SUSTAINABLE SURFACE PROTECTION BY GLASS-LIKE HYBRID AND BIOMATERIALS COATINGS

BIO-SUSHY

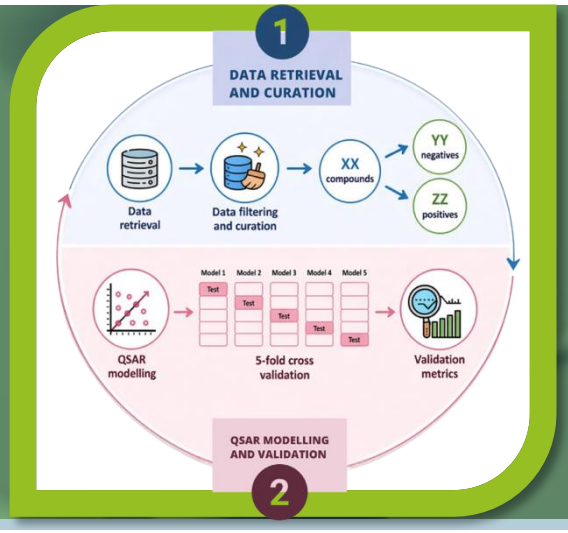
5th Training

Application of QSAR Predictive Models in Toxicology:

Supported by Safe-and-sustainable-by-Design(SSbD) Assessment

November 12, 2026

Online



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Horizon's Europe GA number: 101091464

Agenda

10:00 Opening Remarks and Introduction	• Welcome, housekeeping & BIO-SUSHY project intro. • Goal of the training and overview. (10 min)	Axia Innovation
10:10 Module 1: QSAR Fundamentals	• Introduction to QSAR models and regulatory context. (25 min)	ProtoQSAR
10:35 Module 2: QSAR in BIO-SUSHY	• QSAR in BIO-SUSHY and SSbD. (20 min)	ProtoQSAR
10:55 Module 3: Hands-on QSAR exercise	• Interactive hands-on QSAR exercise. (15 min)	ProtoQSAR
11:10 Module 4: Results analysis	• Results analysis and link to SSbD. (30 min)	ProtoQSAR
11:40 Q&A & BIO-SUSHY applications	• Q&A and BIO-SUSHY applications. (15 min)	Axia Innovation, ProtoQSAR
11:55 Wrap-up & Next Steps	• Summary of key takeaways. • Closing remarks and acknowledgment. (5 min)	Axia Innovation, ProtoQSAR

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Introduction

PFAS, What?

PFAS (per and polyfluorinated alkyl substances) provide excellent water and oil repellency properties.

Why is it a problem?

PFAS are known as 'forever chemicals' due to their resistance, widespread, and linked to environmental and health problems like cancer and decreased fertility.

How?

Exposure could happen through eating, drinking, or using consumer products containing PFAS.

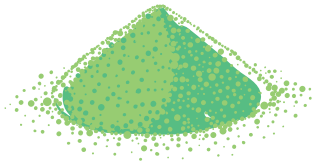
You may have assumed PFAS without knowing it



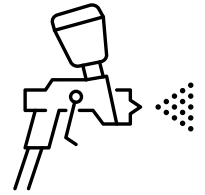
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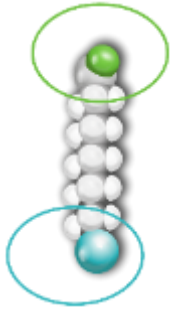
Objectives

Develop **3 PFAS-free bio-based coatings**



Thermoplastic bio-based **powder**

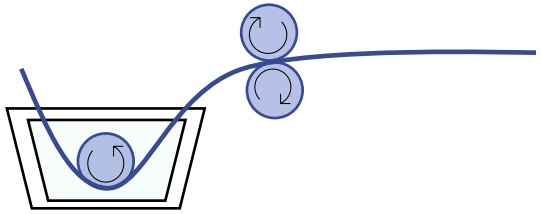








Water-based **hybrid sol-gel** organic

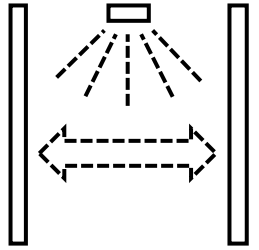


Hydro/oleophobic

additives



Solvent-based **hybrid sol-gel** inorganic



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R&I Coating Development



- Development of **3 novel SSbD coatings materials** with water and oil repellency
- **Validation** of coating materials with 3 case studies
  - Textile
  - Food packaging
  - Glass packaging

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BIO-SUSHY Methodology – Based on 3 pillars



R&I COATING DEVELOPMENT

- Development of 3 novel SSbD coatings materials with water and oil repellency
- Validation of coating materials with 3 case studies (cellulose food trays, textile, glass packaging)



MODELING

- Development of the BIO-SUSHY set of computation tools for SSbD of coatings
- Development of integrated approaches supported by the BIO-SUSHY HUB for effective data management and sharing

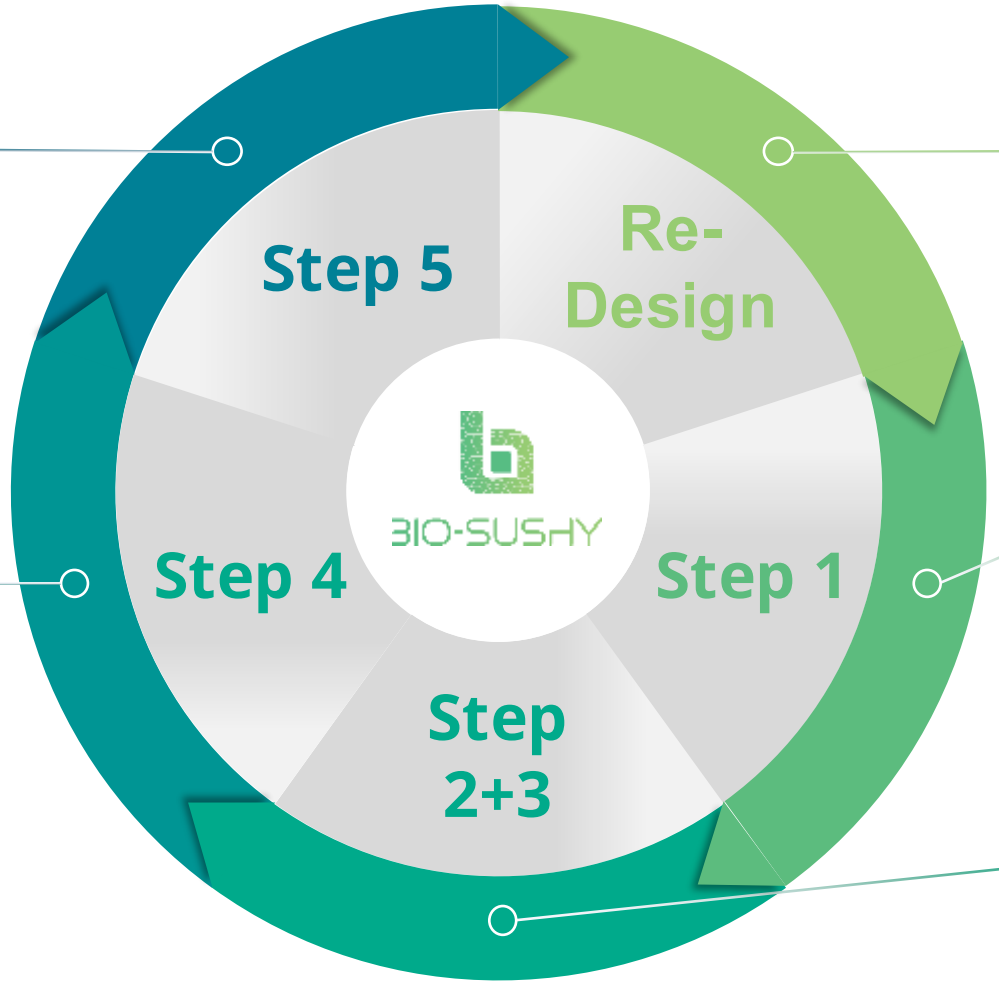


SAFE AND SUSTAINABLE BY DESIGN

- Development of an SSbD Framework applied to PFAs-free coatings (safe by material design, safe by process design, toxicological studies, LCA, LCC, SLCA)
- Standardisation roadmap

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The 5 steps SSbD framework



- Life Cycle Costing (LCC)
- Social-LCA

- Coating development
- Functional modelling
- Data mining
- Up-scaling

- LCA
- Circularity
- End of life

- Data mining
- QSAR

- Occupational monitoring
- Risk assessment
- Tox testing

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Value Chain

BIO-SUSHY consortium combines **materials science, sustainability assessment, and industrial validation**

Materials & Technology Development | **SSbD Methodology & Sustainable Assessment** | **Modelling & Computational Tools** | **Social Acceptance** | **Industrial Validation** | **Market Entry, Dissemination & Standardization**

Applications

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Impacts



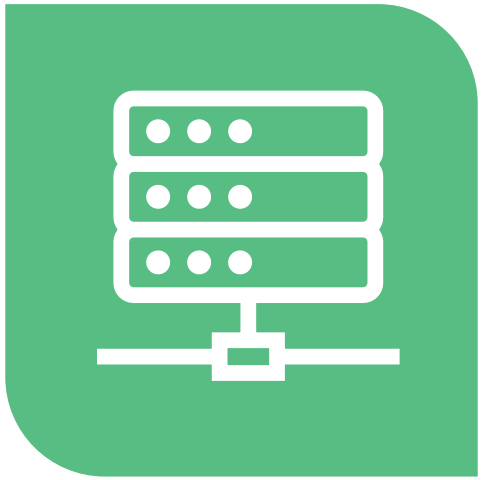
25% reduction of environmental impact



Contribution to SSbD criteria and guiding principles



Reduction of PFAS in the environment



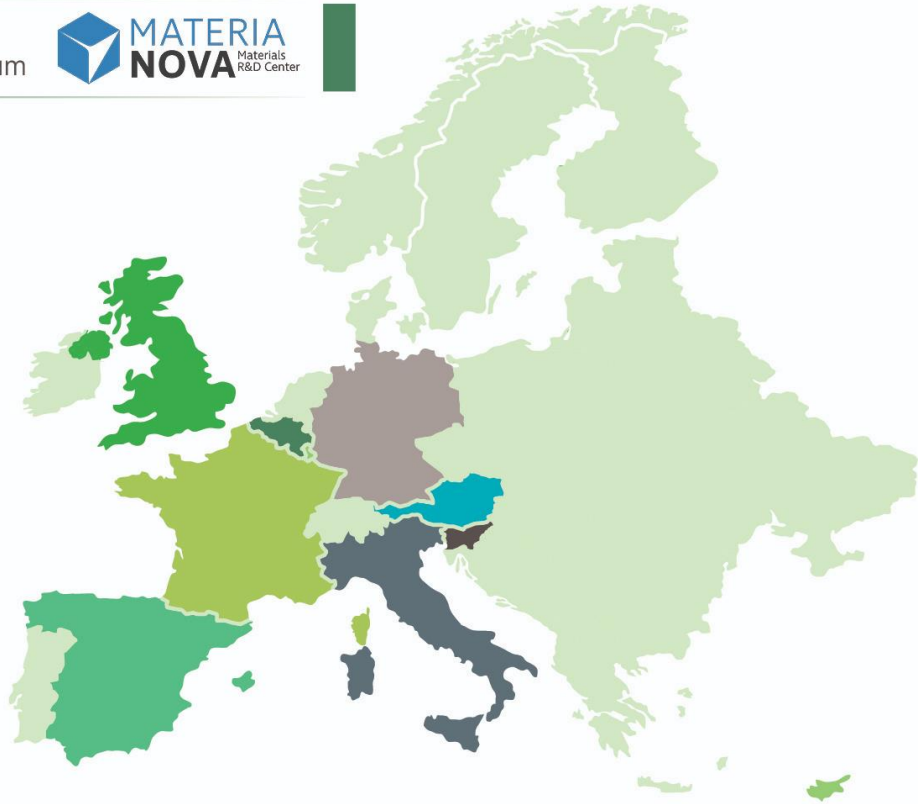
Computational tools to support SSbD concepts

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Team

The BIO-SUSHY project is a collaboration between 14 partners from 7 EU countries and 1 EU-associated country: 6 RTDs, 6 SMEs, 1 university, and 1 national association.

BIO-SUSHY COORDINATOR:
Materia Nova, Av. Nicolas Copernic 3, 7000 Mons, Belgium



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BIO-SUSHY SSbD Guidelines



SSbD Guidelines - Food Packaging



SSbD Guidelines - Glass Cosmetic Packaging



SSbD Guidelines - Textile



SSbD Guidelines Infographic - Food Packaging



SSbD Guidelines Infographic - Glass Cosmetic Packaging



SSbD Guidelines Infographic - Textile

https://www.bio-sushy.eu/dc-materials/

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CEN Workshop Agreements (CWAs) BIO-SUSHY Kicked-off

CEN/WS BIO-SUSHY Kick-off Meeting took place, officially marking the start of the Workshop and the collaborative development of the three CEN Workshop Agreements (CWAs).



CEN Project Officer, introduced the CEN Workshop concept and provided guidance on the standardization process and requirements.

The three CWA drafts were presented by their respective leaders:

- **WOOD K PLUS – Christoph Jocham & Ivana Burzic**
- **MANO – Eric Khousakoun**
- **ULEEDS – Andrew Nelson**

Led and coordinated by the Spanish Association for Standardization (UNE), which is responsible for the organization of the CEN Workshop and its standardization process.

The target publication date for the three CWAs is **December 2026**.

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Upcoming Event

🔬 PFAS, Regulatory Challenges & Sustainable Alternatives!

BIO-SUSHY Project partner Applus+ Rescoll is organising a dedicated event exploring hashtag#PFAS regulations, material obsolescence and innovative alternatives.

📅 19 November 2026
📍 Pessac & Talence, France

🔗 Register here: https://lnkd.in/dWMYznw7



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BIO-SUSHY FINAL EVENT

From PFAS-Free Coating Innovation to real world applications!

