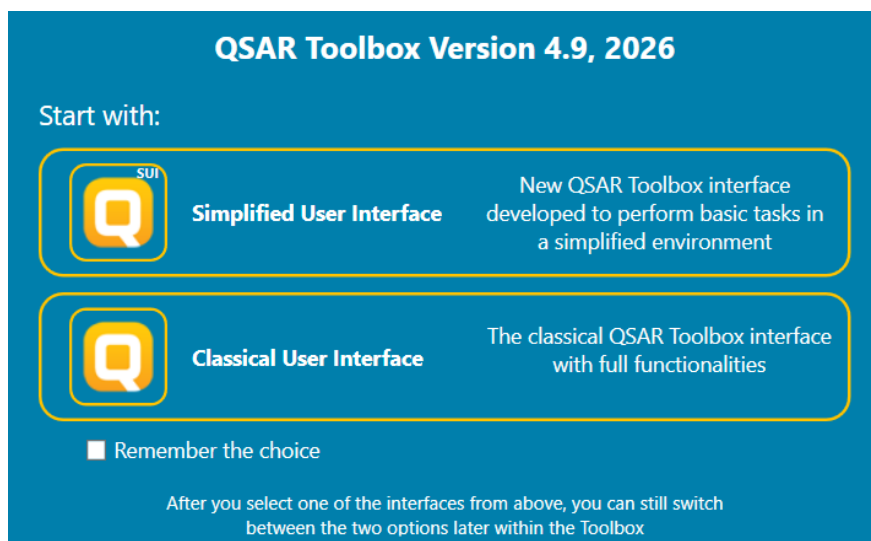


QSAR TOOLBOX

The OECD QSAR Toolbox
for Grouping Chemicals
into Categories

GETTING STARTED: QUICK REFERENCE GUIDE FOR THE CLASSICAL USER INTERFACE

Choose which user interface you want to work with: *Simplified User Interface* or *Classical User Interface*.



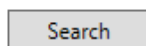
If you want to use the same user interface every time when you open the software then check **Remember the choice** checkbox before selecting one of the two interfaces.

Step 1: Input - Define chemical of interest or "target chemical"

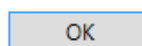
Define your target chemical by Chemical Name, CAS number, SMILES, drawing the molecule or selecting it from a list. To define a chemical by CAS number:



Click **CAS#** → enter the number, and then click



→ the program displays the structure →



The structure is displayed on the data matrix.

The screenshot shows the QSAR TOOLBOX interface. The 'Input' tab is active, and the 'CAS#' button is clicked. The 'Search' button is also visible. The 'Structure' field displays the chemical structure of 4-Nitrobenzoyl chloride. The 'Chemical List' table shows the following information:

EC Number	CAS Number	Chemical Name	SMILES
2045174	122-04-3	High	4-Nitrobenzoyl chloride

The 'Structure info' section is expanded, showing the following details:

- Additional Ids
- CAS Number
- CAS-SMILES relation
- Chemical name(s)
- Comment
- Identity
- Molecular formula
- Predefined substance type
- SMILES

The 'Parameters' section is also expanded, showing the following details:

- Physical Chemical Properties
- Environmental Fate and Transport
- Ecotoxicological Information
- Human Health Hazards
- Intermediate effects - mechanistic information
- Observer metabolism

