QSAR TOOLBOX

The OECD QSAR Toolbox for Grouping Chemicals into Categories

OECD QSAR Toolbox v.4.1

Step by step example how to predict acute aquatic toxicity to Daphnia for the 3-ethyl-5-methyl-3-methoxyphenol by the trend analysis approach

Outlook

- **Background**
- Objectives
- Specific Aims
- Trend analysis
- The exercise
- Workflow of the exercise

Background

- This is a step-by-step presentation designed to take the user of the Toolbox through the workflow of a data gap filling exercise by trend analysis approach.

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Objectives

- **This presentation reviews a number of functionalities of the Toolbox:**
  - Identify analogues for a target chemical
  - Retrieve experimental results available for those analogues
  - Fill data gaps by trend-analysis

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Specific Aims

- To review the workflow of the Toolbox.
- To review the six modules of the Toolbox.
- To reacquaint the user with the basic functionalities within each module.
- To explain the rationale behind each step of the exercise.

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Trend Analysis
Overview

- For a given (eco)toxicological endpoint, the members of a category are often related by a trend (e.g. increasing, decreasing or constant). The trend could be related to molecular mass, carbon chain length, or to some other physicochemical property.
- A demonstration of consistent trends in the behaviour of a group of chemicals is one of the desirable attributes of a chemical category and one of the indicators that a common mechanism for all chemicals is involved. When some chemicals in a category have measured values and a consistent trend is observed, missing values can be estimated by simple scaling from the measured values to unmeasured values as a means of filling data gaps.

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Exercise

- In this exercise we will predict the acute toxicity to daphnids for an untested compound, (3-ethyl-5-methyl-4-methoxyphenol), which is the "target" chemical.
- This prediction will be accomplished by collecting a set of test data for chemicals considered to be in the same category as the target molecule.
- The category will be defined using the following categorization schemes:

  - *Acute aquatic toxicity classification by ECOSAR* – for structural grouping.

  - *Acute aquatic toxicity MOA by OASIS* – for mechanistic grouping.

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- **Workflow of the exercise**

Workflow

- **Toolbox has six modules which are used in a sequential workflow:**
  - Chemical Input
  - Profiling
  - Data
  - Category Definition
  - Filling Data Gaps
  - Report

Outlook

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- **Workflow of the exercise**
  - **Chemical Input**

Chemical Input
Overview

- This module provides 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

User Alternatives for Chemical ID:

A. Single target chemical
- Chemical Name
- Chemical Abstract Services (CAS) number (#)
- SMILES (simplified molecular information line entry system) notation/InChi
- Drawing chemical structure
- Select from User List/Inventory/Databases
- Substructure by using SMART

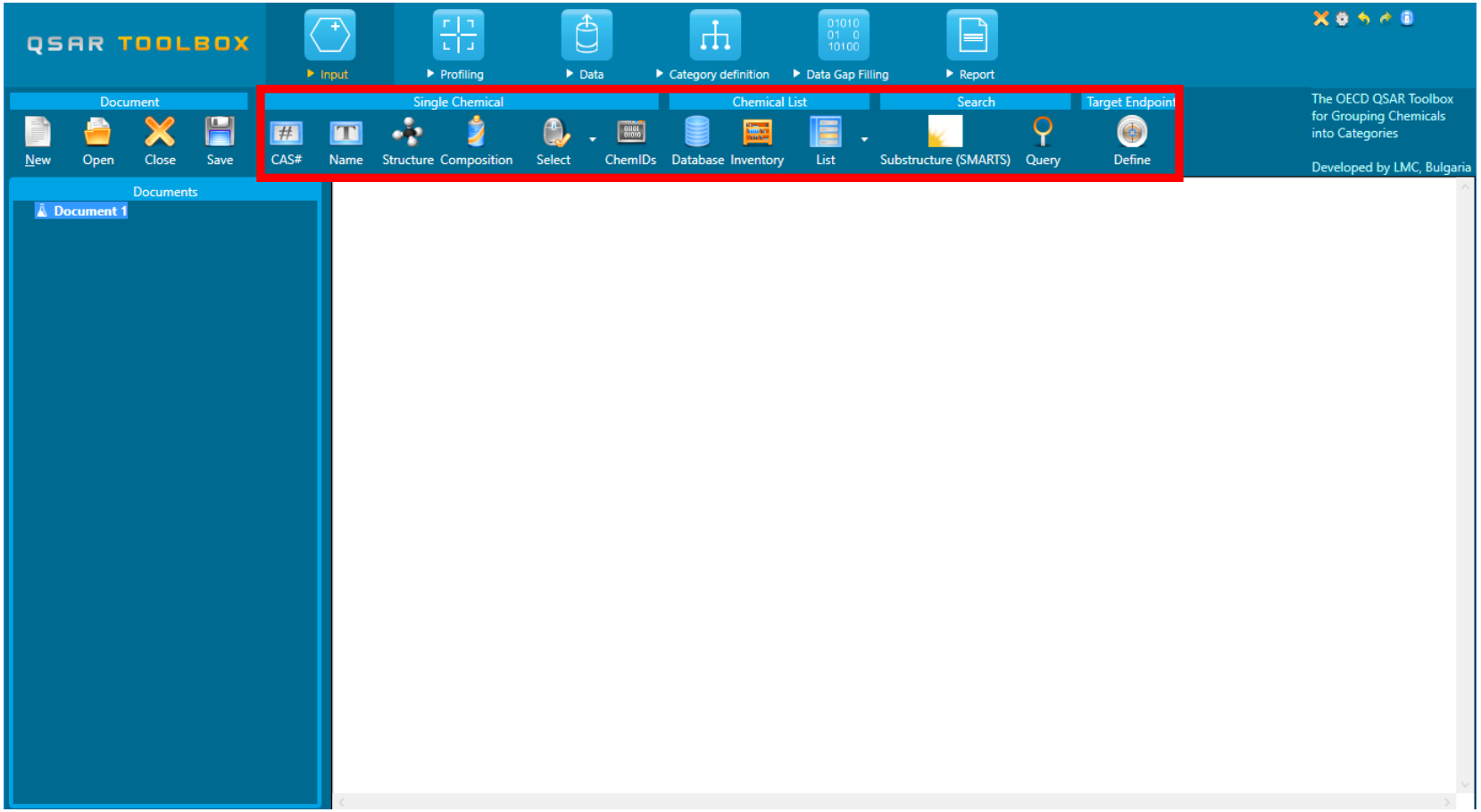
B. Group of chemicals
- User List/Inventory
- Specialized Databases

Getting Started

- Open Toolbox.
- The six modules in the workflow are seen listed next to “QSAR TOOLBOX”.
- Click “Input” (see next slide).

Chemical Input Screen

Input screen

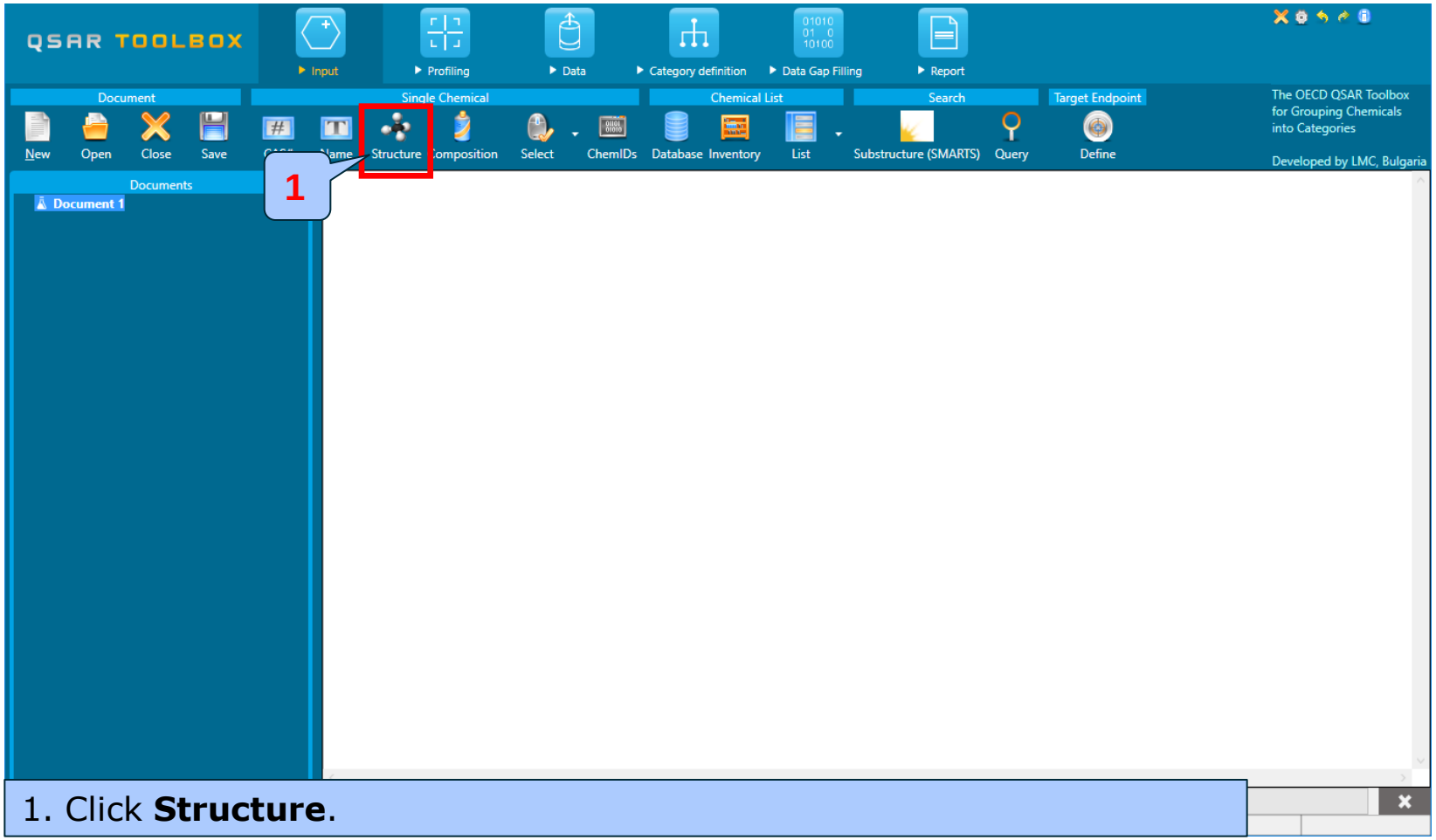


Chemical Input by Drawing

- Inputting the target chemical by drawing varies in difficulty with the structural complexity of the molecule.
- It is accomplished by a series of point-click-move-click operations within the 2D-editor which drops down when you click on "structure" (see next screen shot).
- The subsequent series of slides will take you through the process for the target chemical.

Chemical Input Screen

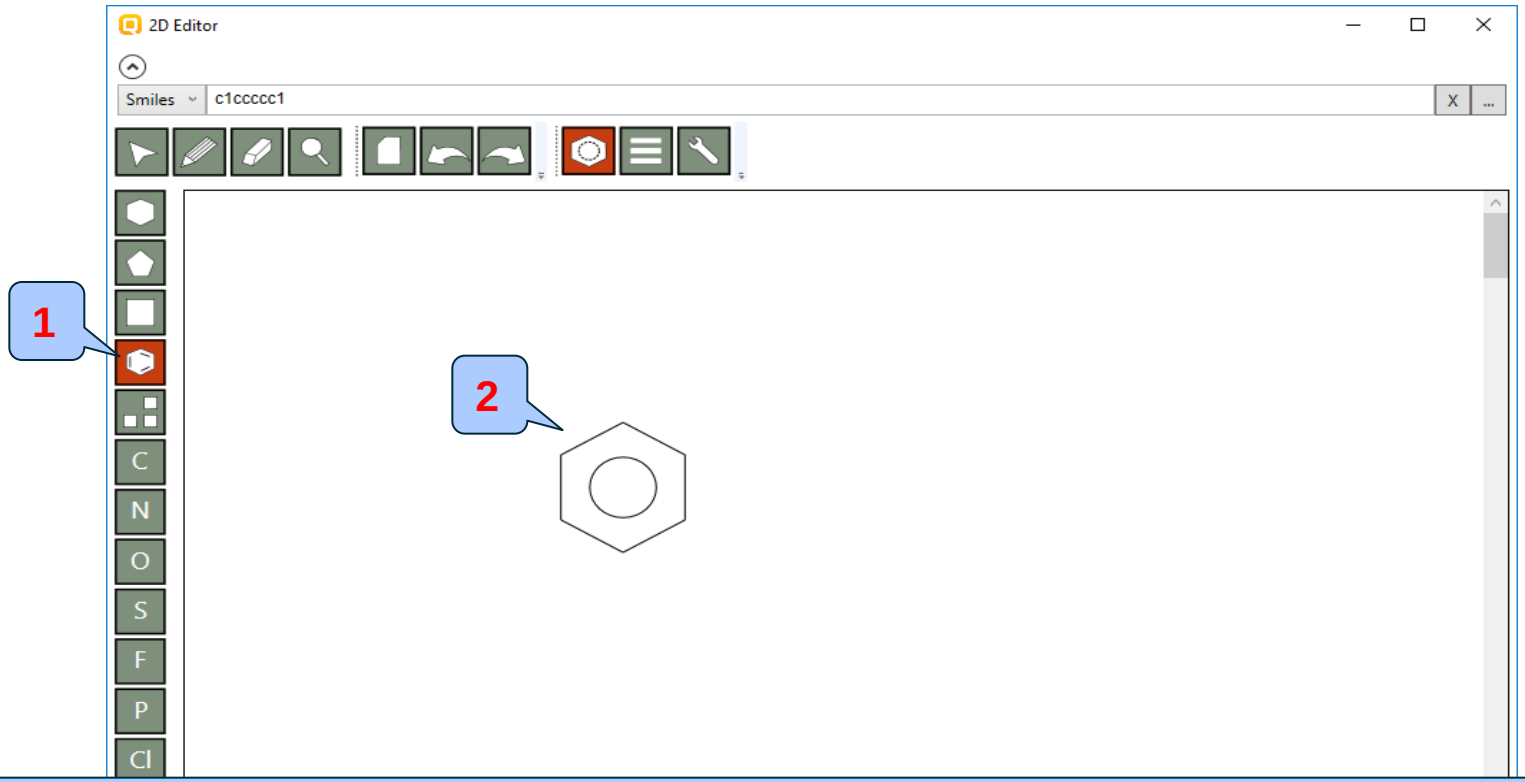
Input target chemical by drawing



1. Click **Structure**.

Chemical Input

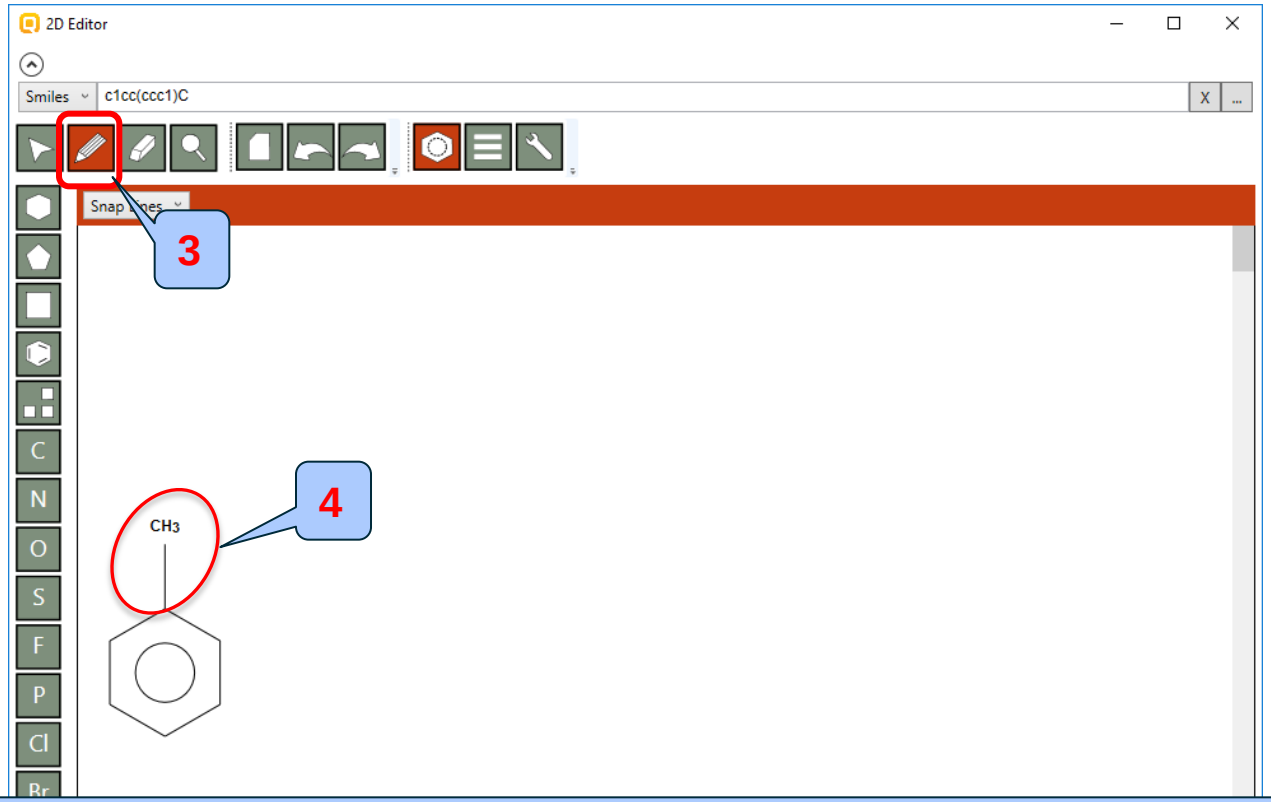
Drawing the target "3-ethyl-5-methyl-4-methoxyphenol" by 2-D editor



1. **Left Click** on the appropriate template form.
2. Move the curser to the large clear area and **left click** again, this puts the selected template on the plot.

Chemical Input

Drawing the target "3-ethyl-5-methyl-4-methoxyphenol" by 2-D editor



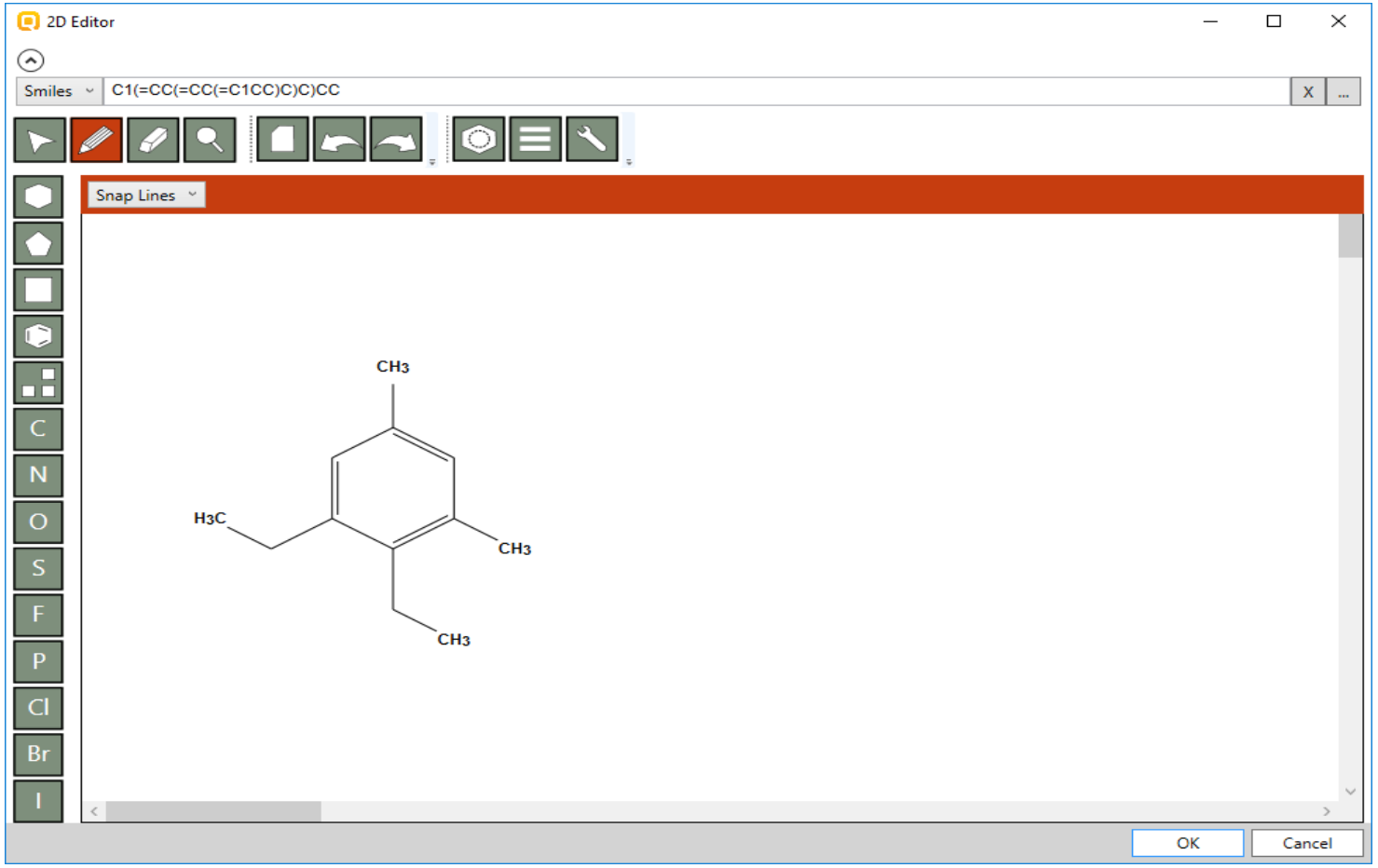
3. Click pencil button to draw a single bond.
4. Drag the mouse (pointing finger) to the appropriate atom and **left click** to create a single bond.

Chemical Input by Drawing

- Note the default is addition of a CH_3-group.
- By moving the 'finger' to other C-atoms and left clicking the mouse adds other hydrocarbon fragments.
- If you make an incorrect entry you can click the 'undo' icon () in the upper corner of the screen to remove the addition.
- This process allows you to build the hydrocarbon skeleton of the target molecule (see next screen shot).

