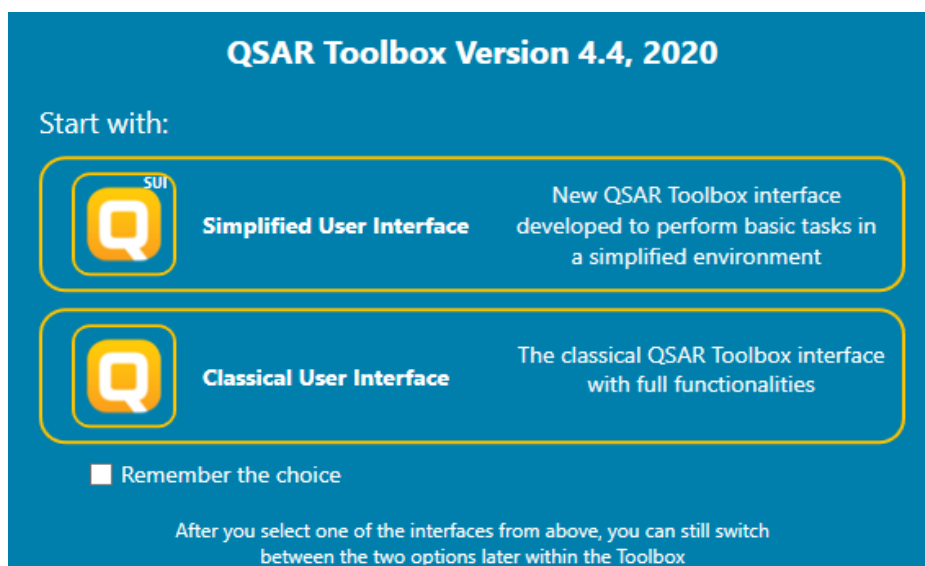


## GETTING STARTED: QUICK REFERENCE GUIDE FOR THE CLASSICAL USER INTERFACE


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.

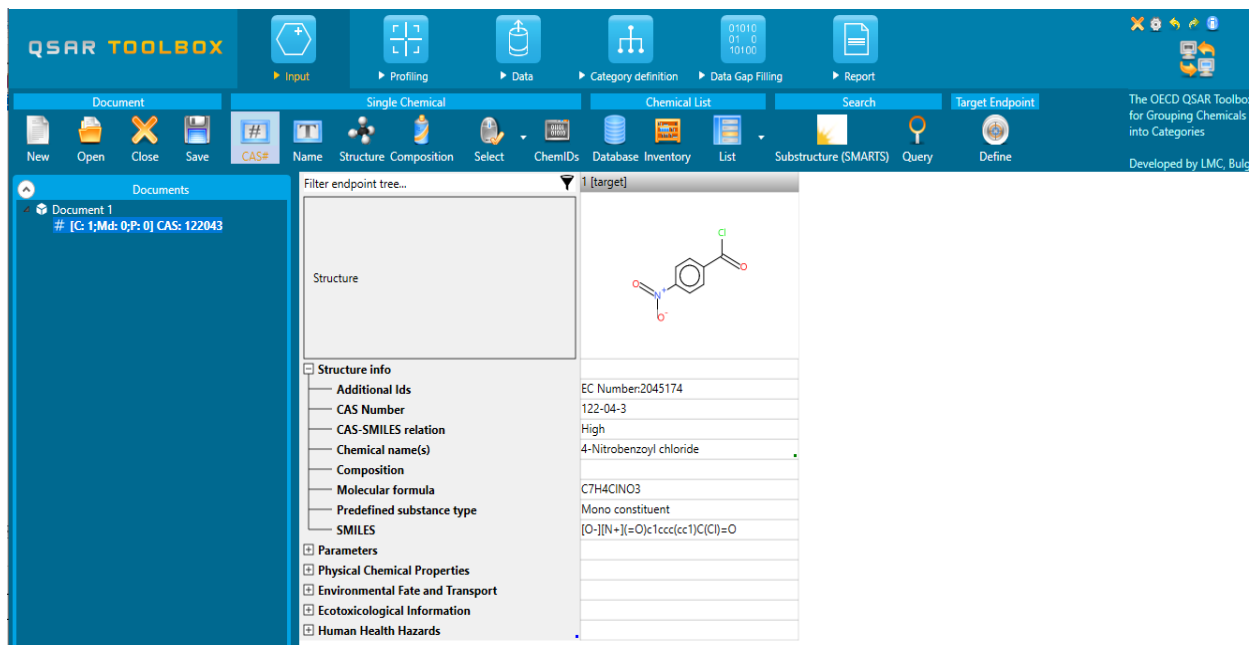
### Step 1: Input - Define chemical of interest or "target chemical"

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  → enter the number, and then click

 → the program displays the structure → 


The structure is displayed on the data matrix.



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.