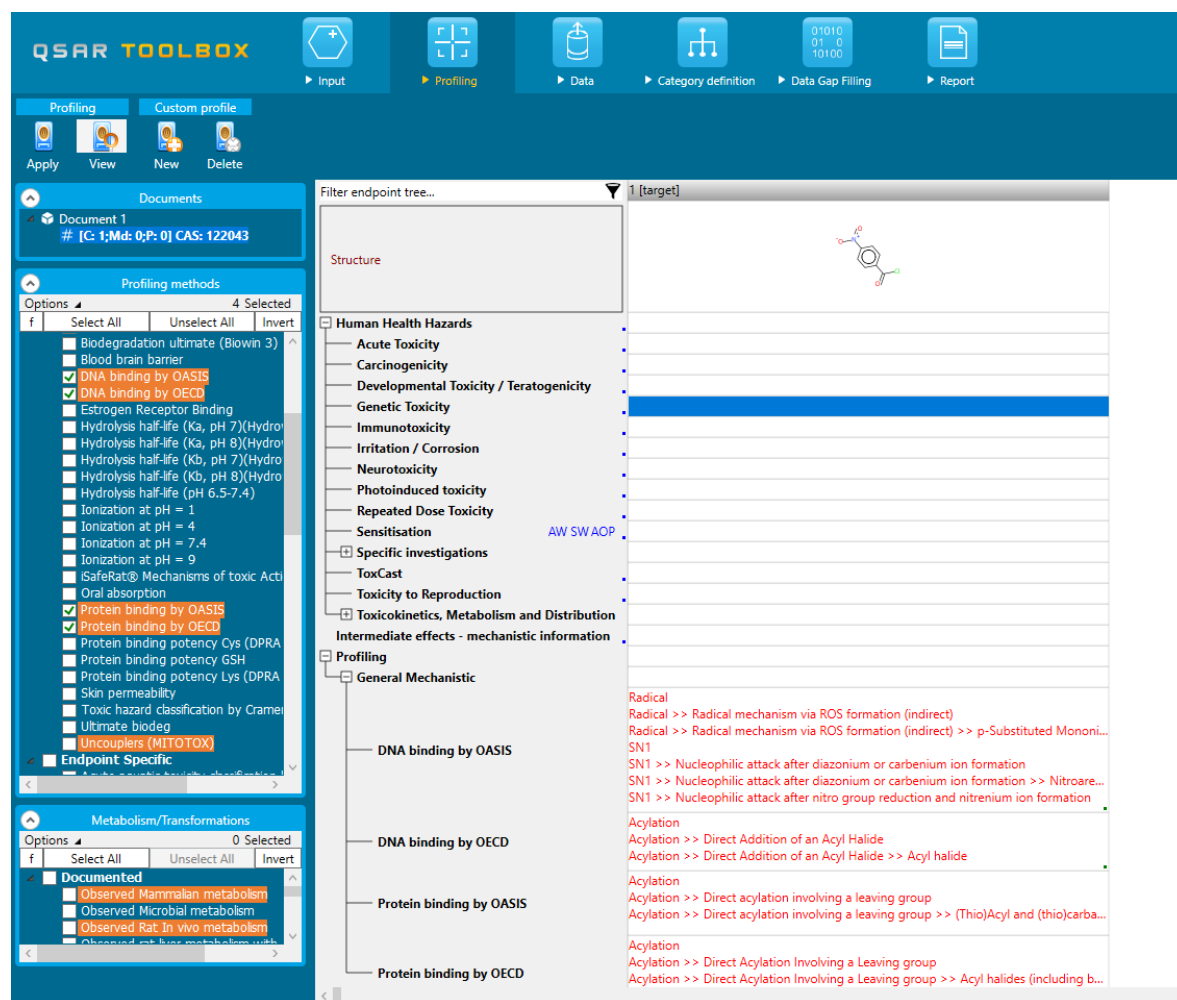


To define the target endpoint, which will be used for the predictions click



Step 2: Profiling - Retrieve information based on the identity of the substance or its structure

Select profilers by ticking the corresponding boxes → . The program establishes a "profile" of the chemical based on its structure.



The screenshot shows the QSAR TOOLBOX software interface. The top toolbar includes buttons for Input, Profiling, Data, Category definition, Data Gap Filling, and Report. Below the toolbar, there are tabs for Profiling and Custom profile. The Profiling tab is active, showing a list of profiling methods on the left and a tree of endpoints on the right. The 'DNA binding by OASIS' and 'Protein binding by OASIS' methods are selected. The 'DNA binding by OASIS' endpoint is highlighted in the tree, and its corresponding scientific information is displayed on the right side of the interface.

