

OECD (Q)SAR Toolbox v.4.4.1

Tutorial of how to predict ecotoxicological endpoint
of chemicals by standardized workflow

Outlook

- **Background**
- Keywords
- Objectives
- Specific Aims
- Standardized workflow for Ecotoxicity
- The exercise
- Standardized workflow execution

Background

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

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Keywords

TARGET CHEMICAL - chemical of interest

MODULE – a Toolbox module is a section dedicated to specific actions and options (e.g. Profiling)

WORKFLOW – the use, in combination, of the different modules (e.g. prediction workflow: from input to report)

PROFILER - algorithm (rule set) for the identification of specific features of the chemicals. Several types of profilers are available, such as structural (e.g. Organic functional groups), mechanistic (e.g. Protein binding by OECD) and endpoint-specific (e.g. in vitro in vitro mutagenicity (Ames test) alerts by ISS) profilers.

ALERT - the profilers consist of sets of rules or alerts. Each of the rules consists of a set of queries. The queries could be related to the chemical structure, physicochemical properties, experimental data, comparison with the target or list with substances and external queries from other predefined profilers (reference queries).

CATEGORY – “group” of substances sharing same characteristics (e.g. the same functional groups or mode of action). In a typical Toolbox workflow, it consists of the target chemical and its analogues gathered according to the selected profilers

ENDPOINT TREE – Endpoints are structured in a branched scheme, from a broader level (Phys-Chem properties, Environmental Fate and transport, Ecotoxicology, Human health hazard) to a more detailed one (e.g. EC3 in LLNA test under Human health hazard-Skin sensitization)

DATA MATRIX – Table reporting the chemical(s) and data (experimental results, profilers outcomes, predictions). Each chemical is in a different column and each data in a different row

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Objectives

This presentation demonstrates a number of functionalities of the Toolbox:

- Identify analogues for a target chemical;
- Retrieve experimental results available for those analogues;
- Color the profiling schemes according to their suitability for subcategorization;
- Fill data gaps by standardized workflow;

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Specific Aims

- To introduce to the Toolbox user to the standard workflow for predicting of ecotox endpoint (LC50);
- To familiarize the user with the new Toolbox interface;
- To explain to the user the rationale behind each step of the exercise.

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Standardized workflow for Ecotoxicity endpoints

Overview

Standardized workflow for Ecotox covers the following acute aquatic toxicity endpoints:

- Fish, LC50 (EC50), 96h, mortality
or
- Invertebrates, EC50(LC50), 48h, mortality, immobilization, intoxication
or
- Algae, LC50 (EC50), 72-96h, population or growth

Standardized workflow for Ecotox endpoints

Overview

- The standardized workflow (SW) is designed to apply data gap filling for discrete chemicals only
- The SWs has been developed to be applicable for the same endpoints used for application of the AWs (i.e. LC50, Mortality, 96h, *Pimephales promelas*).
- Once started, the SW follows the implemented logic under the user control.
- As opposite to the automated workflow (AW), the domain of application is expanded in the SWs (including other endpoints, effects, species, durations, etc.) and SWs allow interactions by the user.
- In case more than one further application is possible, the workflow stops and waits for the decision of the user.
- SW can be executed for a single chemical only.

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The Exercise

- In this exercise we will predict the acute aquatic toxicity endpoint (LC50) of N-Octylamine [CAS# 111-47-8], which will be the “target” chemical.
- This prediction will be accomplished by using of the developed standardized workflow for ecotoxicity (LC50, Mortality, 96h, *P.promelas*).

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Standardized workflow execution

- Only three of the general Toolbox modules are used in a sequential workflow:
 - Input
 - Data Gap Filling
 - Report

The rest of the modules – *Profiling*, *Data* and *Category definition* are included as a part of the algorithm of the standardized workflow. The workflow stops at them and waits for the decision of the user.

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 - 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

I. Single target chemical:

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

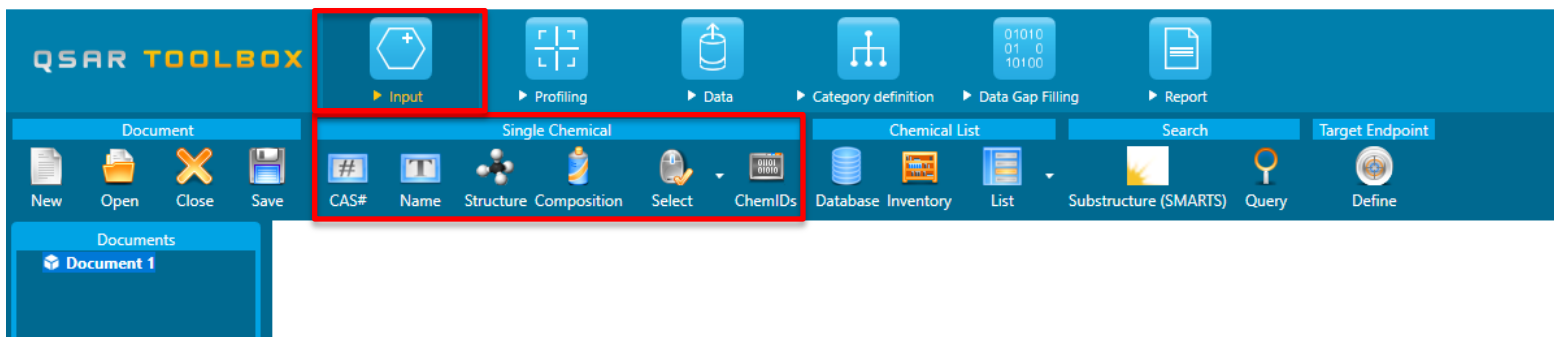
II. Group of chemicals:

- User's List
- Inventory/Database

Chemical Input

Single chemical

As mentioned before SW is allowed for single chemical only. In this respect below are provided different ways for entering a single chemical



- Chemical Name
- Chemical Abstract Services (CAS) number (#)
- Drawing chemical structure
- Select from User List/Inventory/Databases

Chemical Input

Single chemical: CAS RN

1. Press **CAS#** (1);

2. Enter the CAS of N-Octylamine # 111-86-4 (2);

3. Click on **Search** (3);

4. Press **OK** (4).

1	CAS	111-86-4
	SMILES	CCCCCCCCN
	CS Relation	High
	Substance	Mono constituent
	Composition	
	Name	1-amino-octane; 1-Octanamine; 1-octan-1-amine
	Sources	NICNAS Reaxys-DSI

Chemical Input

Target chemical identity

The screenshot displays the QSAR Toolbox software interface. The top menu bar includes options like Document, Single Chemical, Chemical List, Search, and Target Endpoint. Below this is a toolbar with icons for New, Open, Close, Save, and various chemical data management functions. The main workspace shows a document titled 'Document 1' with chemical identifiers: # [C: 1;M:4; 0:P: 0] CAS: 111864. A red box highlights the 'Filter endpoint tree...' dialog, which is set to '1 [target]'. This dialog shows the chemical structure of 1-octanamine (H₂C₈H₁₉N) and its associated 'Structure info' data:

Structure info	Value
Additional ids	EC Number:2039160
CAS Number	111-86-4
CAS-SMILES relation	High
Chemical name(s)	1-aminooctane 1-Octanamine
Composition	
Molecular formula	C ₈ H ₁₉ N
Predefined substance type	Mono constituent
SMILES	CCCCCCCCN

Below the 'Structure info' section, there are expandable sections for 'Parameters', 'Physical Chemical Properties', 'Environmental Fate and Transport', 'Ecotoxicological Information', and 'Human Health Hazards'. A blue callout box with the number '1' points to the 'Structure info' section. At the bottom, a blue instruction bar reads: '1. Open **Structure info** level to see chemical ID of the target molecule'.

