QSAR TOOLBOX

The OECD QSAR Toolbox for Grouping Chemicals into Categories

OECD QSAR Toolbox v.4.2

Category elements for assessing category consistency

Outlook

- **Background**
- Objectives
- Aim
- Category consistency
- Examples

Background

- This is a step-by-step presentation designed to introduce to the user the category elements applicable for assessing the category consistency

- Further to illustrate some simple examples of assessing category consistency targeting Fate and Human toxicity endpoints

Outlook

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Objectives

This presentation demonstrates a number of functionalities of the Toolbox:

- Including category elements in the process of category consistency assessment.

- Generation of the category report including category consistency elements.

Outlook

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Aim

- To introduce and make the user familiar with:
  - the similarity elements (physicochemical parameters, profilers) used in category consistency assessment;
  - the default settings of category consistency elements for reporting

Outlook

- Background
- Objectives
- Aim
- Category consistency
  - **Overview**
  - Adopted concept
  - Category consistency elements
  - Implementation in Toolbox
- Examples

Overview
What is a category ?

- Based on REACH a "Chemical category" is defined as a group of chemicals which have similar physicochemical and structural characteristics and similar mechanism of interaction with respect to a defined endpoint.

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  - Overview
  - **Adopted concept**
  - Category consistency elements
  - Implementation in Toolbox
- Examples

Adopted concept

- The read-across methodology is based on the premise that similar chemical structures (forming the category) are expected to have similar biological/toxicological action with respect to the endpoint
- Category consistency is endpoint specific;
- Category consistency check (using category elements) can be applied to:
  - a list with chemicals with defined target endpoint - there is no need of enter into the data gap filling (i.e. it could be done without accepted prediction)
  - Analogues developed during read across workflow (in the data gap filling)

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  - **Category consistency elements**
  - Implementation in Toolbox
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Category consistency elements

Three layers of information are considered important in analyzing consistency of the chemical categories:

- **Physicochemical similarity** (e.g. *MW, VP, logKow etc*.) and experimental data
- **Structural similarity** (e.g. *Organic functional groups*)
- **Mechanistic similarity** (e.g. *Protein binding alerts for skin sensitization* accounting for (a)biotic activation in case the target endpoint is skin sensitization)

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  - Category consistency elements
  - **Implementation in Toolbox**
- Examples

Category consistency elements

Implementation in Toolbox

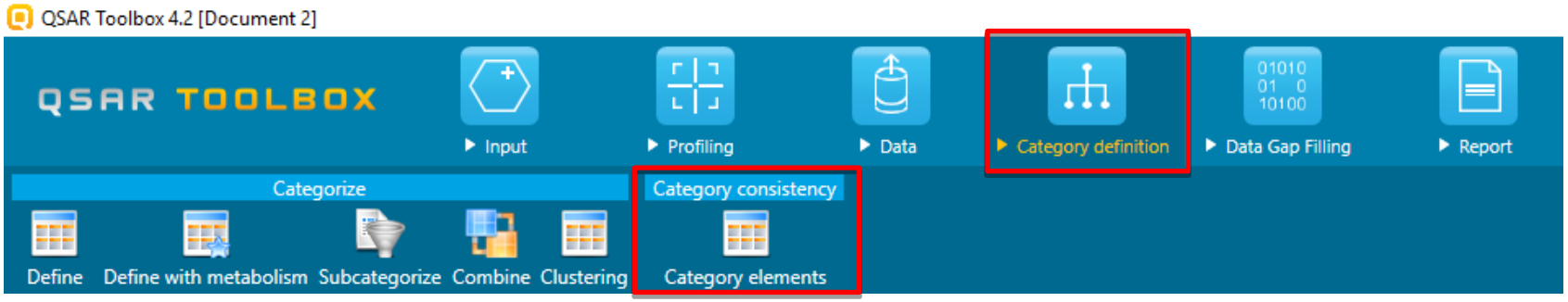
- New functionality related to Category consistency assessment has been implemented in Toolbox 4.2
- It is located in the "Category definition" module and provides default selection of category consistency elements as follows:
  - **Physicochemical similarity** – does not depend on the endpoint
    - ***Parameters* -** Boiling point, logKow, Molecular weight, Vapor pressure, Water solubility
    - ***Physico-chemical exp. data* -** Boiling point, logKow, Vapor pressure, Water solubility
  - **Structural similarity** – does not depend on the endpoint
    - Organic functional groups
    - Structure similarity
  - **Mechanistic similarity** – depends on the pre-defined target endpoint

  The profilers and metabolism simulators highlighted as "suitable" for the target endpoint are selected by default (e.g. for target endpoint Skin sensitization/LLNA/EC3 all *Protein binding alerts for skin sensitization* profilers along with the simulators for *Autoxidation* and *Skin metabolism* are selected by default)
  - **(Eco)toxicological experimental data** – depends on the pre-defined target endpoint
- Different selection of the category consistency elements than the default one is allowed

Category consistency elements

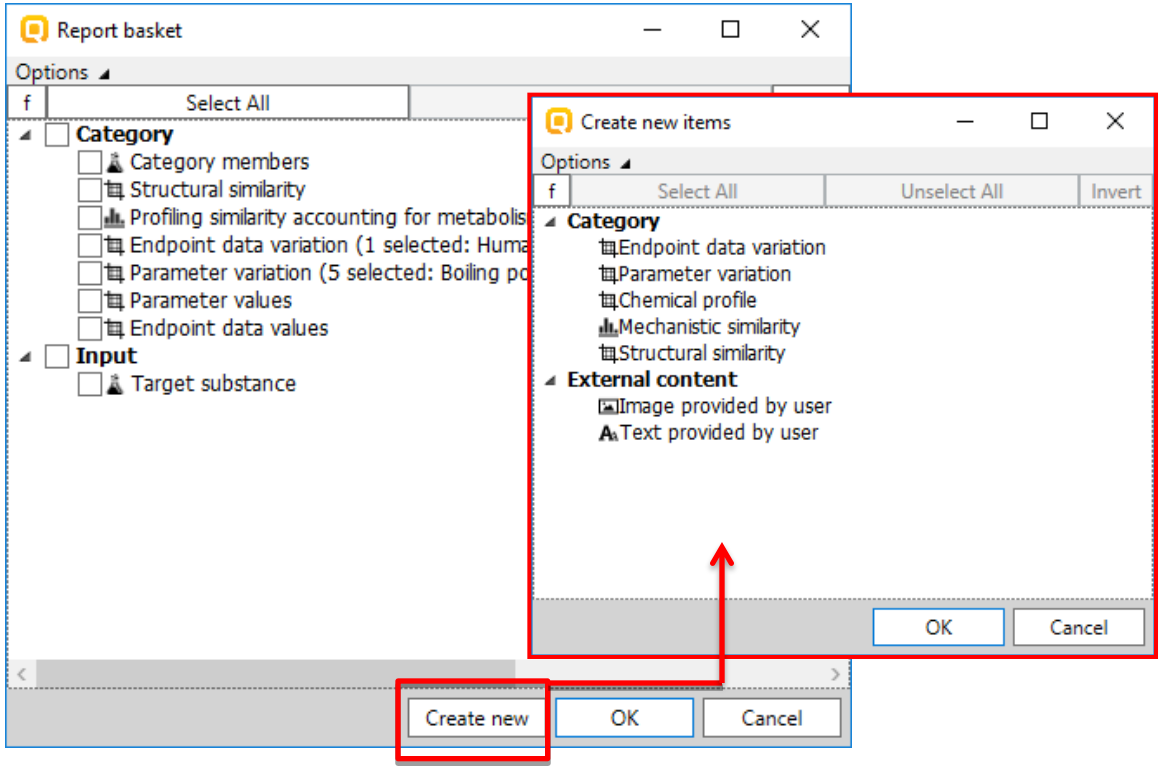
Implementation in Toolbox

- "Category consistency" is located in *Category definition* module
- It allows to filter and collect physico-chemical properties, structural similarity, profiling results accounting for metabolic activation and experimental data
- All selected category elements are automatically stored in the so-called *"Report basket"*
- Evaluation of category consistency is possible even if the target endpoint is defined



Category consistency elements

Report basket

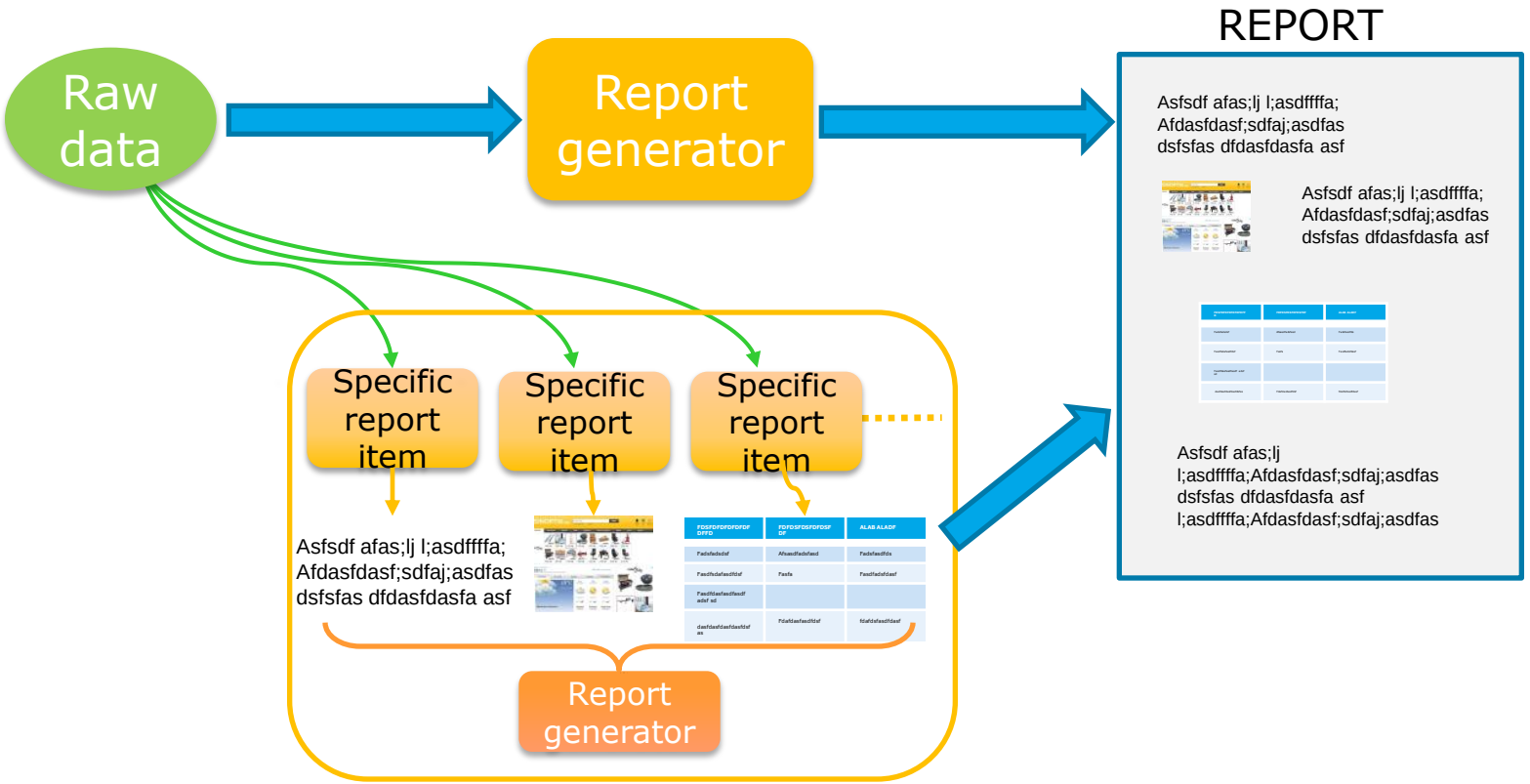


- The selected category elements are automatically stored in the so-called *"Report basket"*
- Additional report items (such as parameter variation for the closest analogues, text, pictures etc.) could be added.

Examples of the report items generated in the basket are given on the next slide

Sidebar on the Report basket

- The specific report items are collected during the workflow or from external modeling sources.
- All items are stored in the "*Report basket*" and can be used in the report to support or justify the consistency of a category.



Category consistency elements

Report items stored in Report basket (examples)

Specific report items and their description

#	Specific report item	Related to:	Options	Actions which trigger saving results in the basket	Result
1	Target information	Target chemical		Target is defined	Depiction of chemical; CAS; Names; SMILES
2	Purity/ Impurity	Target chemical; Category		Target or category members have compositions	Table with description of composition with depictions, quantities of each structure
3	Category members	Category		Category is defined or a list with structures is loaded/ created	Table with depiction; CAS; Name; SMILES of all chemicals
4	Physical chemical similarity	Category	Select 2D parameters and/or physical chemical properties	Category is defined or a list with structures is loaded/created	Table with calculated 2D parameters; Table with experimental physical chemical properties
5	Structural similarity	Category	Adjust structure similarity options	Category is defined or a list with structures is loaded/ created	Table with calculated similarity and variation of similarity with other chemicals
6	Mechanistic similarity	Category	Select metabolism and profiler; Add table; add summary chart; add individual charts	Category is defined with accounting for metabolism	Tables with generated metabolites and their profiling result; Table summarizing number of metabolites and found alerts; Graphic with distribution of alerts across metabolites
7	Common product	Metabolism		Category is defined with accounting for metabolism with map similarity option "exact" metabolite	Depiction of common compound (defined in grouping options) and used simulator
8	Alert performance	Category		Alert performance is calculated	Alert performance table
9	Reliability/ adequacy	Data	Select which metadata to be reported	Prediction is accepted	Table with used data and their metadata
....	……..	……	……..		

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Category consistency elements

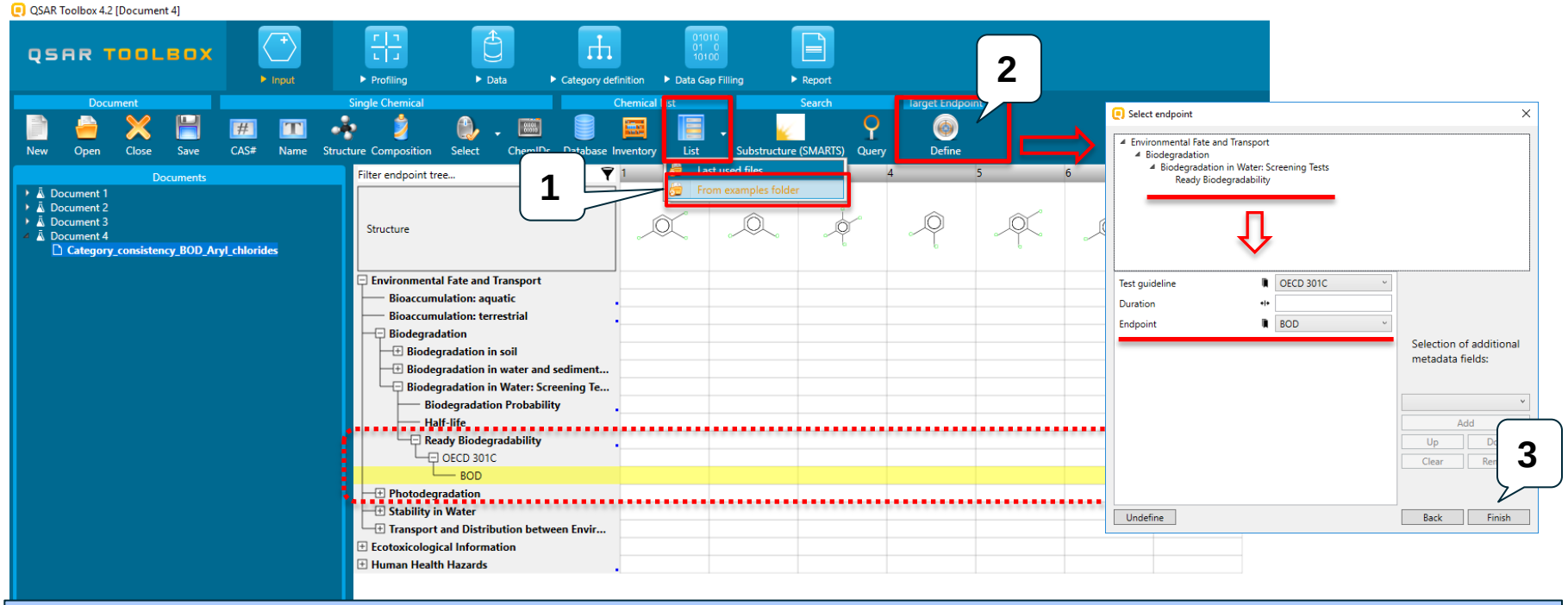
Examples

- Three examples addressing category consistency elements used in the read-across assessment of Fate and Human health endpoints will be illustrated:
  - *Fate endpoint* – BOD
  - *Ecotoxicity endpoint* – LC50
  - *Human health hazard* – skin sensitization (EC3)

