What is new in Toolbox 4.5?

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QSAR Toolbox

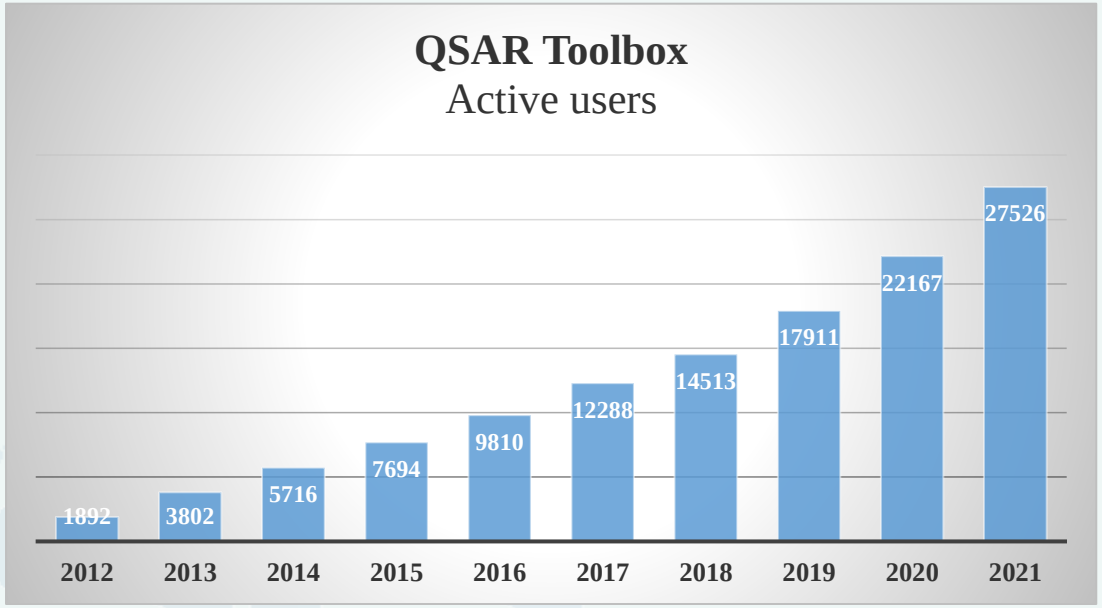
History

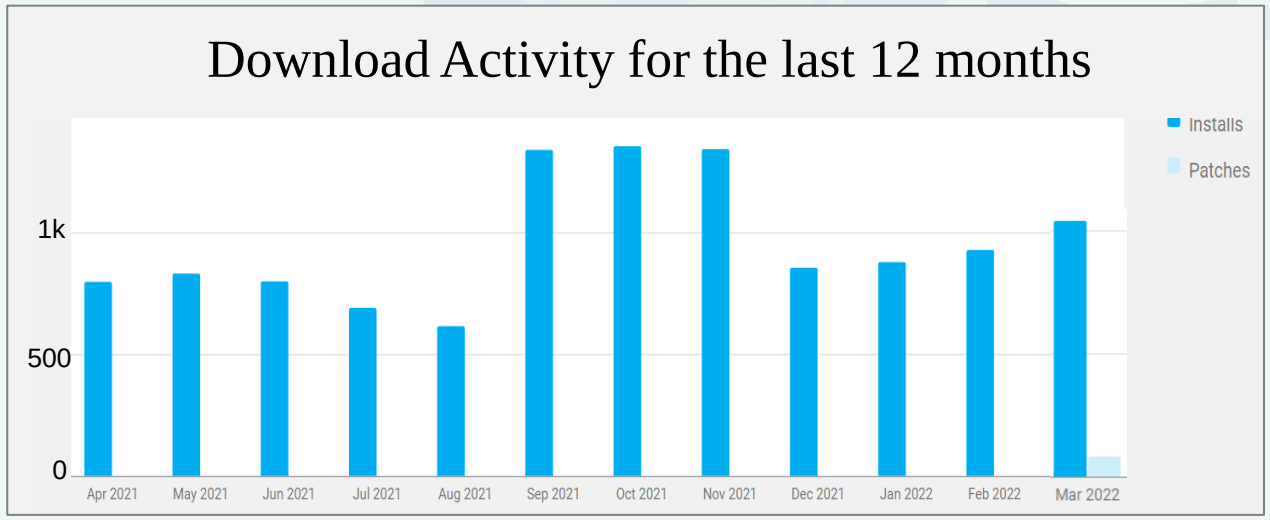
- Initiated as a proof-of-concept in 2006
- Version 1.0 released in October 2008
- Latest public version: 4.5 released in October 2021
- Update of version 4.5 – 4.5*SP1* released in March 2022

QSAR Toolbox

Statistics

- Active users: 27 796
- Toolbox 4.x downloads: 25 761
- Toolbox 4.5 downloads: 4 839





Live statistics here: https://qsartoolbox.org/download/statistics/

What is new in QSAR Toolbox v.4.5?

