QSAR TOOLBOX

The OECD QSAR Toolbox for Grouping Chemicals into Categories

OECD QSAR Toolbox v.4.1

Tutorial of how to use Standardized workflow for ecotoxicological prediction

Aim

This is a step-by-step presentation designed to take the user of Toolbox through the Standardized workflow for ecotoxicity prediction.

Outlook

- Aim
- Ecotoxicological prediction
- Workflow of the exercise
- Report

Outlook

- Aim
- **Ecotoxicological prediction**
- Workflow of the prediction
- Report

Outlook

Ecotoxicological prediction:

- Acute aquatic toxicity

- *Fish*, LC50 (EC50), 96h, mortality

or

- *Invertebrates*, EC50(LC50),48h,mortality, immobilization, intoxication

or

- *Algae*, LC50 (EC50), 72-96h, population or growth

Outlook

- Aims
- Ecotoxicological prediction
- **Workflow of the prediction**
- Report

Workflow: Steps

- Input of target chemical(s)
- Data gap filling: Standardized workflow
- Report

Outlook

- Aims
- Ecotoxicological prediction
- **Workflow of the prediction**
    - **Chemical input**
    - Standardized workflow in Data-gap filling section
- Report

Chemical Input

- This module provides the user with several means of entering the chemical of interest or the target chemical.
- Since all subsequent functions are based on chemical structure, the goal here is to make sure the molecular structure assigned to the target chemical is the correct one.

Chemical Input
Ways of Entering a Chemical

I. Single target chemical:

- Chemical Name
- Chemical Abstract Services (CAS) number (#)
- SMILES (simplified molecular information line entry system) notation
- Chemical with defined composition
- Drawing chemical structure
- Select from User List/Inventory/Databases

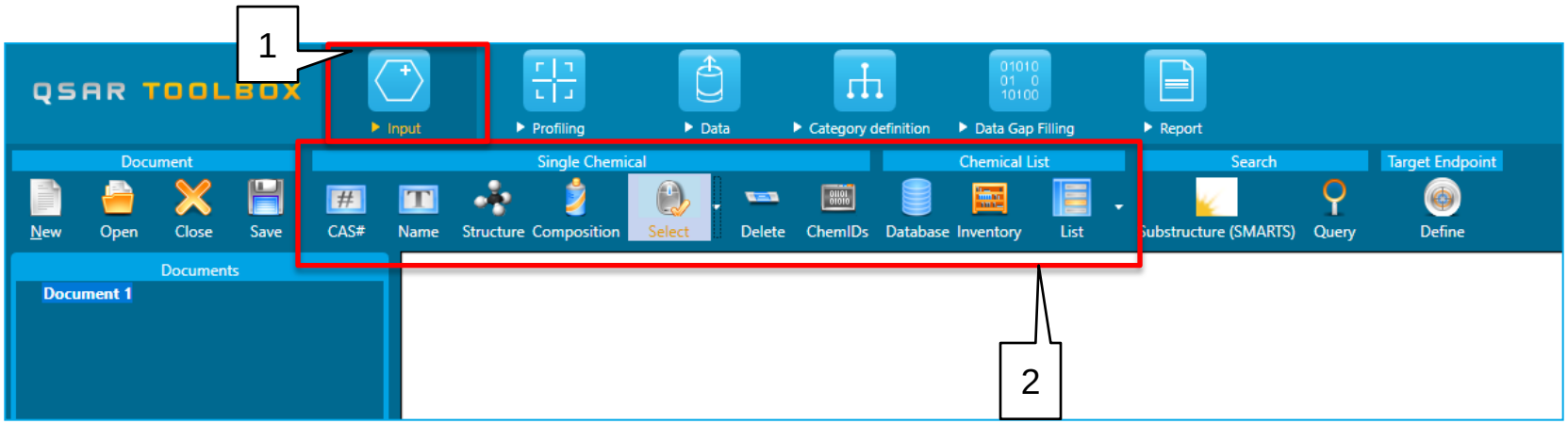
II. Group of chemicals:

- User's List
- Inventory/Database

Chemical Input: Single chemical

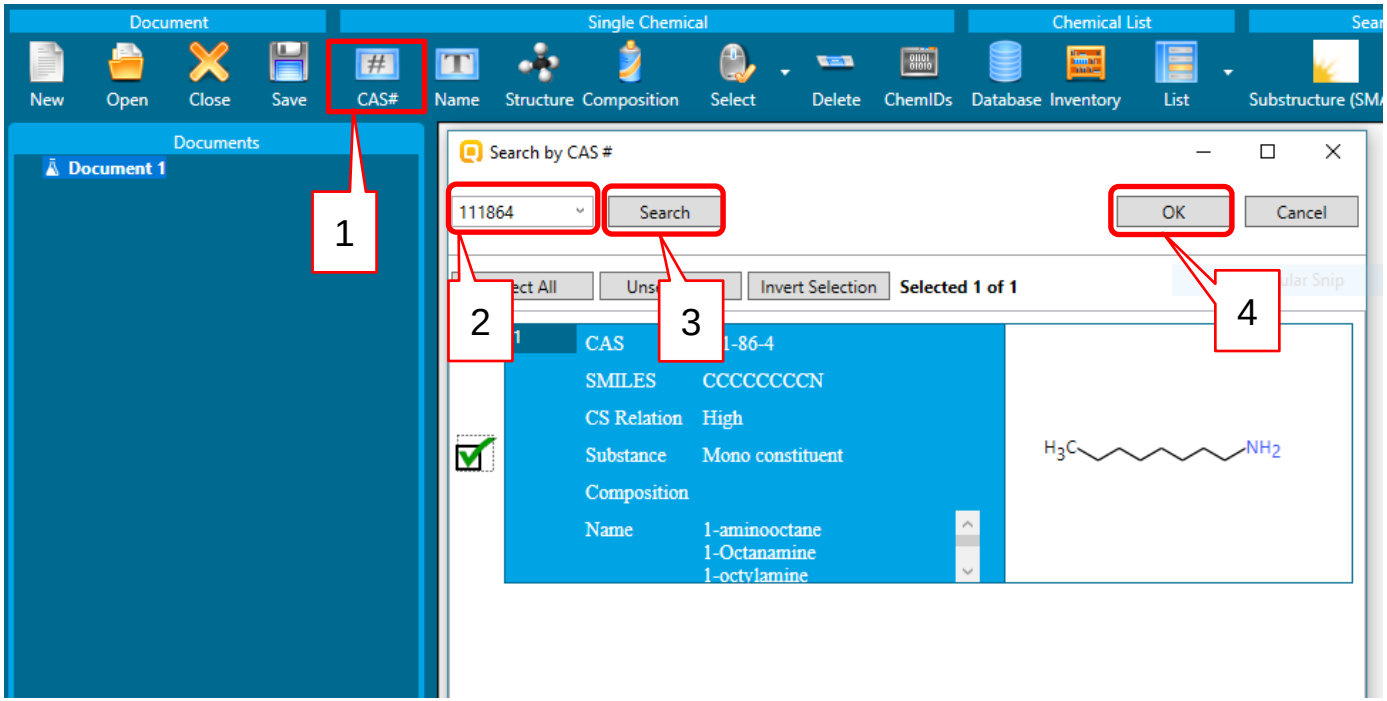
- Open the Toolbox.
- Click on “Input” (see next screen shot).

Chemical Input
Single chemical



1. Click on *Input (1)* to display the main Input section (2).

Chemical Input
Single chemical: CAS RN



1. Press CAS# (1); 2. Type in the CAS # (2) ; 3. Click on *Search* (3);
4. Press *OK* (5).

Outlook

- Aims
- Ecotoxicological prediction
- **Workflow of the prediction**
  - Chemical input
  - **Standardized workflow in Data gap filling section**
- Report

Data gap filling
An overview

- "Data Gap Filling" module gives access to three different data gap filling tools:
  - Read-across
  - Trend analysis
  - (Q)SAR models

- Depending on the situation, the most relevant data gap mechanism should be chosen, taking into account the following considerations:
  - Read-across is the appropriate data-gap filling method for "qualitative" endpoints like skin sensitisation or mutagenicity for which a limited number of results are possible (e.g. positive, negative, equivocal). Furthermore read-across is recommended for "quantitative endpoints" (e.g., 96h-LC50 for fish) if only a low number of analogues with experimental results are identified.
  - Trend analysis is the appropriate data-gap filling method for "quantitative endpoints" (e.g., 96h-LC50 for fish) if a high number of analogues with experimental results are identified.
  - "(Q)SAR models" can be used to fill a data gap if no adequate analogues are found for a target chemical.

Data gap filling
Standardized workflow: An overview

- Algorithms for standardized data gap filling (SWs) have been developed for skin sensitization (LLNA and GPMT data) and acute aquatic toxicity to fish, invertebrates and algae. Once started, the standardized workflows (SWs) follow an implemented logic.

- The main differences compared to the automated workflows (AWs) are that the domain of application is expanded in the SWs (including other species, durations, etc.) and SWs allow interactions by the user and thus, different selection than those in AW could be done.