Category consistency elements

Example 1 – *Fate endpoint*

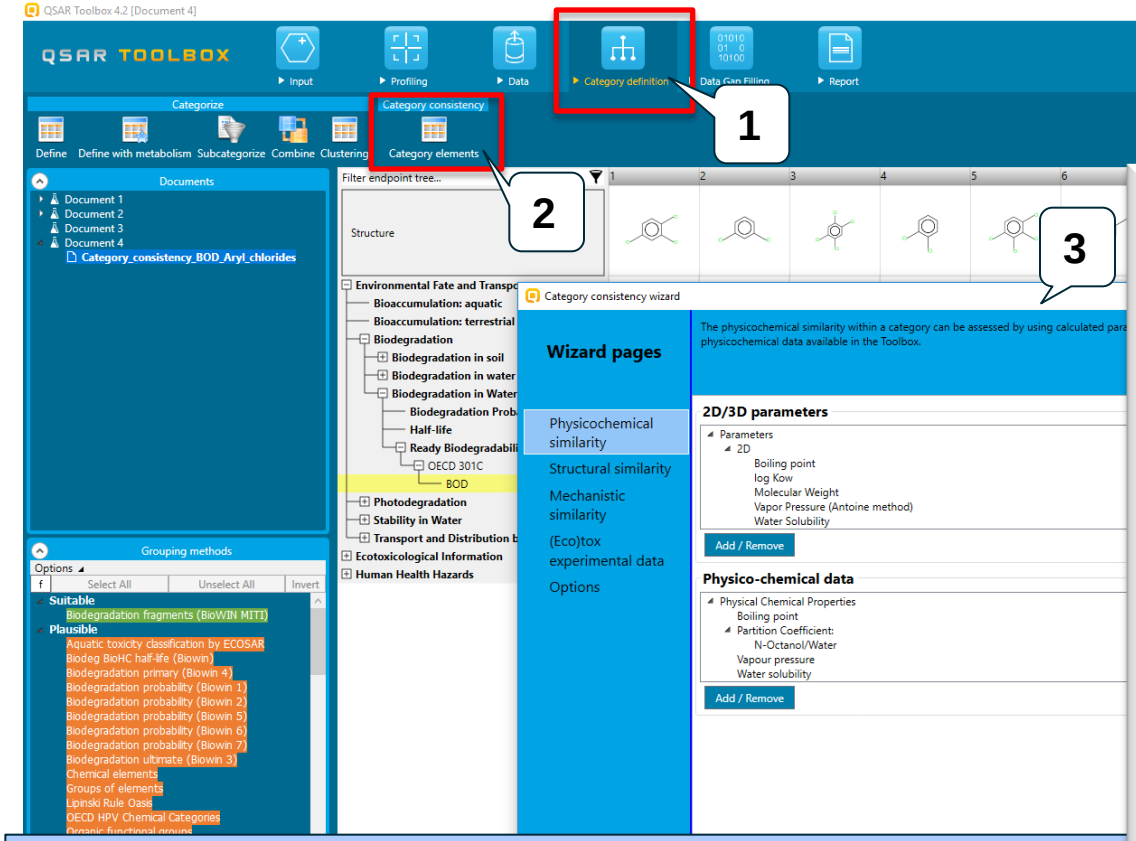
- A list of 7 aromatic halogens is submitted as a category
- The defined target endpoint is: Ready Biodegradability/BOD/OECD 301C



1. Open the list with chemicals **"Category_consistency_BOD_Aryl_chlorides.smi"** from the example folder
2. Click **Define** and select **Ready Biodegradability,** after that select Endpoint: **BOD;** Test guideline: **OECD 301C**
3. Click **Finish**

Category consistency elements

Example 1 – *Fate endpoint*



1. Go to **Category Definition** module
2. Click ***Category elements*** button
3. The **"Category consistency wizard"** appears

Wizard pages

This wizard allows selection of properties in the data matrix relevant to the assessment of the category consistency. The selection could be used for an expert judgment considerations and it is also saved for the Category report. It works by filtering the endpoint tree according to the selected properties.

The endpoint tree elements are grouped as follow:

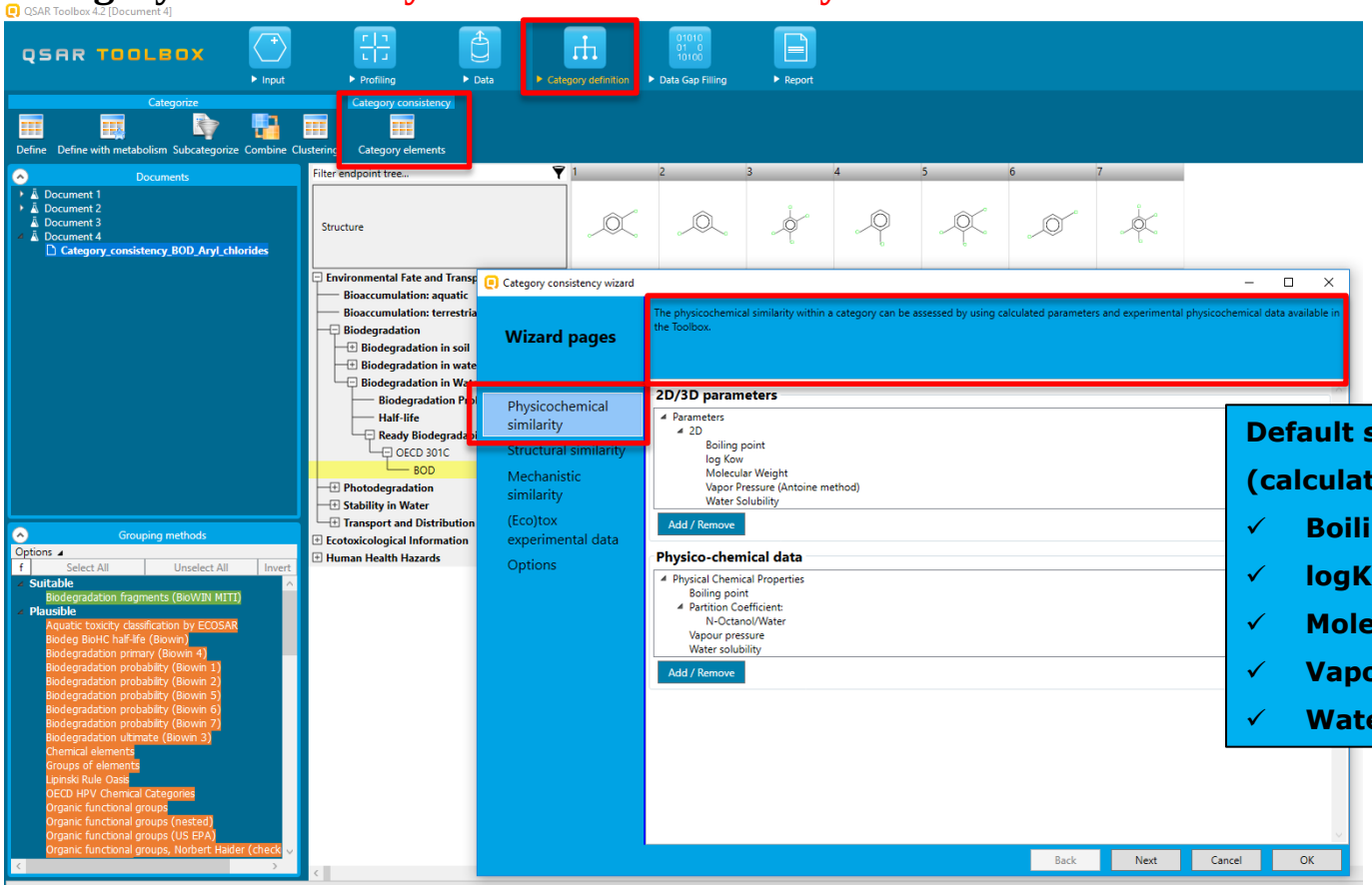
1. **Physicochemical similarity**: calculated and experimental physicochemical parameters.
2. **Structural similarity**: empirical profilers.
3. **Mechanistic similarity**: mechanistic and endpoint specific profilers, and metabolic simulators.
4. **(Eco)tox data**: experimental data from Toolbox databases

The Toolbox automatically highlights profilers and metabolic simulators relevant to the target endpoint.

Category consistency elements

Example 1 – *Fate endpoint*

Category element: Physicochemical similarity



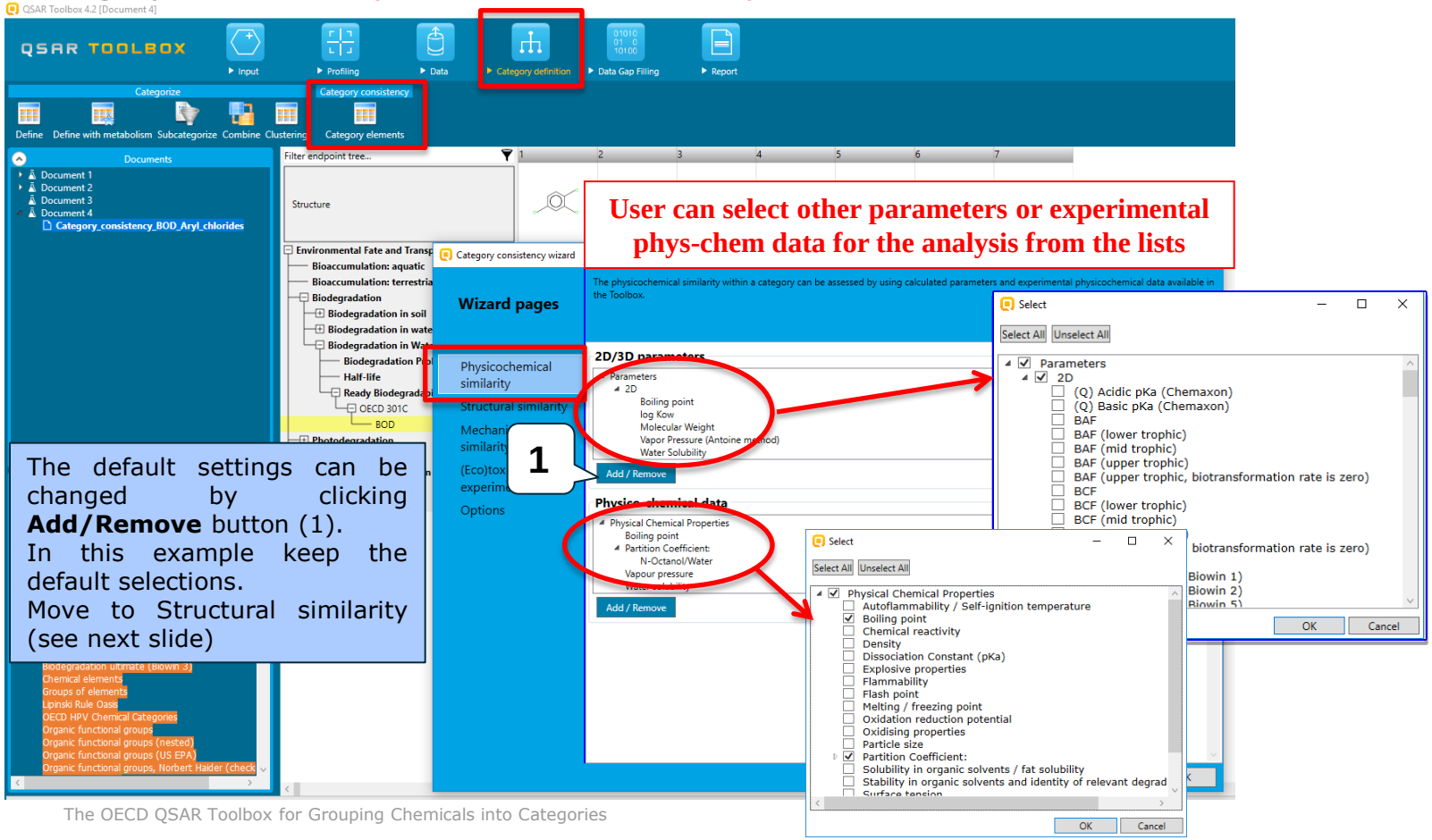
Default selection of 2D parameters (calculated values and exp. data):

- ✓ **Boiling point**
- ✓ **logKow**
- ✓ **Molecular weight**
- ✓ **Vapor pressure**
- ✓ **Water solubility**

Category consistency elements

Example 1 – *Fate endpoint*

Category element: Physicochemical similarity

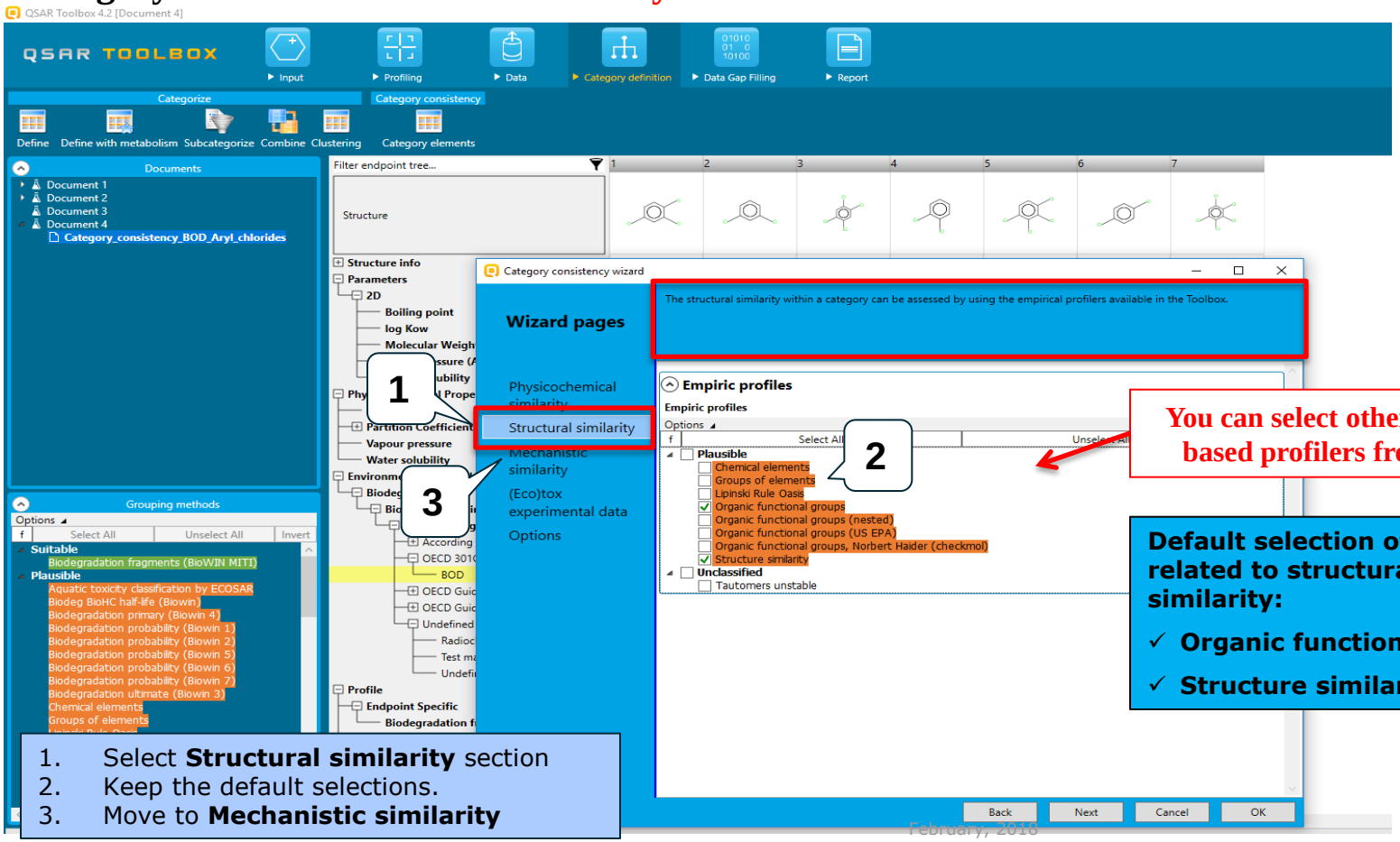


The default settings can be changed by clicking **Add/Remove** button (1).
In this example keep the default selections.
Move to Structural similarity (see next slide)