General:

- **Web client**

  Providing basic features known from the Simplified UI along with a dedicated module for searching in imported IUCLID databases

Important new functionalities/improvements:

- **Substance information & IUCLID compatibility**

  Import/export data from(to) IUCLID to(from) Toolbox;
  Searching capabilities allowing composition search in IUCLID databases

- **Workflow editor (WE)**

  A feature of Toolbox which helps the user define their own (custom) automated workflow schemes for predicting or grouping of chemicals.

- **Automated workflow for DASS**

  A workflow for searching for analogues and read-across, which automatically controls the Toolbox stages and finishes with a prediction for skin sensitization that could be used in a defined approach for skin sensitization (DASS)

Additional new features/improvements:

- New form for easier definition of the target endpoint – following the endpoint tree organization;
- Possibility to define additional endpoints, relevant to the target endpoint;
- Creating custom calculator using experimental data;
- Caching of generated metabolites in Toolbox database;
- Installation of external modules without administrative rights;
- Preparing of additional user manual for the Workflow editor;
- etc.

Resources:

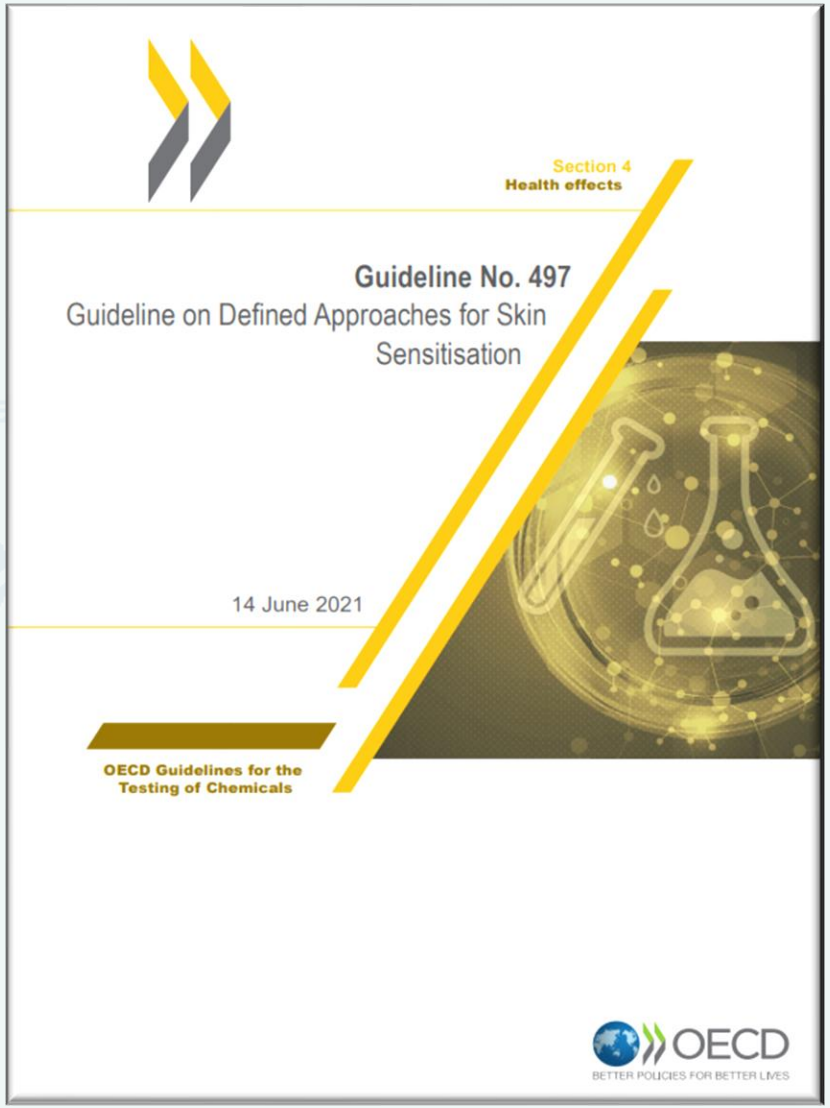
- 10 updated databases & 1 updated inventory;
- 2 new databases;
- 28 updated profilers;
- 12 updated metabolic simulators.

See the full list with *What is new in QSAR Toolbox v.4.5* here: https://qsartoolbox.org/wp-content/uploads/2021/09/Toolbox-4.5-Release-Notes.pdf

Automated workflow for defined approaches for skin sensitization (DASS AW)

DASS – Introduction:

- OECD Test Guideline on Defined Approaches on Skin Sensitisation (DASS) has been published (OECD TG 497).
- This is the first guideline that uses non-animal methods to predict whether a chemical can cause skin allergies.
- Three DAs are currently included.
- One of the DAs - *Integrated Testing Strategy (ITS) v.2* uses predictions from *OECD QSAR Toolbox*, obtained by a specifically created automated workflow (DASS AW)