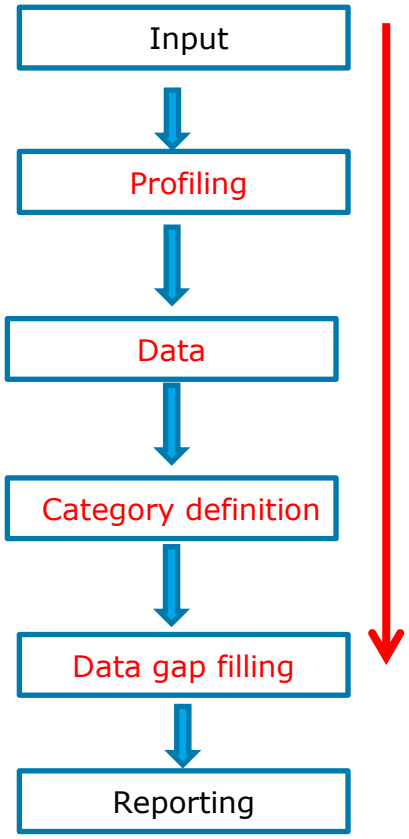
Data gap filling
Standardized workflow: An overview

- The Standardized workflow can be used in a single chemical mode or in a batch mode.

- In this tutorial only single chemical mode for acute aquatic toxicity to fish is discussed.

Data Gap Filling
Overview

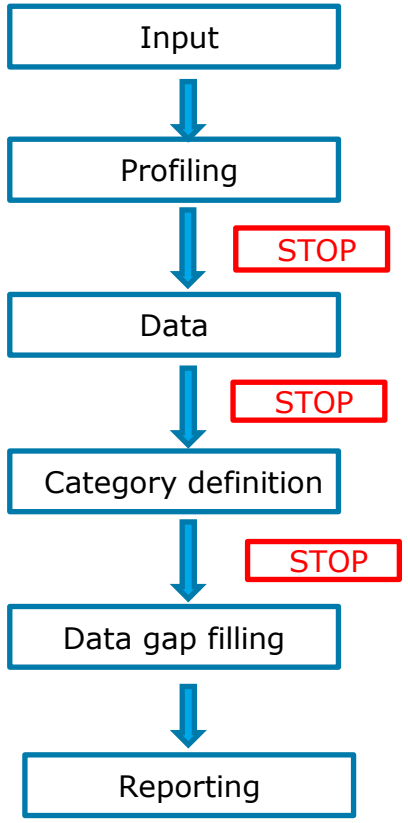
Automated workflow (AW)



Same components as defined in the AW are used in the SW

The SW pauses at each of the stages and user is able to make different selection than those implemented in the AW

Standardized workflow (SW)



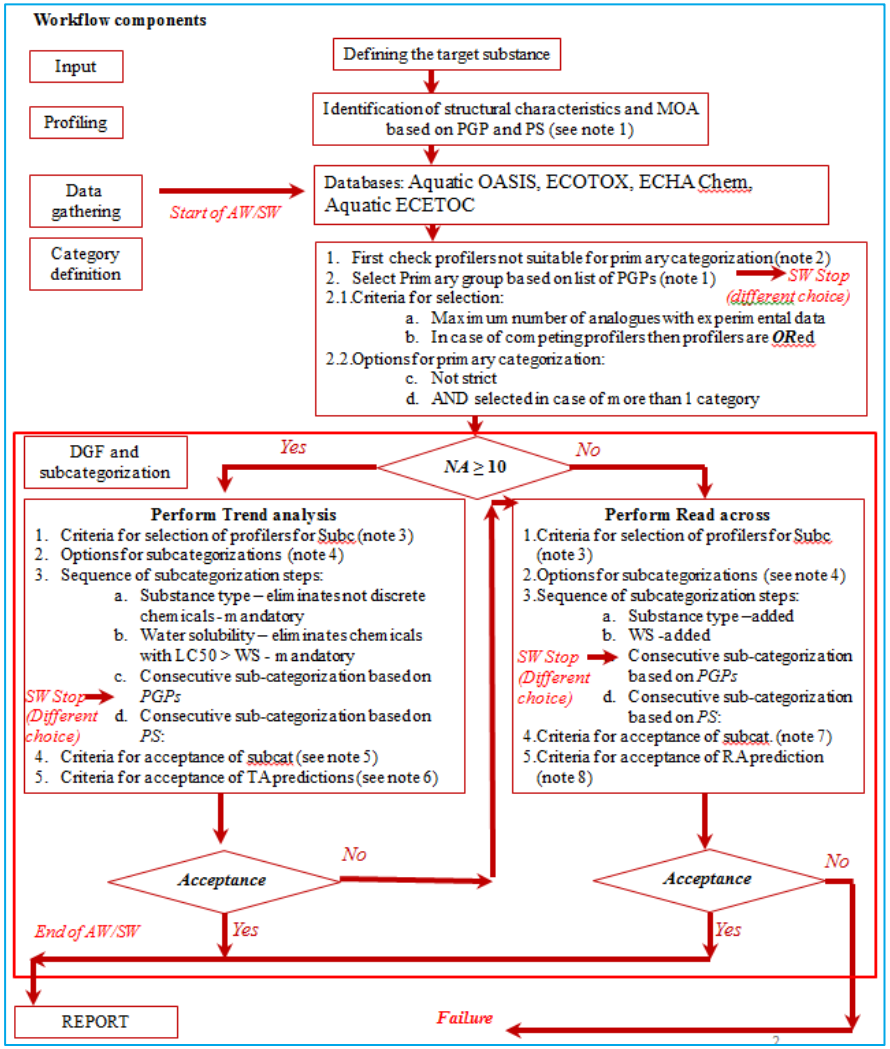
Databases with data for the target endpoint are listed and user select to use all of them or make specific selection

Relevant to the workflow profilers appropriate for DGF are listed and ordered hierarchically based on the population of the group and user is able to select any of them

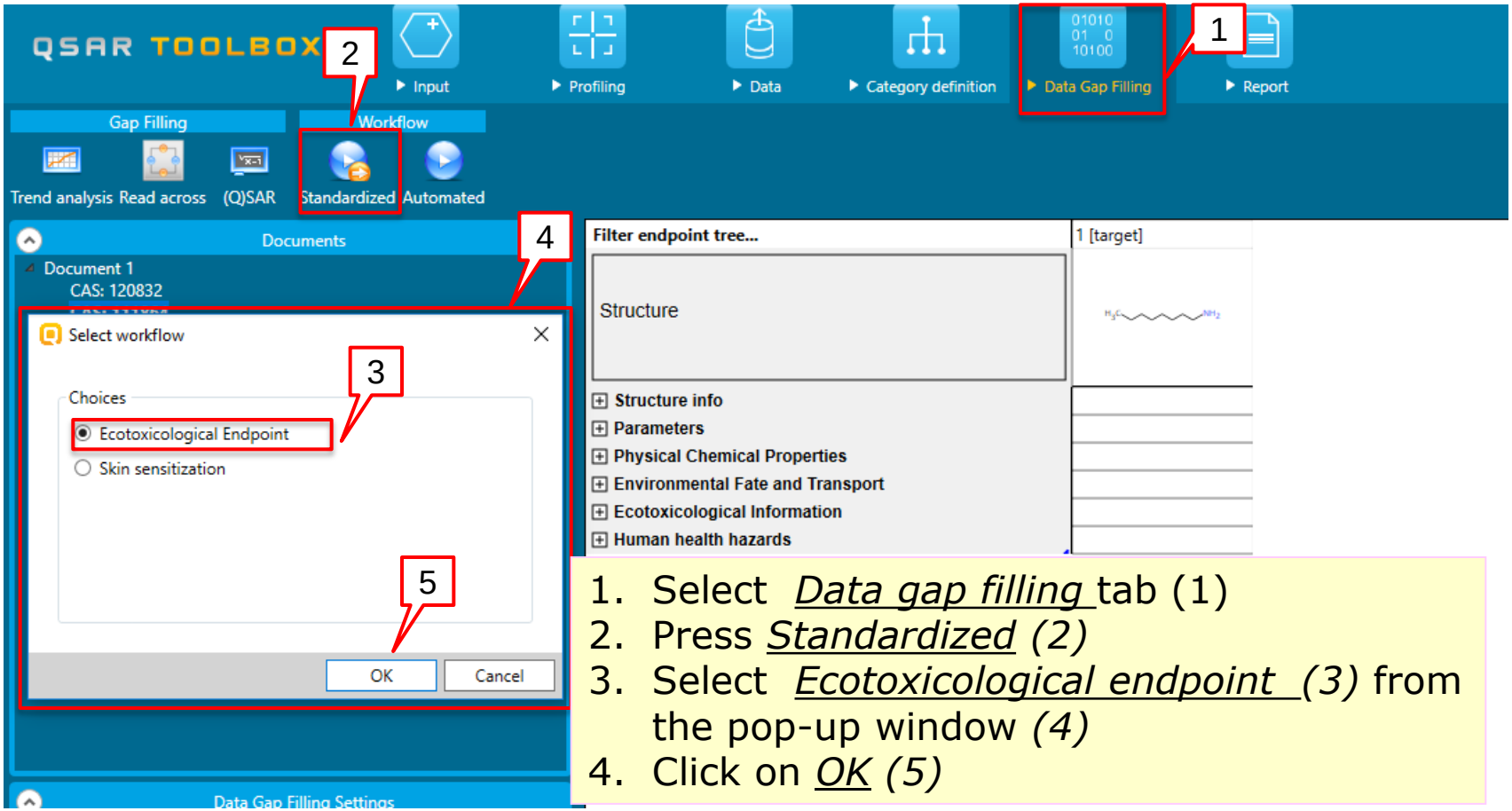
Additional data filtering could be applied (e.g. different species selection)

