

OECD QSAR Toolbox v.4.1

Tutorial on how to predict skin sensitisation potential by standardized workflow

Outlook

- **Background**
- Objectives
- Specific Aims
- Standardized workflow for Skin sensitization
- The exercise
- Standardized workflow execution

Background

- This is a step-by-step presentation designed to take the Toolbox user through the filling of skin sensitization data gaps using a standardized workflow.

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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 the standard workflow for predicting of skin sensitization potential;
- To familiarize the user with the new Toolbox interface;
- To familiarize the user with the new notification messages;
- To explain to the user the rationale behind each step of the exercise.

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Standardized workflow for Skin sensitization

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. Skin sensitization, in vivo, LLNA and GPMT).
- 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 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 one chemical as well as for a batch of chemicals.

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The Exercise

- In this exercise we will predict the skin sensitization potential of Ethylparaben [CAS# 120-47-8], which will be the “target” chemical.
- This prediction will be accomplished by using of the developed standardized workflow for skin sensitization.

The Exercise

Sidebar On Sensitization

- Allergic contact dermatitis that results from skin sensitization is a significant health concern.
- Skin sensitization is a toxicological endpoint that is complex and conceptually difficult.
- However, there is growing agreement that most organic chemicals must react covalently with skin proteins in order to behave as skin sensitizers.
- Therefore, mechanisms by which organic chemicals bind with proteins are relevant to grouping chemicals that may be skin sensitizing agents.

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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.

Outlook

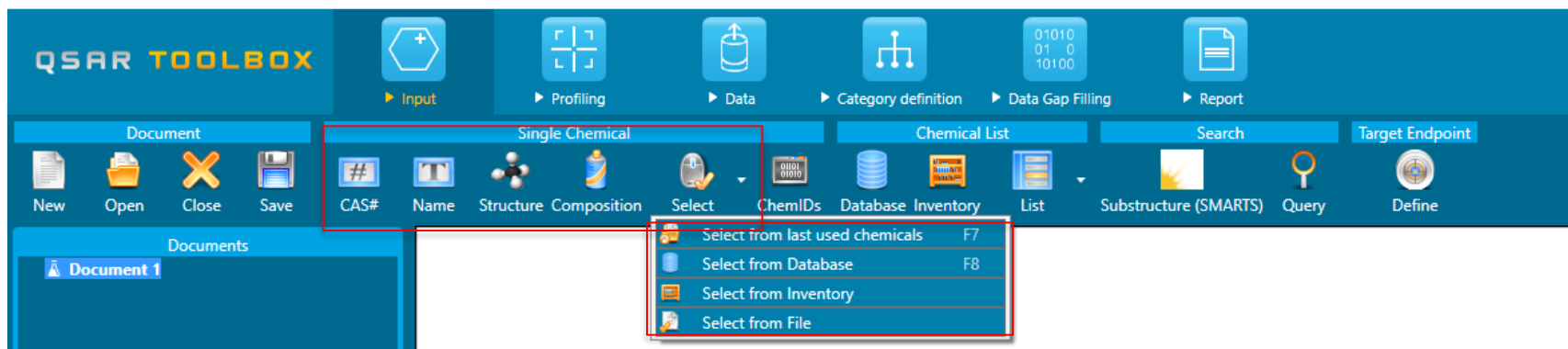
- Background
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 - Input

Input Overview

- This module provides the user with several means of entering the chemical of interest (i.e. 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.

Input

Ways of Entering a Chemical



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

Input Screen

Input target chemical by CAS#

1. Click on **CAS#**;

2. Enter the CAS# of Ethylparaben (CAS **120-47-8**);

3. Click on **Search**.

Input

Target chemical identity

The Toolbox now searches the databases to find out if the CAS# you entered is linked to a molecular structure stored in the Toolbox. It is displayed as a 2-dimensional depiction. Click on **OK** (1).

Search by CAS #

120478 Search

Select All Unselect All Invert Selection Selected 1 of 1

1	CAS	120-47-8
	SMILES	CCOC(=O)c1ccc(O)cc1
	CS Relation	High
<input checked="" type="checkbox"/>	Substance	Mono constituent
	Composition	
	Name	4-Hydroxy-benzoic acid eth... 4-hydroxybenzoic acid ethy... 4-hydroxybenzoic acid, eth...

CCOC(=O)c1ccc(O)cc1



In case the entered CAS# corresponds to more than one structure or to one structure but with different predefined substance type, more than one chemical identity could be retrieved. In this case the user can decide which substance is to be retained for the subsequent workflow.

Input

Target chemical identity

The screenshot displays the QSAR Toolbox software interface. The top menu bar includes 'Input', 'Profiling', 'Data', 'Category definition', 'Data Gap Filling', and 'Report'. Below this, a secondary toolbar contains icons for 'New', 'Open', 'Close', 'Save', 'CAS#', 'Name', 'Structure', 'Composition', 'Select', 'ChemIDs', 'Database', 'Inventory', 'List', 'Substructure (SMARTS)', 'Query', and 'Define'. The main workspace is divided into three panes: 'Documents' on the left, 'Filter endpoint tree...' in the center, and a chemical structure panel on the right. The 'Documents' pane shows 'Document 1' with CAS number 120478. The 'Filter endpoint tree...' pane has 'Structure' selected, and its 'Structure info' sub-section is expanded and highlighted with a red box. A callout box with the number '1' points to this section. The 'Structure info' list includes: CAS Number, CAS Smiles relation, Chemical name(s), Composition, Molecular Formula, Predefined substance type, and Structural Formula. The right-hand panel shows the chemical structure of 4-hydroxybenzoic acid and its associated data: 1 [target], 120-47-8, High, 4-hydroxybenzoic ac, C9H10O3, Mono constituent, and the SMILES string CCOC(=O)c1ccc(O)cc1.