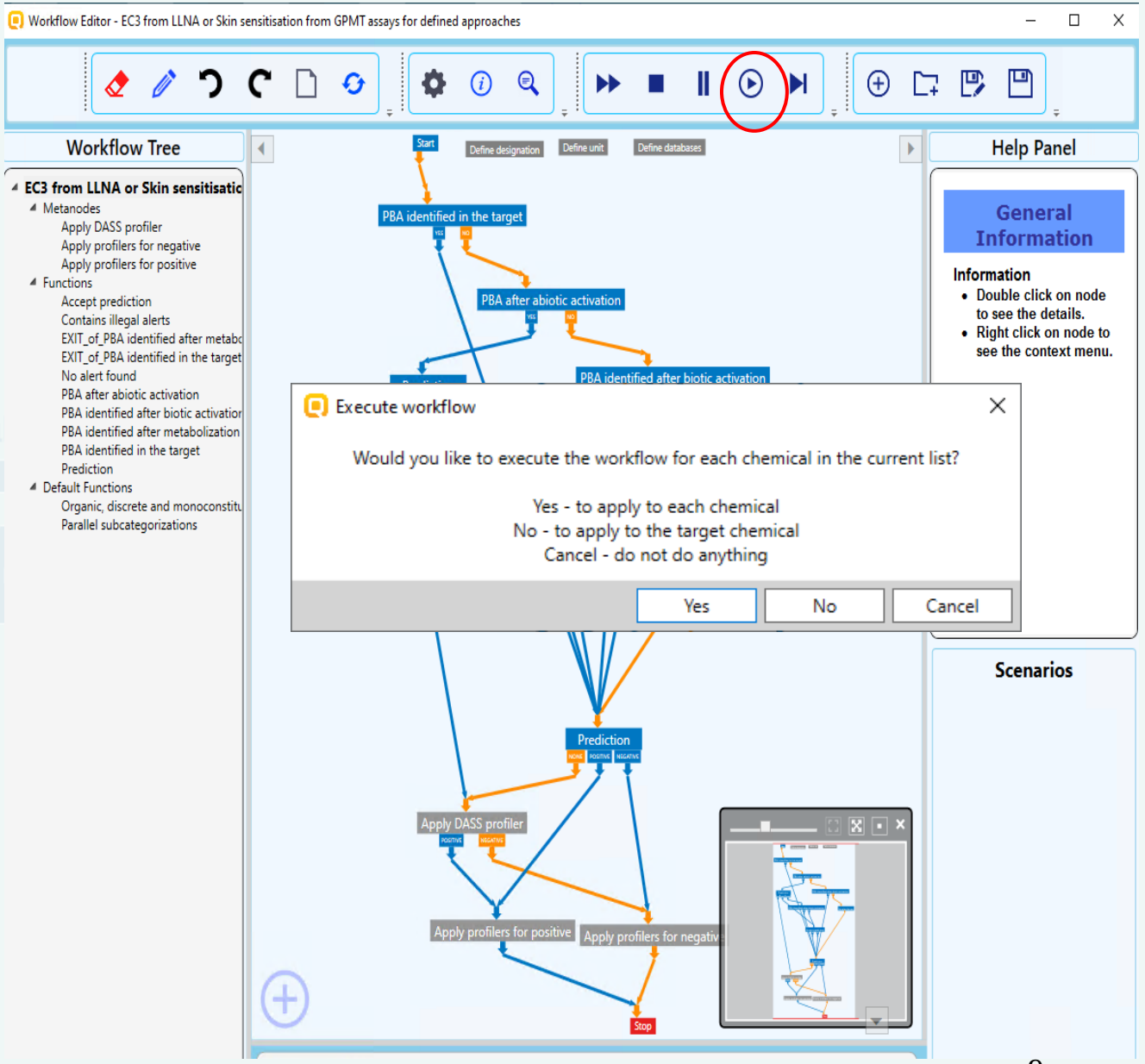
Guideline No. 497: Defined Approaches on Skin Sensitisation: https://doi.org/10.1787/b92879a4-en

DASS AW - implementation

- The WE has been used for development and implementation of the specific AW for SS predictions, including automated definition of the applicability domain.

- The DASS AW can be used to obtain a prediction for a single target chemical or to be applied in batch mode obtaining predictions for a chemical list.

- The DASS AW is applicable to discrete organic chemicals. It is not applicable to mixtures, salts, UVCBs, polymers, etc.