Data Gap Filling

Algorithm of Ecotoxicological workflow



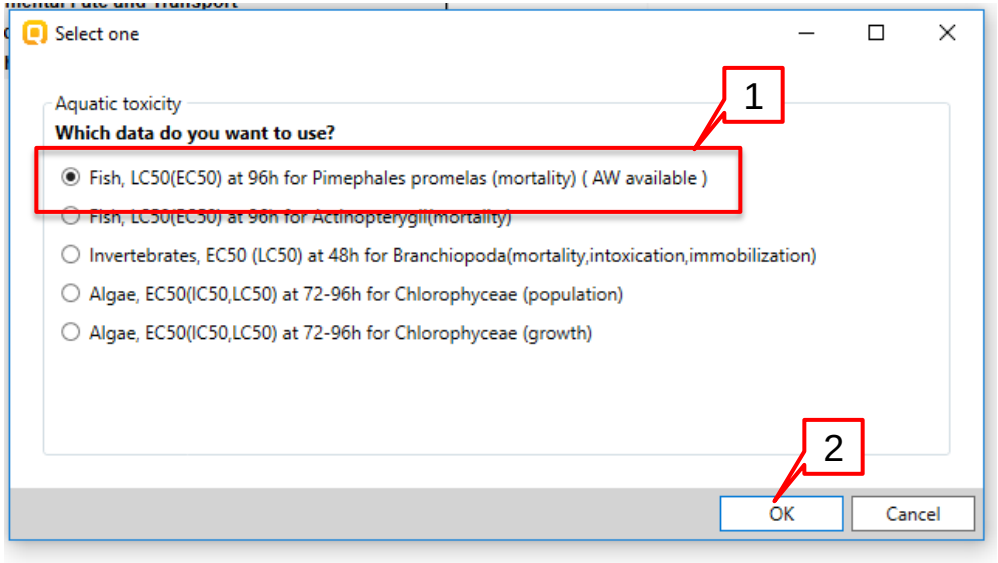
Data Gap Filling
Standardized workflow: single chemical



1. Select *Data gap filling* tab (1)
2. Press *Standardized (2)*
3. Select *Ecotoxicological endpoint (3)* from the pop-up window *(4)*
4. Click on *OK (5)*

Data Gap Filling
Standardized workflow: single chemical

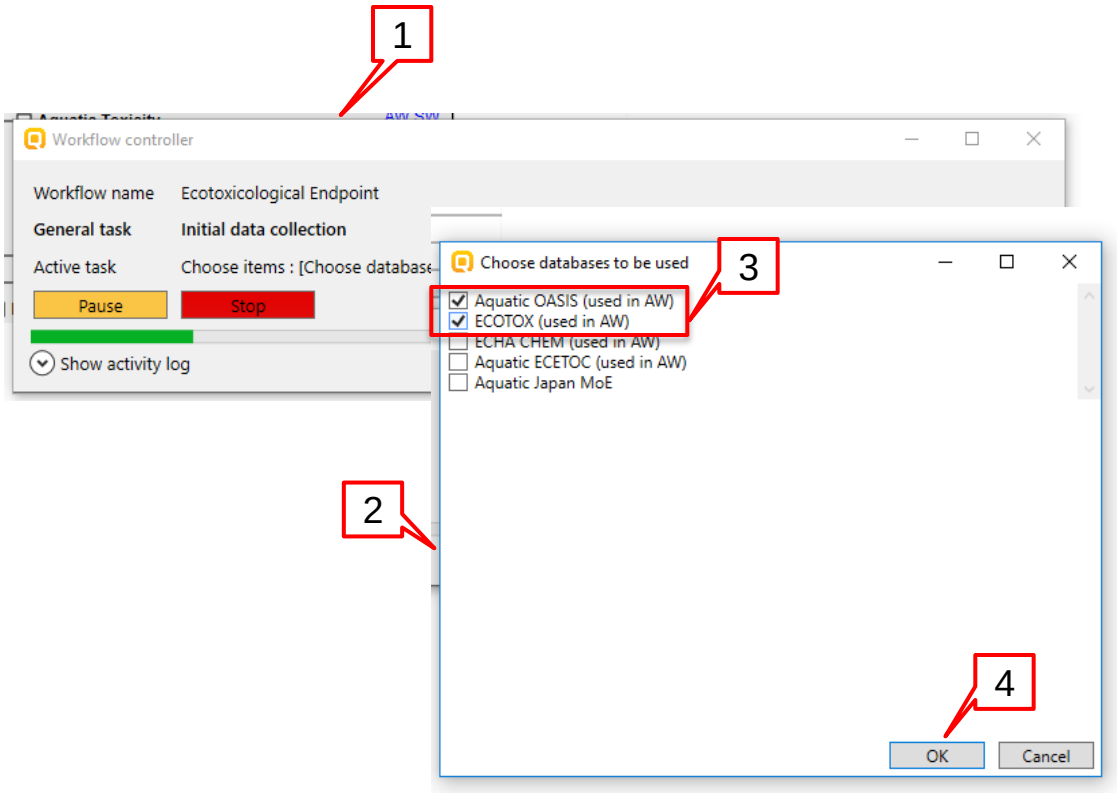
- A dialogue window gives the user a choice to select the end-point (1)
- *AW available in brackets* means that the endpoint is used in the automated workflow
- Click on *OK* (2)



Data Gap Filling
Standardized workflow: single chemical

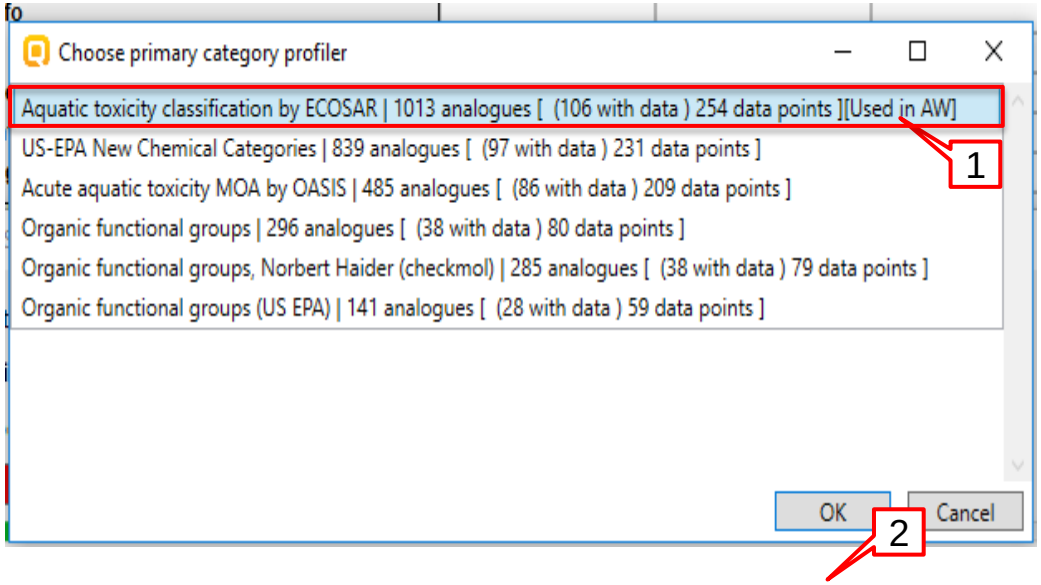
A workflow controller window (1) is displayed for a second and then a dialogue window for selection (2) of databases, which are recommended for use in the SW is displayed

- Indication about which databases are used in the AWs is also included in brackets
- Select the databases (3)
- Click on *OK*(4)



Data Gap Filling
Standardized workflow: single chemical

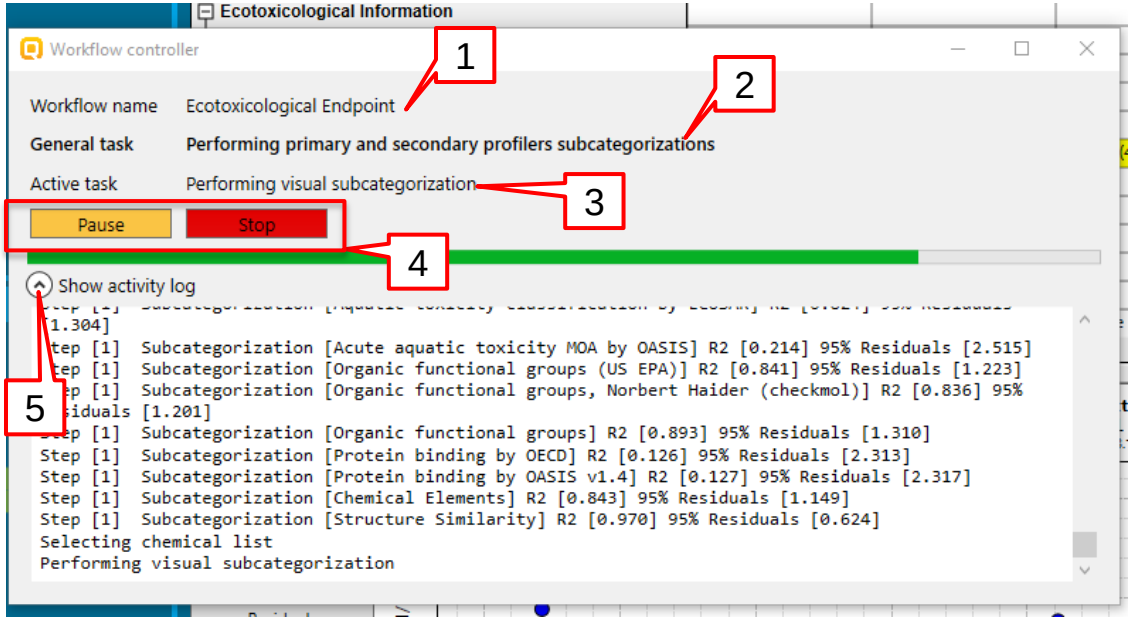
- A list with all primary category profilers is displayed, where you have to select the most suitable one
- Here, select *Aquatic toxicity classification by ECOSAR* (1) and then click on *OK* (2)



