

OECD QSAR Toolbox v.3.4

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
- Save the prediction result

Background

- This is a step-by-step presentation designed to take the user of the Toolbox through the workflow of a data filling exercise by the 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 to the user 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

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

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 - **Chemical Input**

Chemical Input Overview

- 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

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
- Chemical IDs such as EC number, Einescs number

B. Group of chemicals

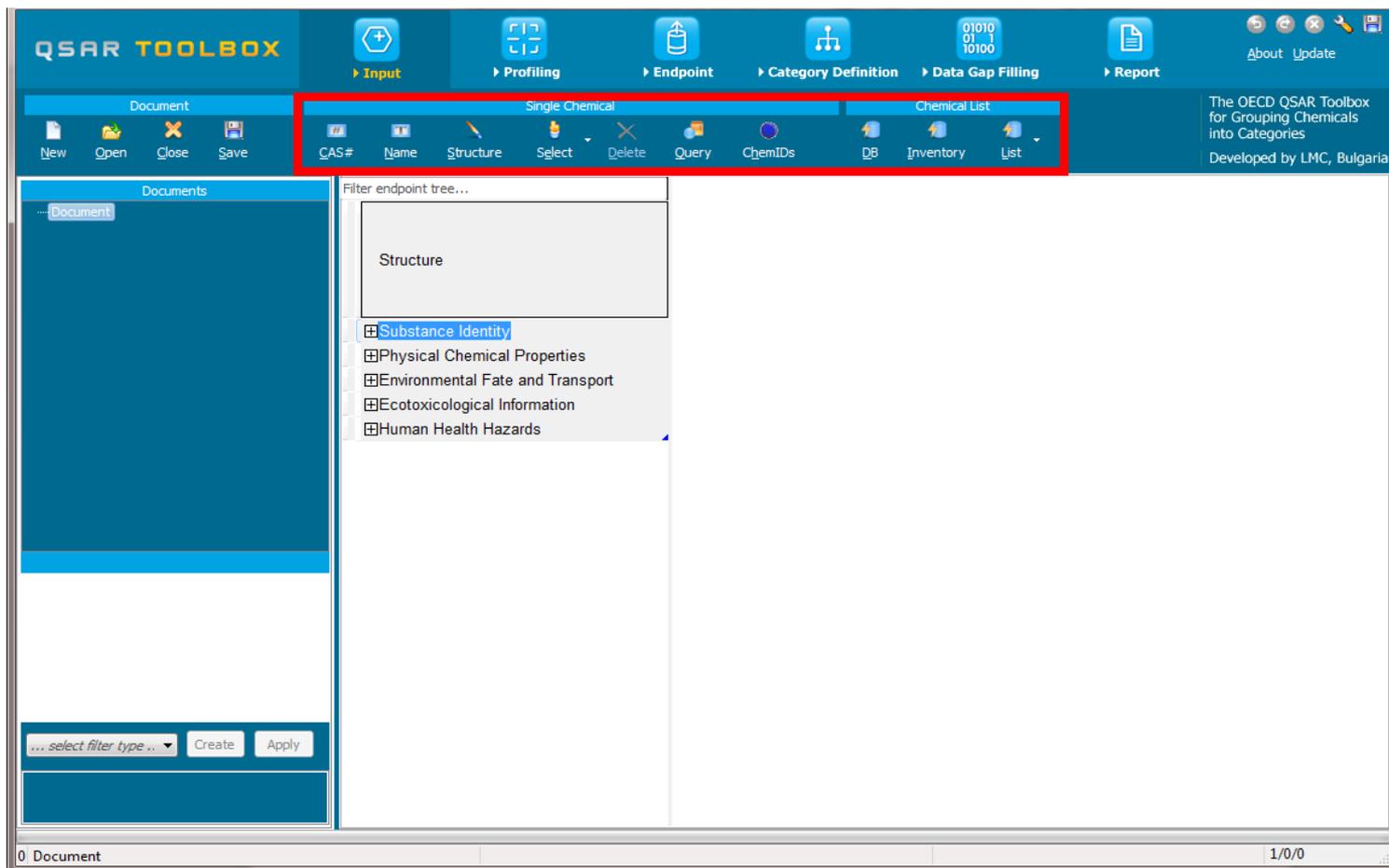
- User List/Inventory
- Specialized Databases

Getting Started

- Open the Toolbox.
- The six modules in the workflow are seen listed next to "QSAR TOOLBOX".
- **Click** on "Input" (see next screen shot).

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 screen shots will take you through the process for the target chemical.

Chemical Input Screen

Input target chemical by drawing

The screenshot displays the QSAR Toolbox software interface. The top menu bar includes options for 'Profiling', 'Endpoint', 'Category Definition', 'Data Gap Filling', and 'Report'. Below the menu bar is a toolbar with icons for 'New', 'Open', 'Close', 'Save', 'CAS#', 'Name', 'Structure', 'Select', 'Delete', 'Query', 'ChemIDs', 'DB', 'Inventory', and 'List'. The 'Structure' button is highlighted with a red box, and a callout bubble with the number '1' points to it. The main workspace is divided into a left sidebar with a 'Documents' panel and a central panel with a 'Filter endpoint tree...' section. The 'Filter endpoint tree...' section contains a list of categories: 'Structure', 'Substance Identity', 'Physical Chemical Properties', 'Environmental Fate and Transport', 'Ecotoxicological Information', and 'Human Health Hazards'. At the bottom of the interface, there is a blue banner with the text '1. Click on **Structure**'.

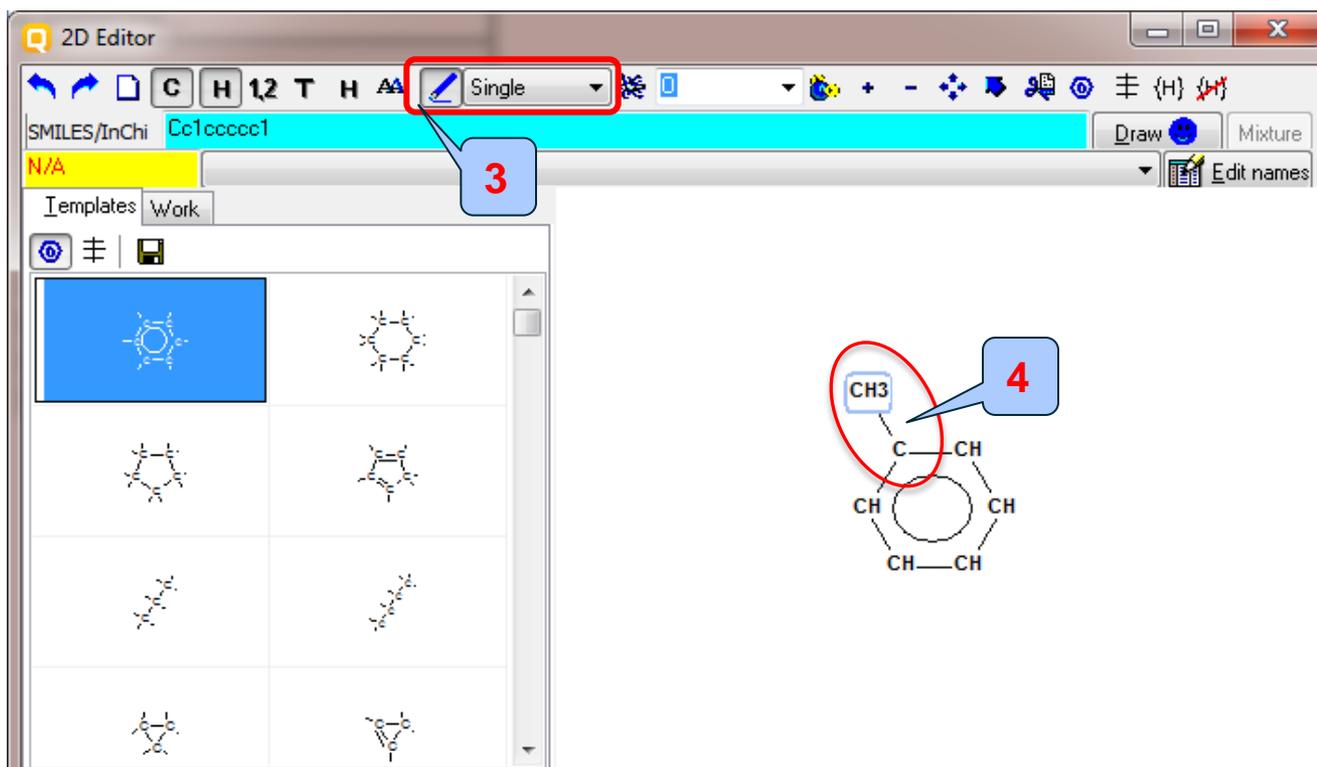
Chemical Input

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

1. **Left Click** on the appropriate template form from "templates".
2. Move the cursor 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