December 01 & 03, 2026

Lyon, France

In Person / Online for general public

ifth

Sustainable surface protection by glass-like hybrid and biomaterials coatings

Final event in Lyon (France)
& MS Teams:

AGENDA

Meeting Details	
Date:	December 01-03 2026
Time:	From 01/12/26 12:30 pm to 02/12/26 17:30 pm
Hosted By:	IFTH
Venue:	Hotel Mercure Lyon Centre Saxe Lafayette 29 rue de Bonnel, 69003 Lyon, France
MS Teams Link	https://events.teams.microsoft.com/event/f7ca99de-f345-4b1a-84f3-da642da5a3cb@80fafee0-594c-4c91-9731-63aa75c0bb55

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First Day (01.12.2026)

Time	Topic	Presenter
12:30	WELCOME and LUNCH	
13:30	BIO-SUSHY main achievements in SSbD development of PFAS-free coatings General Introduction	Coord
	Food tray Case study – Achievements, KPIs, Demos	Case studies responsibles
15:00	AFTERNOON BREAK (30 min)	
15:30	Textile Case study - Achievements, KPIs, Demos Glass Packaging Case study - Achievements, KPIs, Demos	Case studies responsibles
17:30	End of Day 1	

Second Day (02.12.2026)

Time	Topic	Presenter
9:00	PFAS regulation status	External speaker
9:25	BIO-SUSHY SSbD framework	ITENE
9:50	Sustainability assessment and SSbD related scoring	MANO
10:15	MORNING BREAK	
10:45	Rapid screening tools to support safety assessment	UNIVLEEDS
11:10	QSAR modelling tools to support safety assessment	PROTOQSAR
11:35	Physical modelling to support SSbD coating development	CNR
12:00	Data hub and BIO-SUSHY data FAIRness	7P9
12:25	LUNCH BREAK	
14:00	Challenges in PFAS replacement	External speaker
14:25	Bio-SUSHY Social acceptance and willingness-to-pay	ZSI
14:50	BIO-SUSHY contribution to standardization	UNE
15:15	AFTERNOON BREAK	
15:45	Market uptake and BIO-SUSHY exploitation routes	AXIA
16:10	Textile industry testimony on PFAS alternatives uptake	External speaker
16:35	Round table	ZSI
17:30	End of meeting	

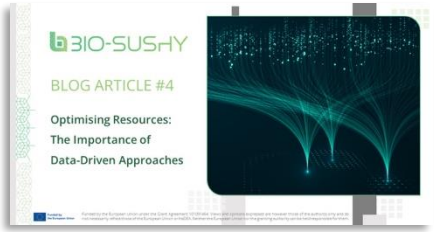


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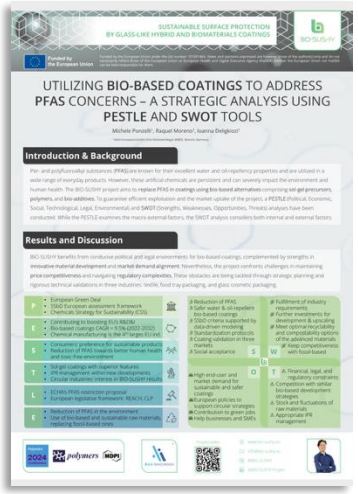
Stay up to date with our progress











www.bio-sushy.eu

info@bio-sushy.eu

@BIO-SUSHY Project

@BIO_SUSHY

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José Luis Valles Pardo

Senior Researcher, ProtoQSAR

José Luis Vallés Pardo is a computational chemist with more than 15 years of experience, including data analysis, development of predictive models, and participation in national and European research projects during the last 5 years. Currently, he is the head of ProtoPRED®, the predictive platform from ProtoQSAR. He is also the responsible of some of the SSbD projects of the company. Outside the work, he enjoys playing basketball, computer games, and doing puzzles, especially with his children.



ProtoQSAR

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ProtoPRED®

Registration link to the platform: free-tokens

https://protopred.protoqsar.com/Register

Main page of the prediction platform:

https://protopred.protoqsar.com/

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BIO-SUSHY

BlueSky: **@BIO_SUSHY**

LinkedIn: **@BIO-SUSHY Project**

WEB: **www.bio-sushy.eu**

EMAIL: **info@bio-sushy.eu**

THANK YOU!

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SUSTAINABLE SURFACE PROTECTION BY GLASS-LIKE HYBRID AND BIOMATERIALS COATINGS

BIO-SUSHY

Module 1: QSAR Fundamentals & Regulatory Context

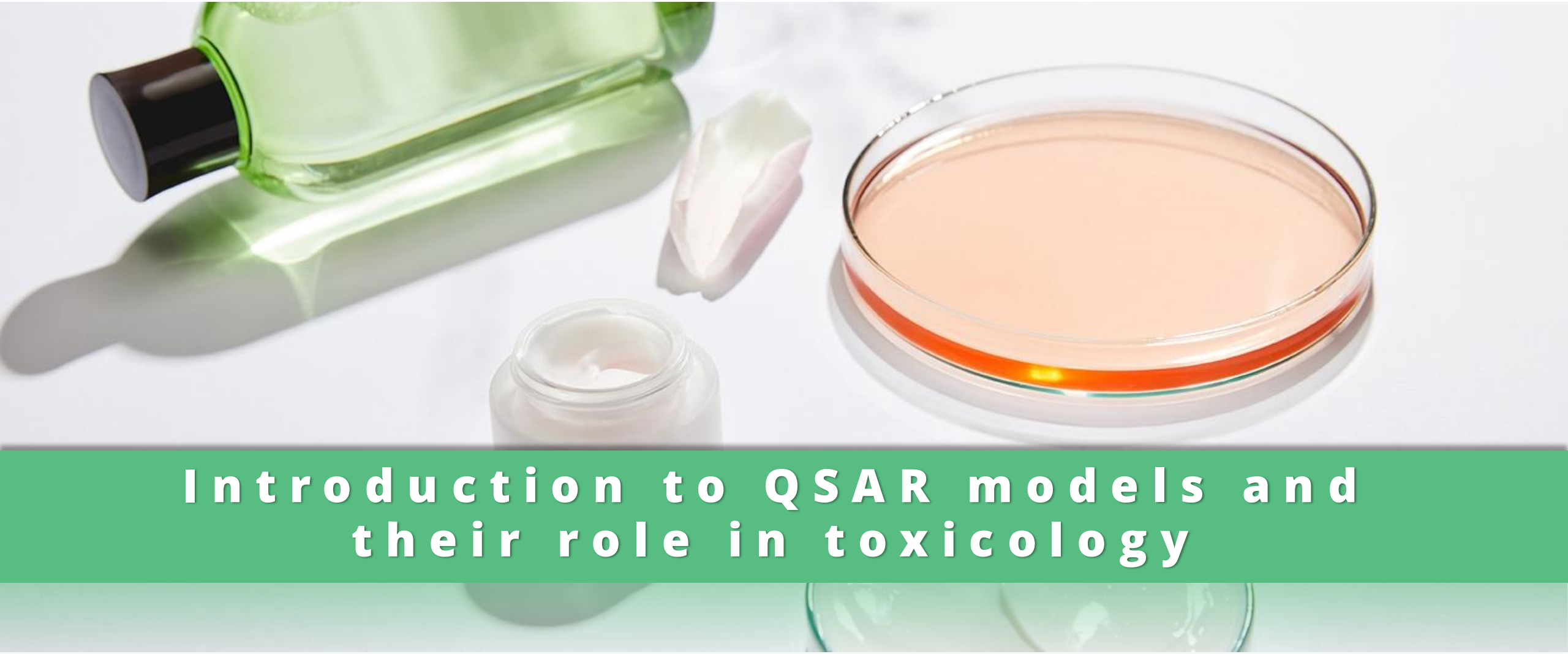
BIO-SUSHY TRAINING #5

José Luis Vallés Pardo

12/11/2026

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Introduction to QSAR models and their role in toxicology

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Increased concern about the potential adverse effects of chemicals has prompted regulatory and health agencies to expand the range and sensitivity of hazard detection tests for humans and the environment.

https://www.ema.europa.eu/

https://www.ich.org/page/ich-guidelines

https://echa.europa.eu/es/home



https://echa.europa.eu/es/regulations/reach/understanding-reach



https://echa.europa.eu/es/regulations/clp/understanding-clp



https://echa.europa.eu/es/regulations/biocidal-products-regulation/understanding-bpr

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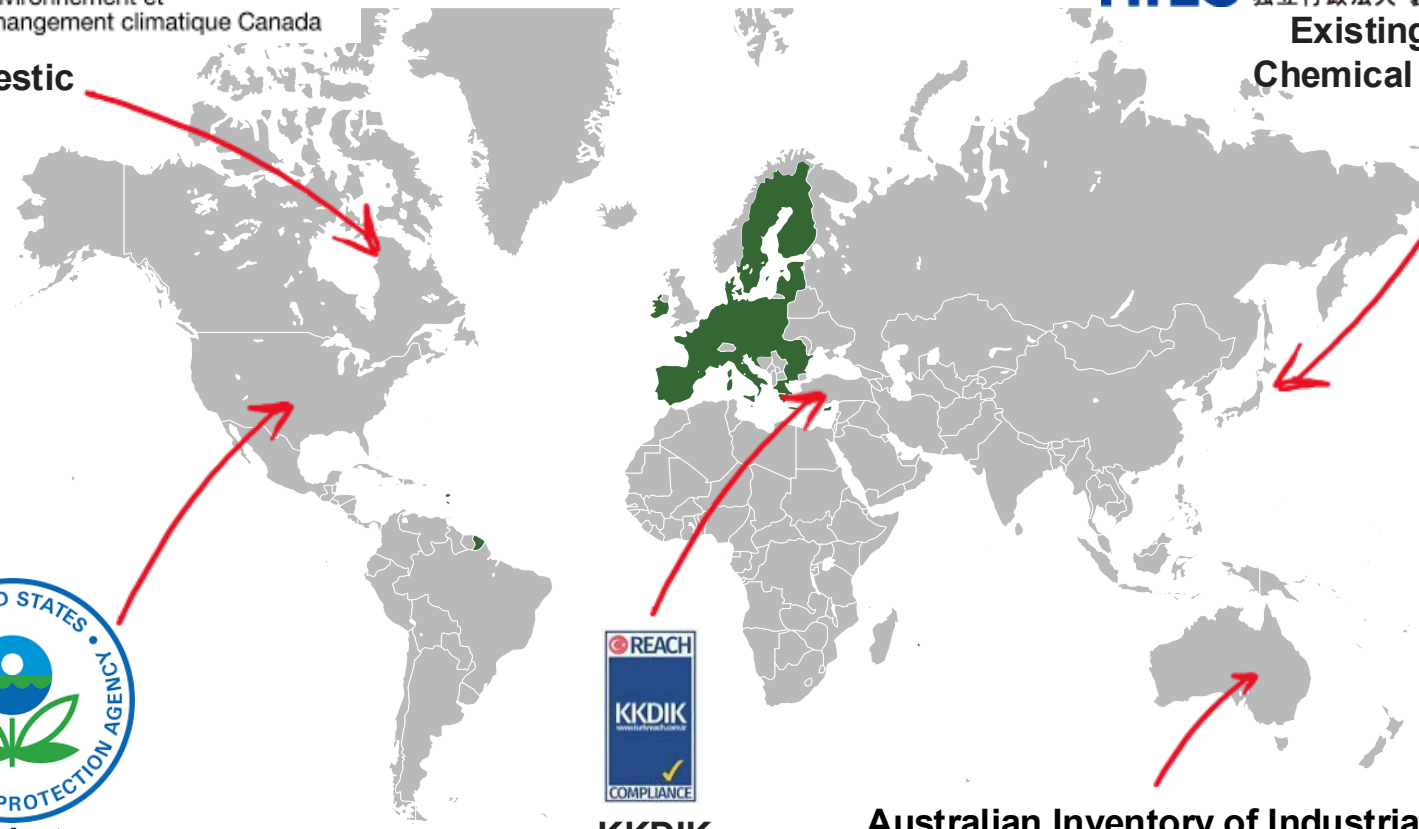
Environment and Climate Change Canada
Environnement et Changement climatique Canada

Domestic and Non-Domestic substance lists

ECHA EUROPEAN CHEMICALS AGENCY
https://echa.europa.eu/es/home

nite National Institute of Technology and Evaluation 独立行政法人 製品評価技術基盤機構

Existing and New Chemical Substances



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

Toxic Substances Control Act

REACH KKDIK COMPLIANCE

KKDIK

Australian Inventory of Industrial Chemicals

Australian Government
Department of Health

Australian Industrial Chemicals Introduction Scheme

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ANNEX VII: > 1 TONNE/YEAR

- **7. Physico-chemical properties**
  - 7.1 State of the substance
  - 7.2 Melting point/freezing point
  - 7.3 Boiling point
  - 7.4 Relative density
  - 7.5 Vapor pressure
  - 7.6 Surface tensión
  - 7.7 Water solubility
  - 7.8 n-octanol/water partition coefficient
  - 7.9 Flash point
  - 7.10 Flammability
  - 7.11 Explosive properties
  - 7.12 Self-ignition temperature
  - 7.13 Oxidizing properties
  - 7.14 Particle size distribution

Physicochemical

- **8. Toxicological properties**
  - 8.1 Skin corrosion/irritation
  - 8.2 Serious eye damage/eye irritation
  - 8.3 Skin sensitisation
  - 8.4 Mutagenicity
  - 8.5 Acute toxicity (oral)

Toxicological

- **9. Ecotoxicological properties**
  - 9.1 Aquatic toxicity (daphnia & algae)
  - 9.2 Degradation (Ready biodegradability)

Ecotoxicological

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ANNEX VIII: > 10 TONNE/YEAR

+ ANNEX VII

- **8. Toxicological properties**
  - 8.1.1 *In vivo* skin corrosion/irritation
  - 8.2.1 *In vivo* serious eye damage/eye irritation
  - 8.4.2 *In vitro* mutagenicity
  - 8.5.2/3 Acute toxicity (inhalation & dermal route)
  - 8.6 Repeated dose toxicity
  - 8.7 Reproductive toxicity

Toxicological

- **9. Ecotoxicological properties**
  - 9.1.53/4 Aquatic toxicity (fish & activated sludge)
  - 9.2.2.1 Hydrolysis as a function of pH
  - 9.3 Adsorption/desorption screening

Ecotoxicological

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ANNEX IX: > 100 TONNE/YEAR

+ ANNEX VII
+ ANNEX VIII

- **7. Physico-chemical properties**
  - 7,15 Stability in organic solvents and identity of relevant degradation products
  - 7,16 Dissociation constant
  - 7,17 Viscosity

Physicochemical

- **8. Toxicological properties**
  - 8.6.1 Short-term repeated dose toxicity study (28 days)
  - 8.6.2 Sub-chronic toxicity study (90-day)
  - 8.7.2 Pre-natal developmental toxicity study
  - 8.7.3 Extended One-Generation Reproductive Toxicity Study

Toxicological

- **9. Ecotoxicological properties**
  - 9.1.5/6 Aquatic toxicity (fish & activated sludge)
  - 9.2 Degradation (water, sediment & soil)
  - 9.3.2 Bioaccumulation in aquatic species
  - 9.3.3 Further information on adsorption/desorption
  - 9.4 Effects on terrestrial organisms

Ecotoxicological

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ANNEX X: > 1000 TONNE/YEAR

+ ANNEX VII
+ ANNEX VIII
+ ANNEX IX

- **8. Toxicological properties**
  - 8.7.2 Developmental toxicity study
  - 8.7.3 Extended One-Generation Reproductive Toxicity Study
  - 8.9.1 Carcinogenicity study

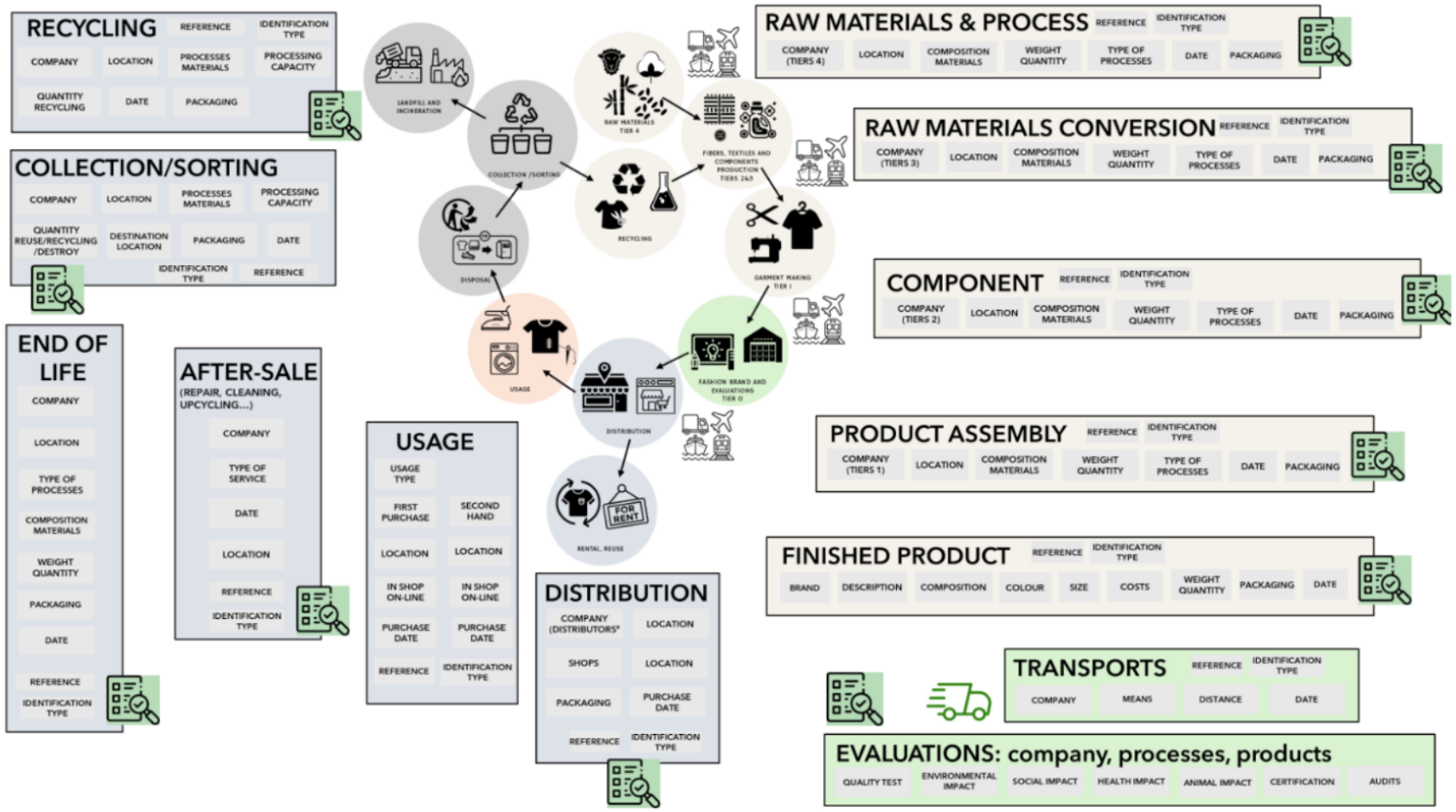
Toxicological

- **9. Ecotoxicological properties**
  - 9.2 Further biotic degradation
  - 9.3 Further information on the environmental fate
  - 9.4 Long-term toxicity testing on invertebrates and plants
  - 9.5.1 Long-term toxicity to sediment organisms
  - 9.6.1 Long-term or reproductive toxicity to birds