Data Gap Filling
Standardized workflow: single chemical

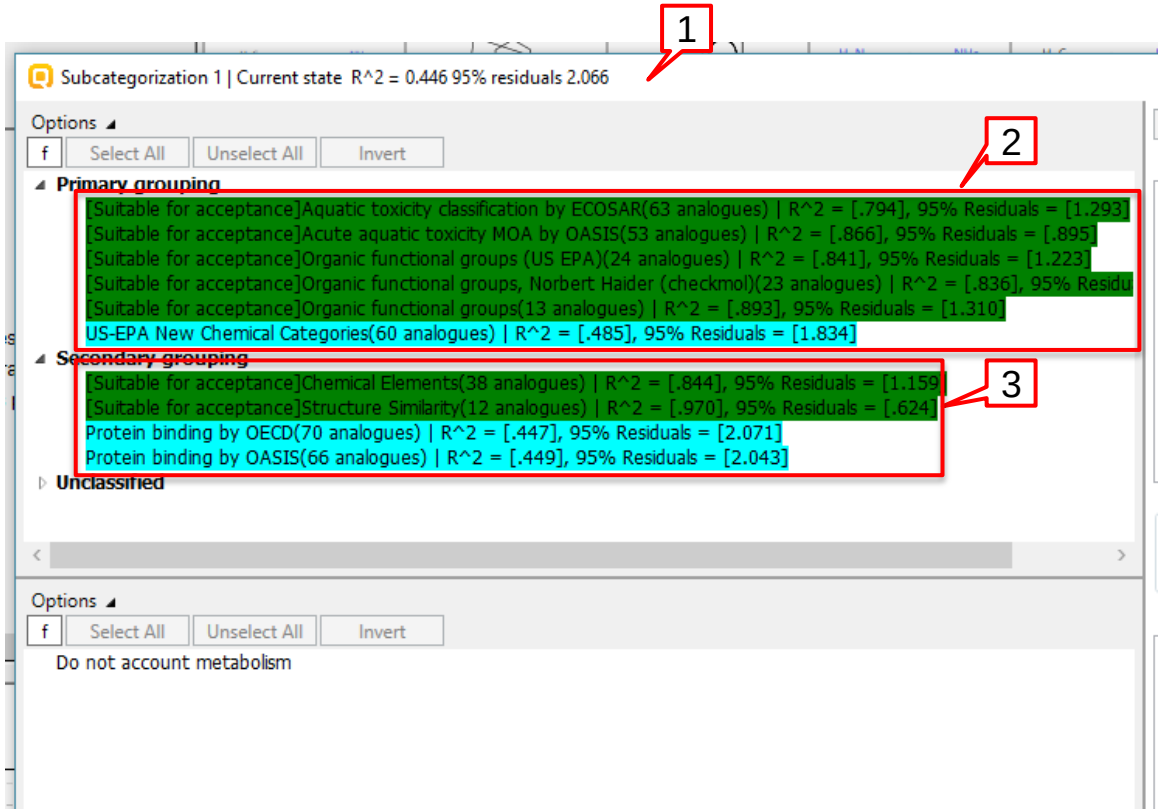
A workflow controller window is displayed throughout the standardized workflow procedure. It includes:

- Workflow name (1)
- General task (2)
- Active task (this is subtask of the general task, which is currently being performed)(3)
- Navigation options (4)
- Activity log (5)



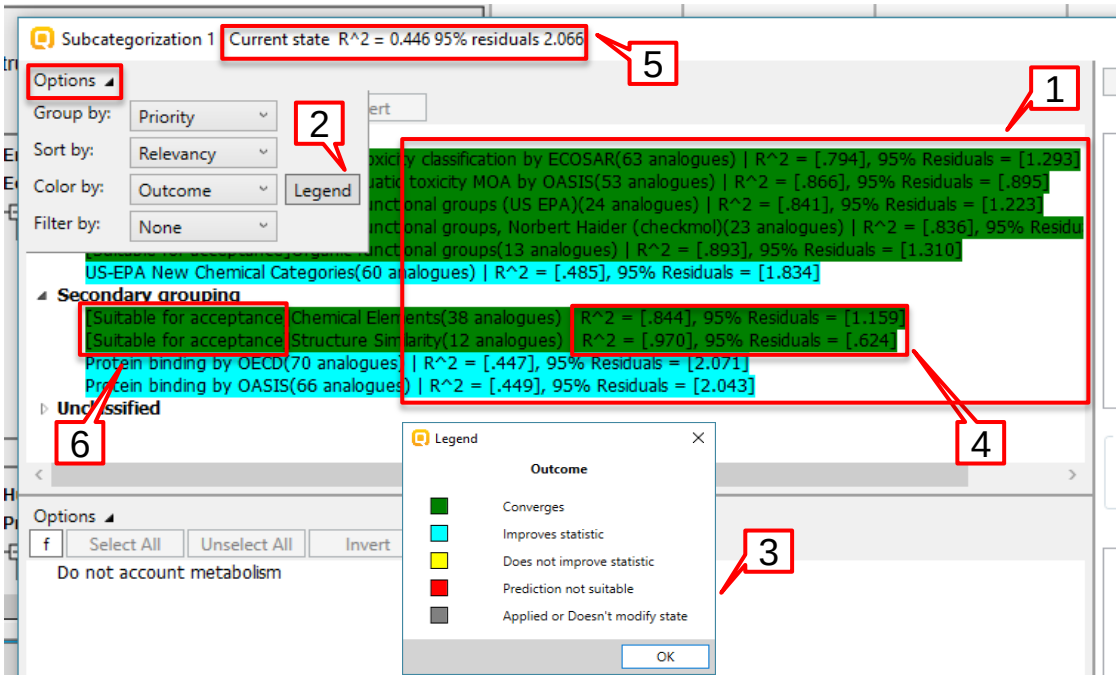
Data Gap Filling
Standardized workflow: single chemical

The subcategorisation window (1) is separated into two sections:
Primary grouping (2) and secondary grouping (3)



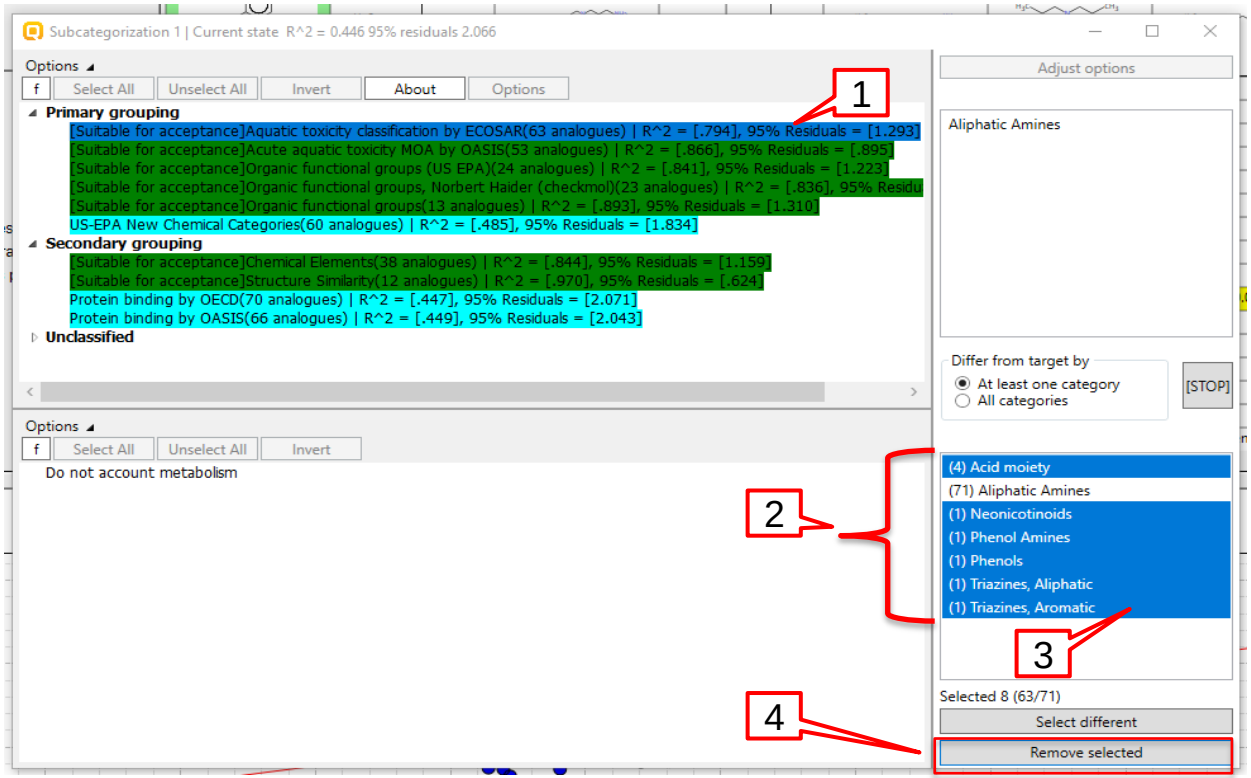
Data Gap Filling
Standardized workflow: single chemical