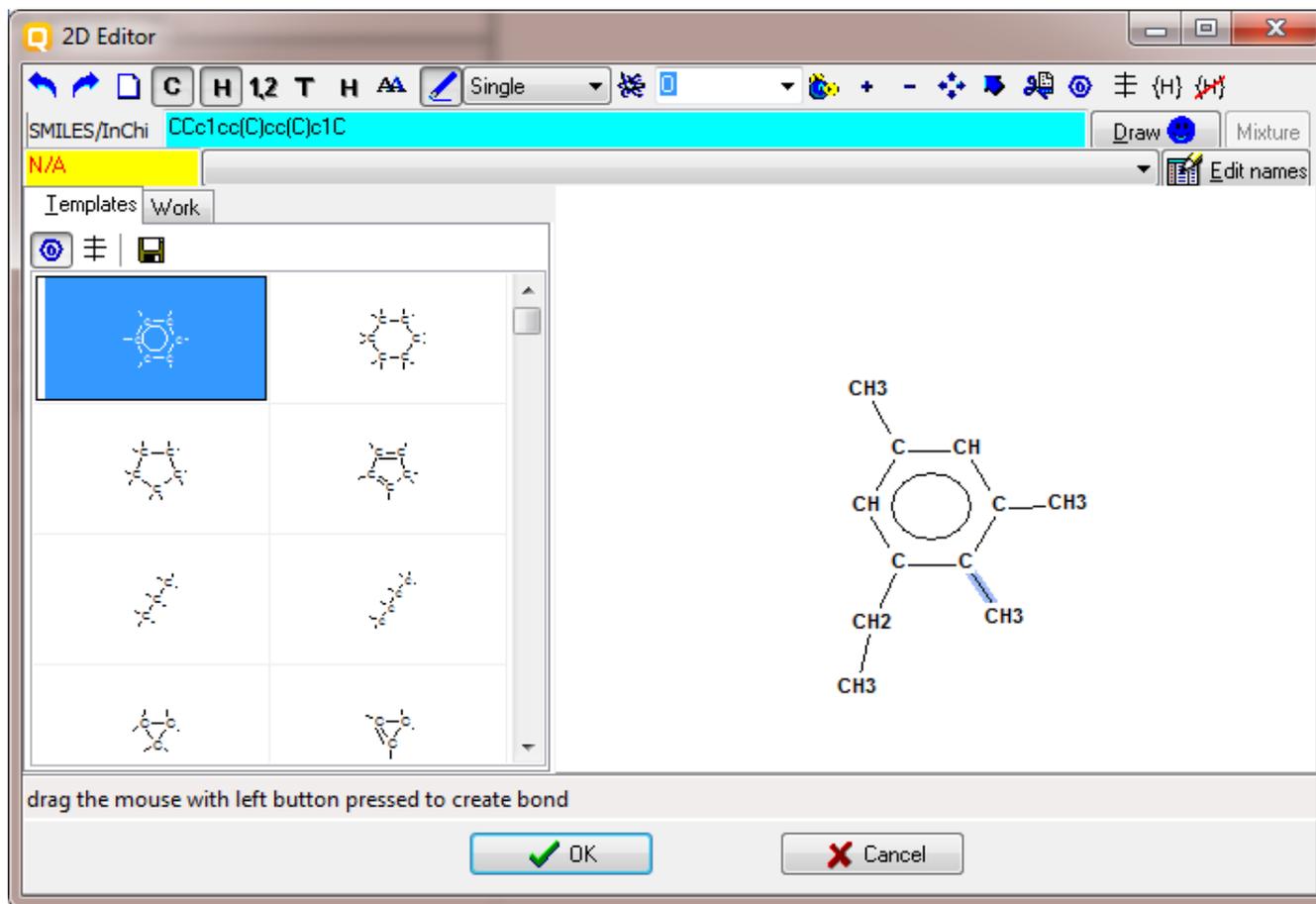
3. Click on  button to add a bond of selected type ("Single" in this case).
4. Drag the mouse (pointing finger) to the appropriate atom and **left click** to create a single bond.

Chemical Input by Drawing

- Note the default is addition of a CH₃-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 on 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

2D Editor

SMILES/InChi CCc1cc(C)cc(C)c1C

1

2

drag the mouse with left button pressed to create bond

1. Click on  button to add a hetero atom in this case an oxygen atom.
2. Left click with mouse over the methyl group to insert an oxygen atom.

Chemical Input

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

The screenshot shows the 2D Editor window with the following elements:

- 3:** A red box highlights the 'Single' bond button in the toolbar.
- 4:** A blue circle highlights the O-CH3 group in the chemical structure.
- 5:** A blue box highlights the 'Draw' button in the toolbar.
- 6:** A blue box highlights the 'OK' button at the bottom of the window.

The SMILES string in the input field is CCc1cc(O)cc(C)c1OC. The chemical structure shows a benzene ring with an OH group, a CH₂-CH₃ group, a CH₃ group, and an O-CH₃ group.

3. Click on  button

5. Click **Draw**

4. Drag the mouse from the O-atom to create a single bond

6. 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 screenshot shows the QSAR Toolbox software interface. The top menu bar includes 'Input', 'Profiling', 'Endpoint', 'Category Definition', 'Data Gap Filling', and 'Report'. The main window is divided into several sections:

- Documents:** A list of documents with the selected document showing the SMILES string: CCc1cc(O)cc(C)c1OC.
- Structure:** A chemical structure diagram of 4-methoxy-3-methylbenzoic acid.
- Substance Identity:** A tree view showing various identity fields:
 - CAS Number
 - Chemical IDs
 - Chemical Name
 - Molecular Formula: C10H14O2
 - Structural Formula: CCc1cc(O)cc(C)c1OC
 - Physical Chemical Properties
 - Environmental Fate and Transport
 - Ecotoxicological Information
 - Human Health Hazards
- Filter endpoint tree...:** A field containing the text '1 [target]'.

A red circle highlights the 'Molecular Formula' and 'Structural Formula' fields in the Substance Identity section.

The workflow on the first module is now complete, and the user can proceed to the next module. Click on “Profiling”.

Outlook

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 - Chemical Input
 - **Profiling**

Profiling Overview

- “Profiling” 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".

The screenshot shows the QSAR Toolbox software interface. The top menu bar includes 'Input', 'Profiling', 'Endpoint', 'Category Definition', 'Data Gap Filling', and 'Report'. The left sidebar has 'Profiling methods' and 'Metabolism/Transformations'. The main window displays a 'Filter endpoint tree...' with '1 [target]' and a chemical structure. The 'About' dialog box is open, showing details for the 'US-EPA New Chemical Categories' profiler. The dialog box includes a 'Name' field, a 'Short description', a 'Disclaimer', and a 'Details' table. Three numbered callouts (1, 2, 3) indicate the steps: 1. Highlight the profiler in the 'Profiling methods' list; 2. Right-click and select 'About'; 3. Click the 'Close' button in the 'About' dialog box.

Details	
Version	2.0
Adopted	QSAR Toolbox 2.0 beta, April 2010
Number of categories	66
Number of help	66

1. Highlight the profiler, then perform right click; 2. Select **About**;
3. After acquiring the information you desire, **click** on "close".

Profiling

- For most of the profilers, background information can be retrieved by highlighting one of the profilers (for example, DNA binding by OASIS v1.4) and clicking on “View” (see next screenshot).

Profiling

The screenshot displays the QSAR Toolbox 3.4.0.7 Profiling interface. On the left, a list of profiling methods is shown, with 'DNA binding by OASIS v.1.4' highlighted. A red circle and arrow labeled '1' point to this method. A second red circle and arrow labeled '2' point to the 'View' button. A third red circle and arrow labeled '3' point to the 'Alkyl nitrites' structural alert in the profile description window. The profile description window shows a tree of category definitions and a detailed description of the 'Alkyl nitrites' alert, including its mechanistic domain, alert, and structural fragments.

1. Highlight the profiler
2. Click **View**
3. Click on one of the Structural alerts (for example Alkyl nitrites)

Profiling

Side-Bar to Profiling

- The outcome of the profiling determines the most appropriate way to search for analogues (detailed information in Manual for getting started– Toolbox 2.0 (Chapter 4). <http://www.oecd.org/dataoecd/58/56/46210452.pdf>
- Table 4-1 in chapter 4 (Manual for getting started – Toolbox 2.0) lists a selection of profilers and their relevance for different endpoints of regulatory relevance.
- For this example, the following mechanistic profiling methods are relevant to the aquatic toxicity:
 - ECOSAR – for structural grouping
 - Acute aquatic toxicity MOA by OASIS – mechanistic grouping
 - Protein binding by OASIS v.1.4– mechanistic grouping
 - Acute aquatic toxicity classification by Verhaar (Modified) – grouping by reactivity
 - Organic functional groups – empiric knowledge

Profiling

Profiling the target chemical

- Select the “Profiling methods” related to the target endpoint by ticking the box next to the profilers name.
- This selects (a green check mark appears) or deselects (the green check disappears) profilers.
- For this example, select the following profilers which are relevant to the aquatic toxicity (see next screen shot):
 - ECOSAR – for structural grouping
 - Acute aquatic toxicity MOA by OASIS – mechanistic grouping
 - Protein binding by OASIS v.1.4 – mechanistic grouping
 - Acute aquatic toxicity classification by Verhaar(Modified) – grouping by reactivity
 - Organic functional groups – empiric knowledge

Profiling

Profiling the target chemical

The screenshot shows the QSAR Toolbox Profiling interface. The 'Profiling' tab is selected. In the 'Profiling Schemes' toolbar, the 'Apply' button is circled and labeled with a '2'. In the 'Profiling methods' list, the 'plus' icon next to 'DNA binding by OASIS v.1.4' is circled and labeled with a '1'. The 'Organic Functional groups' endpoint is also checked. The 'Filter endpoint tree...' panel shows a tree structure with 'Structure' selected. The '1 [target]' panel displays the chemical structure and associated data.