1. Open Structure info level to see chemical ID of the target molecule

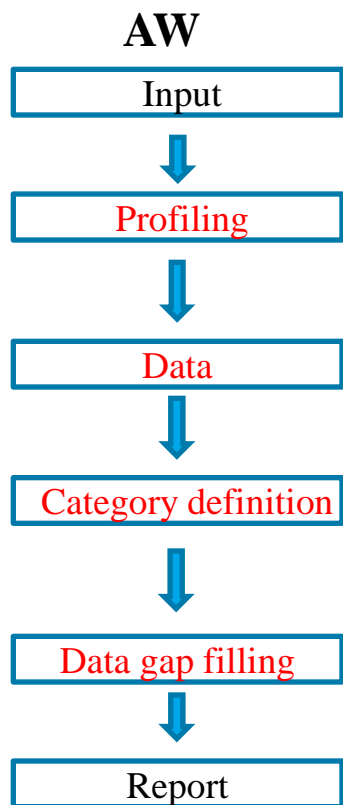
Outlook

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- **Standardized workflow execution**
 - Input
 - **Data Gap Filling**

Data Gap Filling Overview

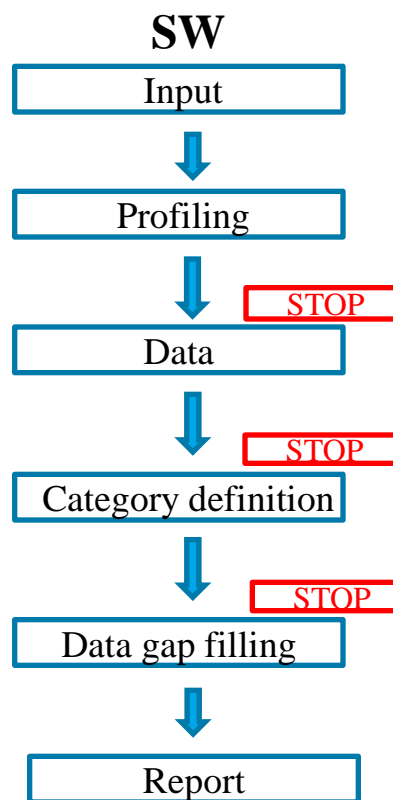
- “Data Gap Filling” (DGF) module give access to five different data gap filling tools:
 - Read-across
 - Trend analysis
 - (Q)SAR models
 - Standardized workflow
 - Automated workflow
- Depending on the situation, the most relevant data gap mechanism should be chosen, taking into account the following 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.
 - Standardized and Automated workflows are developed to facilitate the users work. Once started, they follow the implemented logic and finish with prediction. The general differences between the two types of workflows are represented on the next slide.

Data Gap Filling Overview



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



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

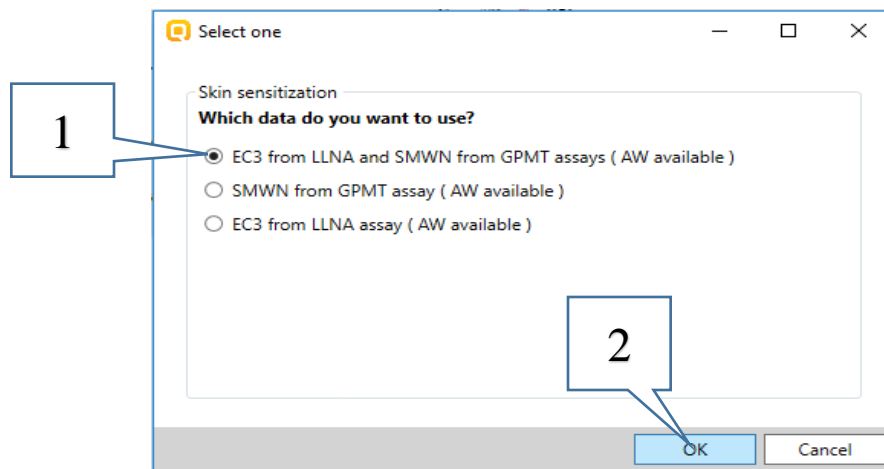
The screenshot displays the QSAR Toolbox software interface. The top menu bar contains several icons, with 'Data Gap Filling' highlighted in a red dashed box and labeled '1'. Below the menu bar, the 'Standardized' button in the workflow bar is highlighted in a red box and labeled '2'. The 'Filter endpoint tree...' panel shows a tree structure with 'Skin sensitization' selected, labeled '3'. A 'Select workflow' dialog box is open, showing 'Skin sensitization' selected in the 'Choices' list, labeled '4'. The dialog box has 'OK' and 'Cancel' buttons. At the bottom, a blue box contains the following instructions:

1. Go to **Data Gap Filling**; 2. Click on **Standardized** button; 3. Select **Skin sensitization**; 4. Confirm with **OK**

Data Gap Filling

Apply Standardized workflow

There are three options for selection of endpoint and user should select one of them. The first option allows more analogues to be found because of the using of two types of data – EC3 and SMWN. During the workflow process all skin data of these endpoints will be converted to the default scale for Skin Sensitisation - “Skin Sensitisation ECETOC”. It converts all skin data into: Positive and Negative.