Category consistency elements

Example 1 – *Fate endpoint*

Category element: Structural similarity

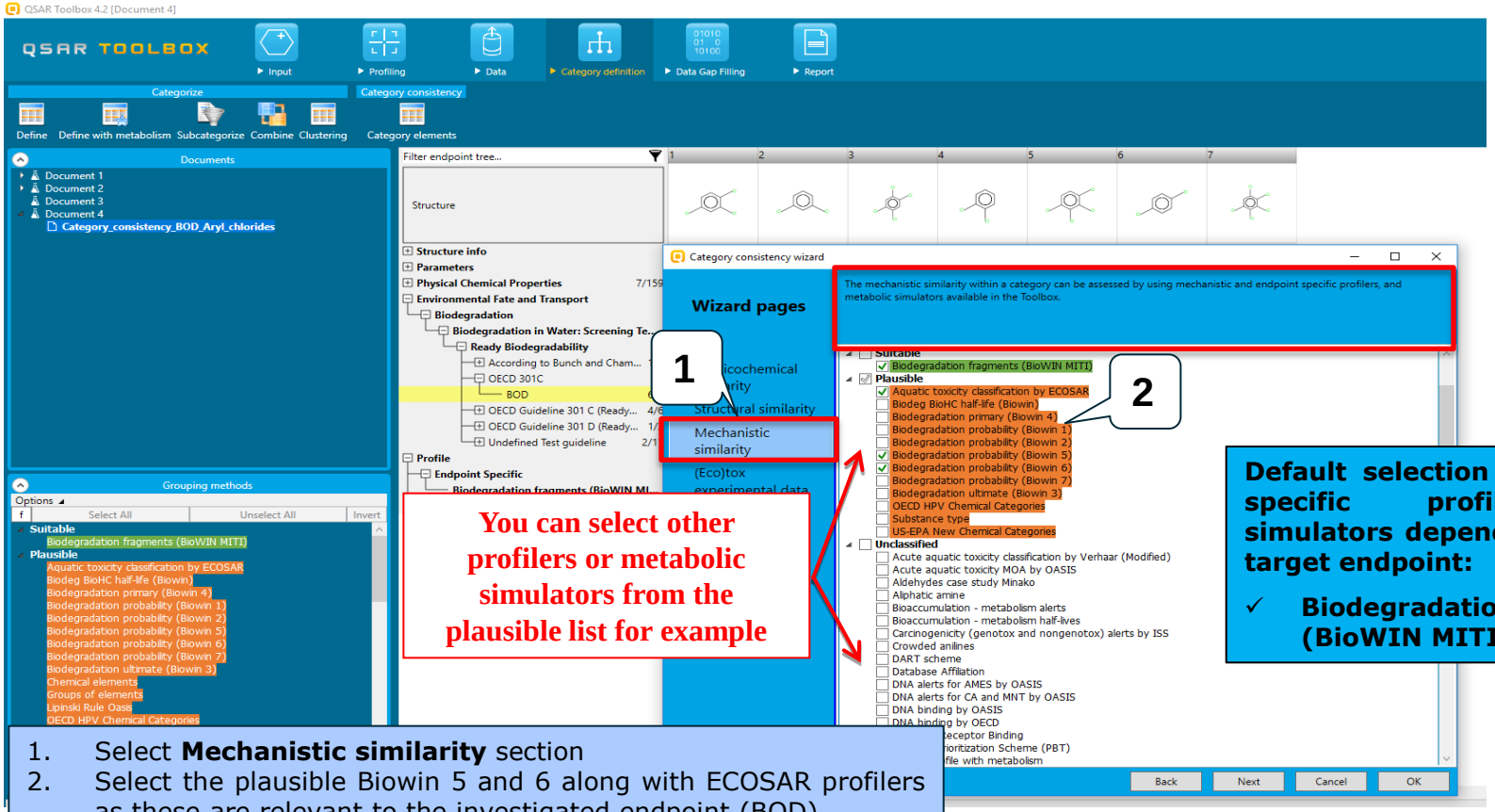


1. Select **Structural similarity** section
2. Keep the default selections.
3. Move to **Mechanistic similarity**

Category consistency elements

Example 1 – *Fate endpoint*

Category element: Mechanistic similarity

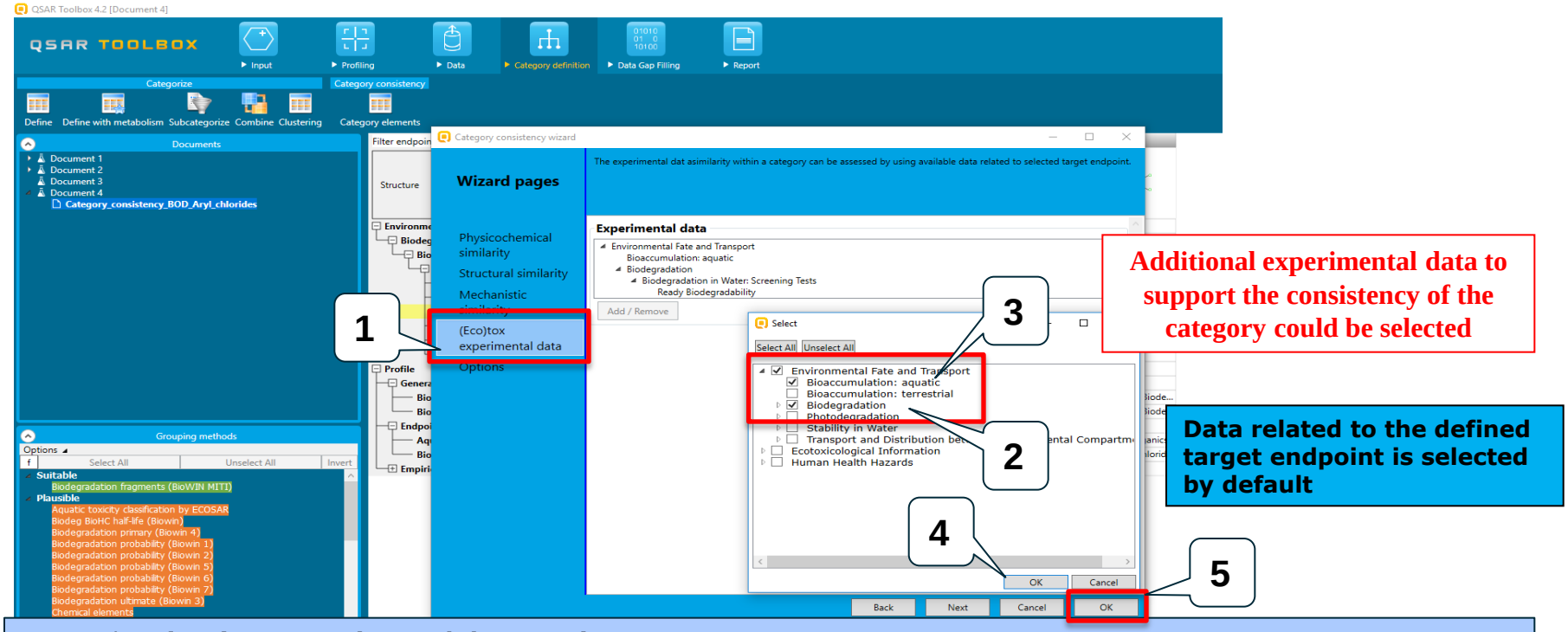


1. Select **Mechanistic similarity** section
2. Select the plausible Biowin 5 and 6 along with ECOSAR profilers as these are relevant to the investigated endpoint (BOD)

Category consistency elements

Example 1 – *Fate endpoint*

Category element: (Eco)tox experimental data

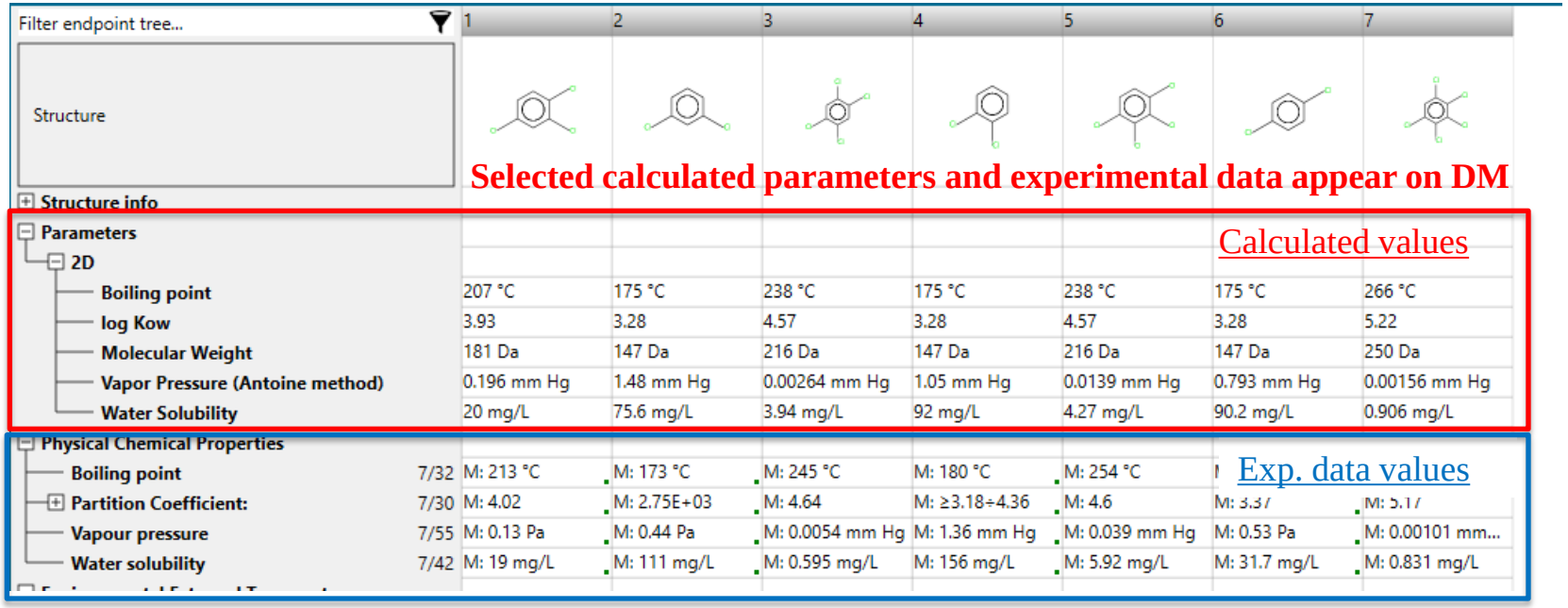


1. Select **(Eco)tox experimental data section**
2. Biodegradation is selected by default
3. In addition **select** *Bioaccumulation: aquatic* node in order to investigate BCF data for the analogues within the category
4. Click **OK** button in the Select window
5. Finally, click **OK** Category consistency wizard window in order to execute the consistency check

Category consistency elements

Example 1 – *Fate endpoint*

Selection of parameters and experimental data related to "Physicochemical similarity" (slide #23) are calculated/extracted from databases and filtered in the DM



Category consistency elements

Example 1 – *Fate endpoint*

Profiling results from the profilers related to "Structural similarity" (slide #24) appeared on DM

Filter endpoint tree...		1	2	3	4	5	6	7
Structure								
Structure info								
Parameters								
Physical Chemical Properties	7/159	M: 0.13 Pa	M: 0.44 Pa	M: 0.0054 mm Hg	M: ≥3.18÷4.36	M: 0.039 mm Hg	M: 0.53 Pa	M: 0.00101 mm...
Environmental Fate and Transport	7/28	M: 0	M: 0	M: 0 %	M: 0	M: 0 %	M: >95	M: 0 %
Profile								
Endpoint Specific								
Empiric								
Organic functional groups		Aryl Aryl halide	Aryl Aryl halide	Aromatic perhal... Aryl	Aryl Aryl halide	Aromatic perhal... Aryl	Aryl Aryl halide	Aromatic perhal... Aryl
Structure similarity		58.8÷73.7 %	31.6÷75 %	22.2÷66.7 %	42.1÷70.6 %	44.4÷76.2 %	21.1÷75 %	21.1÷76.2 %

Profiling results from the selected structure-based profilers appeared on DM

Category consistency elements

Example 1 – *Fate endpoint*

Profiling results from the profilers related to "Structural similarity" (slide #24) appeared on DM

Filter endpoint tree...		1	2	3	4	5	6	7
Structure								
Structure info								
Parameters								
Physical Chemical Properties	7/159	M: 0.13 Pa	M: 0.44 Pa	M: 0.0054 mm Hg	M: ≥3.18÷4.36	M: 0.039 mm Hg	M: 0.53 Pa	M: 0.00101 mm...
Environmental Fate and Transport	7/28	M: 0	M: 0	M: 0 %	M: 0	M: 0 %	M: >95	M: 0 %
Profile								
Endpoint Specific								
Empiric								
Organic functional groups		Aryl Aryl halide	Aryl Aryl halide	Aromatic perhal... Aryl	Aryl Aryl halide	Aromatic perhal... Aryl	Aryl Aryl halide	Aromatic perhal... Aryl
Structure similarity		58.8÷73.7 %	31.6÷75 %	22.2÷66.7 %	42.1÷70.6 %	44.4÷76.2 %	21.1÷75 %	21.1÷76.2 %

Calculated structure similarity

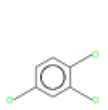
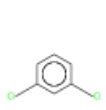
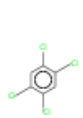
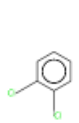
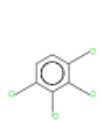
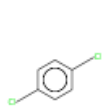
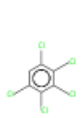
	Chemical 1	Chemical 2	Chemical 3	Chemical 4	Chemical 5	Chemical 6	Chemical 7
Chemical 1	100%	70.6 %	63.2 %	70.6 %	73.7 %	58.8 %	60 %
Chemical 2	70.6 %	100%	33.3 %	62.5 %	44.4 %	75 %	31.6 %
Chemical 3	63.2 %	33.3 %	100%	44.4 %	60 %	22.2 %	66.7 %
Chemical 4	70.6 %	62.5 %	44.4 %	100%	66.7 %	50 %	42.1 %
Chemical 5	73.7 %	44.4 %	60 %	66.7 %	100%	44.4 %	76.2 %
Chemical 6	58.8 %	75 %	22.2 %	50 %	44.4 %	100%	21.1 %
Chemical 7	60 %	31.6 %	66.7 %	42.1 %	76.2 %	21.1 %	100%

Structural similarity could be estimated by analyzing variations of similarity values between category members (analogues). The table on the left is taken from the Category report and it shows the calculated structural similarity between different members.

Category consistency elements

Example 1 – *Fate endpoint*

Profiling results from the profilers related to "Mechanistic similarity" (slide #25) appeared on DM

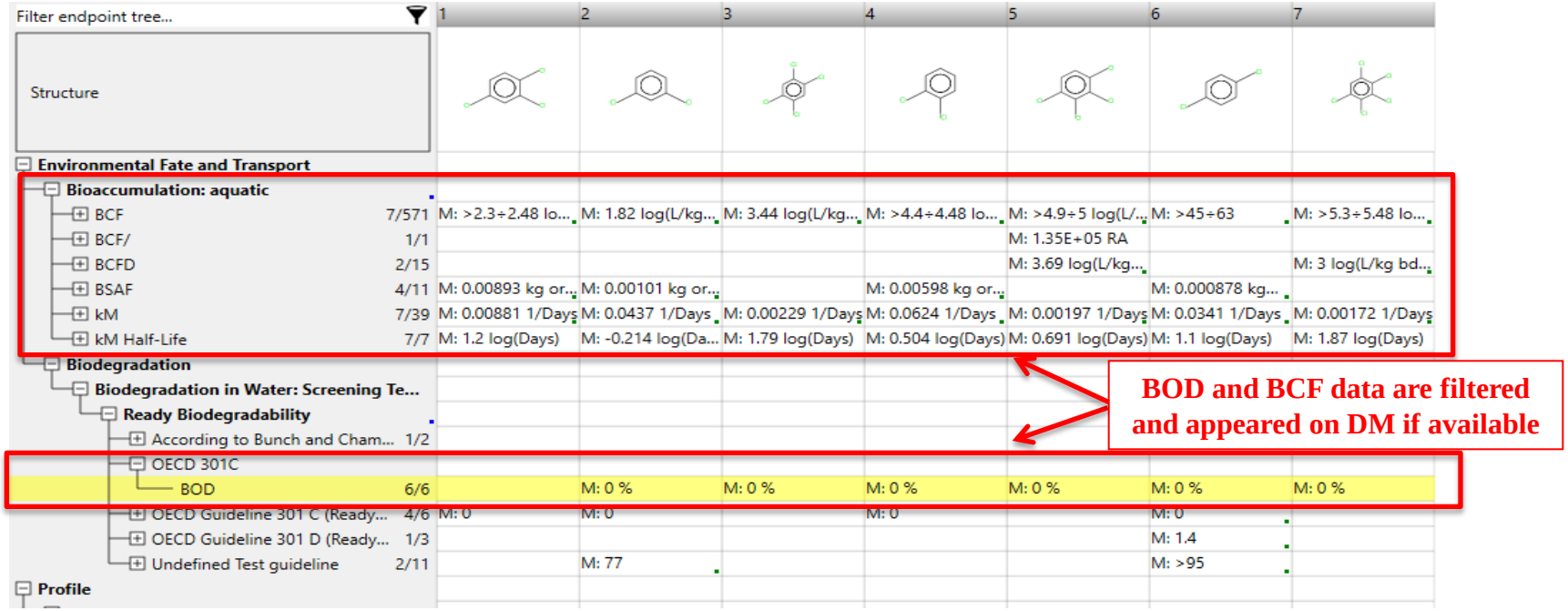
Filter endpoint tree...		1	2	3	4	5	6	7
Structure								
Structure info								
Parameters								
Physical Chemical Properties	7/159	M: 0.13 Pa	M: 0.44 Pa	M: 0.0054 mm Hg	M: ≥3.18÷4.36	M: 0.039 mm Hg	M: 0.53 Pa	M: 0.00101 mm...
Environmental Fate and Transport								
Biodegradation								
Biodegradation in Water: Screenin...	7/28	M: 0	M: 0	M: 0 %	M: 0	M: 0 %	M: >95	M: 0 %
Profile								
General Mechanistic								
Biodegradation probability (Biowin 5)		Does NOT Biode...	Does NOT Biode...	Does NOT Biode...	Does NOT Biode...	Does NOT Biode...	Does NOT Biode...	Does NOT Biode...
Biodegradation probability (Biowin 6)		Does NOT Biode...	Does NOT Biode...	Does NOT Biode...	Does NOT Biode...	Does NOT Biode...	Does NOT Biode...	Does NOT Biode...
Endpoint Specific								
Aquatic toxicity classification by ECOS...		Neutral Organics	Neutral Organics	Neutral Organics	Neutral Organics	Neutral Organics	Neutral Organics	Neutral Organics
Biodegradation fragments (BioWIN MI...		Aromatic chlorid...	Aromatic chlorid...	Aromatic chlorid...	Aromatic chlorid...	Aromatic chlorid...	Aromatic chlorid...	Aromatic chlorid...
Empiric								

All the chemicals within the category are consistent with respect to mechanism-based profilers