Ecotoxicological

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SSbD approach



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Economic considerations



Toxicity Testing

Acute Inhalation Toxicity (OPPTS 870.1300, OECD 403) - P330
Limit Test, 10 rats, 4 hour exposure, 14 days.....$8900
Second exposure level $6900
Each additional level beyond the second.....$2300
Grinding of solids.....$550
Analytical concentration determination[2].....$7100

28 Day Oral Toxicity (OPPTS 870.3050, OECD 407, EU B.7, FDA IV.C3a) – P712
5 rats/sex/group, 4 Groups, 7-Day Dosing.....$67700
10 rats/sex/group, 4 Groups, 7-Day Dosing.....$103300

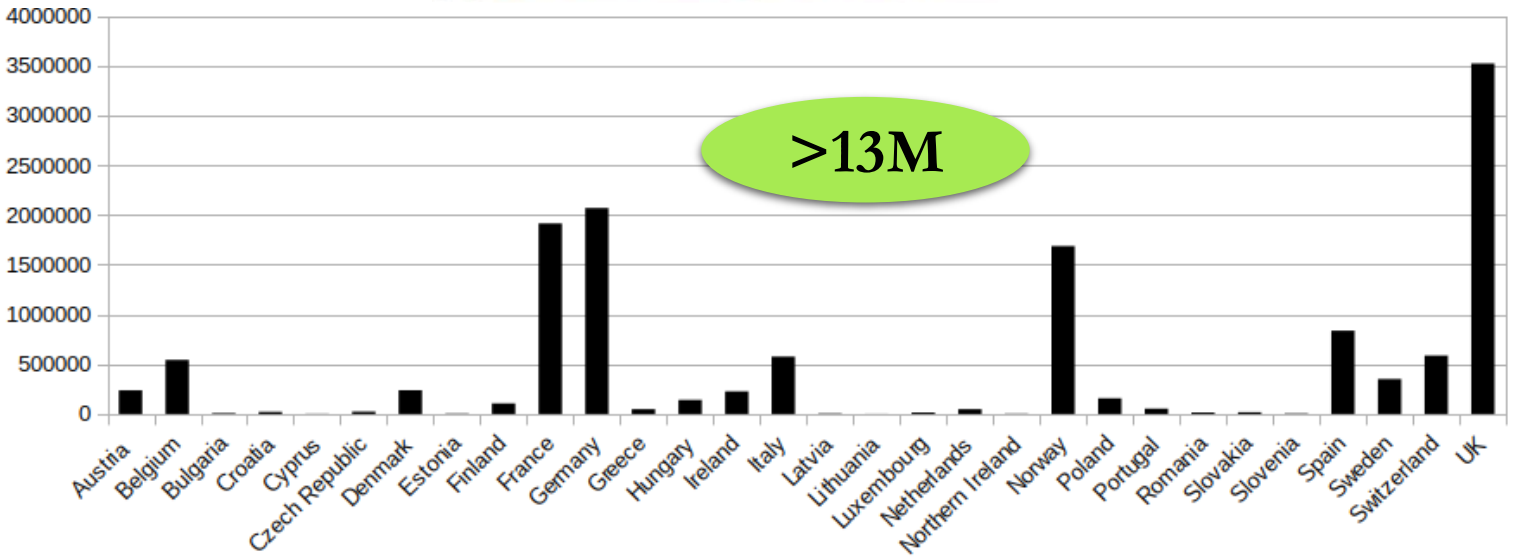
28 Day Dietary Toxicity (OPPTS 870.3050, OECD 407, EU B.7, FDA IV.C3a) –P702
5 rats/sex/group, 4 Groups, 7-Day Dosing.....$62850
10 rats/sex/group, 4 Groups, 7-Day Dosing.....$94700

28 Day Dermal Toxicity (OPPTS 870.3200, OECD 410, EU B.9,) – P722
5 rats/sex/group, 4 Groups, 5-Day Dosing.....$61500
10 rats/sex/group, 4 Groups, 5-Day Dosing.....$101600

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Ethical concerns





Vertebrate animals killed annually in Europe for research. Data from 2016 to 2018, depending on the country.
(https://www.eara.eu/animal-research-statistics)

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Alternative methods

Weight of evidence



Is there already enough information?

In vitro methods



Use of isolated organs, tissues or cells instead of whole organisms

Grouping & read-across



Extrapolation of results based on similarity between substances

QSAR models



Endpoint predictions

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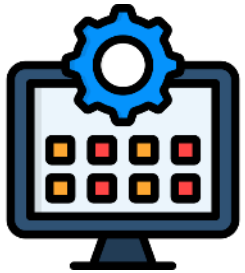
Advantages of the computational methodology



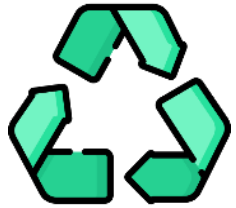
Save time, money, and resources



Predictive efficacy for the discovery or improvement of chemical compounds



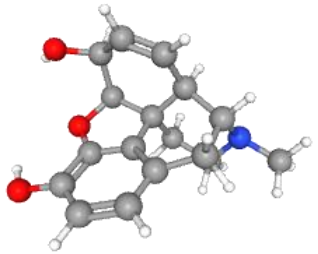
Easy and immediate applicability of the models to new structures



Compliance with European directives regarding animal testing (3Rs)

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Advantages of the computational methodology





Unknown activity

x Mutagenicity?
x LD_{50}?
x Skin irritation?

Prediction

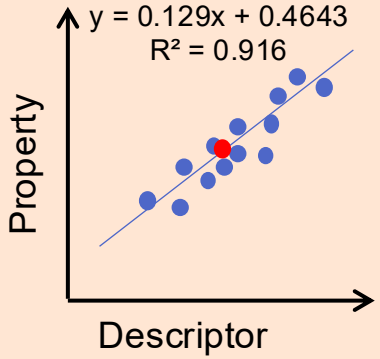
✓ Mutagenic/Non-mutagenic
✓ LD_{50} = 0.1 μM
✓ Irritant/Non-irritant

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Computational approaches

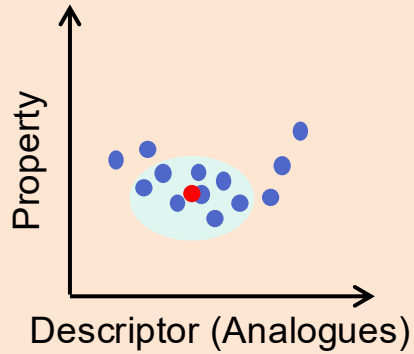
TREND ANALYSIS

Interpolation of the value of a linear relationship between a descriptor and the property of interest



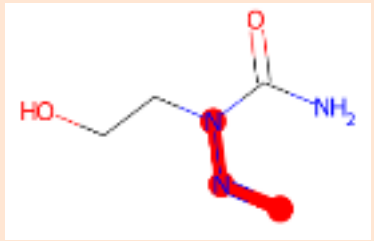
READ-ACROSS

Inference of the value of the property of interest from a group of molecules considered similar



SAR

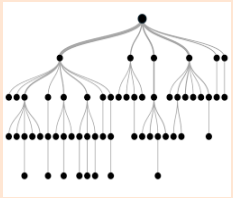
Classification of a substance according to the presence (or absence) of certain (sub)structures.

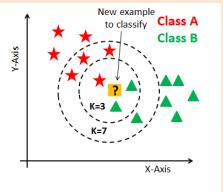


QSAR

Complex mathematical models that relate various molecular properties to the property of interest

MLR = 0.113LK + 0.22 HOMO + 0.16 NAI - 0.118





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Overview of model development, validation and applicability domain.

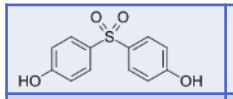
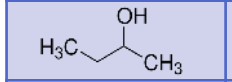
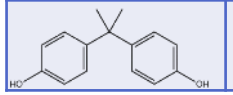
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QSAR models

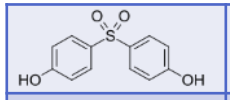
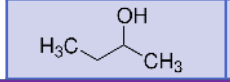
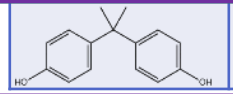
Initial dataset



Calculation of molecular descriptors

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	6.98	4.23	1.35	2.96	2.67
	3.46	8.24	2.14	5.35	5.68

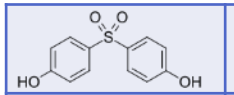
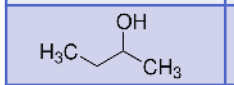
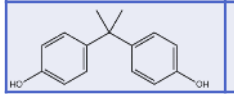
Training and validation subsets splitting

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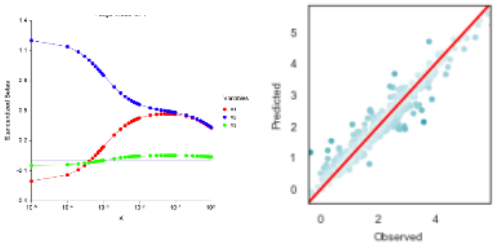
Training set



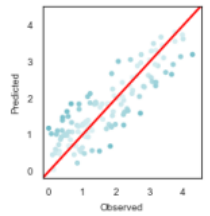
Selection of relevant descriptors

	3.21	8.64	5.49
	6.98	1.35	2.67
	3.46	2.14	5.68

Model generation



Model validation





Validation set

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QSAR models

Initial dataset

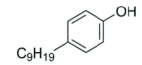
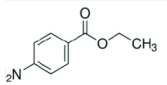
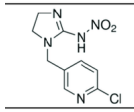
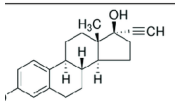
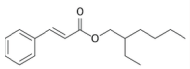
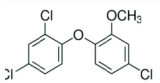


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Initial dataset

- The first thing we need is a database of experimental data for the model we want to generate. The quantity, quality, and robustness of the input data are important for generating reliable models. Defining properly the endpoint that we want to model is crucial at this step.



Structural formula	Chemical properties	
4-Nonylphenol (NP)		
	Compound group	Industrial additives
	Molecular mass, g/mol	220.35
	Solubility in water, mg/L	7.0
	log K_{ow}	5.76
Benzocaine (BE)		
	Compound group	Pharmaceuticals
	Molecular mass, g/mol	165.19
	Solubility in water, mg/L	1310
	log K_{ow}	1.86
Imidacloprid (IM)		
	Compound group	Pharmaceuticals
	Molecular mass, g/mol	255.66
	Solubility in water, mg/L	0.61
	log K_{ow}	0.57
17α-Ethinylestradiol (EE2)		
	Compound group	Hormones
	Molecular mass, g/mol	296.40
	Solubility in water, mg/L	11.3
	log K_{ow}	3.67
Octyl-methoxycinnamate (OMC)		
	Compound group	UV blockers
	Molecular mass, g/mol	290.40
	Solubility in water, mg/L	0.2
	log K_{ow}	6.1
Triclosan (TCS)		
	Compound group	Pesticides
	Molecular mass, g/mol	289.54
	Solubility in water, mg/L	0.1
	log K_{ow}	4.76

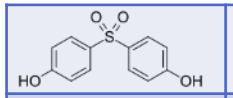
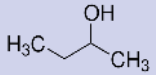
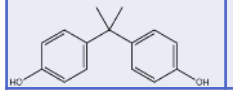
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QSAR models

Initial dataset



Calculation of molecular descriptors

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Molecular descriptors

- There is a direct (although complex) relationship between the molecular structure of a compound and its chemical behaviour.
- Predicting this behaviour is possible through an abstract representation of its structure in terms of chemical similarity parameters, the so-called "descriptors".

Simple structural features

- Number of heteroatoms
- Presence of chlorine

Fragments or substructures

- Number of carbonyl groups
- Presence of carboxyl

Physicochemical properties

- Molecular weight
- LogP
- Solubility

Three-dimensional indices

- They depend on the structural configuration

Topological indices: They take into account exclusively the planar structure or molecular graph: Wiener index, branching indices, “kappa shape” indices, electro-topological indices, topological torsions of atom pairs, etc.

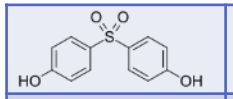
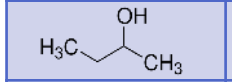
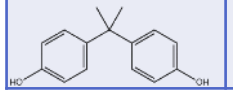
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QSAR models

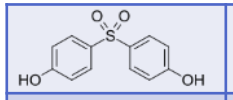
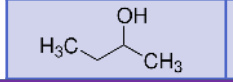
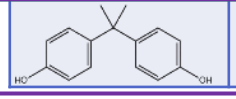
Initial dataset



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Training set



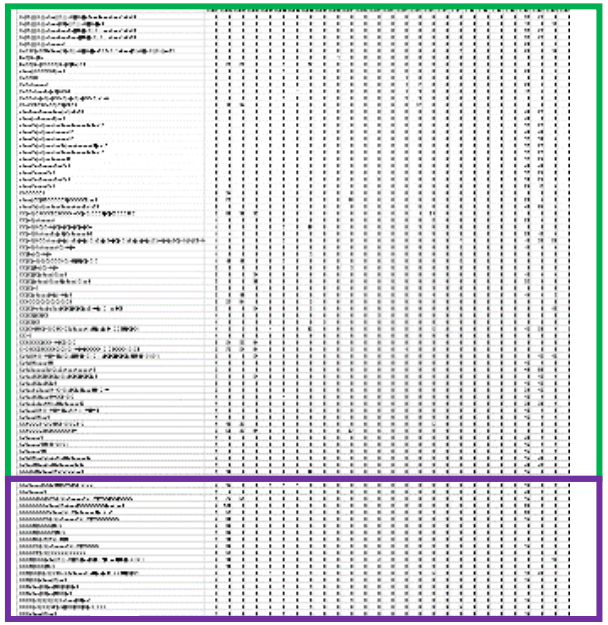


Validation set

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Subsets splitting

- With all the available data, we separated it into two groups. The training group is the one we will use to generate the model, while the validation group will serve to check the reliability of the model.