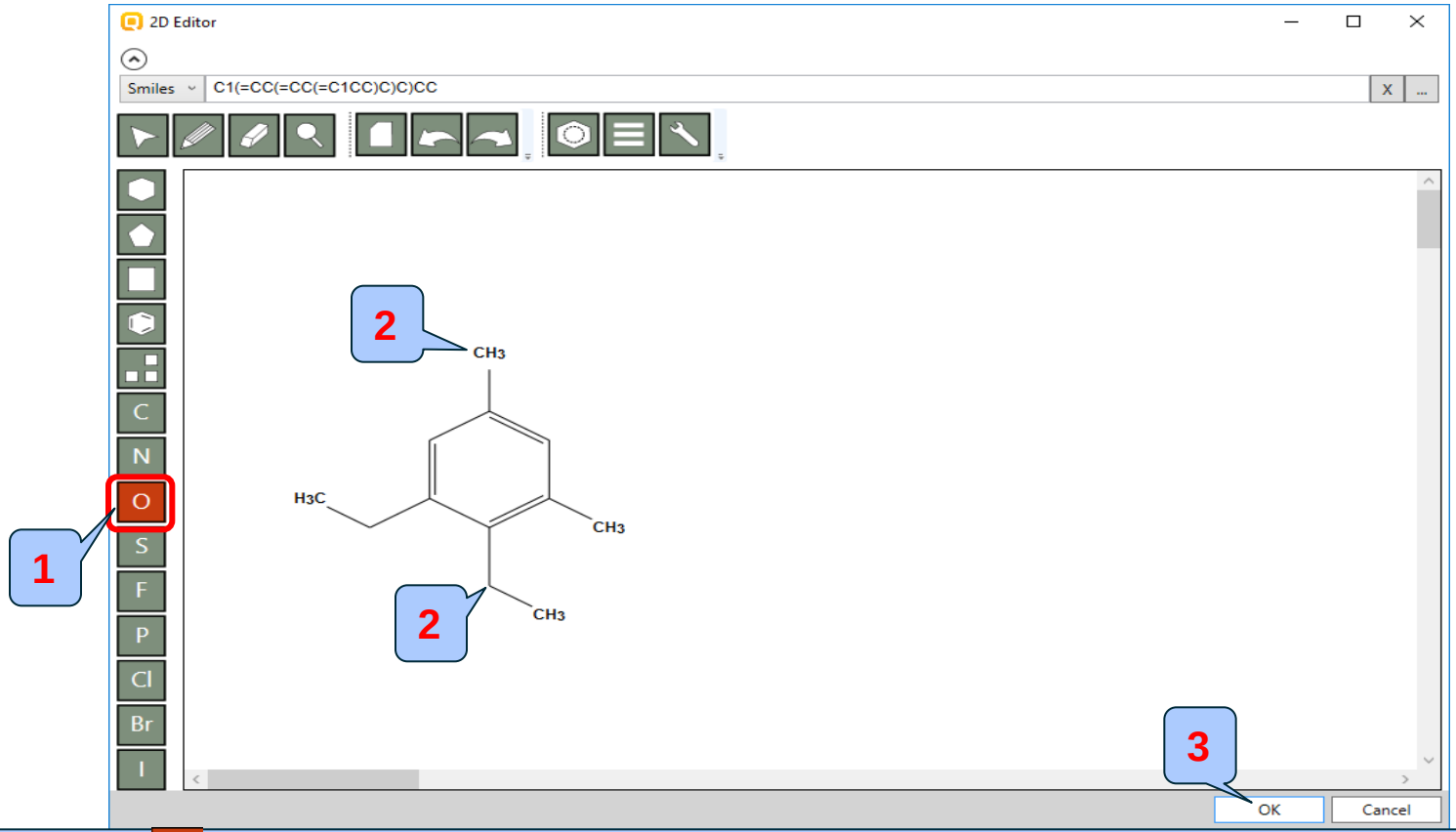
Chemical Input

Drawing the target "3-ethyl-5-methyl-4-methoxyphenol" by 2-D editor



Chemical Input

Drawing the target "3-ethyl-5-methyl-4-methoxyphenol" by 2-D editor

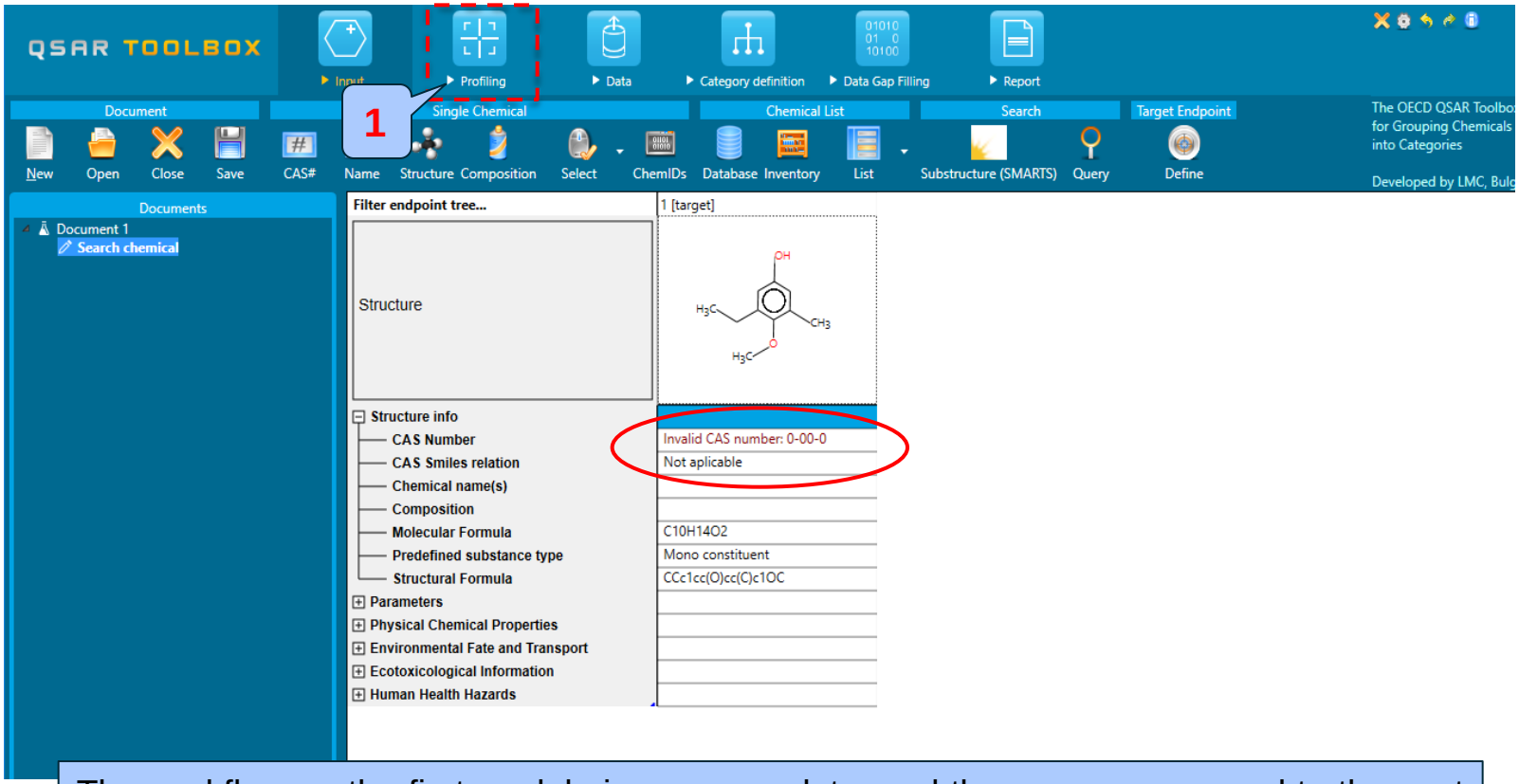


1. Click O to add an oxygen atom; 2. Left click with mouse over the methyl group to insert an oxygen atom; 3. Click **OK**.

Chemical Input
Target chemical identity

- The already drawn target structure automatically appears on the data matrix
- Note that no CAS number or name is displayed for this chemical. This means the target chemical is not listed in the chemical inventories/databases implemented in the Toolbox (see next slide).

Chemical Input
Target chemical identity



The workflow on the first module is now complete, and the user can proceed to the next module. Click ***Profiling*** (1).

Outlook

- Background
- Objectives
- Specific Aims
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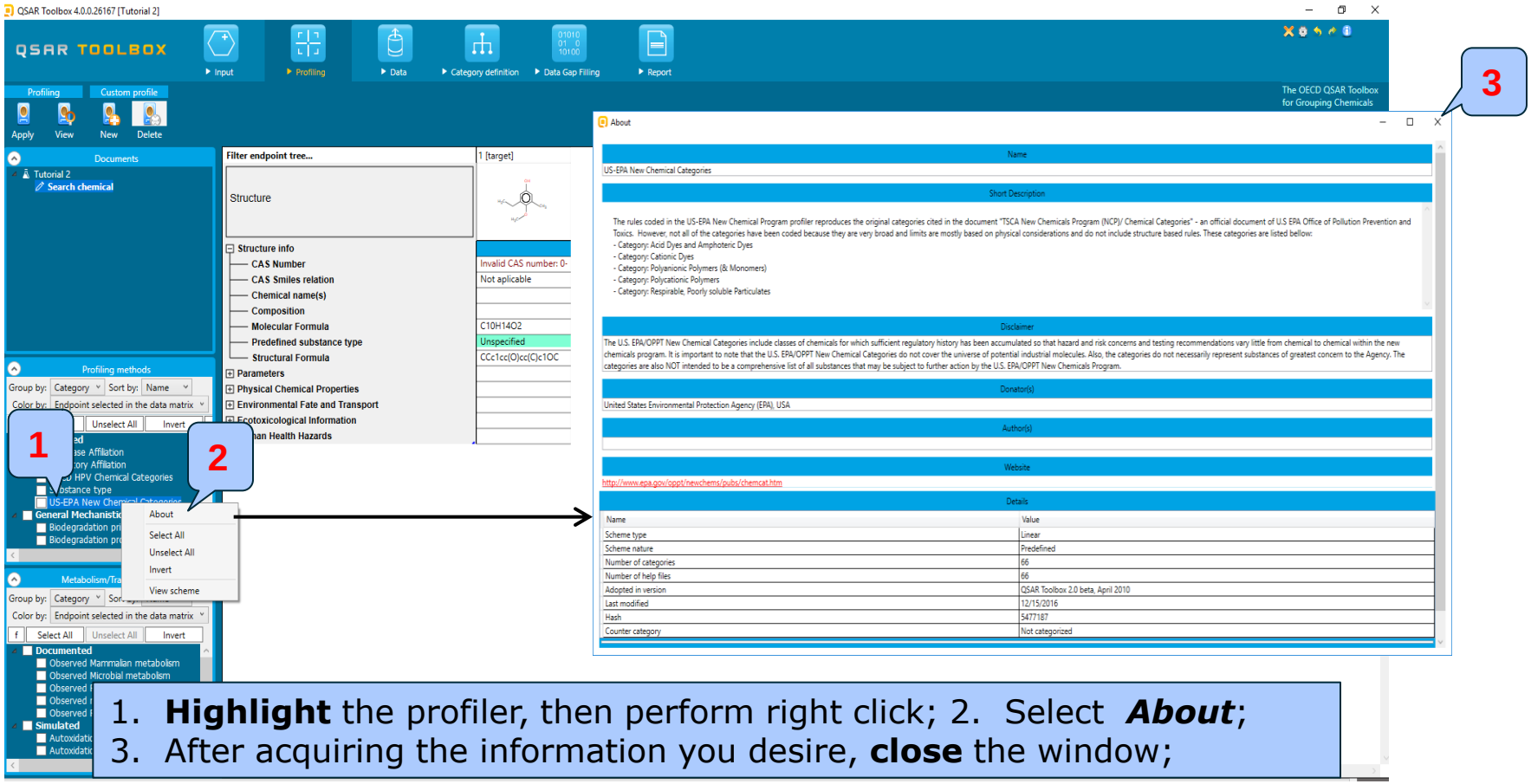
- The exercise
- **Workflow of the exercise**
  - Chemical Input
  - **Profiling**

Profiling
Overview

- *Profiling* module refers to the electronic process of retrieving relevant information on the target compound, other than environmental fate, ecotoxicity and toxicity data, which are stored in the Toolbox database.
- Available information includes likely mechanism(s) of action, as well as observed or simulated metabolites.

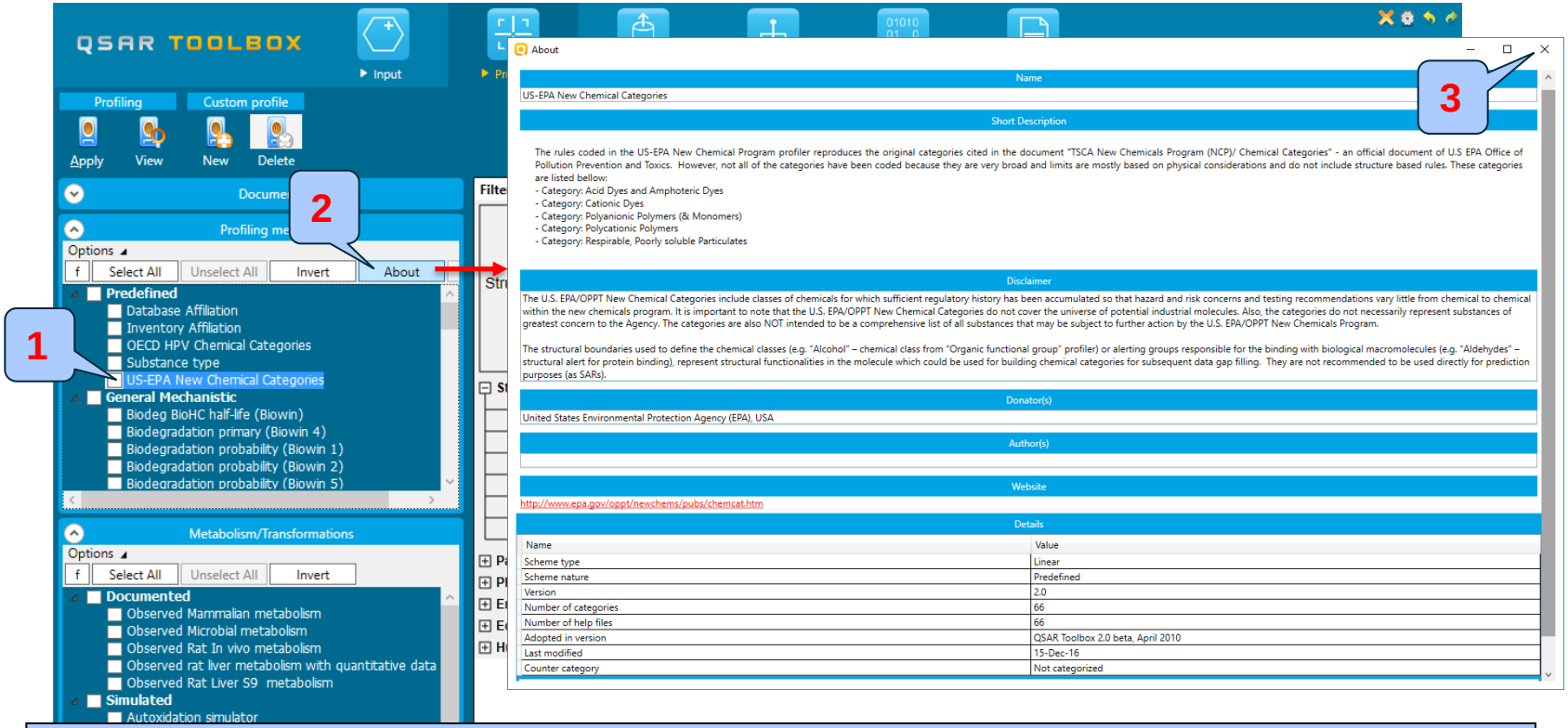
Profiling

Summary information of the different profilers are provided in the "About".



Profiling

Summary information of the different profilers are provided in the "About".

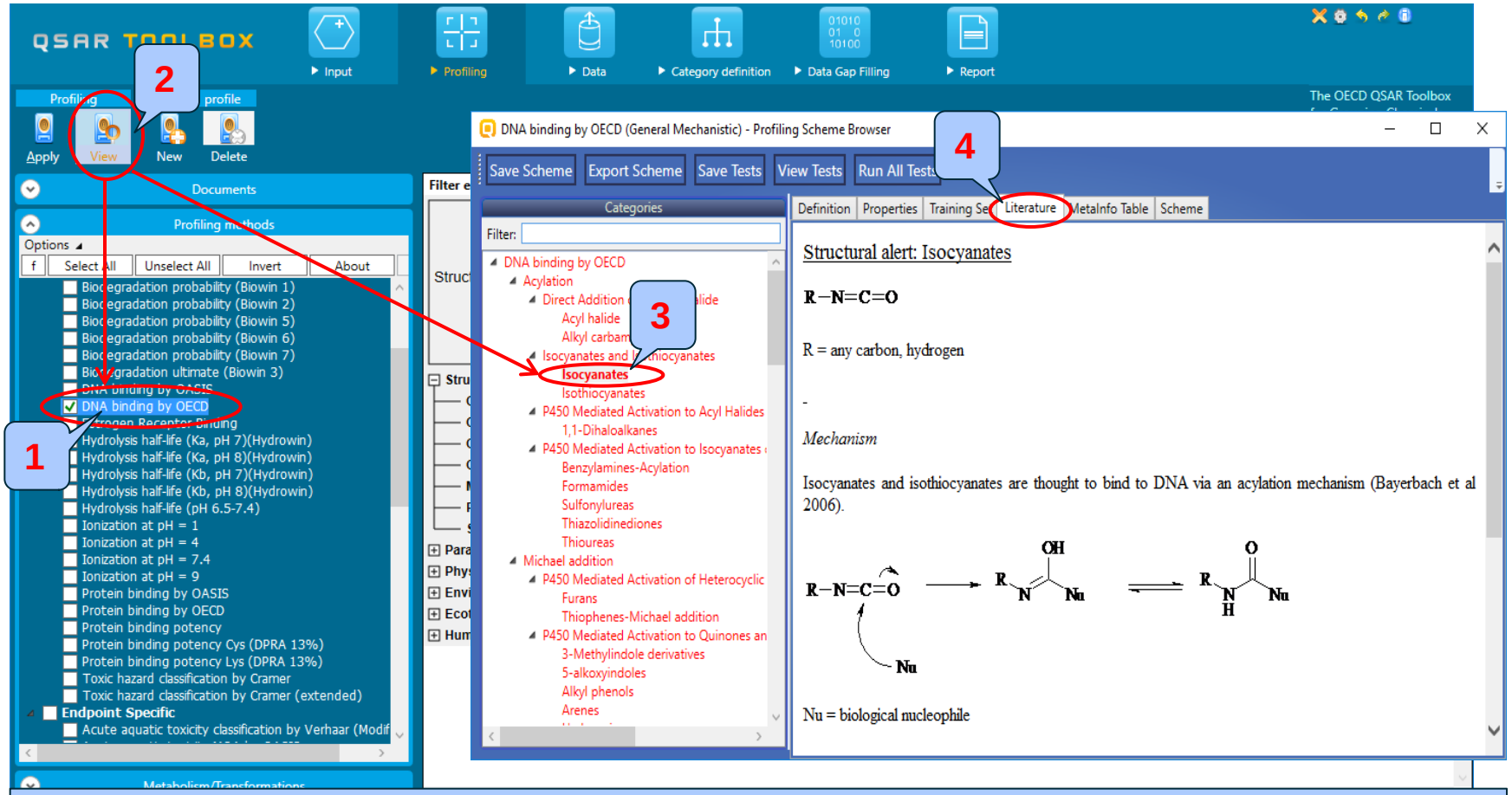


1. Click the profiler of interest; 2. Click **About** or right-click the profiler and select *About*; 3. **Close** the window.

Profiling

- For most of the profilers, background information can be retrieved by highlighting one of the profilers (for example, *DNA binding by OECD*) and clicking **View** (see next slide).

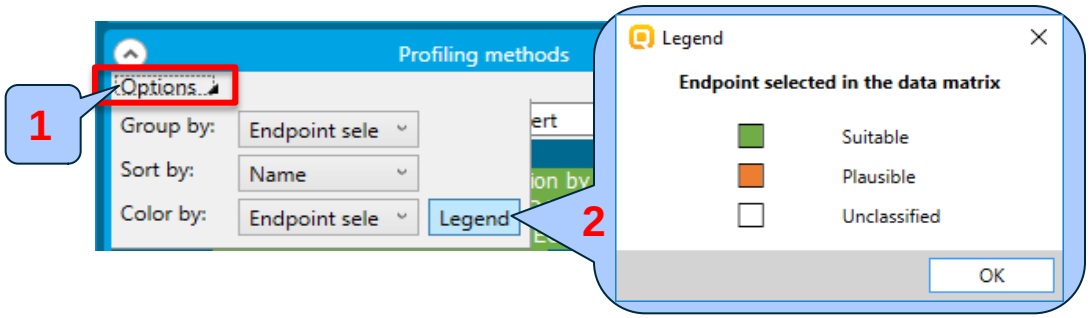
Profiling



1. Click the profiler; 2. Click **View**; 3. Click one of the structural alerts (for example *Isocyanates*); 4. Go to the **Literature** tab to see the background information.

Profiling
Profiling the target chemical

- Once the endpoint is selected, the relevant profiles and metabolic transformations are highlighted. Meaning of the colors could be seen within the **Options** (1) by click **Legend** (2).

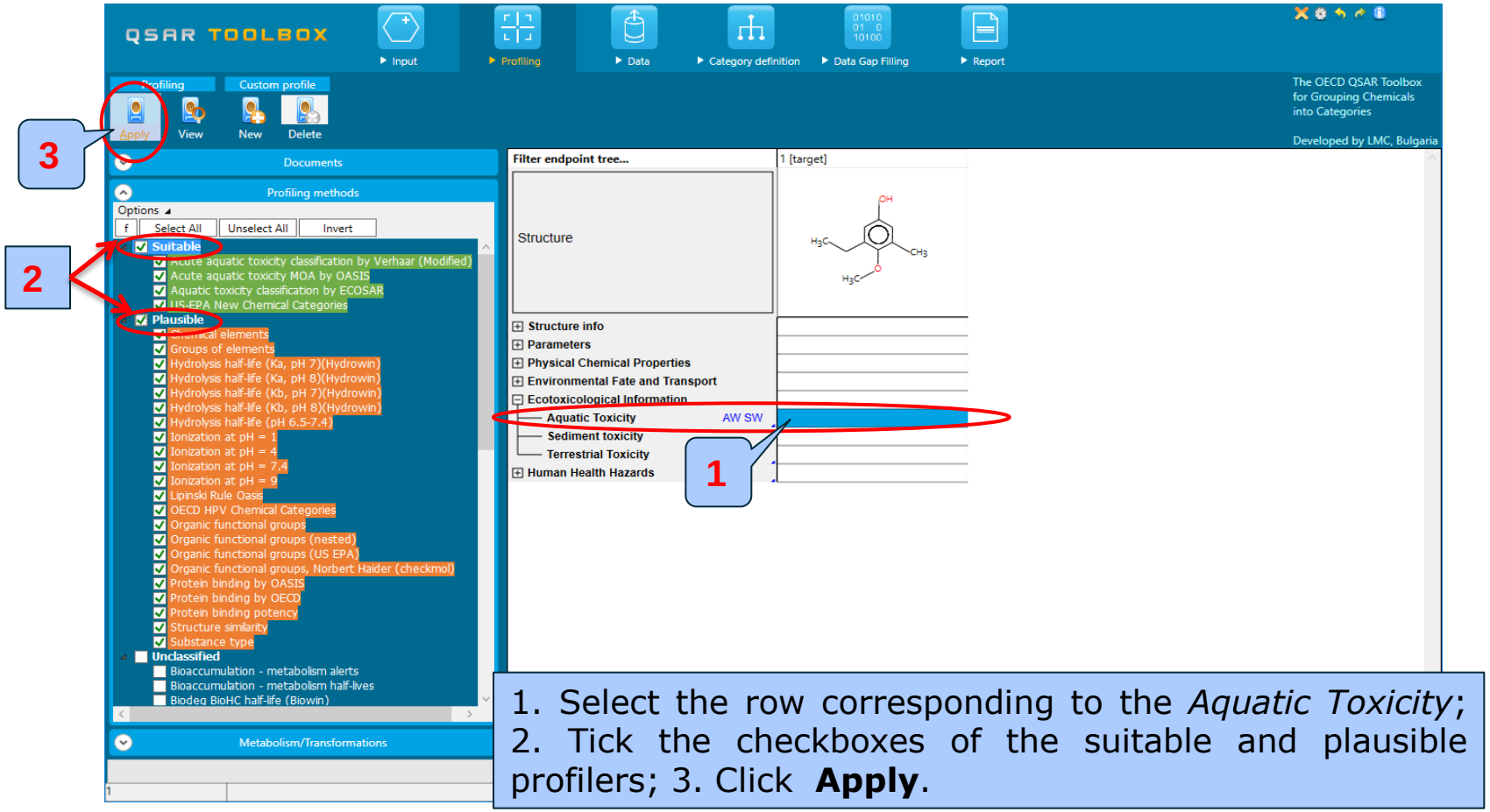


  - **Suitable** - developed using data/knowledge for the target endpoint;
  - **Plausible** – not endpoint specific; structure-based; form broader group of analogues;
  - **Unclassified** – all profilers, which are not classified in any of the categories above.

- Select the Profiling methods related to the target endpoint by ticking the checkbox next to the profilers name.
- This selects (a green check mark appears) or deselects (the green check disappears) profilers.

