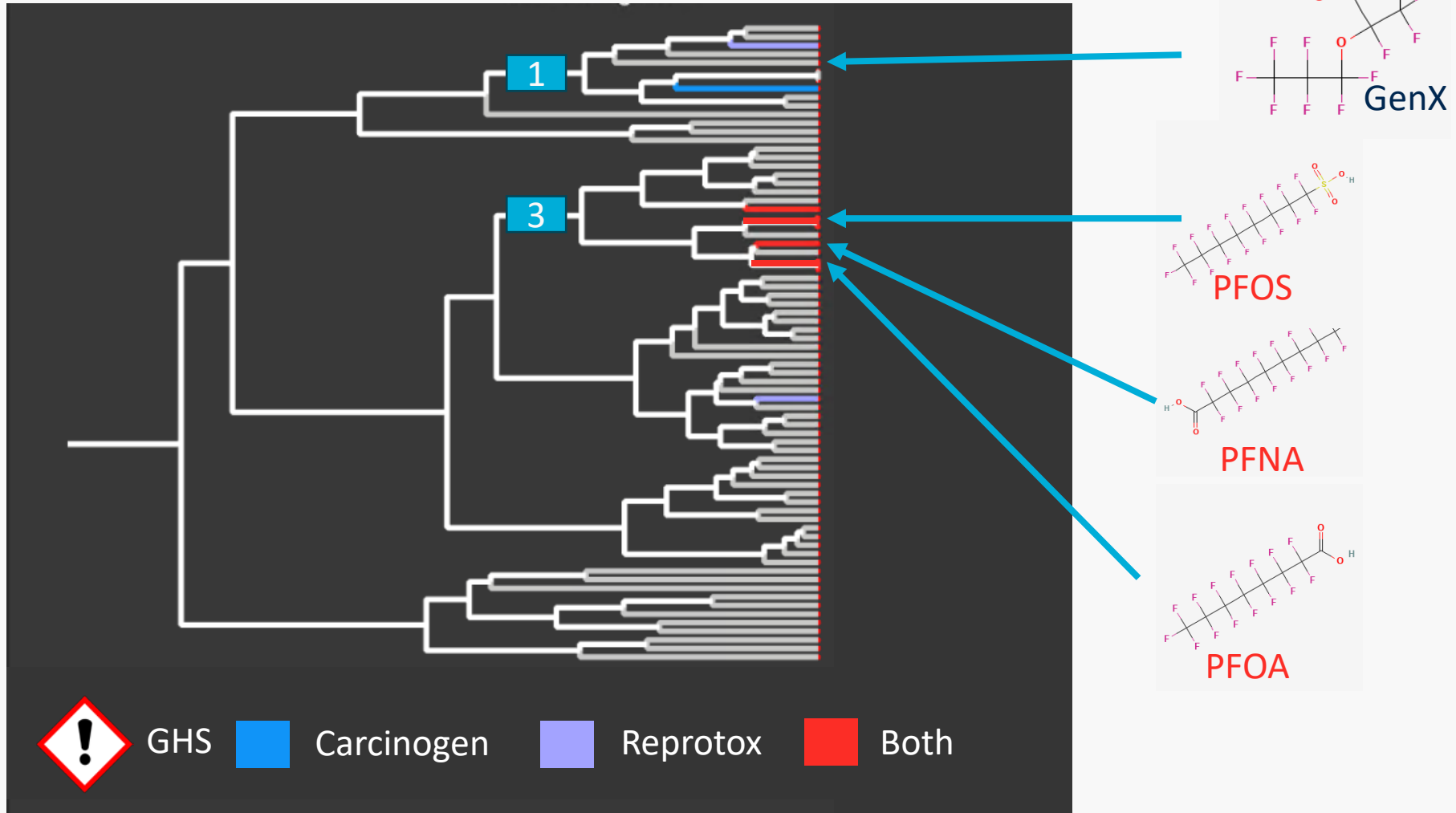




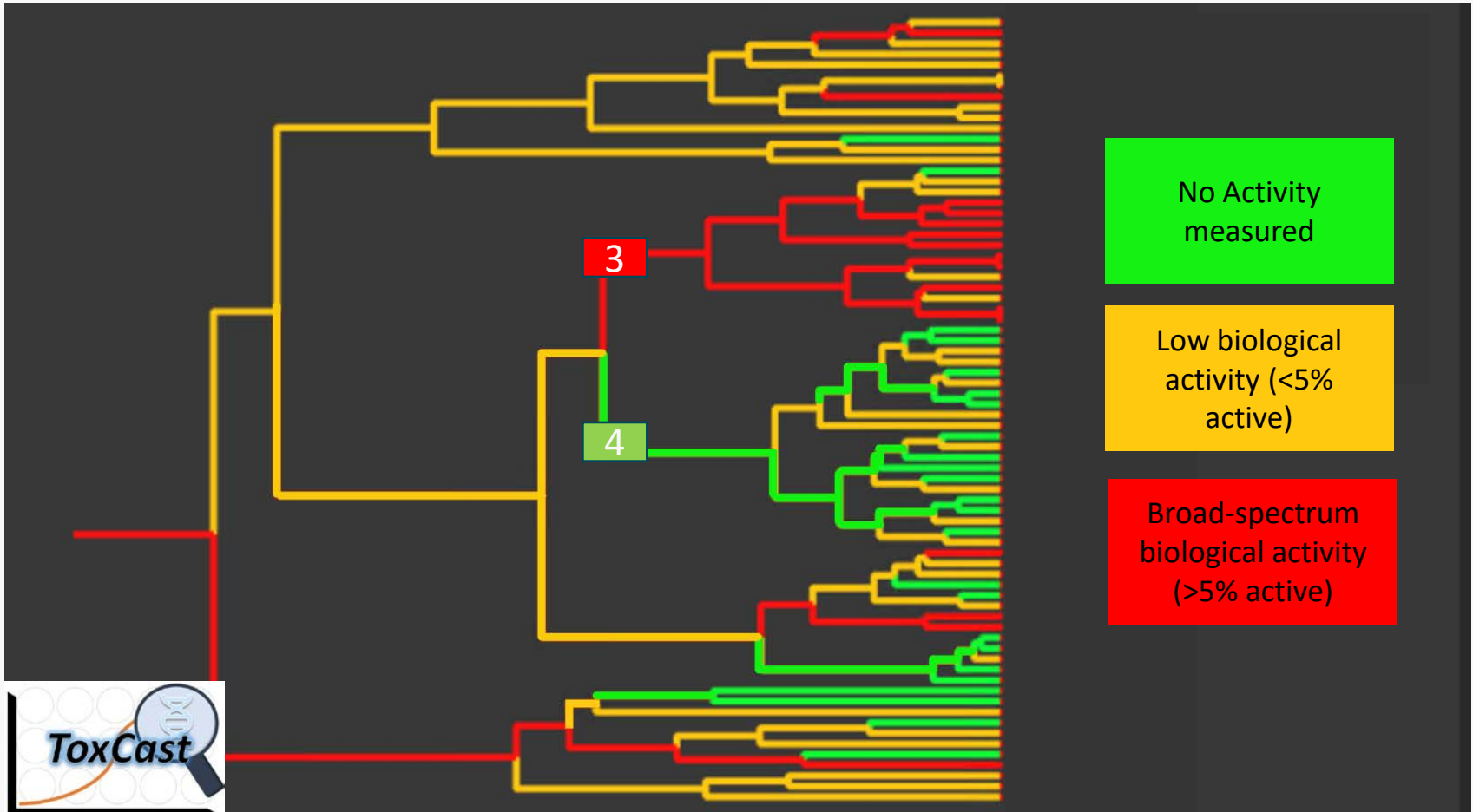
8 groups of PFAS with similar molecule shape and chemical features.



Recognised Hazard (GHS)

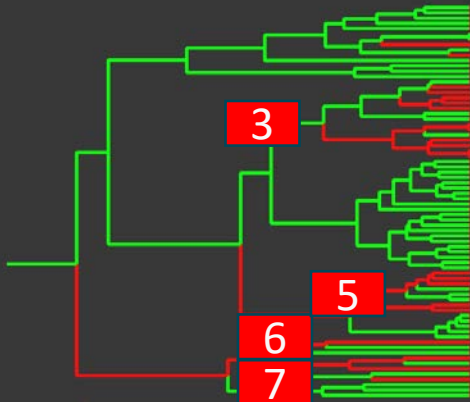


GHS classification were gathered from state reglementary agency from Europe (ECHA), Australia (AICIS) and Japan (NITE)

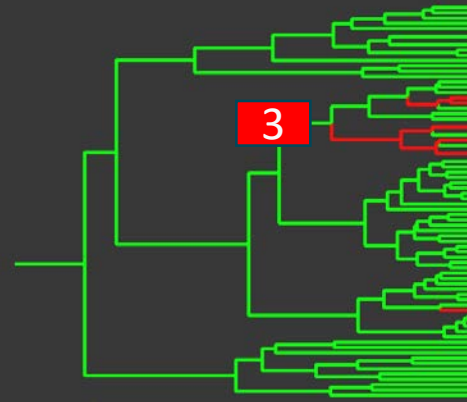


Toxcast is an EPA program that screen chemicals for biological activity, all 74 PFAS had at least 100 in Vitro (cells) tests.