Category consistency elements

Example 1 – *Fate endpoint*

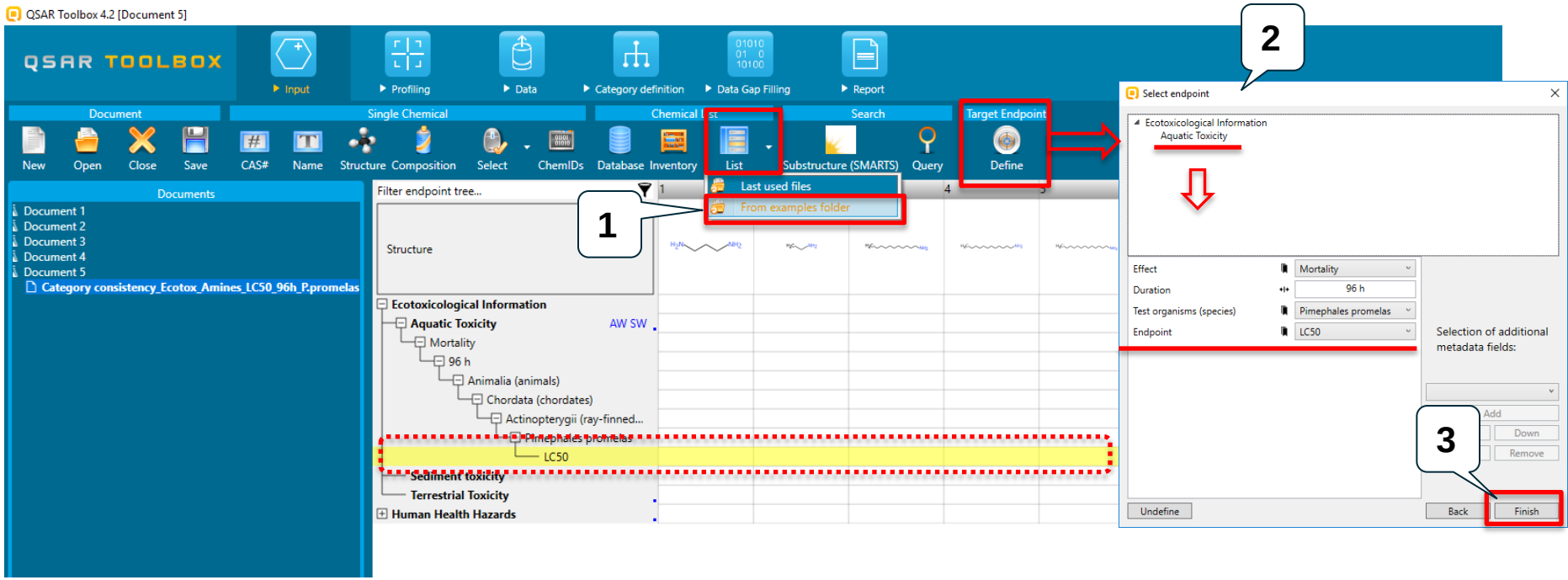
Experimental data related to the target endpoint and additionally added (slide #26) appeared on DM



Category consistency elements

Example 2 – *Ecotox endpoint*

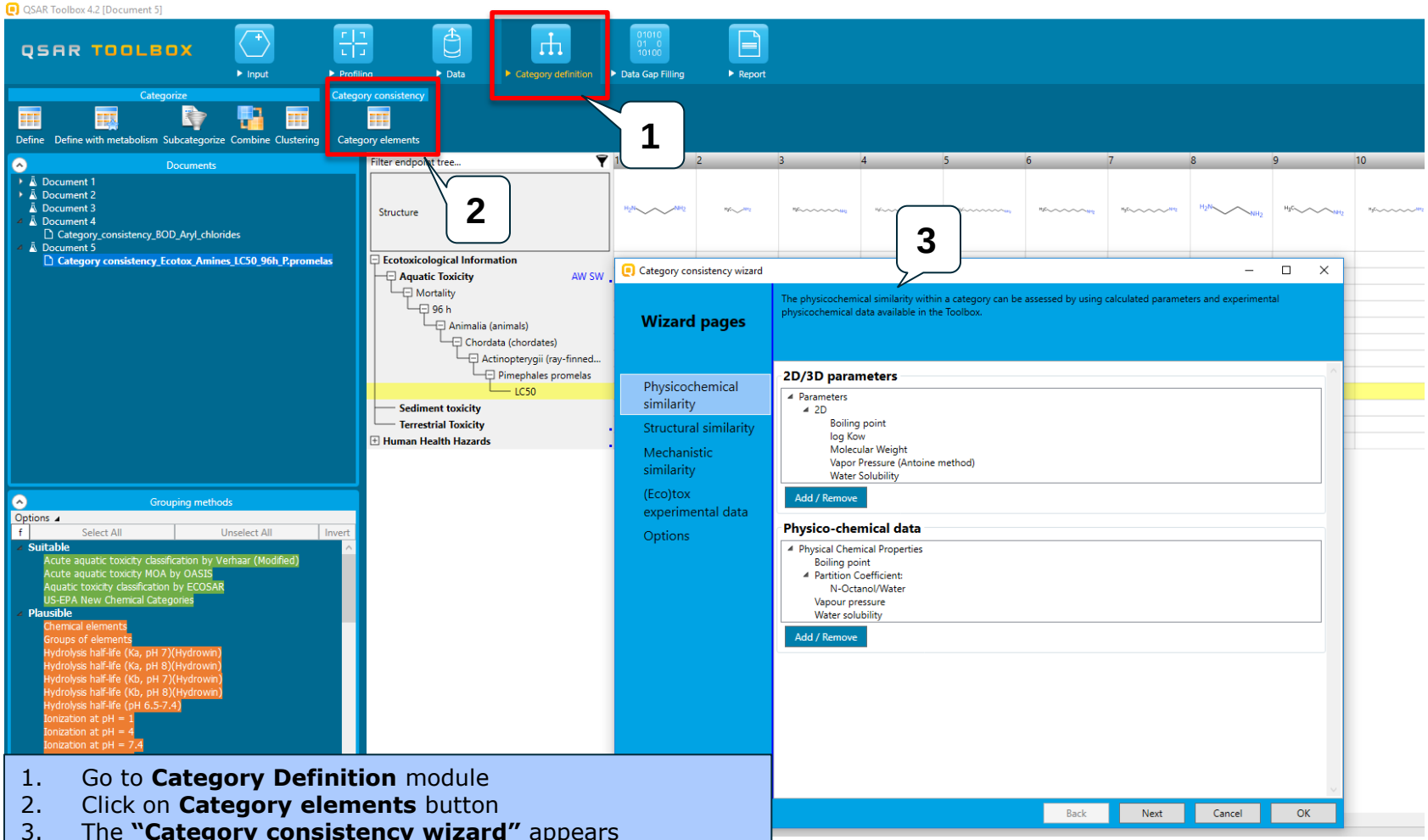
- A list of 15 Aliphatic amines is submitted as a category
- The defined target endpoint is: Aquatic toxicity/LC50/96h/P.promelas/Mortality



1. Open the list with chemicals "Category consistency_Ecotox_Amines_LC50_96h_P.promelas.smi" from the example folder
2. Click **Define** and fill in the fields of the target endpoint as shown on the snapshot
3. Click **Finish**

Category consistency elements

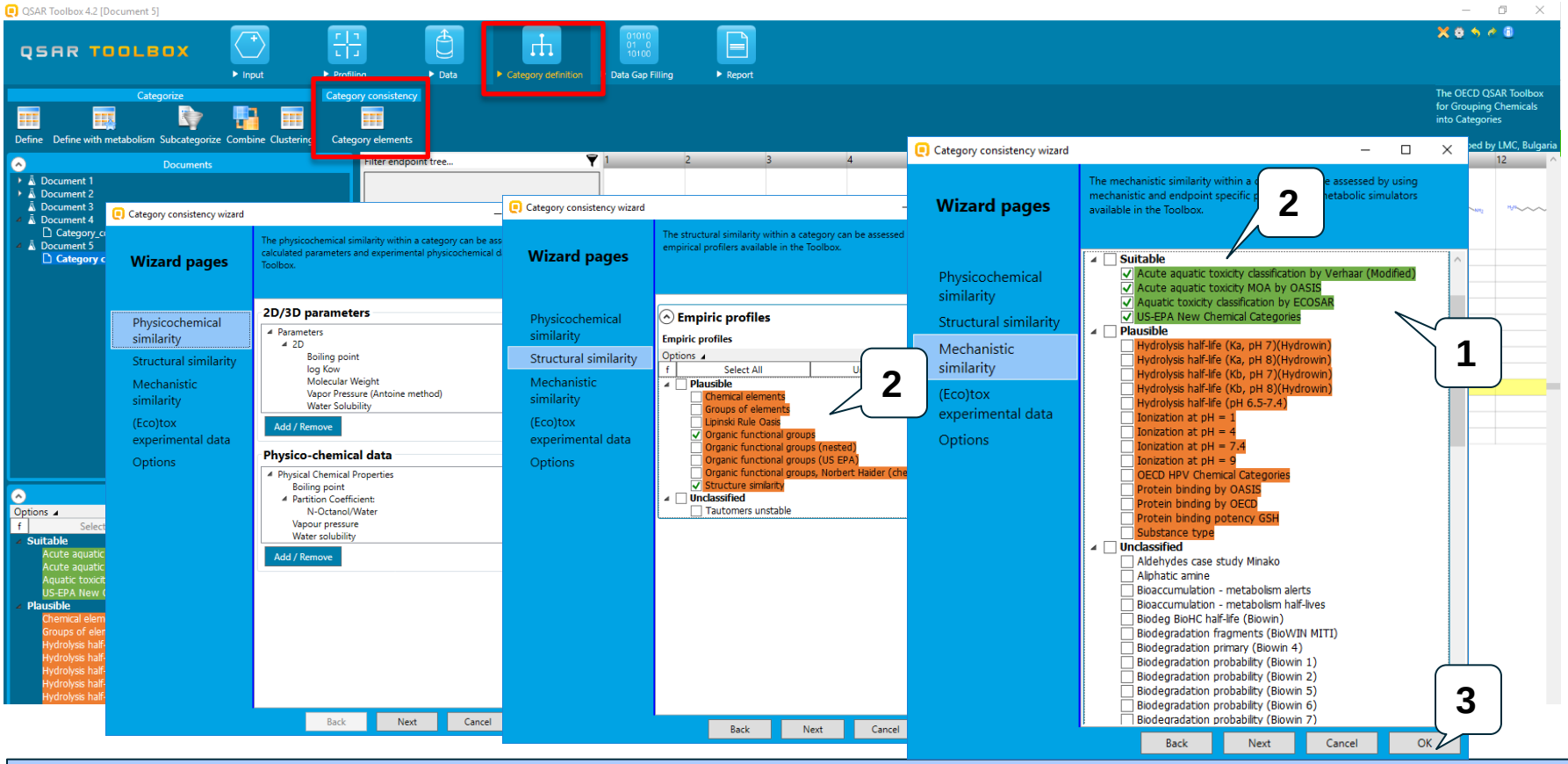
Example 2 – *Ecotox endpoint*



1. Go to **Category Definition** module
2. Click on **Category elements** button
3. The **"Category consistency wizard"** appears

Category consistency elements

Example 2 – *Ecotox endpoint*

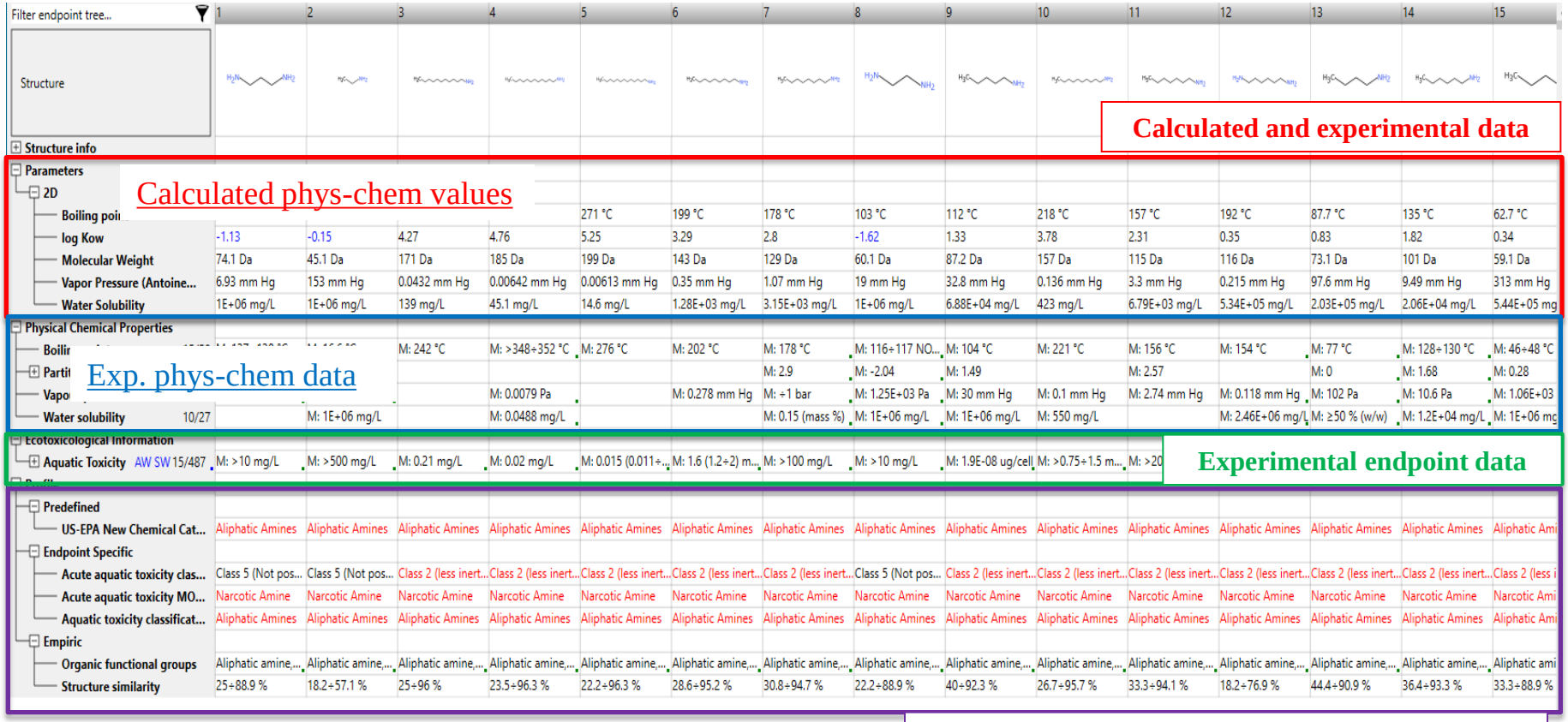


1. The only difference with the previous example is the default selection of mechanism-based profilers. The latter depends on the defined target endpoint
2. Keep the default selections of profilers and phys-chem parameters
3. Click **OK** button

Category consistency elements

Example 2 – *Ecotox endpoint*

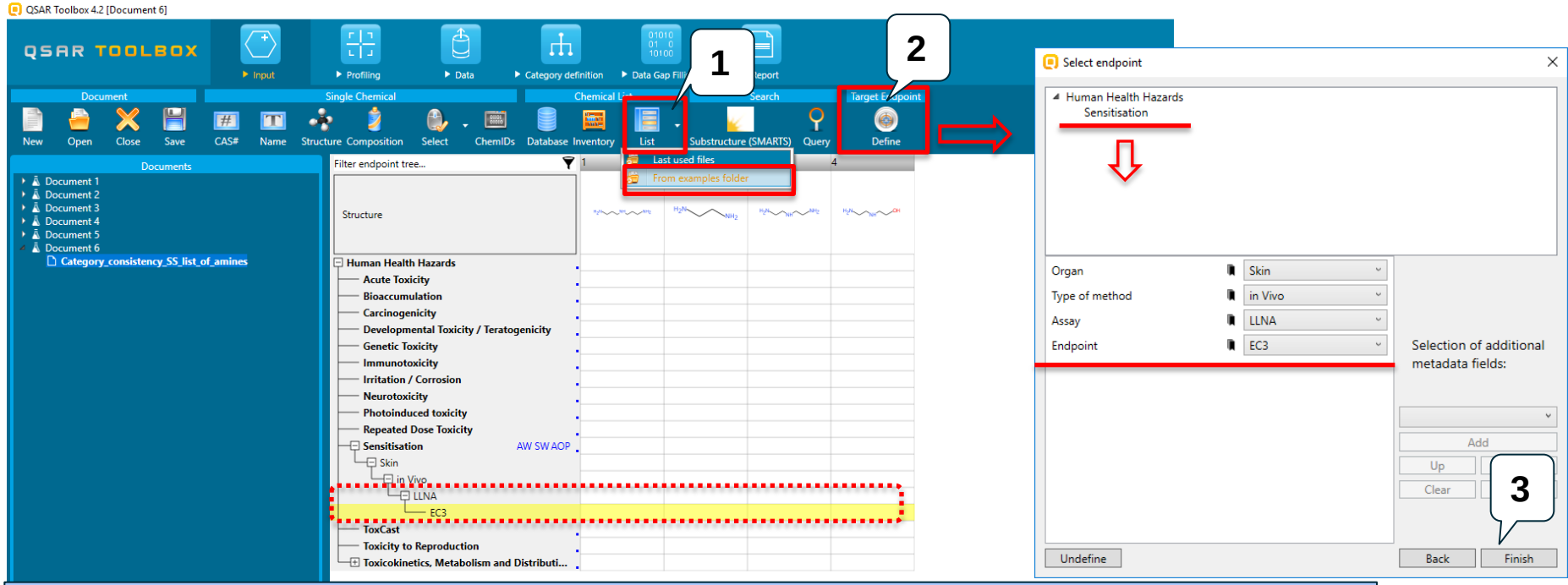
Selected data and profilers related to the specific Category elements appeared on DM