- Profilers are highlighted in different color (1)
- Click on *Options - Legend* (2) to display the colors' meaning (3)
- "Priority" factor along with criteria for acceptance of the prediction (4) as compared with the statistics of *the current state* (5)
- An indication for *suitability* (6) of the profiler for acceptance of the prediction is included

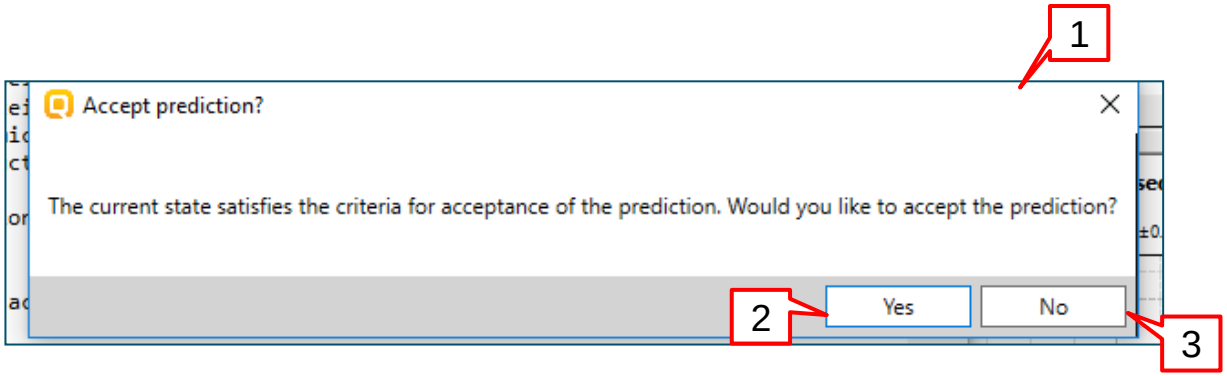


Data Gap Filling
Standardized workflow: single chemical

- Clicking on the first profiler (1) shows all categories found in the analogues (2) as the ones colored in blue (3) are the ones that are not applicable to the target chemical and hence can be removed (4)



Data Gap Filling
Standardized workflow: single chemical

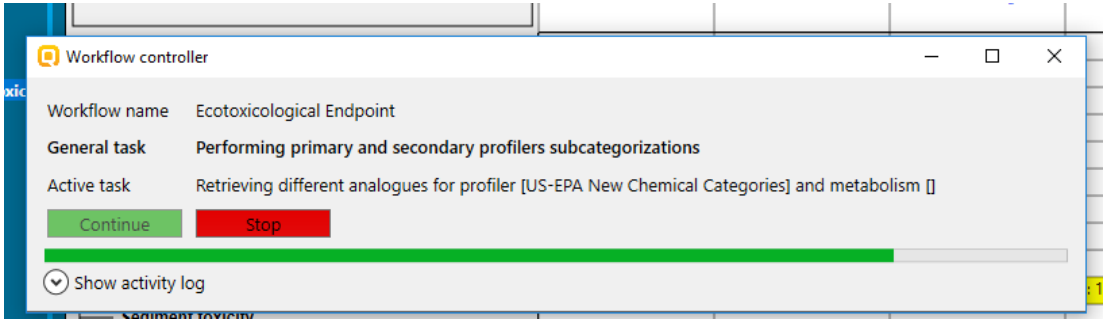


- An *Accept prediction?* window is visualized (1)
- Press Yes (2) , if you want to accept the prediction (next see slide 30)
- Press No (3) and continue with the workflow if you are not satisfy with the outcome (see slide 29)

Data Gap Filling
Standardized workflow: single chemical

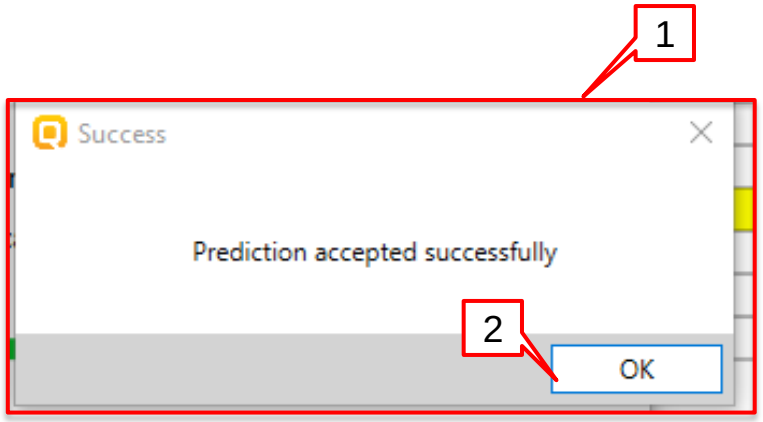
- **Press No (3) and continue with the workflow if you are not satisfy with the outcome.**

- Press *Continue* button (1) in the workflow controller
- Then repeat the steps described in slides 25-27



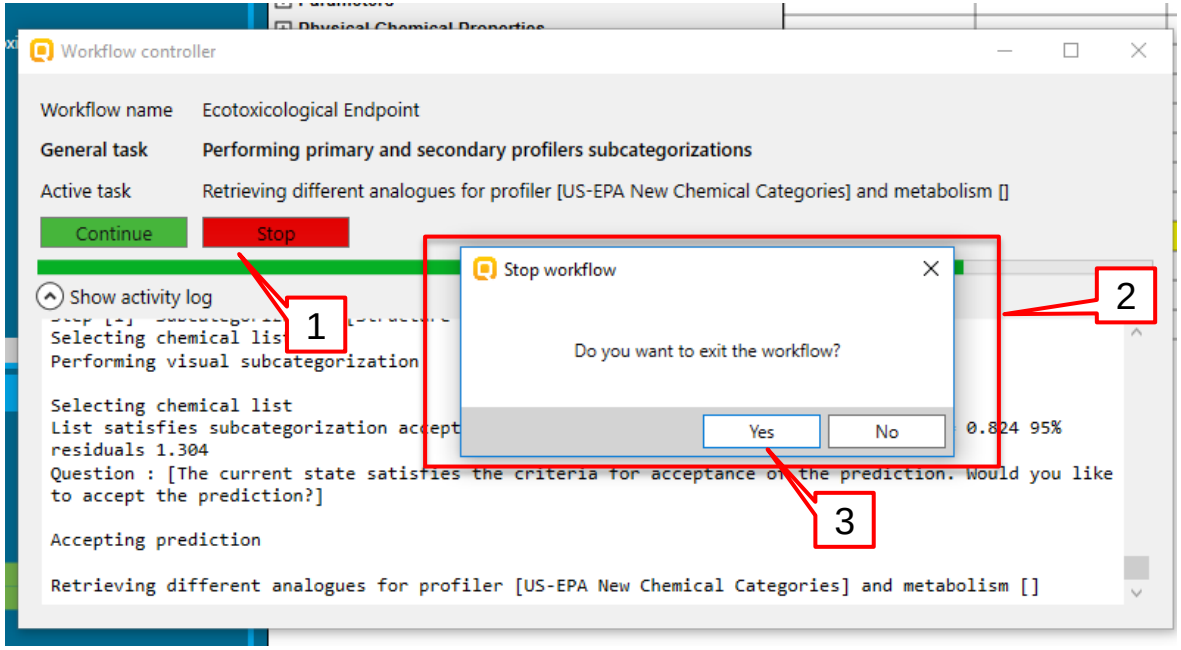
Data Gap Filling
Standardized workflow: single chemical

- A pop-up window (1) is displayed informing that the prediction is accepted
- Press *OK* (2)



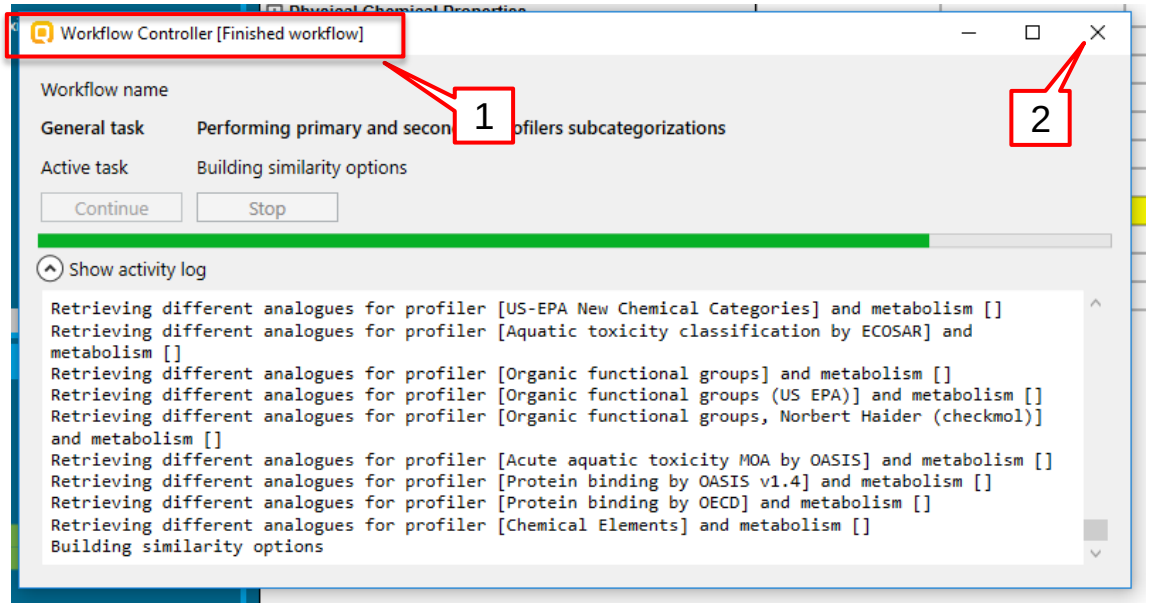
Data Gap Filling
Standardized workflow: single chemical