- Training (70-80%)
- Validation (20-30%)

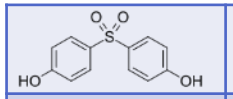
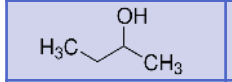
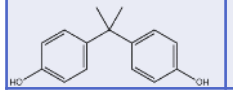
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QSAR models

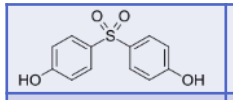
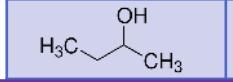
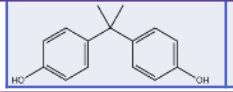
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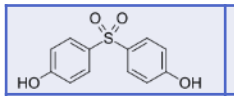
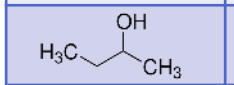
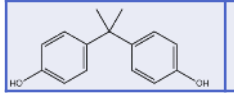
Training set



Validation set



Selection of relevant descriptors

	3.21	8.64	5.49
	6.98	1.35	2.67
	3.46	2.14	5.68

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Selection of relevant descriptors

- Of the descriptors calculated for each molecule, those that do not provide information must be eliminated, and those that best represent the property under study for the training group must be selected. Various statistical filters are used for this purpose.

Elimination (unsupervised methods):

- Descriptors with a single value
- Descriptors with a high percentage of NaNs
- Highly correlated descriptors

Selection (supervised methods):

- Use of algorithms
- Chemometric methods (PCA, MLR…)

IMPORTANT: This is done ONLY on the train set, and then applied to the test set as well.

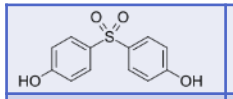
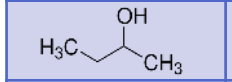
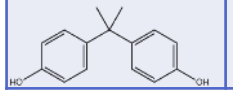
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QSAR models

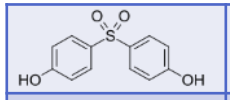
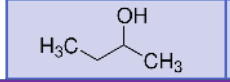
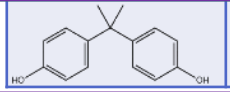
Initial dataset



Calculation of molecular descriptors

	3.21	2.10	8.64	6.53	5.49
	6.98	4.23	1.35	2.96	2.67
	3.46	8.24	2.14	5.35	5.68

Training and validation subsets splitting

	3.21	2.10	8.64	6.53	5.49
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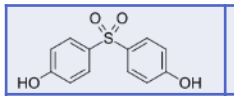
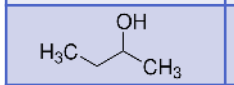
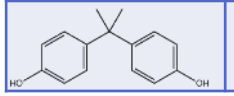
Training set



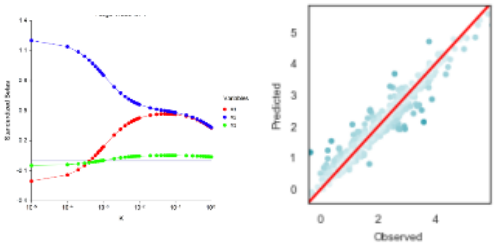
Validation set



Selection of relevant descriptors

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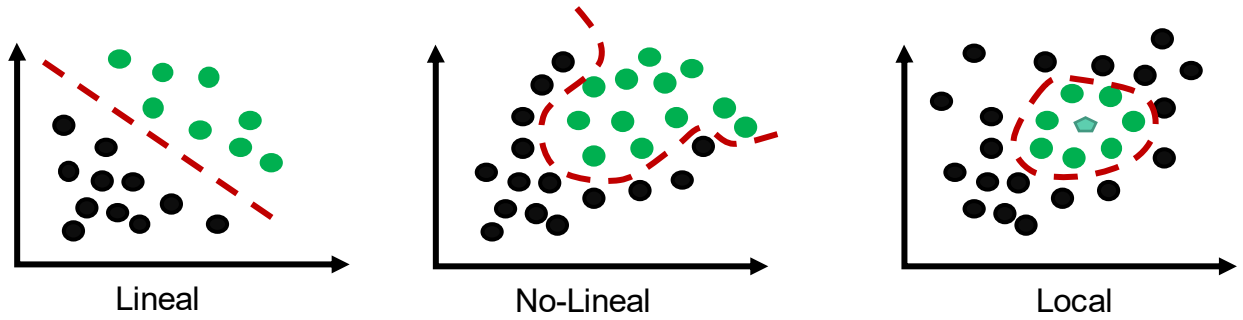
Model generation



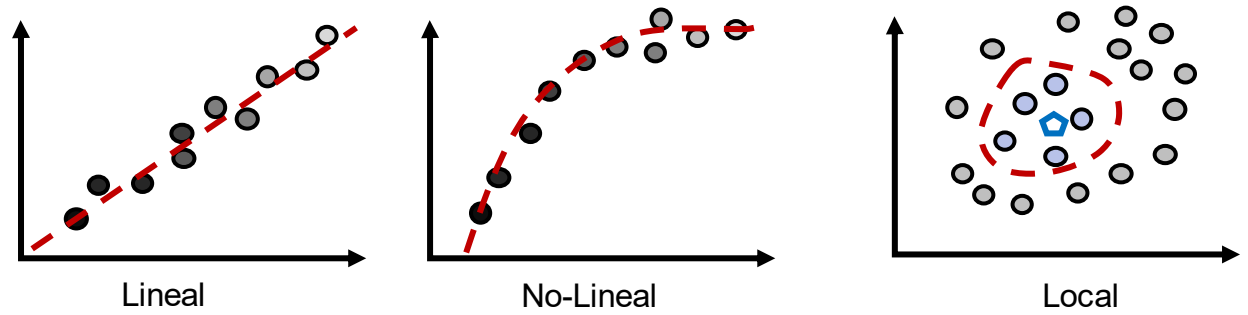
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Model generation

- **Qualitative or classification methods:** allow obtaining binary classifications, such as “active/inactive”.



- **Quantitative or regression methods:** allow for the quantification of the parameter that is intended to be predicted.



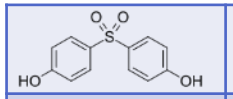
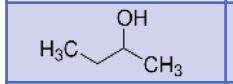
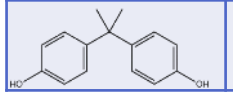
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QSAR models

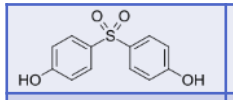
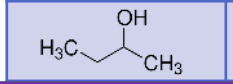
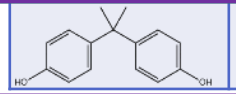
Initial dataset



Calculation of molecular descriptors

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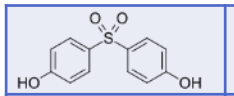
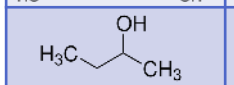
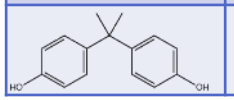
Training and validation subsets splitting

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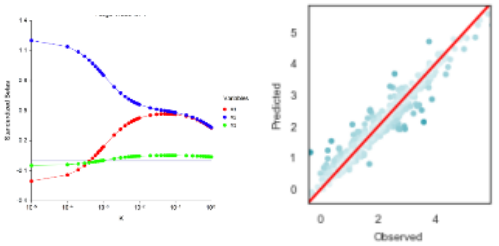
Training set



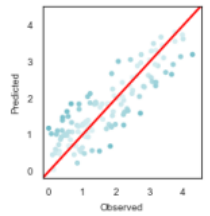
Selection of relevant descriptors

	3.21	8.64	5.49
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Model generation



Model validation



Validation set



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Model validation

- The validation group is now used to determine the reliability of the model, they are experimental results for which we know the real value of the property in question, and we will be able to compare it with the value predicted by our model.

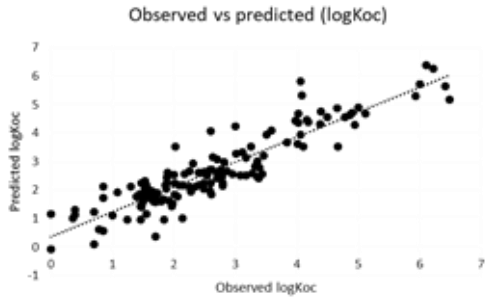
$$\mathbf{ACTIVITY/TOXICITY} = \sum_{ci} \mathbf{DESCRIPTOR(i)}$$

Structures	ID	MW	Num_carbons	Num_heteroatoms	Carbon-hetero_ratio	Halide_count	a_acc	diameter	a_nH	Solubility (mg/L)
ClC(Cl)C(=O)N[C@@H]([C@H](O)c1ccc([N+](=O)[O-])cc1)CO	[illegible]	[illegible]	[illegible]	9	1,22	2	3	11	12	???
Clc1cc2N(c3c(Sc2cc1)cccc3)CCCN(C)C	[illegible]	318,86	17	4	4,25	1	1	9	19	???
Fc1cc2c(N(C=C(C(O)=O)C2=O)C2CC2)cc1N1CCNCC1	[illegible]	319,34	17	7	2,43	1	4	11	18	???
Clc1cccc(Cl)c1NC=C(C(O)=O)C#N	[illegible]	230,09	9	5	1,80	2	1	7	9	???
O=C1CC[C@@]2([C@@H]3[C@H]([C@@H]4[C@](O)(C(=O)CO)[C@]4(CC3=O)C)CCC2=C1)C	[illegible]	[illegible]	[illegible]	5	4,20	0	5	12	28	???
o1ncc2C[C@@]3([C@@H]4[C@H]([C@@H]5[C@](O)(C#C)[C@]5(CC4)C)CCC3=Cc12)C	[illegible]	[illegible]	[illegible]	[illegible]	7,33	0	2	11	27	???
N(CCCN1c2c(CCc3cccccc3)cccc2)C	[illegible]	266,38	18	2	9,00	0	1	9	22	???

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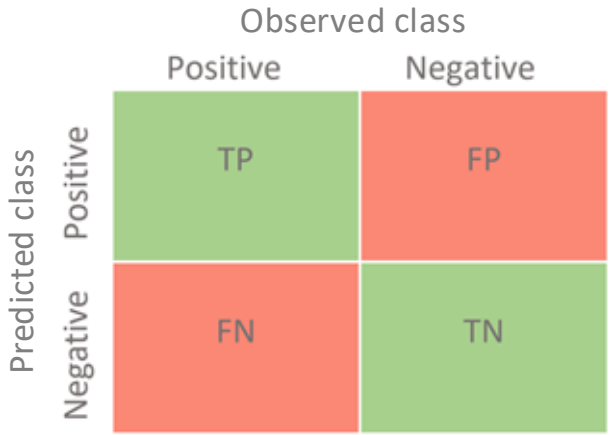
Statistical parameters

- Regression



- Correlation coefficient (R^2)
- Mean absolute error (MAE)

- Classification

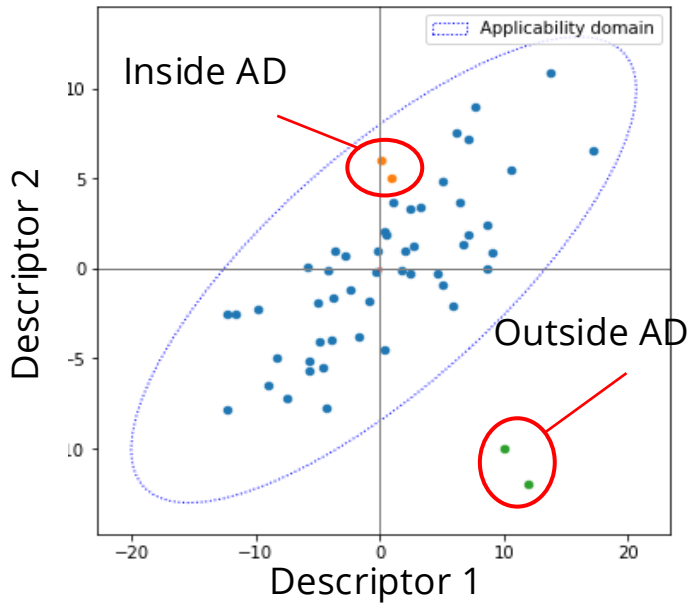


- Accuracy = (VP + VN)/(VP + VN + FP + FN)
- Sensibility = VP/(VP + FP)
- Specifity = VN/(VN+FN)

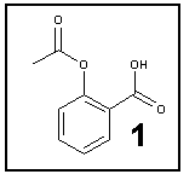
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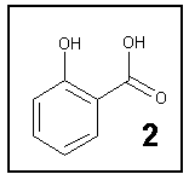
Applicability domain

- The domain of applicability defines the chemical space of the molecules used to construct the model.
- There are several strategies for studying the domain of applicability, some based on the compound's structure and others based on chemical similarity.



El coeficiente de Tanimoto





1	1	1	0	1	1	0	1	0
2	1	1	0	1	0	0	0	0

A = Number of bits set in both = 3
B = Number of bits set in (1), but not in (2) = 2
C = Number of bits set in (2), but not in (1) = 0

TANIMOTO COEFFICIENT = A / (A + B + C)
= 3 / (3 + 2 + 0) = 0.6 or 60%

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Regulatory acceptance and main limitations of QSAR predictions.

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United States - EPA

United States Environmental Protection Agency

US EPA (40CFR158 subpart W)

In this rule, the EPA indicates that it will consider any report that uses SAR analysis and QSAR models suitable to supplement or meet the data requirements for antimicrobial pesticide chemicals.

US EPA, Office of Pollution Prevention and Toxics (OPPT)

The OPPT allows the use of (Q)SAR methods for the identification of potential mutagenic, carcinogenic and other ecotoxicological hazards and for the subsequent regulation of new industrial chemicals.

US FDA, Office of Food Additive Safety (OFAS)

OFAS, as part of the FDA, has been using (Q)SAR analysis for several years in the pre-market review of substances in contact with food.

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Canada - PMRA



Pest Management Regulatory Agency (PMRA), Health Canada

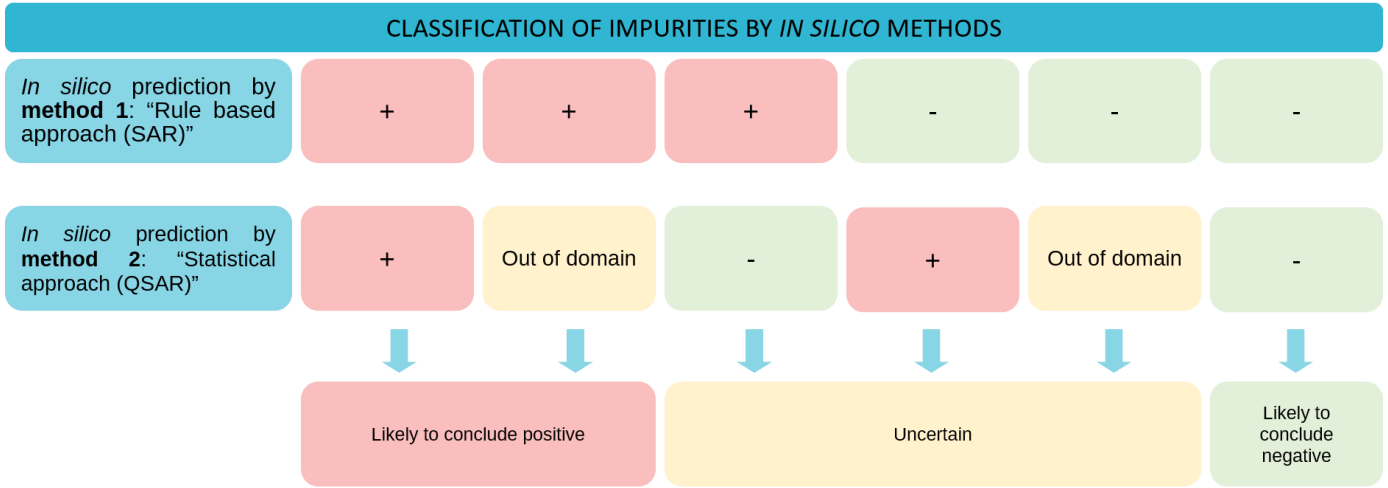
In terms of the application of (Q)SAR, the PMRA may include a request for (Q)SAR predictions on metabolites or degraded compounds when it requires the submission of existing data and may also generate (Q)SAR predictions to help identify potential hazards.