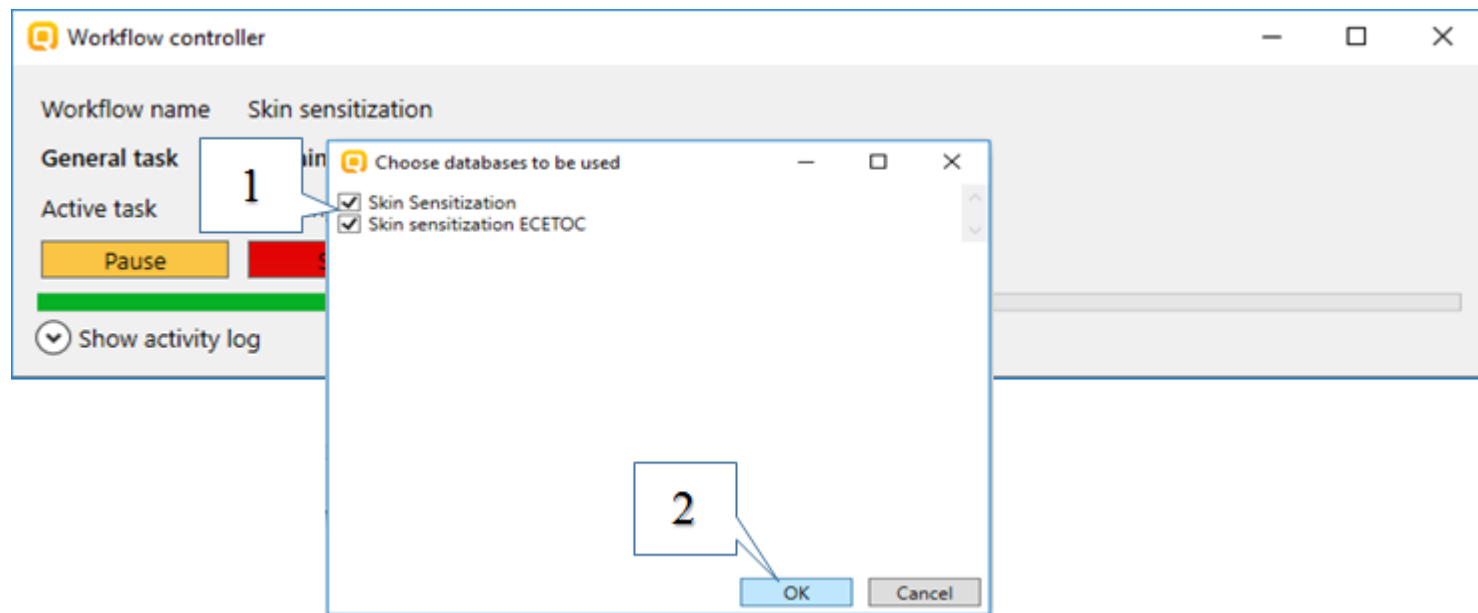


1. Select the first combined endpoint – EC3 from LLNA and SMWN from GPMT assays; 2. Confirm with **OK**

Data Gap Filling

Apply Standardized workflow

Once the workflow is started, *Workflow controller* appears. The first choice, which the user have to make is to select one or all skin sensitization databases, where the analogues will be searched.

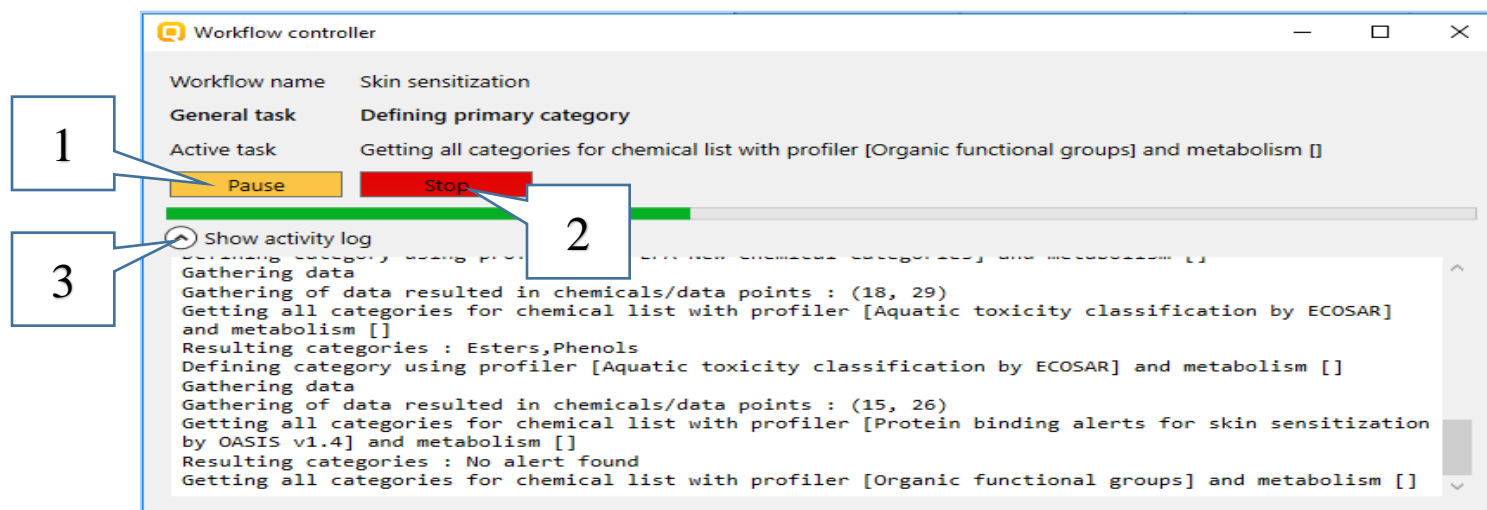


1. Select the both databases – **Skin Sensitization** and **Skin sensitization ECETOC**;
2. Click on **OK**

Data Gap Filling

Apply Standardized workflow

The **Workflow controller** has two main buttons **Continue/Pause** (1) allowing to continue or pause and **Stop** (2) – which will stop the workflow. Additionally, all actions that will be done during the execution of the workflow are tracked down and could be seen from the **Show activity log** part (3) of the Workflow controller.



Data Gap Filling

Algorithm of Skin sensitization workflow

Once finished with the selection of databases, the workflow continues with application of the relevant profilers. There are three possible cases to form an analogues set:

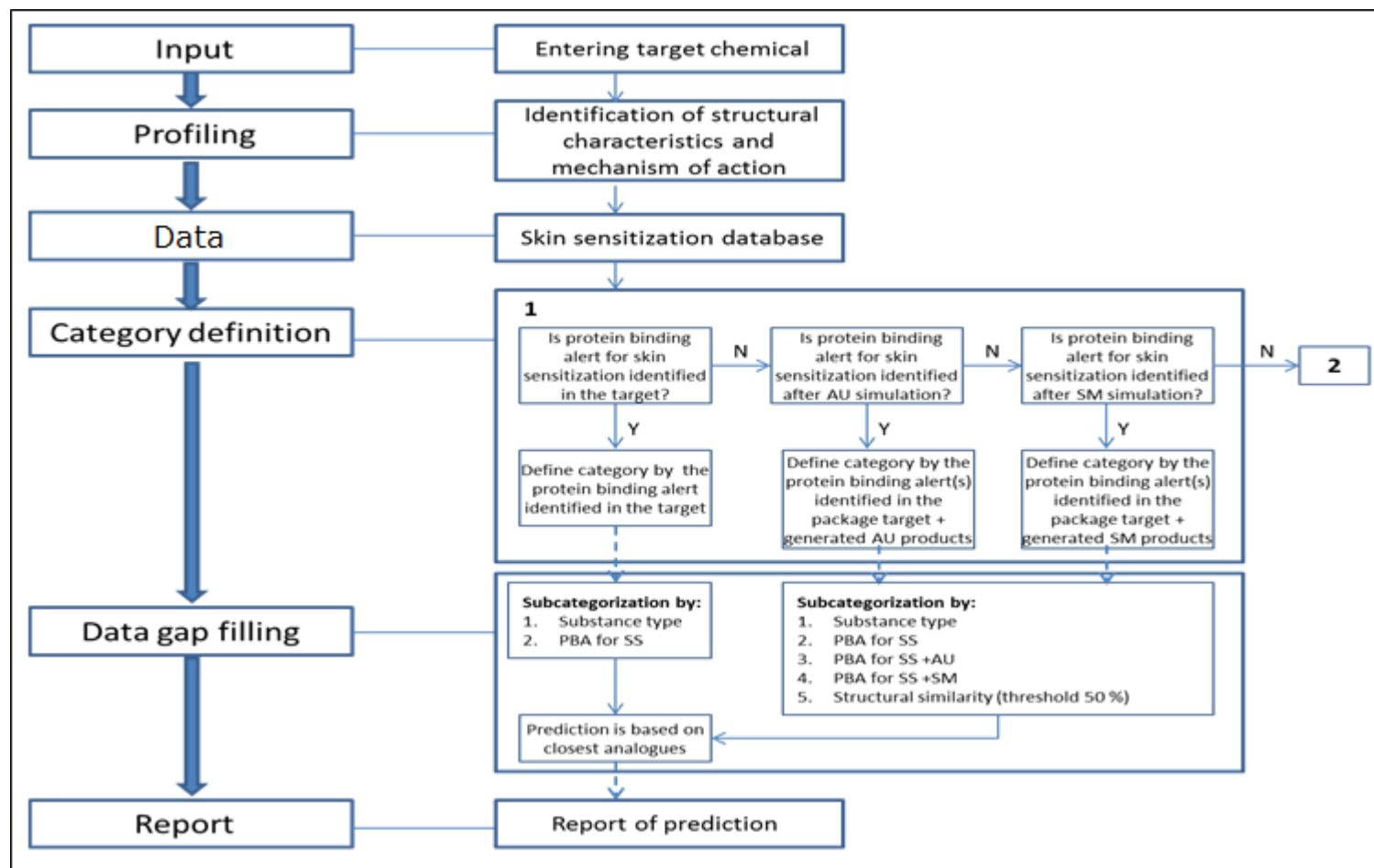
- 1) if the target have an active alert as a parent;
- 2) if the target have an active alert as a result of autoxidation or skin metabolism activation;
- 3) if no alert is found in the target or its metabolites.

If a protein binding alert is identified in the target or is produced as a result of autoxidation or skin metabolism (case 1 or 2) then primary grouping is based on this alert.

In the last case (case 3) the primary group is defined using structurally based profiling schemes.

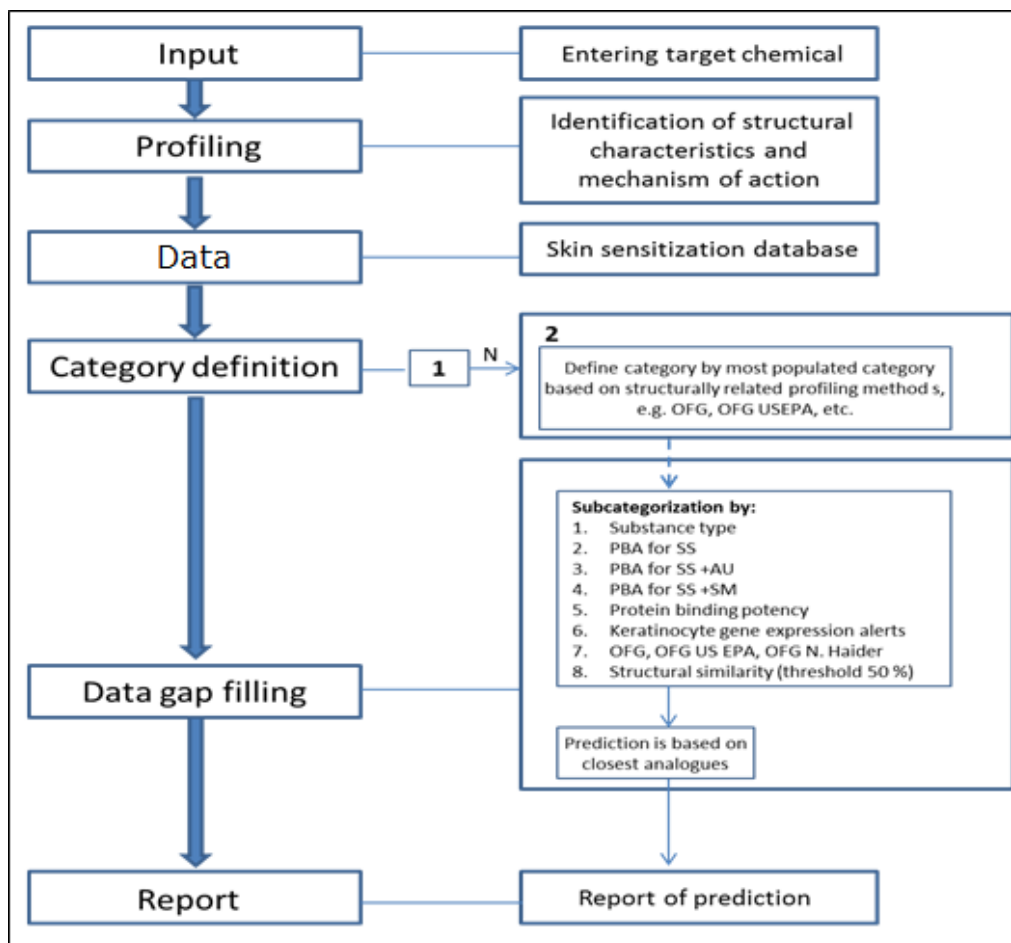
Data Gap Filling

Scenario 1 – an alert is identified in the parent or produced as a result of autoxidation or skin metabolism activation