- Press *Stop* button (1) on the Workflow controller.
- A pop-up window (2) asks to confirm the exit of the workflow
- Press *Yes button*(3)

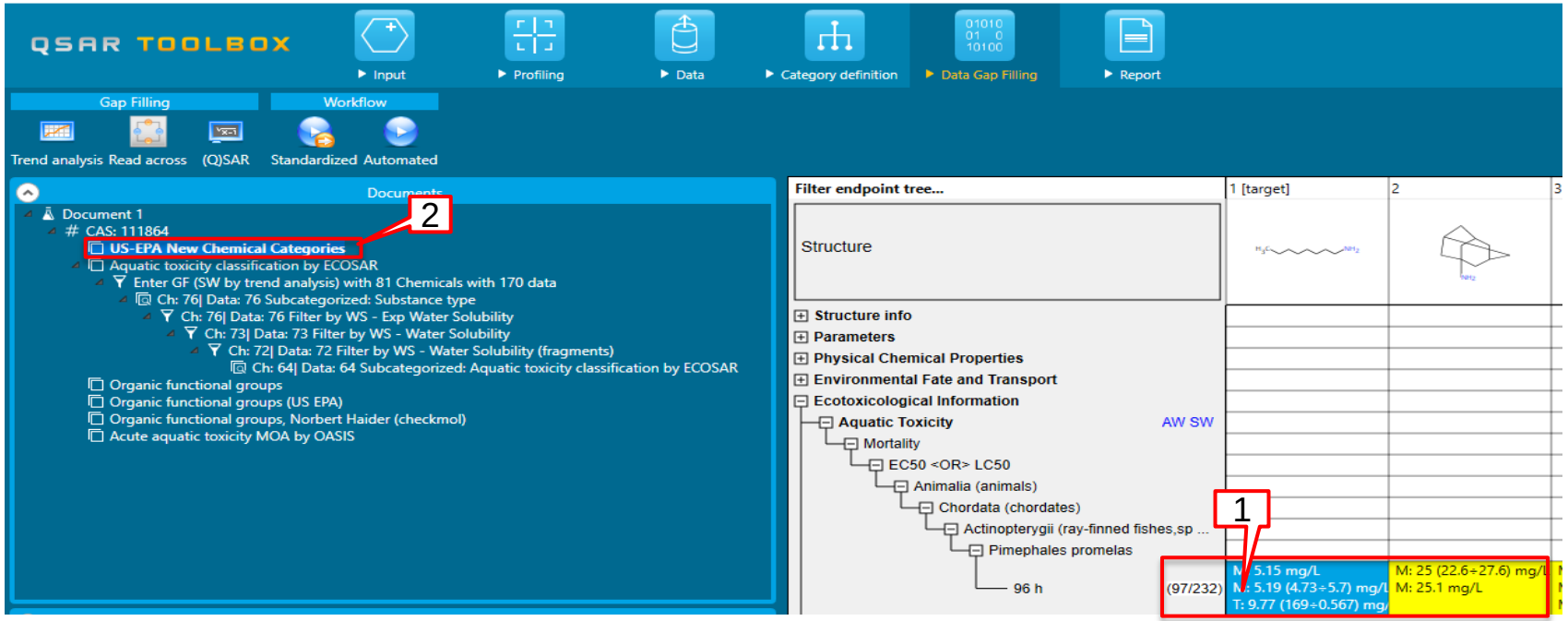


Data Gap Filling
Standardized workflow: single chemical

- A message is displayed that the workflow has finished (1)
- Press **X** button (2)



Data Gap Filling
Standardized workflow: single chemical

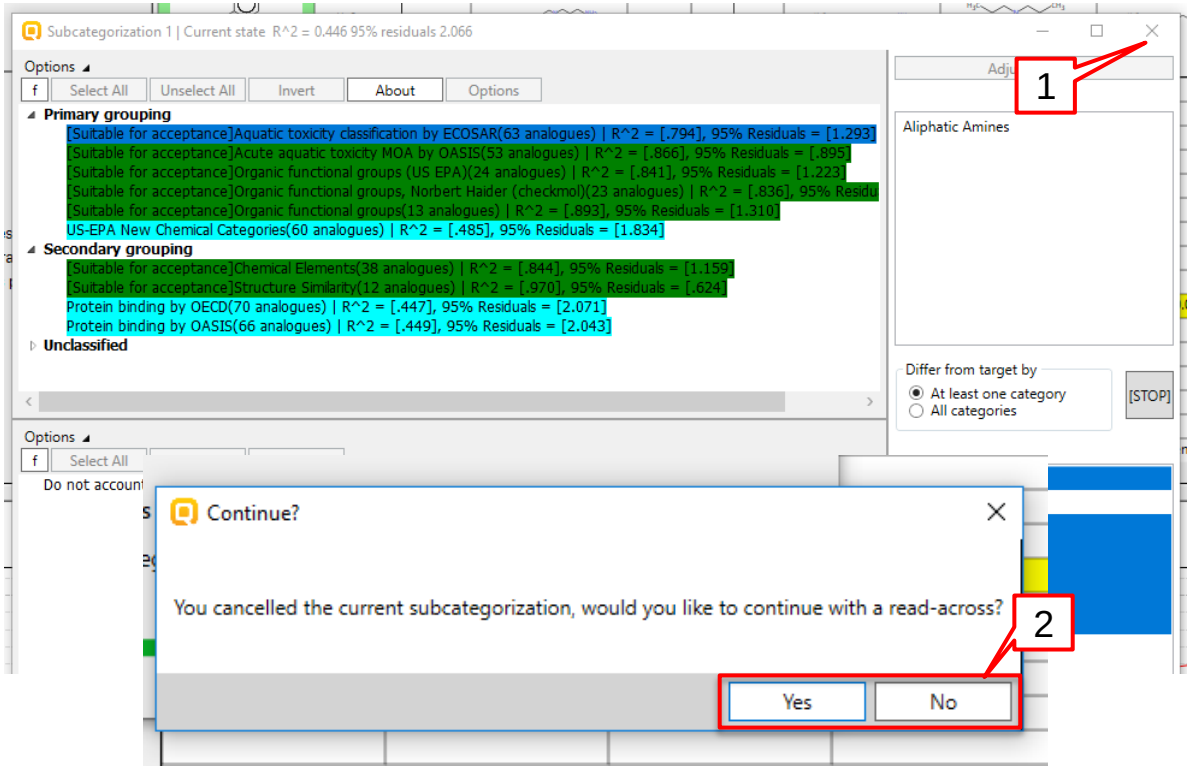


- The result is displayed on the data matrix (1) marked with “T”(“M” stands for measured data)
- The workflow finishes on the document level of the primary grouping(2)