1. Tick in the plus box next to the profilers related to the target Endpoint (see previous slide 35);
2. 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 by 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"

QSAR Toolbox 3.4.0.17 [Document_4]

QSAR TOOLBOX

Input Profiling Endpoint Category Definition Data Gap Filling Report

Profiling Profiling Schemes

Apply New View Delete

Profiling methods

Select All Unselect All Invert About

- 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 v1.4
- Protein binding by OECD
- Protein binding potency
- Superfragments
- Toxic hazard classification by Cramer
- Toxic hazard classification by Cramer (or
- Ultimate biodeg

Endpoint Specific

- Acute aquatic toxicity classification by Verhaar
- Acute aquatic toxicity MOA by OASIS
- Aquatic toxicity classification by ECOSAR
- Bioaccumulation - metabolism alerts
- Bioaccumulation - metabolism half-lives
- Biodegradation fragments (BioWIN MITI)
- Carcinogenicity (genotox and nongenotox)
- DART scheme v.1.0
- DNA alerts for AMES by OASIS v.1.4
- DNA alerts for CA and MNT by OASIS v.1.4

Metabolism/Transformations

Select All Unselect All Invert About

Documented

- Observed Mammalian metabolism
- Observed Microbial metabolism
- Observed Rat In vivo metabolism
- Observed Rat Liver S9 metabolism

Simulated

- Autoxidation simulator
- Autoxidation simulator (alkaline medium)

Filter endpoint tree...

Structure

Substance Identity

Physical Chemical Properties

Environmental Fate and Transport

Ecotoxicological Information

Human Health Hazards

Profile

Endpoint Specific

- Acute aquatic toxicity classification by Verhaar (Class 2 (less inert ... Phenols and Anilines Phenols
- Acute aquatic toxicity MOA by OASIS
- Aquatic toxicity classification by ECOSAR

Empiric

Organic Functional groups

Alkoxy

Alkyl arenes

Aryl

Ether

Phenol

1 [target]

CC1=CC(=C(C=C1)OC)C

1. Double click on the box  to open the nodes of the tree

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 - Chemical Input
 - Profiling
 - **Endpoint**

Endpoint

- “Endpoint” refer to the electronic process of retrieving the environmental fate, ecotoxicity and toxicity data that are stored in the Toolbox database.
- Data gathering can be executed in a global fashion (i.e., collecting all data of all endpoints) or on a more narrowly defined basis (e.g., collecting data for a single or limited number of endpoints).
- 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).

Endpoint

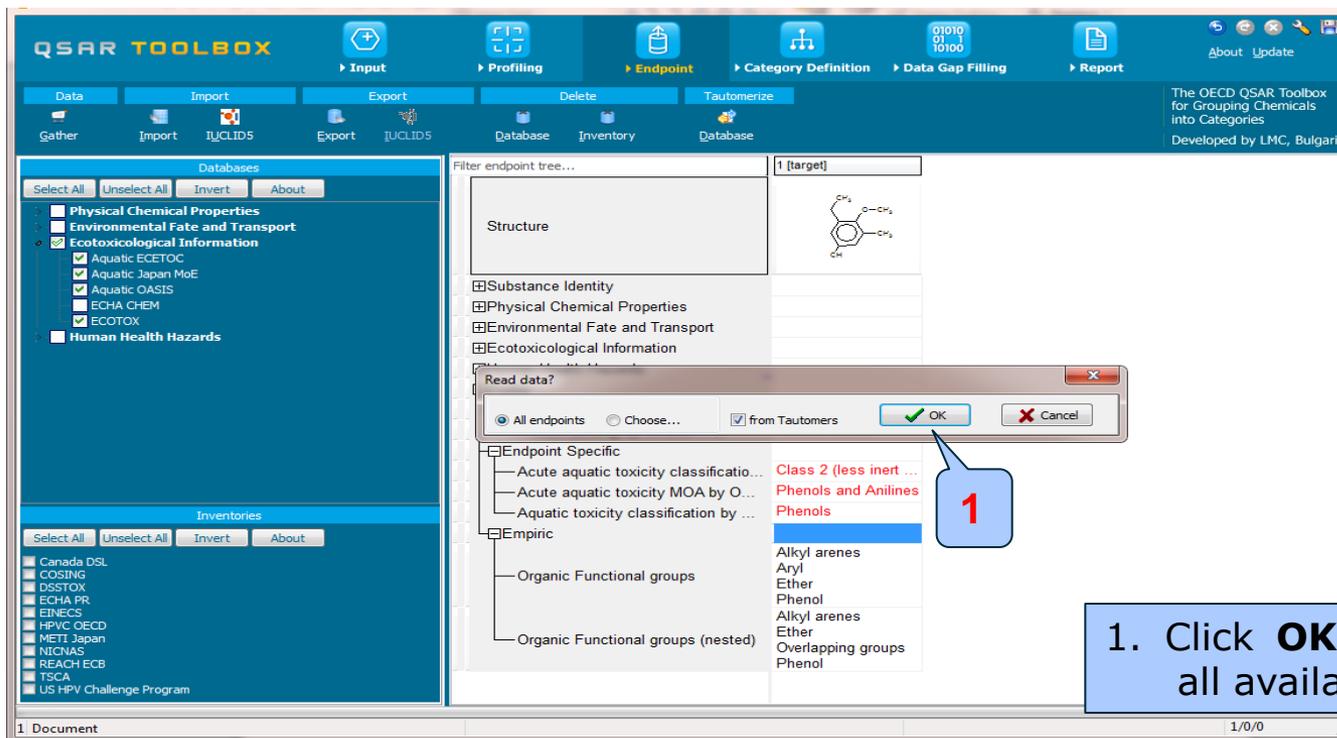
The screenshot shows the QSAR Toolbox interface with the 'Endpoint' tab selected. The 'Databases' panel on the left is expanded to 'Ecotoxicological Information', and several databases are checked with green checkmarks. The 'Gather' button is circled in red. The main panel shows a tree view of endpoints and a list of alerts on the right.

1. Expand the **Ecotoxicological Information** section;
2. Select databases related to the target endpoint by adding a **green** check in the box before the database name;
3. Click **Gather**

Endpoint 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.

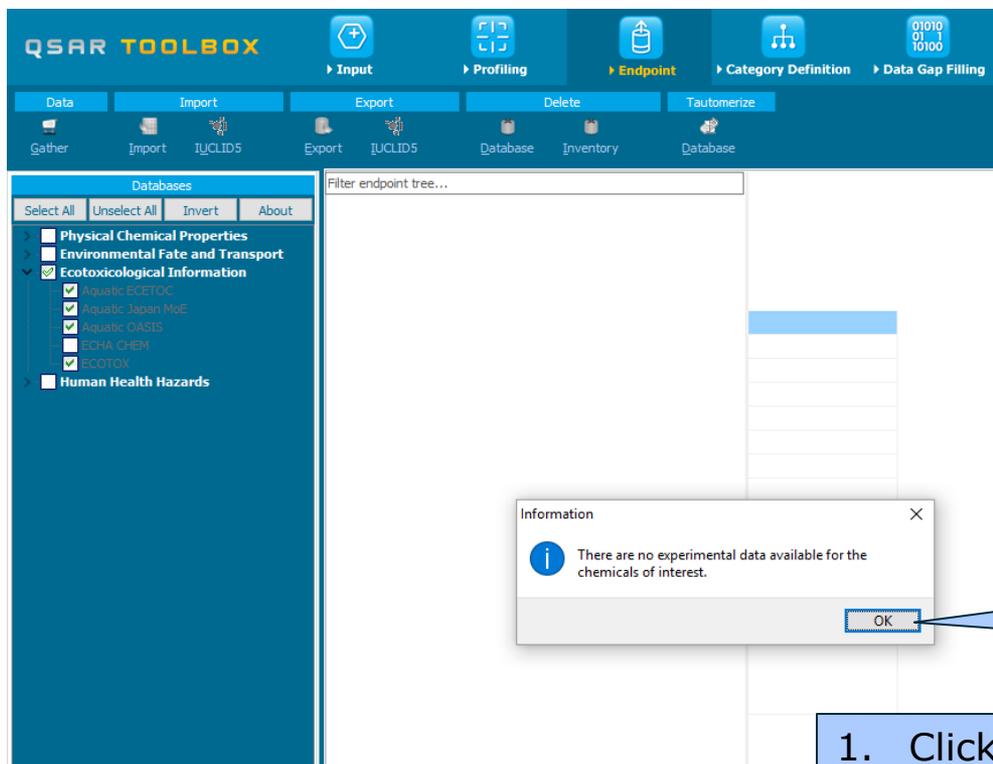


1. Click **OK** to read all available data

Endpoint

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
 - Endpoint
 - **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.
- Detailed information about grouping chemical (Chapter 4) could be downloaded from:
<http://www.oecd.org/dataoecd/58/56/46210452.pdf>
- 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.
- “Aquatic toxicity classification by ECOSAR” 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

The screenshot displays the QSAR Toolbox software interface. The top navigation bar includes 'Input', 'Profiling', 'Endpoint', 'Category Definition', 'Data Gap Filling', and 'Report'. The 'Category Definition' section is active, showing a 'Categorize' button and a 'Delete' button. A list of grouping methods is visible, with 'Endpoint Specific' expanded. The 'Aquatic toxicity classification by ECOSAR' option is highlighted. A dialog box titled 'Filter endpoint tree...' is open, showing a tree structure with 'Phenols' selected. Another dialog box titled 'target(s) profiles' is open, showing a list of chemical classes with 'Phenols' selected. The 'OK' button in the 'target(s) profiles' dialog is highlighted.