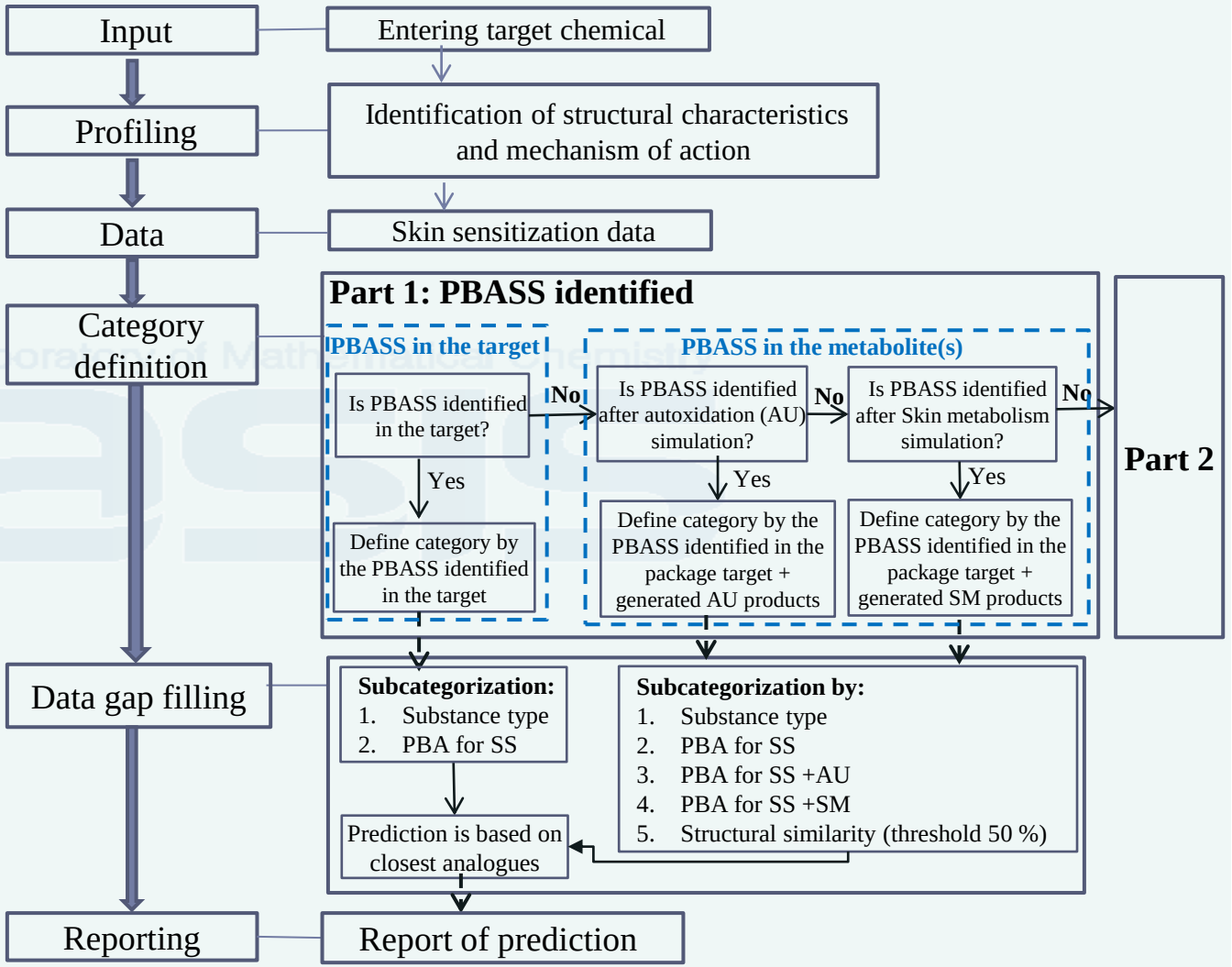


DASS AW - logic

- The algorithms, implemented in all AWs for predicting skin sensitization are based on the presence/absence of protein binding alert(s) for skin sensitization (PBASS).

- If PBASS is identified in the target as parent or as a result of abiotic or biotic metabolic activation, the AW searches for analogues, acting by the same mechanism

Part 1: Identified protein binding alert(s) for skin sensitization (PBASS) in the target chemical as parent or as a result of metabolic activation



DASS AW - logic

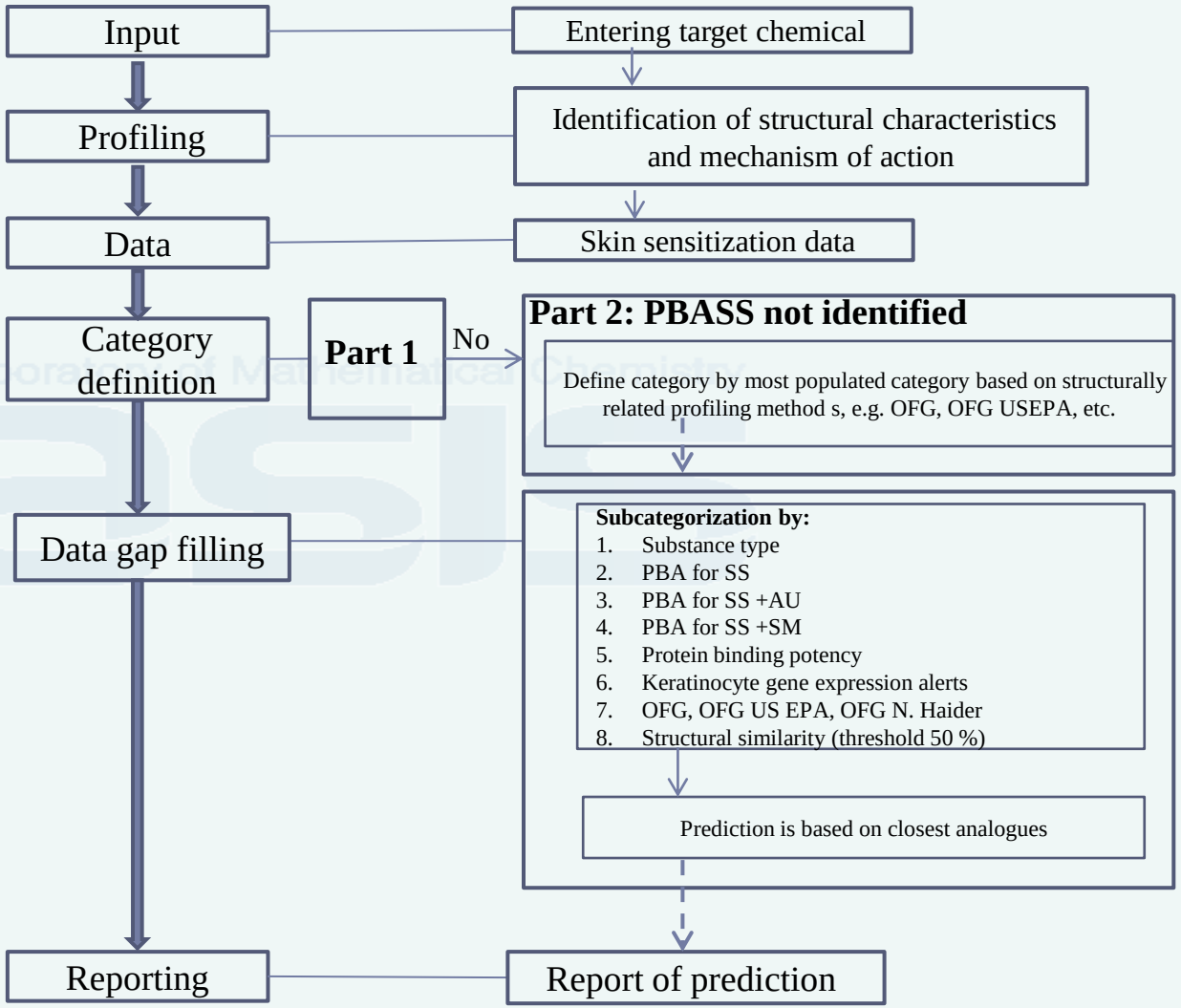
- The algorithms, implemented in all AWs for predicting skin sensitization are based on the presence/absence of protein binding alert(s) for skin sensitization (PBASS).