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 - Input
 - **Data Gap Filling**

Data gap filling

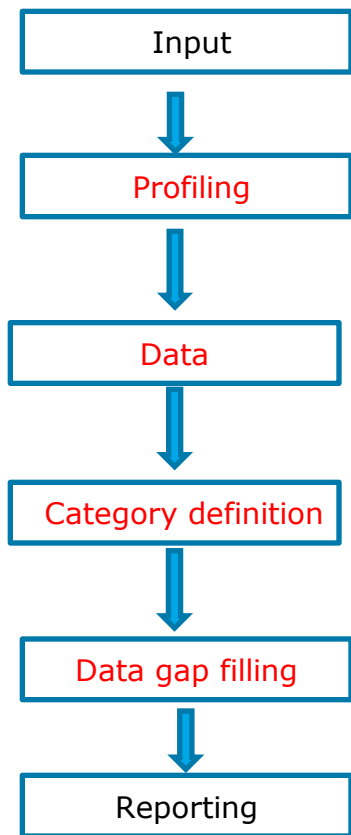
An overview

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

Data gap filling

An overview

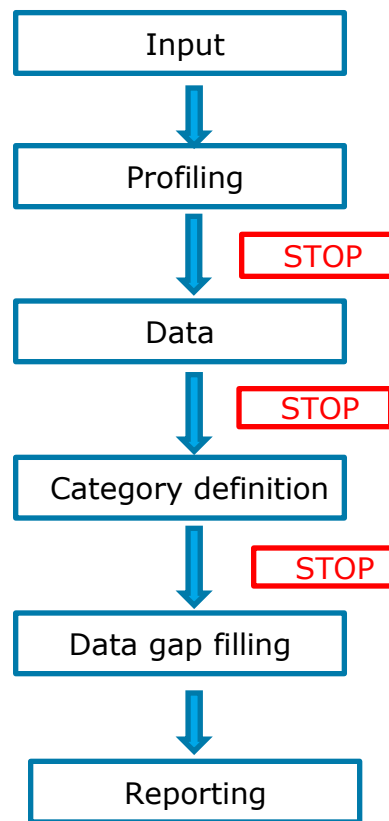
Automated workflow (AW)



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

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

Standardized workflow (SW)



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

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

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

In this example, we will use the Standardized workflow approach.

Data Gap Filling

Apply Standardized workflow

1. Go to **Data Gap Filling**;

2. Press **Standardized**;

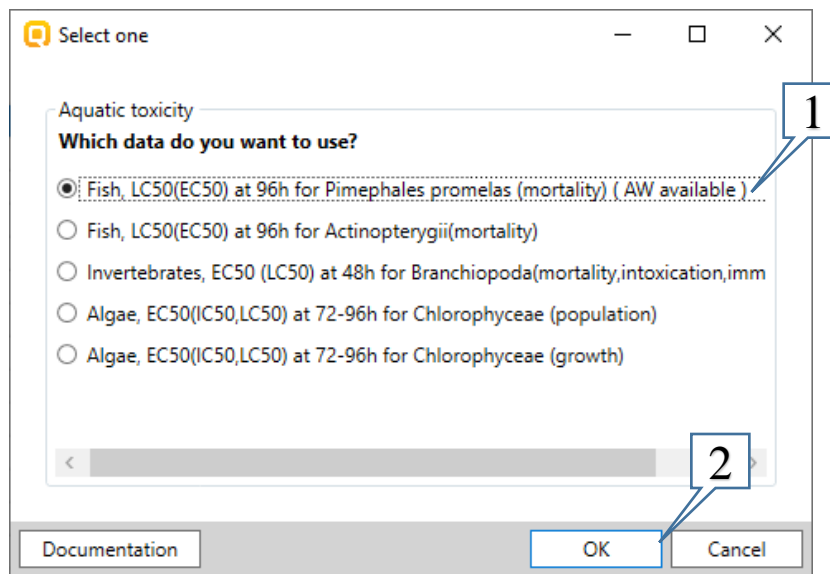
3. Select **Ecotoxicological endpoint**

4. Click **OK**

Data Gap Filling

Apply Standardized workflow

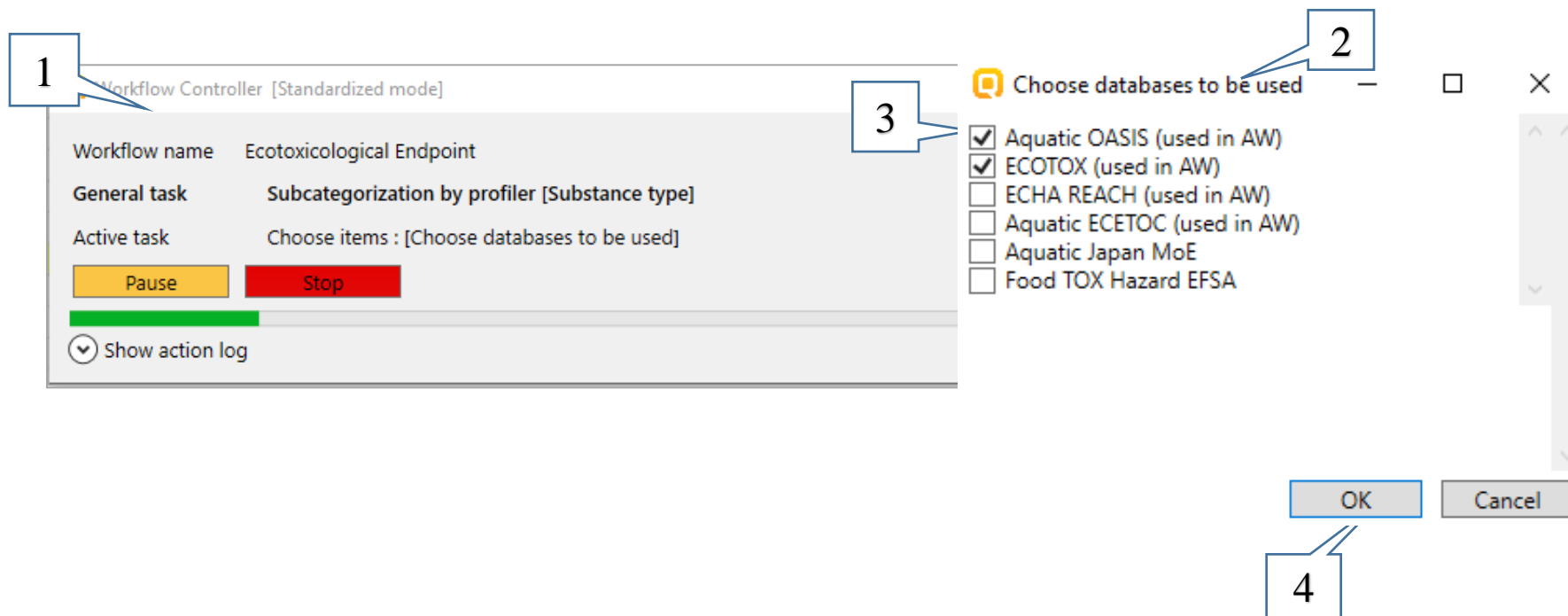
There are several options for selection of endpoint and user should select one of them. The first option covers the same endpoint and metadata as the automated workflow, while the others are associated with different endpoints.



In our case select the first endpoint – **Fish, LC50(EC50) at 96h for Pimephales promelas** (1). The user could make other selection. *AW available in brackets* means that the endpoint is used in the automated workflow;
2. Click on **OK** (2)