1. Highlight "Aquatic toxicity classification by ECOSAR";
2. Click **Define**;
3. Confirm the category **Phenols** and
4. Click **OK**

Category Definition

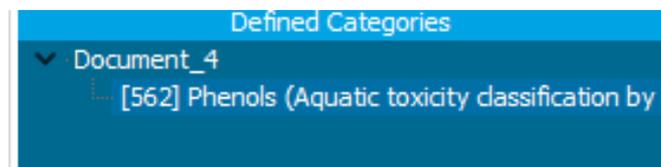
Defining ECOSAR category

The screenshot shows the QSAR Toolbox software interface. The top navigation bar includes 'Input', 'Profiling', 'Endpoint', 'Category Definition', 'Data Gap Filling', and 'Report'. The 'Category Definition' step is active, showing a toolbar with 'Categorize' and 'Delete' options. The main window displays a 'Filter endpoint tree...' dialog with a search for '1 [target]' and a chemical structure of a phenol derivative. The 'Endpoint Specific' tree is expanded to 'Aquatic toxicity classification by ECOSAR'. A dialog box is open for defining a category name, with 'henols (Aquatic toxicity classification by ECOSAR)' entered. A red circle with the number '1' points to the 'OK' button.

1. Click **OK** to confirm the name of the category and to gather experimental data

Category Definition Analogues

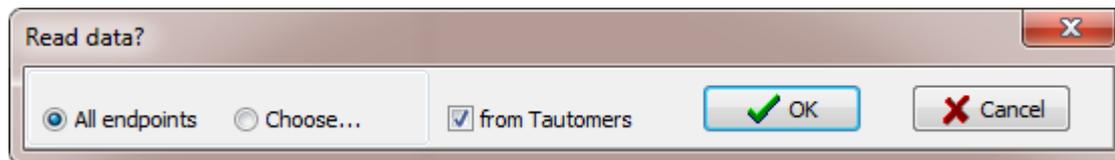
- The Toolbox now identifies all chemicals corresponding to the ECOSAR classification of “phenols” which are listed in the databases selected under “Endpoint”.
- 562 analogues are identified. Along with the target they form a category (Phenols) which can be used for data gap filling.
- The name of the category appears in the “Defined Categories” window, along with the number of substances belonging to the category.



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 ecotoxicological endpoints are selected, both options give the same results.
- As the Toolbox must search the database, this may take some time.

Category Definition

Read data for Analogues

Due to overlap between the Toolbox databases for intersecting chemicals the same data may be found simultaneously. Data redundancies are identified and the user has the opportunity to select either a single data value or all data values.

Repeated values for: 6271 data-points, 2049 groups, 946 chemicals

Data points...

	Endpoint	CAS	Structure	Value	additional_comm
<input checked="" type="checkbox"/>	LOEC	59-02-9		100 milligrams per kilogram	CONC1/ONLY CONC TESTED//
<input checked="" type="checkbox"/>	LOEC	59-02-9		100 milligrams per kilogram	CONC1/ONLY CONC TESTED//
<input checked="" type="checkbox"/>	LOEC	59-02-9		100 milligrams per kilogram	CONC1/ONLY CONC TESTED//
<input checked="" type="checkbox"/>	LOEC	59-02-9		100 milligrams per kilogram	CONC1/ONLY CONC TESTED//
<input checked="" type="checkbox"/>	LOEC	59-02-9		100 milligrams per kilogram	CONC1/ONLY CONC TESTED//
<input checked="" type="checkbox"/>	LOEC	59-02-9		100 milligrams per kilogram	CONC1/ONLY CONC TESTED//

1. Click **Select one** and then

2. Click **OK**

1. Click **Select one** and then
2. Click **OK**

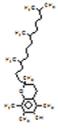
Category Definition

Summary of Analogues

Profiling
 Endpoint
 Category Definition
 Data Gap Filling
 Report

Clustering
 Delete
 Delete All

Filter endpoint tree...

	1 [target]	2	3	4	5	6	7
Structure							
Substance Identity							
Physical Chemical Properties							
Environmental Fate and Transport							
Ecotoxicological Information							
Aquatic Toxicity (525/28510)		M: 100 mg/kg, 100...	M: 102 mg/L, 238 ...	M: 3.21 mg/L, 102 ...	M: 0.868 mg/L	M: 2.05 mg/L, 0.00...	M: 3.97 mg/L, 0.01
Sediment Toxicity							
Terrestrial Toxicity (163/4152)		M: 2.15E3 mg/L		M: 4 kilograms per...		M: 825(658;1.08E3...	
Human Health Hazards							
Profile							

Category Definition

Summary information of Analogues

Profiling
Endpoint
Category Definition
Data Gap Filling
Report

Clustering
Delete
Delete All

Filter endpoint tree...

Structure

- Substance Identity
- Physical Chemical Properties
- Environmental Fate and Transport
- Ecotoxicological Information
 - Aquatic Toxicity
 - Sediment Toxicity
 - Terrestrial Toxicity
- Human Health Hazards
- Profile

(525/28510)

(163/4152)

1 [target]	2	3	4	5	6	7
	M: 100 mg/kg, 100...	M: 102 mg/L, 238 ...	M: 3.21 mg/L, 102 ...	M: 0.868 mg/L	M: 2.05 mg/L, 0.00...	M: 3.97 mg/L, 0.01.
	M: 2.15E3 mg/L		M: 4 kilograms per...		M: 825(658;1.08E3...	



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

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 562 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 screen shots)

Category Definition

Navigation through the endpoint tree

Endpoint	1 [target]	2	3	4
Structure				
Substance Identity				
Physical Chemical Properties				
Environmental Fate and Transport				
Ecotoxicological Information				
Aquatic Toxicity				
Accumulation	(7/115)			
Avoidance	(8/25)			
Behavior	(91/559)			
Biochemistry	(73/1598)	M: 100 mg/kg, 100...		M: 3.31 mg/L,
Cell(s)	(27/258)			M: 10 mg/L, 2
Development	(52/749)			M: 20 mg/L
Ecosystem Process	(3/34)			M: 0.551 mg/L
Enzyme(s)	(45/666)			M: 1.79 mg/L
Feeding Behavior	(20/58)			
Genetics	(44/2023)	M: 100 milligrams ...		
Growth	(329/2132)		M: 238 mg/L	M: 102 mg/L, 1
Histology	(26/133)			M: 0.2 mg/L, 3
Hormone(s)	(27/394)			
Immobilisation	(49/100)			
Immunological	(12/113)			
Injury	(26/34)			
Intoxication	(117/926)			M: 2.7 mg/L, 2
Morphology	(32/900)			
Mortality				
EC50	(2/85)			

1. Expand the following nodes: **Aquatic toxicity**; Mortality; LC50; Animalia; Arthropodata (Invertebrates); Branchiopoda (branchiopodos)
2. Find *Daphnia magna* - this is the species related to target endpoint

Category Definition

Navigation through the endpoint tree

The screenshot displays the QSAR Toolbox software interface. At the top, the 'Category Definition' workflow is highlighted. Below the toolbar, the 'Grouping methods' list on the left includes 'LC50'. The 'Filter endpoint tree...' window shows a tree structure with 'LC50' selected and circled in red. A blue callout box with the number '1' points to this selection. The right side of the interface shows a table with chemical structures and counts for various endpoints.

Endpoint	Count
Undefined Duration	(11/77)
2 Minutes	(1/1)
18 Minutes	(1/2)
24 Minutes	(1/1)
27 Minutes	(1/1)
36 Minutes	(1/3)
1 h	(14/184)
1.5 h	(1/2)

1. Expand the following nodes: Aquatic toxicity; **Mortality**; LC50; 48h; Animalia; Arthropoda (Invertebrates); Branchiopoda (branchiopodos)
2. Find *Daphia magna* - this is the species related to target endpoint

Category Definition

Navigation through the endpoint tree

The screenshot shows the QSAR Toolbox software interface. The top navigation bar includes tabs for 'Input', 'Profiling', 'Endpoint', 'Category Definition', 'Data Gap Filling', and 'Report'. Below the navigation bar are buttons for 'Categorize' and 'Delete'. The main area displays a list of endpoints with checkboxes and counts. A callout box labeled '1' points to the '48 h' endpoint, and another callout box labeled '2' points to the 'Daphnia magna' species. The interface also shows a 'Grouping methods' list on the left and a 'Defined Categories' list at the bottom.

Endpoint	Count
36 h	(3/3)
44 h	(3/3)
46 h	(1/1)
48 h	(1/1)
Animalia	
Annelida (Invertebrates)	(8/39)
Arthropoda (Crustacea, Invertebrates)	M: 5.8
Arachnida (Spiders)	(1/19)
Branchiopoda (Branchiopods, Crustac...)	
Artemia parthenogenetica	(1/1)
Artemia salina	(7/9)
Artemia sp.	(2/10)
Bosmina coregoni	(1/1)
Ceriodaphnia dubia	(10/37)
Ceriodaphnia pulchella	(1/1)
Ceriodaphnia reticulata	(2/5)
Chydorus sphaericus	(1/1)
Daphnia carinata	(2/2)
Daphnia cucullata	(3/4)
Daphnia galeata ssp. mendotae	(1/1)
Daphnia longispina	(1/1)
Daphnia magna	(54/215)
Daphnia pulex	(10/51)

1. Expand the following nodes: Aquatic toxicity; Mortality; LC50; 48h; **Animalia**; Arthropoda (Invertebrates); **Branchiopoda (branchiopodos)**
2. Find **Daphnia magna** - this is the species related to target endpoint

Category Definition

Navigation through the endpoint tree

- Navigation through the tree by "Filtering"

The screenshot shows the QSAR Toolbox interface with the 'Category Definition' step selected. The 'Input' tab is active, and the 'daphnia magna' endpoint is selected in the tree. A callout box with '1' points to the 'Filter' button, and another callout box with '2' points to the 'daphnia magna' node in the tree.