Data Gap Filling

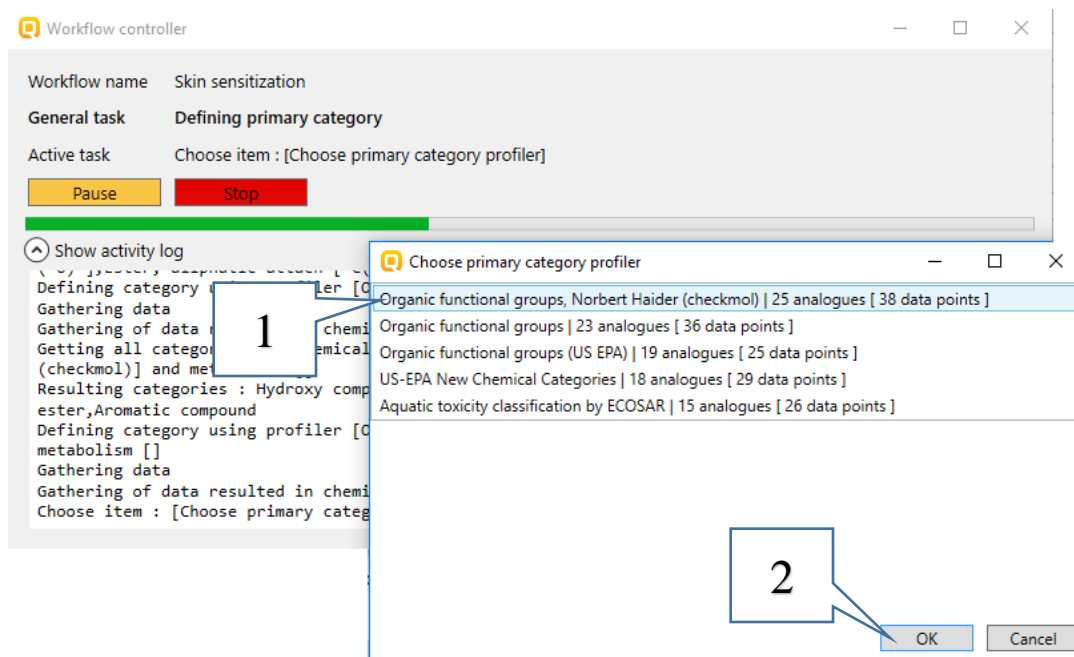
Scenario 2 – no alert is identified in the parent neither in generated metabolites (autoxidation products and skin metabolites)



Data Gap Filling

Apply Standardized workflow

When a group cannot be defined by the workflow (more than one alert available in the target chemical or different primary groupings based on structure based profilers) then the standardized workflow wait for action from the user.



1. Select the most populated category; 2. Confirm with **OK**

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

The screenshot shows the 'Subcategorization' window in the QSAR Toolbox. The interface is divided into two main sections. The top section has 'Group by: Priority', 'Sort by: Relevancy', and 'Color by: Outcome'. A callout '1' points to the 'Sort by: Relevancy' dropdown. Below this, a list of profilers is shown, with several highlighted in cyan. A callout '2' points to the 'Primary grouping' header, which contains the highlighted profilers: 'Protein binding potency', 'Protein binding alerts for skin sensitization', 'Keratinocyte gene expression', 'Structure Similarity', 'Organic functional groups', 'Organic functional groups (US EPA)', and 'Organic functional groups, Norbert Haider (checkmol)'. A callout '3' points to the 'Unclassified' group, which contains 'Substance type'. The bottom section has 'Group by: Category', 'Sort by: Name', and 'Color by: Outcome'. A callout '4' points to the 'Simulated' group, which contains 'Autoxidation simulator' and 'Skin metabolism simulator'. A 'Legend' dialog box is open on the right, titled 'Outcome', with a list of outcomes and their corresponding colors: 'Converges' (green), 'Improves statistic' (cyan), 'Does not improve statistic' (yellow), 'Prediction not suitable' (red), and 'Applied or Doesn't modify state' (grey). The dialog also has an 'OK' button.

The profilers are sorted by **Relevancy** (1) and the highlighted profilers appear in group **Primary grouping** (2). All the rest profilers are under group **Unclassified** (3). Although the highlighted profiles are relevant to the endpoint, recommended and facilitating the user in their further choice, the rest of the profilers are not removed and user can select each of them for subcategorization. In case the target have no alert as a parent, the related metabolic simulator will be also highlighted (4).

Data Gap Filling

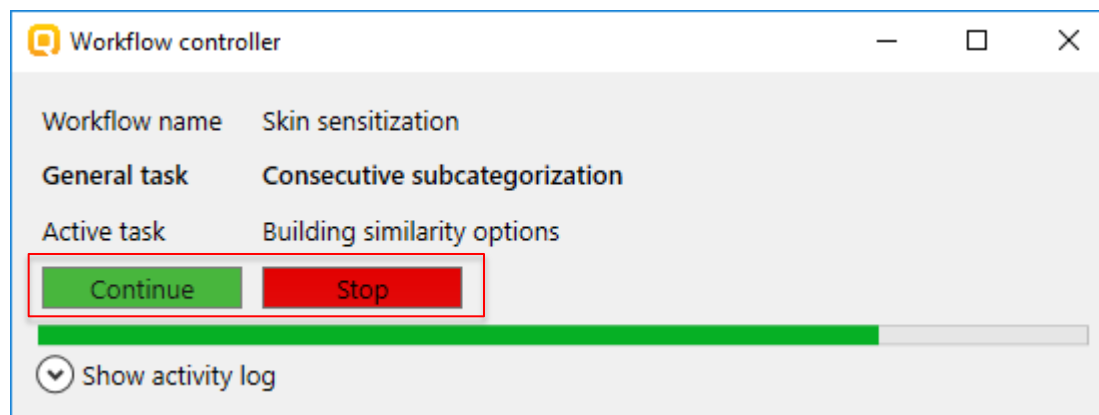
Apply Standardized workflow

The screenshot displays the QSAR Toolbox interface during a data gap filling workflow. The 'Workflow Controller' window shows the task 'Consecutive subcategorization' with the active task 'Performing visual subcategorization'. The 'Subcategorization' panel on the left shows 'Primary grouping' with 'Protein binding alerts for skin sensitization by OASIS' and 'Skin metabolism simulator' selected. The 'Data Gap Filling' table shows a grid of chemical structures and their predicted values for various endpoints. The 'Read-across prediction' plot shows the relationship between log Kow and predicted values for EC3.5 M W N.

Select **Protein binding alerts for skin sensitization by OASIS**. in combination with **Skin metabolism simulator** (1). No alerts for SS are found in the target, neither in its metabolites (2). Click on **Remove selected** (3).

Data Gap Filling

Apply Standardized workflow



When the chemicals, which fulfill the requirements are removed, the *Workflow controller* stops before the next subcategorization. The user can continue to subcategorize or to stop, accepting the current state of the prediction.