Profiling

Profiling the target chemical



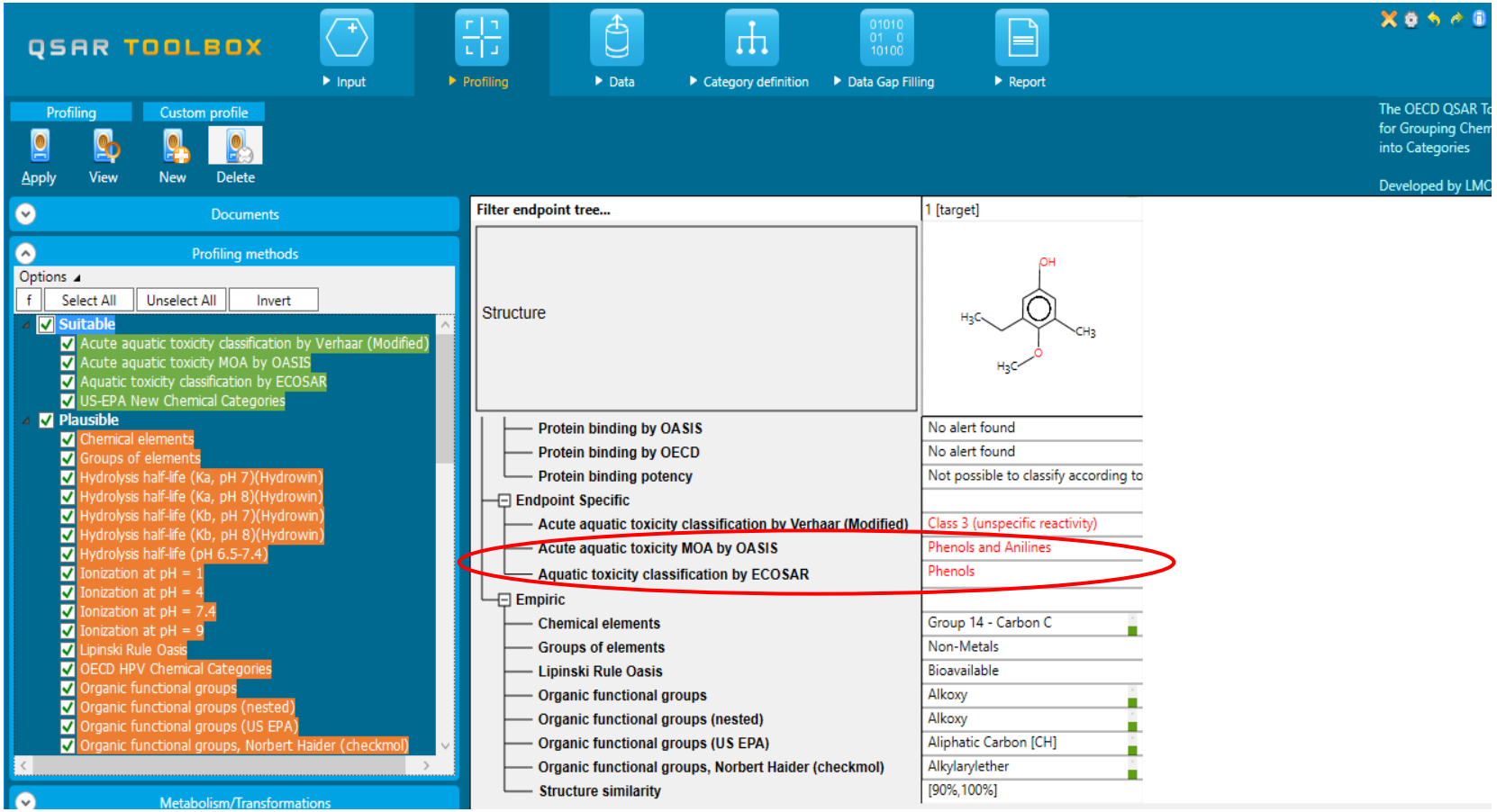
1. Select the row corresponding to the *Aquatic Toxicity*; 2. Tick the checkboxes of the suitable and plausible profilers; 3. Click **Apply**.

Profiling
Profiling the target chemical

- The actual profiling will take several seconds depending on the number and type of selected profilers.
- The results of profiling automatically appear as a dropdown box under the target chemical.
- Please note the specific profiling results of *Classification by ECOSAR* and *MOA by OASIS* (see next slide).
- These results will be used to search for suitable analogues in the next steps of the exercise.

Profiling

Profiles of the target "3-ethyl-5-methyl-4-methoxyphenol



Outlook

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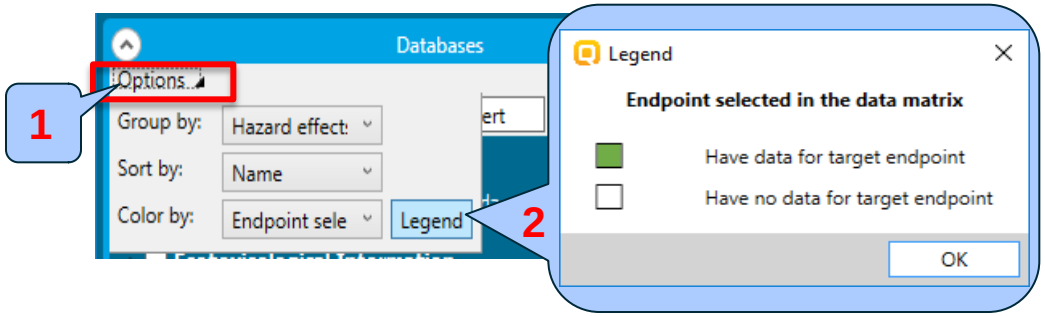
- **Workflow of the exercise**
  - Chemical Input
  - Profiling
  - **Data**

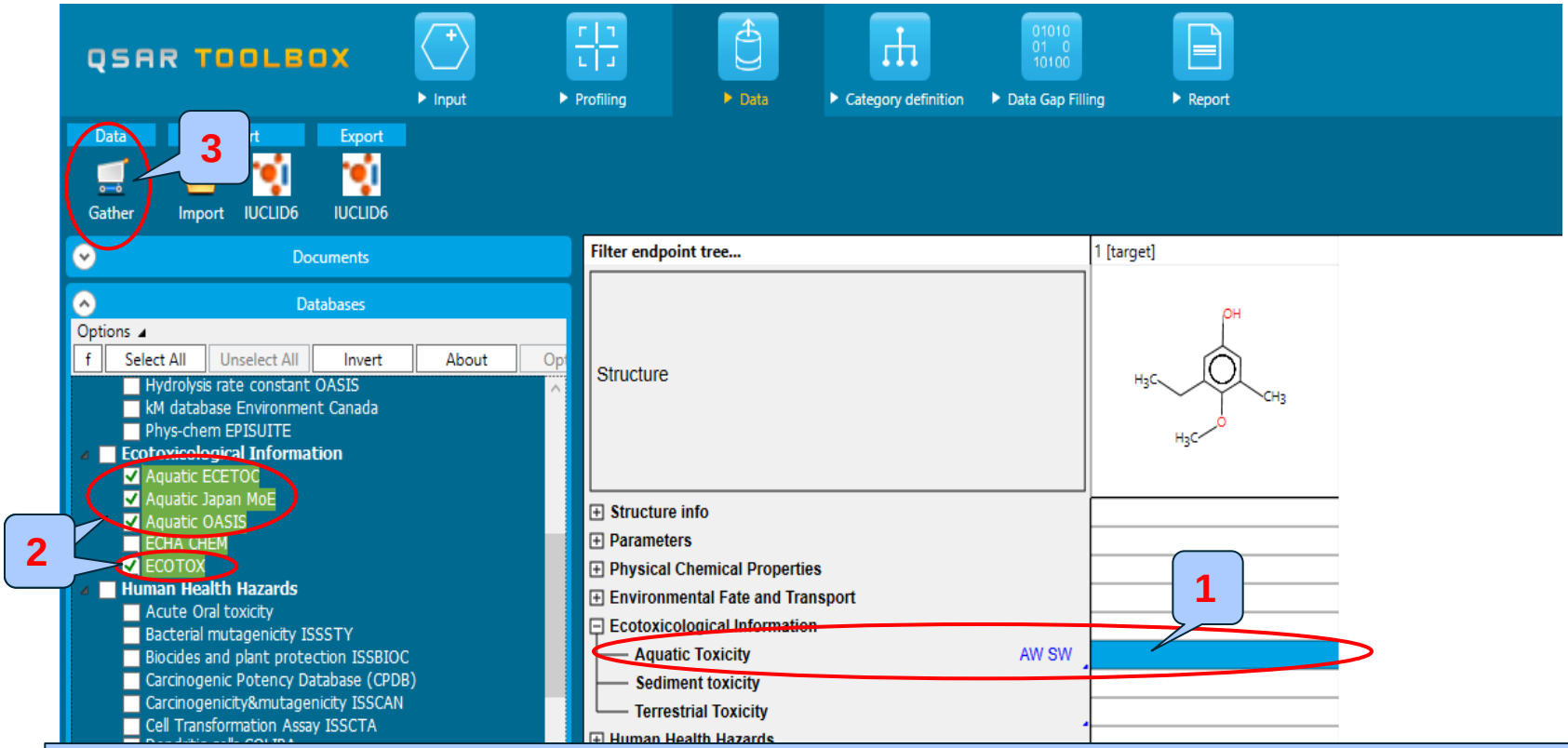
Data

- *Data* module refers to the electronic process of retrieving the environmental fate, ecotoxicity and toxicity data that are stored in the Toolbox databases.
- Data gathering can be executed in a global fashion (i.e. collecting all data of all endpoints) or on a more narrowly defined basis (i.e. collecting data for a single or limited number of endpoints).
- Once the endpoint is selected, the relevant databases are highlighted. Meaning of the colors could be seen within the **Options** (1) by click **Legend** (2).



- In this example, we limit our data gathering to the common aquatic toxicity endpoints from databases containing aquatic toxicity data (Aquatic ECETOC, Aquatic Japan MoE, ECOTOX, and Aquatic OASIS).

Data
Gather data using database` relevancy

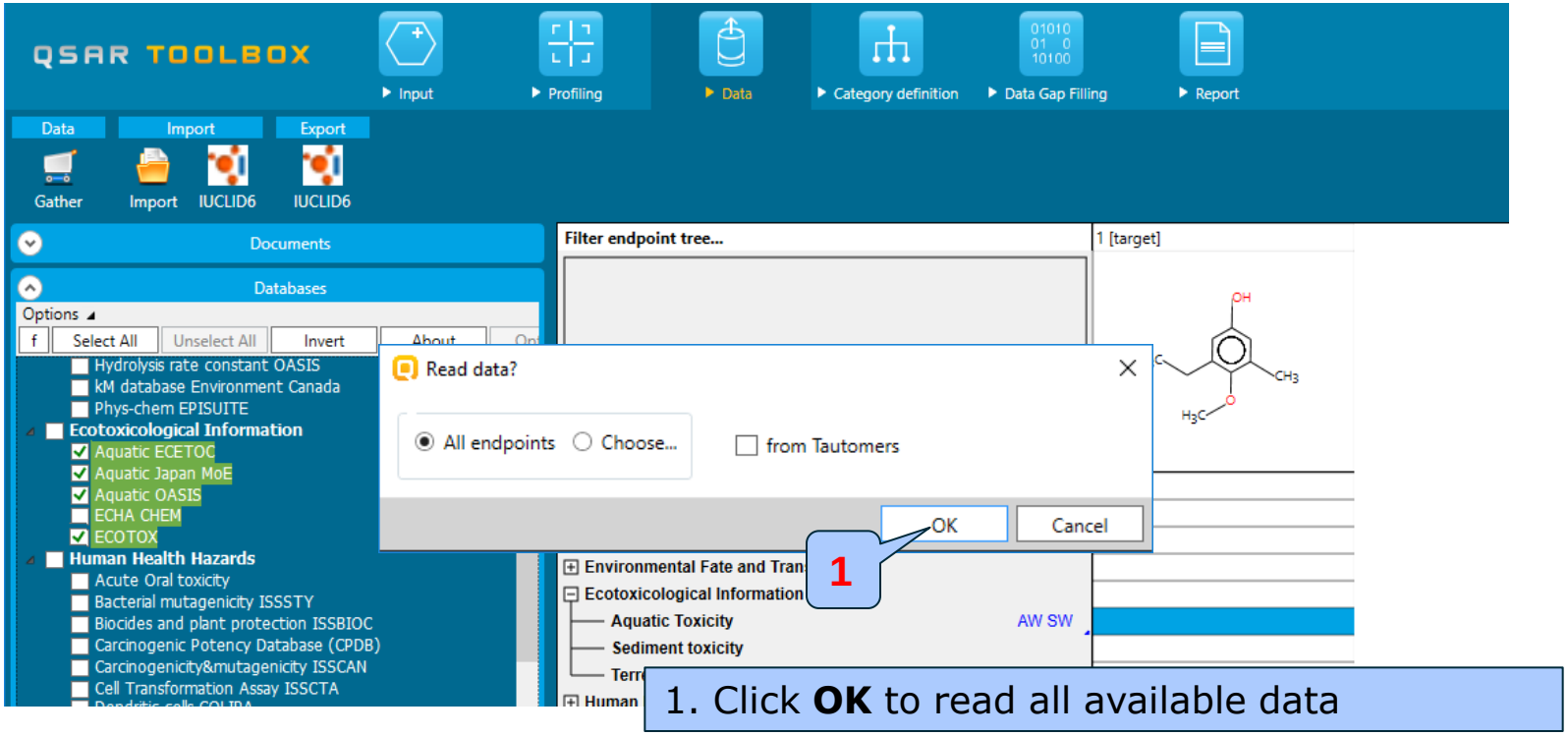


1. Select the row corresponding to the *Aquatic toxicity;* 2. Select all highlighted databases except ECHA CHEM; 3. Click **Gather**.

Data
Process of collecting data

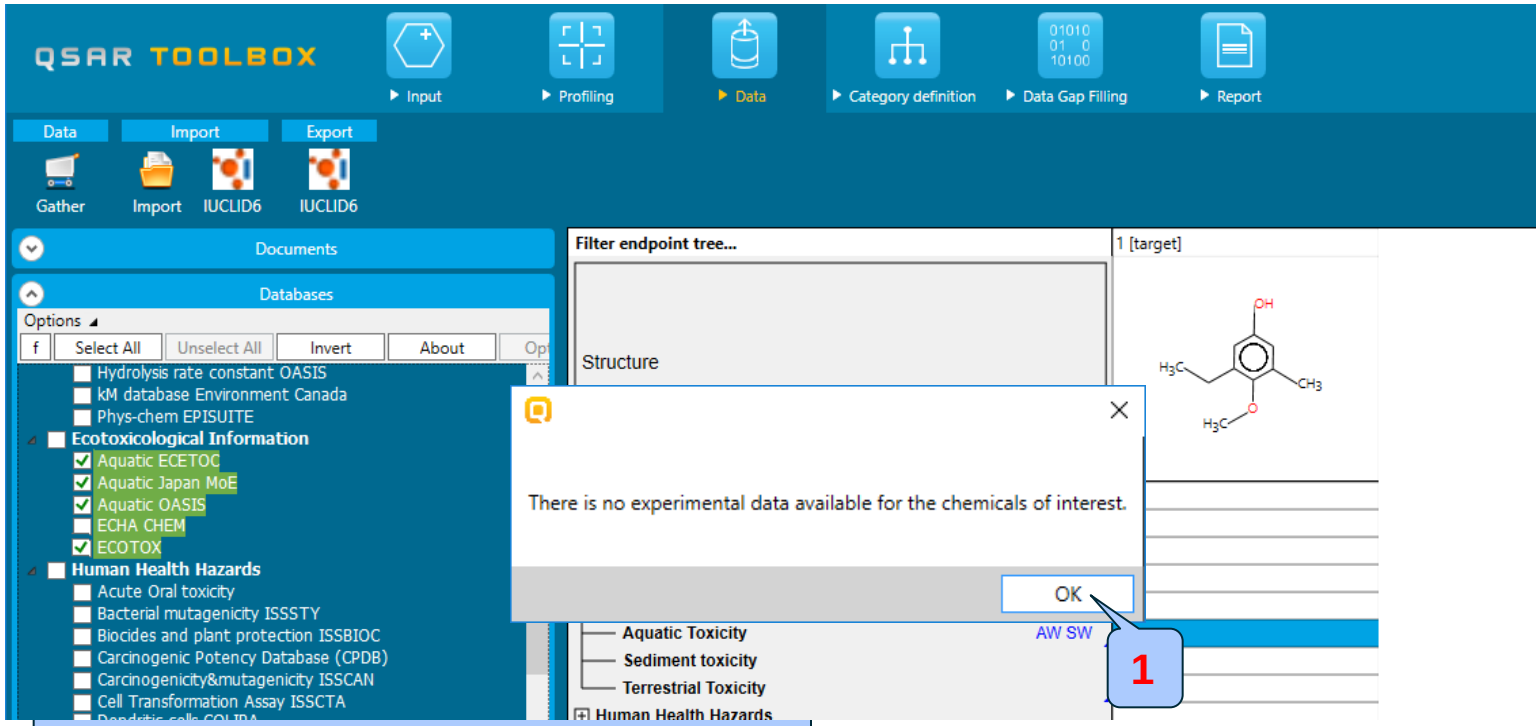
Toxicity information on the target chemical is electronically collected from the selected datasets.

A window with "Read data?" appears. Now the user could choose to collect "all" or "endpoint specific" data.



Data
Process of collecting data

In this example, an insert window appears stating that no experimental data is available for the chemical of interest.



1. Click **OK** to close the window

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  - Profiling
  - Data
  - **Category definition**

Recap

- You have entered the target chemical being sure of the correct structure.
- You have profiled the target chemical and found no experimental data is currently available for this structure.
- In other words, you have identified a data gap, which you would like to fill.
- Now you are ready to continue with next step of the workflow - *Category Definition*.

Category Definition
Overview

- This module provides the user with several means of grouping chemicals into a toxicologically meaningful category that includes the target molecule.
- This is the critical step in the workflow.
- Several options are available in the Toolbox to assist the user in defining the category definition.

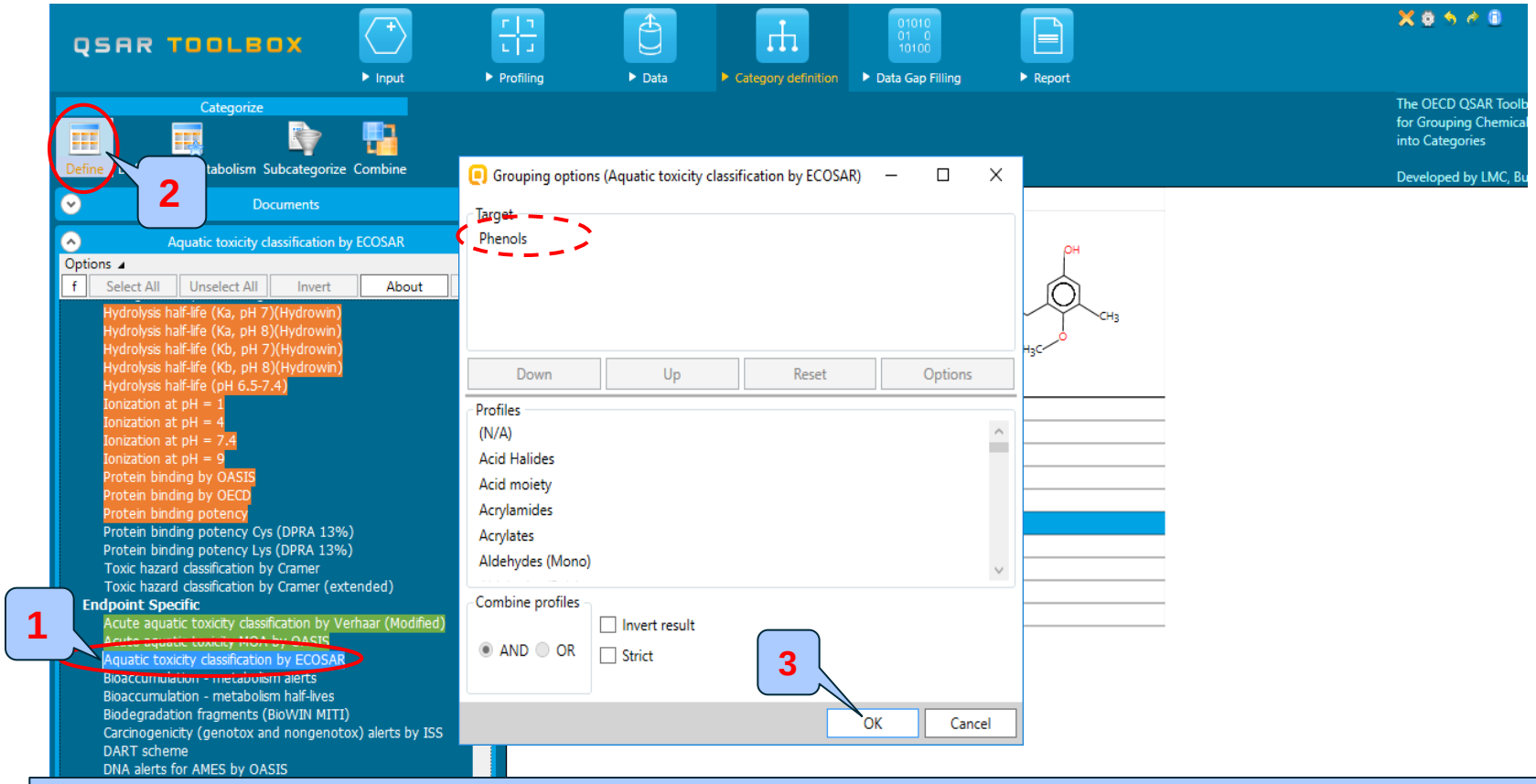
Category Definition
Grouping methods

- The different grouping methods allow the user to group chemicals into chemical categories according to different measures of "similarity" so that within a category data gaps can be filled by trend-analysis.
- For this example, starting from the target chemical a specific ECOSAR classification is identified, subsequently analogues are found within the same specific classification for which experimental results are available.

Category Definition
ECOSAR categories

- ECOSAR has been used by the U.S. Environmental Protection Agency since 1981 to predict the aquatic toxicity of new industrial chemicals in the absence of test data.
- The *Aquatic toxicity classification by ECOSAR* profiling scheme in the Toolbox is used for grouping of chemicals by structural similarity which may or may not have mechanistic meaning. Experience has shown ECOSAR to be a robust profiler which makes it a logical choice in an initial profiling scheme.

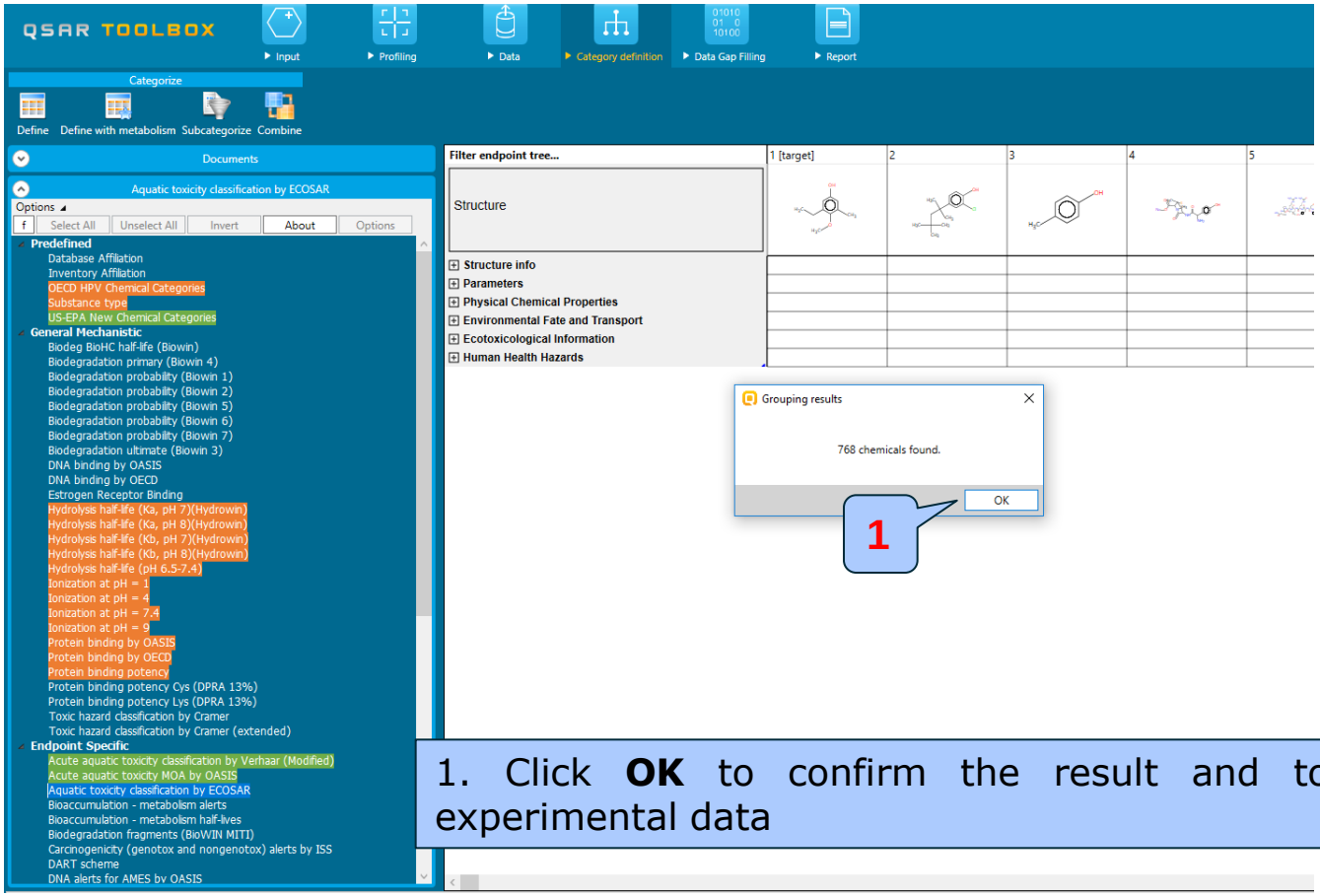
Category Definition
Defining ECOSAR category



1. Select the highlighted ***Aquatic toxicity classification by ECOSAR***; 2. Click **Define**; 3. Confirm the category "Phenols" by clicking **OK**.