Grouping methods	Structure	1 [target]	2	3	4
LC0	(1/1)				
LC50	(2/2)				
Undefined Duration	(1/4)				
3 h	(37/115)				
24 h	(1/2)				M:
25 h					
48 h					
Animalia					
Arthropoda (Crustacea, Invertebrates)					
Branchiopoda (Branchiopods, Crustac...)	(54/215)				M:
Daphnia magna	(1/2)				
50 h	(2/7)				
72 h	(9/19)				
96 h	(1/1)				
4.2 Days	(7/9)				
7 Days					

1. Insert type "Daphnia magna" in the filter box, then press **Enter**;
2. Open the tree to the target endpoint by double left clicking.

Recap

- You have now retrieved the available experimental data on aquatic toxicity for 562 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 on “Data Gap Filling” (see next screen shot).

Outlook

- Background
- Objectives
- Specific Aims
- Trend analysis
- The exercise
- **Workflow of the exercise**
 - Chemical Input
 - Profiling
 - Endpoint
 - Category definition
 - **Data Gap Filling**

Data Gap Filling

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.
- In this example, we use trend analysis.

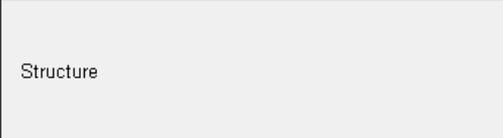
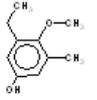
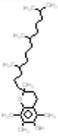
Data Gap Filling

Data Gap window

QSAR TOOLBOX

Filling

⚡ Apply

Data Gap Filling Method	daphnia magna	1 [target]	2	3
<input checked="" type="radio"/> Read-across <input type="radio"/> Trend analysis <input type="radio"/> (Q)SAR models	Structure 			
Target Endpoint Ecotoxicological Information Aquatic Toxicity Mortality LC50 48 h Animalia Arthropoda Branchiopoda Daphnia magna	<ul style="list-style-type: none"> [-] LC0 (1/1) [-] LC50 <ul style="list-style-type: none"> [+] Undefined Duration (2/2) [+] 3 h (1/4) [+] 24 h (37/115) [+] 25 h (1/2) [-] 48 h <ul style="list-style-type: none"> [-] Animalia <ul style="list-style-type: none"> [-] Arthropoda (Crustacea, Invertebrates) <ul style="list-style-type: none"> [-] Branchiopoda (Branchiopods, Crustac... <ul style="list-style-type: none"> - <i>Daphnia magna</i> (54/215) [+] 50 h (1/2) [+] 72 h (2/7) [+] 96 h (9/19) [+] 4.2 Days (1/1) [+] 7 Days (7/9) [+] 9 Days (1/1) 			

Data Gap Filling

Results of Trend analysis

QSAR TOOLBOX

Input Profiling Endpoint Category Definition Data Gap Filling Report

Filling

Apply

The OECD QSAR Toolbox for Grouping Chemicals into Categories

Data Gap Filling Method

- Read-across
- Trend analysis**
- (Q)SAR models

Target Endpoint

Ecotoxicological Information Aquatic Toxicity Mortality LC50 48 h
Animalia Arthropoda Branchiopoda Daphnia magna

daphnia magna

1 [target] 4 6 13 17

Structure

Daphnia magna (54/215)

M: 3.21 mg/L, 3.1 (...)

M: 0.242 mg/L

M: >0.032 mg/L, 2...

M: 0.24 mg/L, 1...

Descriptors Prediction Adequacy Cumul. freq. Statistics Residuals

Trend analysis prediction of LC50, making a linear approximation, based on 54 values from 54 analogue chemicals, Observed target value: N/A, Predicted target value: 1.60 mg/L, Model equation: $LC50 = +3.44 + 0.495 * \log Kow$

LC50 (obs.), log(1 mol/L)

log Kow

Accept prediction

Return to matrix

- Select/filter data
- Selection navigation
- Gap filling approach
- Descriptors/data
- Model/(Q)SAR
- Calculation options
- Visual options
- Information
- Miscellaneous

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** dot represents the predicted value for the target chemical.
- The **BLUE** dots represent the experimental results available for the analogues used in the trend analysis.
- Before accepting the estimated result for the target chemical, the trend analysis should be further refined by subcategorisation (see following slides).

Data Gap Filling

Side-Bar of Subcategorisation

- 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”.
- Subcategorisation refers to the process of applying additional profilers to the previously defined category; subcategorisation identifies chemicals which have differing profiling results and eventually eliminating these chemicals from the final category.

Data Gap Filling

Side-Bar of Subcategorisation

In this example, subcategorisation 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 chemicals, mixtures, polymers, inorganics, organometalics. The current target is a discrete chemical 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

Subcategorisation is demonstrated in the next 4 screen shots.

Data Gap Filling

Side-Bar of Subcategorisation

The screenshot displays the QSAR Toolbox interface during a 'Data Gap Filling' session. The left sidebar lists various 'Grouping methods' under 'Predefined' and 'General Mechanistic' categories. A callout box labeled '3' points to the 'Substance Type' option under 'Predefined'. The top navigation bar shows the current step as 'Data Gap Filling'. The central area features a 'Trend analysis prediction of LC50' plot with the equation $LC50 = +3.44 + 0.495 * \log Kow$. A callout box labeled '1' points to the 'Select/filter data' option in the right sidebar. Another callout box labeled '2' points to the 'Subcategorize' option in the right sidebar. The right sidebar also includes options like 'Mark chemicals by W5', 'Mark outliers points', and 'Filter points by test conditions'.

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

Data Gap Filling

Side-Bar of Subcategorisation

The screenshot displays the QSAR Toolbox 3.4.0.8 interface. On the left, a side-bar lists various chemical categories and simulation options. The main window shows a scatter plot of log Kow values. A red regression line is drawn through the data points. A callout '1' points to an outlier green dot. A callout '2' points to the 'Close' button in the chemical details window. A callout '3' points to the 'Remove' button in the side-bar. The side-bar shows a list of chemicals with 'Discrete chemical' and 'Dissociating chemical' selected. The details window shows the chemical structure of sodium pentachlorophenate and its properties.

Descriptor	Units	Value	Endpoint reference	Units	Value
log Kow		2.05	Endpoint obs. data (recalculated)	log(1/mol/L)	5.84
Molecular weight	Da	288			

- 1. Double click** above the outlier to see why this chemical is different to the target
The chemical is dissociating chemical and has to be eliminated being different substance type compared to the target, which is a discrete chemical.
- 2. Close;** 3. Click **Remove** to eliminate dissimilar chemical

Data Gap Filling

Subcategorisation by Acute-aquatic toxicity MOA

1

2

Subcategorization

Grouping methods

- Hydrolysis half-life (Ka, pH 8)(Hydrowi
- Hydrolysis half-life (Kb, pH 7)(Hydrowi
- Hydrolysis half-life (Kb, pH 8)(Hydrowi
- Hydrolysis half-life (pH 6.5-7.4)
- Tonization at pH = 1
- Tonization at pH = 4
- Tonization at pH = 7.4
- Tonization at pH = 9
- Protein binding by OASIS v1.4
- Protein binding by OECD
- Protein binding potency
- Superfragments
- Toxic hazard classification by Cramer (e
- Toxic hazard classification by Cramer (d
- Ultimate biodeg

Endpoint Specific

- Acute aquatic toxicity classification by
- Acute aquatic toxicity MOA by OASIS
- Aquatic toxicity classification by ECOS
- Bioaccumulation - metabolism alerts
- Bioaccumulation - metabolism half-lives
- Biodegradation fragments (BioWIN MIT
- Carcinogenicity (genotox and nongenod
- DART scheme v.1.0
- DNA alerts for AMES by OASIS v.1.4
- DNA alerts for CA and MNT by OASIS v
- Eye irritation/corrosion Exclusion rules
- Eye irritation/corrosion Inclusion rules
- in vitro mutagenicity (Ames test) alerts
- in vitro mutagenicity (Micronucleus) ale
- Keratinocyte gene expression

Metabolism/Transformations

Do not account metabolism

Documented

- Observed Mammalian metabolism
- Observed Microbial metabolism
- Observed Rat in vivo metabolism
- Observed Rat Liver S9 metabolism

Simulated

- Autoxidation simulator
- Autoxidation simulator (alkaline mediu
- Dissociation simulation
- Hydrolysis simulator (acidic)
- Hydrolysis simulator (basic)
- Hydrolysis simulator (neutral)
- in vivo Rat metabolism simulator

Adjust options

Target

Phenols and Anilines

Differ from target by:

- At least one category
- All categories

Correlation

Analogues

- (1) Aldehydes
- (48) Phenols and Anilines
- (3) Reactive unspecified

Selected 4 (48/52)

Select different

Remove

point

Category Definition

Data Gap Filling

Report

214	215	216	217
Structure	<chem>Oc1ccc(Cl)cc1</chem>	<chem>Oc1ccc(Cl)c(Cl)c1</chem>	<chem>CCCCCc1ccc(O)cc1</chem>
<i>Daphnia magna</i>	(52/190) M: 0.396 mg/L, 0.4...	M: 0.218 mg/L, 0.1...	M: 0.0857 mg/L

ptors Prediction Adequacy Cumul. freq. Statistics Residuals

Accept prediction

Return to matrix

- Select/filter data
- Subcategorize
- Mark chemicals by WS
- Mark chemicals by descriptor value
- Mark outlier points
- Filter points by test conditions
- Mark focused chemical
- Mark focused points
- Invert existing marks
- Remove marked chemicals/points
- Clear existing marks
- Selection navigation
- Go back
- Go forward
- Go to first
- Go to last
- Gap filling approach
- Descriptors/data
- Model/(Q)SAR
- Calculation options
- Visualization

Trend analysis prediction of LC50, making a linear approximation, based on 52 values from 52 analogue chemicals, Observed target value: N/A, Predicted target value: 1.68 mg/L, Model equation: LC50 = +3.51 +0.468 * log Kow

LC50 (mg/L)

log Kow

descriptor X: log Kow

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

Data Gap Filling

Subcategorisation by Chemical elements

The screenshot displays the QSAR Toolbox interface during a data gap filling process. The central plot shows a scatter of points representing chemical analogues, with a red regression line. A specific point is highlighted as an outlier. The interface includes a sidebar on the left with various grouping methods, a top navigation bar with 'Endpoint', 'Category Definition', 'Data Gap Filling', and 'Report' tabs, and a right sidebar with 'Accept prediction' and 'Return to matrix' options. Four callouts (1, 2, 3, 4) indicate the steps for subcategorisation by chemical elements.