In this example we will continue with consecutive subcategorization. Click on Continue button

Data Gap Filling

Apply Standardized workflow

The screenshot displays the QSAR Toolbox interface during a data gap filling workflow. A 'Workflow Controller' window is open, showing the workflow name 'Skin sensitization' and the general task 'Consecutive subcategorization'. The active task is 'Performing visual subcategorization'. Below this, a 'Subcategorization' window is open, showing a list of profiling schemes. Three callouts are present: (1) points to greyed-out options in the 'Do not account for' section; (2) points to the 'Organic functional groups (US-EPA)' option; (3) points to the 'Remove selected' button. The main window shows a table of 24 chemical structures with their predicted values for 'M: Negative' and 'M: Positive'. Below the table is a 'Read-across prediction for EC3, S M W N, based on 5 values' plot showing observed vs. predicted values.

The used profiling schemes and metabolism simulators are colored in grey (1).
 Now we select **Organic functional groups (US-EPA)** (2) and remove the different chemicals (3).

Data Gap Filling

Apply Standardized workflow

The screenshot displays the QSAR Toolbox software interface. On the left, the 'Workflow Controller' dialog box is open, showing a progress bar and 'Continue' and 'Stop' buttons. A callout box with the number '2' points to the 'Stop' button. Below the dialog, the 'Data Gap Filling Settings' panel is visible, with a callout box containing the number '1' pointing to the 'Standardized workflows' option. The main window shows a 'Filter endpoint tree...' dialog with a list of endpoints including Acute Toxicity, Bioaccumulation, Carcinogenicity, etc. To the right, a table displays chemical structures for four different endpoints. At the bottom, a 'Read-across prediction for EC3, S M W N, based on 3 values' plot shows a horizontal axis for 'log Kow' ranging from 1.9 to 3.5 and a vertical axis for 'EC3, S M W N' with 'Positive' and 'Negative' labels. A red box highlights a horizontal line at the 'Negative' level, with four data points marked by red dots. A callout box with the number '1' points to this red box.

We see that all remained chemicals after the second subcategorization possess negative data (1). Therefore, here we click on the **Stop** button (2) of the workflow controller.

Data Gap Filling

Apply Standardized workflow

The screenshot displays the QSAR Toolbox interface during a data gap filling workflow. A 'Stop workflow' dialog box is prominently featured, asking the user 'Do you want to exit the workflow?' with 'Yes' and 'No' buttons. A red box highlights this dialog, and a callout with the number '1' points to the 'Yes' button. The background shows a 'Filter endpoint tree...' window with a list of endpoints such as Acute Toxicity, Bioaccumulation, and Carcinogenicity. Below this, a 'Data Gap Filling Settings' panel is visible, with checkboxes for 'Only endpoint relevant' and 'Only chemical relevant'. At the bottom, a scatter plot titled 'Read-across prediction for EC3, S M W N, based on 3 values' shows 'Observed: Negative; Predicted: Negative' with data points plotted against log Kow and EC3, S M W N.

“Stop workflow” dialogue appears to ask the user if they are sure to exit the workflow. Confirm with “Yes” (1)

Data Gap Filling

Apply Standardized workflow

The screenshot displays the QSAR Toolbox interface during a data gap filling workflow. A 'Workflow Controller' dialog box is open, showing a 'Finished workflow' with the name 'Consecutive subcategorization'. The active task is 'Retrieving different analogues for profiler [Substance type] and'. Below this, a list of toxicity endpoints is visible, including Acute Toxicity, Bioaccumulation, Carcinogenicity, etc. A 'Confirm' dialog box asks 'Are you sure you want to accept this prediction?' with 'Yes' and 'No' buttons. A callout box with the number '2' points to the 'Yes' button. In the background, a scatter plot titled 'Read-across prediction for EC3, S, M, W, N, based on 3 values' shows 'Observed: Negative; Predicted: Negative'. The x-axis is 'log Kow' (ranging from 1.9 to 3.3) and the y-axis is 'EC3, S, M, W, N' (Positive/Negative). Four data points are plotted, all in the negative region. A callout box with the number '1' points to the 'Accept prediction' button (marked with a green checkmark) at the bottom right of the plot area.

Now we can accept the prediction by click on **Accept prediction** (1) and to confirm this activity by the “**Yes**” button (2).

Data Gap Filling

Apply Standardized workflow

The screenshot displays the QSAR Toolbox interface. On the left, there is a 'Documents' pane with a tree view of chemical categories and a 'Data Gap Filling Settings' pane with checkboxes for 'Only endpoint relevant' and 'Only chemical relevant'. The main area shows a 'Workflow Controller' window with the following details:

- Workflow name: Consecutive subcategorization
- General task: Consecutive subcategorization
- Active task: Retrieving different analogues for profiler [Substance type] and metabolism []
- Buttons: Continue, Stop
- Show activity log:

A 'Success' dialog box is open in the center, displaying the message 'Prediction accepted successfully' and an 'OK' button. A red box highlights the dialog box, and a blue callout box with the number '2' points to the 'OK' button.

Below the dialog box, a table shows the results of the prediction. A red box highlights the first cell of the table, which contains '(25/39) M: Negative'. A blue callout box with the number '1' points to this cell.

(25/39) M: Negative	M: Negative	M: Negative	M: Positive	M: Positive	M: Positive	M: Positive	M: Positive
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The bottom of the interface shows a status bar with '(25/39)'.

The next message informs that the prediction is accepted successfully and it appears on the matrix (1). Click on “OK” (2)

Data Gap Filling

Apply Standardized workflow

The screenshot displays the QSAR Toolbox software interface. On the left, the 'Documents' pane shows a list of files, with 'Data: 9 Subcategorized: Protein binding' selected. Below it, the 'Data Gap Filling Settings' pane has 'Only endpoint relevant' and 'Only chemical relevant' checked, and 'Standardized workflows' selected under 'At this position:'. The main window is titled 'Filter endpoint tree...' and contains a 'Workflow Controller [Finished workflow]' dialog box. The dialog box has a 'Workflow name' field, a 'General task' of 'Consecutive subcategorization', and an 'Active task' of 'Retrieving different analogues for profiler [Substance type] and metabolism'. Below the task information are 'Continue' and 'Stop' buttons. A callout box with the number '2' points to the 'Close' button (represented by an 'X' icon) in the dialog box's title bar. The 'Show activity log' section is expanded, showing a detailed log of the workflow steps, including target retrieval, data collection, alert detection, and category definition. A callout box with the number '1' points to the 'Show activity log' button. In the background, a table with chemical structures and 'M: Positive' labels is visible.