Category consistency elements

Example 3 – *Human health hazard endpoint*

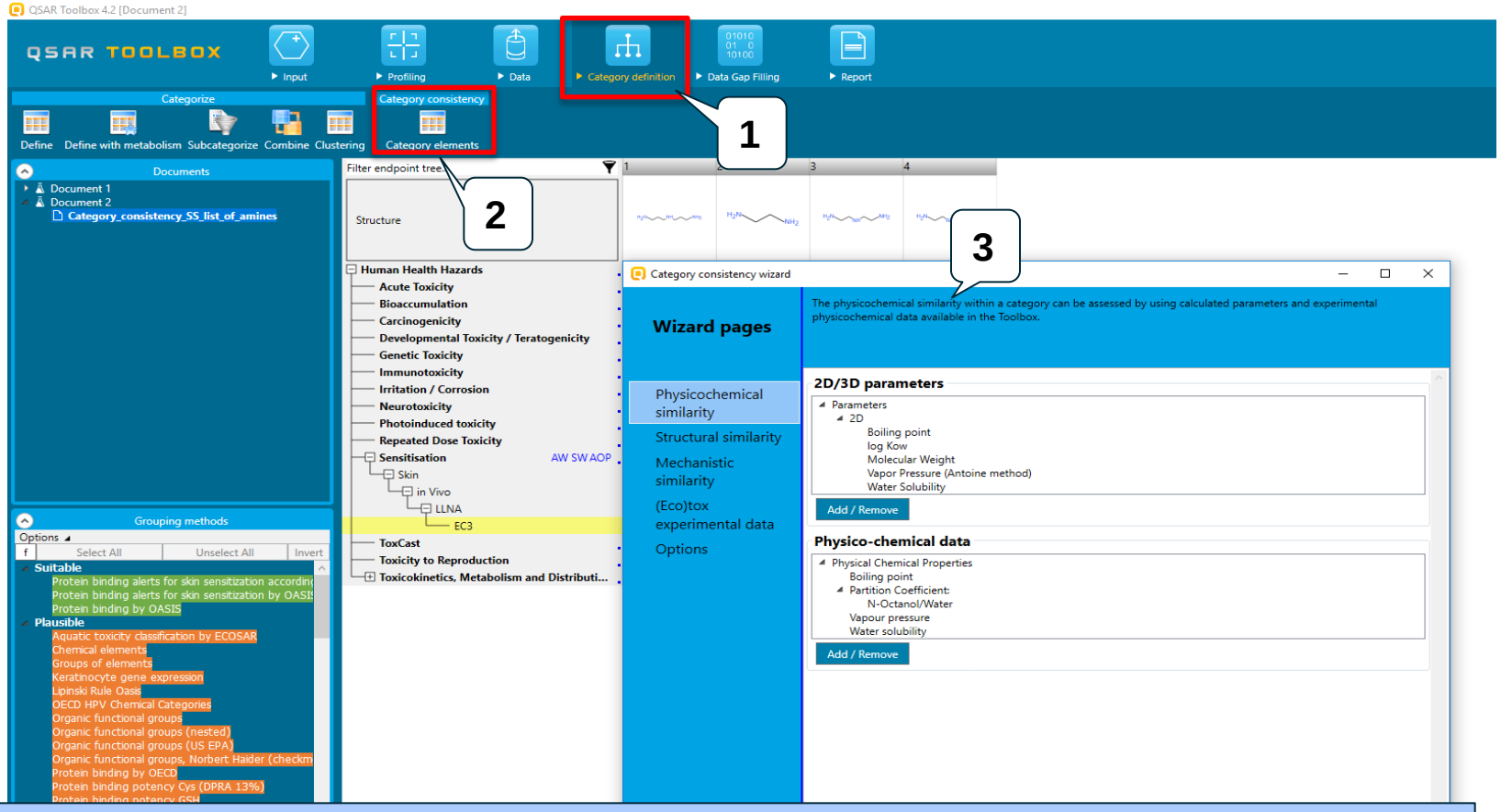
- A list of four amines is submitted as a category
- The defined target endpoint is: EC3/LLNA/Skin sensitisation



1. Open the list with 4 amines "Category_consistency_SS_list_of_amines.smi" from the example folder
2. **Define target endpoint** as shown on the snapshot
3. Click **Finish**

Category consistency elements

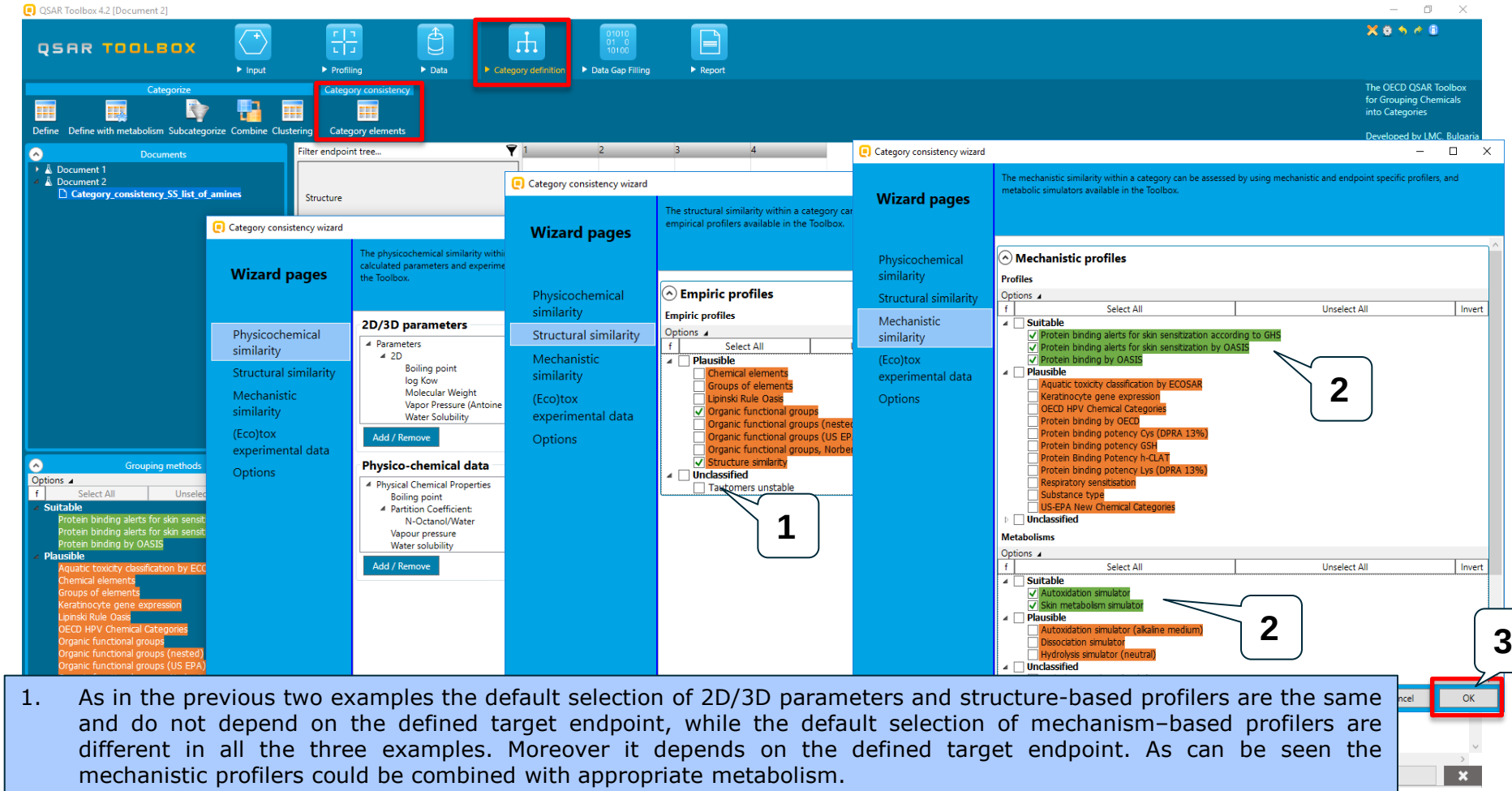
Example 3 – *Human health hazard endpoint*



1. Go to **Category Definition** module
2. Click **Category elements** button
3. The **"Category consistency wizard"** appears

Category consistency elements

Example 3 – *Human health hazard endpoint*

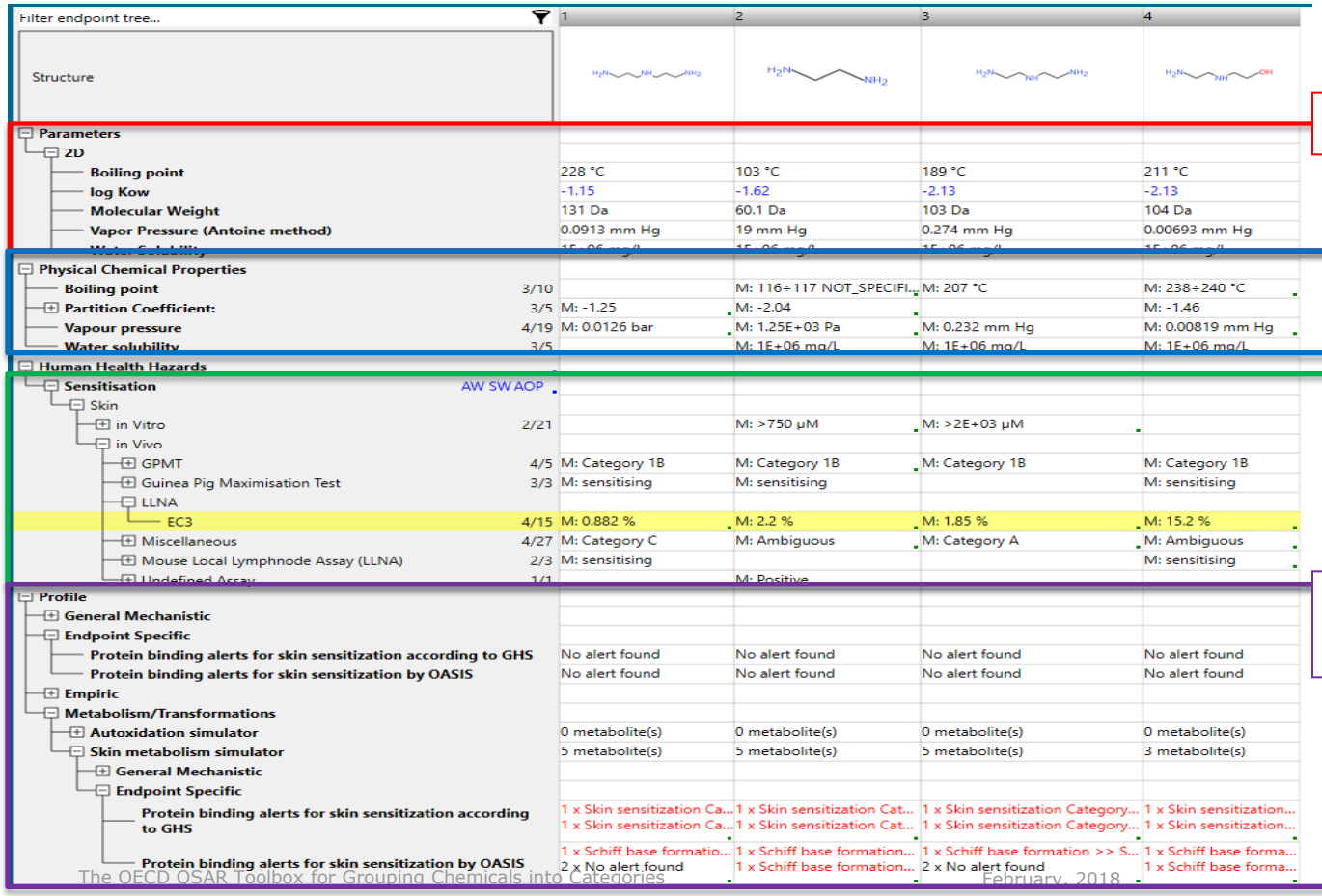


1. As in the previous two examples the default selection of 2D/3D parameters and structure-based profilers are the same and do not depend on the defined target endpoint, while the default selection of mechanism–based profilers are different in all the three examples. Moreover it depends on the defined target endpoint. As can be seen the mechanistic profilers could be combined with appropriate metabolism.
2. Keep the default selection of profilers and metabolic simulators.
3. Click **OK** button.

Category consistency elements

Example 3 – *Human health hazard endpoint*

Selected data and profilers related to the specific Category elements appeared on DM



Filter endpoint tree...		1	2	3	4
Structure					
Parameters					
2D					
Boiling point		228 °C	103 °C	189 °C	211 °C
log Kow		-1.15	-1.62	-2.13	-2.13
Molecular Weight		131 Da	60.1 Da	103 Da	104 Da
Vapor Pressure (Antoine method)		0.0913 mm Hg	19 mm Hg	0.274 mm Hg	0.00693 mm Hg
Physical Chemical Properties					
Boiling point	3/10		M: 116÷117 NOT_SPECIFI...	M: 207 °C	M: 238÷240 °C
Partition Coefficient:	3/5	M: -1.25	M: -2.04		M: -1.46
Vapour pressure	4/19	M: 0.0126 bar	M: 1.25E+03 Pa	M: 0.232 mm Hg	M: 0.00819 mm Hg
Water solubility	3/5		M: 1E+06 mg/L	M: 1E+06 mg/L	M: 1E+06 mg/L
Human Health Hazards					
Sensitisation	AW SW AOP				
Skin					
in Vitro	2/21		M: >750 µM	M: >2E+03 µM	
in Vivo					
GPMT	4/5	M: Category 1B	M: Category 1B	M: Category 1B	M: Category 1B
Guinea Pig Maximisation Test	3/3	M: sensitising	M: sensitising		M: sensitising
LLNA					
EC3	4/15	M: 0.882 %	M: 2.2 %	M: 1.85 %	M: 15.2 %
Miscellaneous	4/27	M: Category C	M: Ambiguous	M: Category A	M: Ambiguous
Mouse Local Lymphnode Assay (LLNA)	2/3	M: sensitising			M: sensitising
Undefined Assay	1/1		M: Positive		
Profile					
General Mechanistic					
Endpoint Specific					
Protein binding alerts for skin sensitization according to GHS		No alert found	No alert found	No alert found	No alert found
Protein binding alerts for skin sensitization by OASIS		No alert found	No alert found	No alert found	No alert found
Empiric					
Metabolism/Transformations					
Autoxidation simulator		0 metabolite(s)	0 metabolite(s)	0 metabolite(s)	0 metabolite(s)
Skin metabolism simulator		5 metabolite(s)	5 metabolite(s)	5 metabolite(s)	3 metabolite(s)
General Mechanistic					
Endpoint Specific					
Protein binding alerts for skin sensitization according to GHS		1 x Skin sensitization Ca... 1 x Skin sensitization Ca...	1 x Skin sensitization Cat... 1 x Skin sensitization Cat...	1 x Skin sensitization Category... 1 x Skin sensitization Category...	1 x Skin sensitization... 1 x Skin sensitization...
Protein binding alerts for skin sensitization by OASIS		1 x Schiff base formatio... 2 x No alert found	1 x Schiff base formation... 1 x Schiff base formation...	1 x Schiff base formation >> S... 2 x No alert found	1 x Schiff base forma... 1 x Schiff base forma...