Category Definition

Defining ECOSAR category



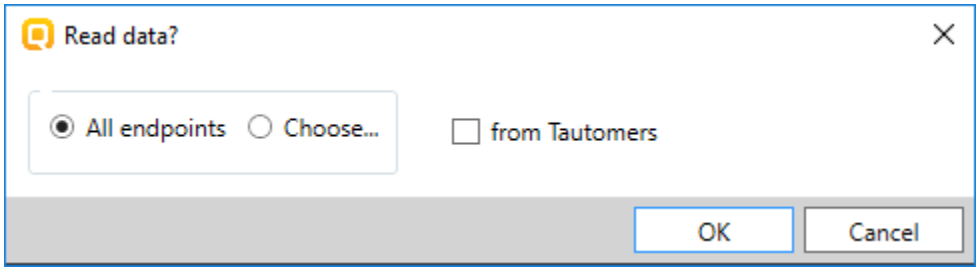
1. Click **OK** to confirm the result and to gather experimental data

Category Definition
Analogues

- The Toolbox now identifies all chemicals corresponding to the ECOSAR classification of *Phenols* which are listed in the selected databases within the *Data* module.
- 768 analogues are identified. Along with the target they form a category (Phenols) which can be used for data gap filling.

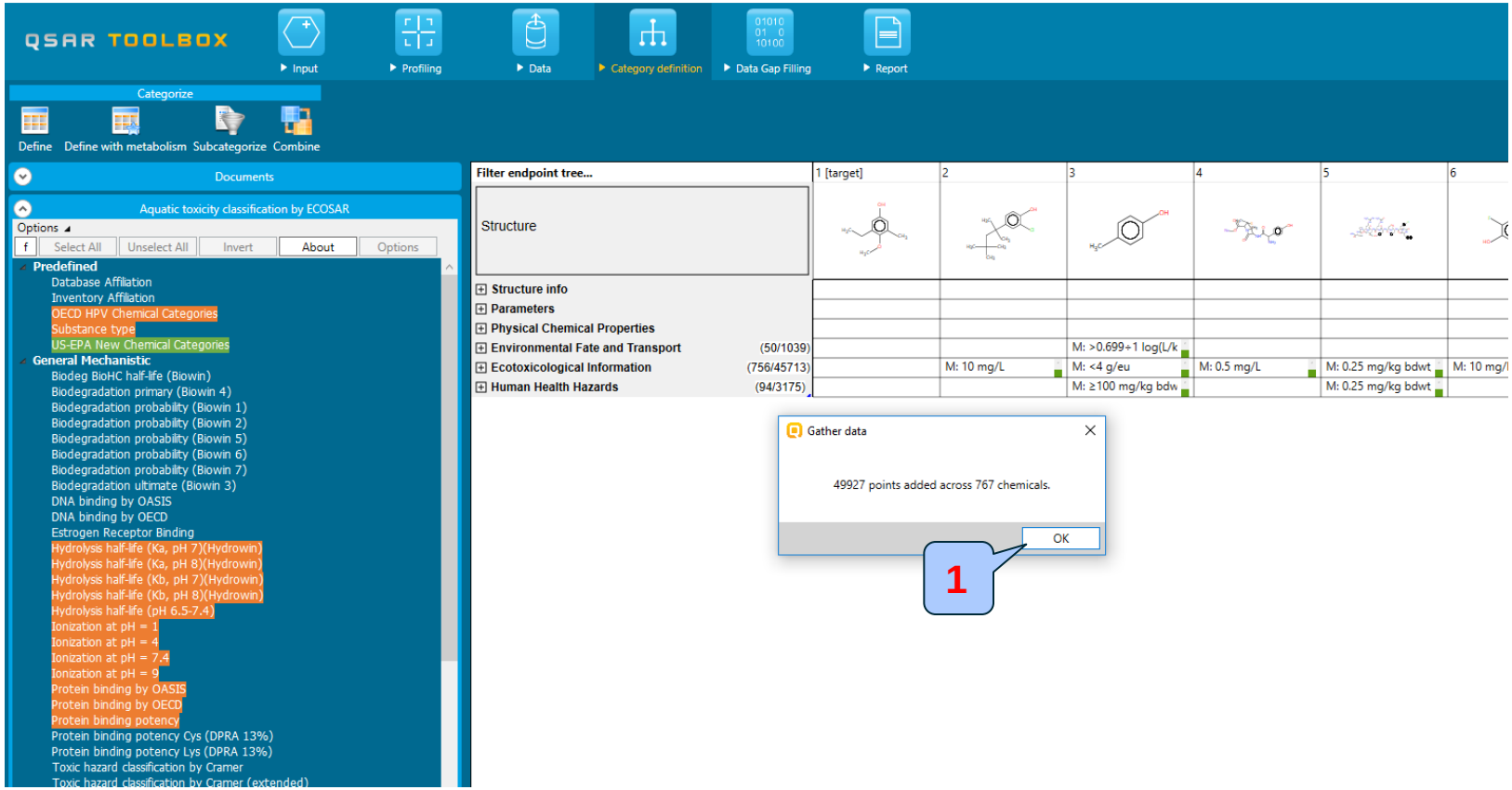
Category Definition
Read data for Analogues

- The Toolbox automatically request the user to select the endpoint that should be retrieved.
- The user can either select the specific endpoint or by default choose to retrieve data on all endpoints (see below).



- In this example, since only databases that contain information for Eco-toxicological endpoints are selected, both options give the same results.
- As the Toolbox must search the database, this may take some time.

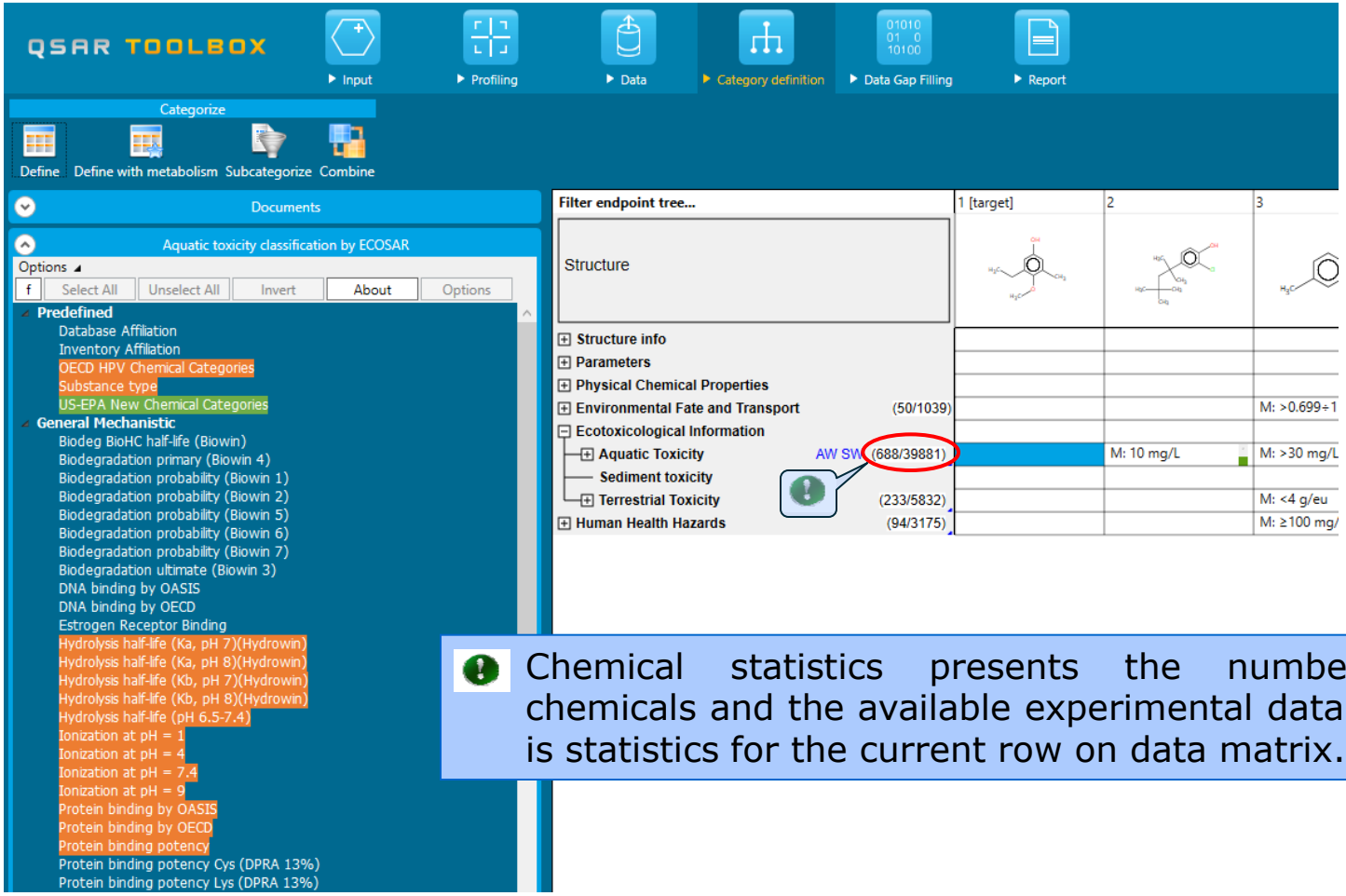
Category Definition
Summary information of Analogues



1. Click **OK** on window that provides information for common number gathered data across the number of chemicals.

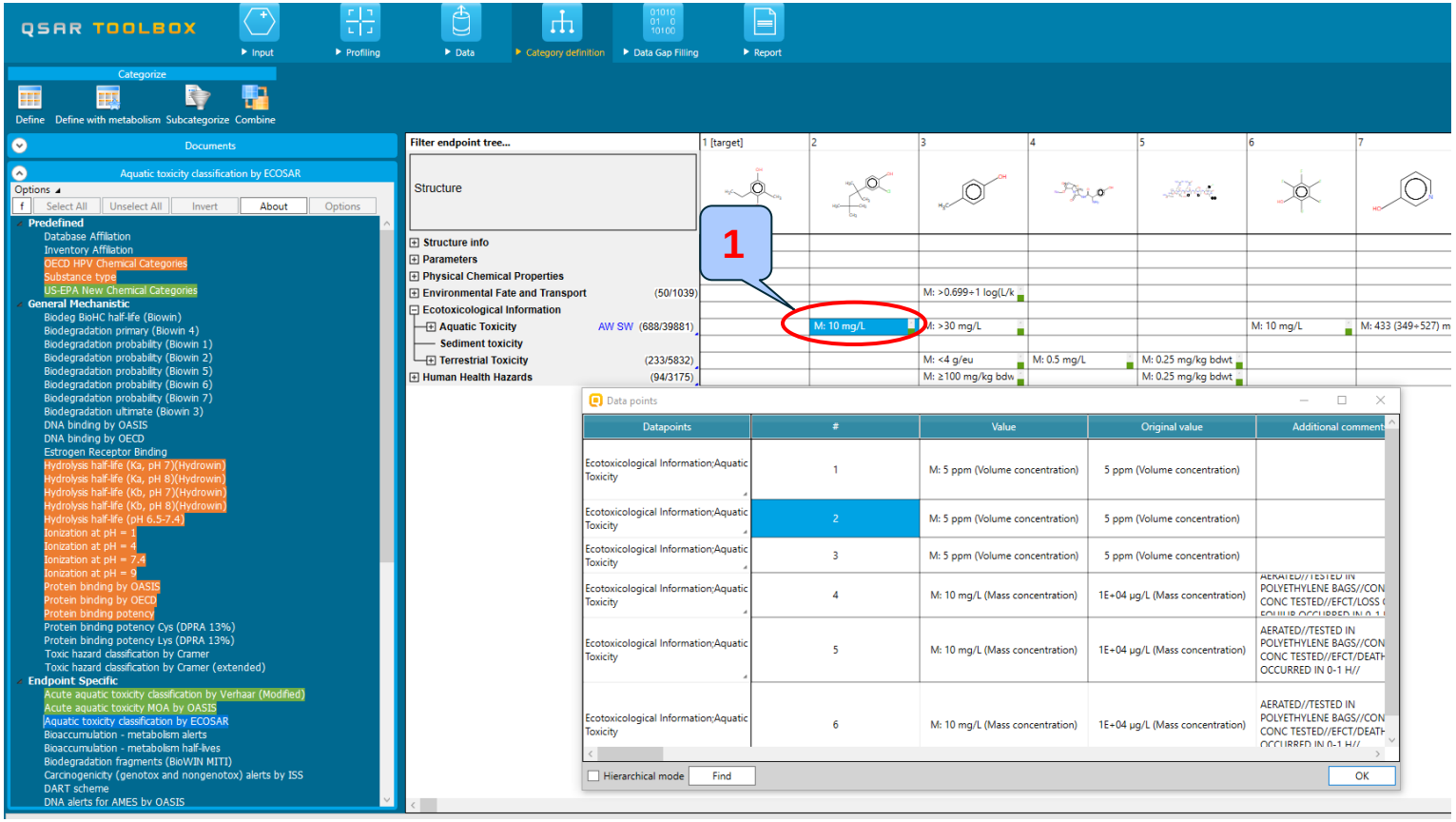
Category Definition

Summary information of Analogues



Chemical statistics presents the number of chemicals and the available experimental data. This is statistics for the current row on data matrix.

Category Definition
Summary information of Analogues



1. Double-click on the cell with measured data opens a table which provides detailed information for all experimental data of the focused chemical.

Recap

- You have identified a category (*Phenols*) with the *Aquatic toxicity classification by ECOSAR* profiler for the target chemical 3-ethyl-5-methyl-4-methoxyphenol.
- The available experimental results for these 767 analogues have been collected from the selected databases (Aquatic ECETOC, Aquatic Japan MoE, ECOTOX, and Aquatic OASIS).
- But before the user can proceed with the *Filling Data Gap* module, he/she should navigate through the endpoint tree and find the specific gap that will be filled.

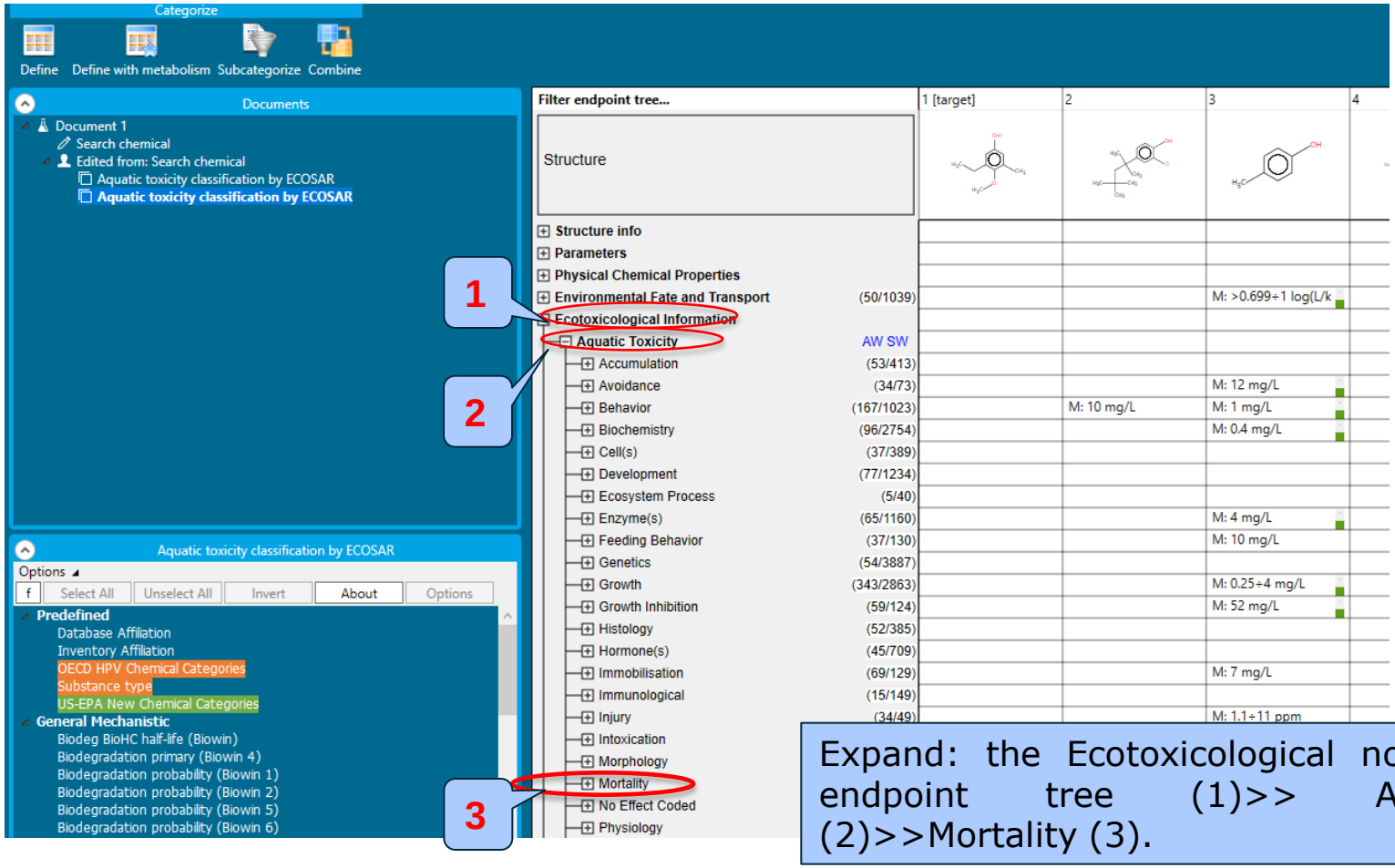
Category Definition

Navigation through the endpoint tree

- The user can navigate through the data tree by opening (or closing) the nodes of the tree.
- The data tree is extensive but logically constructed. It can be mastered with a practice.
- In this example, the "48 h LC50 Mortality for *Daphnia magna*" is the target endpoint.
- You can navigate through the endpoint tree by typing the species "Daphnia magna" in the "Filter endpoint tree…" box and clicking (Aquatic Toxicity, Mortality, LC50, 48 h, Animalia, etc to *Daphnia magna* - the specific endpoint (see next two slides).

Category Definition

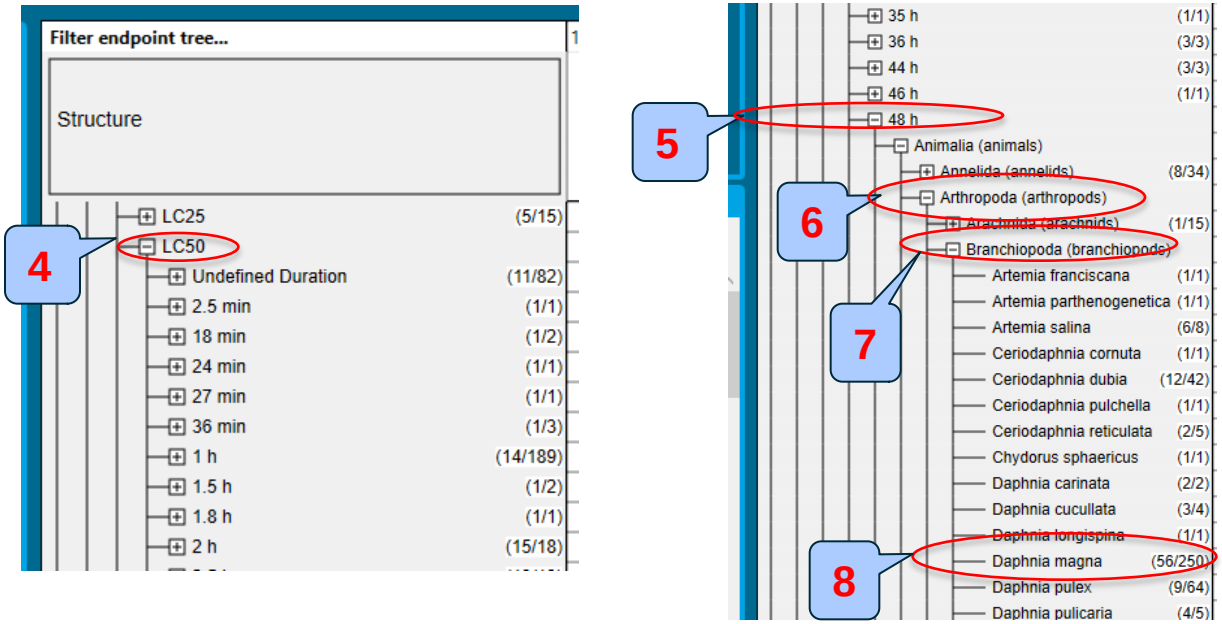
Navigation through the endpoint tree



Expand: the Ecotoxicological node of endpoint tree (1)>> Aquatic (2)>>Mortality (3).

Category Definition

Navigation through the endpoint tree



>> *LC50 (4)* >> *48h (5)* >>Arthropoda (arthropods) (6)>>Branchiopoda (branchiopods) (7)>>**Daphnia magna** (8) - this is the species related to target endpoint.

Recap

- You have now retrieved the available experimental data on aquatic toxicity for 767 chemicals classified as "phenols" by the "Aquatic toxicity classification by ECOSAR" profiler found in the databases Aquatic ECETOC, Aquatic Japan MoE, ECOTOX, and Aquatic OASIS.
- You have identified the target endpoint of "48 h LC50 Mortality for *Daphnia magna*".
- You are ready to fill in the data gap so click *Data Gap Filling* (see next slide).