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International - EMA

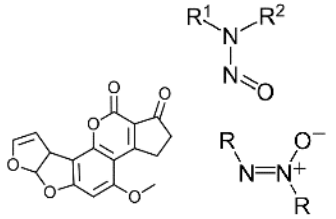
The ICH-M7 guidelines for predicting mutagenicity of drug impurities requires the application of two types of models:

- A model based on "expert rules" (SAR)
- A statistical nature model (QSAR)



Barber *et al.*, 2015. Regulatory Toxicology and Pharmacology
Amberg *et al.*, 2016. Regulatory Toxicology and Pharmacology

Cohort of concern



Aflatoxins
N-nitrosamines
Alkyl-azoxy

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Europe - REACH

ECHA asks registrants to show how they considered alternative methods before consulting on testing proposals

ECHA/PR/15/13

To further ensure that testing on animals is only done as a last resort, ECHA has started requesting additional information from registrants who submit new testing proposals for vertebrate animal tests. This follows the European Ombudsman's recent decision about ECHA's role in evaluating testing proposals.

Helsinki, 2 November 2015 - ECHA has sent the first requests to registrants asking them to inform ECHA of their considerations of alternative methods to support their testing proposals involving vertebrate animals. This affects testing proposals made since 11 September 2015.

The information received will be published together with the testing proposals on ECHA's testing proposals consultation web

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OECD principles

OCDE principle 1: Well defined endpoint

OCDE principle 2: Unambiguous algorithm

OCDE principle 3: A defined domain of applicability

OCDE principle 4: Appropriate measures of goodness-of-fit, robustness and predictivity

OCDE principle 5: Mechanistic interpretation (if possible)

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Reporting QSAR

(Q)SAR Model Reporting Format (QMRF)

Standardized model for summarizing and reporting **information from a (Q)SAR model**:

- model development
- data source
- parameter characteristics
- robustness and predictive metrics
- applicability domain

(Q)SAR Prediction Reporting Format (QPRF)

Standardized model for describing the **evaluation of a substance in a model**:

- outcome
- domain of applicability
- interpretation
- analogous

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Limitations of QSAR models

Well defined structure of the molecule

Amount of experimental data

Quality of experimental data

Usually limited to organic molecules

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BIO-SUSHY

AXIA INNOVATION

José Luis Vallés Pardo

jlvalles@protoqsar.com

ProtoQSAR

THANK YOU!

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SUSTAINABLE SURFACE PROTECTION BY GLASS-LIKE HYBRID AND BIOMATERIALS COATINGS

BIO-SUSHY

Module 2: QSAR in BIO-SUSHY & SSbD

BIO-SUSHY TRAINING #5

José Luis Vallés Pardo

12/11/2026

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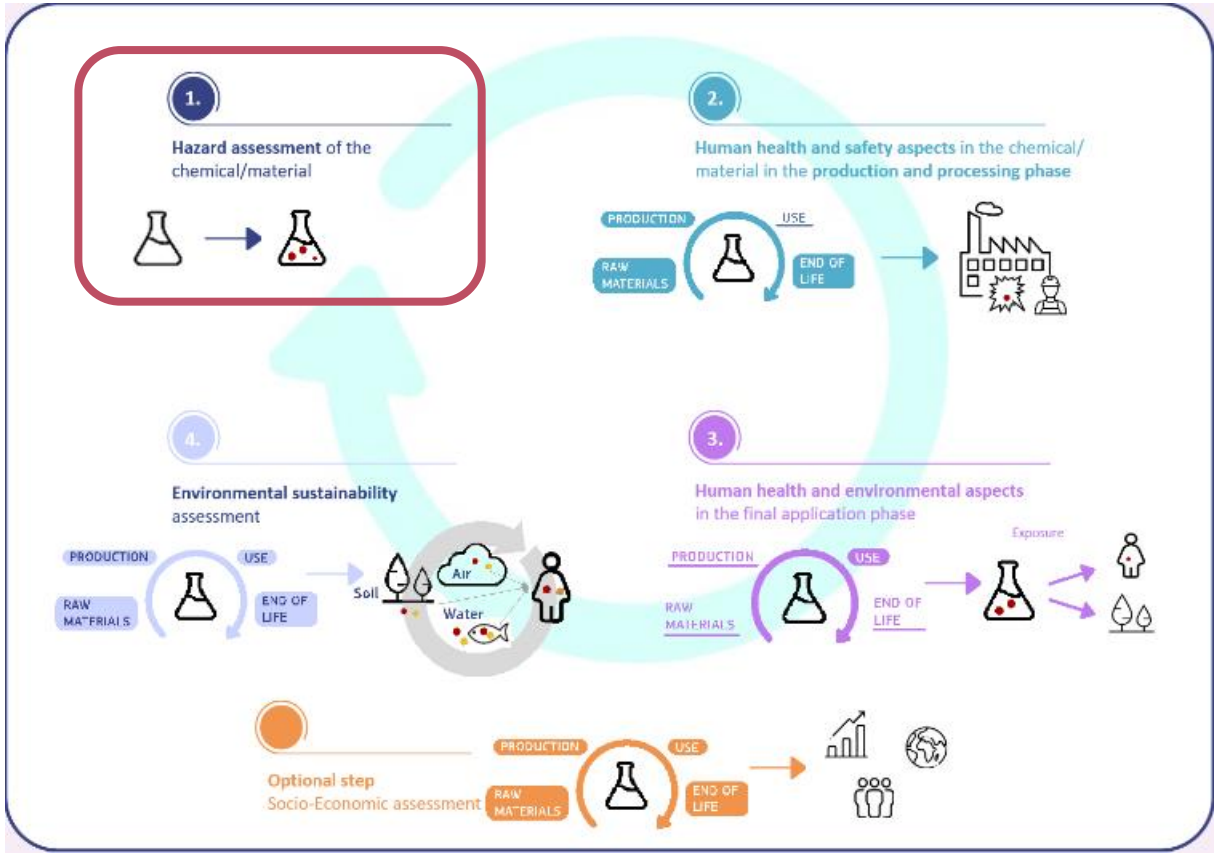


Role of predictive toxicology in SSbD-hazard assessment

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SSbD approach

An **holistic approach** including hazard, exposure, and LCA is applied along the whole process life cycle, **from** the initial **raw materials to** the **final product.** A **scoring system** is defined to assess and compare the compounds involved in all the different steps.



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SSbD approach

Group definition	Human health hazards	Environmental hazards	Physical hazards
Group A: Includes the most harmful substances (according to the Chemicals Strategy for Sustainability), including substances of very high concern (SVHC) (i.e., substances meeting the criteria laid down in REACH Art. 57(a-f) and identified in accordance with REACH Art. 59(1)[16],[17]	• Carcinogenicity Cat. 1A and 1B • Germ cell mutagenicity Cat. 1A and 1B • Reproductive/developmental toxicity Cat. 1A and 1B • Endocrine disruption Cat. 1 (human health) • Respiratory sensitisation Cat. 1 • Specific target organ toxicity - repeated exposure (STOT-RE) Cat. 1, including immunotoxicity and neurotoxicity	• Persistent, bioaccumulative and toxic/very persistent and very bioaccumulative (PBT/vPvB) • Persistent, mobile and toxic/very persistent and mobile (PMT/vPvM)[18] • Endocrine disruption Cat. 1 (environment)	
Group B: Includes substances of concern, as described in the Chemicals Strategy for Sustainability and defined in Article 2(28) of the ecodesign proposal for sustainable products[19], but not included in Group A	• Skin sensitisation Cat 1 • Carcinogenicity Cat. 2 • Germ cell mutagenicity Cat. 2 • Reproductive/developmental toxicity Cat. 2 • Specific target organ toxicity - repeated exposure (STOT-RE) Cat. 2 • Specific target organ toxicity - single exposure (STOT-SE) Cat. 1 and 2 • Endocrine disruption Cat. 2 (human health)	• Hazardous for the ozone layer • Chronic environmental toxicity (chronic aquatic toxicity) • Endocrine disruption Cat. 2 (environment)	
Group C: Includes the other hazard classes not in Groups A or B	• Acute toxicity • Skin corrosion • Skin irritation • Serious eye damage/eye irritation • Aspiration hazard (Cat. 1) • Specific target organ toxicity - single exposure (STOT-SE) Cat. 3	• Acute environmental toxicity (acute aquatic toxicity)	• Explosives • Flammable gases, liquids and solids • Oxidising gases, liquids, solids • Gases under pressure • Self-reactive • Pyrophoric liquids, solids • Self-heating • In contact with water emits flammable gas • Organic peroxides • Corrosivity • Desensitised explosives

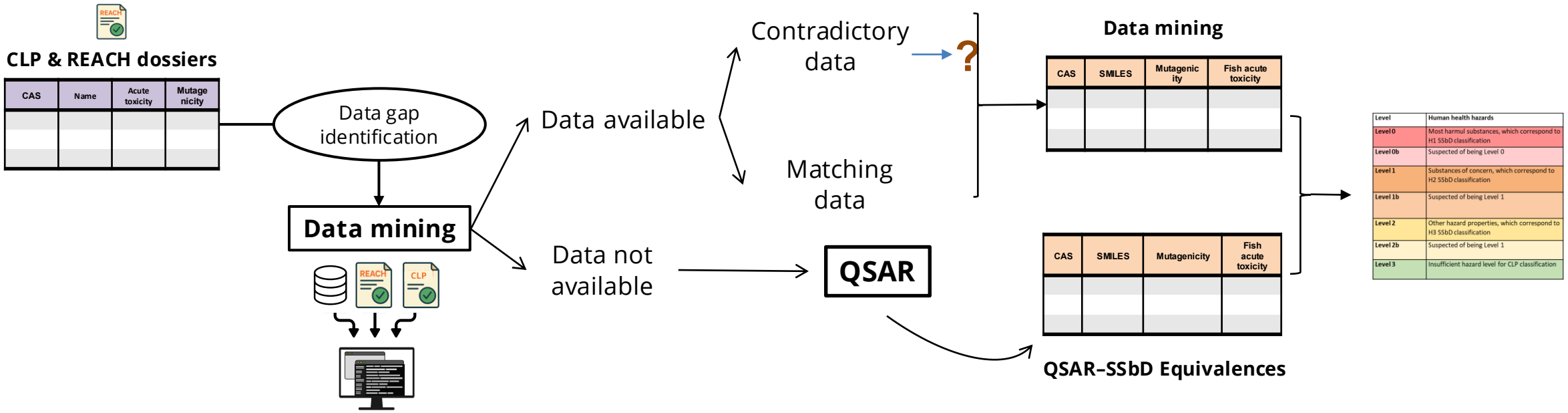
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SSbD approach

Level	Human health hazards	Environmental hazards	Physical hazards
Level 0 (Most harmful substances- Criteria H1)	- Carcinogenicity Cat. 1A and 1B - Germ cell mutagenicity Cat. 1A and 1B - Reproductive/developmental toxicity Cat. 1A and 1B - Endocrine disruption Cat. 1 (human health) - Respiratory sensitisation Cat. 1 - Specific target organ toxicity - repeated exposure (STOT-RE) Cat. 1, including immunotoxicity and neurotoxicity	- Persistent, bioaccumulative and toxic / very persistent and very bioaccumulative (PBT/vPvB) - Persistent, mobile and toxic / very persistent and very mobile (PMT/vPvM) - Endocrine disruption Cat. 1 (environment)	
Level 1 (Substances of concern – Criteria H2)	- Skin sensitisation Cat. 1 - Carcinogenicity Cat. 2 - Germ cell mutagenicity Cat. 2 - Reproductive/developmental toxicity Cat. 2 - Specific target organ toxicity - repeated exposure (STOT-RE) Cat. 2 - Specific target organ toxicity - single exposure (STOT-SE) Cat. 1 and 2 - Endocrine disruption Cat. 2 (human health)	- Hazardous for the ozone layer - Chronic environmental toxicity (chronic aquatic toxicity) - Endocrine disruption Cat. 2 (environment)	
Level 2 (Other hazard properties – Criteria H3)	- Acute toxicity - Skin corrosion - Skin irritation - Serious eye damage / eye irritation - Aspiration hazard (Cat. 1) - Specific target organ toxicity - single exposure (STOT-SE) Cat. 3	- Acute environmental toxicity (acute aquatic toxicity)	-Explosives - Flammable gases, liquids and solids - Oxidising gases, liquids, solids - Gases under pressure -Self-reactive - Pyrophoric liquids, solids - Self-heating - In contact with water emits flammable gas - Organic peroxides - Corrosivity - Desensitised explosives
Level 3 (No hazards)	No hazard associated	No hazard associated	No hazard associated

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SSbD approach



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Role of QSAR in SSbD

- Gathering (eco)toxicity data for low-level SSbD tiers, when more compounds and alternatives are tested.
- Giving indications of possible toxicity when data is not available.
- Giving advice about possible toxicities for further exposure analysis.
- Possible use in other SSbD steps, such as extra ecotoxicity parameters for LCA, or toxicokinetic parameters for exposure assessment.

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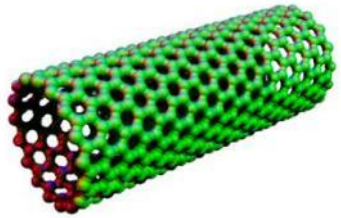


Limitations and possible approaches for QSAR integration in the SSbD assessment

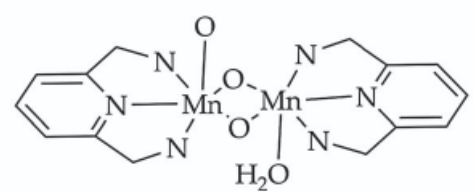
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Limitations

Four main limitations:



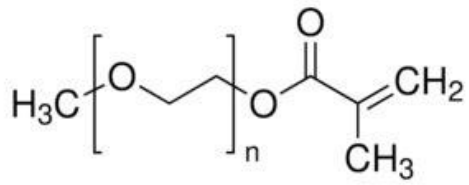
- Nanomaterials



- Inorganic/organometallic compounds



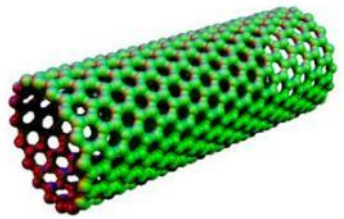
- Mixtures



- Polymers

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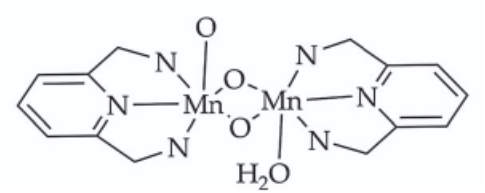
Nanomaterial



- Lack of computational methods to **describe** properly its **structure**
- Existing robust experimental **data is sparse**
- **Experimental parameters** can be related with (eco)toxicity
- **Different families of NMs**, different behaviour

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Inorganic/organometallic compounds



- (Q)SAR models are **feasible**
- **Lack of** enough experimental **data** to have robust models
- **Models trained** only **with organic compounds not reliable** for organometallic compounds

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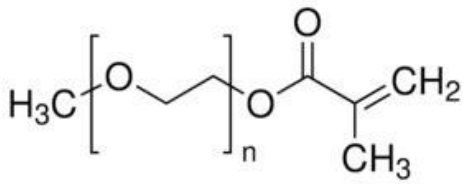
Mixtures

- **(Q)SAR** predictions relies in **single compounds**
- **Predictions** can be done for **individual components**
- Assumption that if one **component** is **(eco)toxic**, the **mixture** is also **(eco)toxic**
- This assumption is **not applicable to physicochemical** properties



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Polymers



- Not defined **structure**
- If **principal oligomer** is known, the **prediction can be done** for it
- **Predictions** can be done **for monomer, dimer, trimer**, etc.