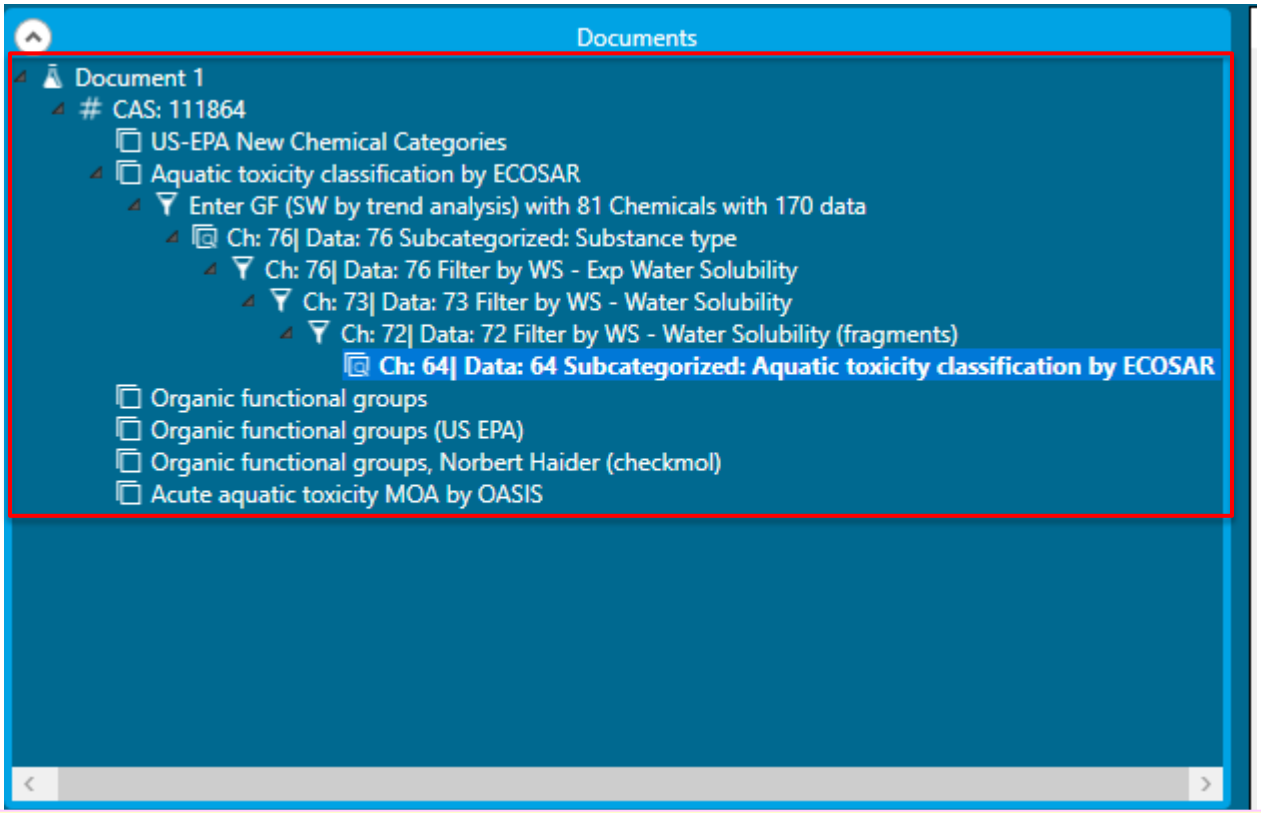
Data Gap Filling
Standardized workflow: single chemical

If the subcategorisation window is closed by pressing **X** button (1) without performing any subcategorization, a dialogue window is displayed (2):

- Press *Yes* if you want to exit the trend analysis and continue with read-across analysis.
- Press *No* if you want to finish the workflow.



Data Gap Filling
Standardized workflow: single chemical



The steps executed in the SW are listed in the Documents panel.

Outlook

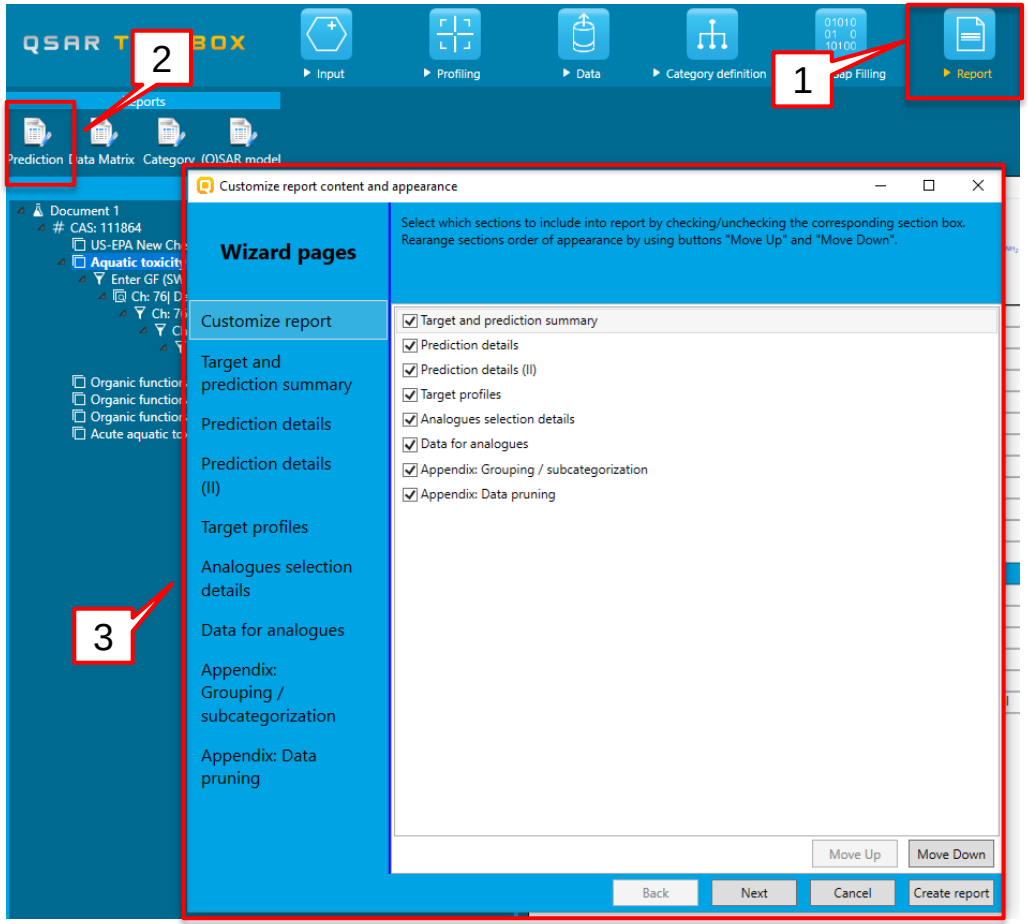
- Aims
- Ecotoxicological prediction
- Workflow of the prediction
  - Chemical input
  - Standardized workflow in Data gap filling section
- **Report**

Report
Overview

- Report module could generate report of any of predictions performed with the Toolbox.
- Report module contains Wizard pages which navigate you through predefined and user-editable report templates.

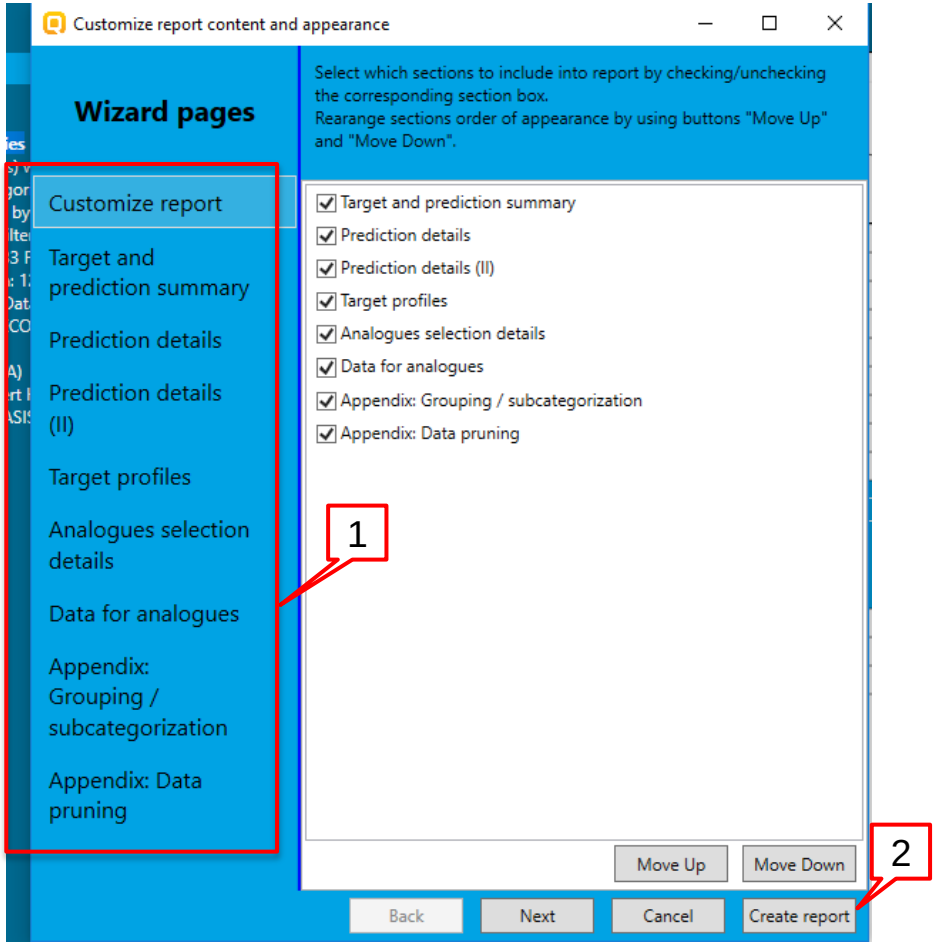
Report
Generation report

- Go to *Report* module (1)
- Select *Prediction* (2)
- A Wizard pages window is displayed (3)



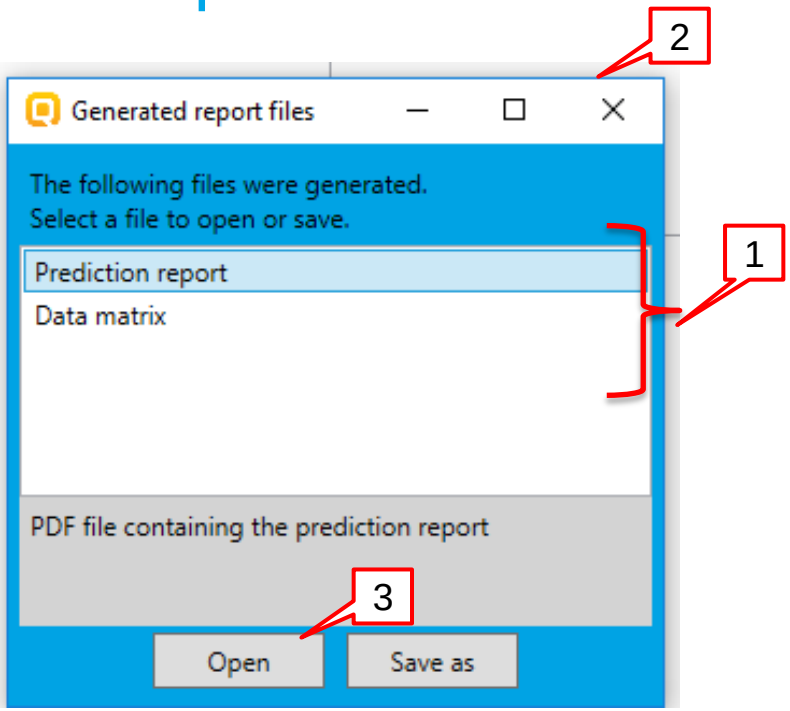
Report
Generation report

- Select different levels to customize the information that is going to be shown in the report (1);
- Select *Create report* (2) to display the report.