Data Gap Filling

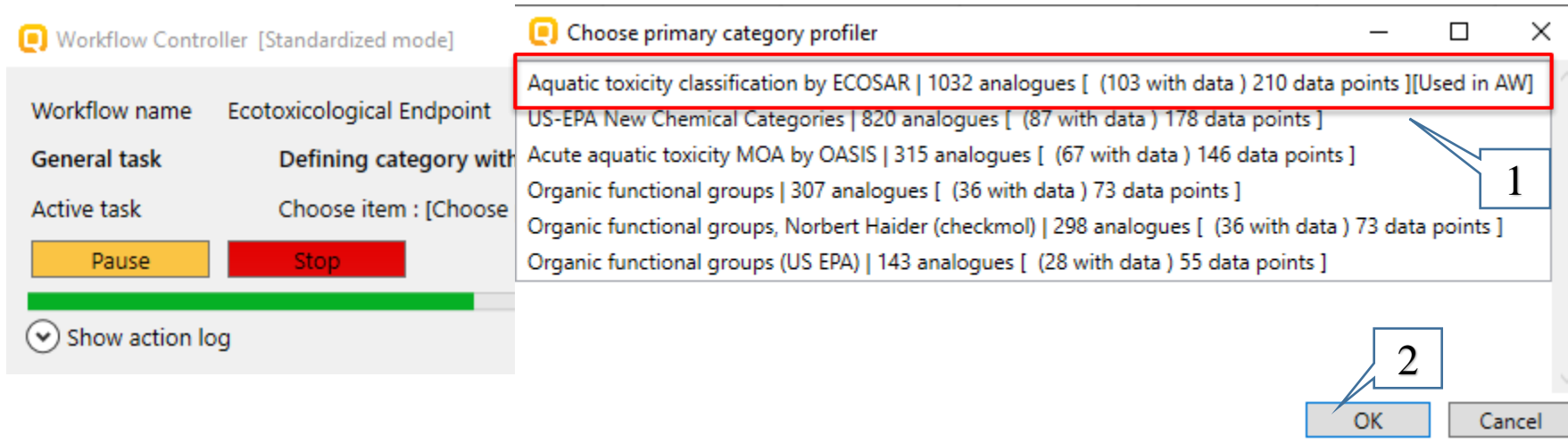
Apply Standardized workflow



A workflow controller window (1) is displayed and then a dialogue window for selection (2) of databases appears. Indication about which databases are used in the AWs is also included in brackets. Select the databases which you would like to be used in SW. In our case the first two databases are selected (3); Click on **OK**(4)

Data Gap Filling

Apply Standardized workflow



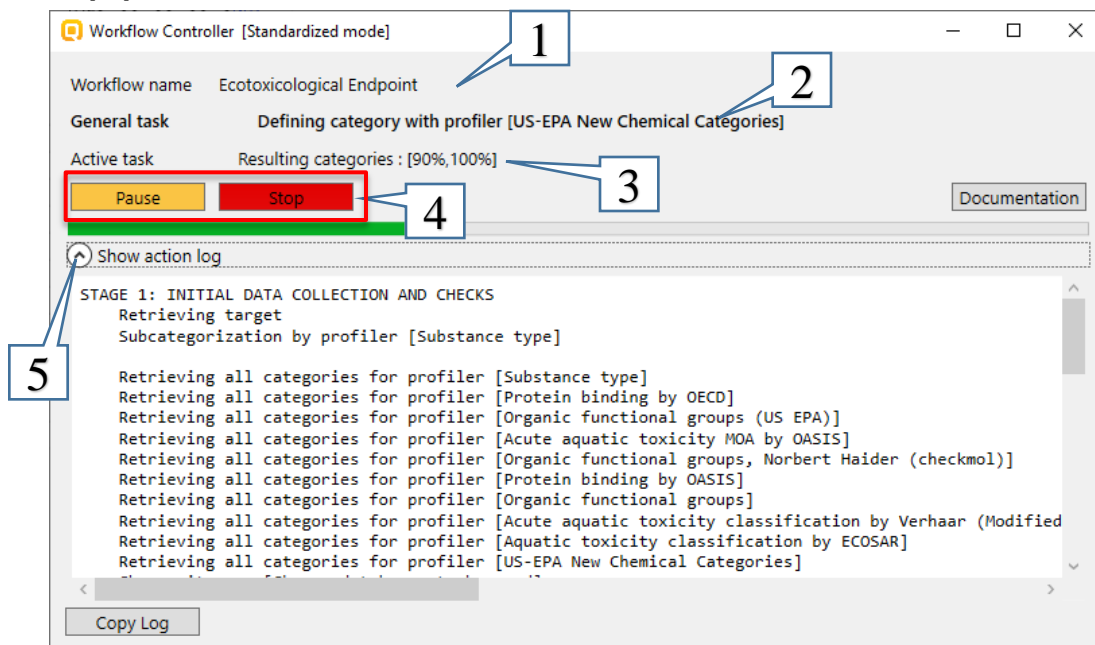
Now the system define groups with analogues and provide a list with the most appropriate for primary grouping profilers starting with the most populated one. Here, we select **Aquatic toxicity classification by ECOSAR** (1) and then click on **OK** (2).

Data Gap Filling

Apply Standardized workflow

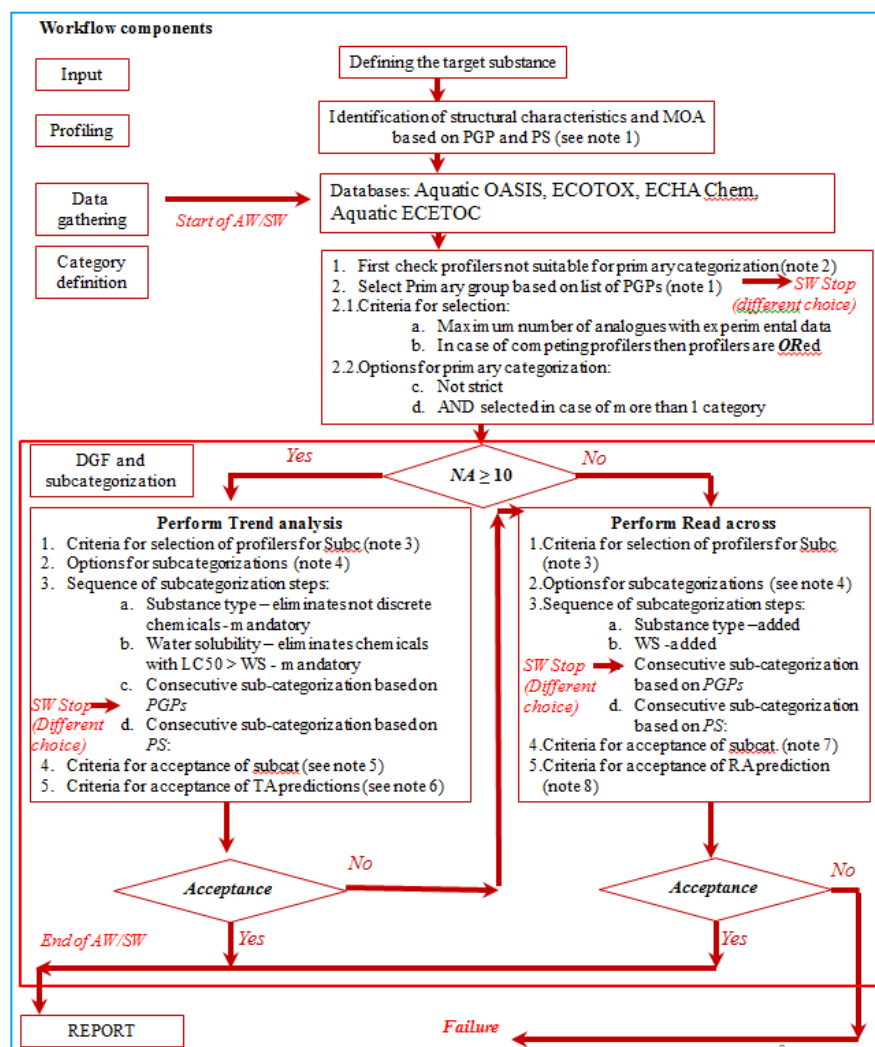
A workflow controller window is displayed throughout the standardized workflow procedure. It includes:

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



Data gap filling

Algorithm of Ecotoxicological workflow



Data Gap Filling

Apply Standardized workflow

When the profiling scheme for primary categorization is selected, the workflow makes a category and enters in Data Gap Filling, where the next step is subcategorization. Depending on the outcome obtained by the applied subcategorization, the profilers are colored as follows:

- **Green** – application of the profiler will satisfy the criteria for acceptance of the prediction
- **Blue** – application of the profiler increase the confidence of the prediction only
- **Yellow** – application of the profiler does not change the current state
- **Red** – criteria for acceptance the subcategorization will be not reached
- **Grey** – already applied profiler