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- **Workflow of the exercise**
  - Chemical Input
  - Profiling
  - Data
  - Category definition
  - **Data Gap Filling**

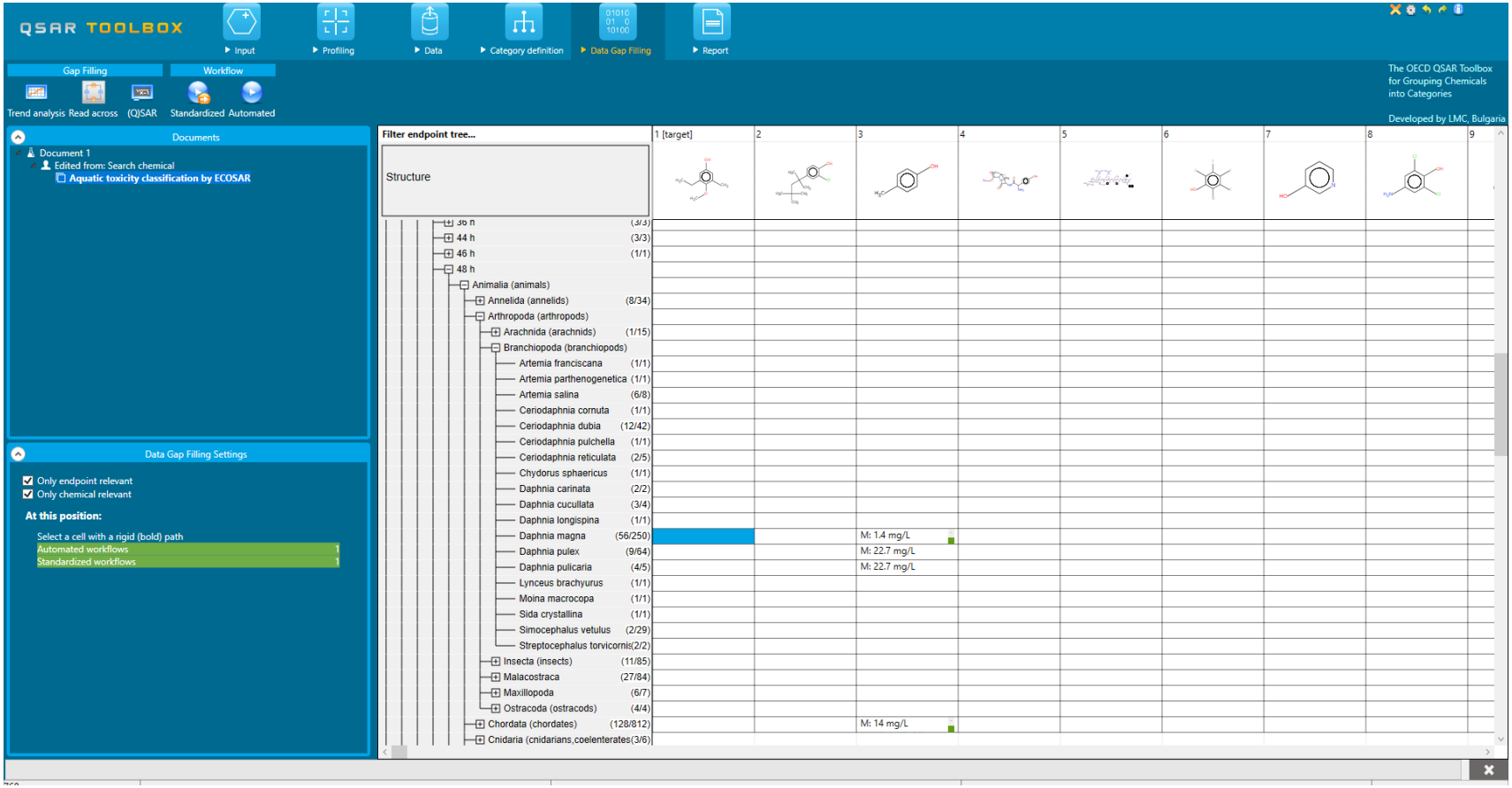
Data Gap Filling

Overview

- *Data Gap Filling* module gives access to five different data gap filling tools:
  - Read-across
  - Trend analysis
  - (Q)SAR models
  - Standardized workflow (SW)
  - Automated workflow (AW)
- The most relevant data gap mechanism is used , 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.
  - *Automated and standardized workflows* follow preliminary implemented logic. The AW is not affected by the user activities (proceeding or subsequent), while the SW stops at the each step of the workflows allowing the user to make different selection.
- In this example we use trend analysis.

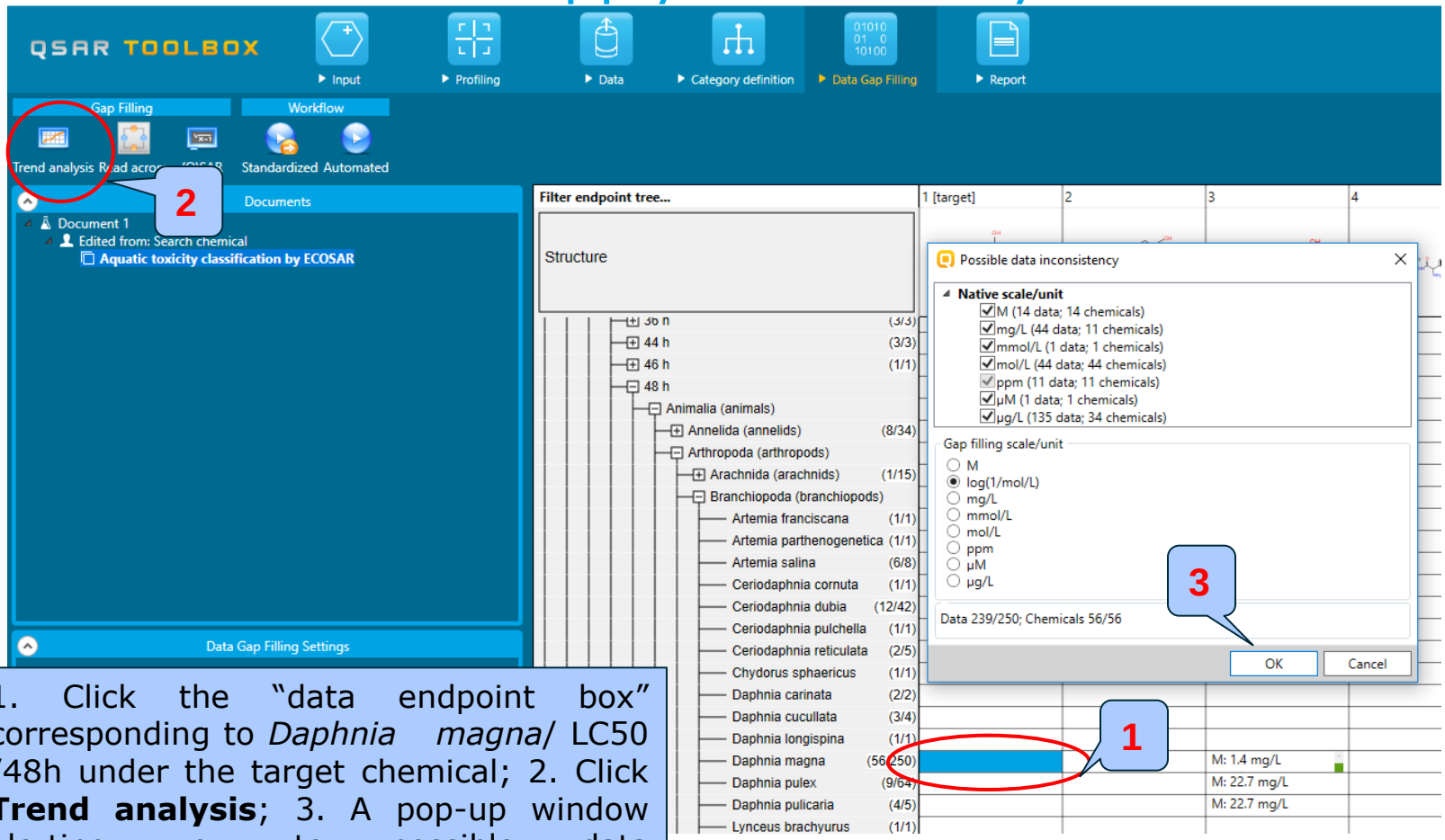
Data Gap Filling

Data Gap window



Data Gap Filling

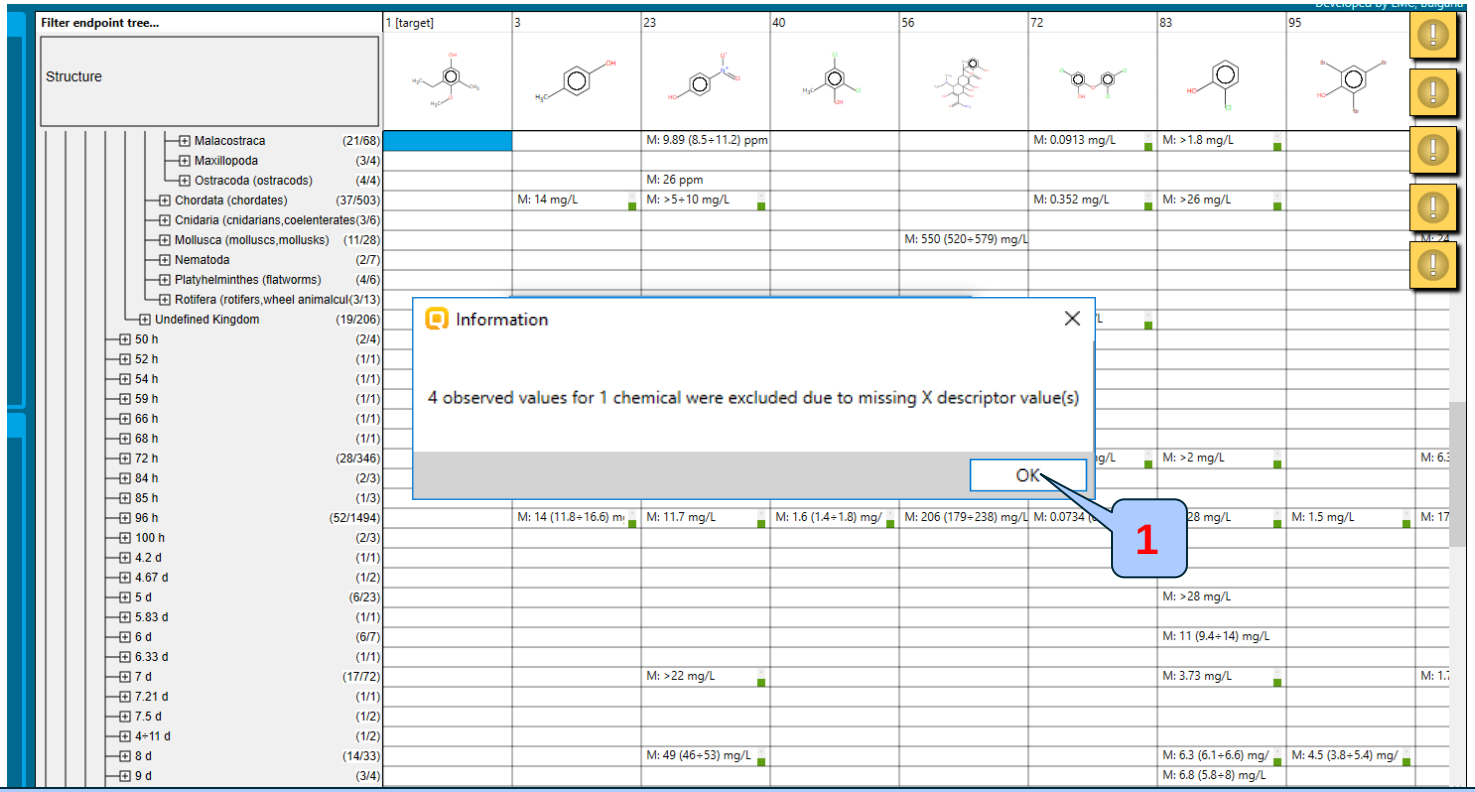
Apply Trend analysis



1. Click the "data endpoint box" corresponding to *Daphnia magna*/ LC50 /48h under the target chemical; 2. Click **Trend analysis**; 3. A pop-up window alerting you to possible data inconsistencies appears. Click **OK**.

Data Gap Filling

Results of Trend analysis



A pop-up message informs about the number of data points across the number of chemicals (e.g. mixtures or UVCB substances) that will not be included in the Trend analysis prediction due to missing X descriptor value(s), which by default is Log*Kow*. Click OK (1).

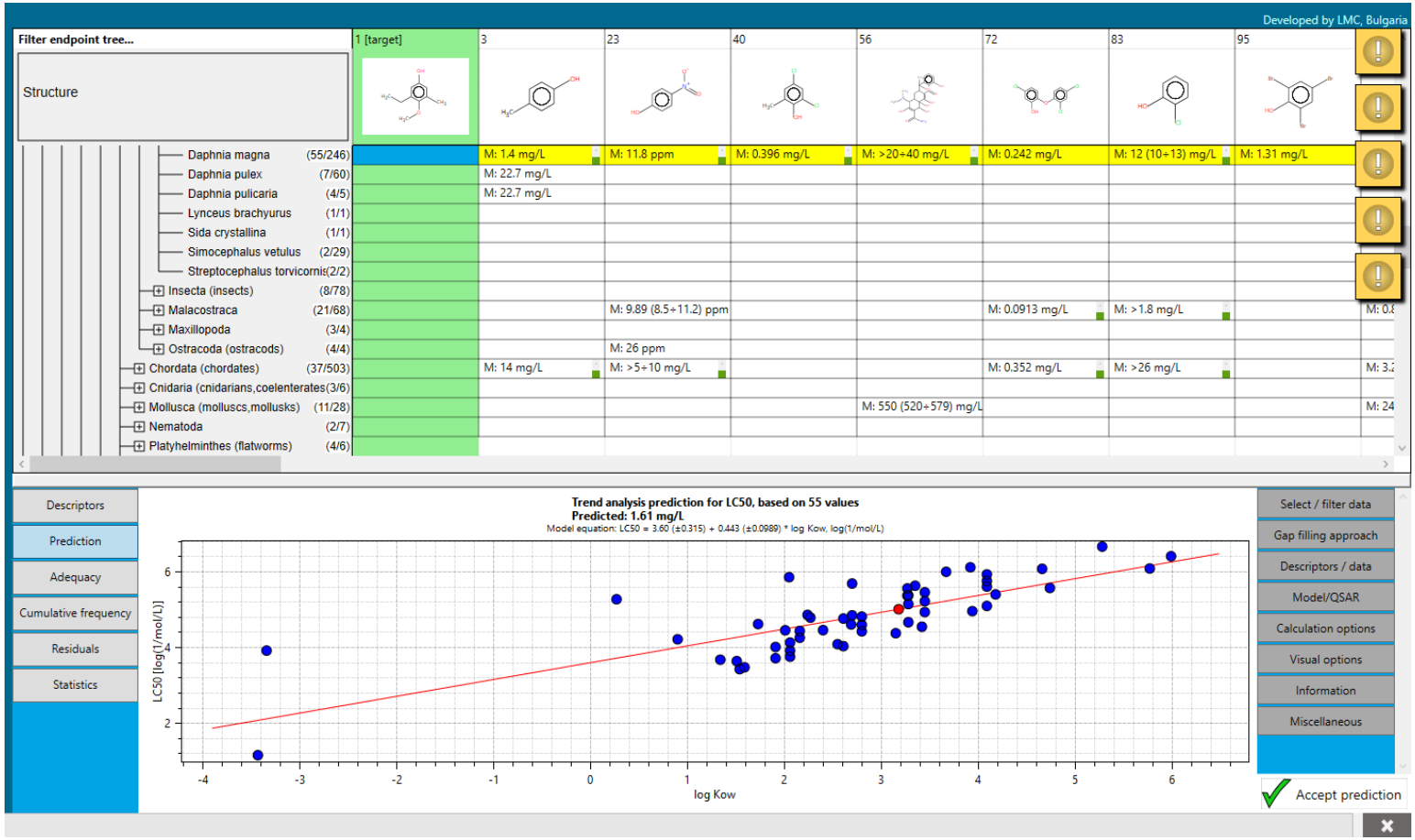
Data Gap Filling

Interpreting Trend analysis

- The resulting plot outlines the log of the experimental LC50 results of all analogues (Y axis) according to a descriptor (X axis) with Log *Kow* being the default descriptor (see next slide).
- The **RED** points represents the predicted value for the target chemical.
- The **BLUE** points represent the experimental results available for the analogues used in the trend analysis.
- The square-shaped signs in the right side of the data gap filling window are the so-called "helpers". The helpers are notifying messages that provide different type of information related to the used data points in the prediction.
- Before accepting the estimated result for the target chemical, the trend analysis should be further refined by subcategorization (see the next slides).

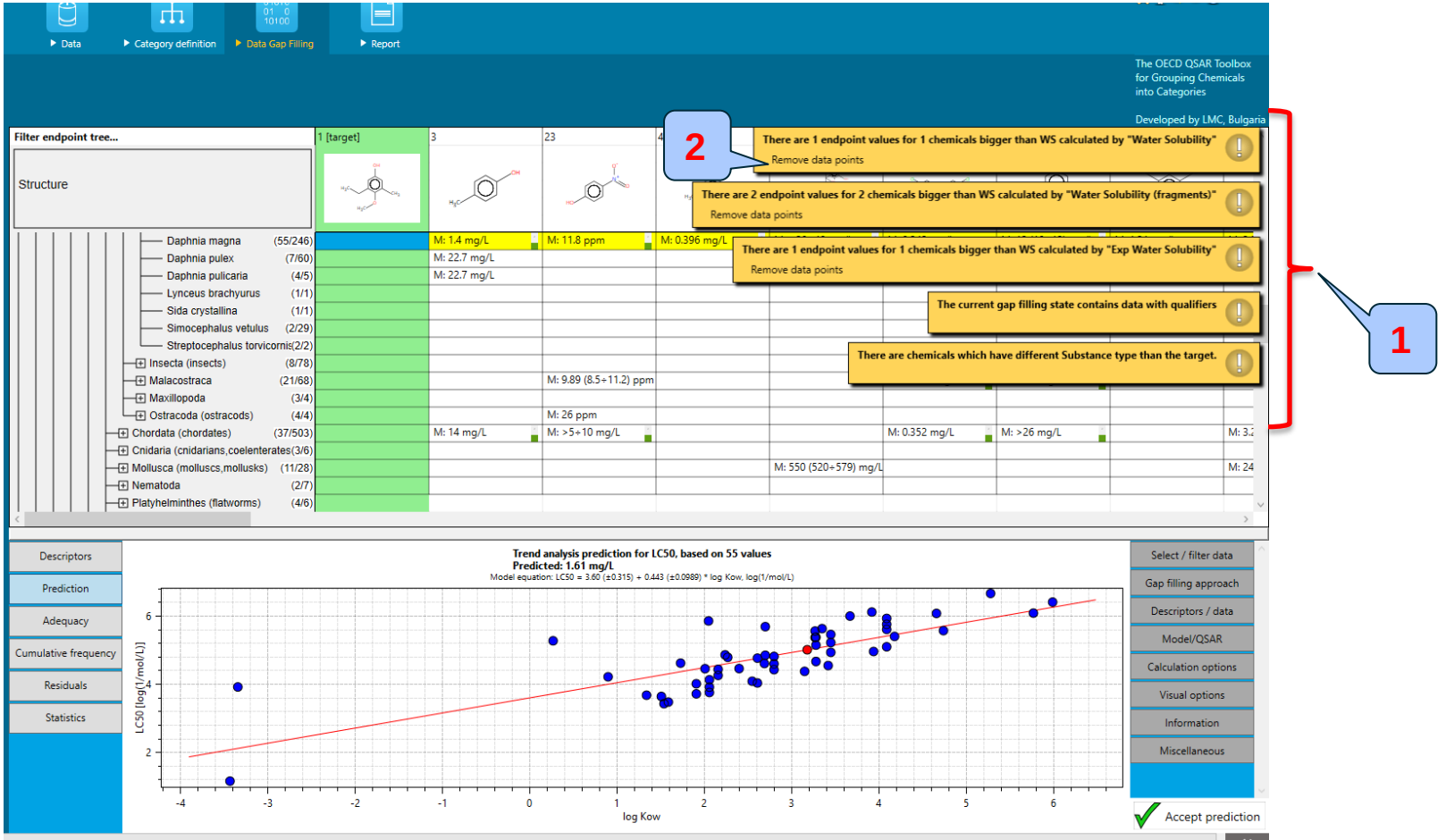
Data Gap Filling

Results of Trend analysis



Data Gap Filling

Results of Trend analysis



1. Click the helpers to see the information that they provide; 2. Click ***Remove data points*** in order to eliminate the data points that have values bigger than WS. Once the data points are removed the helpers disappear.

Data Gap Filling

Subcategorization

- Remember in the Toolbox, a category refers to a group of chemicals which have the same profiling result according to one of the profilers listed in the module *Profiling*.

- Subcategorization refers to the process of applying additional profilers to the previously defined category. The subcategorization identifies chemicals which have differing profiling results and eventually eliminating these chemicals from the final category.

Data Gap Filling

Subcategorization

In this example, subcategorization allows for the elimination of analogues which are dissimilar to the target chemical with respect to:

- Substance type (mixtures and hydrolizing chemicals)

  The categorisation based on substance type allows keeping among the analogues only those that are of the same chemical type: discrete chemical, organic, mixture, polymer(predefined), inorganic, mono constituent(predefined) or multi constituent(predefined). The current target is a discrete chemical, organic, mono constituent(predefined) hence the analogues should also be discrete chemicals.

- OASIS Mode of action (all except phenols and anilines)

  The categorization based on mode of action identifies analogues having the same mode of action as the target which is in the group of phenols and anilines.

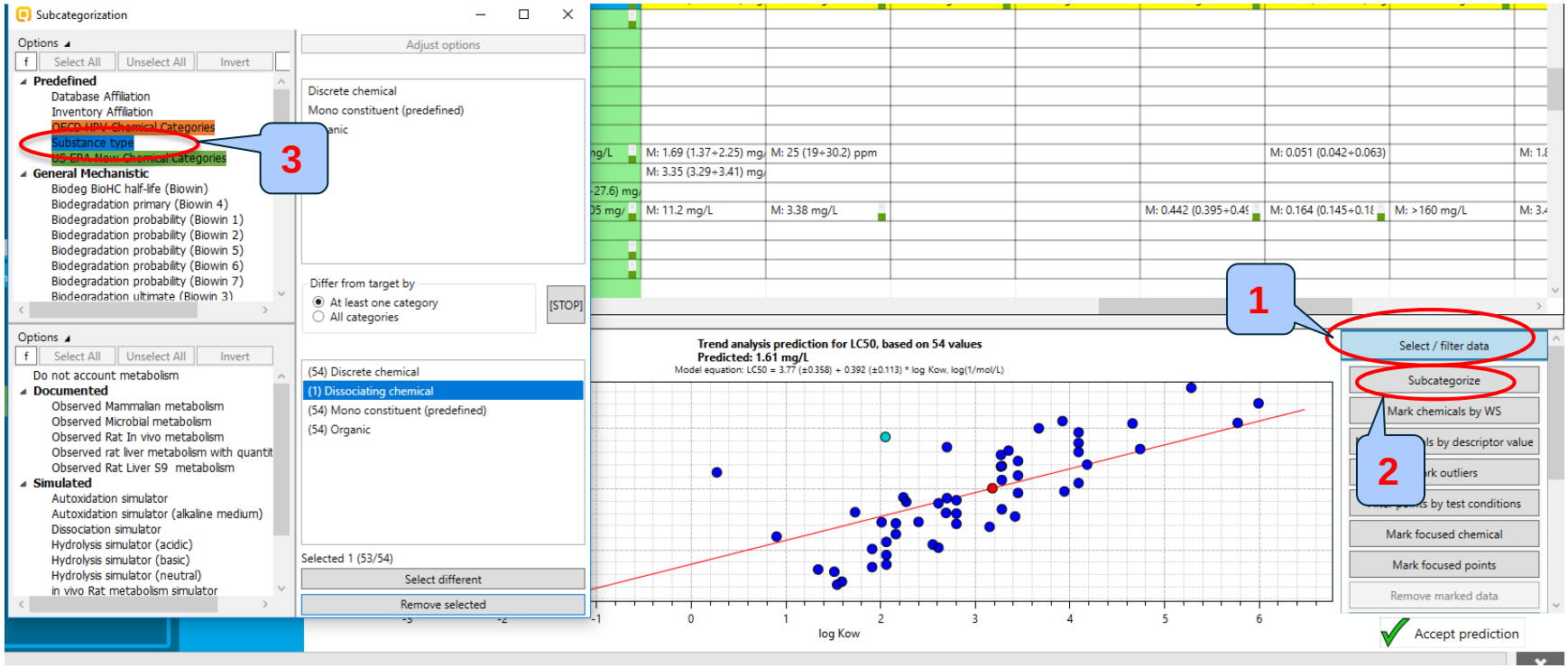
- Chemical elements

The profiler aimed to identify analogues consisting of same elements as those presented in the target chemical

Subcategorization is demonstrated in the next 4 slides.

