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 everytime 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"

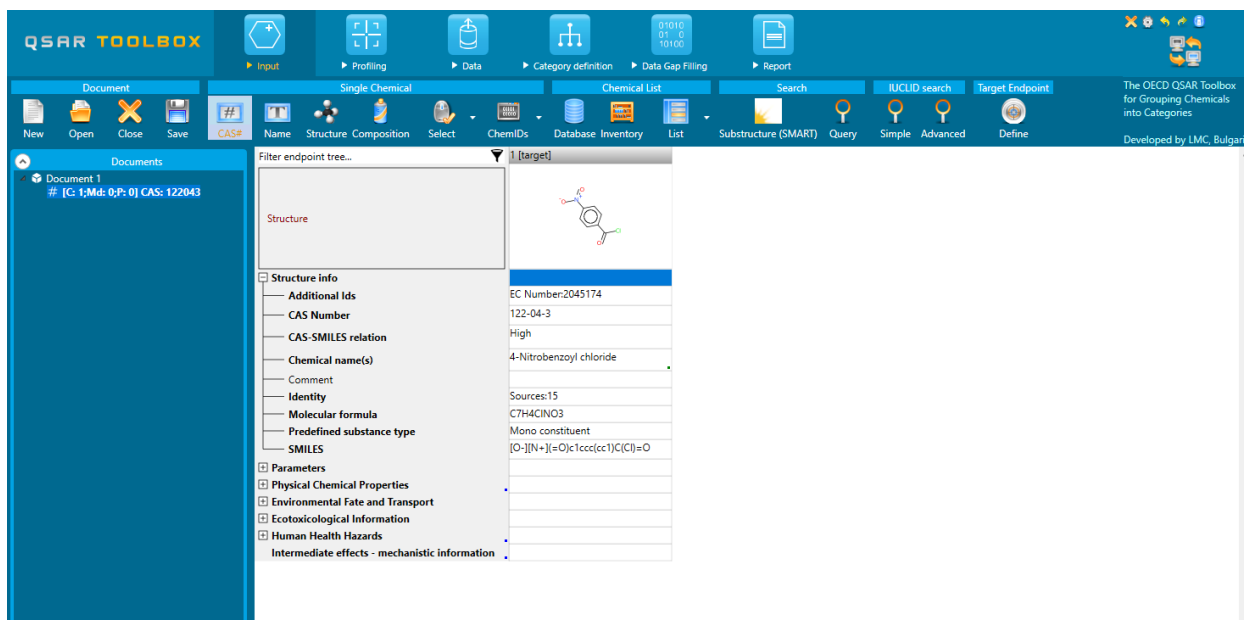Define your target chemical by Chemical Name, CAS number, SMILES, drawing the molecule or selecting it from a list. To define a chemical by CAS number:

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

Search → the program displays the structure → **OK**

The structure is displayed on the data matrix.

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

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

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

💡 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 [View].

💡 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 → [Gather] . The retrieved information is displayed according to five subsections in the endpoint tree:
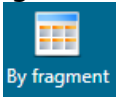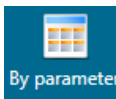

💡 To open the data tree: left-click on the nodes. To access detailed information on the experimental results: double-click on the result in the matrix.
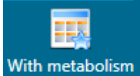
💡 The highlighted databases correspond to the selected endpoint in the data matrix or to the previously defined endpoint if any.

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

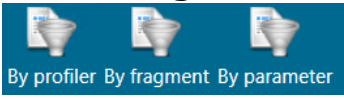Select one of the grouping methods available in the **Categorization section**.

To collect analogues of a target chemical based on its profiling result, use → .

Analogues of a target chemical could be searched also based on the fragment(s) defined by user → or by a parametric criterion → .

To identify the analogues of the target chemical accounting for its metabolic activation or based on specific criteria defined for the parent and/or generated metabolites, 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:
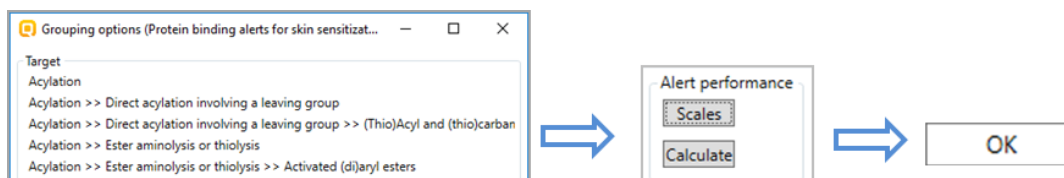
Select of the criteria available within the **Subcategorization section** to refine a chemical category on the data matrix → .

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. →
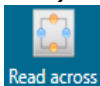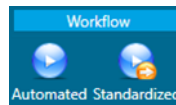

- Trend analysis: for "quantitative" endpoints if many analogues with experimental results are identified. →
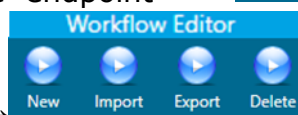
- (Q)SAR models: if no analogue with experimental results is identified or to build a weight of evidence case. →

- 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 → . To create or import/export your own workflows → .
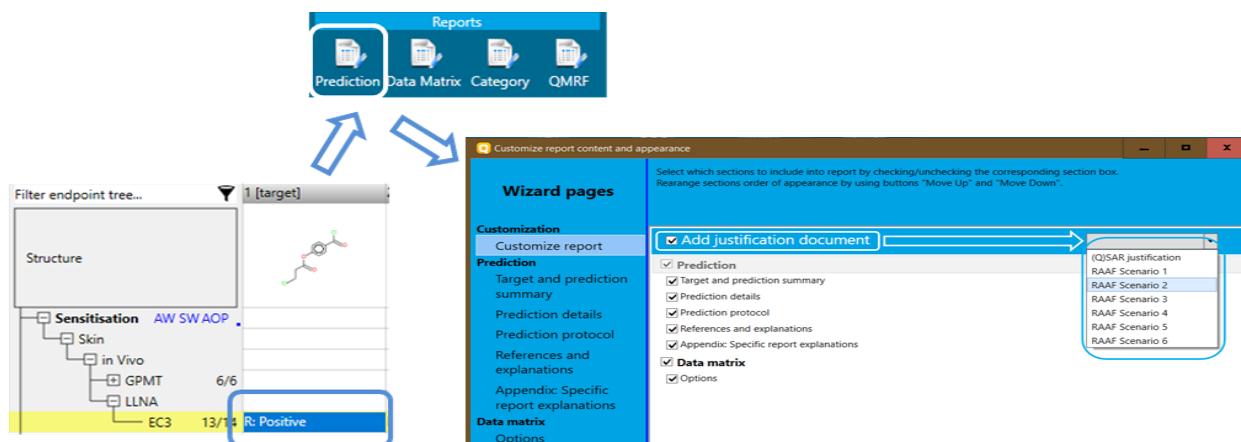
Step 6: Report – Obtain a detailed report for your prediction or category

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 TB 4.7. →
The Export allows exporting of various information from the current data matrix.
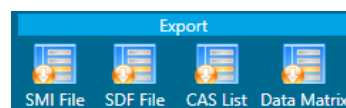
🛈 Each of the above illustrated functionalities is explained in details in the F1 help file available with installation (press F1).