Data Gap Filling

Apply Standardized workflow

Subcategorization 1 | Current state $R^2 = 0.392$ 95% residuals 2.142

Options ▾ Select All Unselect All Invert

Profilers 0 Selected

Adjust options Target

Primary grouping

- [Suitable for acceptance]Aquatic toxicity classification by ECOSAR(64 analogues) | $R^2 = [0.777]$, 95% Residuals = [1.38]
- [Suitable for acceptance]Acute aquatic toxicity MOA by OASIS(53 analogues) | $R^2 = [0.866]$, 95% Residuals = [0.9]
- [Suitable for acceptance]Organic functional groups (US EPA)(24 analogues) | $R^2 = [0.841]$, 95% Residuals = [1.22]
- [Suitable for acceptance]Organic functional groups, Norbert Haider (checkmol)(23 analogues) | $R^2 = [0.836]$, 95% Residuals = [1.2]
- [Suitable for acceptance]Organic functional groups(13 analogues) | $R^2 = [0.893]$, 95% Residuals = [1.31]
- US EPA New Chemical Categories(61 analogues) | $R^2 = [0.437]$, 95% Residuals = [1.86]

Secondary grouping

- [Suitable for acceptance]Chemical Elements(38 analogues) | $R^2 = [0.844]$, 95% Residuals = [1.16]
- [Suitable for acceptance]Structure Similarity(12 analogues) | $R^2 = [0.97]$, 95% Residuals = [0.624]
- Protein binding by OASIS(71 analogues) | $R^2 = [0.393]$, 95% Residuals = [2.11]
- Protein binding by OECD(74 analogues) | $R^2 = [0.392]$, 95% Residuals = [2.14]

Unclassified

Options ▾ Select All Unselect All Invert

Metabolisms 0 Selected

Do not account metabolism

Differ from target by

☒ At least one category

☐ All categories

STO

Analogues

Once the primary group is selected, the implemented logic of Ecotoxicological workflow is applied. As result a list with profilers appears highlighted and ordered appropriately. The profilers are separated into two sections in the subcategorization window (1): *Primary grouping* (2) and *Secondary grouping* (3).

Data Gap Filling

Apply Standardized workflow

6 Subcategorization 1 | Current state $R^2 = 0.392$ 95% residuals 2.142

Options f Select All Unselect All 1 Selected Invert About Options

Primary grouping

(Suitable for acceptance) Aquatic toxicity classification by ECOSAR(64 analogues) | $R^2 = [0.777]$, 95% Residuals = [1.38]

(Suitable for acceptance) Active Aquatic Toxicity MoA by OASIS(53 analogues) | $R^2 = [0.800]$, 95% Residuals = [1.31]

(Suitable for acceptance) Organic functional groups (US EPA)(24 analogues) | $R^2 = [0.841]$, 95% Residuals = [1.22]

(Suitable for acceptance) Organic functional groups, Norbert Haider (checkmol)(23 analogues) | $R^2 = [0.836]$, 95% Residuals = [1.32]

(Suitable for acceptance) Organic functional groups(13 analogues) | $R^2 = [0.893]$, 95% Residuals = [1.31]

US-EPA New Chemical Categories(61 analogues) | $R^2 = [0.437]$, 95% Residuals = [1.86]

Secondary grouping

(Suitable for acceptance) Chemical Elements(38 analogues) | $R^2 = [0.844]$, 95% Residuals = [1.16]

(Suitable for acceptance) Structure Similarity(12 analogues) | $R^2 = [0.97]$, 95% Residuals = [0.624]

Protein binding by OASIS(71 analogues) | $R^2 = [0.393]$, 95% Residuals = [2.11]

Protein binding by OECD(74 analogues) | $R^2 = [0.392]$, 95% Residuals = [2.14]

Unclassified

Options f Select All Unselect All 0 Selected Invert

Do not account metabolism

Metabolisms

Adjust options

Target

Aliphatic Amines

ECOSAR(64 analogues) | $R^2 = [0.777]$, 95% Residuals = [1.38]

Differ from target by

☒ At least one category

☐ All categories

[STOP]

Analogues

(5) Acid moiety

(74) Aliphatic Amines

(1) Neonicotinoids

(2) Phenol Amines

(2) Phenols

(1) Triazines, Aliphatic

(1) Triazines, Aromatic

Selected 10 (64/74)

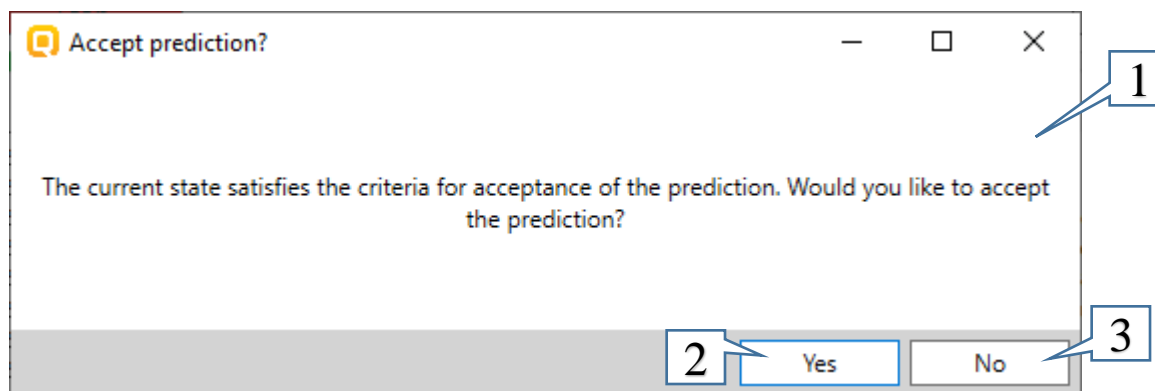
Select different

Remove selected

Clicking on the first profiler (1) shows all categories found in the analogues (2) as the ones colored in blue (3) are the ones that are not applicable to the target chemical (different to the target) and hence can be removed (4). Moreover a statistic coefficients which will be obtained if the profiler is applied are provided after profilers' name (5). The statistics of the current state is available too (6) and user could easily compare them.

Data Gap Filling

Apply Standardized workflow



- If obtained results after applied subcategorization satisfy the criteria for acceptance the prediction, then the message appears:
- *The current state satisfy the criteria for acceptance the prediction. Would you like to accept the prediction ?(1)*
- Press Yes (2) , if you want to accept the prediction (next slide)
- Press No (3) and continue with the workflow if you are not satisfy with the outcome and want to continue

Data Gap Filling

Apply Standardized workflow

The screenshot displays the QSAR Toolbox interface during a Data Gap Filling workflow. The 'Data Gap Filling' tab is active, showing a filter endpoint tree on the left and a table of chemical data on the right. Two pop-up windows are overlaid on the main interface:

- Pop-up window (1):** A 'Success' dialog box with the text 'Prediction accepted successfully' and an 'OK' button.
- Pop-up window (2):** A 'Workflow Controller [Standardized mode]' dialog box. It shows the workflow name 'Ecotoxicological Endpoint' and the general task 'Retrieving different analogues for profiler [Structure Similarity]'. The active task is 'Continue'. Below the task, there is a 'Show action log' section with the following text:


```
Step [1] Subcategorization [Structure Similarity] R2 [0.970] 95% Residuals [0.624]
Selecting chemical list
Performing visual subcategorization
Selecting chemical list
List satisfies subcategorization acceptance criteria : [Suitable for acceptance] R^2 =
Question : [The current state satisfies the criteria for acceptance of the prediction.]
Accepting prediction
```

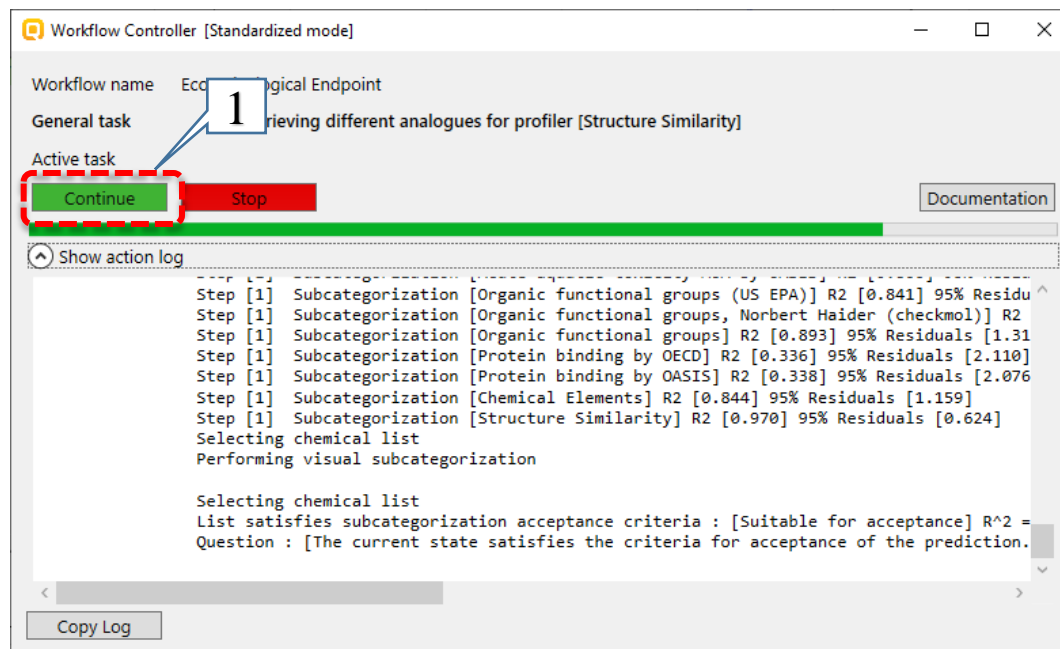
 A 'Copy Log' button is located at the bottom of the log section.