Data Gap Filling

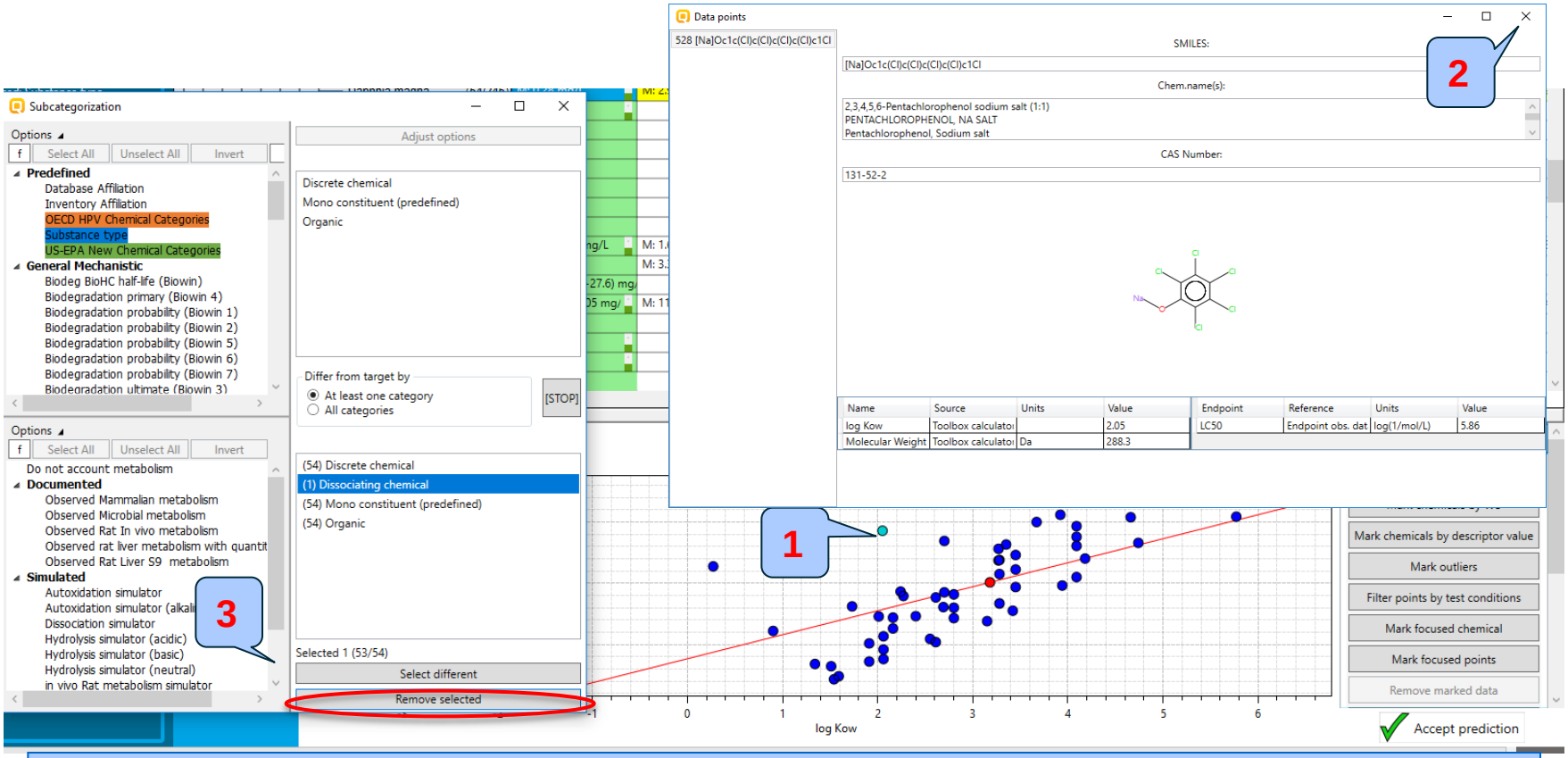
Subcategorization by Substance type



1. Open **Select/filter data**; 2. Select **Subcategorize**; 3. Select ***Substance type***

Data Gap Filling

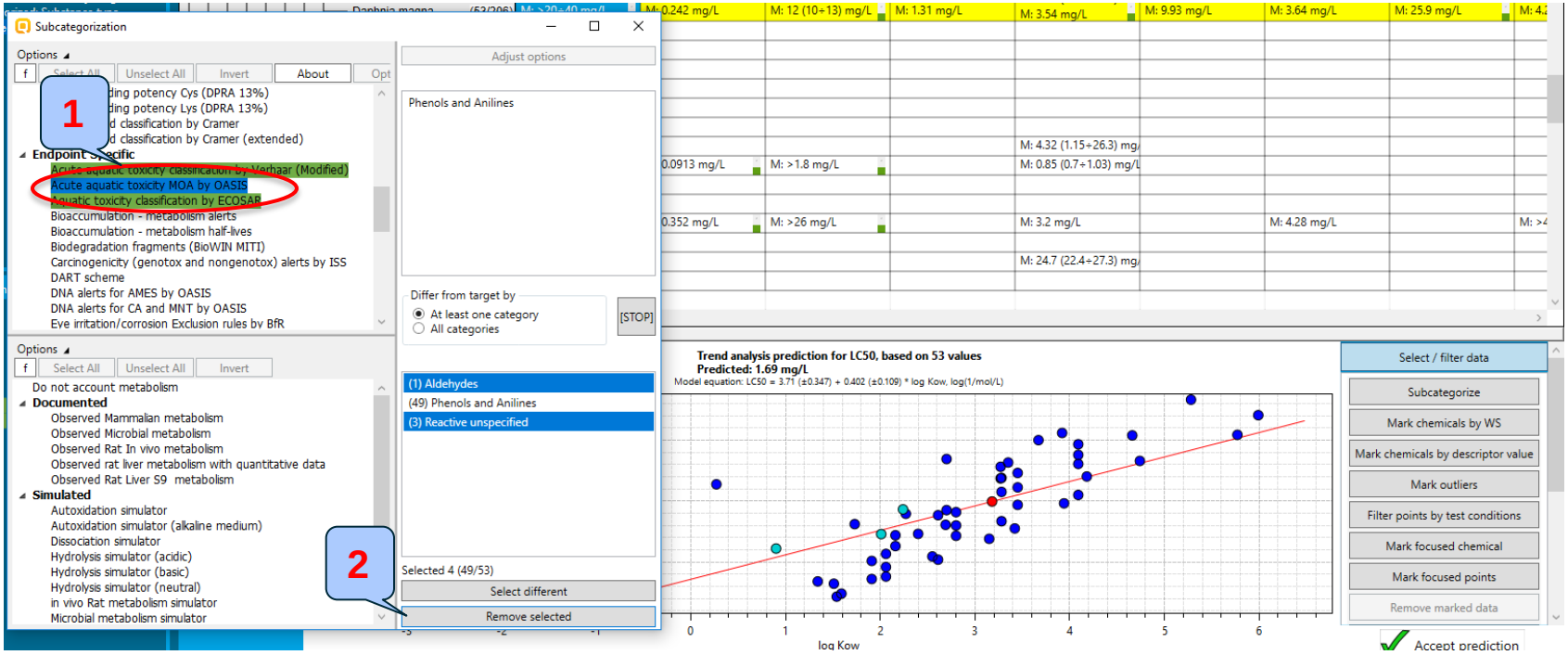
Subcategorization by Substance type



1. **Double click** on the highlighted outlier to see why this chemical is different to the target. The chemical is dissociating chemical, mono constituent and organic and should to be eliminated being different substance type compared to the target. 2. Click **Close**; 3. Click **Remove selected** to eliminate dissimilar chemicals.

Data Gap Filling

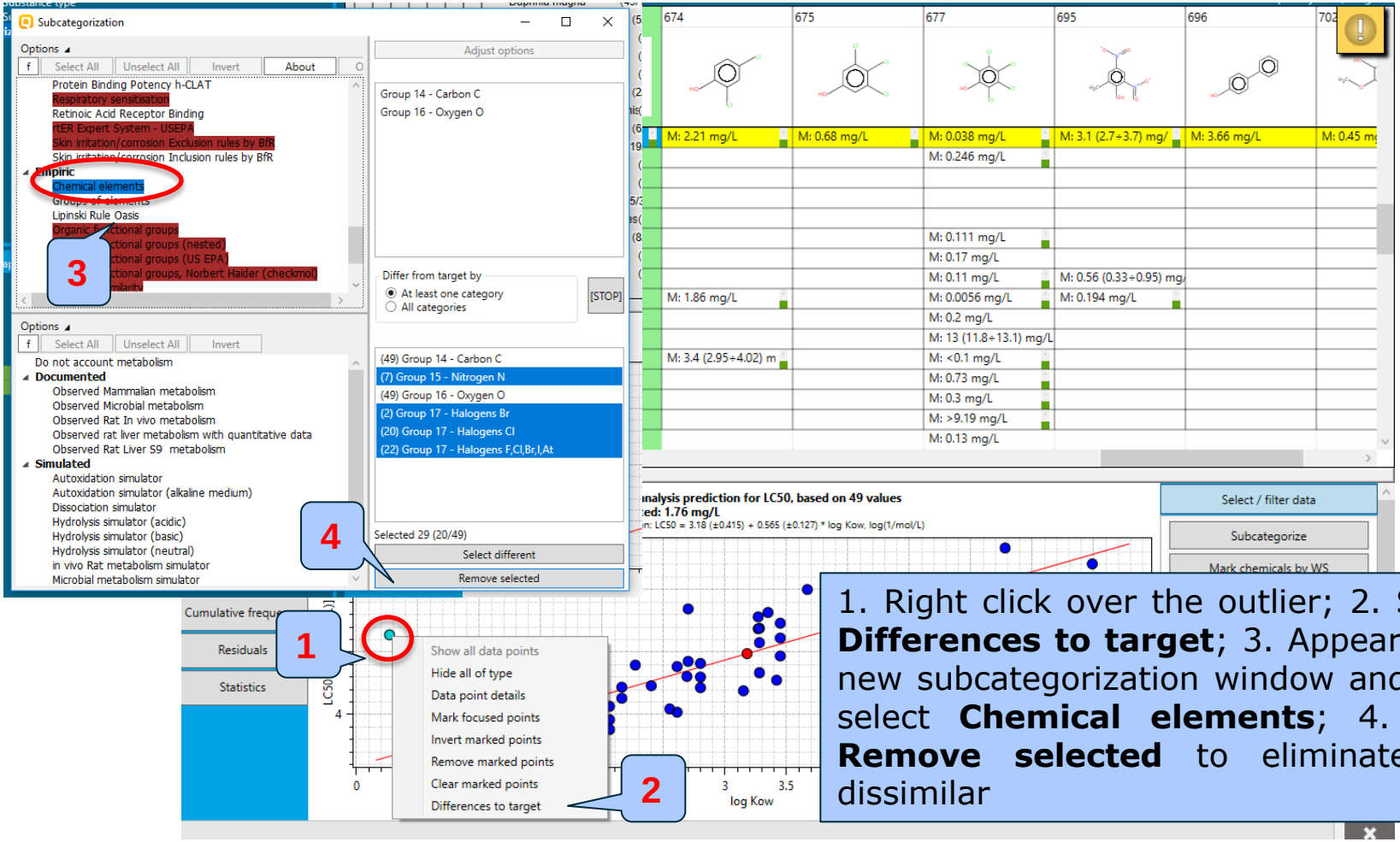
Subcategorization by Acute-aquatic toxicity MOA



1. Select ***Acute aquatic toxicity MOA by OASIS***; 2. Click **Remove selected** to eliminate the dissimilar chemicals.

Data Gap Filling

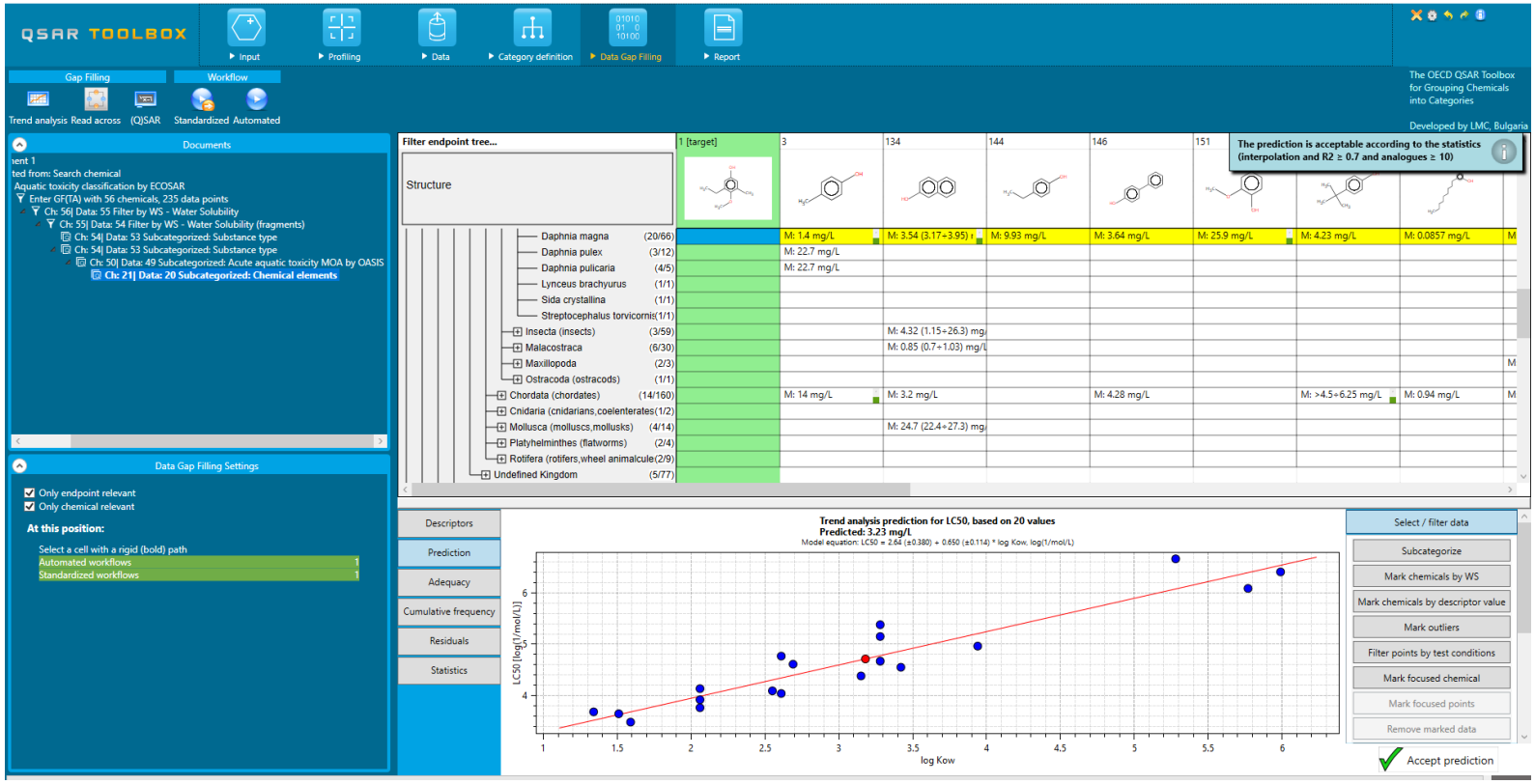
Subcategorization by Chemical elements



1. Right click over the outlier; 2. Select **Differences to target**; 3. Appearing of new subcategorization window and then select **Chemical elements**; 4. Click **Remove selected** to eliminate the dissimilar

Data Gap Filling

Results



Helper indicating that the prediction is acceptable according to the statistic appears.

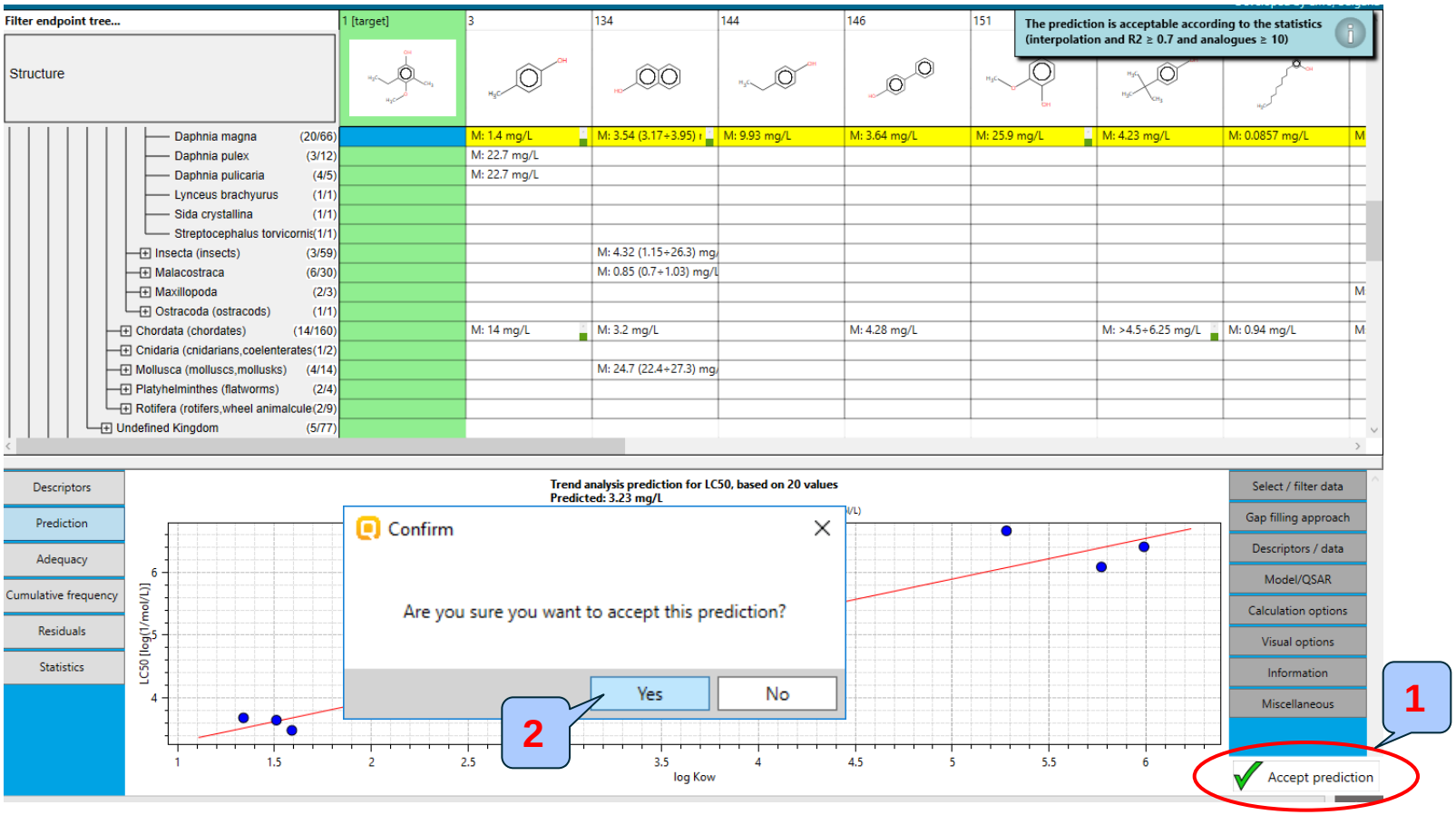
Data Gap Filling

Results

- The remaining chemicals in the graph now all have a consistent profile relevant for aquatic toxicity (i.e. Substance type, Classification by ECOSAR, MOA by OASIS and Chemical elements).
- By accepting the prediction the data gap is filled (see next screen shot).

Data Gap Filling

Accepting prediction result



1. Click **Accept prediction**; 2. Click **Yes** to confirm the prediction. The prediction is accepted successfully and the system automatically returns you to the data matrix.

Outlook

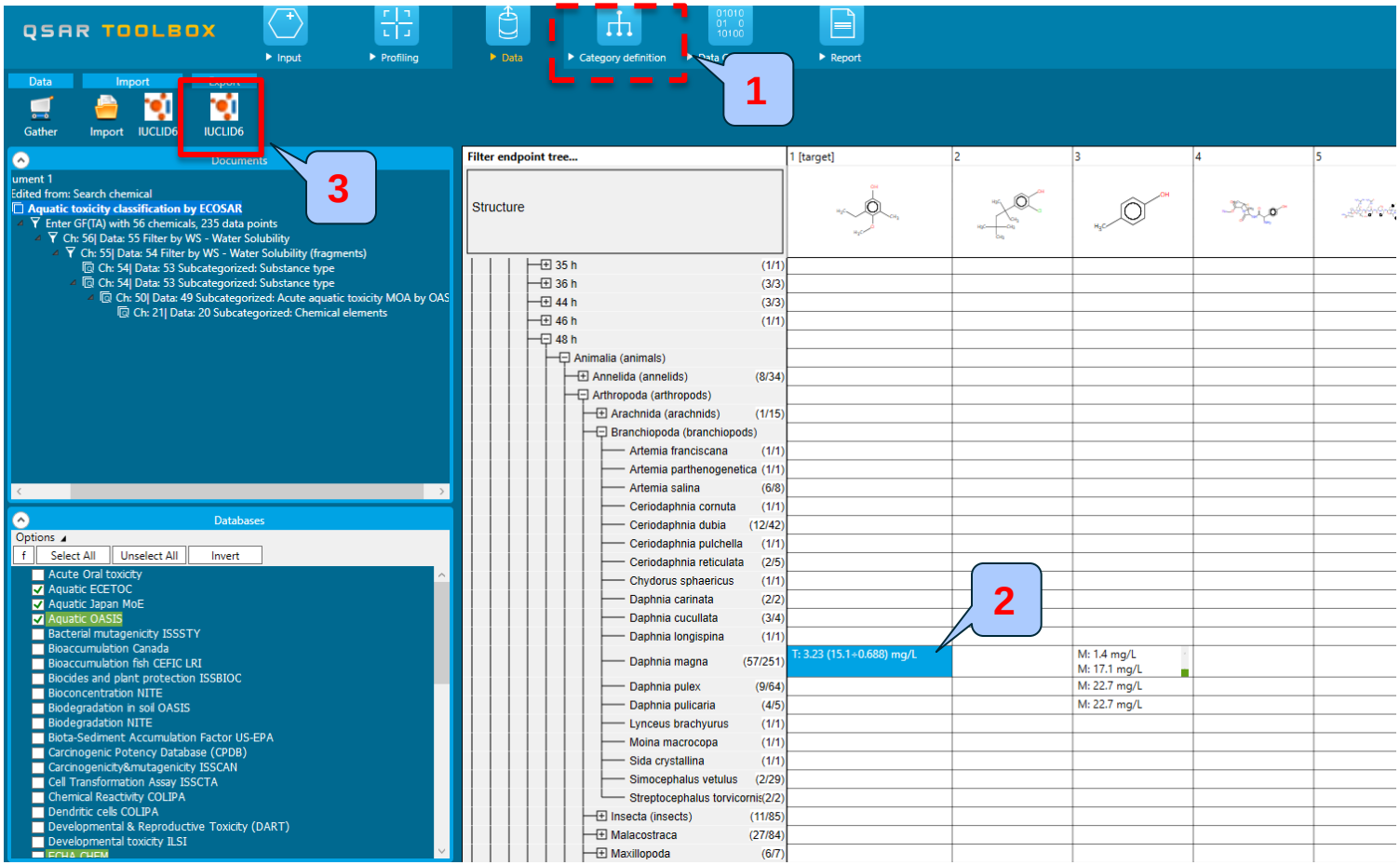
- Background
- Objectives
- Specific Aims
- Trend analysis
- The exercise
- **Workflow of the exercise**
  - Chemical Input
  - Profiling
  - Data
  - Category definition
  - Data Gap Filling
  - **Export a prediction to IUCLID6**

Export prediction to the IUCLID 6
Overview

- The OECD QSAR Toolbox allows the users to export predicted data (by means of the Filling Data Gap tools) to IUCLID 6.
- The way of exporting is connect to an IUCLID 6 server (via WebServices) and assigning the predicted endpoint data to a selected substance.
- A wizard will guide the user through the different steps of exporting (see next screenshot).