The **Workflow Controller** **does not** close itself automatically. The user can expand the **activity log** (1) and to examine all performed steps during the Standardized workflow execution. After that the controller have to be closed by click on the close button (2).

Data Gap Filling Recap

The application of the SW for skin sensitization requires user activities such as:

- specification of the endpoint;
- selection of databases;
- selection of primary grouping in case no alert is identified in the target as parent and after autoxidation and skin metabolism activation;
- selection of highlighted profiling schemes for subcategorization in order to increase the confidence of the prediction;
- accepting the prediction.

Outlook

- Background
- Objectives
- Specific Aims
- Read across and analogue approach
- The exercise
- **Workflow**
 - Input
 - Data Gap Filling
 - **Report**

Report Overview

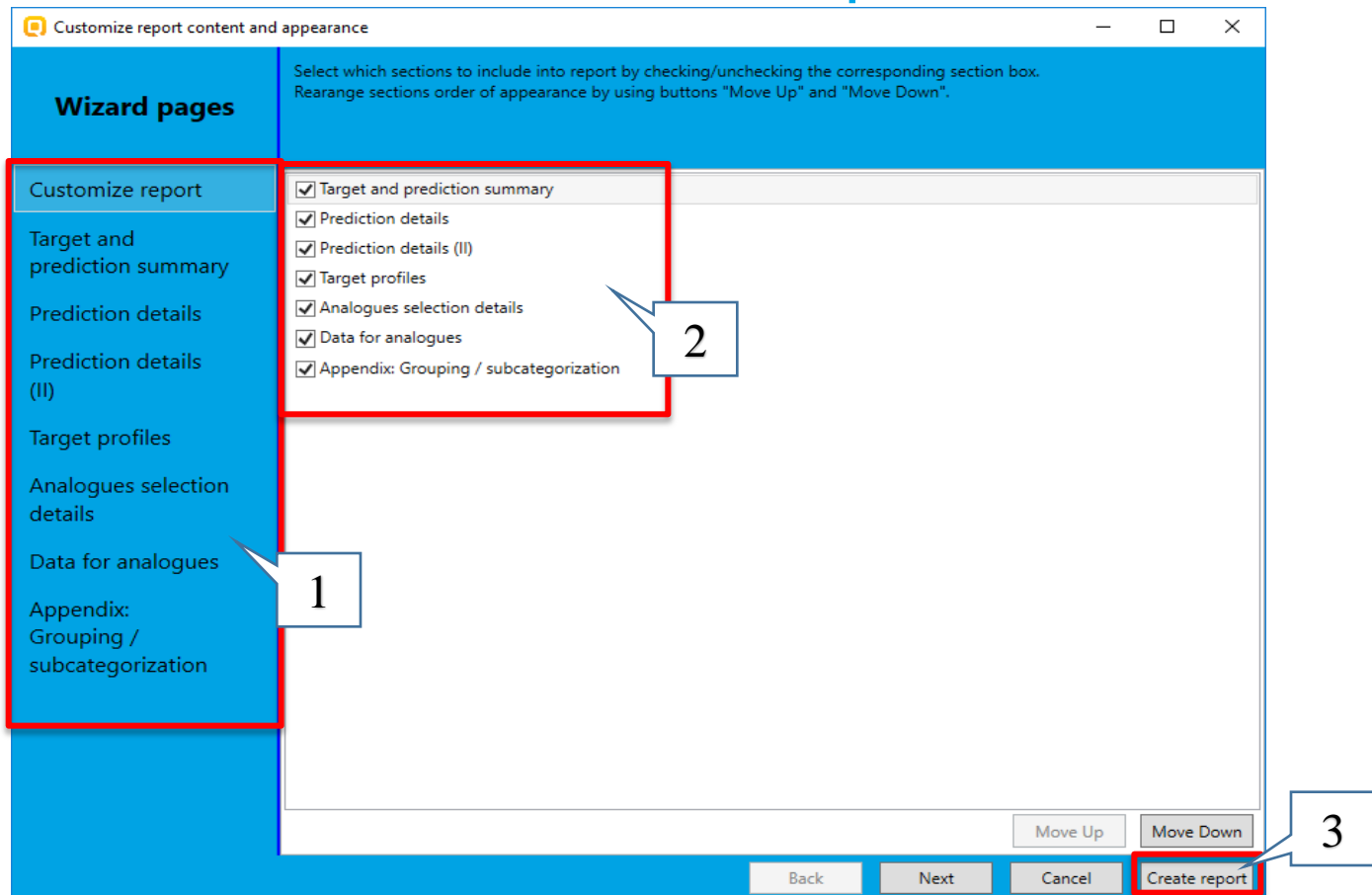
- Report module could generate report on any of predictions performed with the Toolbox.
- Report module contains predefined report template which users can customized.
- Two type of report files are generated:
 - *Prediction report* – containing information for the target
 - *Data matrix* – containing information for the analogues used for the prediction
 - *Category report* – containing information for the analogues in the category
 - *QMRF report* – containing information for the applied QSAR model.

Report Generation report

The screenshot shows the QSAR Toolbox software interface. The top navigation bar includes icons for Input, Profiling, Data, Category definition, Data Gap Filling, and Report. The 'Report' icon is highlighted with a callout box labeled '1'. On the left sidebar, the 'Prediction' icon is highlighted with a callout box labeled '3'. A 'Create prediction report' dialog box is open, providing instructions on how to generate a report. The main workspace displays a 'Filter endpoint tree...' on the left, a table of chemical structures in the center, and a prediction table on the right. The prediction table has 10 columns and 10 rows. The first row is highlighted in blue, and the first cell contains 'M: Negative' and 'R: Negative', with a callout box labeled '2' pointing to it. The rest of the cells in the first row are highlighted in yellow. The prediction table also includes a 'Discrete chemical' checkbox at the bottom.

1. Go to the **Report** section; 2. Click on the cell with the prediction; 3. Click on **Prediction**

Report Generation report



The user can customize the report content (1) and appearance (2). Generation of the reports happens by click on the **Create report** button (3).