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

Data Gap Filling

Apply Standardized workflow

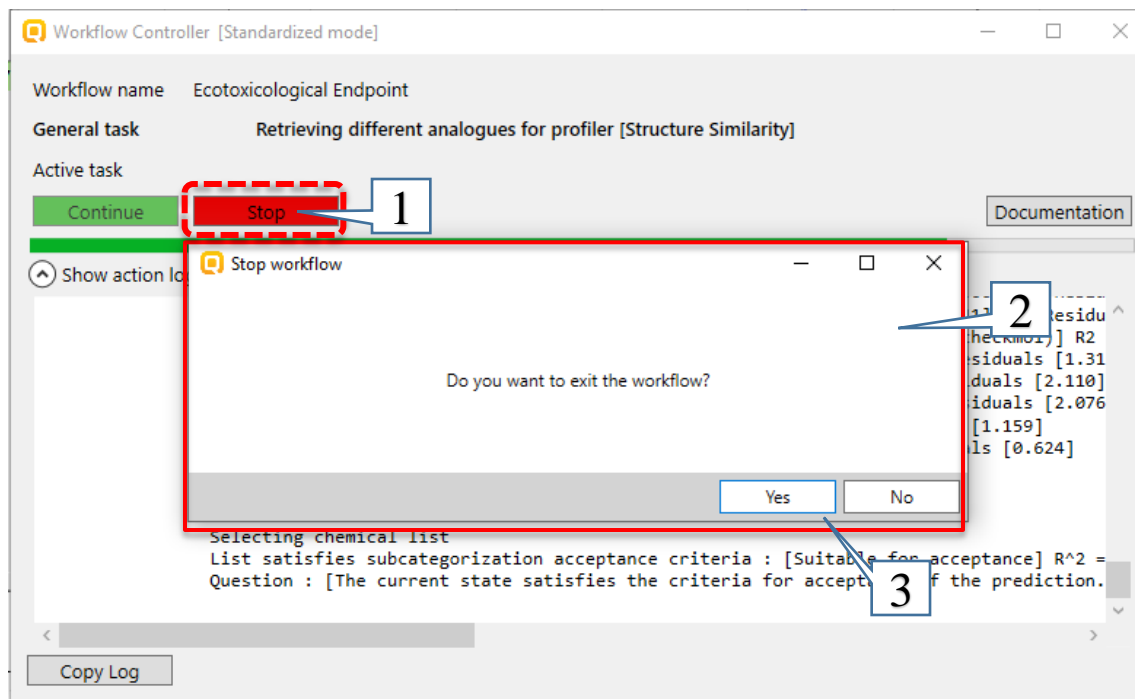
- Continue the workflow if you are not satisfied with the outcome.



- Press Continue button (1) in the workflow controller
- Then repeat the steps described on slide 34

Data Gap Filling

Apply Standardized workflow

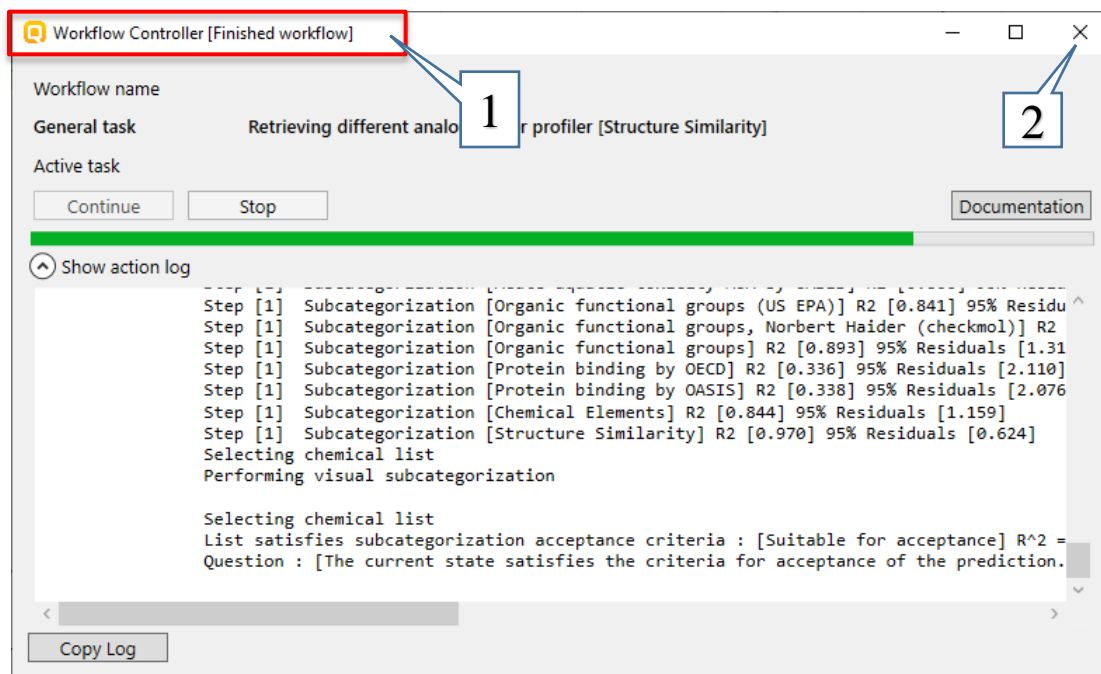


- Press Stop button (1) on the Workflow controller, once you are satisfied with the prediction
- A pop-up window (2) asks to confirm the exit of the workflow
- Press Yes button(3)