- If PBASS is identified in the target as parent or as a result of abiotic or biotic metabolic activation, the AW searches for analogues, acting by the same mechanism

- If PBASS is NOT identified in the target as parent or as a result of metabolic activation, the AW searches for structurally similar analogues, having no PBASS

- In case the DASS AW falls to make a prediction by read-across, the prediction is based only on the theoretical knowledge (i.e. PBASS)

Part 2: Protein binding alert(s) for skin sensitization (PBASS) is not identified in the target chemical as parent or as a result of metabolic activation



DASS AW – applicability domain:

- The applicability domain (AD) is automatically defined once the DASS AW finishes with a prediction.

- Three different domain layers (parametric, structural and mechanistic) could be considered depending on the prediction:
  - ***structural*** and ***parametric layers*** – based on the structural fragments (atom centered fragments (ACFs)) and phys-chem parameter properties (MW, logKow, VP, WS) of the correctly predicted chemicals from the training set (TS)*
  - ***mechanistic layer*** – based on the presence/absence of PBASS, identified by the endpoint-specific *Protein binding alerts for skin sensitization by OASIS* profiler, combined with (a)biotic metabolism simulators (*Autoxidation* and *Skin metabolism* simulators)

Toolbox DASS AW outcome		Applicability domain layer		
		Structural	Parametric	Mechanistic
Positive	Read-across	Not considered	Not considered	**Considered**
	Profiling	Not considered	Not considered	**Met by definition**
Negative	Read-across	Not considered	Not considered	**Considered**
	Profiling	**Considered**	**Considered**	**Met by definition**

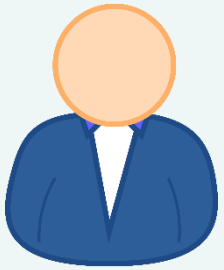
*TS of the DASS AW consists of above 2200 chemicals having SS (LLNA and/or GPMT) experimental data available in the Toolbox Skin sensitization and REACH Skin sensitization (normalized) databases

What is new in Toolbox 4.5?

Toolbox Web Client 2.0

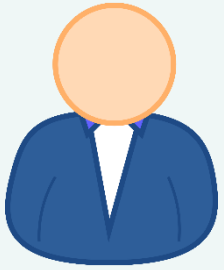
Potential users, new features and deployment scenarios

