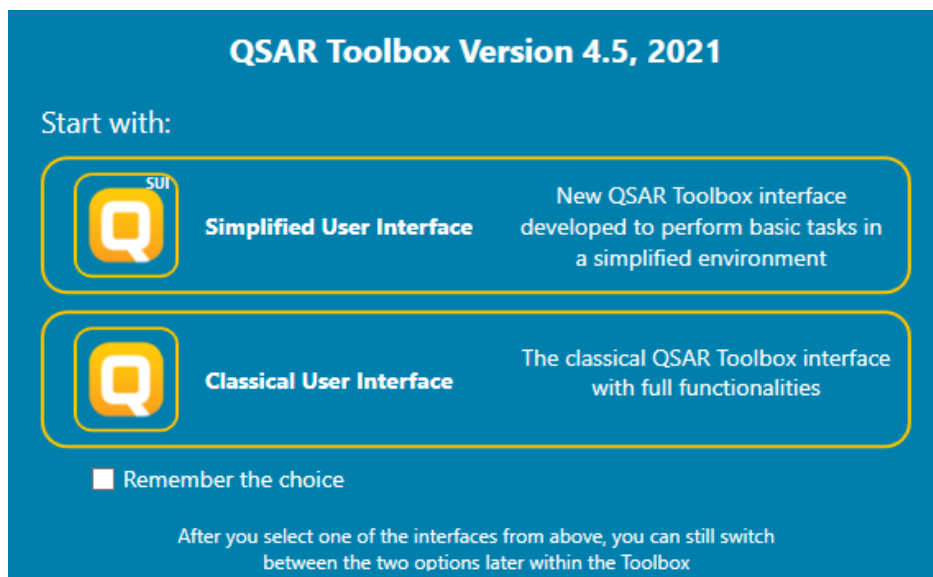



## GETTING STARTED: QUICK REFERENCE GUIDE FOR THE CLASSICAL USER INTERFACE


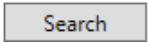
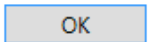
Choose which user interface you want to work with: *Simplified User Interface* or *Classical User Interface*.



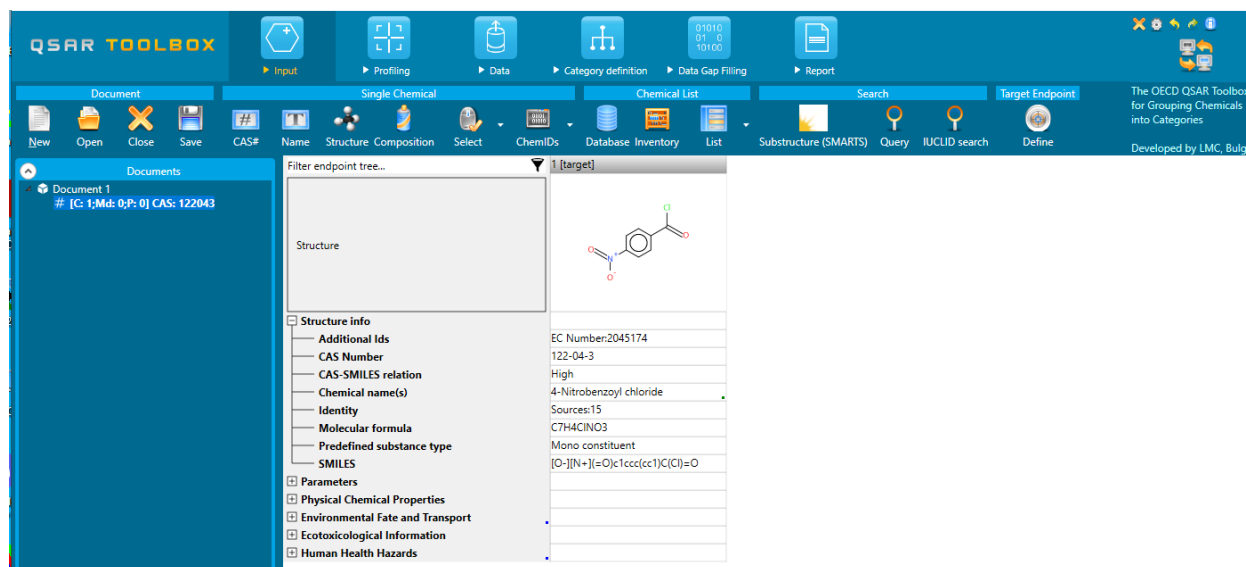
 If you want to use the same user interface everytime when you open the software then check **Remember the choice** checkbox before selecting one of the two interfaces.