Report Wizard pages

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

Report

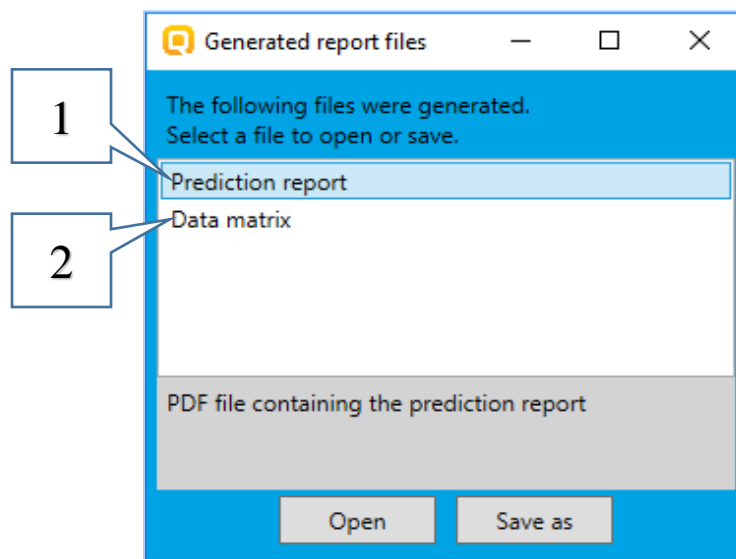
Wizard pages

- **Analogues selection details** – This section illustrates how analogues were selected. It displays selected databases, category boundaries and applicability domain.
- **Data for analogues** – This section provides details information about the analogues used for obtaining the prediction including parameters, profilers and experimental data. Additional data, available for the used analogues into Toolbox, could be also included by the user.
- **Appendix: Grouping / subcategorization** – This section includes the categories used for primary categorization as well as the categories and metadata removed during the subcategorization automatically populated by the system.

Report Generation report

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

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



Report

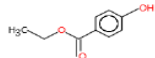
Generated report files

Prediction of EC3, S M W N for Ethylparaben

1 / 9

QSAR Toolbox prediction for single chemical

Date: 25 Jul 2017
 Author(s):
 Contact details:

Target information		
Structural information SMILES: <chem>CCOC(=O)c1ccc(O)cc1</chem> Structure 	Numerical identifiers EC#: N/A CAS#: 120-47-8 Other: N/A	Chemical names 4-Hydroxy-benzoic acid ethyl ester 4-hydroxybenzoic acid ethyl ester 4-hydroxybenzoic acid, ethyl ester

Prediction summary
Predicted endpoint: EC3, S M W N; No effect specified; No species specified; No duration specified; No guideline specified Predicted value: Negative Unit/scale: Skin sensitisation II (ECETOC) Data gap filling method: Read-across analysis Summary: <i>manually editable field</i> Not provided by the user

Using of a standardized workflow for predicting of skin sensitization potential is noted in the *Prediction report*.

Report

Generated report files

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O		
1			Target chemical		Neighbour #1		Neighbour #2		Neighbour #3								
2	Substance identity																
3	Structure																
4	CAS number		120-47-8		94-13-3		99-76-3		94-26-8								
5	Chemical name		Ethylparaben		Propylparaben		Methylparaben		Butylparaben								
6	Other identifier																
7	SMILES		CCOC(=O)c1ccc(O)cc1		CCCC(=O)c1ccc(O)cc1		COC(=O)c1ccc(O)cc1		CCCCOC(=O)c1ccc(O)cc1								
8	Parameters		unit														
9	Parameters		unit														
10	Parameters		unit														
11	Profilers																
12	Profiles used for grouping/subcategorization																
13	Organic functional groups, Norbert Haider (checkmol) (primary grouping)		Hydroxy compound; Phenol; Carboxylic acid derivative; Carboxylic acid ester; Aromatic compound		Hydroxy compound; Phenol; Carboxylic acid derivative; Carboxylic acid ester; Aromatic compound		Hydroxy compound; Phenol; Carboxylic acid derivative; Carboxylic acid ester; Aromatic compound		Hydroxy compound; Phenol; Carboxylic acid derivative; Carboxylic acid ester; Aromatic compound								
14	Protein binding alerts for skin sensitization by		No alert found		No alert found		No alert found		No alert found								
15	Organic functional groups (US EPA) (subcategorization)		Aliphatic Carbon [CH]; Aliphatic Carbon [-CH2-]; Aliphatic Carbon [-CH3]; Aromatic Carbon [C]; Carbonyl, one aromatic attach [-C(=O)-]; Ester, aliphatic attach [-C(=O)O]; Hydroxy, aromatic attach [-OH]; Miscellaneous sulfide (=S) or oxide (=O); Olefinic carbon [=CH- or =C<]; Oxygen, one aromatic attach [-O-]		Aliphatic Carbon [CH]; Aliphatic Carbon [-CH2-]; Aliphatic Carbon [-CH3]; Aromatic Carbon [C]; Carbonyl, one aromatic attach [-C(=O)-]; Ester, aliphatic attach [-C(=O)O]; Hydroxy, aromatic attach [-OH]; Miscellaneous sulfide (=S) or oxide (=O); Olefinic carbon [=CH- or =C<]; Oxygen, one aromatic attach [-O-]		Aliphatic Carbon [CH]; Aliphatic Carbon [-CH2-]; Aliphatic Carbon [-CH3]; Aromatic Carbon [C]; Carbonyl, one aromatic attach [-C(=O)-]; Ester, aliphatic attach [-C(=O)O]; Hydroxy, aromatic attach [-OH]; Miscellaneous sulfide (=S) or oxide (=O); Olefinic carbon [=CH- or =C<]; Oxygen, one aromatic attach [-O-]		Aliphatic Carbon [CH]; Aliphatic Carbon [-CH2-]; Aliphatic Carbon [-CH3]; Aromatic Carbon [C]; Carbonyl, one aromatic attach [-C(=O)-]; Ester, aliphatic attach [-C(=O)O]; Hydroxy, aromatic attach [-OH]; Miscellaneous sulfide (=S) or oxide (=O); Olefinic carbon [=CH- or =C<]; Oxygen, one aromatic attach [-O-]		Aliphatic Carbon [CH]; Aliphatic Carbon [-CH2-]; Aliphatic Carbon [-CH3]; Aromatic Carbon [C]; Carbonyl, one aromatic attach [-C(=O)-]; Ester, aliphatic attach [-C(=O)O]; Hydroxy, aromatic attach [-OH]; Miscellaneous sulfide (=S) or oxide (=O); Olefinic carbon [=CH- or =C<]; Oxygen, one aromatic attach [-O-]						

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.

Congratulation

- You have completed the tutorial on the standardized workflow for skin sensitization data gap filling.
- You have now been introduced to the consecutive steps of the standardized workflow of the QSAR Toolbox and the rationale behind each step.
- Note proficiency comes with practice.