  Assessment done **with all** the predictions together.
- This approaches are **not applicable to physicochemical** properties

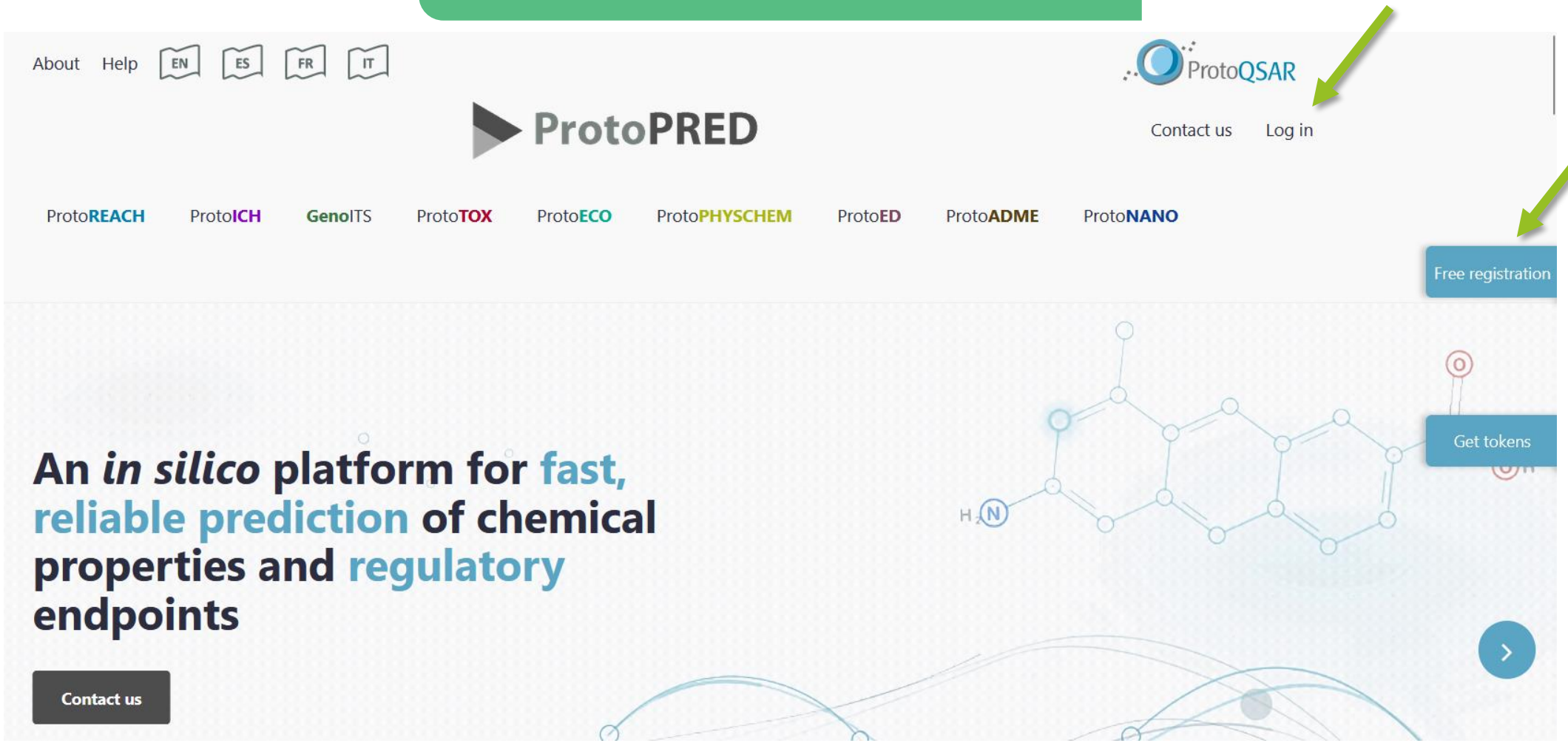
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Introduction to the platform used during the practical exercise

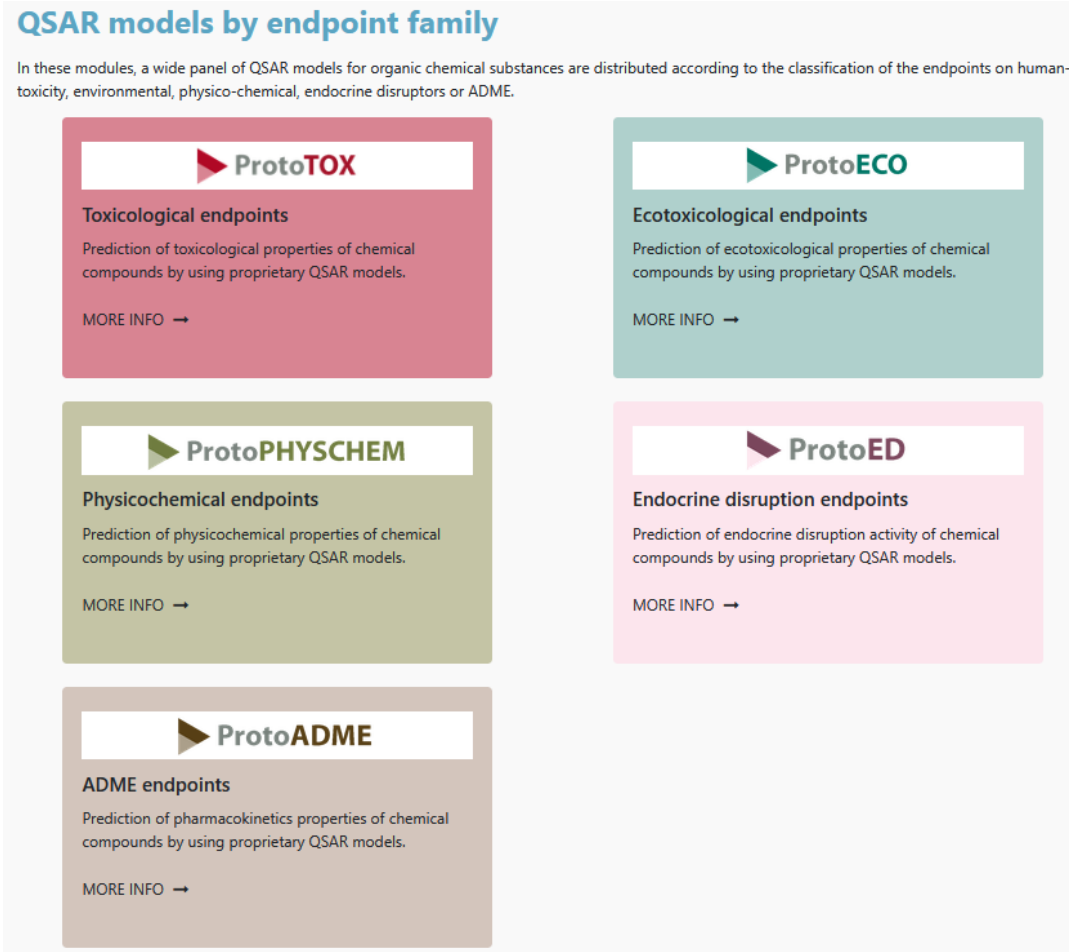
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Introduction to ProtoPRED®



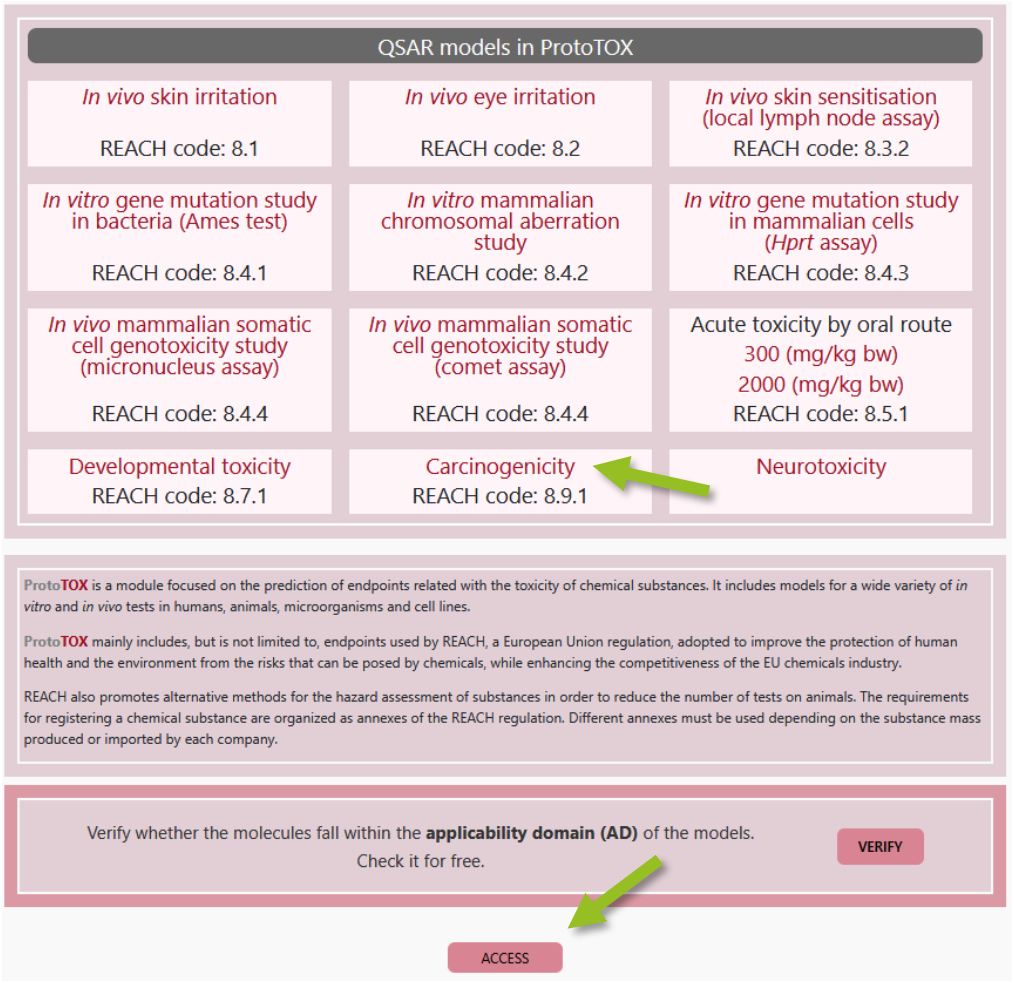
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Endpoint

Human health effects: Carcinogenicity. Carcinogenicity Studies.

Chemicals are defined as carcinogenic if they induce tumours, increase tumour incidence and/or malignancy or shorten the time to tumour occurrence.

Metrics

Training set

Experimental values	QSAR predictions: Non-carcinogen	QSAR predictions: Carcinogen
Non-carcinogen	286	14
Carcinogen	13	174

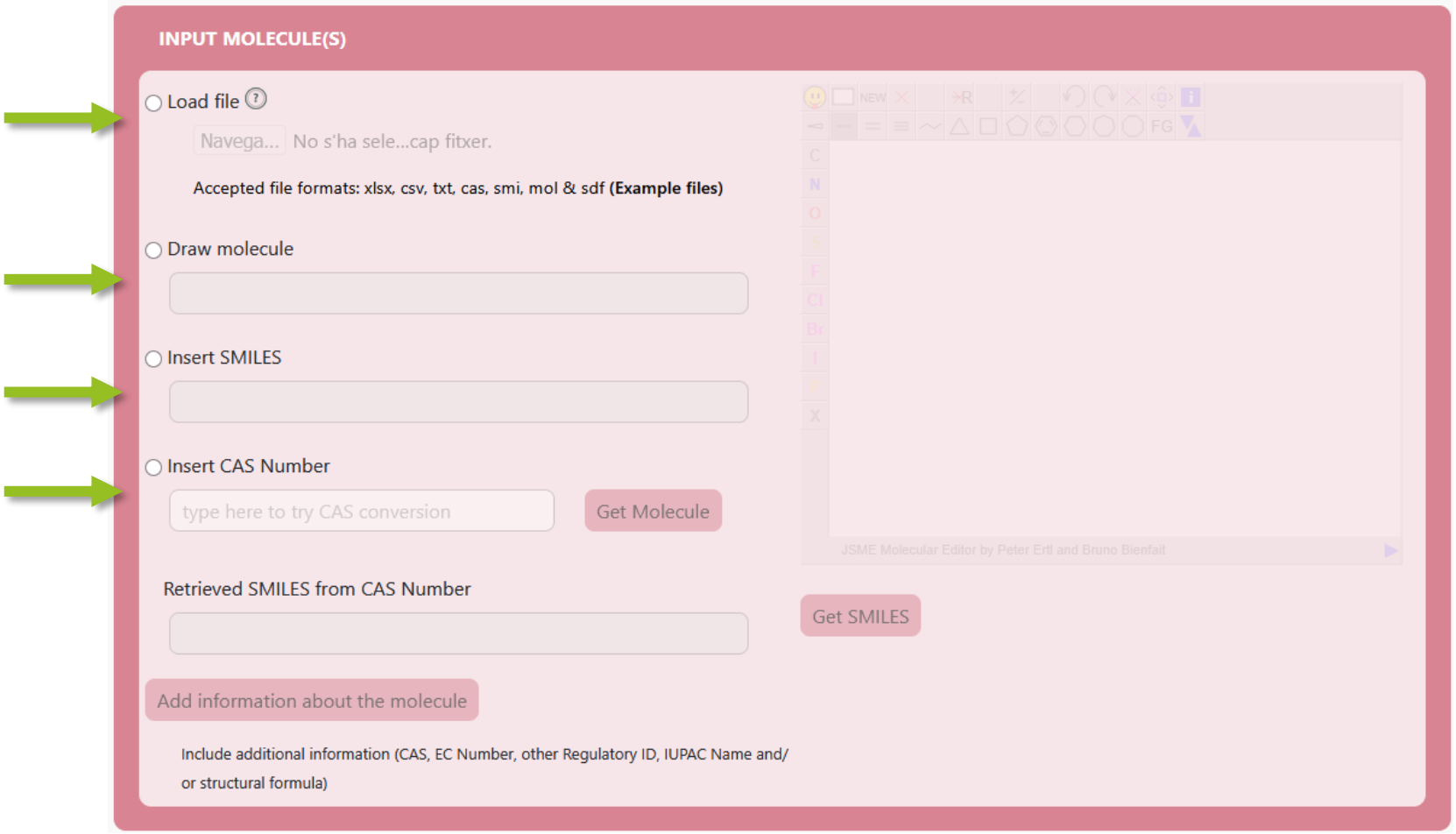
Validation set

Experimental values	QSAR predictions: Non-carcinogen	QSAR predictions: Carcinogen
Non-carcinogen	74	27
Carcinogen	20	44

Parameters	Training	Validation
Accuracy	0.94	0.72
Sensitivity / recall	0.93	0.69
Specificity	0.95	0.73
Precision	0.93	0.62
Negative predictive value	0.96	0.79
F-score	0.93	0.65
Matthews Correlation Coefficient	0.88	0.41
Critical Success Index	0.87	0.48
Area under the ROC	0.94	0.71