Toolbox Web Client: Potential users



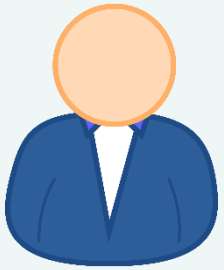
New users *(unfamiliar with Toolbox)*

To get familiar with the basics without being overwhelmed by the full interface



Users of the SUI

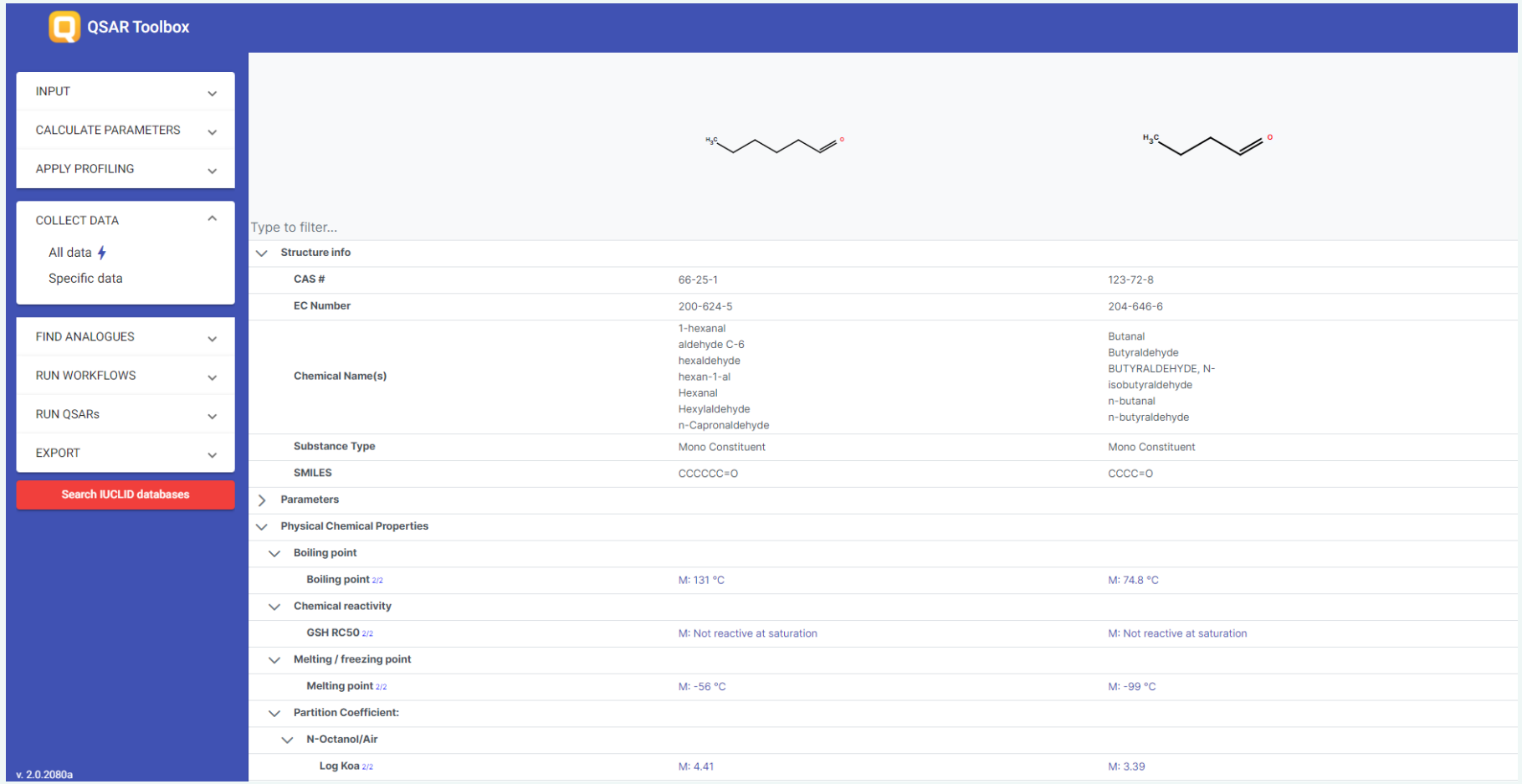
To solve everyday tasks in a simpler environment



Regular users *(already experienced with the desktop version)*

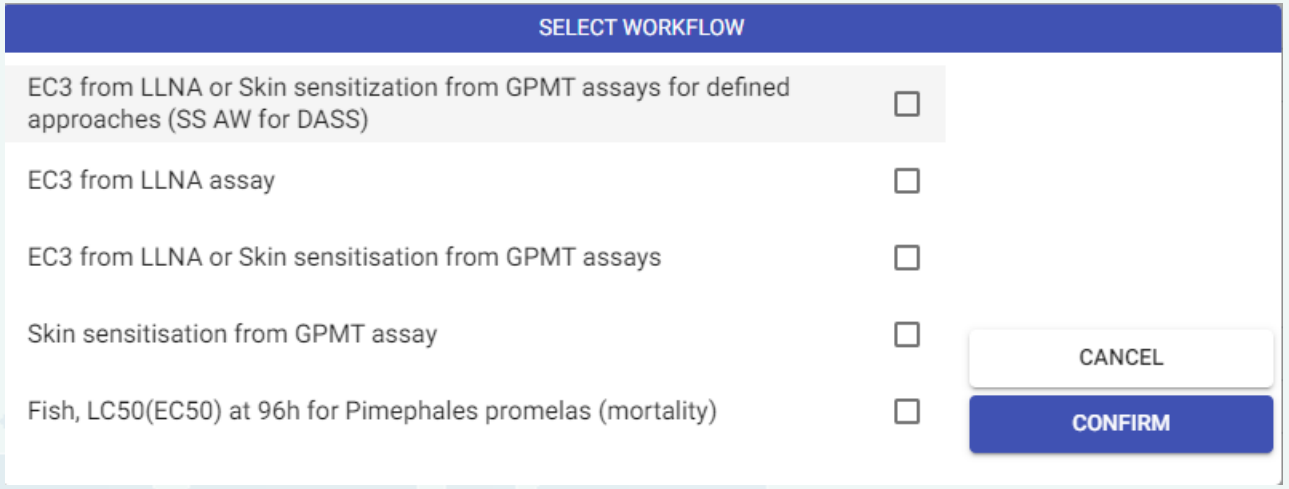
To utilize the benefits of a shared deployment and/or mobile usage