Data Gap Filling

Apply Standardized workflow

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

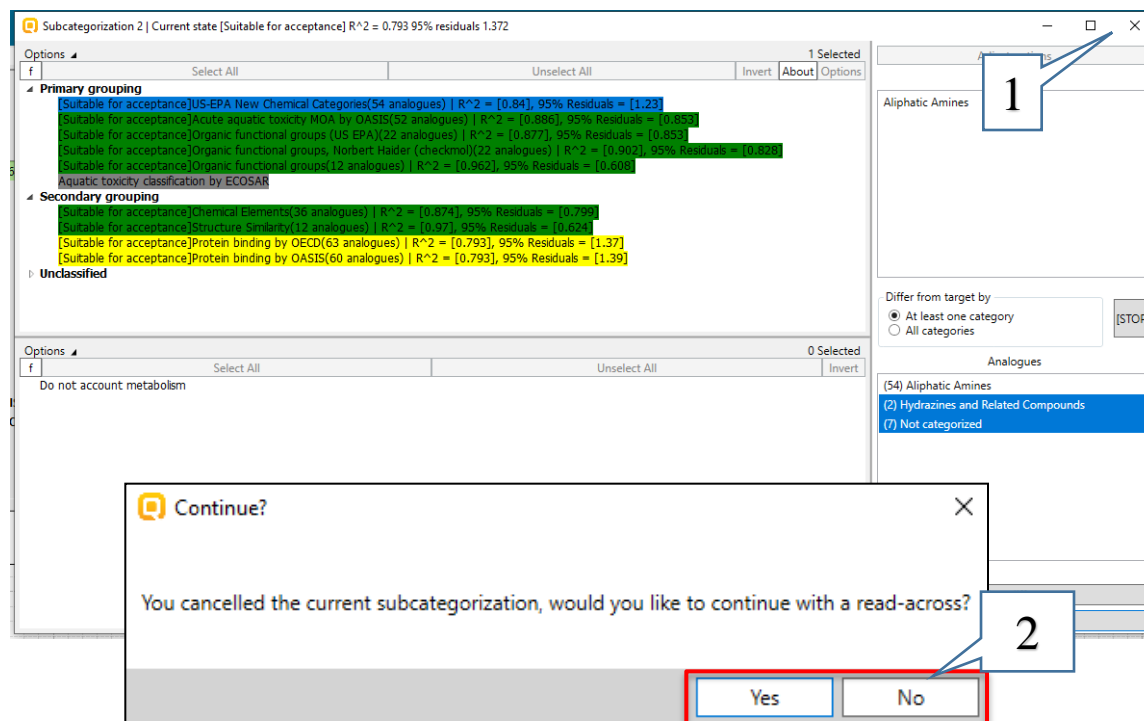


Data Gap Filling

Apply Standardized workflow

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

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



Data Gap Filling

Apply Standardized workflow

The screenshot displays the QSAR Toolbox software interface during a Data Gap Filling workflow. The top menu bar includes options for Input, Profiling, Data, Category definition, Data Gap Filling, and Report. The 'Documents' panel on the left lists chemical categories, with '[C: 1032;Md: 210;P: 1] Aliphatic Amines (Aquatic toxicity classification by ECOSAR)' highlighted by a red box and labeled with a '2'. The 'Filter endpoint tree...' panel in the center shows a hierarchical tree of endpoints, with 'Aquatic Toxicity' expanded and 'Mortality' selected, highlighted by a red box and labeled with a '1'. The 'Data matrix' on the right shows a table with columns for different endpoints and rows for chemical categories. The row corresponding to the selected category is highlighted in yellow, showing measured data (M) and predicted data (P) for various endpoints. The bottom panel shows 'Data Gap Filling Settings' with 'Only endpoint relevant' checked.

Documents

Document 1

[C: 1;Md: 0;P: 1] CAS: 111864

[C: 820;Md: 178;P: 1] Aliphatic Amines (US-EPA New Chemical Categories)

[C: 1032;Md: 210;P: 1] Aliphatic Amines (Aquatic toxicity classification by ECOSAR)

[C: 84;Md: 184;P: 1] Enter GF (SW by trend analysis)

[C: 75;Md: 171;P: 1] Subcategorized: Substance type

[C: 78;Md: 170;P: 1] Filter by WS - Exp Water Solubility

[C: 76;Md: 160;P: 0] Filter by WS - Water Solubility

[C: 75;Md: 155;P: 0] Filter by WS - Water Solubility (fragments)

[C: 76;Md: 160;P: 1] Filter by WS - Water Solubility

[C: 75;Md: 155;P: 0] Filter by WS - Water Solubility (fragments)

[C: 75;Md: 155;P: 1] Filter by WS - Water Solubility (fragments)

[C: 65;Md: 137;P: 1] Subcategorized: Aquatic toxicity classification by E

[C: 56;Md: 125;P: 1] Subcategorized: US-EPA New Chemical Catego

[C: 307;Md: 73;P: 1] Amine, primary<AND>Aliphatic amine, primary (Organic functional grou

[C: 143;Md: 55;P: 1] Aliphatic Carbon [-CH3]<AND>Aliphatic Carbon [-CH2-]<AND>Aliphatic

[C: 298;Md: 73;P: 1] Amine<AND>Primary amine<AND>Primary aliphatic amine (Organic fur

[C: 315;Md: 146;P: 1] Narcotic Amine (Acute aquatic toxicity MOA by OASIS)

Data Gap Filling Settings

Only endpoint relevant

Filter endpoint tree...

Structure

Parameters

Physical Chemical Properties

Environmental Fate and Transport

Ecotoxicological Information

Aquatic Toxicity

Mortality

EC50 <OR> LC50

Animalia (animals)

Chordata (chordat...

Actinopterygii...

Pinnipedia...

103/211

1 [target]

2

3

4

5

6

M: 5.15 mg/L

M: 5.19 (4.73+5....

T: 8.64 (0.547+1...

M: 25 (22.6+27.6...

M: 25.1 mg/L

M: 102 (97.9+10...

M: 102 mg/L

The result is displayed on the data matrix (1) marked with "T"("M" stands for measured data)

The workflow finishes on the document level of the primary grouping(2)

Data Gap Filling

Apply Standardized workflow

```

Document 1
: [C: 1;Md: 0;P: 1] CAS: 111864
  ☐ [C: 820;Md: 178;P: 1] Aliphatic Amines (US-EPA New Chemical Categories)
  ☒ [C: 1032;Md: 210;P: 1] Aliphatic Amines (Aquatic toxicity classification by ECOSAR)
    ☒ [C: 84;Md: 184;P: 1] Enter GF (SW by trend analysis)
      ☒ [C: 79;Md: 171;P: 1] Subcategorized: Substance type
        ☒ [C: 78;Md: 170;P: 1] Filter by WS - Exp Water Solubility
          ☒ [C: 76;Md: 160;P: 1] Filter by WS - Water Solubility
            ☒ [C: 75;Md: 155;P: 1] Filter by WS - Water Solubility (fragments)
              ☒ [C: 65;Md: 137;P: 1] Subcategorized: Aquatic toxicity classification by ECOSAR
        ☐ [C: 307;Md: 73;P: 1] Amine, primary<AND>Aliphatic amine, primary (Organic functional groups)
        ☐ [C: 143;Md: 55;P: 1] Aliphatic Carbon [-CH3]<AND>Aliphatic Carbon [-CH2-]<AND>Aliphatic Carbon [CH]<AND>Amino, aliphatic attach [-NH2]
        ☐ [C: 298;Md: 73;P: 1] Amine<AND>Primary amine<AND>Primary aliphatic amine (Organic functional groups, Norbert Haider (checkmol))
        ☐ [C: 315;Md: 146;P: 1] Narcotic Amine (Acute aquatic toxicity MOA by OASIS)
  
```

All the steps executed in the SW are listed in the Document's panel.
The grey highlighted level(s) of documented tree indicates that a prediction is accepted at this level.

Outlook

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- Specific Aims
- Standardized workflow for Ecotoxicity
- The exercise
- **Standardized workflow execution**
 - Input
 - Data Gap Filling
 - **Report**

Report Overview

- The report module can generate reports on predictions performed with the Toolbox.
- The report module contains a predefined report template which users can customized.
- Three types of report files are generated:
 - Prediction report – containing information for the target
 - Category report – containing information for the analogues in the category
 - Data matrix – containing information for the analogues used for the prediction

Report Generation report

The screenshot shows the QSAR Toolbox software interface. The top menu bar has 'Report' highlighted. The left sidebar has 'Prediction' selected. The central window displays the 'Customize report content and appearance' wizard. The wizard has three pages: 'Customization', 'Prediction', and 'Category'. The 'Prediction' page is currently active, showing options to include 'Prediction', 'Category', and 'Data matrix' sections in the report. The 'Prediction' section is checked, and the 'Data matrix' section is also checked. The 'Category' section is unchecked. The 'Data matrix' section has a note: 'Remove password protection of the PDF files. Note: If the protection is removed, this will be specified in the first page of the report.' The wizard has 'Back', 'Next', 'Cancel', and 'Create report' buttons at the bottom.