QSAR TOOLBOX

Input Profiling Data Category definition Data Gap Filling Report

Profiling Custom profile

Apply View New Delete

Documents

Profiling methods

Options

Select All Unselect All Invert

Predefined

- Database Affiliation
- Inventory Affiliation
- OECD HPV Chemical Categories
- Substance type
- US-EPA New Chemical Categories

General Mechanistic

- Biodeg BioHC half-life (Biowin)
- Biodegradation primary (Biowin 4)
- Biodegradation probability (Biowin 1)
- Biodegradation probability (Biowin 2)
- Biodegradation probability (Biowin 5)
- Biodegradation probability (Biowin 6)
- Biodegradation probability (Biowin 7)
- Biodegradation ultimate (Biowin 3)
- DNA binding by OASIS
- DNA binding by OECD
- Estrogen Receptor Binding
- Hydrolysis half-life (Ka, pH 7)(Hydrowin)
- Hydrolysis half-life (Ka, pH 8)(Hydrowin)
- Hydrolysis half-life (Kb, pH 7)(Hydrowin)
- Hydrolysis half-life (Kb, pH 8)(Hydrowin)
- Hydrolysis half-life (pH 6.5-7.4)
- Ionization at pH = 1
- Ionization at pH = 4
- Ionization at pH = 7.4
- Ionization at pH = 9
- Protein binding by OASIS
- Protein binding by OECD
- Protein binding potency Cys (DPRA 13%)
- Protein binding potency GSH
- Protein binding potency Lys (DPRA 13%)
- Toxic hazard classification by Cramer
- Toxic hazard classification by Cramer (extended)
- Ultimate biodeg

Endpoint Specific

- Acute aquatic toxicity classification by Verhaar
- Acute aquatic toxicity MOA by OASIS
- Aquatic toxicity classification by ECOSAR
- Bioaccumulation - metabolism alerts

Filter endpoint tree...

1 [target]

Structure

Human Health Hazards

- Acute Toxicity
- Bioaccumulation
- Carcinogenicity
- Developmental Toxicity / Teratogenicity
- Genetic Toxicity
- Immunotoxicity
- Irritation / Corrosion
- Neurotoxicity
- Photoinduced toxicity
- Repeated Dose Toxicity
- Sensitisation
- ToxCast
- Toxicity to Reproduction
- Toxicokinetics, Metabolism and Distribution

Profile

- General Mechanistic
- DNA binding by OASIS
- DNA binding by OECD
- Protein binding by OASIS
- Protein binding by OECD

Radical

- Radical >> Radical mechanism via ROS...
- Radical >> Radical mechanism via ROS...
- Radical >> Radical mechanism via ROS...
- SN1
- SN1 >> Nucleophilic attack after diazo...


Acylation

- Acylation >> Direct Addition of an Acyl...
- Acylation >> Direct Addition of an Acyl...
- SN1
- SN1 >> Nitrenium Ion formation

Acylation



- Acylation >> Direct acylation involving...
- Acylation >> Direct acylation involving...
- Acylation
- Acylation >> Direct Acylation Involving...
- Acylation >> Direct Acylation Involving...

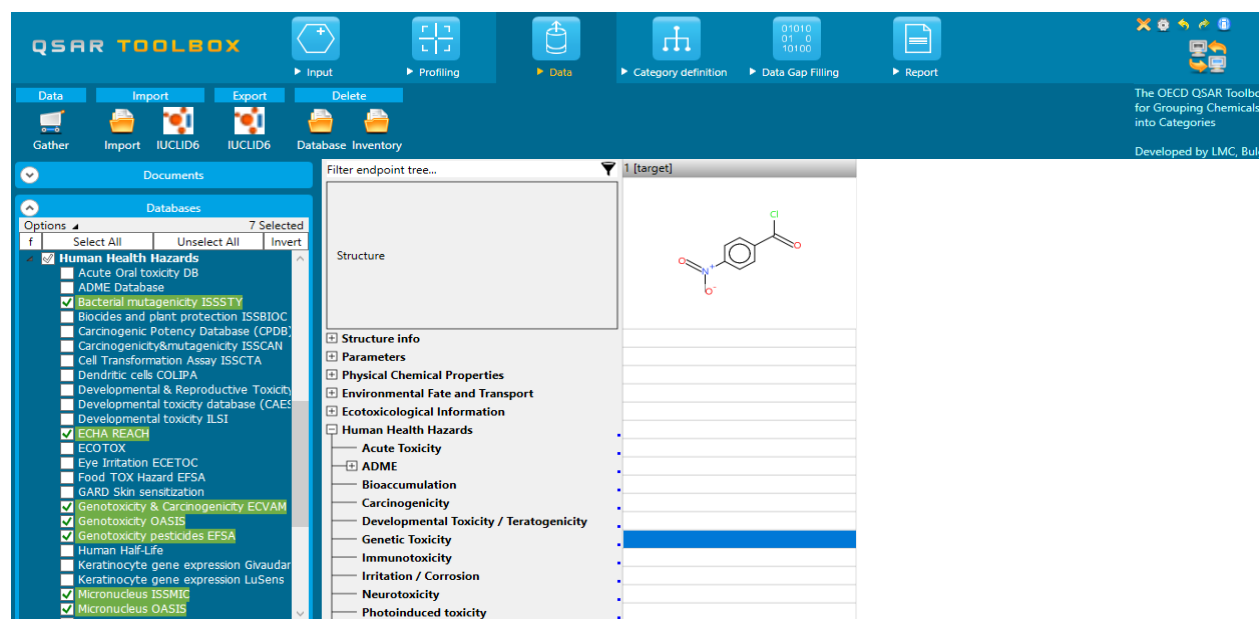
! To obtain the general background information on any profiler, right click on it and select **About**. To obtain the scientific information used to build the profiler,