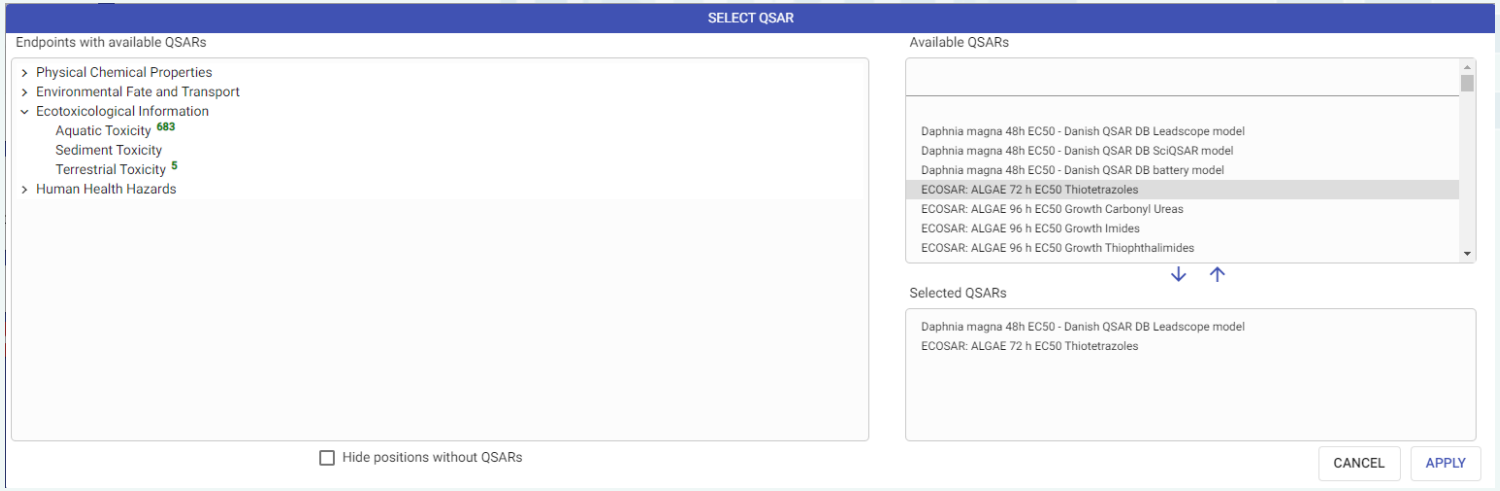
Toolbox Web Client: New features



Real data matrix

Toolbox Web Client: New features





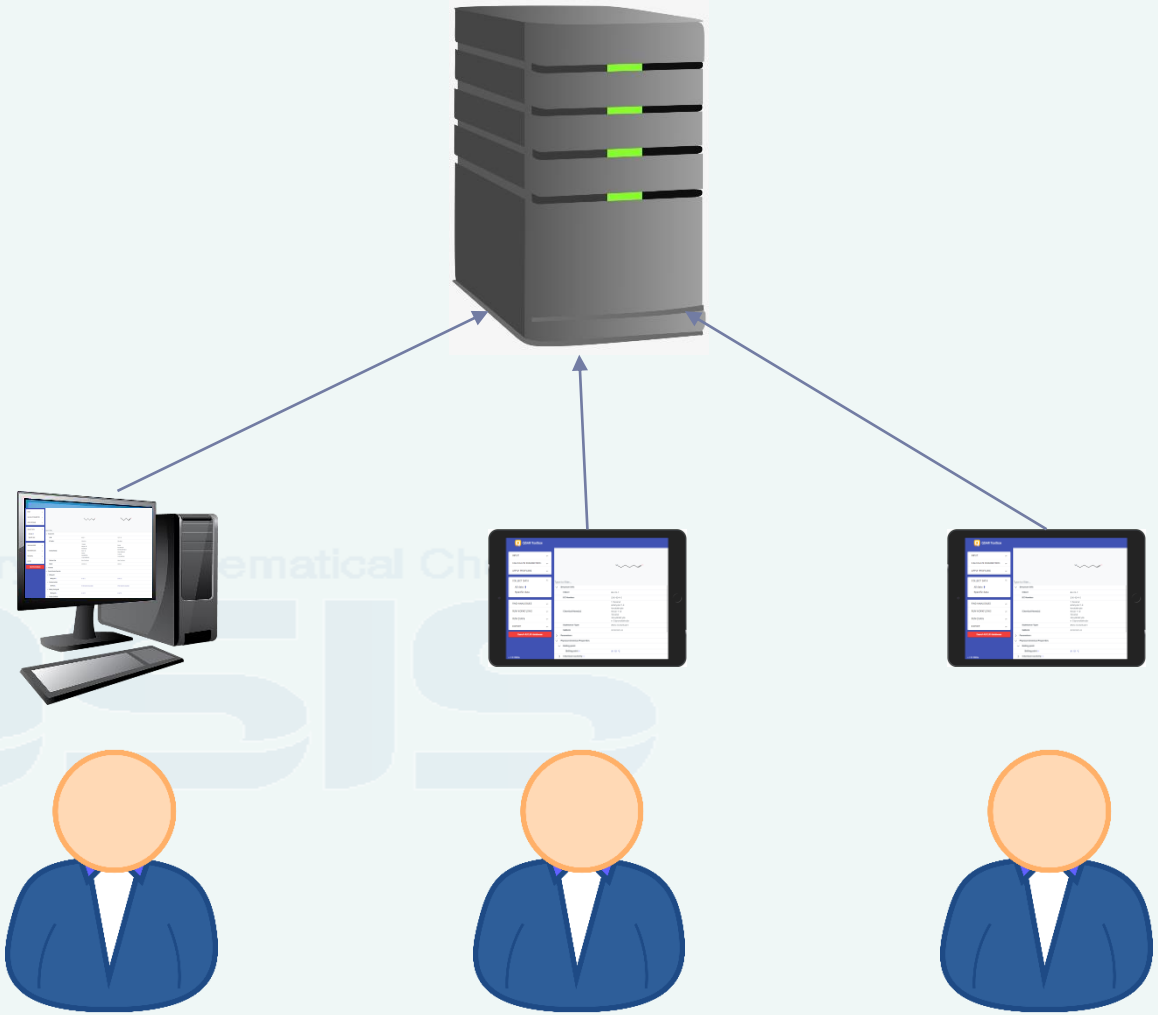
Executing workflows and QSARs

Toolbox Web Client: Improvements

- Input structures with a 2D editor
- Selecting multiple chemicals from a search result
- Improved displaying of data points
- Richer explain service
- Better export

Toolbox Web Client: Deployment scenarios