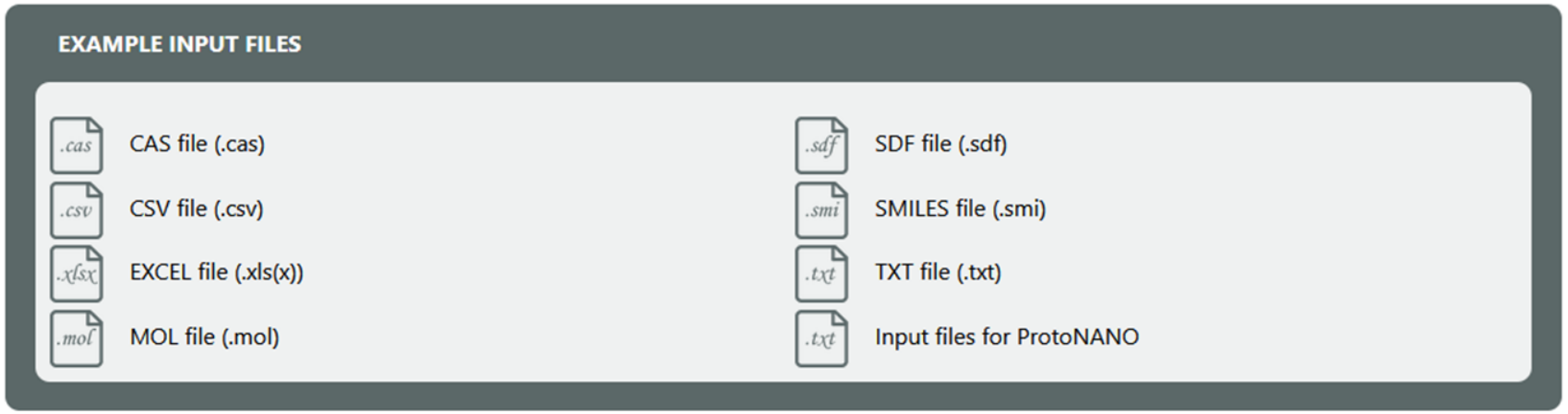
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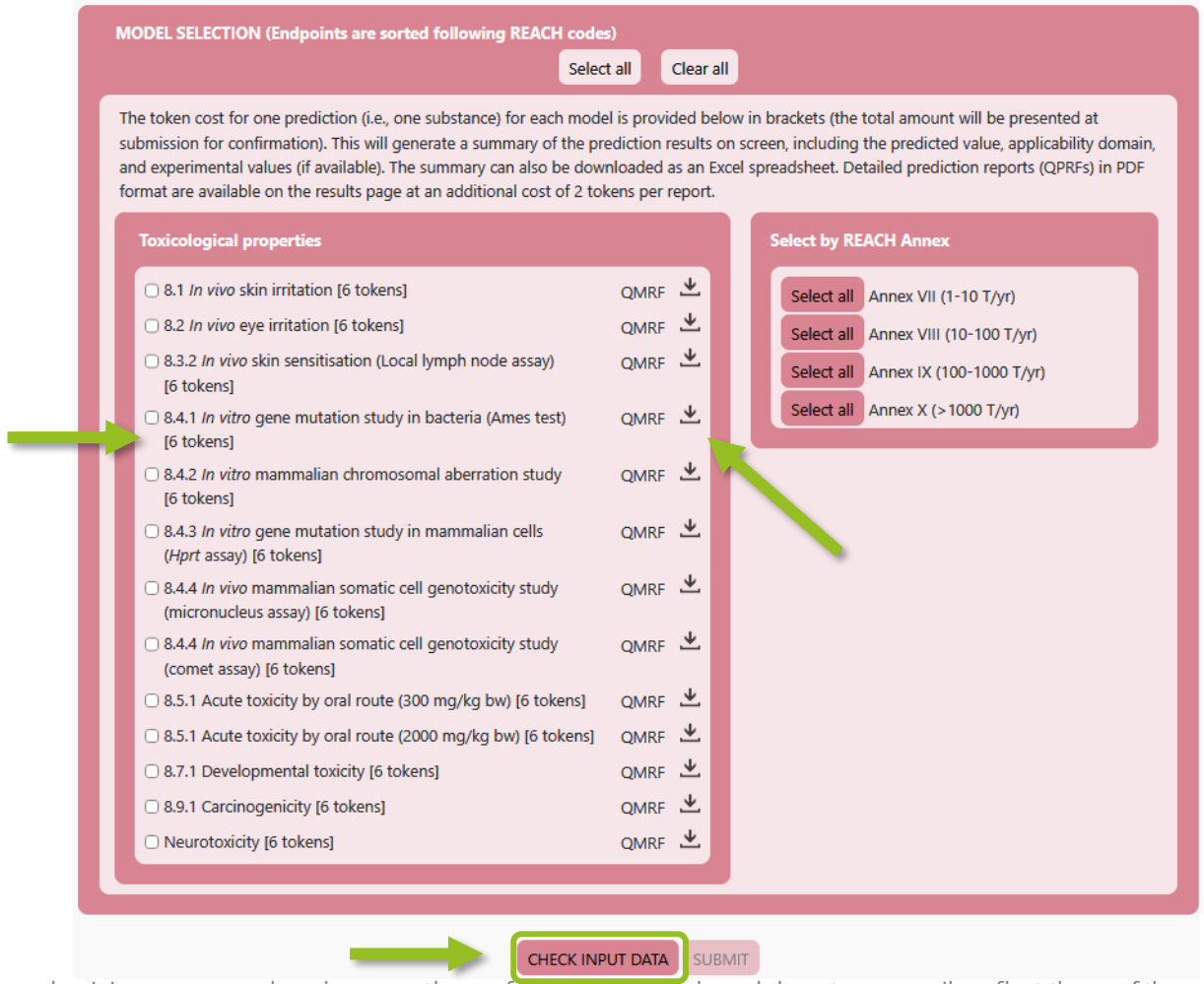
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3. Defining the endpoint - OECD Principle 1

3.1. Species:

Bacteria (Salmonella Typhimurium)

3.2. Endpoint:

Human health effects: Mutagenicity. OECD 471: Bacterial reverse mutation test.

3.3. Comment on endpoint:

Mutagenicity refers to the induction of permanent transmissible changes in the amount or structure of the genetic material of cells or organisms. The Bacterial reverse mutation test evaluates gene mutations. The test uses amino-acid requiring strains of bacteria to detect (reverse) gene mutations (point mutations and frameshifts) (see reference for "Guidance on information requirements and chemical safety assessment, Chapter R.7a" in section 9.2).

3.4. Endpoint units:

N/A

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4. Defining the algorithm - OECD Principle 2

4.1. Type of model:

QSAR

4.2. Explicit algorithm:

Random Forest Classifier. This method is an ensemble learning method fundamentally based on decision trees, that implements a meta estimator that fits a number of decision tree classifiers on various sub-samples of the dataset and uses averaging to improve the predictive accuracy and control over-fitting.

4.3. Descriptors in the model:

- **GATS5c:** Geary autocorrelation of lag 5 (log function) weighted by Gasteiger charge.
- **GATS1d:** Geary autocorrelation of lag 1 (log function) weighted by sigma electrons.
- **BELd-1:** Lowest eigenvalue of Burden matrix weighted by sigma electrons.

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7.7. Predictivity - Statistics obtained by external validation:

Experimental values	QSAR predictions: non-mutagenic	QSAR predictions: mutagenic	
non-mutagenic	553	196	73.8% (TNR)
mutagenic	190	685	78.3% (TPR)
	74.4 % (NPV)	77.8% (PPV)	**76.2% (ACC)**

Parameters	Validation
Accuracy (ACC)	0.762
Sensitivity, recall or true positive rate (TPR)	0.783
Specificity or true negative rate (TNR)	0.738

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BIO-SUSHY

AXIA INNOVATION

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ProtoQSAR

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SUSTAINABLE SURFACE PROTECTION BY GLASS-LIKE HYBRID AND BIOMATERIALS COATINGS

BIO-SUSHY

Module 3: Hands-on QSAR Exercise

BIO-SUSHY TRAINING #5

José Luis Vallés Pardo

12/11/2026

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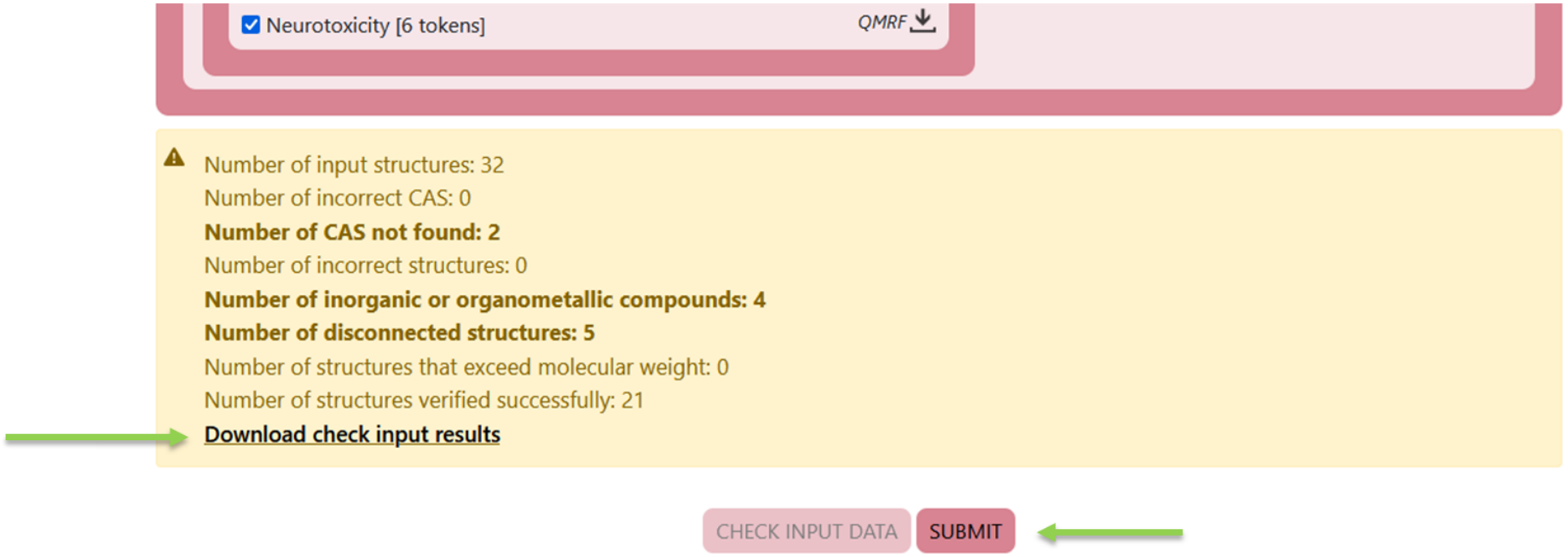
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Demonstration of a predefined QSAR prediction

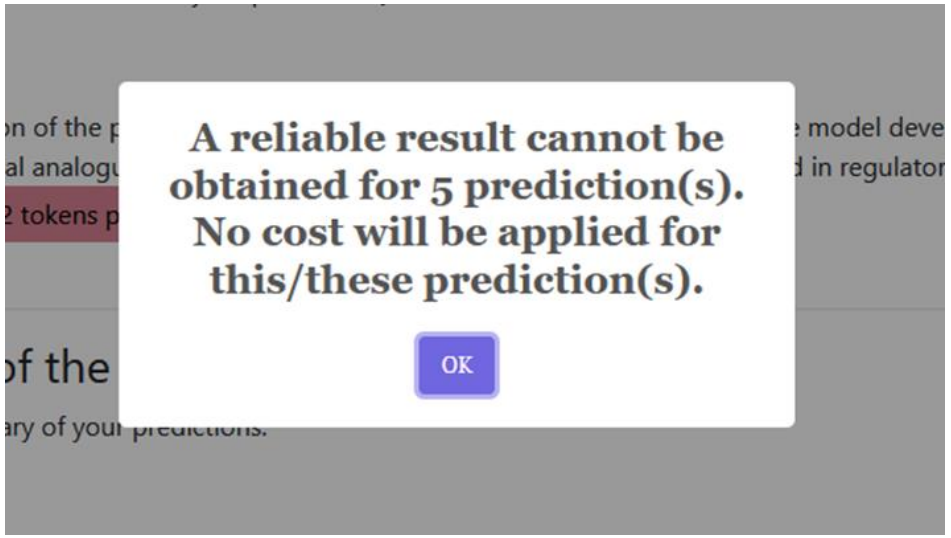
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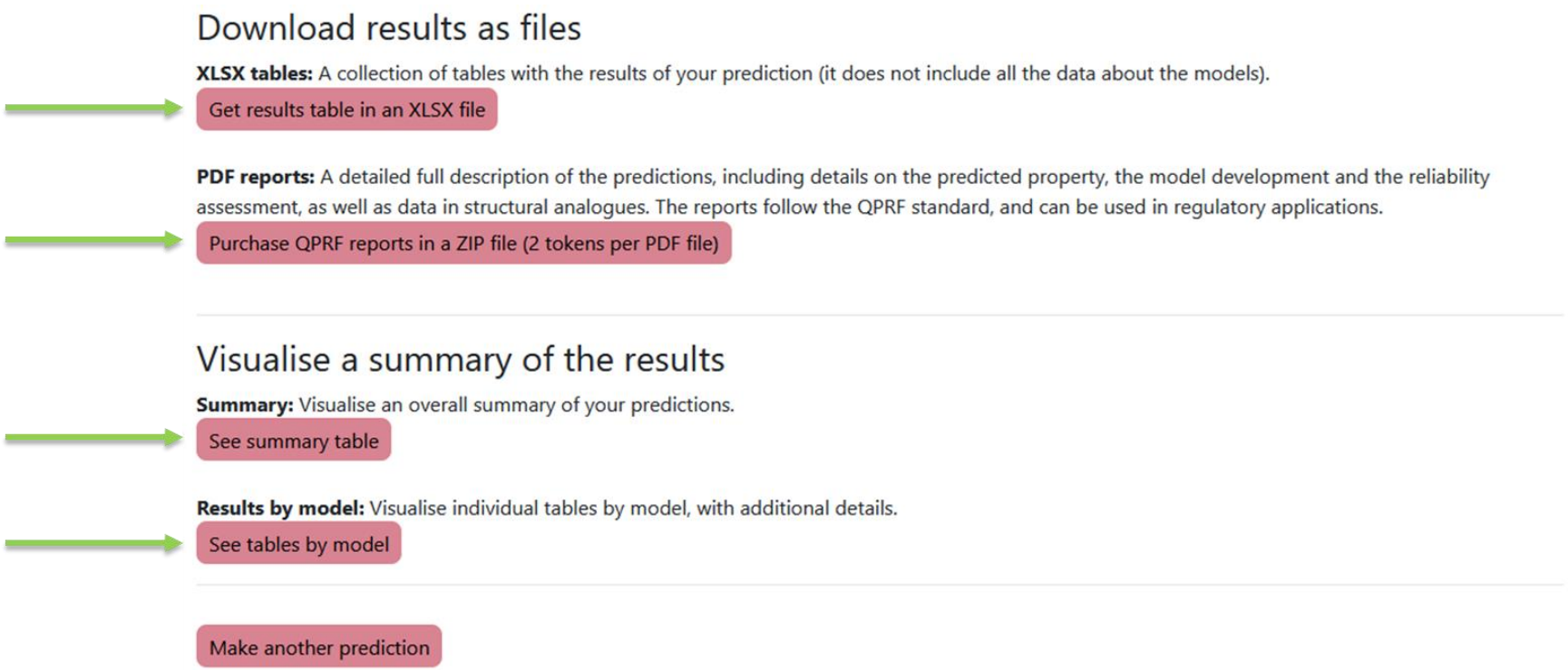
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ID	SMILES	*In vivo* skin sensitisation (local lymph node assay)	*In vitro* gene mutation study in bacteria (Ames test)	*In vivo* mammalian somatic cell genotoxicity study (comet assay)	Carcinogenicity
0_C(C(=O)O)O	C(C(=O)O)O	Sensitizer	Non-mutagenic*	Non-mutagenic	Non-carcinogen
1_C(C_O)O	C(C(=O)O)C(CC(=O)O)(C(=O)O)O	Non-sensitizer	Non-mutagenic*	Non-mutagenic*	Non-carcinogen*
2_CCO_OCC	CCO[Si](OCC)(OCC)OCC	Sensitizer	Non-mutagenic	Mutagenic	Carcinogen
3_CCO_O)O	CCOCC1C(C(C(C(O1)OC)OCC)OCC)OC2C(C(C(C(O2)CO)OC)O)O	Non-sensitizer	Non-mutagenic	Non-mutagenic	Non-carcinogen