! To obtain the general background information on any profiler, right click on it and select **About**. To obtain the scientific information used to build the profiler, select

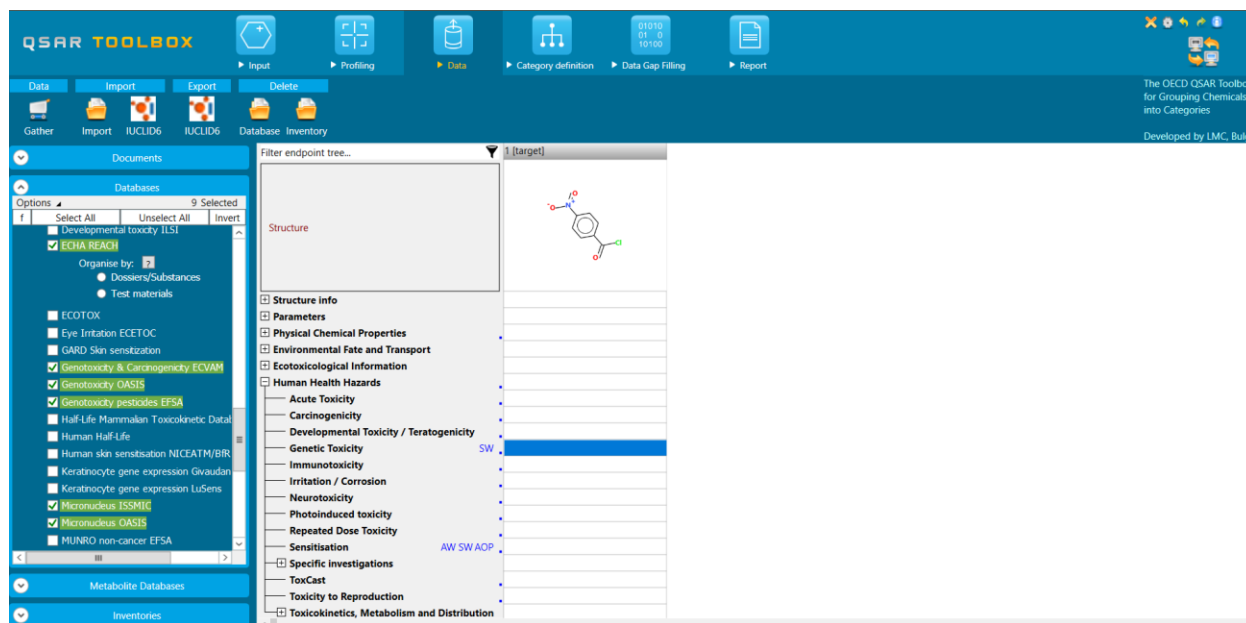
it and click .

! The highlighted profiles correspond to the selected endpoint in the data matrix or to the previously defined endpoint if any.

Step 3: Endpoint - Retrieve experimental results from the resident databases



Select databases by ticking ☒ the corresponding databases → . The retrieved information is displayed according to four subsections in the endpoint tree:

The screenshot shows the QSAR TOOLBOX software interface. At the top is a blue header bar with the 'QSAR TOOLBOX' logo and several icons for 'Input', 'Profiling', 'Data', 'Category definition', 'Data Gap Filling', and 'Report'. Below this is a secondary bar with 'Data', 'Import', 'Export', and 'Delete' tabs. The 'Data' tab is active, showing a 'Gather' button and a 'Database Inventory' section. The 'Database Inventory' lists various databases with checkboxes; several are checked, including 'ECHA REACH', 'Genotoxicity & Carcinogenicity ECVAH', 'Genotoxicity OASIS', 'Genotoxicity pesticides EFSA', 'Microtox', 'Microtox DASH', and 'HUMAN non-cancer EFSA'. To the right of the inventory is a 'Filter endpoint tree...' window showing a hierarchical tree of endpoints. The 'Genetic Toxicity' node is highlighted in blue. To the right of the tree is a chemical structure of a nitro-substituted benzene ring. At the bottom right, there is a small text box that reads 'The OECD QSAR Toolbox for Grouping Chemicals into Categories' and 'Developed by IMC, Bulgaria'.