Calculated phys-chem values

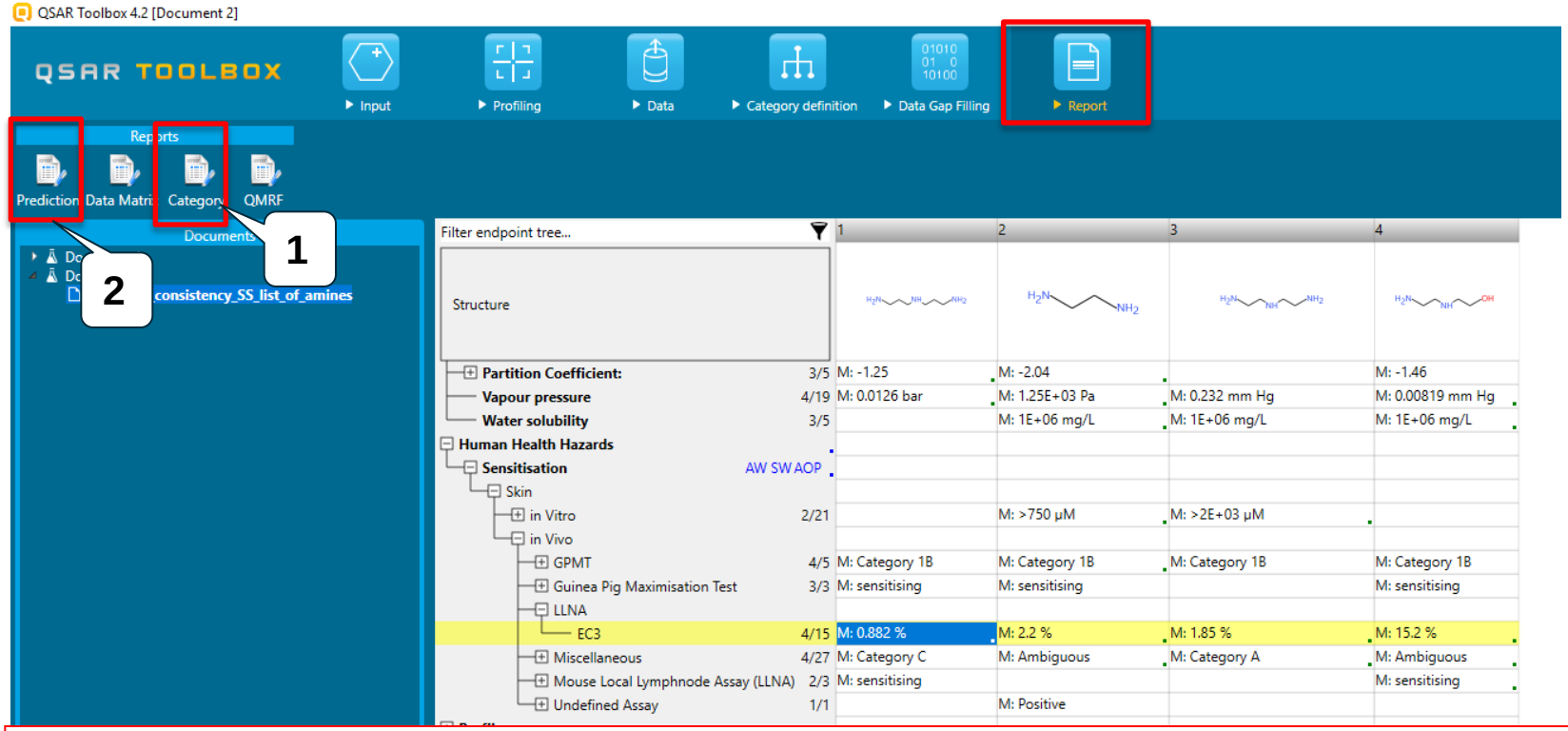
Exp. phys-chem data

Experimental endpoint data

Mechanistic and structure-based profiling results

Category consistency elements

Report



A report can be obtained for

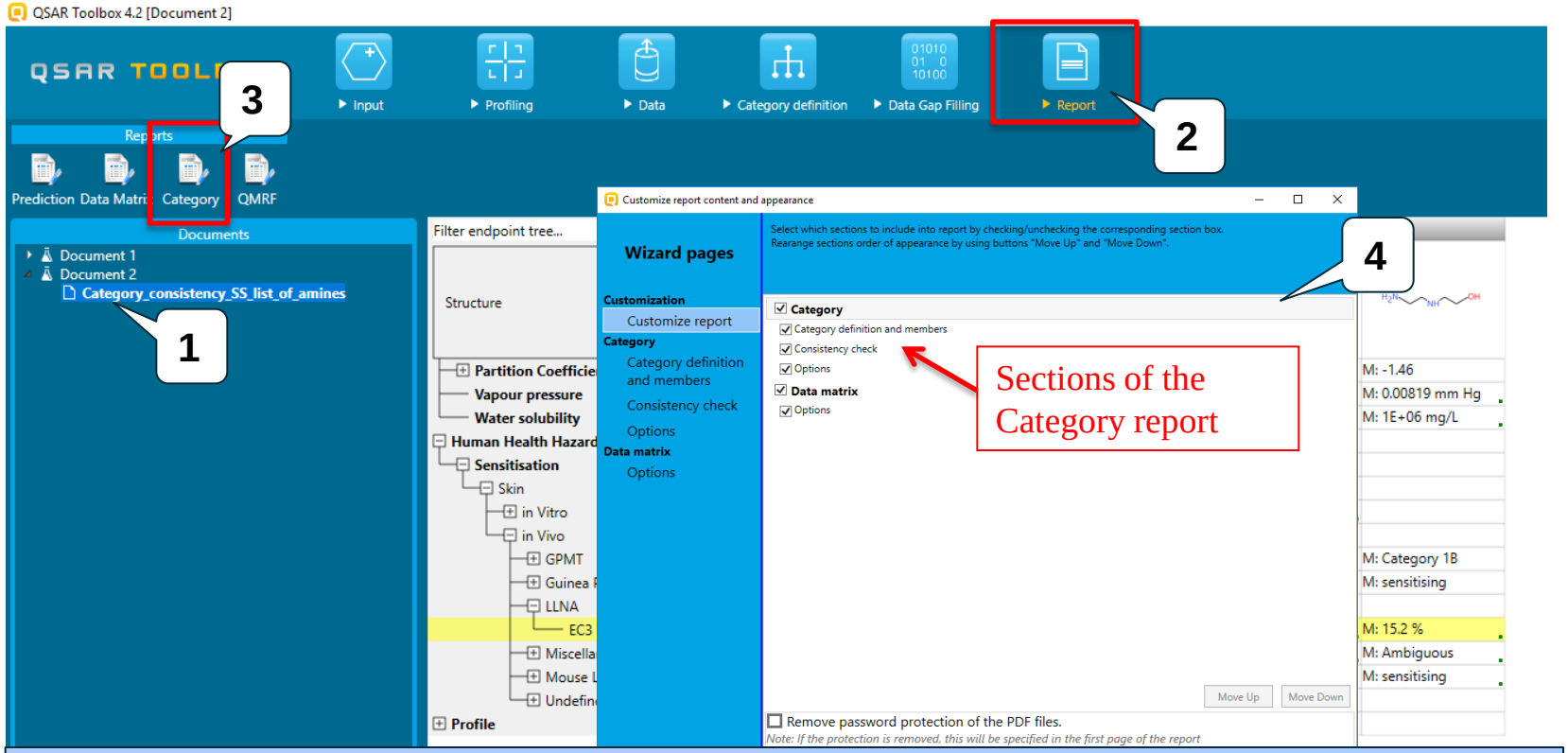
- A category (list of chemicals) with defined target endpoint without entering the data gap filling (1) OR
- The analogues grouped during the read-across workflow (in the data gap filling) (2)

A report for a list of chemicals without entering data gap filling will be illustrated in the next few slides

Category consistency elements

Report

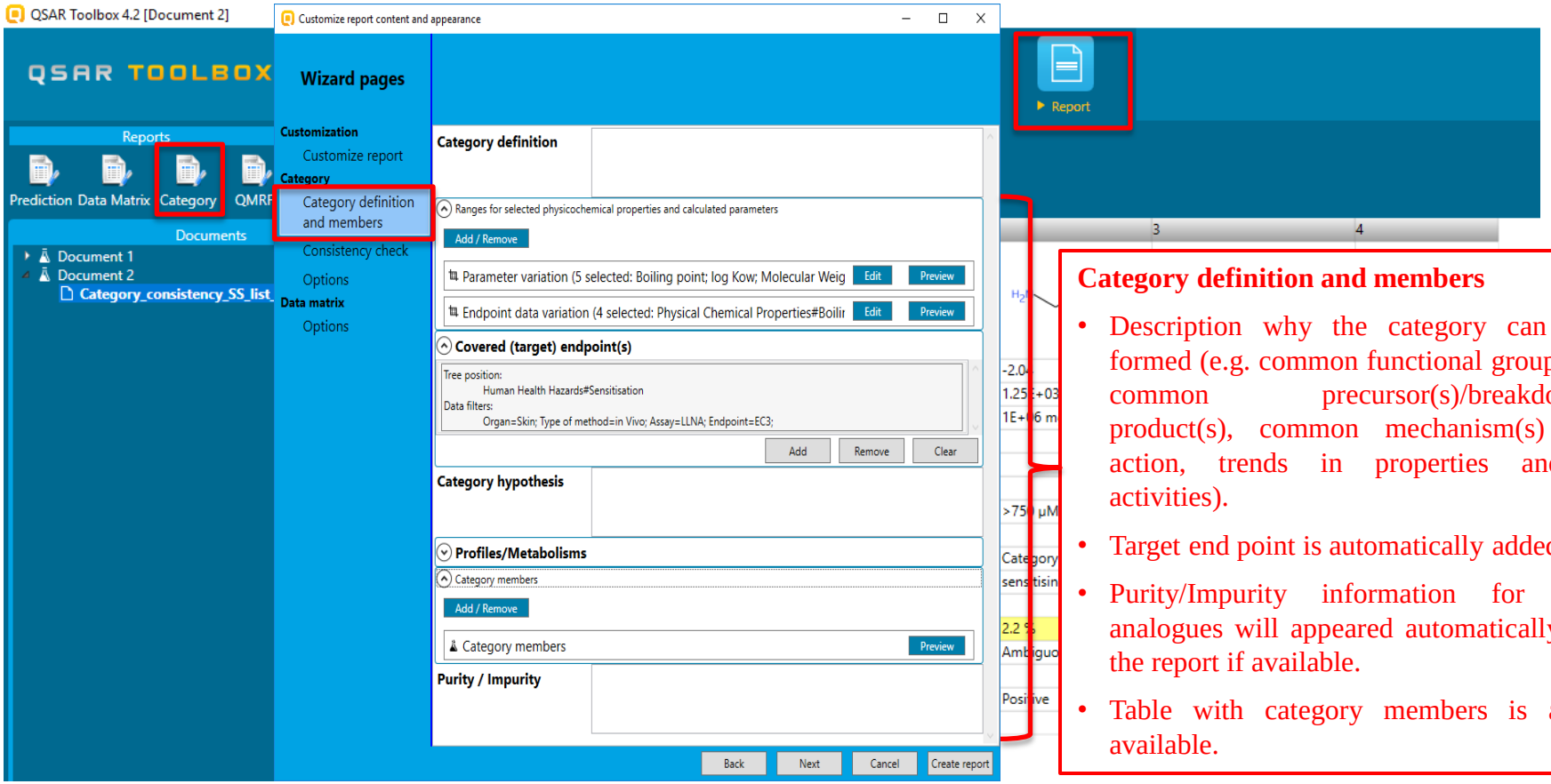
A report for the list of aliphatic amines associated with skin sensitization endpoint (Example 3) will be illustrated



1. Once you are in the document for assessing category of amines related to skin sensitization endpoint
2. Go to **Report module**
3. Click on **Category report**
4. The wizard window with sections of the category report appeared

Category consistency elements

Report



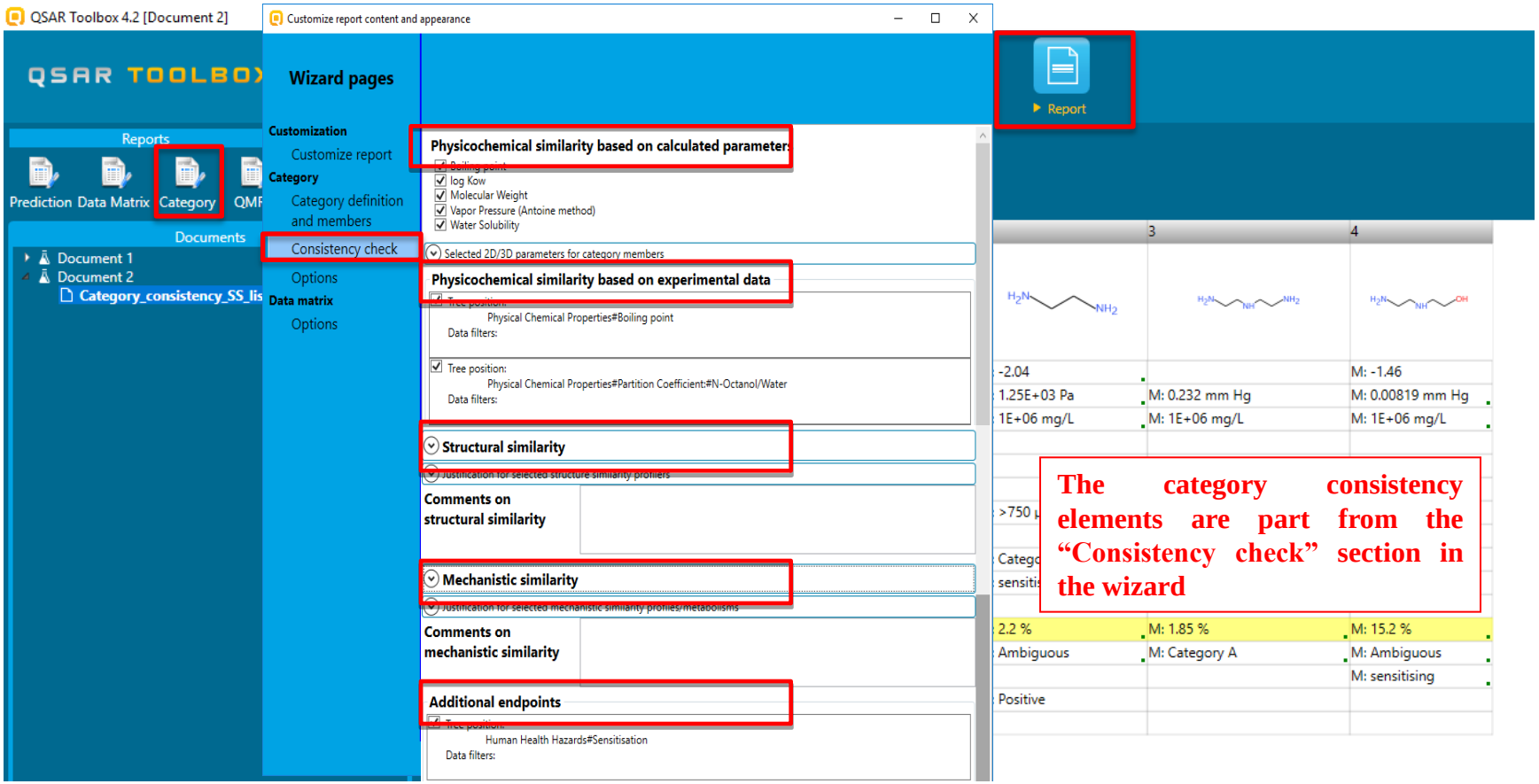
Category definition and members

- Description why the category can be formed (e.g. common functional group(s), common precursor(s)/breakdown product(s), common mechanism(s) of action, trends in properties and/or activities).
- Target end point is automatically added.
- Purity/Impurity information for the analogues will appeared automatically in the report if available.
- Table with category members is also available.