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:




 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.

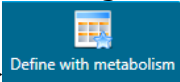
 The highlighted databases correspond to the selected endpoint in the data matrix or to the previously defined endpoint if any.

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

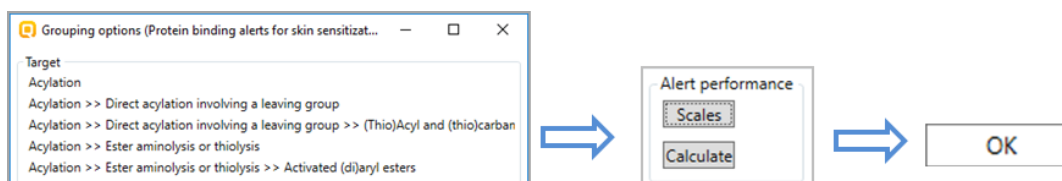
Select one grouping method according to the profile of your target chemical in the


window **Grouping methods** → .

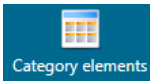
To identify the analogues of the target accounting for metabolic activation of the

chemicals based on specific criteria select → .

To check how much relevant to a target endpoint an alert is, once the **Define (with metabolism) button** is selected then calculate the Alert performance:



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 → 

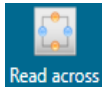
! The category consistency is endpoint specific. Three layers of information are considered important: Physicochemical similarity; Structural similarity and Mechanistic similarity.

! 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

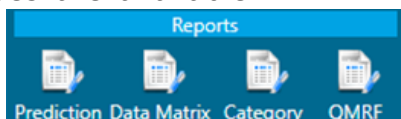
analysis method depending on the endpoint →



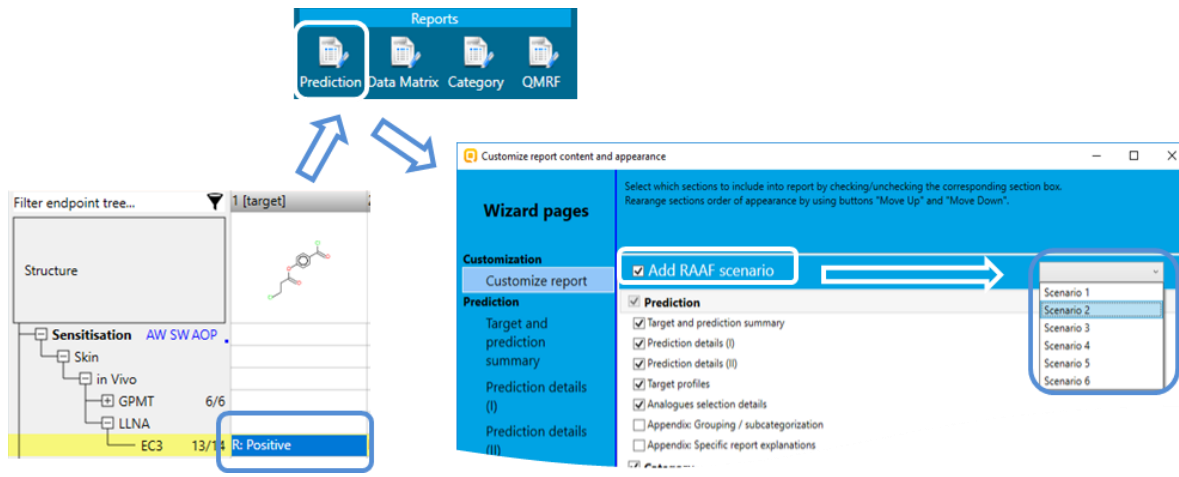
## Step 6: Report – Obtain a detailed report for your prediction or category

Four report types are available in TB 4.4. Prediction is needed for the *Prediction*

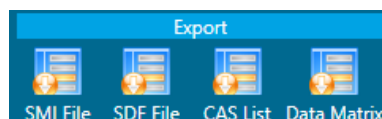
report, only. →



Read across Assessment Elements could be included to the report automatically by selection of **RAAF scenario**



Four export types are also available in TB 4.4. → 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).