Exporting the prediction to IUCLID 6

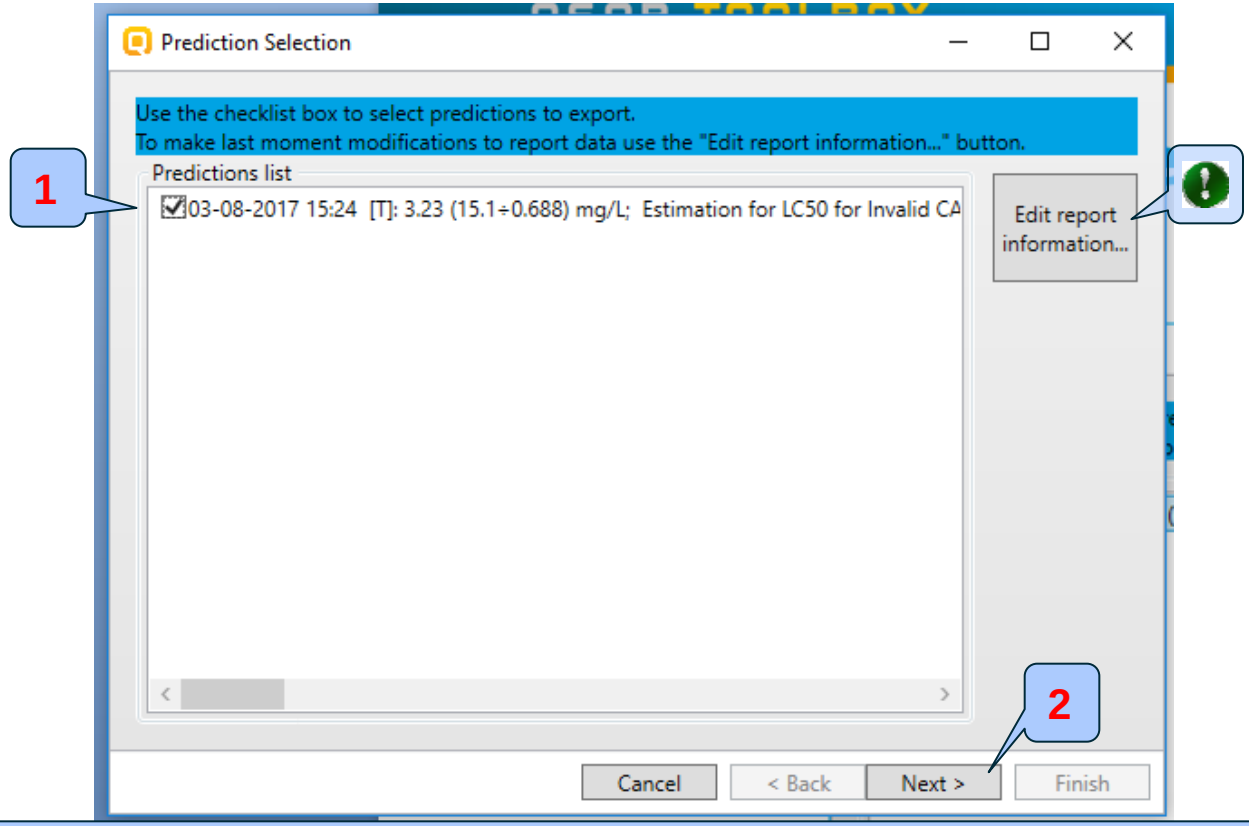
Case study



1. Go to **Data** section; 2. Click the prediction; 3. Click **IUCLUD6**.

Exporting the prediction to IUCLID 6

Case study

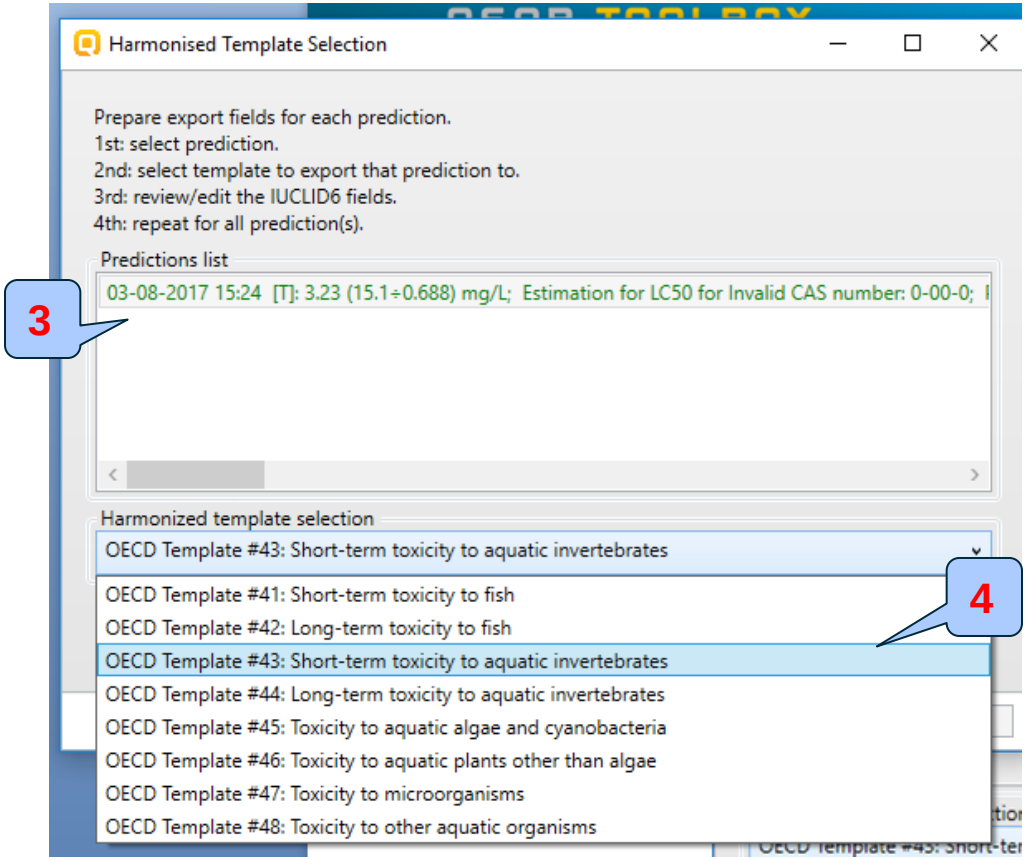


1. Tick the prediction to export 2. Click **Next** to move through the next step of the export.

The user could also edit the report information

Exporting the prediction to IUCLID 6

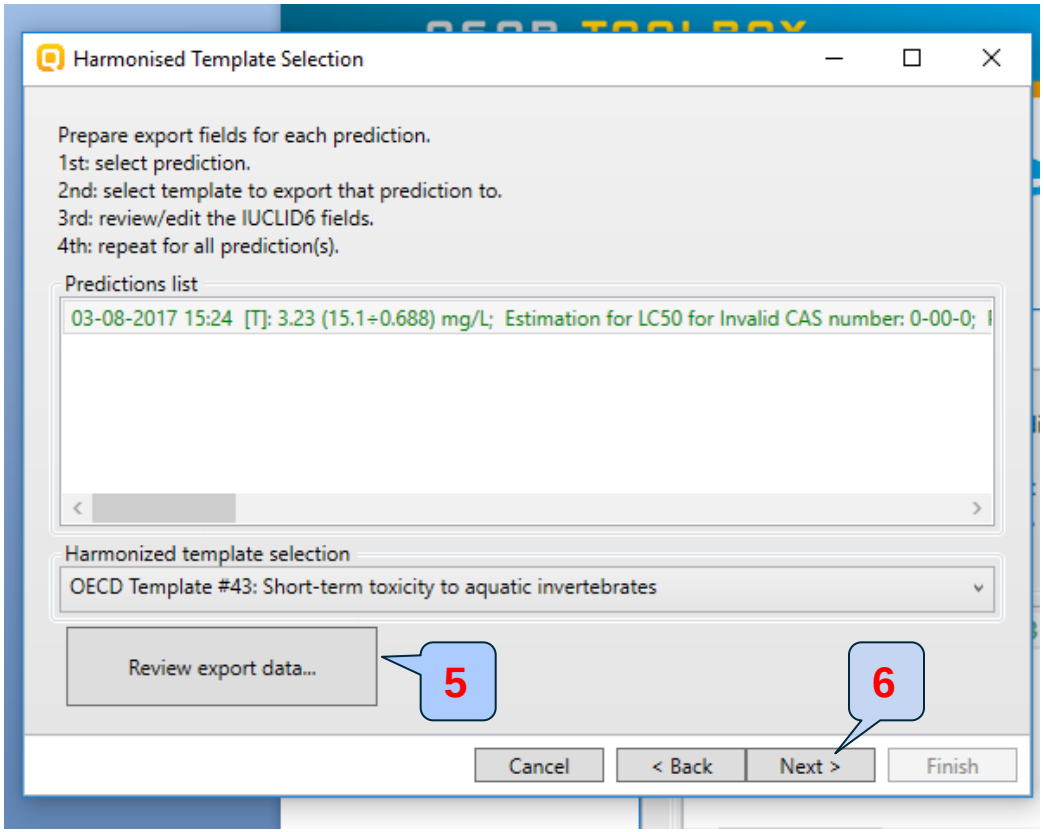
Case study



3. Select a prediction; 4. Select a template to export the prediction

Exporting the prediction to IUCLID 6

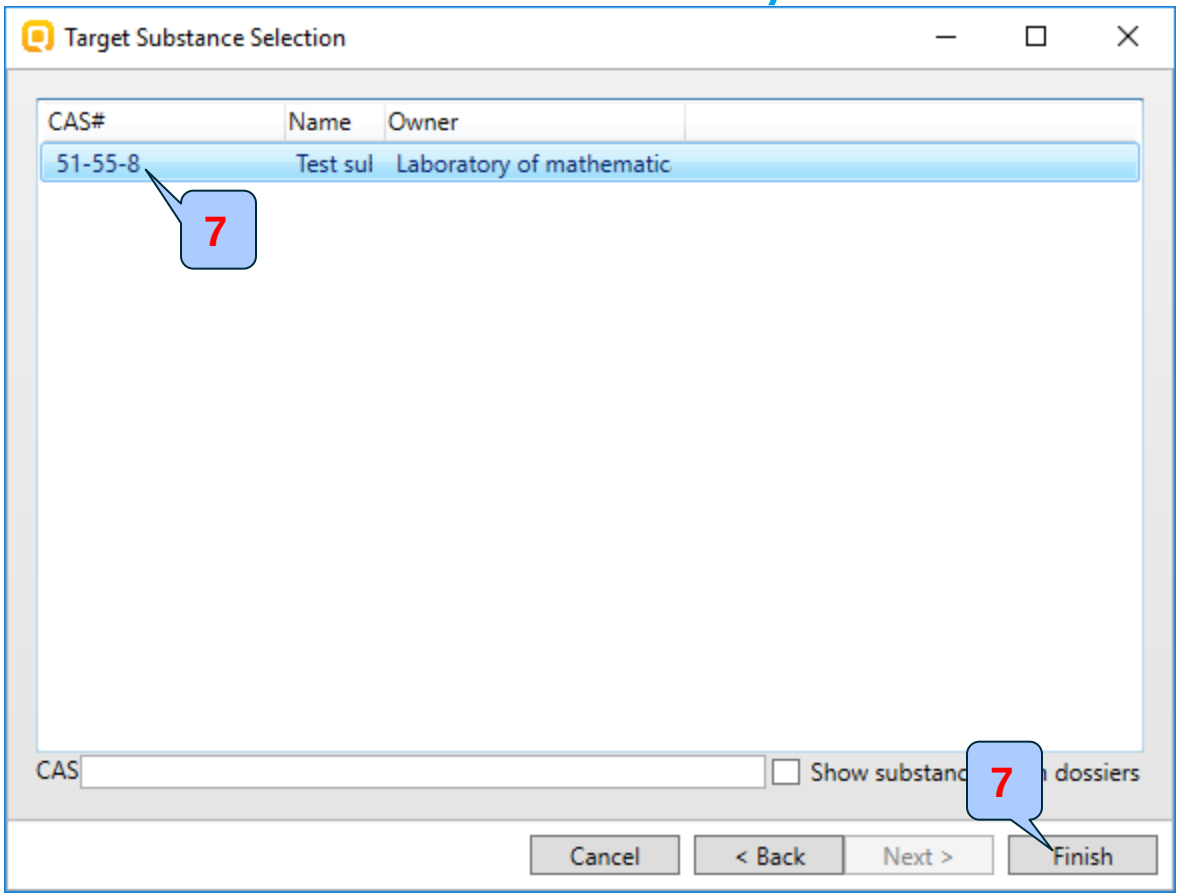
Case study



5. Review/edit the IUCLID6 fields; 6. Click **Next**

Exporting the prediction to IUCLID 6

Case study



7. Select a substance to assigning the predicted endpoint data; 8. Click **Finish**

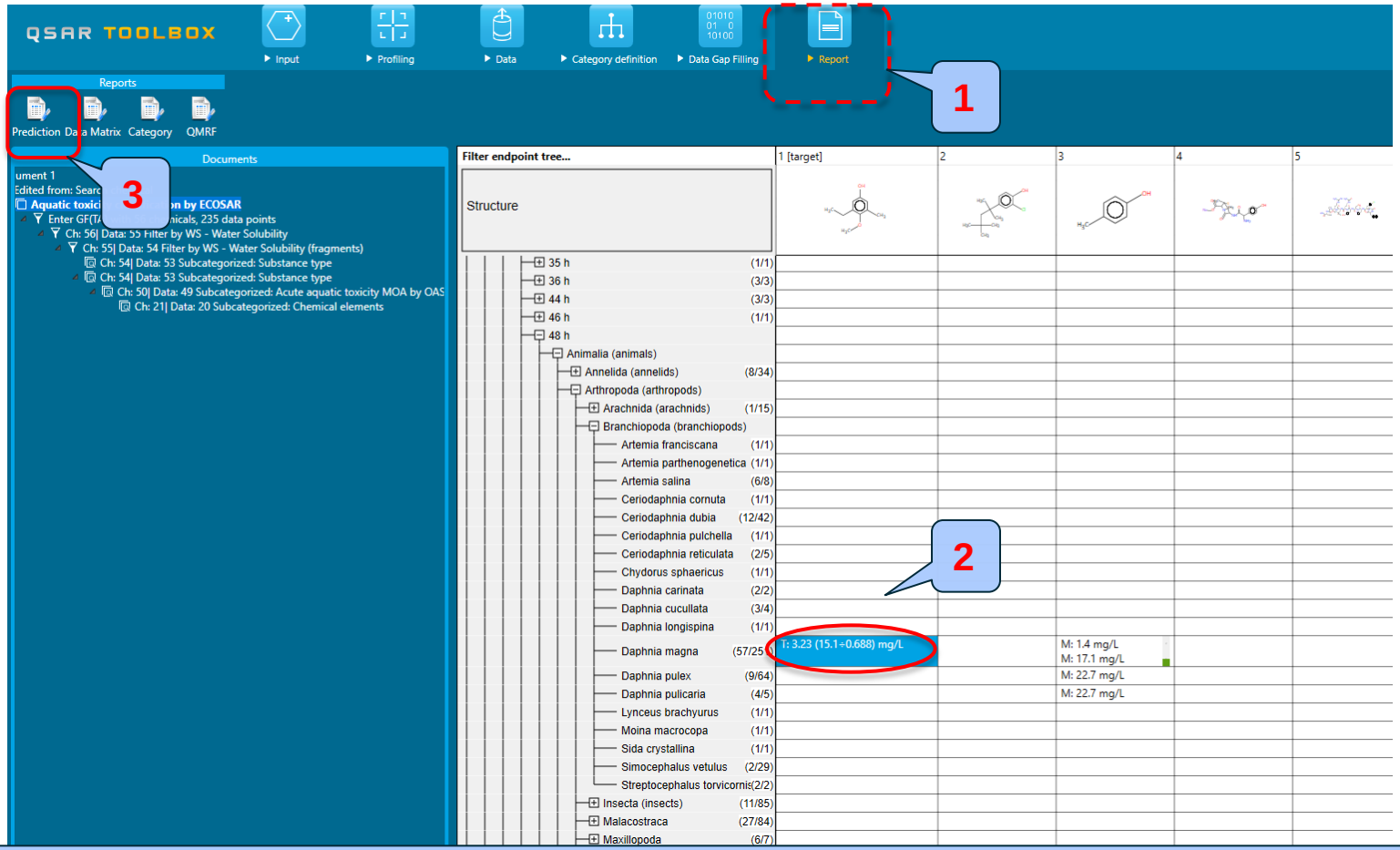
Outlook

- Background
- Objectives
- Specific Aims
- Trend analysis
- The exercise
- **Workflow of the exercise**
  - Chemical Input
  - Profiling
  - Data
  - Category definition
  - Data Gap Filling
  - Export a prediction to IUCLID5
  - **Report**

Report
Overview

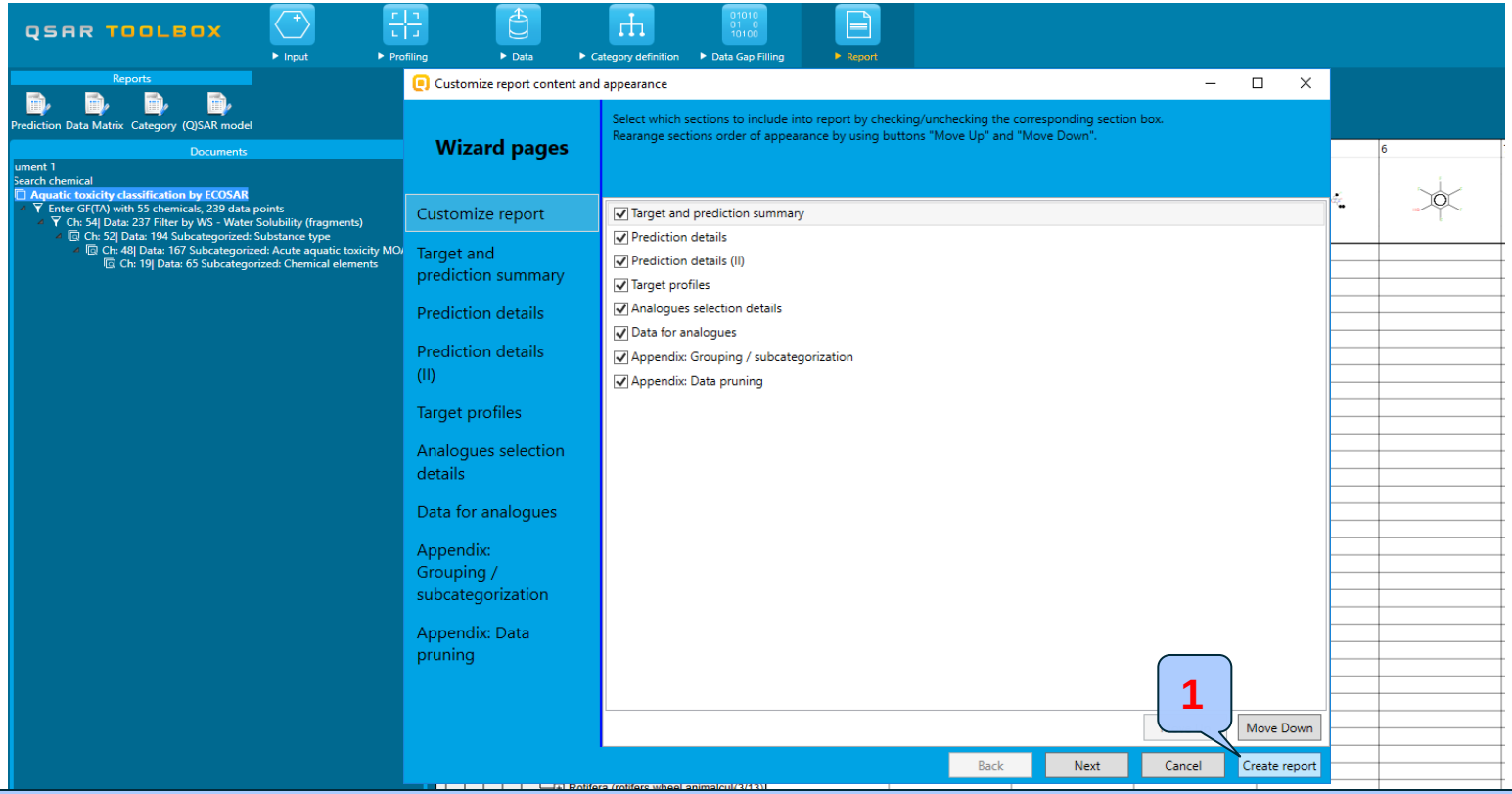
- Report module could generate report on any of predictions performed with the Toolbox.
- Report module contains predefined report templates, which could be customized.
- The report can then be printed or saved in different formats.

Report
Generation report



1. Go to the **Report** module; 2. Highlight the prediction result; 3. Click **Prediction** to create a report

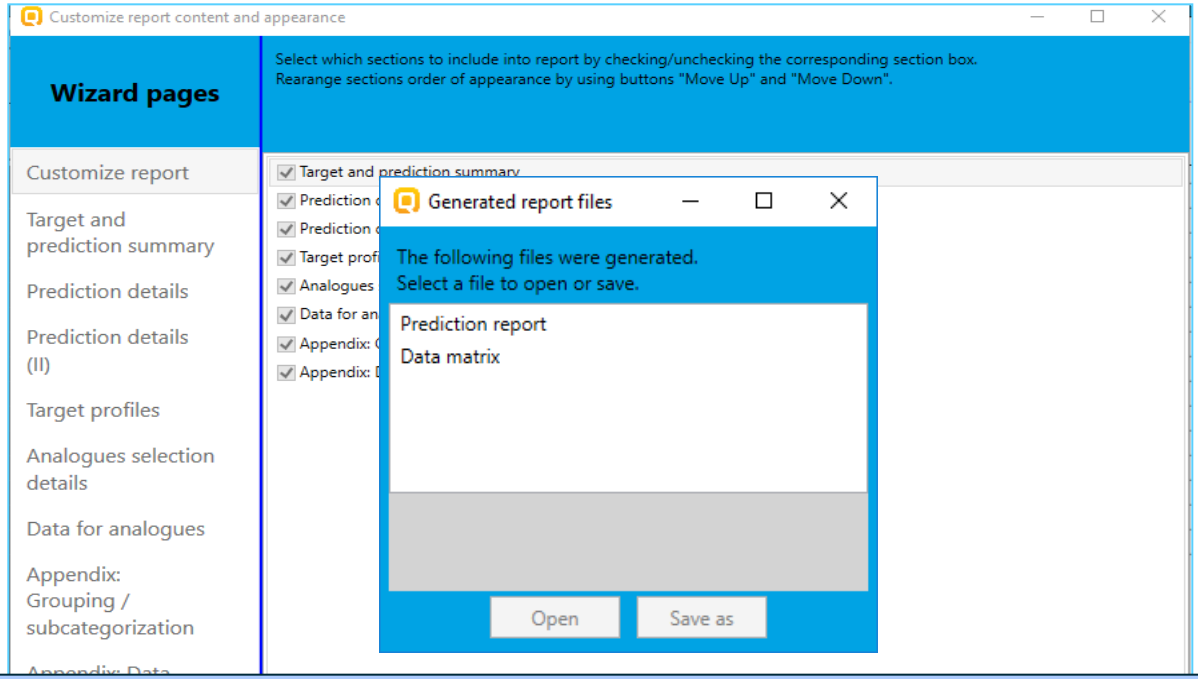
Report
Generation report



Report wizard pages appear, where the user could customize the report content and appearance. Some of the fields in the report are automatically populated by the system.

1. Click **Create report** to generate the report.

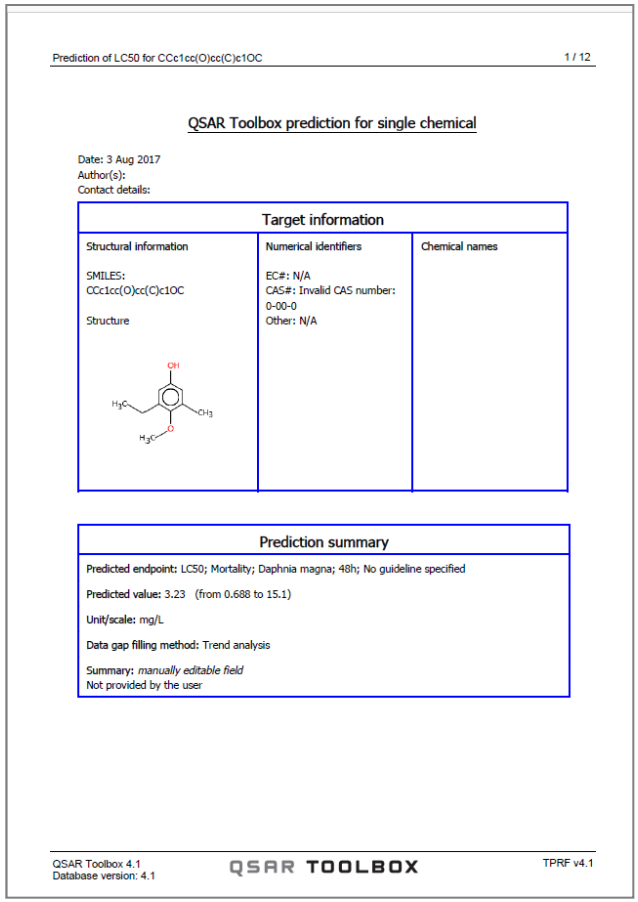
Report
Generation report



Additional window appears with two options: ***Prediction report*** or ***Data matrix***. The user can open and/or save the files.