Keep the default settings

Category consistency elements

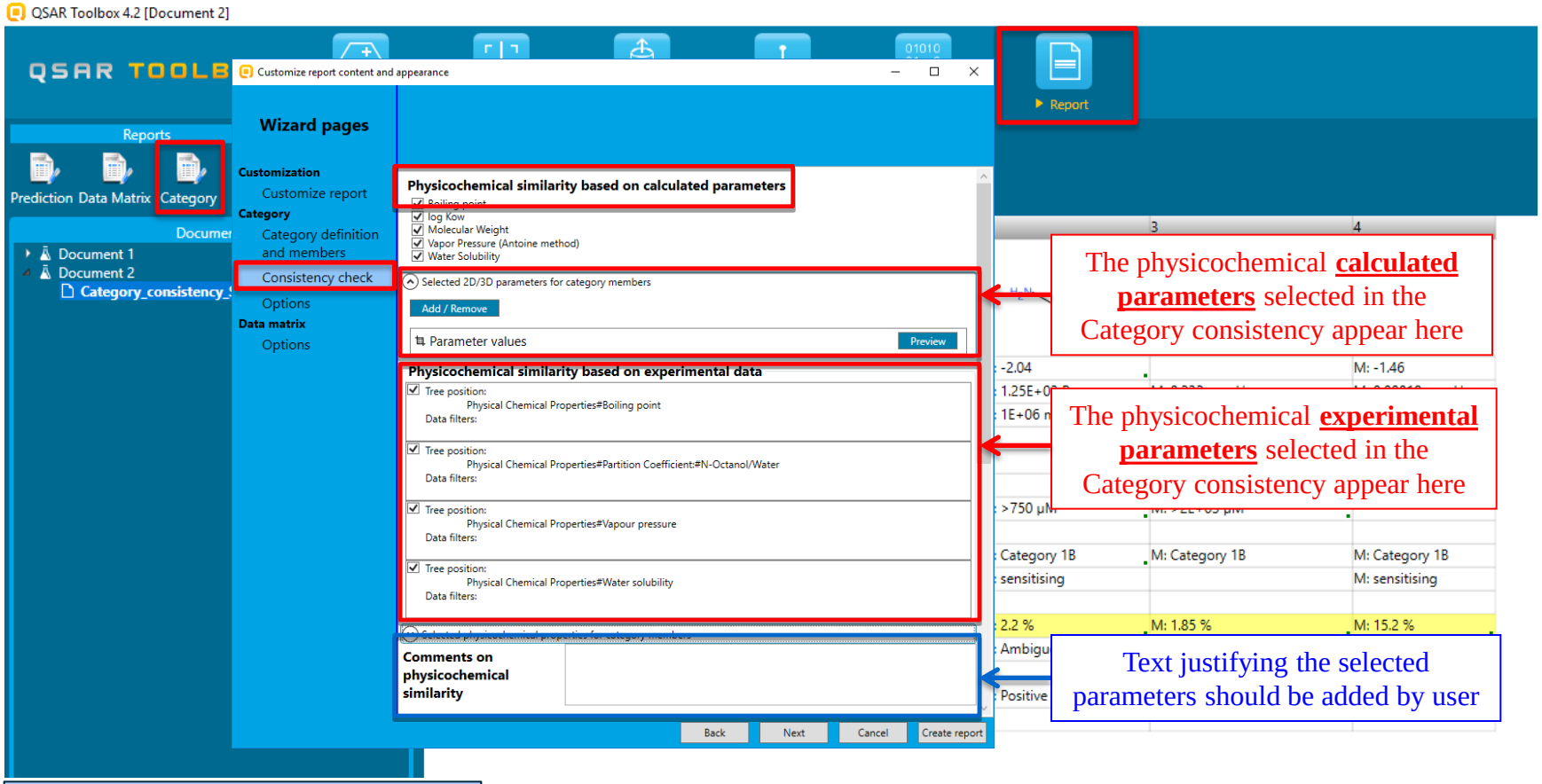
Report



Keep the default settings

Category consistency elements

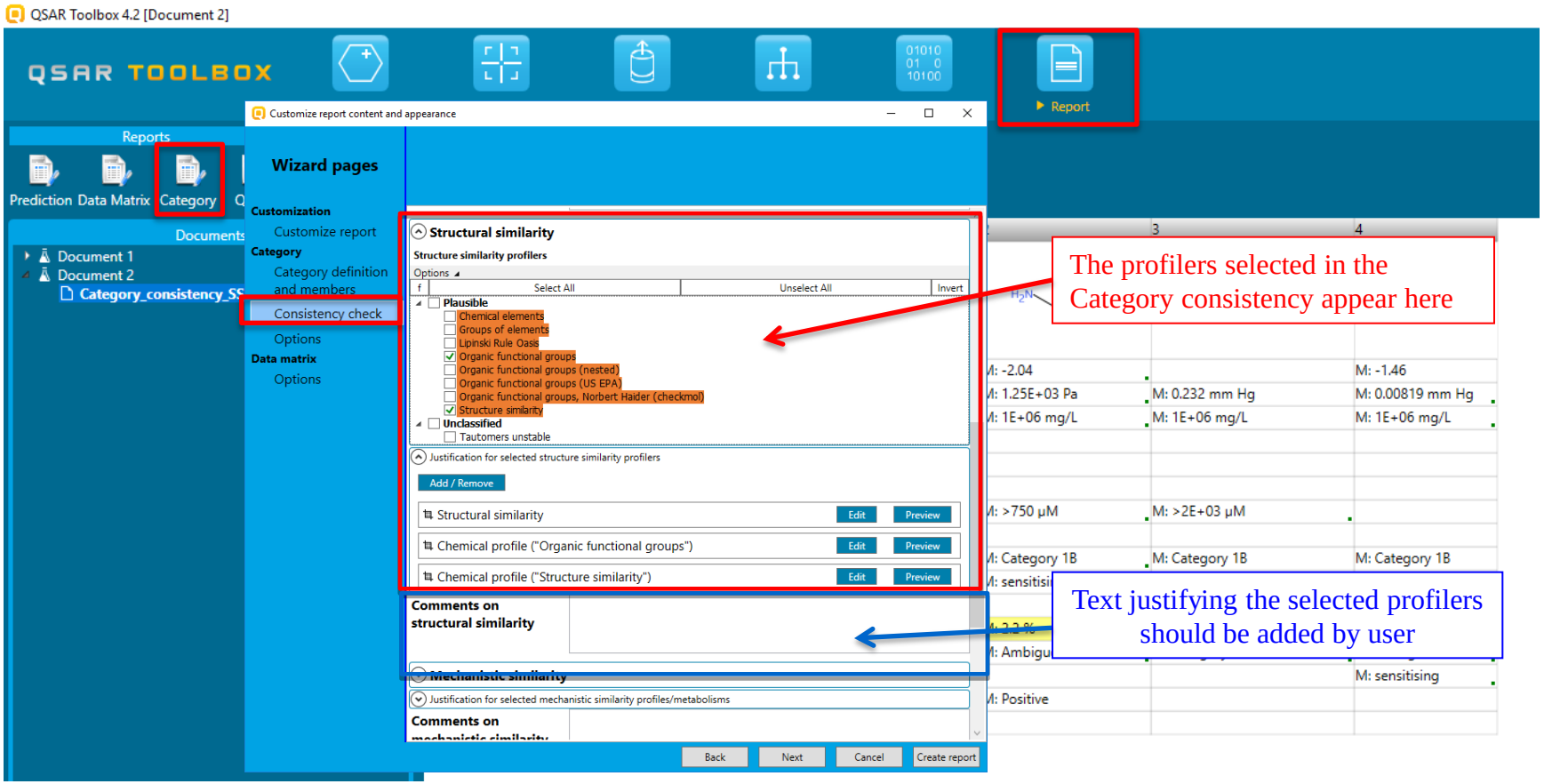
Report



Keep the default settings

Category consistency elements

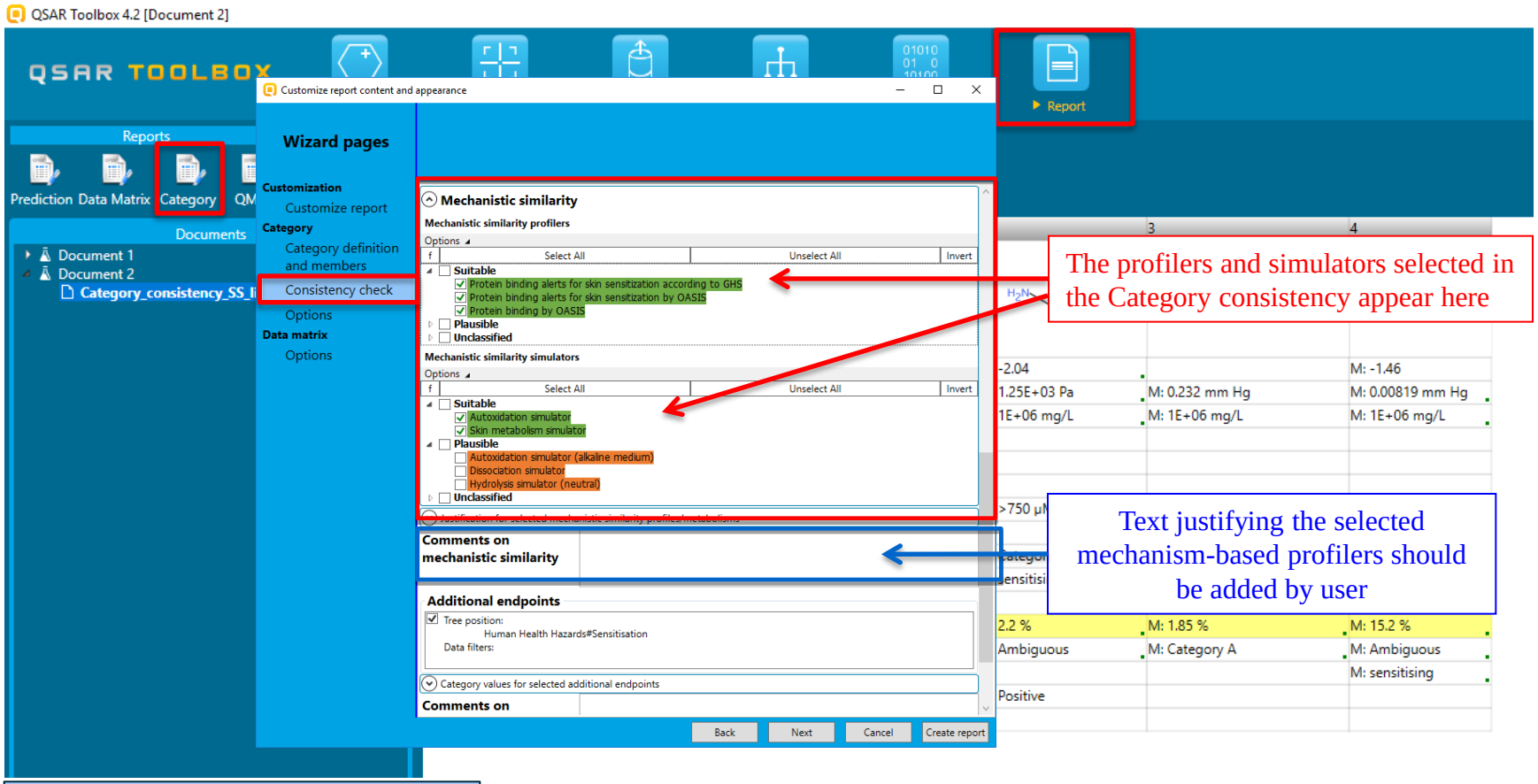
Report



Keep the default settings

Category consistency elements

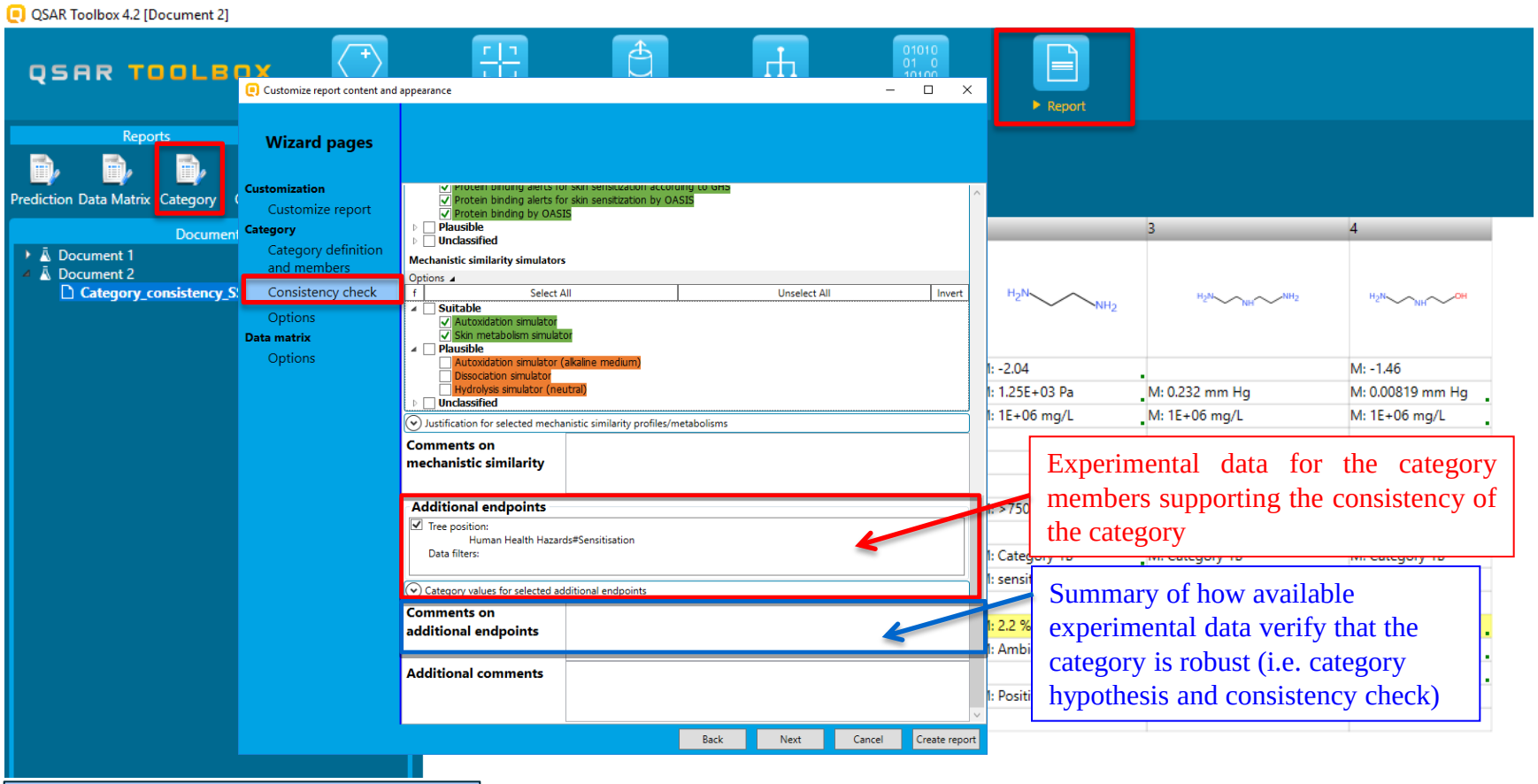
Report



Keep the default settings

Category consistency elements

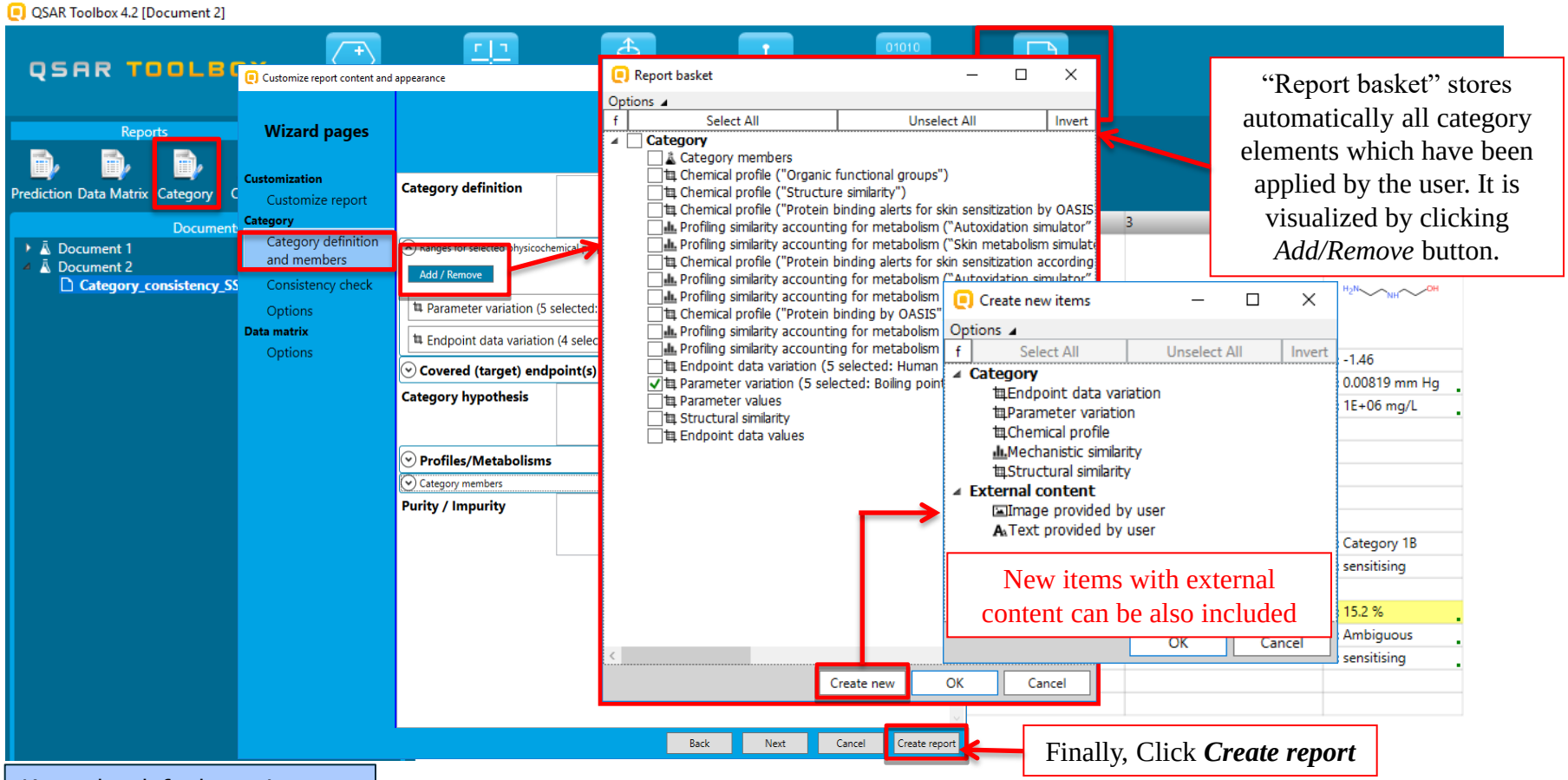
Report



Keep the default settings

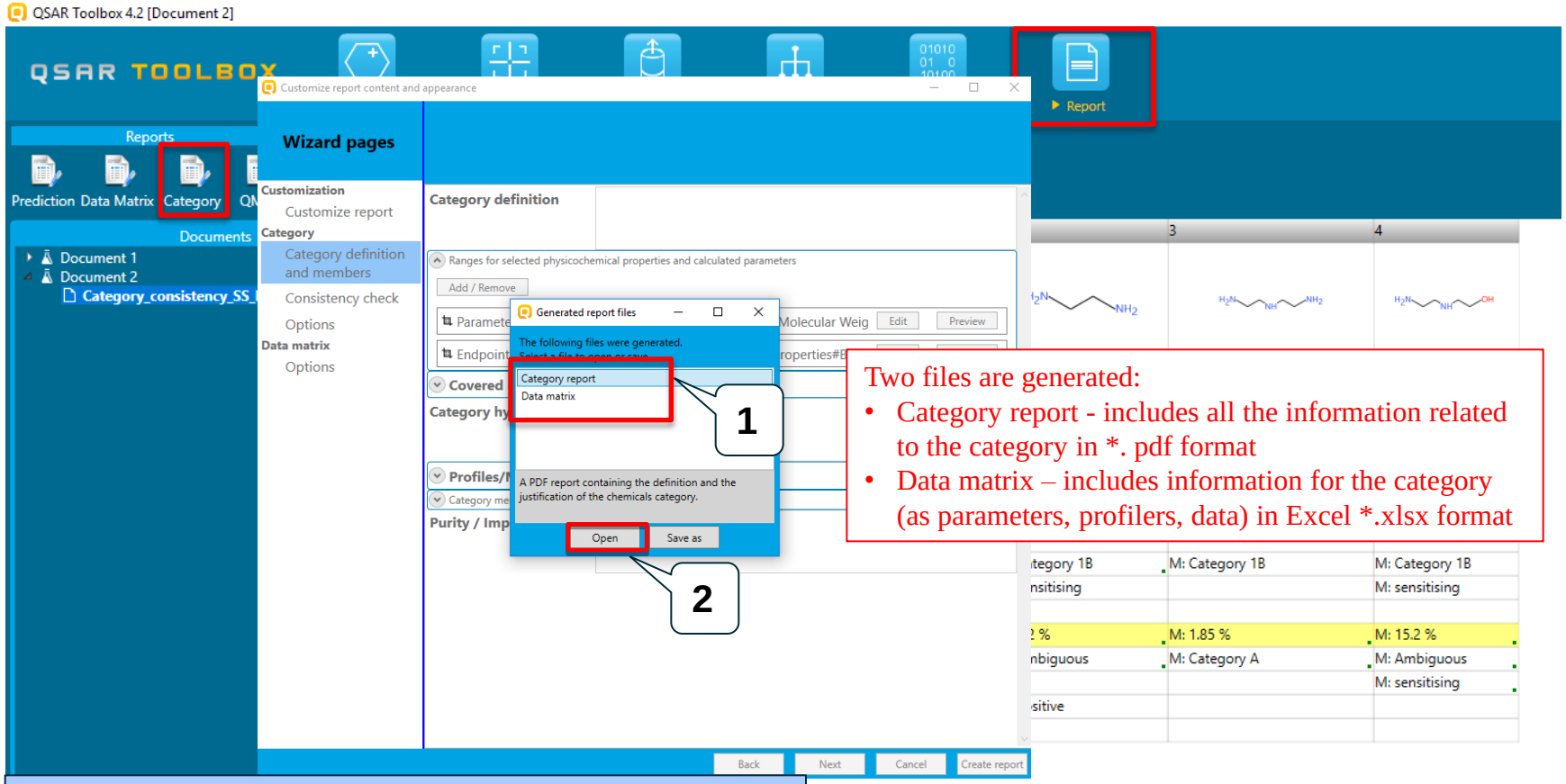
Category consistency elements

Report



Category consistency elements

Report



1. Select **Category report**
2. Click **Open**

Category consistency elements

Report

1. Category definition section:

QSAR Toolbox report for category

1. Category definition

1.1. Category definition

manually editable field

Not provided by the user

Ranges for selected physicochemical properties and calculated parameters

Parameter variation (5 selected: Boiling point; log Kow; Molecular Weight; Vapor Pressure (Antoine method); Water Solubility)

2D parameters data variation

Parameter name	Variation	unit (family)
Boiling point	103 ÷ 228	°C
log Kow	-2.13 ÷ -1.15	<no units>
Molecular Weight	60.1 ÷ 131	Da
Vapor Pressure (Antoine method)	0.00693 ÷ 19	mm Hg
Water Solubility	1E+06	mg/L

Endpoint data variation (4 selected: Physical Chemical Properties#Boiling point; Physical Chemical Properties#Vapour pressure; Physical Chemical Properties#Water solubility; Physical Chemical Properties#Partition Coefficient:#N-Octanol/Water)