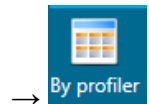
! To open the data tree: left-click on the nodes. To access detailed information on the experimental results: double-click on the result in the matrix.

! The highlighted databases correspond to the selected endpoint in the data matrix or to the previously defined endpoint if any.

Step 4: Category definition - Identify chemicals which could form a category with the "target" chemical

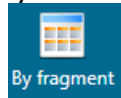
Select one of the grouping methods available in the **Categorization section**.

To identify the analogues of the target based on the profile of your target chemical



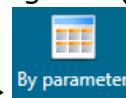
→

To identify the analogues of the target based on the fragment(s) identified in the

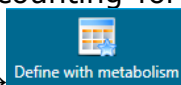


target →

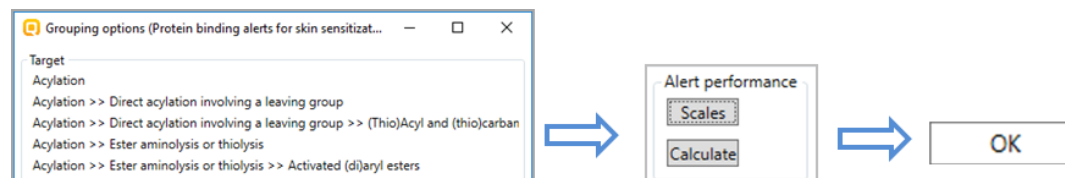
or by a specific 2D or 3D parameters →



To identify the analogues of the target accounting for metabolic activation of the chemicals based on specific criteria select →

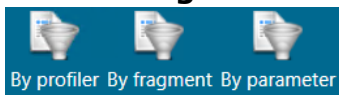


To check how much relevant to a target endpoint an alert is, once search **by profiler/with metabolism** is selected then calculate the Alert performance:



Select of the criteria available within the **Subcategorization section** to refine a

chemical category on the data matrix →



To identify the subgroups within an existing category that are determined by the

definitions of the currently selected profiling method →



To assess the consistency of the defined category →



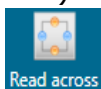
! The category consistency is endpoint specific. Four layers of information are considered important: Physicochemical similarity; Structural similarity and Mechanistic similarity and ADME similarity.

! The highlighted profiles correspond to the selected endpoint in the data matrix or to the previously defined endpoint if any.

Step 5: Data gap filling - Predict missing data by read-across, trend analysis, QSAR models or automated/standardized workflows

Select data gap filling by clicking in the corresponding cell in the data matrix, and then select one of the data gap filling methods:

- Read-across: for “qualitative” endpoints (skin sensitization or mutagenicity e.g. positive, negative, equivocal) or for “quantitative endpoints” (e.g., 96h-LC50 for fish) if only very few analogues with experimental results are identified. →



- Trend analysis: for “quantitative” endpoints if many analogues with experimental results are identified. →

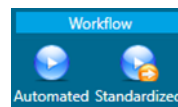


- (Q)SAR models: if no analogue with experimental results is identified or to build a weight of evidence case. →

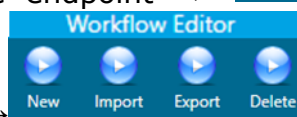


- Standardized and Automated workflows: once started, they follow the implemented logic and finish with prediction. They include read-across or trend