1. Right click over the outlier; 2. Select **information** and select **Different to target**;
3. Select **Chemical elements**; 4. Click **Remove** to eliminate dissimilar

Data Gap Filling Results

QSAR TOOLBOX

Input Profiling Endpoint Category Definition Data Gap Filling Report

The OECD QSAR Toolbox for Grouping Chemicals into Categories
Developed by LMC, Bulgaria

Data Gap Filling Method

- Read-across
- Trend analysis
- (Q)SAR models

Target Endpoint

Ecotoxicological Information Aquatic Toxicity Mortality LC50 48 h Animalia Arthropoda Branchiopoda Daphnia magna

daphnia magna

25	26	27	33	50	
Structure	<chem>Oc1ccccc1</chem>	<chem>Oc1ccc(cc1)-c2ccccc2</chem>	<chem>Oc1ccc(cc1)-c2ccc(cc2)Cl</chem>	<chem>Cc1ccc(cc1)C(=O)c2ccccc2</chem>	<chem>Cc1ccc(cc1)C(=O)c2ccc(O)cc2</chem>
Daphnia ... (18/62)	M: 26.5 mg/L, 12(7...	M: 0.71 mg/L, 1.2...	M: 3.64 mg/L, 3.66	M: 4.23 mg/L	M: 25.9 mg/L

Descriptors Prediction Adequacy Cumul. freq. Statistics Residuals

Trend analysis prediction of LC50, making a linear approximation, based on 18 values from 18 analogue chemicals, Observed target value: N/A, Predicted target value: 3.47 mg/L,

Model equation: $LC50 = +2.66 + 0.635 * \log Kow$

Descriptor X: log Kow

Accept prediction

Return to matrix

- Remove marked chemicals/points
- Clear existing marks
- Selection navigation
 - Go back
 - Go forward
 - Go to first
 - Go to last
- Gap filling approach
- Descriptors/data
- Model/(Q)SAR
- Calculation options
 - Data usage
 - Prediction approach options
 - Set level of significance
- Visual options
- Information

542 Phenols (Aquatic toxicity classification by ECOSAR) Create prediction by gap filling 1/1/0

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).
- By **clicking** on Return to Matrix, the user can close the read-across and proceed with the workflow (see next screen shot).

Data Gap Filling

Accepting prediction results

The screenshot shows the QSAR Toolbox interface during the Data Gap Filling process. The main workspace displays a table of chemical structures and their predicted LC50 values. The table has columns for chemical structures and predicted LC50 values. The predicted values are: 3.47(0.726,16.6), 2.97(2.76,4.11), 30.1 mg/L, 100, 0.71 mg/L, 1.2, and 3.64 mg/L, 3.66. A scatter plot shows the relationship between log Kow (Descriptor X) and LC50 (obs., log(l mol/L)). An 'Information' dialog box is open, stating 'The current prediction was accepted'. A red circle highlights the 'Accept prediction' and 'Return to matrix' buttons in the right sidebar. Three callout boxes with numbers 1, 2, and 3 point to these buttons respectively.

1. Click **Accept prediction**; 2. Click **OK**; 3. Click **Return to matrix**

Outlook

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

Export prediction to the IUCLID5

Overview

- The OECD QSAR Toolbox allows the users to export predicted data (by means of the Filling Data Gap tools) to IUCLID 5.
- There are two ways of exporting:
 - create an *.i5z file which can then be imported into an IUCLID 5 database.
 - connect to an IUCLID 5 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 screen shot).
- More detailed information could be found in the following link: <http://www.oecd.org/dataoecd/54/27/47136326.pdf>

Exporting the prediction to IUCLID5

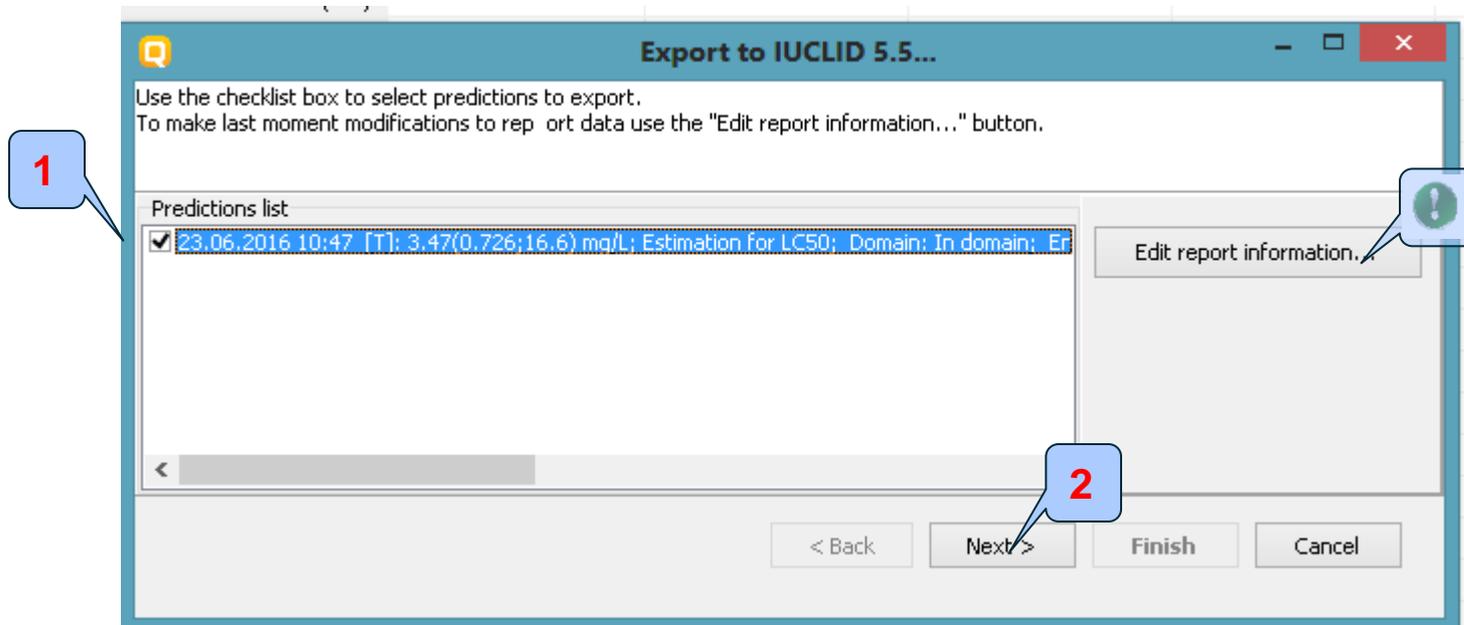
Case study

The screenshot displays the QSAR Toolbox interface during a 'Data Gap Filling' operation. The 'Target Endpoint' is set to 'Ecotoxicological Information Aquatic Toxicity Mortality LC50 48 h Animalia Arthropoda Branchiopoda Daphnia magna'. The taxonomic tree for 'daphnia magna' is shown, with a right-click context menu open over the 'Daphnia magna' node. The menu options include 'Copy', 'Explain', 'Delete prediction', 'Display prediction domain', 'Explain prediction', 'Edit prediction info', 'Report', and 'IUCLID5'. A callout box with the number '1' points to the 'Daphnia magna' node, and another callout box with the number '2' points to the 'IUCLID5' option in the menu. The prediction value 'T: 3.47(0.726,16.6)' is visible next to the node.