### 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 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...

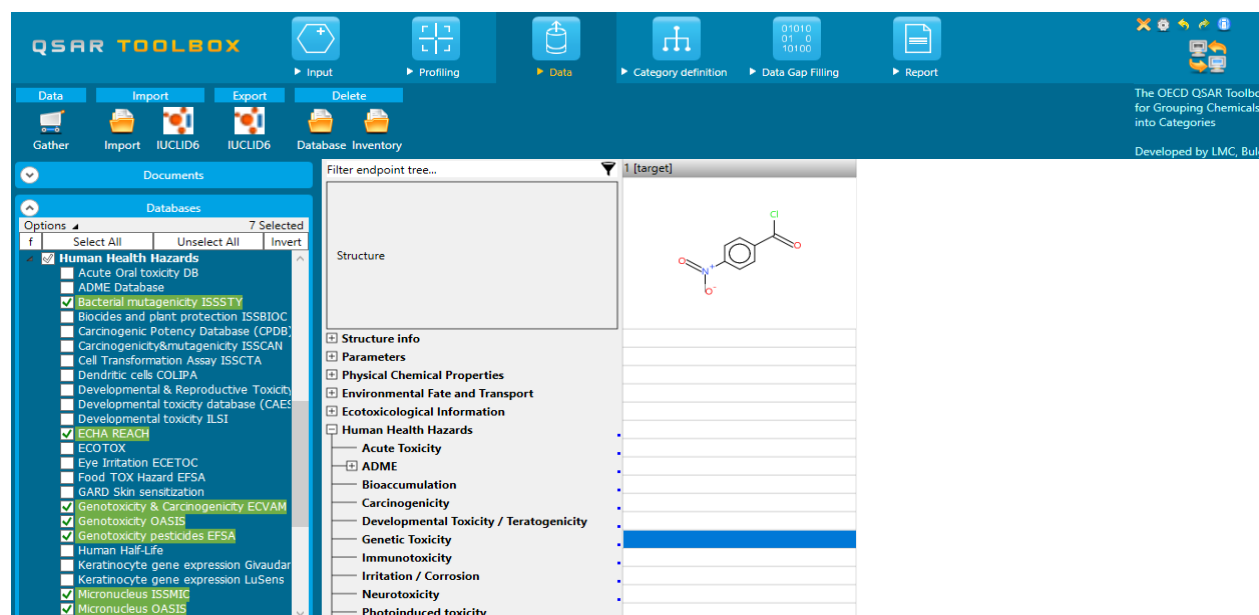
! To obtain the general background information on any profiler, right click on it and select **About**. To obtain the scientific information used to build the profiler,

select it and click .

! The highlighted profiles correspond to the selected endpoint in the data matrix or to the defined target 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.

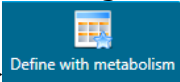
! The highlighted databases correspond to the selected endpoint in the data matrix or to the previously defined endpoint if any.

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

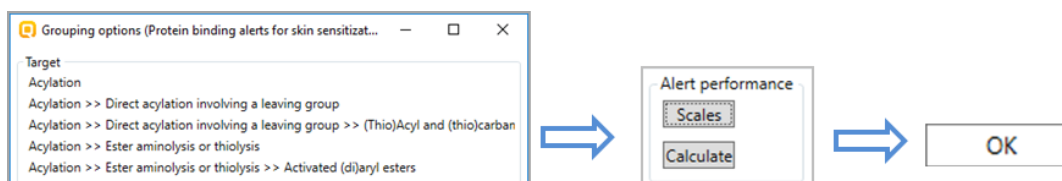
Select one grouping method according to the profile of your target chemical in the


window **Grouping methods** → .

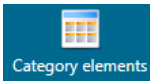
To identify the analogues of the target accounting for metabolic activation of the

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 → 

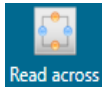
! The category consistency is endpoint specific. Three layers of information are considered important: Physicochemical similarity; Structural similarity and Mechanistic similarity.

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

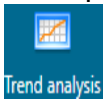
## **Step 5: Data gap filling - Predict missing data by read-across, trend analysis, QSAR models or automated/standardized workflows**

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

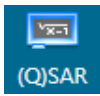
- Read-across: for “qualitative” endpoints (skin sensitization or mutagenicity e.g. positive, negative, equivocal) or for “quantitative endpoints” (e.g., 96h-LC50 for fish) if only very few analogues with experimental results are

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. Custom workflows can be

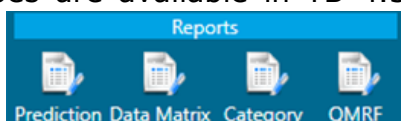
created, imported, exported or deleted →



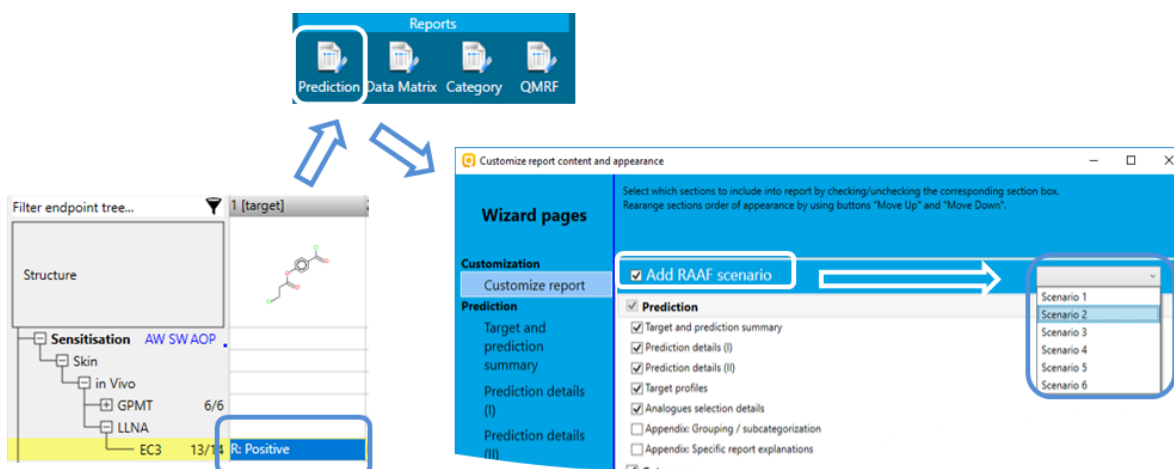
## Step 6: Report – Obtain a detailed report for your prediction or category

Four report types are available in TB 4.5. Prediction is needed for the *Prediction*

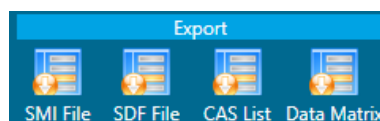
report, only. →



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



Four export types are also available in TB 4.5. → 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).