analysis method depending on the endpoint →



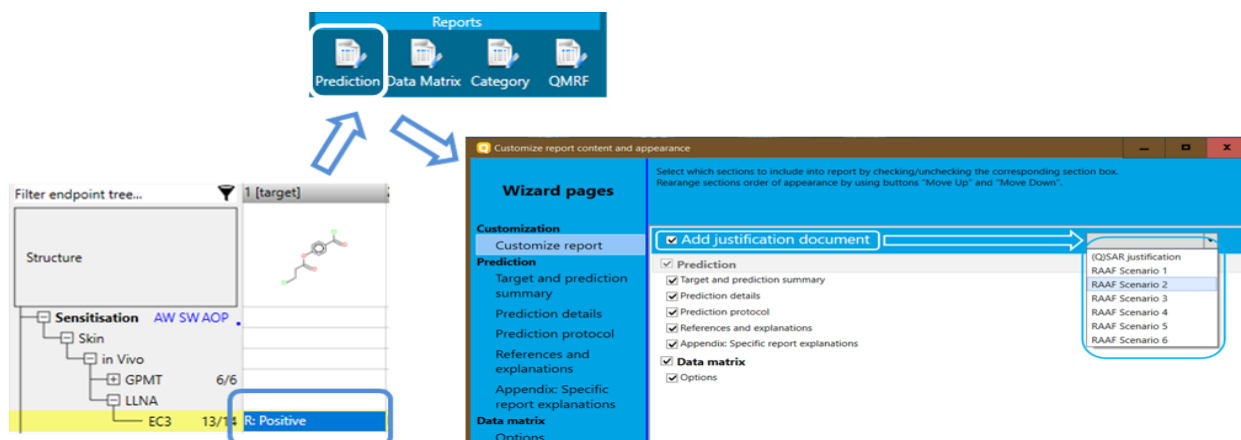
import/export your own workflows →



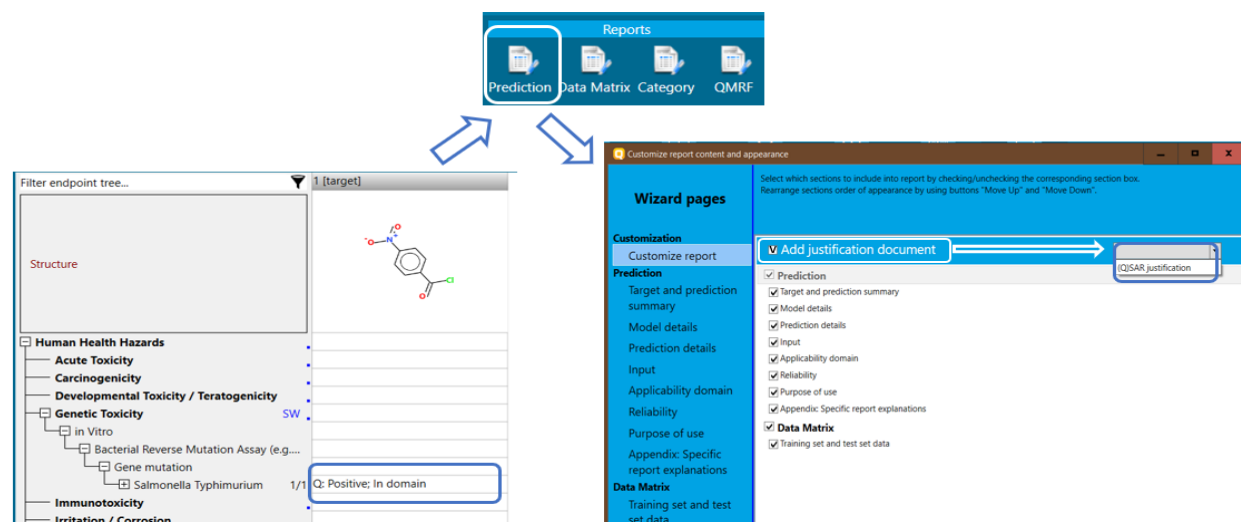
Step 6: Report – Obtain a detailed report for your prediction or category

Prediction is needed to generate a *Prediction* report.

Read across Assessment Elements could be included in a separate justification document in case of regulatory interest, by selection of a **RAAF scenario**.

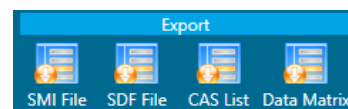


For predictions from a (Q)SAR model, the **(Q)SAR justification** document including (Q)SAR assessment elements, can be selected.



Four export types are also available in Toolbox v.4.9 →

The Export allows exporting of various information from the current data matrix.



! Each of the above illustrated functionalities is explained in details in the F1 help file available with installation (press F1).