1. Move the mouse in the column of the target substance and click the **right mouse** button; **2. Select IUCLID**

Exporting the prediction to IUCLID5

Case study

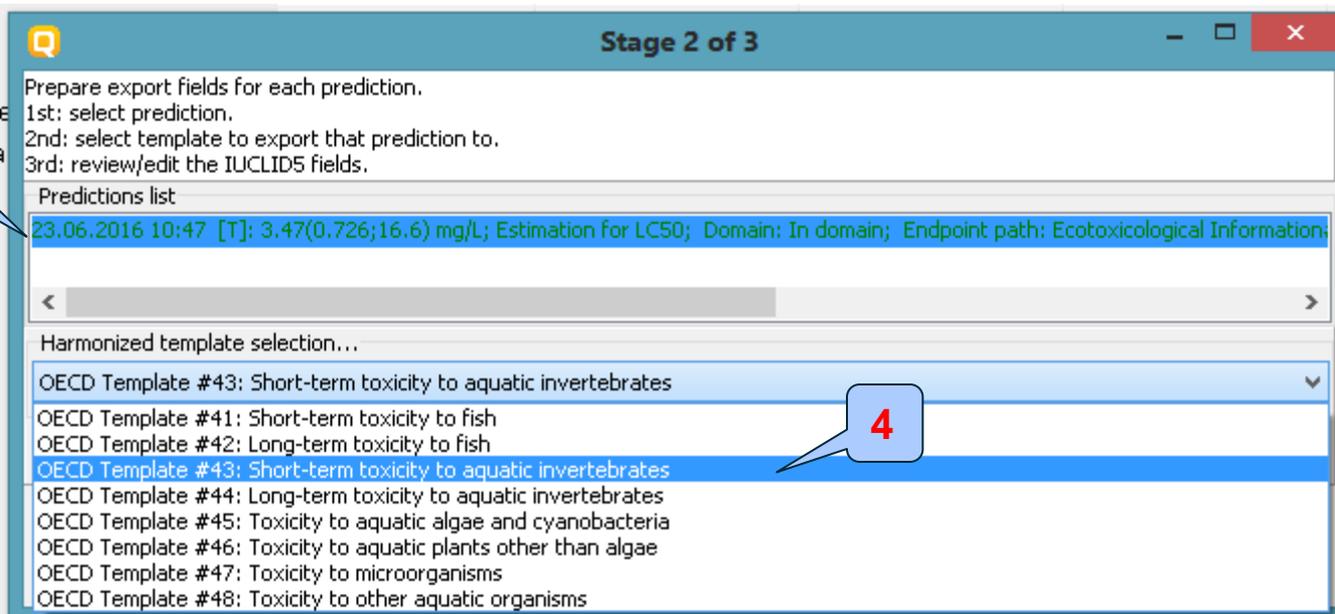


1. Select the **prediction** to export;
2. Click **Next** to move to the next step of the export.

 The user could also edit the report information

Exporting the prediction to IUCLID5

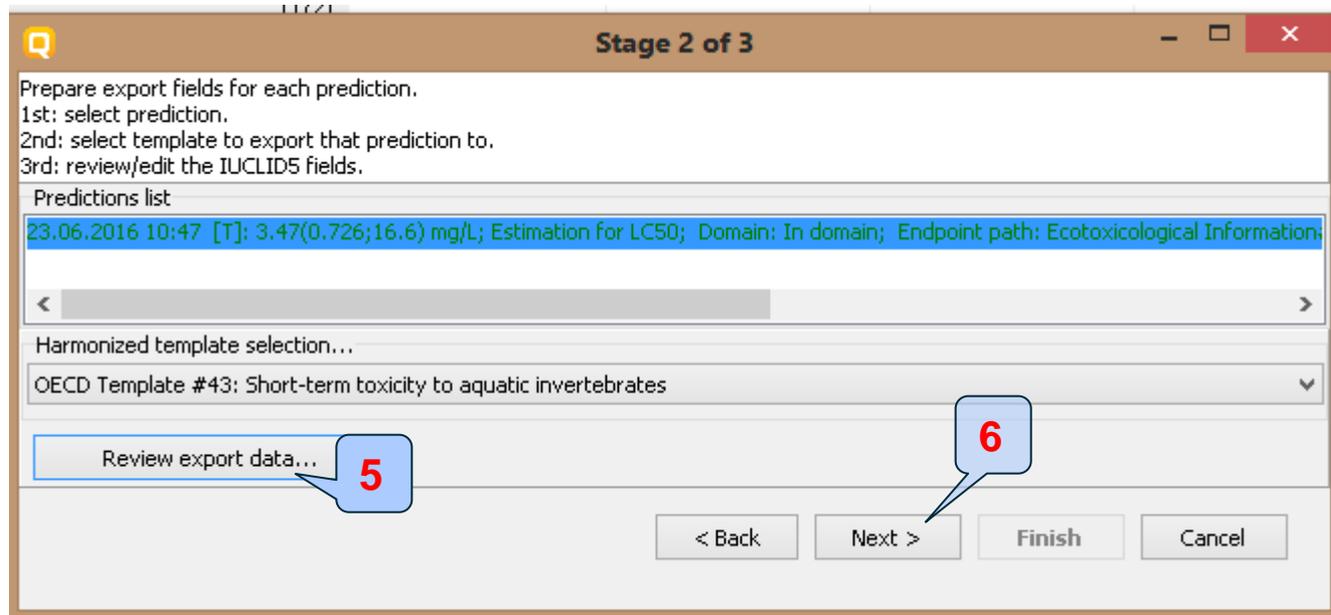
Case study



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

Exporting the prediction to IUCLID5

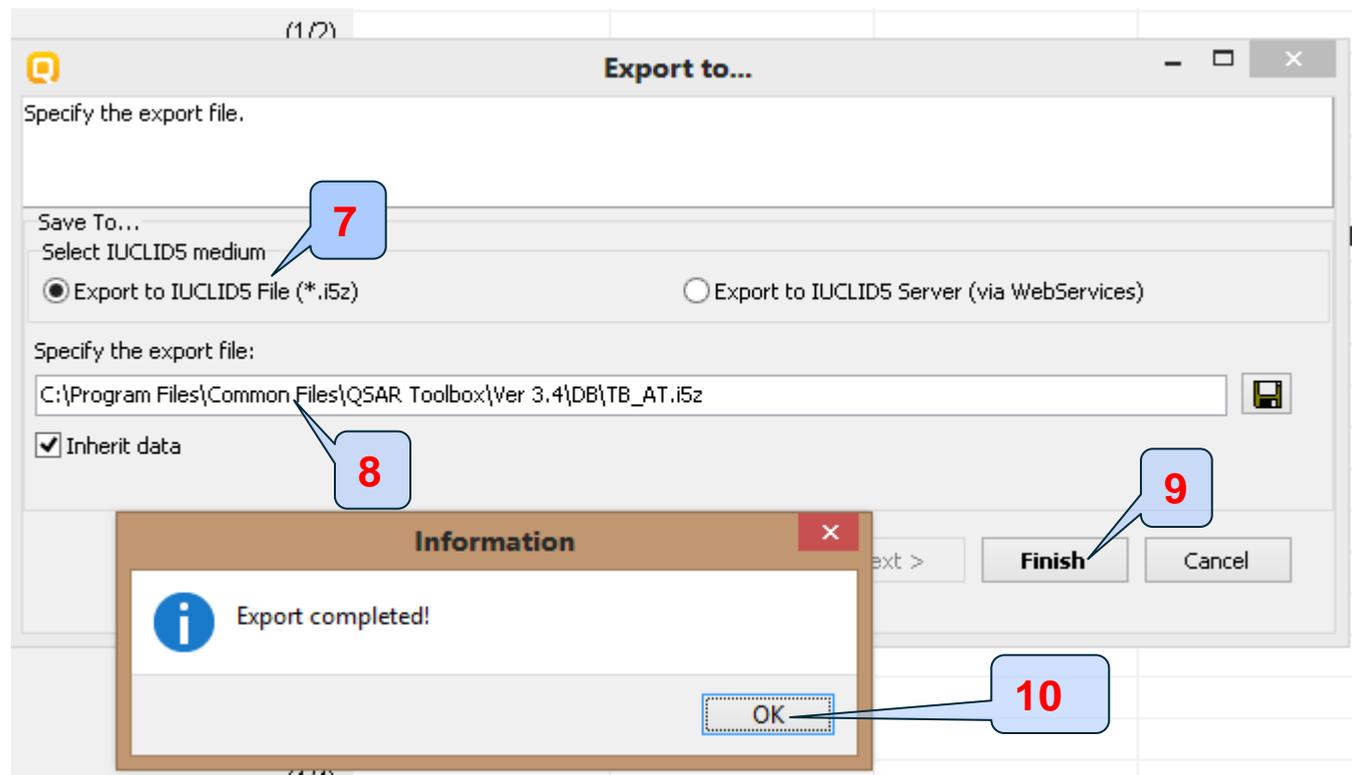
Case study



5. Review/edit the IUCLID5 fields **6. Click Next**

Exporting the prediction to IUCLID5

Case study



7. Select **medium** to export, i5z file or export via WebServices;
 8. Specify the export file; 9. Click **Finish**; 10. Click **OK**