1. Go to **Report** module

2. Select **Prediction**

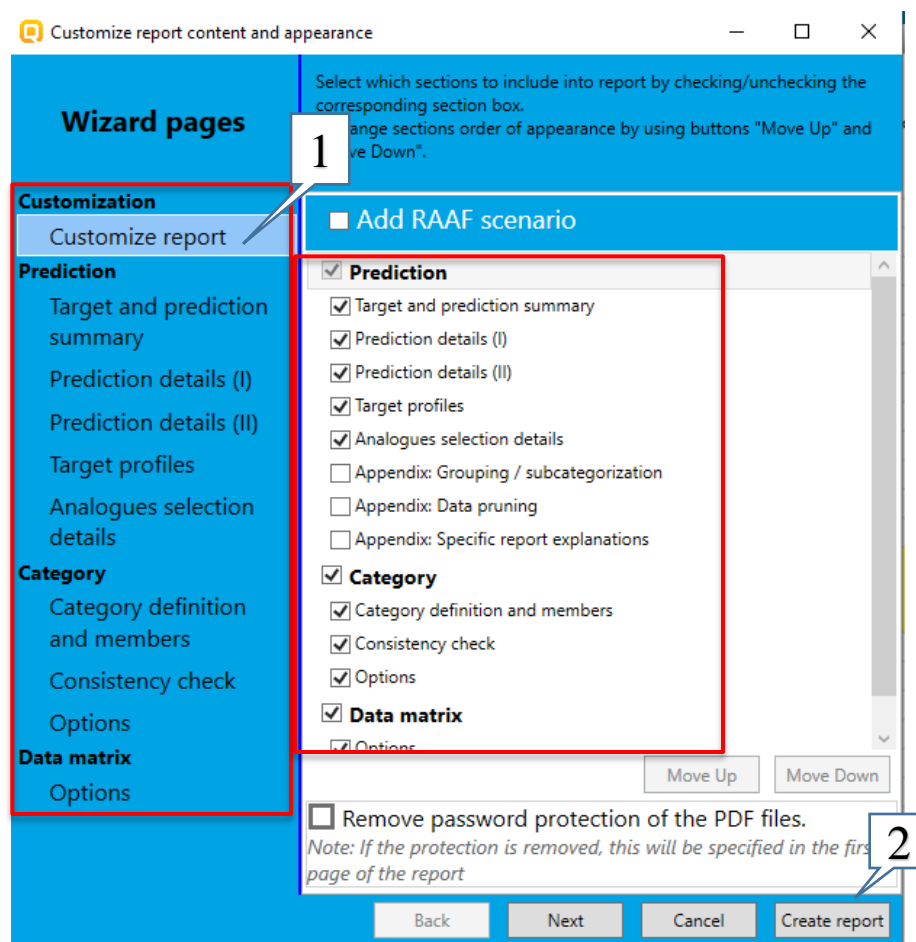
3. A Wizard pages window is displayed

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

Report Generation report

The user can customize the report content (1) and appearance.

Generation of the reports happens by click on the **Create report** button (2).



Report Wizard pages

I. Customized report - the user is able to include or exclude the sections in the report;

II. Prediction report:

- **Target and prediction summary** – This section includes substance ID of the target chemical and the prediction outcome. Fields which are automatically populated by the system are indicated. Here the user could add information for the author, contact details and summary information;
- **Prediction details** and **Prediction details (II)** – section prediction details provides details about the prediction and its reliability. Prediction details (II) is optional it provides specific information about the prediction depending on the gap filling approach;
- **Target profiles** – this section summarize profiles used for the prediction. Additional profiles could be also included by the user;
- **Analogues selection details** – This section illustrates how analogues were selected. It displays selected databases, category boundaries and applicability domain.

Report Wizard pages

III. Category report:

- **Category definition and members** – This part includes sections related to list of category members, basic definition of the target endpoint and category hypothesis. Also information for calculated physico-chemical parameters for the category members are provided. Some of the sections are automatically populated while for the others a report items from Report basket could be added manually.
- **Consistency check** – This part includes sections related to the layers of the consistency check: physicochemical similarity; structural similarity, mechanistic similarity and additional endpoint data. Similarly to the previous section some of the sections are automatically populated and for the others items from the Report basket could be added.;
- **Options** – in this section number of the category members used for reporting could be changed;

IV. Data matrix report

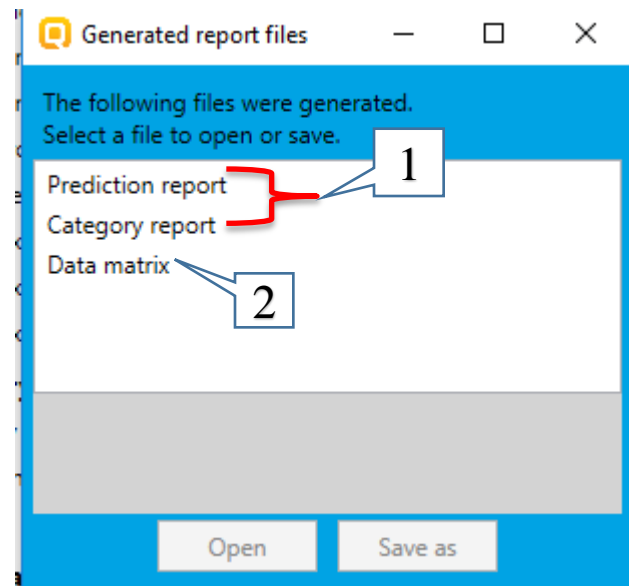
- Data matrix report gives the possibility to export information for the chemicals in the data matrix including parameters, profilers and experimental data.

Report

Generation report

After clicking on the Create report button, *Generated report files* window appears. It contains two types of files:

- 1) Prediction report** - a PDF file containing the prediction information related to the target.
- 2) Category report** - a PDF file containing information for the consistency of the final category (target plus used analogues).
- 3) Data matrix** - a MS Excel file containing chemicals used for prediction along with their data for selected parameters, profiles and endpoint tree positions.



Report

Prediction report

Using of a standardized workflow for predicting of ecotoxicological endpoint is noted in the *Prediction report*.

Prediction of LC50 for octylamine

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Prediction report

QSAR Toolbox prediction for single chemical

Date: 14 Apr 2020

Author(s):

Contact details:

Target information		
Structural information	Numerical identifiers	Chemical names
SMILES: <chem>CCCCCCCCN</chem>	CAS#: 111-86-4 Other: EC Number:2039160	1-aminooctane 1-Octanamine 1-octylamine
Structure 		

Prediction summary
Predicted endpoint: LC50; Mortality; Pimephales promelas; 96 h; No guideline specified Predicted value: 8.64 (from 0.547 to 136) Unit/scale: mg/L Data gap filling method: Trend analysis Summary: manually editable field Not provided by the user

Report

Category report

Category report

QSAR Toolbox report for category

Information for the members of the category obtained as a result of SW application is included in the *Category report*.

1. Category definition

1.1. Category definition

Category name

manually editable field

Not provided by the user

Covered (target) endpoint(s)

- Ecotoxicological Information/Aquatic Toxicity: Pimephales promelas, Actinopterygii (ray-finned fishes, spiny rayed fishes), Chordata (chordates), Animalia (animals), EC50 <OR> LC50, Mortality, Duration=96 h

Category hypothesis

manually editable field

Not provided by the user

1.2. Category members

Information of category members




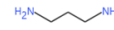
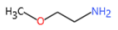


Table of category members

#	CAS	Name	SMILES	Structure
1	111-86-4	octylamine	<chem>CCCCCCCCN</chem>	
2	768-94-5	Amantadine	<chem>NC12CC3CC(C(C3)C1)C2</chem>	
3	100-46-9	Benzylamine	<chem>NCc1ccccc1</chem>	
4	109-76-2	1,3-Diaminopropane	<chem>NCCCN</chem>	
5	109-85-3	2-methoxyethanamine	<chem>COCN</chem>	
6	103-83-3	Benzyltrimethyl	<chem>CN(C)Cc1ccccc1</chem>	