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In vivo mammalian somatic cell genotoxicity study (comet assay)

For additional model details, check the **QMRF file.**

ID	Chemical name	EC number	Other Regulatory ID	Structural Formula	CAS	SMILES	Experimental value*	Predicted value	Applicability domain**
C(C(=O)O)O	-	-	-	-	-	C(C(=O)O)O	NA	Non-mutagenic	Inside (T/L/E/R)
C(C_O)O	-	-	-	-	-	C(C(=O)O)C(CC(=O)O)(C(=O)O)O	Non-mutagenic	Non-mutagenic	Inside (T/L/E/R)
CCO_OCC	-	-	-	-	-	CCO[Si](OCC)(OCC)OCC	NA	Mutagenic	Inside (T/E)
CCO_O)O	-	-	-	-	-	CCOCC1C(C(C(C(O1)OC)OCC)OCC)OC2C(C(C(C(O2)CO)OC)O)O	NA	Non-mutagenic	Inside (T/E)

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AXIA INNOVATION

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SUSTAINABLE SURFACE PROTECTION BY GLASS-LIKE HYBRID AND BIOMATERIALS COATINGS

BIO-SUSHY

Module 4: Results Analysis & Link to SSbD

BIO-SUSHY TRAINING #5

José Luis Vallés Pardo

12/11/2026

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Interpretation of QSAR results

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Summary results

Summary results

ID	SMILES	*In vivo* skin sensitisation (local lymph node assay)	*In vitro* gene mutation study in bacteria (Ames test)	*In vivo* mammalian somatic cell genotoxicity study (comet assay)	Carcinogenicity
0_C(C(=O)O)O	C(C(=O)O)O	Sensitizer	Non-mutagenic*	Non-mutagenic	Non-carcinogen
1_C(C_O)O	C(C(=O)O)C(CC(=O)O)(C(=O)O)O	Non-sensitizer	Non-mutagenic*	Non-mutagenic*	Non-carcinogen*
2_CCO_OCC	CCO[Si](OCC)(OCC)OCC	Sensitizer	Non-mutagenic	Mutagenic	Carcinogen
3_CCO_O)O	CCOCC1C(C(C(C(O1)OC)OCC)OCC)OC2C(C(C(C(O2)CO)OC)O)O	Non-sensitizer	Non-mutagenic	Non-mutagenic	Non-carcinogen

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Results by model

In vivo skin sensitisation (local lymph node assay)

For additional model details, check the **QMRF file.**

ID	Chemical name	EC number	Other Regulatory ID	Structural Formula	CAS	SMILES	Experimental value*	Predicted value	Applicability domain**
C(C(=O)O)O	-	-	-	-	-	C(C(=O)O)O	NA	Sensitizer	Inside (T/L/E/R)
C(C_O)O	-	-	-	-	-	C(C(=O)O)C(CC(=O)O)(C(=O)O)O	NA	Non-sensitizer	Inside (T/L/E/R)
CCO_OCC	-	-	-	-	-	CCO[Si](OCC)(OCC)OCC	NA	Sensitizer	Inside (E/R)
CCO_O)O	-	-	-	-	-	CCOCC1C(C(C(C(O1)OC)OCC)OCC)OC2C(C(C(C(O2)CO)OC)O)O	NA	Non-sensitizer	Inside (T/E)

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Results by model

In vitro gene mutation study in bacteria (Ames test)

For additional model details, check the **QMRF file.**

ID	Chemical name	EC number	Other Regulatory ID	Structural Formula	CAS	SMILES	Experimental value*	Predicted value	Applicability domain**
C(C(=O)O)O	-	-	-	-	-	C(C(=O)O)O	Non-mutagenic	Non-mutagenic	Inside (T/L/E/R)
C(C_O)O	-	-	-	-	-	C(C(=O)O)C(CC(=O)O)(C(=O)O)O	Non-mutagenic	Non-mutagenic	Inside (T/L/E/R)
CCO_OCC	-	-	-	-	-	CCO[Si](OCC)(OCC)OCC	NA	Non-mutagenic	Inside (T/L/E/R)
CCO_O)O	-	-	-	-	-	CCOCC1C(C(C(C(O1)OC)OCC)OCC)OC2C(C(C(C(O2)CO)OC)O)O	NA	Non-mutagenic	Inside (T/L/E/R)

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Results by model

In vivo mammalian somatic cell genotoxicity study (comet assay)

For additional model details, check the **QMRF file.**

ID	Chemical name	EC number	Other Regulatory ID	Structural Formula	CAS	SMILES	Experimental value*	Predicted value	Applicability domain**
C(C(=O)O)O	-	-	-	-	-	C(C(=O)O)O	NA	Non-mutagenic	Inside (T/L/E/R)
C(C_O)O	-	-	-	-	-	C(C(=O)O)C(CC(=O)O)(C(=O)O)O	Non-mutagenic	Non-mutagenic	Inside (T/L/E/R)
CCO_OCC	-	-	-	-	-	CCO[Si](OCC)(OCC)OCC	NA	Mutagenic	Inside (T/E)
CCO_O)O	-	-	-	-	-	CCOCC1C(C(C(C(O1)OC)OCC)OCC)OC2C(C(C(C(O2)CO)OC)O)O	NA	Non-mutagenic	Inside (T/E)

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Results by model

Carcinogenicity

For additional model details, check the **QMRF file.**

ID	Chemical name	EC number	Other Regulatory ID	Structural Formula	CAS	SMILES	Experimental value*	Predicted value	Applicability domain**
C(C(=O)O)O	-	-	-	-	-	C(C(=O)O)O	NA	Non-carcinogen	Inside (T/L/E/R)
C(C_O)O	-	-	-	-	-	C(C(=O)O)C(CC(=O)O)(C(=O)O)O	Non-carcinogen	Non-carcinogen	Inside (T/L/E/R)
CCO_OCC	-	-	-	-	-	CCO[Si](OCC)(OCC)OCC	NA	Carcinogen	Inside (T/E/R)
CCO_O)O	-	-	-	-	-	CCOCC1C(C(C(C(O1)OC)OCC)OCC)OC2C(C(C(C(O2)CO)OC)O)O	NA	Non-carcinogen	Inside (T/L/E/R)

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(Q)SAR Prediction Reporting Format (QPRF)

Standardized model for describing the **evaluation of a substance in a model**:

- Information about input
- Outcome
- Applicability domain
- Reliability score
- Analogues

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Discussion of reliability, applicability and limitations of the predictions

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Applicability and reliability

In vivo mammalian somatic cell genotoxicity study (comet assay)

For additional model details, check the **QMRF file.**

ID	Chemical name	EC number	Other Regulatory ID	Structural Formula	CAS	SMILES	Experimental value*	Predicted value	Applicability domain**
C(C(=O)O)O	-	-	-	-	-	C(C(=O)O)O	NA	Non-mutagenic	Inside (T/L/E/R)
C(C_O)O	-	-	-	-	-	C(C(=O)O)C(CC(=O)O)(C(=O)O)O	Non-mutagenic	Non-mutagenic	Inside (T/L/E/R)
CCO_OCC	-	-	-	-	-	CCO[Si](OCC)(OCC)OCC	NA	Mutagenic	Inside (T/E)
CCO_O)O	-	-	-	-	-	CCOCC1C(C(C(C(O1)OC)OCC)OCC)OC2C(C(C(C(O2)CO)OC)O)O	NA	Non-mutagenic	Inside (T/E)

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ProtoPRED® reliability score

Internal scoring system to evaluate the reliability of a prediction.

It takes in account different criteria:

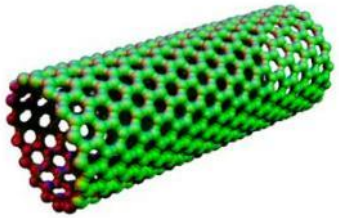
- Reproducibility
- Training/validation performance
- Applicability domain assessment
- Structural space
- Property/Descriptors range
- Analogues performance

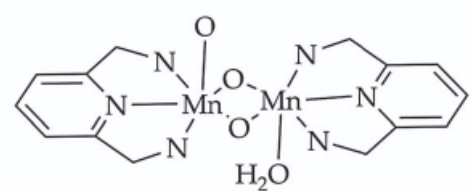
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Limitations (for the input)

Four main limitations:

- Nanomaterials

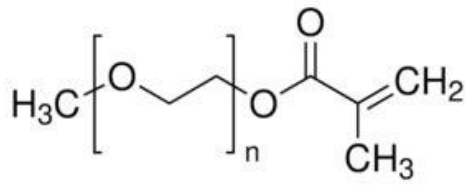




- Inorganic/organometallic compounds

- Mixtures





- Polymers

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Limitations of the predictions

Does align the obtained output with the required information for the SSbD assessment?

In the SSbD assessment, the **Level 0** classification **corresponds** to compounds categorised as **Mutagenicity Cat. 1A/B**.

Mutagenicity Cat. 1A/B corresponds to mutagenicity in **germinal cells**.

We have obtained predictions for **Ames test and comet assay**, both in **somatic cells**.

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Linking QSAR results to hazard assessment and SSbD decision-making

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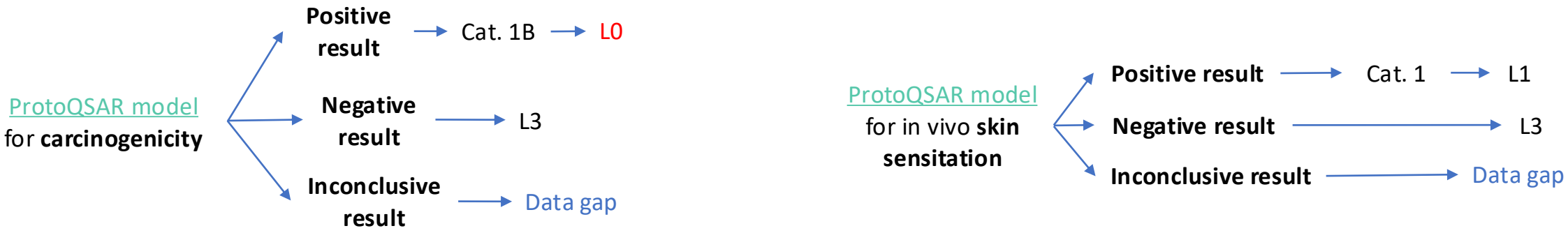
QSAR-SSbD link

- A map **correlating** the outputs of the **QSAR models with** the needed information for the **SSbD-hazard assessment** would be necessary
- A deep **understanding of the model** used (and the SSbD framework requirements) is needed
- This study is useful to made the **SSbD assessment and** to understand the **limitation of our current battery of models**
- The results of these analysis **could vary from one predictive software to another**

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QSAR-SSbD link

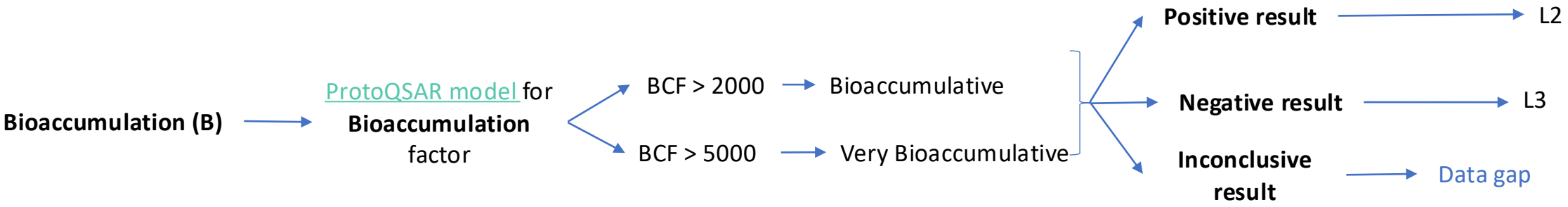
Direct correlation



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QSAR-SSbD link

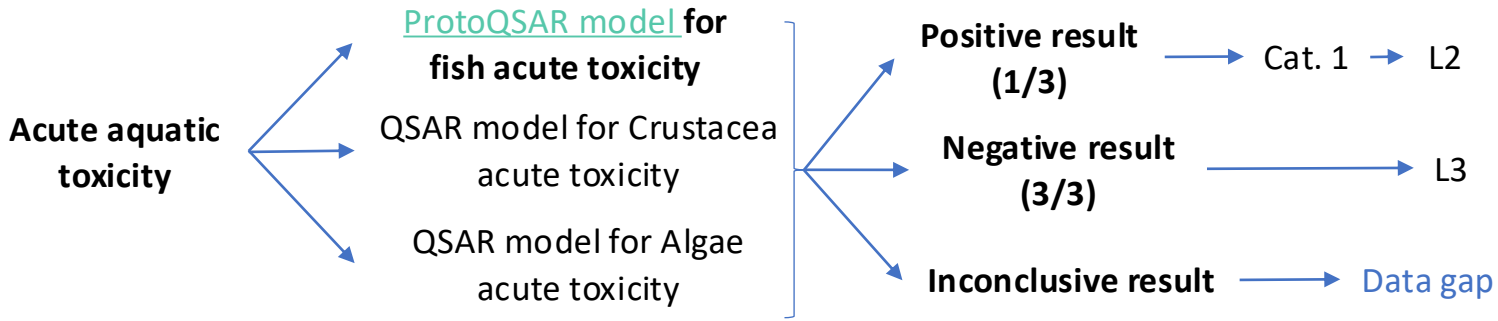
Regression to classification correlation



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QSAR-SSbD link

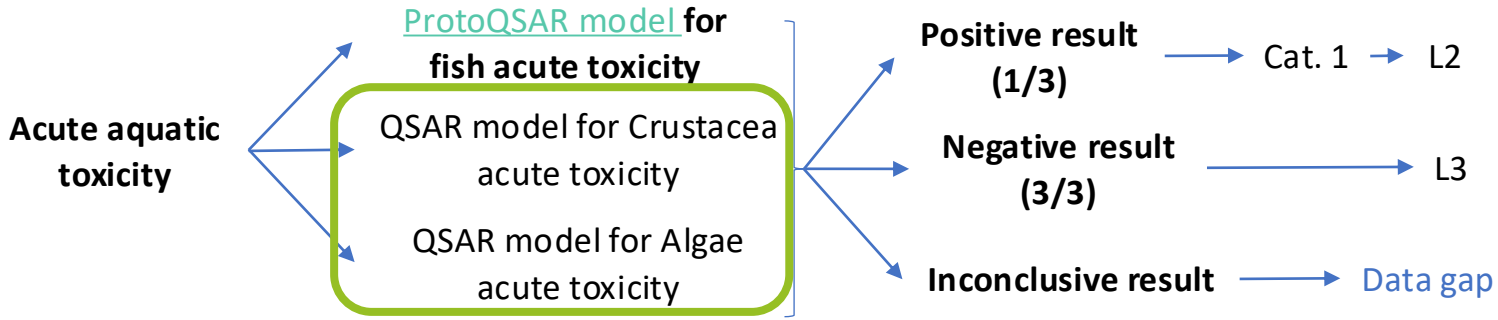
Regression to classification correlation



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QSAR-SSbD link

Missing models for a more robust SSbD assessment



This analysis will highlight also **missing models** and can be used as a **roadmap for** the **development** of new ones

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BIO-SUSHY

AXIA INNOVATION

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THANK YOU!

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