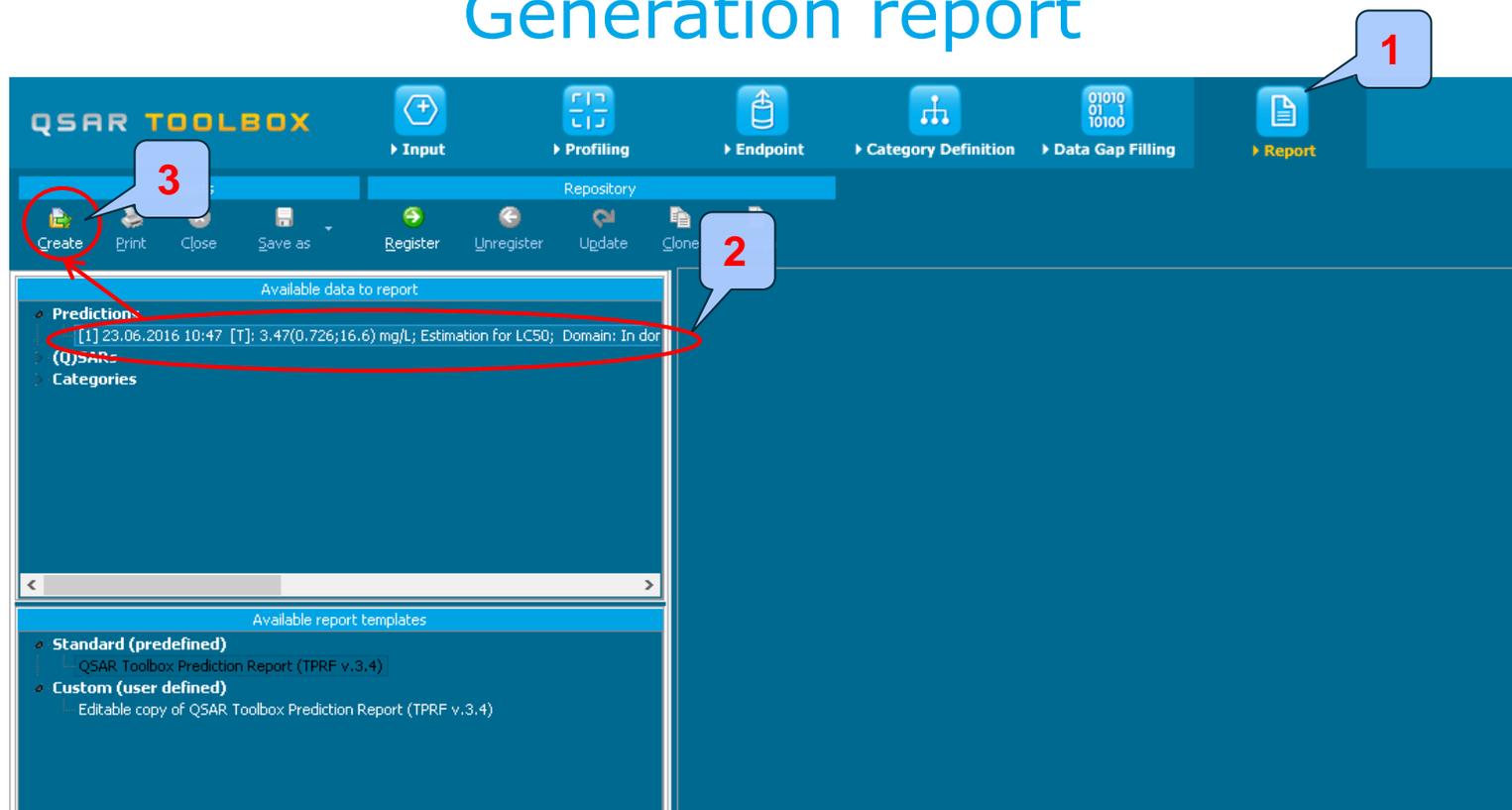
Outlook

- Background
- Objectives
- Specific Aims
- Trend analysis
- The exercise
- **Workflow of the exercise**
 - Chemical Input
 - Profiling
 - Endpoint
 - 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 as well as a template editor with which users can define their own user defined templates.
- The report can then be printed or saved in different formats.

Report Generation report



1. Go to **Report** section; 2. **Select** prediction for the target chemical from the "Available data to report" window; 3. **Click** Create

Report Overview

The screenshot displays the QSAR Toolbox software interface. At the top, there is a navigation bar with icons for Input, Profiling, Endpoint, Category Definition, Data Gap Filling, and Report. Below this is a secondary toolbar with options like Create, Print, Close, Save as, Register, Unregister, Update, Clone, and Design. The main window is divided into several sections:

- Left Panel:** Contains a tree view under 'Available data to report' with sub-items: Predictions, [1] 23.06.2016 10:47 [T]: 3.47(0.726;16.6) mg/L; Estimation for LC50; Do (Q)SARs, and Categories. Below this is a section for 'Available report templates' with two options: 'Standard (predefined)' (QSAR Toolbox Prediction Report (TPRF v.3.4)) and 'Custom (user defined)' (Editable copy of QSAR Toolbox Prediction Report (TPRF v.3.4)). A checkbox at the bottom is checked and labeled 'show only relevant templates'.
- Top Right Panel:** Shows 'The OECD for Grouping into Categories' and 'Develop'.
- Main Content Area:** Titled 'Prediction [1]', it displays the prediction of LC50 for the chemical CCc1cc(O)cc(C)c1OC. The page number '1 / 29' is shown in the top right corner. The main heading is **QSAR Toolbox prediction for single chemical**. Below this, there is a paragraph of text: *The template of the current report is based on "GUIDANCE DOCUMENT ON THE VALIDATION OF (QUANTITATIVE) STRUCTURE-ACTIVITY RELATIONSHIPS MODELS" published by OECD (September, 2007) and "GUIDANCE ON INFORMATION REQUIREMENTS AND CHEMICAL SAFETY ASSESSMENT / CHAPTER R.6: QSARS AND GROUPING OF CHEMICALS" published by ECHA (May, 2008).* This is followed by another paragraph: *The report provides information about the target substance, chemical characteristics used for the grouping, the resulting boundaries of the group of chemicals (applicability domain), the type of data gap filling approach that was applied (read-across, trend analysis or QSAR models), the predicted result(s) and in the Annex information about the category members or training set and test set chemicals.* The final line of text is partially visible: *The chemicals are ordered by the distance to the target substance within the*

Outlook

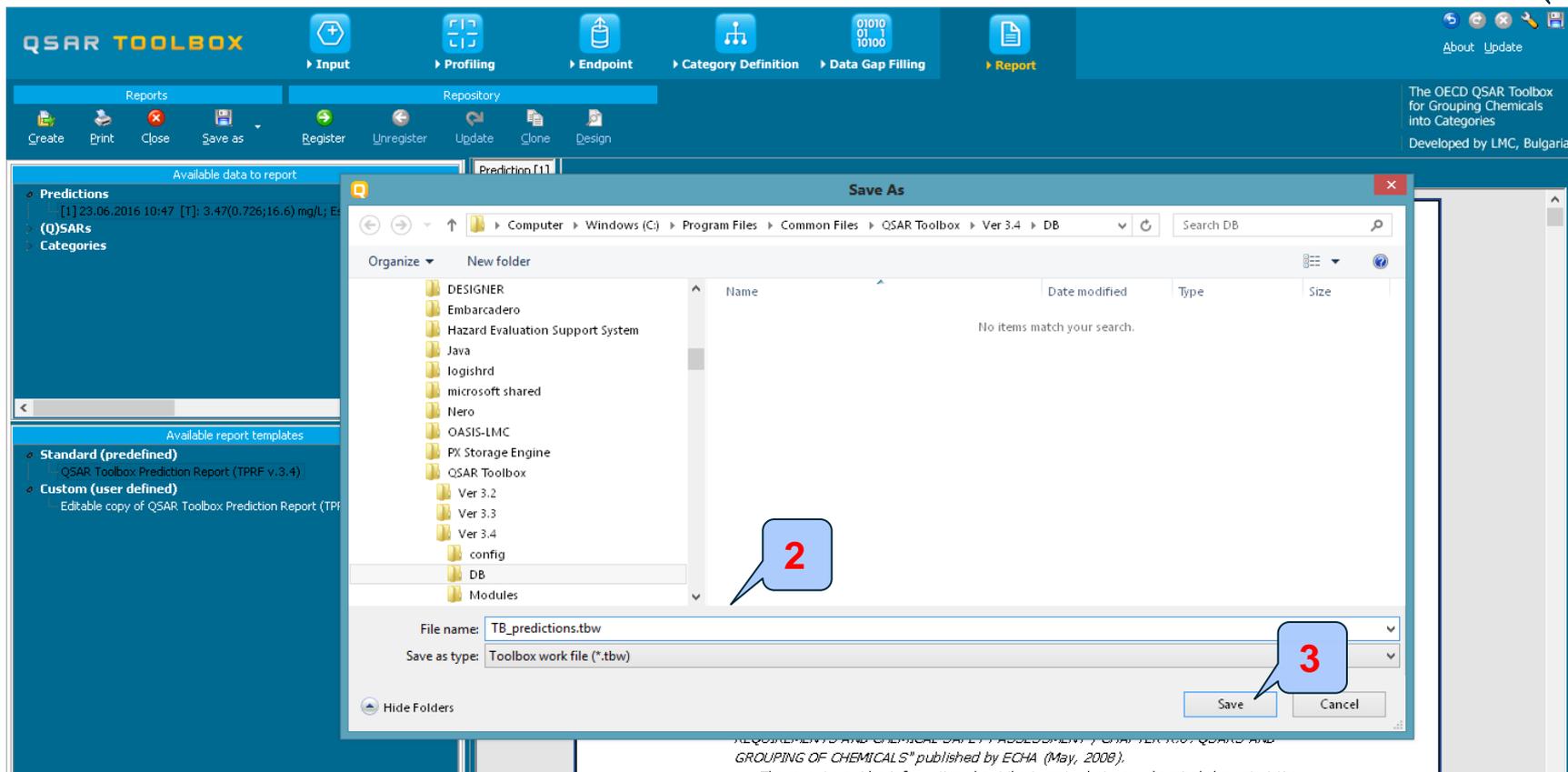
- Background
- Objectives
- Specific Aims
- Trend analysis
- The exercise
- Workflow of the exercise
- **Save the prediction result**

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



1. Click on Save button; **2. Define** name of the file; **3. Click** Save button

REQUIREMENTS AND CHEMICAL SAFETY ASSESSMENT / CHAPTER 10. QSAR AND GROUPING OF CHEMICALS" published by ECHA (May, 2008).
The report provides information about the tested substances, chemical characterisation

Open saved file

1

2

3

4

Once the file has been saved **1. Go** to Input; **2. Click** Open; **3. Find** and **select** file; **4. 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 5
- 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.