Report

data matrix report

Data matrix report

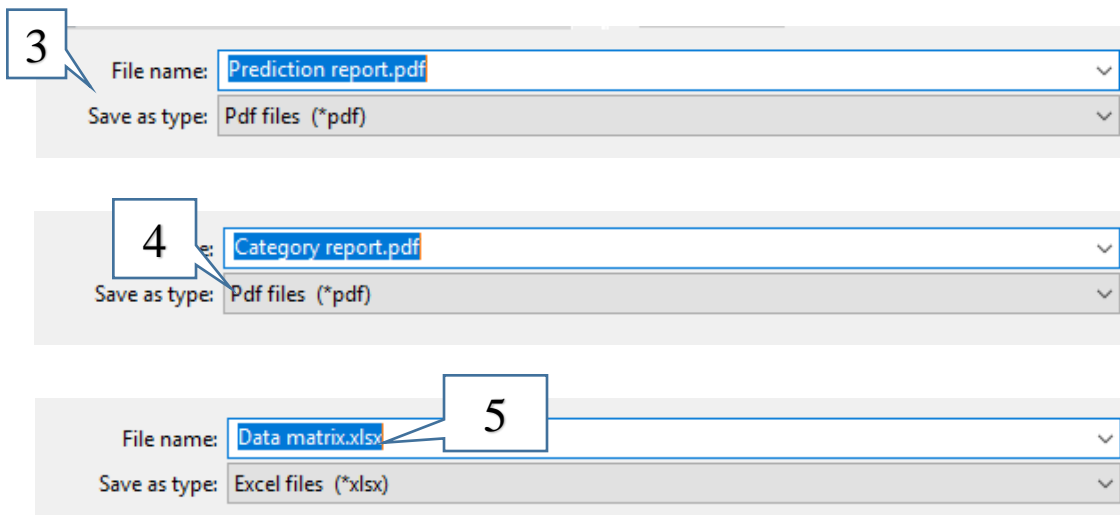
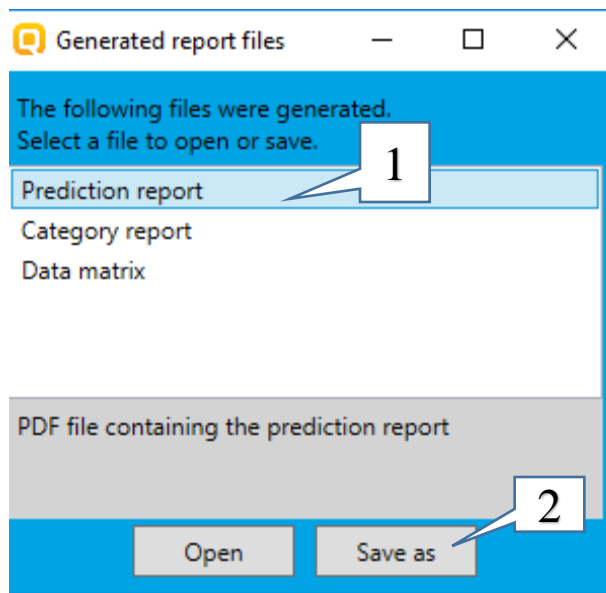
A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W
Substance Identity		Target chemical			Analogue #1			Analogue #2			Analogue #3			Analogue #4			Analogue #5			Analogue #6		
Structure																						
CAS number		111-86-4			768-94-5			100-46-9			109-76-2			109-85-3			103-83-3			15673-00-4		
Chemical name		octylamine			Amantadine			Benzylamine			1,3-Diaminopropane			2-methoxyethanamine			Benzyltrimethyl			3,3-Dimethylbutylamine		
Other Identifier																						
SMILES		CCCCCCCCN			NC12CC3CC(C(C(C3)C1)C2			NCC1CCCC1			NCCCN			COCCN			CN(C)CC1CCCC1			CC(C)(C)CCN		
Parameters	unit																					
Profilers																						
Profiles used for grouping/subcategorization																						
Aliphatic Amines (Aquatic toxicity)		Aliphatic Amines Discrete chemical;			Aliphatic Amines Discrete chemical;			Aliphatic Amines Discrete chemical;			Aliphatic Amines Discrete chemical;			Aliphatic Amines Discrete chemical;			Aliphatic Amines Discrete chemical;			Aliphatic Amines Discrete chemical;		
Substance type (subcategorization)		Mono constituent (predefined); Organic			Mono constituent (predefined); Organic			Mono constituent (predefined); Organic			Mono constituent (predefined); Organic			Mono constituent (predefined); Organic			Mono constituent (predefined); Organic			Mono constituent (predefined); Organic		
Aquatic toxicity classification by ECOSAR		Aliphatic Amines			Aliphatic Amines			Aliphatic Amines			Aliphatic Amines			Aliphatic Amines			Aliphatic Amines			Aliphatic Amines		
US-EPA New Chemical Categories		Aliphatic Amines			Aliphatic Amines			Aliphatic Amines			Aliphatic Amines			Aliphatic Amines			Aliphatic Amines			Aliphatic Amines		
General Mechanistic																						
Protein binding by OASIS		No alert found			No alert found			No alert found			No alert found			No alert found			No alert found			No alert found		
Protein binding by OECD		No alert found			No alert found			No alert found			No alert found			No alert found			No alert found			No alert found		
Endpoint Specific																						
Acute aquatic toxicity MOA by OASIS		Narcotic Amine			Narcotic Amine			Narcotic Amine			Narcotic Amine			Narcotic Amine			Narcotic Amine			Narcotic Amine		
Empiric																						
Organic functional groups (US EPA)		Aliphatic Carbon [-CH3]; Aliphatic Carbon [-CH2-]; Aliphatic Carbon [CH]; Amino, aliphatic attach [-NH2]; Amino, aliphatic attach [-N<]			Fused Aliphatic ring unit; Aliphatic Carbon [-CH2-]; Aliphatic Carbon [CH]; Aliphatic Carbon [C]; Amino, aliphatic attach [-NH2]; Amino, aliphatic attach [-N<]; Tertiary Carbon			Aliphatic Carbon [-CH2-]; Aliphatic Carbon [CH]; Amino, aliphatic attach [-NH2]; Amino, aliphatic attach [-N<]; Aromatic Carbon [C]			Aliphatic Carbon [-CH2-]; Aliphatic Carbon [CH]; Amino, aliphatic attach [-NH2]; Amino, aliphatic attach [-N<]; Amino, aliphatic attach [-N<]			Aliphatic Carbon [-CH3]; Aliphatic Carbon [-CH2-]; Aliphatic Carbon [CH]; Oxygen, aliphatic attach [-O-]; Amino, aliphatic attach [-NH2]; Amino, aliphatic attach [-N<]			Aliphatic Carbon [-CH3]; Aliphatic Carbon [-CH2-]; Aliphatic Carbon [CH]; Amino, aliphatic attach [-NH2]; Amino, aliphatic attach [-N<]; Aromatic Carbon [C]			Aliphatic Carbon [-CH3]; Aliphatic Carbon [-CH2-]; Aliphatic Carbon [CH]; Amino, aliphatic attach [-NH2]; Amino, aliphatic attach [-N<]; Aromatic Carbon [C]		
Organic functional groups		Amine, primary; Aliphatic amine, primary			Amine, primary; Tricyclic amine; Cycloalkane; Bridged-ring carbocycles; Aliphatic amine, primary			Amine, primary; Benzyl; Aryl; Aliphatic amine, primary			Amine, primary; Aliphatic amine, primary			Amine, primary; Ether; Aliphatic amine, primary			Amine, tertiary; Benzyl; Aryl; Aliphatic amine, tertiary			Alkane, branched with quaternary Amine, primary; tert-Butyl; Aliphatic amine, primary		
Structure similarity		[90%,100%]			[0%,10%]			[10%,20%]			[40%,50%]			[20%,30%]			[0%,10%]			[20%,30%]		
Chemical elements		Group 14 - Carbon C; Group 15 - Nitrogen N			Group 14 - Carbon C; Group 15 - Nitrogen N			Group 14 - Carbon C; Group 15 - Nitrogen N			Group 14 - Carbon C; Group 15 - Nitrogen N			Group 14 - Carbon C; Group 15 - Nitrogen N			Group 14 - Carbon C; Group 15 - Nitrogen N			Group 14 - Carbon C; Group 15 - Nitrogen N		

Analogue used for the target prediction can be seen the **Data matrix** report. Their selected profiling results, experimental data and/or parameters are also shown.

Report

Saving the report files

To save any of the reports, select the **report** (1) and then click on **Save as** (2); The prediction and category reports are saved as a **pdf file** (3, 4) while the **data matrix** is saved as an **.xlsx file** (5)



Congratulations!

- You have completed the tutorial on the standardized workflow for ecotoxicological endpoint.
- You have now been introduced to the consecutive steps of the standardized workflow of the (Q)SAR Toolbox and the rationale behind each step.
- Note, proficiency comes with practice!