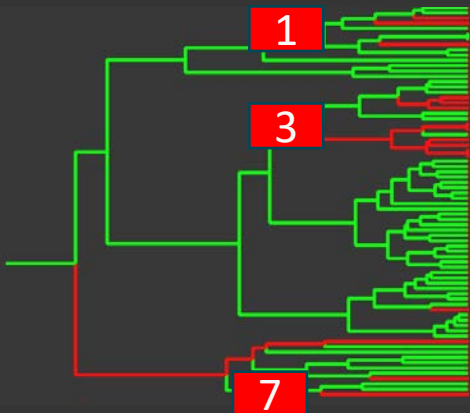
Estrogen receptor



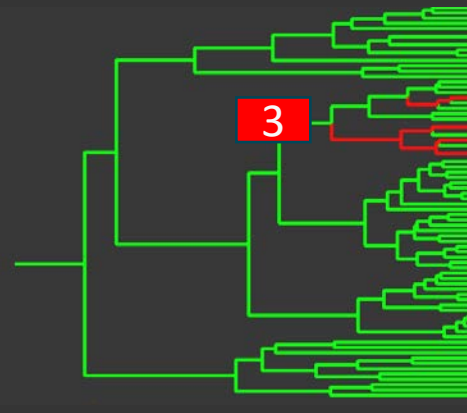
Androgen receptor



PPAR* receptor



Thyroid receptor



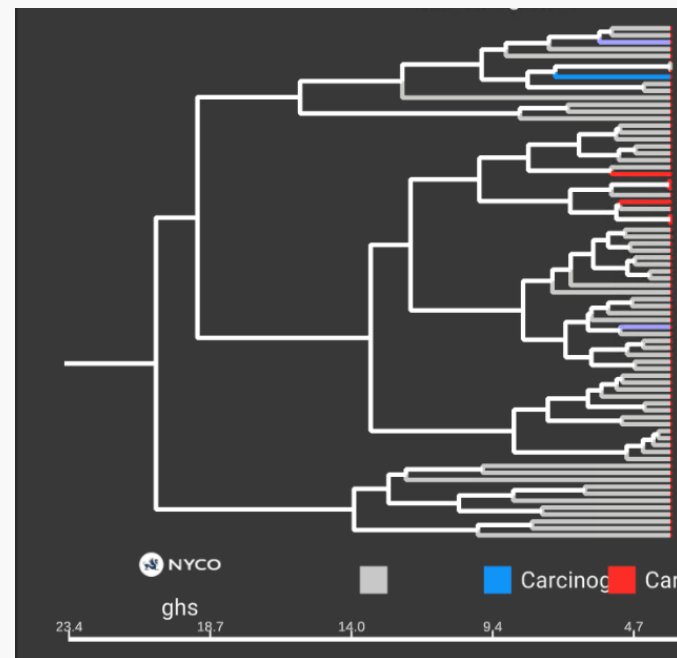
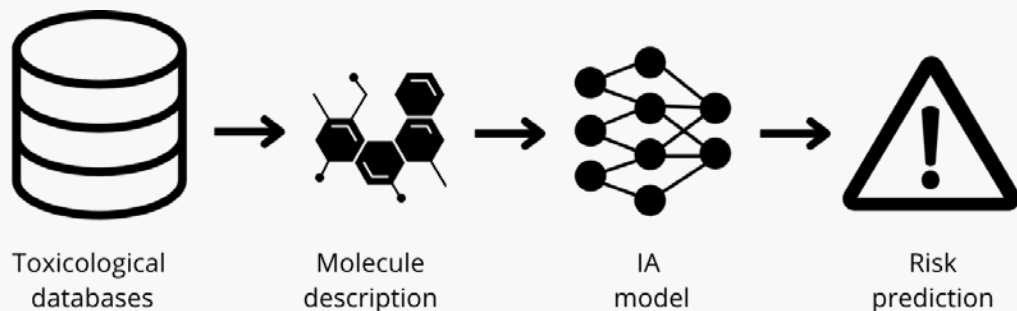
Cluster 4 – less biological activity *in Vitro*



Cluster 4 is composed of shorter PFAS chain with very few Toxcast active tests ($\leq 2\%$) and not on ER/AR/TR/PPAR.

M1 is a drug used for anesthesia, and have some evidence of toxicity on liver, kidney, neurotox and reprotox probably due to its **metabolite**.

As many compounds lacks toxicological data, *in Silico* approach can bridge the gap and highlight particular risk in some group of molecules.



Only a few PFAS have recongized hazard

Estimate the risk of high level toxicological endpoints (Carcinogenicity, Reprotoxicity) that are very costly and ethically controversial (*In Vivo*).