Connecting to your local Toolbox



Using a shared Toolbox server

Toolbox Web Client: Demo

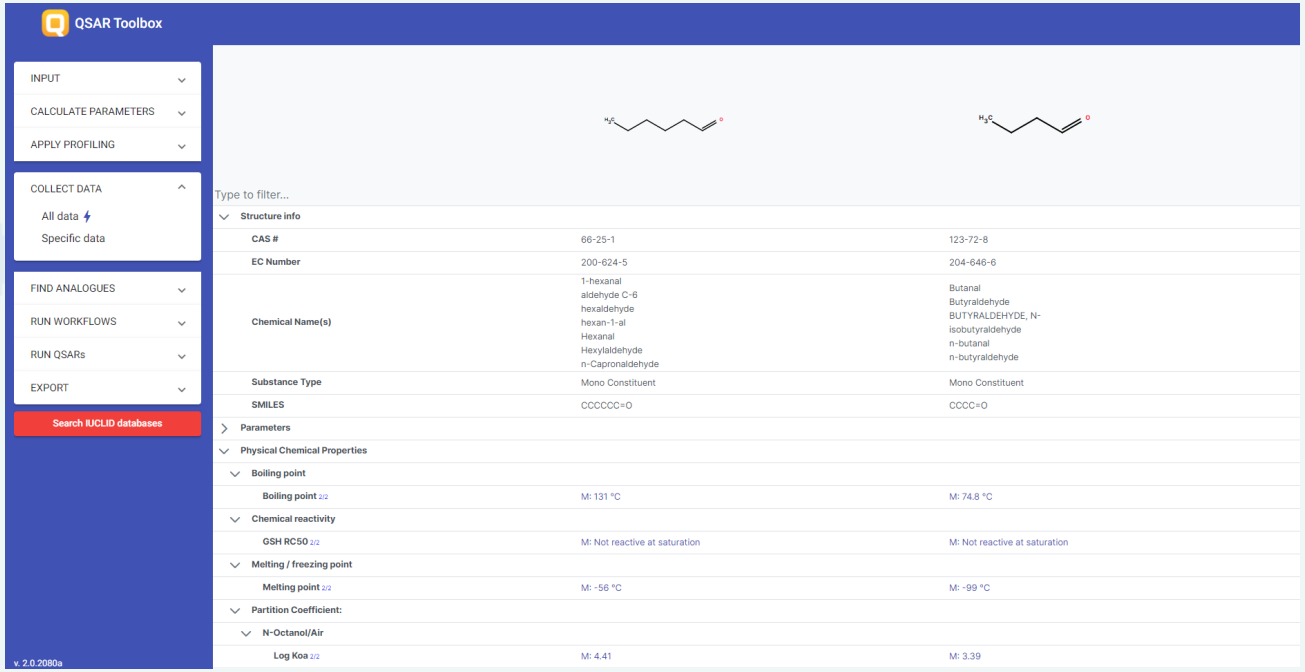
Launching the WebClient

Overview of the available features

Running a chemical through the workflow

Explaining results

Exporting the matrix



Toolbox Web Client: Future developments

- Scalability improvements (for shared use)
- Integrating metabolism
- Implementing reporting standards