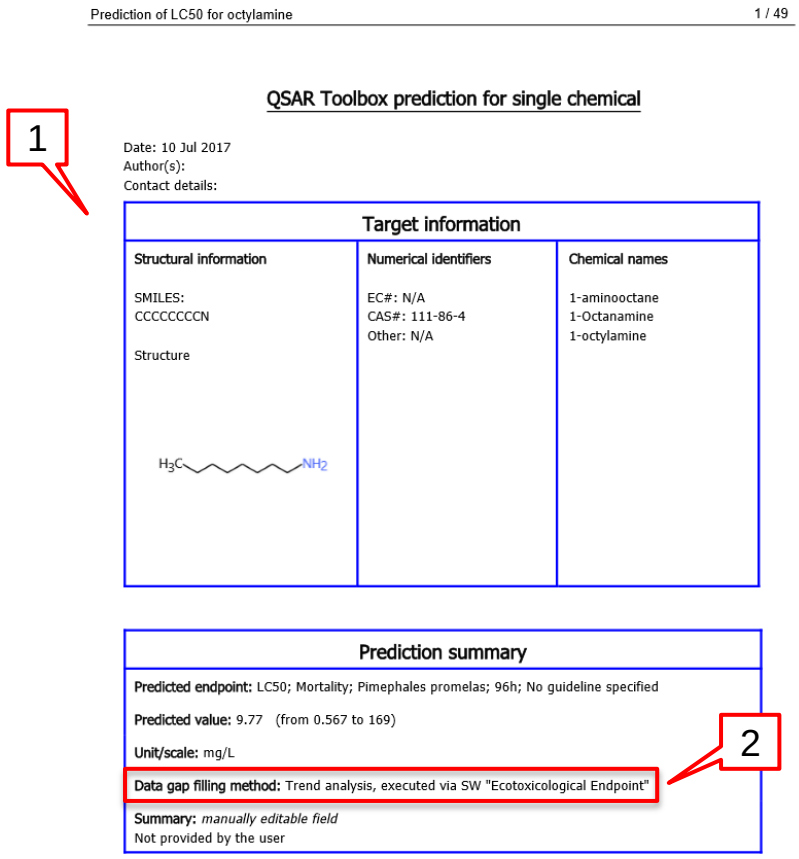
Report
Generation report

- Two files (1) are generated, which can be selected from the *Generated report files window* (2) by clicking *Open (3)*
- Select *Create report* (2) to display the report

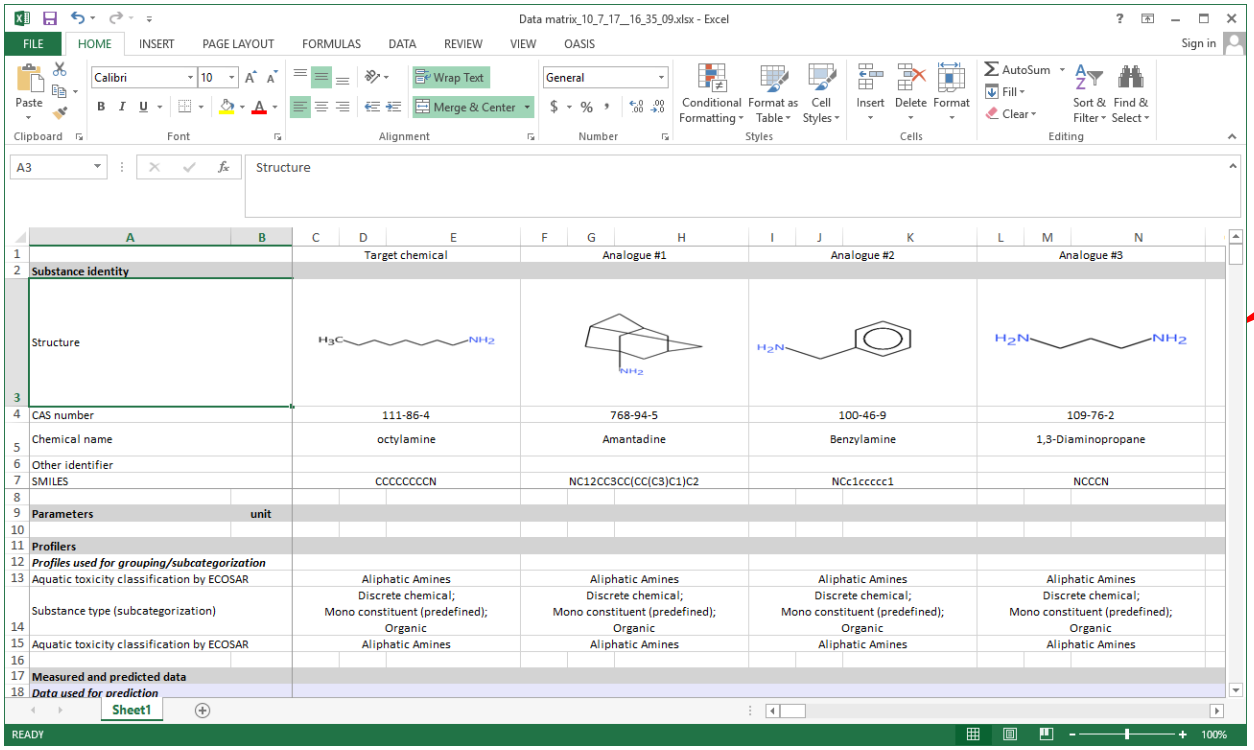


Report
Overview

- The prediction report (1) is a PDF file;
- The execution of SW "Ecotoxicological Endpoint" is included in the Prediction summary (2)



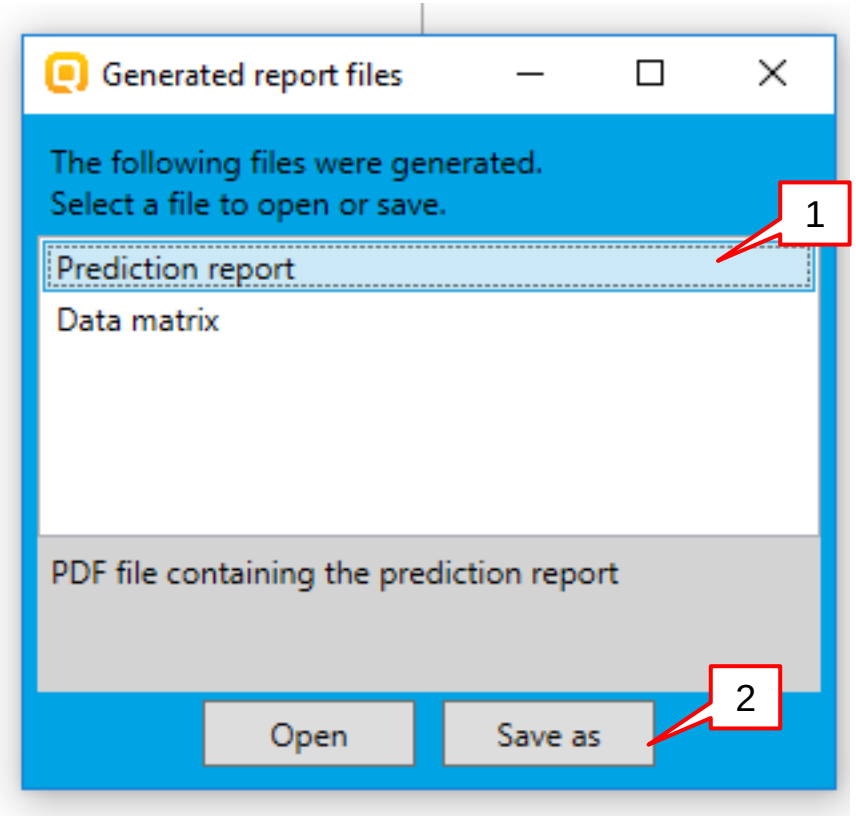
Report
Overview



The data matrix (1) is an *Excel* file, which contains information about the analogues.

Report
Save

To save any of the two files, select the file (1) and then click on *Save as* (2)



Report
Save

The report is saved as a pdf file (1) while the data matrix is saved as an *.xlsx* file (2)