Toxicological
databases

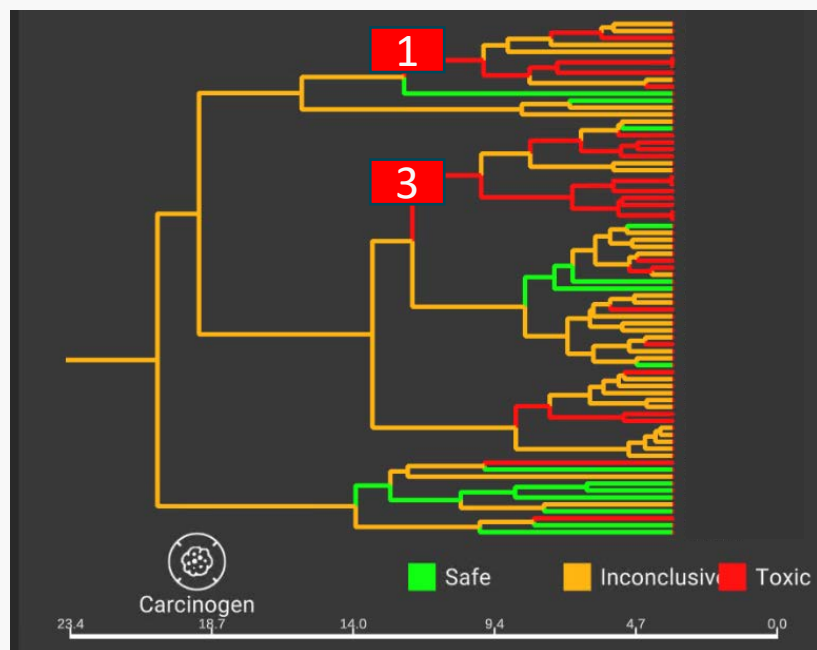


**Artificial
intelligence
(QSAR)**

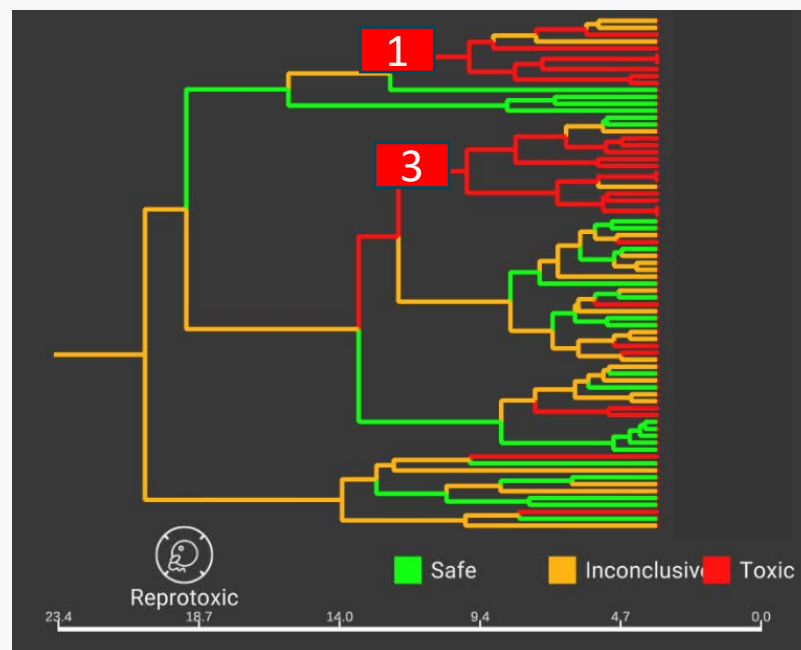
(QSAR SafetyByDesign V2024)

Cluster 1 – The QSARs highlight potential toxicological concerns, guiding further investigation

Cluster 3 – Consistent with existing toxicological data

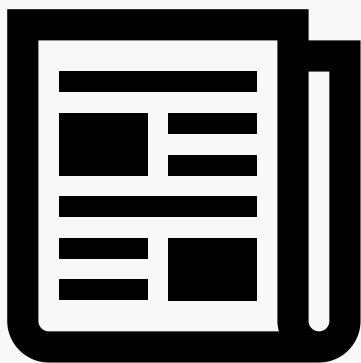


Carcinogenicity QSAR prediction



Reprotoxicity QSAR prediction

Safety By Design is used to create comprehensive chemical maps to visualise and understand the biological activity patterns among large group of molecules to:



**Make the most of available
toxicological information**



**Focus effort, on highest
or lowest risk compounds**

Please don't hesitate to reach out if you're interested in exploring solutions for your use case (e.g., compounds, toxicology).

Concact: aurelien.stab@nyco-group.com

oudin@semaco.fr



NYCO
Solutions ahead



SEMACO
ENVIRONNEMENT

Thank you for your attention