- The **Prediction report** is a PDF file containing the prediction information related to the target.
- The **Data matrix** is a MS Excel file containing chemicals used for prediction along with their data for selected parameters, profiles and endpoint tree positions.

Prediction report
Overview



Prediction of LC50 for CCc1cc(O)cc(C)c1OC 1 / 12

QSAR Toolbox prediction for single chemical

Date: 3 Aug 2017
Author(s):
Contact details:

Target information

Structural information	Numerical identifiers	Chemical names
SMILES: CCc1cc(O)cc(C)c1OC Structure	EC#: N/A CAS#: Invalid CAS number: 0-00-0 Other: N/A	

Prediction summary

Predicted endpoint: LC50; Mortality; Daphnia magna; 48h; No guideline specified

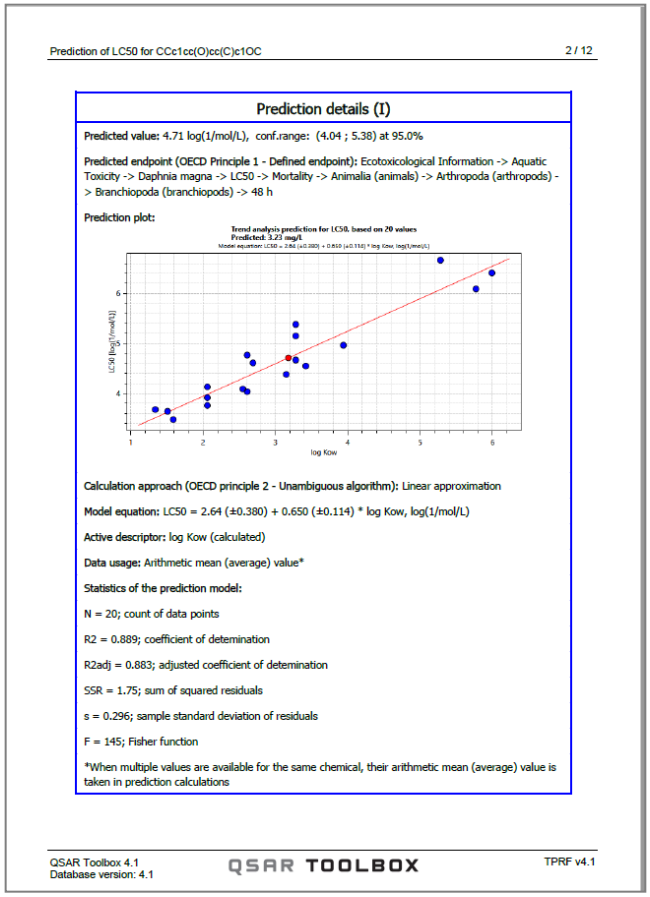
Predicted value: 3.23 (from 0.688 to 15.1)

Unit/scale: mg/L

Data gap filling method: Trend analysis

Summary: *manually editable field*
Not provided by the user

QSAR Toolbox 4.1
Database version: 4.1
QSAR TOOLBOX
TPRF v4.1



Prediction of LC50 for CCc1cc(O)cc(C)c1OC 2 / 12

Prediction details (I)

Predicted value: 4.71 log(1/mol/L), conf.range: (4.04 ; 5.38) at 95.0%

Predicted endpoint (OECD Principle 1 - Defined endpoint): Ecotoxicological Information -> Aquatic Toxicity -> Daphnia magna -> LC50 -> Mortality -> Animalia (animals) -> Arthropoda (arthropods) -> Branchiopoda (branchiopods) -> 48 h

Prediction plot:

Calculation approach (OECD principle 2 - Unambiguous algorithm): Linear approximation

Model equation: LC50 = 2.64 (±0.380) + 0.650 (±0.114) * log Kow, log(1/mol/L)

Active descriptor: log Kow (calculated)

Data usage: Arithmetic mean (average) value*

Statistics of the prediction model:

N = 20; count of data points

R2 = 0.889; coefficient of detemination

R2adj = 0.883; adjusted coefficient of detemination

SSR = 1.75; sum of squared residuals

s = 0.296; sample standard deviation of residuals

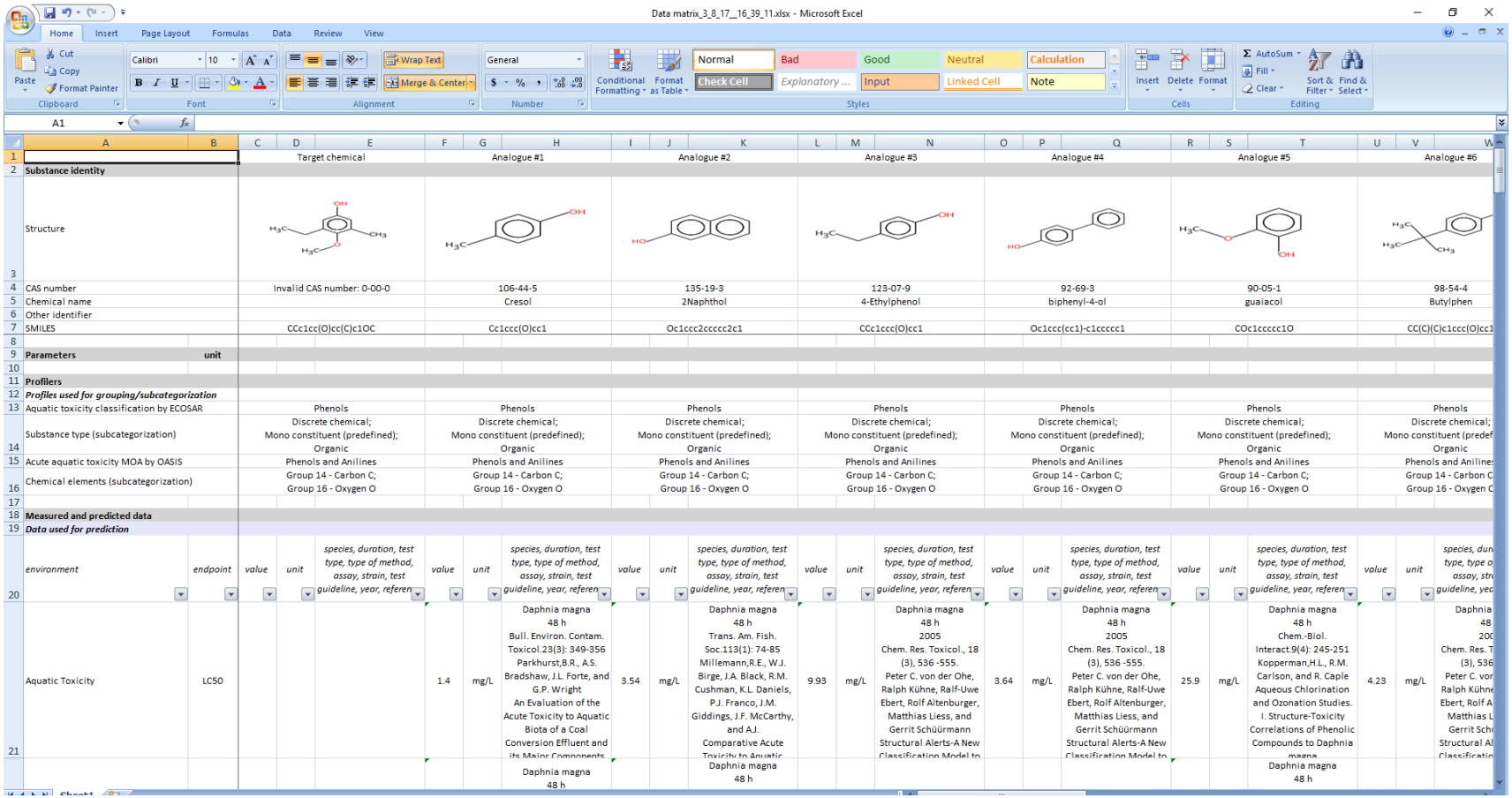
F = 145; Fisher function

*When multiple values are available for the same chemical, their arithmetic mean (average) value is taken in prediction calculations

QSAR Toolbox 4.1
Database version: 4.1
QSAR TOOLBOX
TPRF v4.1

Data matrix

Overview



		Target chemical	Analogue #1	Analogue #2	Analogue #3	Analogue #4	Analogue #5	Analogue #6
Substance identity								
Structure								
CAS number		Invalid CAS number: 0-00-0	106-44-5	135-19-3	123-07-9	92-69-3	90-05-1	98-54-4
Chemical name			Cresol	2Naphthol	4-Ethylphenol	biphenyl-4-ol	guaiacol	Butylphen
Other identifier								
SMILES		CCc1cc(O)cc(C)c1OC	Cc1ccc(O)cc1	Oc1ccc2ccccc2c1	CCc1ccc(O)cc1	Oc1ccc(cc1)-c1ccccc1	COc1ccccc1O	CC(C)(C)c1ccc(O)cc1
Parameters	**unit**							
Profilers								
Profiles used for grouping/subcategorization								
Aquatic toxicity classification by ECOSAR		Phenols	Phenols	Phenols	Phenols	Phenols	Phenols	Phenols
Substance type (subcategorization)		Discrete chemical; Mono constituent (predefined); Organic	Discrete chemical; Mono constituent (predefined); Organic	Discrete chemical; Mono constituent (predefined); Organic	Discrete chemical; Mono constituent (predefined); Organic	Discrete chemical; Mono constituent (predefined); Organic	Discrete chemical; Mono constituent (predefined); Organic	Discrete chemical; Mono constituent (predef Organic
Acute aquatic toxicity MOA by OASIS		Phenols and Anilines	Phenols and Anilines	Phenols and Anilines	Phenols and Anilines	Phenols and Anilines	Phenols and Anilines	Phenols and Anilines
Chemical elements (subcategorization)		Group 14 - Carbon C; Group 16 - Oxygen O	Group 14 - Carbon C; Group 16 - Oxygen O	Group 14 - Carbon C; Group 16 - Oxygen O	Group 14 - Carbon C; Group 16 - Oxygen O	Group 14 - Carbon C; Group 16 - Oxygen O	Group 14 - Carbon C; Group 16 - Oxygen O	Group 14 - Carbon C Group 16 - Oxygen C
Measured and predicted data								
Data used for prediction								

environment	*endpoint*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, referen*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, referen*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, referen*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, referen*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, referen*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, referen*	*value*	*unit*	*species, dur type, type o assay, str guideline, yec*
Aquatic Toxicity	LC50				1.4	mg/L	Daphnia magna 48 h Bull. Environ. Contam. Toxicol.23(3): 349-356 Parkhurst,B.R., A.S. Bradshaw, J.L. Forte, and G.P. Wright An Evaluation of the Acute Toxicity to Aquatic Biota of a Coal Conversion Effluent and its Major Components	3.54	mg/L	Daphnia magna 48 h Trans. Am. Fish. Soc.113(1): 74-85 Millemann,R.E., W.J. Birge, J.A. Black, R.M. Cushman, K.L. Daniels, P.J. Franco, J.M. Giddings, J.F. McCarthy, and A.J. Comparative Acute Toxicity to Aquatic	9.93	mg/L	Daphnia magna 48 h 2005 Chem. Res. Toxicol., 18 (3), 536 -555. Peter C. von der Ohe, Ralph Kühne, Ralf-Uwe Ebert, Rolf Altenburger, Matthias Liess, and Gerrit Schüürmann Structural Alerts-A New Classification Model to	3.64	mg/L	Daphnia magna 48 h 2005 Chem. Res. Toxicol., 18 (3), 536 -555. Peter C. von der Ohe, Ralph Kühne, Ralf-Uwe Ebert, Rolf Altenburger, Matthias Liess, and Gerrit Schüürmann Structural Alerts-A New Classification Model to	25.9	mg/L	Daphnia magna 48 h Chem.-Biol. Interact.9(4): 245-251 Kopperman,H.L., R.M. Carlson, and R. Caple Aqueous Chlorination and Ozonation Studies. I. Structure-Toxicity Correlations of Phenolic Compounds to Daphnia magna	4.23	mg/L	Daphnia 48 200 Chem. Res. T (3), 536 Peter C. vor Ralph Kühn Ebert, Rolf A Matthias L Gerrit Schi Structural Al Classificatio
							Daphnia magna 48 h			Daphnia magna 48 h									Daphnia magna 48 h		

Outlook

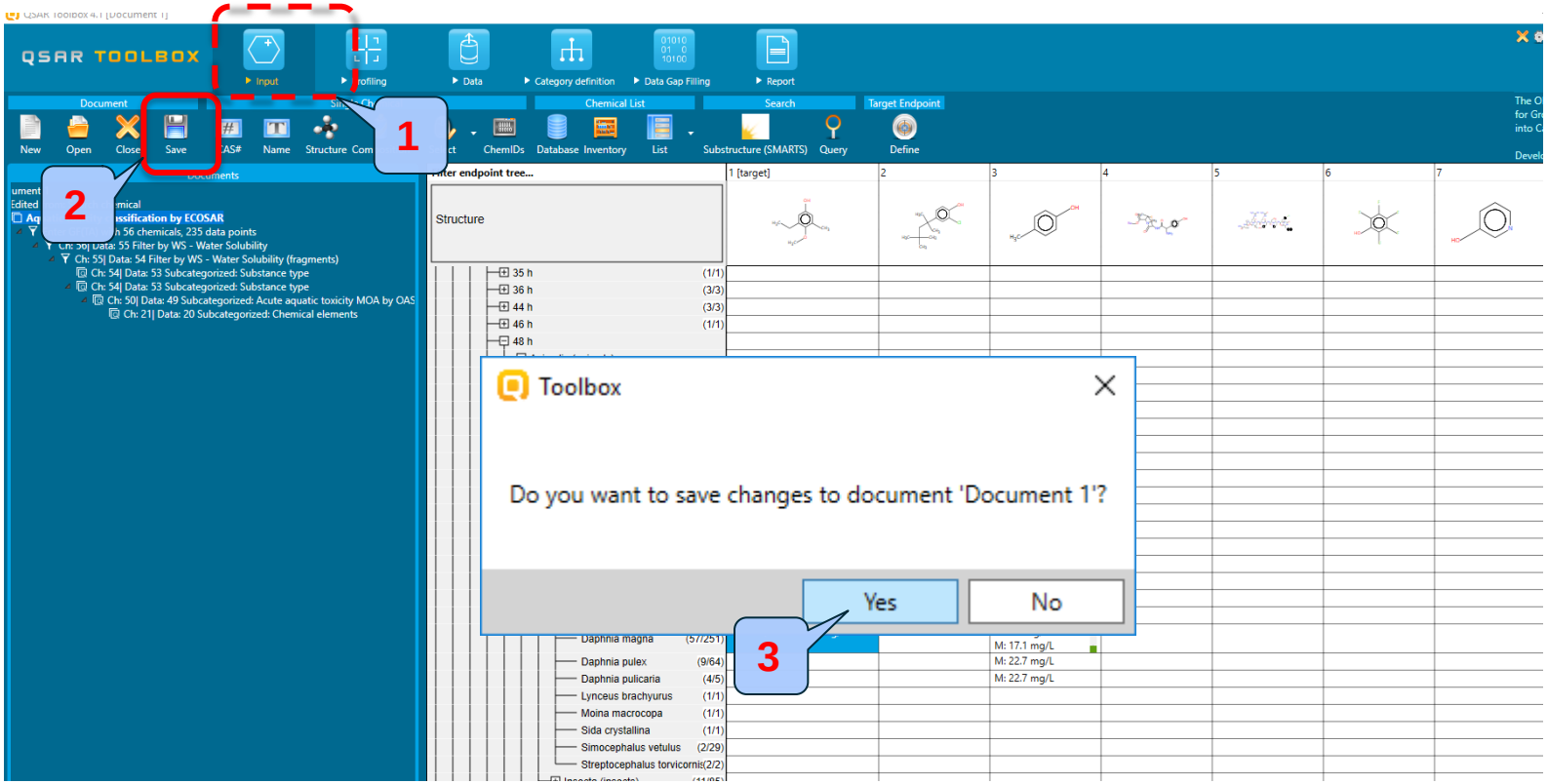
- Background
- Objectives
- Specific Aims
- Trend analysis
- The exercise
- Workflow of the exercise
- **Save the prediction result**

Saving the prediction result

- This functionality allow storing/restoring the current state of Toolbox documents including loaded chemicals, experimental data, profiles, predictions etc., on the same computer. The functionality is implemented based on saving the sequence of actions that led to the current state of the Toolbox document and later executing these actions in the same sequence in order to get the same result(s).

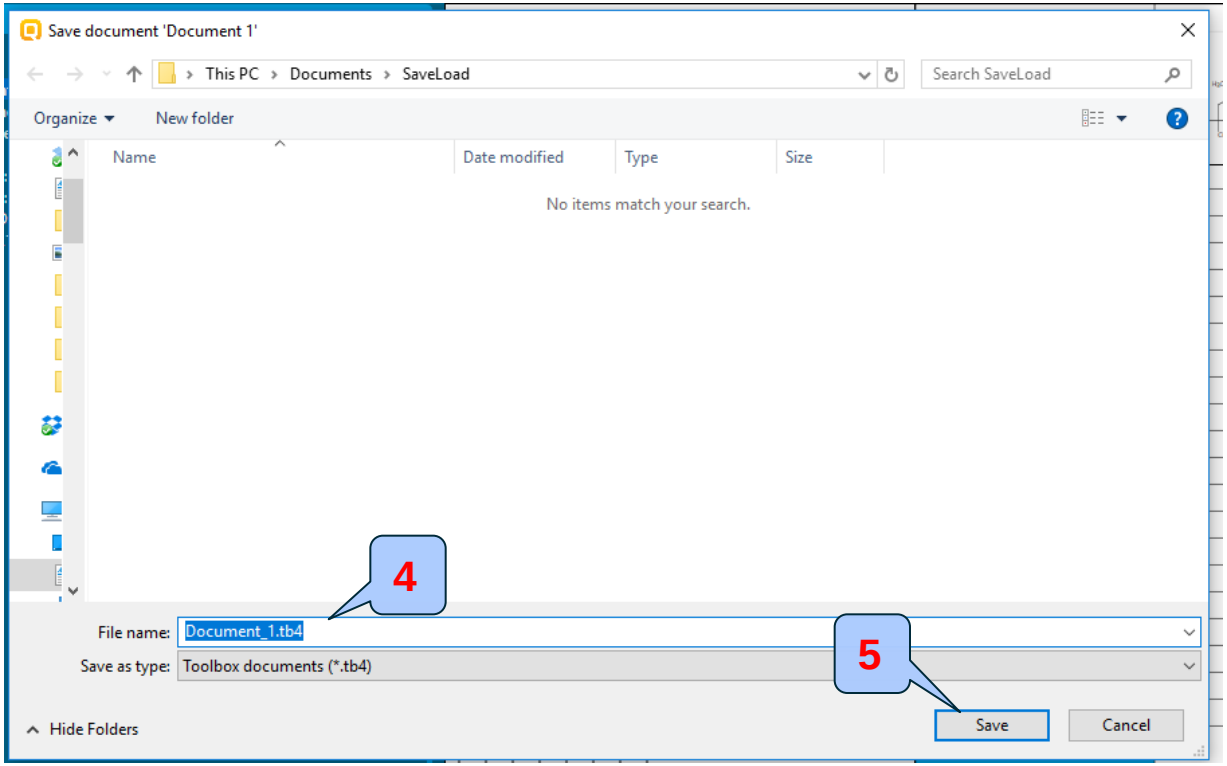
- Saving/Loading the file with TB prediction is shown on next screenshots

Saving the prediction result



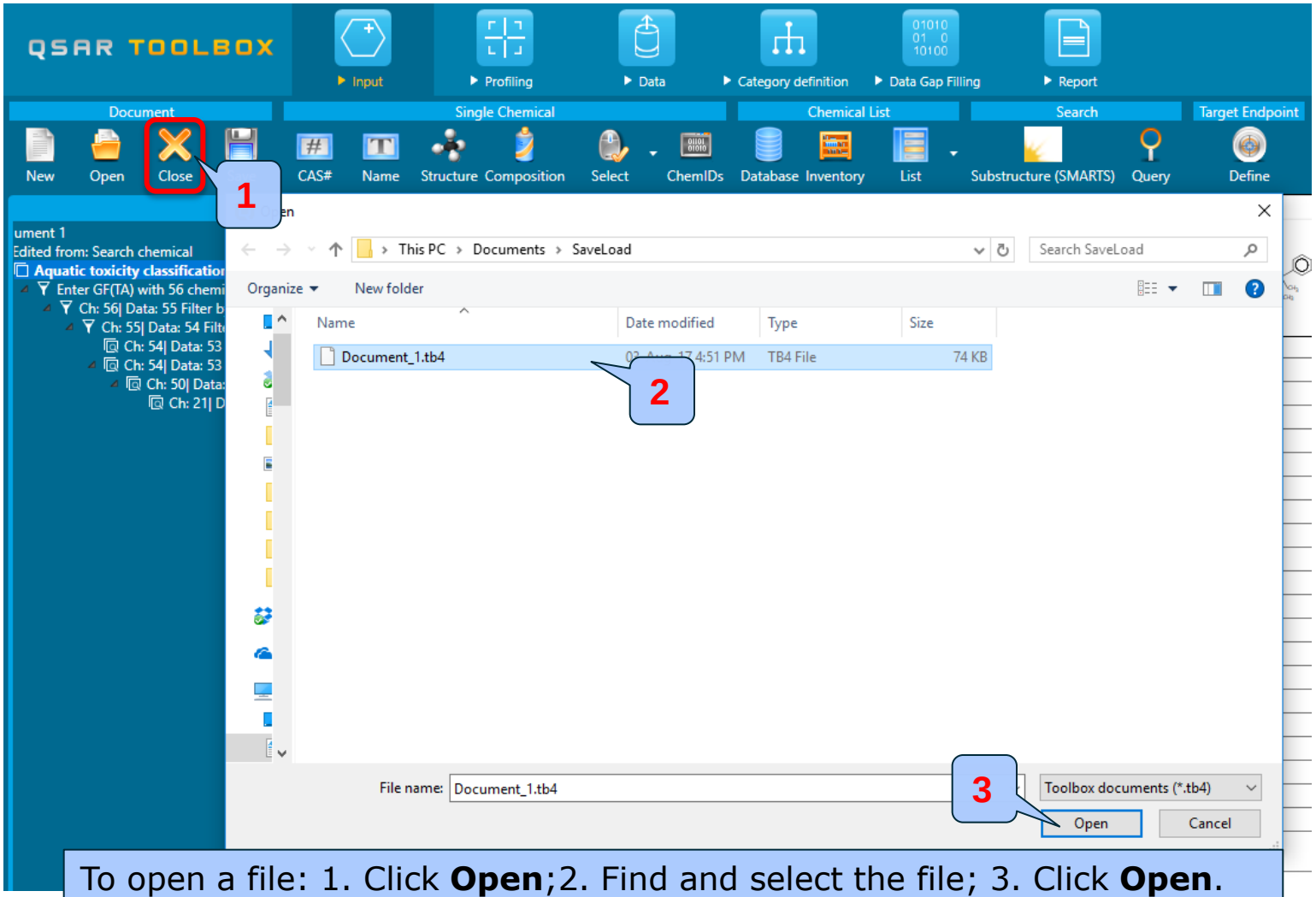
1. Go to the *Input* module; 2. Click **Save** button; 3. Click Yes to confirm;

Saving the prediction result



4. Define name of the file; 5. Click **Save**

Open file



To open a file: 1. Click **Open**;2. Find and select the file; 3. Click **Open**.

Congratulations

- You have now been introduced to the work flow of the Toolbox and completed the tutorial on data gap filling by trend analysis and exported the prediction to IUCLID 6.
- You have been introduced to the six modules of the Toolbox, the basic functionalities within each module and the rationale behind each module.
- Remember proficiency comes with practice.