Physical Chemical Properties data variation

Position	Variation	unit (family)
Boiling point	117 ÷ 244	°C(Temperature)
Boiling point	NOT_SPECIFIED	HT Version 20120101 phrasegroup_C47
Vapour pressure	0.0126 ÷ 99.8	bar(Pressure)
Vapour pressure	0.01 ÷ 1.25E+03	Pa(Pressure)
Vapour pressure	0.00819 ÷ 12	mm Hg(Pressure)
Water solubility	1E+06	mg/L(Mass concentration)
Water solubility	1E+06	mg/L(Mass concentration)
Partition Coefficient:#N-Octanol/Water	-4.96 ÷ -1.25	

1.2. Covered (target) endpoint(s)

manually editable field

- Human Health Hazards/Sensitisation: Skin, in Vivo, LLNA, EC3

1.3. Category hypothesis

manually editable field

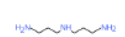
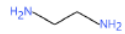
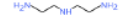
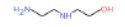
Not provided by the user

1.4. Profiles/Metabolisms

manually editable field

1.5. Category members

manually editable field

#	CAS	Name	SMILES	Structure
1	56-18-8	Iminobis-3-propylamine	NCCCNCCCN	
2	107-15-3	Ethylenediamine	NCCN	
3	111-40-0	Diethylenetriamine	NCCNCCN	
4	111-41-1	dicyclopentylsilanediol	NCCNCCO	

Purity / Impurity

manually editable field

Not provided by the user

2. Consistency check

2.1. Physicochemical similarity

manually editable field

Selected 2D/3D parameters for category members

1. Category definition section:

1.1. Category definition – includes ranges of variation of selected physicochemical parameters (calculated values and exp data);
1.2. Covered (target) endpoint(s) –automatically fulfilled
1.3. Category hypothesis – information could be provided by the user
1.4. Profiling/Metabolisms – additional profilers/metabolisms could be provided
1.5. Category members – a table with category members is provided; information regarding Purity/Impurity could be manually added

Category consistency elements

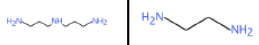
2. Consistency check section:

Report

2. Consistency check

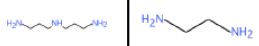
2.1. Physicochemical similarity

Selected 2D/3D parameters for category members

	1	2
		
Boiling point, °C	228	103
log Kow,	-1.15	-1.62
Molecular Weight, Da	131	60.1
Vapor Pressure (Antoine method), mm Hg	0.0913	19
Water Solubility, mg/L	1E+06	1E+06

	3	4
		
Boiling point, °C	189	211
log Kow,	-2.13	-2.13
Molecular Weight, Da	103	104
Vapor Pressure (Antoine method), mm Hg	0.274	0.00693
Water Solubility, mg/L	1E+06	1E+06

Selected physicochemical properties for category members

	1	2
		
Physical Chemical Properties/Boiling point		NOT_SPECIFIED
Physical Chemical Properties/Boiling point		117÷117 °C (x2)
Physical Chemical Properties/Partition Coefficient;/N-Octanol/Water	-4.96÷-1.25 (x2)	-2.04÷-1.65 (x2)
Physical Chemical Properties/Vapour pressure	0.0126÷99.8 bar (x9)	13.3÷1.25E+03 Pa (x2)
Physical Chemical Properties/Vapour pressure		12 mm Hg
Physical Chemical Properties/Water solubility		1E+06 mg/L
Physical Chemical Properties/Water solubility		1E+03 g/L

	3	4
		
Physical Chemical Properties/Boiling point	207 °C	239÷244 °C (x6)
Physical Chemical Properties/Boiling point		
Physical Chemical Properties/Partition Coefficient;/N-Octanol/Water		-1.46
Physical Chemical Properties/Vapour pressure	0.232 mm Hg	0.01÷46.9 Pa (x5)
Physical Chemical Properties/Vapour pressure		0.00819 mm Hg
Physical Chemical Properties/Water solubility	1E+06 mg/L	1E+03 g/L
Physical Chemical Properties/Water solubility		1E+06 mg/L

Comments on physicochemical similarity *manually edit*

Not provided by the user

QSAR Toolbox 4.2
Database version: 4.2

QSAR TOOLBOX

TPRF v4.2

2.2. Structural similarity

Structural similarity

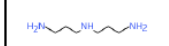
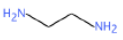
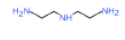
Options

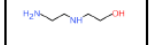
Mode: Hologram, CombineAllFeatures
Measure:
-Dice
Molecular features:
-AtomCenteredFragments
Atom characteristics:
-AtomType
-CountHAttached
-Hybridization

Calculated structure similarity

	Chemical 1	Chemical 2	Chemical 3	Chemical 4
Chemical 1	100%	61.5 %	87.5 %	62.5 %
Chemical 2	61.5 %	100%	72.7 %	36.4 %
Chemical 3	87.5 %	72.7 %	100%	71.4 %
Chemical 4	62.5 %	36.4 %	71.4 %	100%

Chemical profile ("Organic functional groups")

1	2	3
		
Amine, primary Amine, secondary Aliphatic amine, primary Aliphatic amine, secondary	Amine, primary Aliphatic amine, primary	Amine, primary Amine, secondary Aliphatic amine, primary Aliphatic amine, secondary

4


QSAR Toolbox 4.2
Database version: 4.2

QSAR TOOLBOX

2. Consistency check section:

2.1. Physicochemical similarity – provides information for the selected physicochemical parameters (calculated values and exp data)

2.2. Structural similarity – provides profiling results from the selected structural based profilers – Structural similarity and OFG

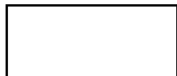
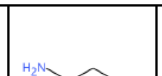
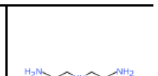
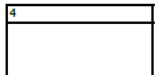
Category consistency elements

2. Consistency check section (cond.): Report

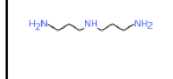
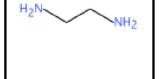
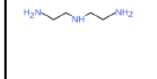
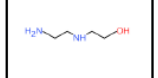
2.3. Mechanistic similarity

Profiling similarity accounting for metabolism ("Skin metabolism simulator" and "Protein binding alerts for skin sensitization by OASIS")
Metabolism: Skin metabolism simulator

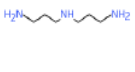
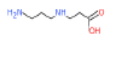
Chemical profile ("Protein binding alerts for skin sensitization by OASIS")

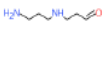
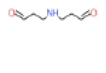
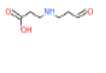
 No alert found	 No alert found	 No alert found
4  No alert found		

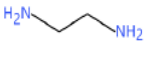
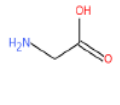
Chemical profile ("Protein binding alerts for skin sensitization according to GHS")

1	2	3
 No alert found	 No alert found	 No alert found
4 		

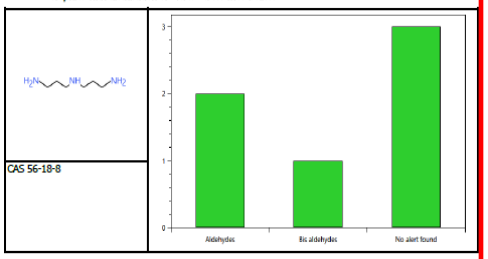
Tables with generated metabolites for each analogue with profiling result

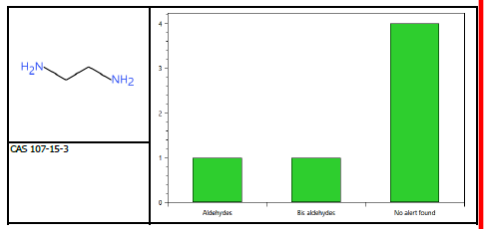
P1	M1 P1	M2 P1
 No alert found	 No alert found	 No alert found

M3 P1	M4 P1	M5 P1
 Aldehydes	 Bis aldehydes	 Aldehydes

P2	M1 P2	M2 P2
 No alert found	 No alert found	 No alert found

Graphics with distribution of alerts across metabolites





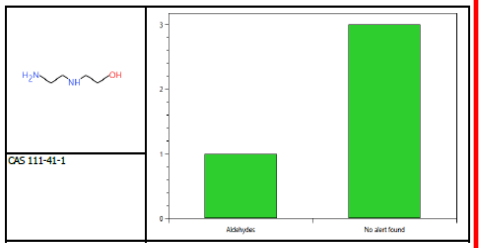


Table summarizing number of metabolites including parent with specific alerts

Protein binding alerts for skin sensitization by OASIS	P1 56-18-8	P2 107-15-3	P3 111-40-0	P4 111-41-1
Aldehydes	2	1	2	1
Bis aldehydes	1	1	1	0
No alert found	3	4	3	3

2. Consistency check section:

2.3. Mechanistic similarity – provides information for the selected profiles (assigned as suitable with respect to the target endpoint and/or manually added by the user to justify the consistency):

- Profiling results for all category members
- Tables for parents and generated metabolites (if any)
- Graphics with distribution of alerts across metabolites
- Tables summarizing the number of metabolites (including parent) with specific alerts

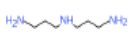
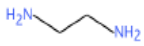
Category consistency elements

2. Consistency check section (cond.): Report

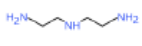
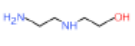
2.4. Additional endpoints

Category values for selected additional endpoints

manually editable field

	1	2
		
Human Health Hazards/Sensitisation	Category C	Positive (x2)
Human Health Hazards/Sensitisation	sensitising (x2)	Category A
Human Health Hazards/Sensitisation	Category 1B	Moderately sensitising (x10)
Human Health Hazards/Sensitisation	0.882÷0.9 % (x3)	Ambiguous

Human Health Hazards/Sensitisation		Not sensitising (x3)
Human Health Hazards/Sensitisation		Strong sensitizer
Human Health Hazards/Sensitisation		Category 1B
Human Health Hazards/Sensitisation		2.2÷2.7 % (x4)
Human Health Hazards/Sensitisation		sensitising
Human Health Hazards/Sensitisation		Positive (x2)
Human Health Hazards/Sensitisation		99.5÷750 µM (x7)
Human Health Hazards/Sensitisation		Negative (x3)
Human Health Hazards/Sensitisation		Positive

	3	4
		
Human Health Hazards/Sensitisation	Category A	Ambiguous
Human Health Hazards/Sensitisation	Moderately sensitising (x6)	Moderately sensitising (x3)
Human Health Hazards/Sensitisation	Category 1B	sensitising (x3)
Human Health Hazards/Sensitisation	1.85÷5.8 % (x5)	Category 1B
Human Health Hazards/Sensitisation	1.26E+03÷2E+03 µM (x3)	5.3÷15.2 % (x3)
Human Health Hazards/Sensitisation	Negative (x4)	
Human Health Hazards/Sensitisation		
Human Health Hazards/Sensitisation		
Human Health Hazards/Sensitisation		

2. Consistency check section:

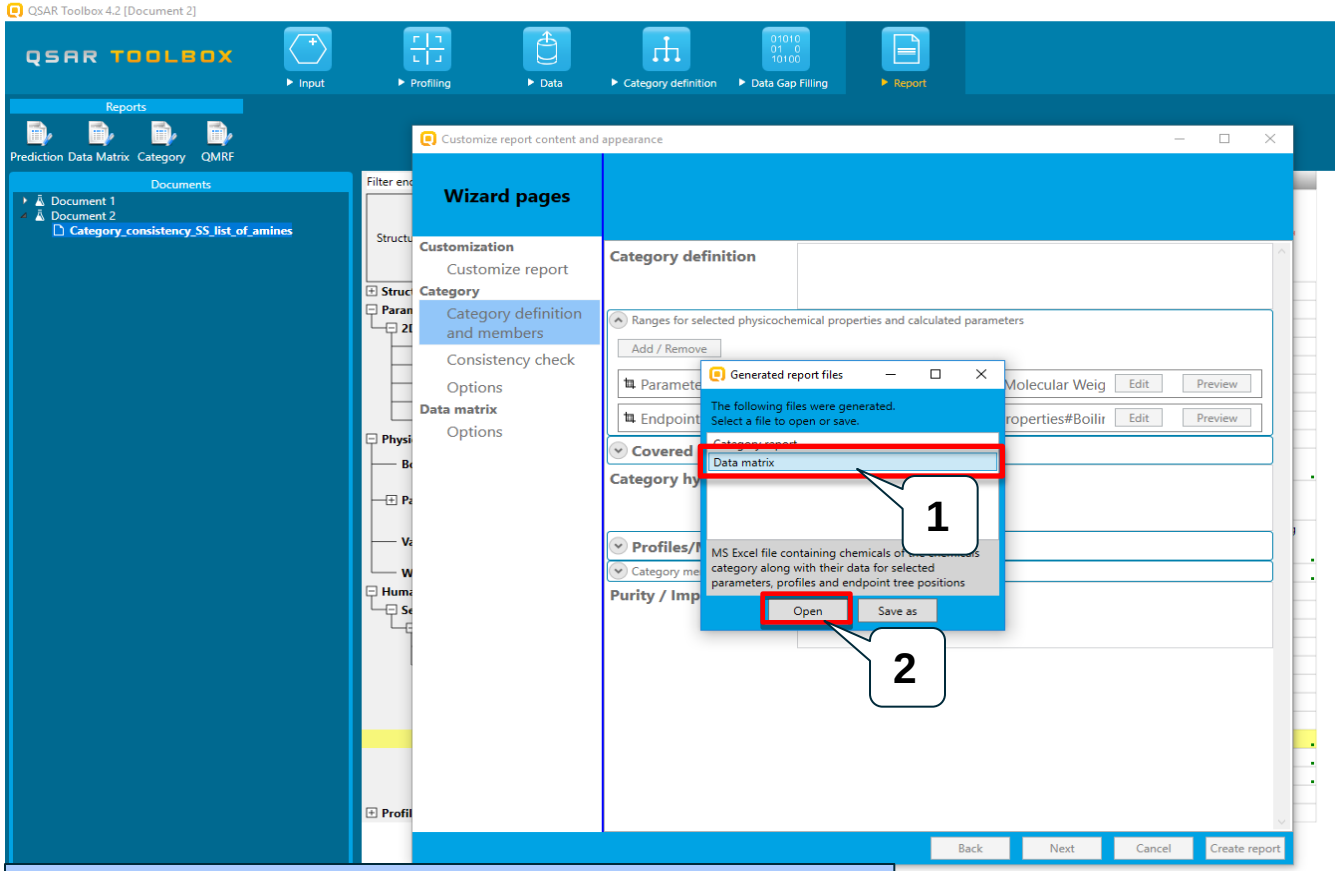
2.4. Additional endpoints – provides experimental data for all category members related to the additionally added endpoints

The number in brackets shows how many times the same experimental result is recorded

Category consistency elements

Report

Data matrix

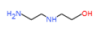
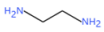
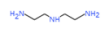


1. Select **Data matrix** report
2. Click **Open**

Category consistency elements

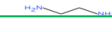
Report

Data matrix

		Chemical #1	Chemical #2	Chemical #3	Chemical #4
Substance identity					
Structure					
CAS number		56-18-8	111-41-1		
Chemical name		Iminobis-3-propylamine	dicyclopentylsilanediol		
Other identifier					
SMILES		NCCCNCCCN	NCCNCCO		
Parameters	**unit**				
Vapor Pressure (Antoine method)	mm Hg	0.0913	0.00693		
log Kow		-1.15	-2.13		
Molecular Weight	Da	131.22498	104.15528	60.10352	103.17322
Boiling point	°C	228.13	210.9	103.44	189.14
Water Solubility	mg/L	1000000	1000000	1000000	1000000
Profilers					
General Mechanistic					
Protein binding by OASIS		No alert found	No alert found	No alert found	No alert found
Protein binding by OASIS, with Autoxidation		No alert found	No alert found	No alert found	No alert found
Protein binding by OASIS, with Skin metabolism simulator		No alert found; Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes; Schiff base formation >> Schiff base formation with carbonyl compounds	No alert found; Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes	No alert found; Sc for	No alert found;
Endpoint Specific					
Protein binding alerts for skin sensitization		No alert found	No alert found		
Protein binding alerts for skin sensitization		No alert found	No alert found	No alert found	No alert found
Protein binding alerts for skin sensitization		No alert found	No alert found	No alert found	No alert found
Protein binding alerts for skin sensitization		No alert found	No alert found	No alert found	No alert found
Protein binding alerts for skin sensitization by OASIS, with Skin metabolism simulator		No alert found; Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes; Schiff base formation >> Schiff base formation with carbonyl compounds	No alert found; Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes	No alert found; Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes; Schiff base formation >> Schiff base formation with carbonyl compounds	No alert found; Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes; Schiff base formation >> Schiff base formation with carbonyl compounds
Protein binding alerts for skin sensitization		Skin sensitization Category 1B >>	No alert found;	Skin sensitization Category 1B >>	Skin sensitization Category 1B >>

Parameters values and profilers used in the workflow

Profilers accounting for metabolism if applied

		Chemical #1			Chemical #2			Chemical #3			Chemical #4		
Substance identity													
Structure													
Physical Chemical Properties#Boiling point													
environment	*endpoint*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, reference*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, reference*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, reference*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, reference*
Boiling point	none				239	°C	SRC	117	°C	SRC	207	°C	SRC
Physical Chemical Properties#Vapour													
environment	*endpoint*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, reference*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, reference*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, reference*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, reference*
Vapour pressure	none				0.00819	mm Hg	SRC	12	mm Hg	SRC	0.232	mm Hg	SRC
environment	*endpoint*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, reference*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, reference*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, reference*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, reference*
N-Octanol/Water	none							-2.04		SRC			
Human Health Hazards#Sensitisation													
environment	*endpoint*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, reference*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, reference*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, reference*	*value*	*unit*	*species, duration, test type, type of method, assay, strain, test guideline, year, reference*
Sensitisation	none	Category C		in Vivo Miscellaneous 2001 Medizin&Wissen Verlagges, Munchen. ISBN 3-86094-163-1 Kayser, D., E. Schlede. (eds.) Chemikalien und Kontaktallergie – eine bewertende	Moderately sensitising		Unified pig in Vivo Miscellaneous Other Guideline: 1980 Dow Chemical USA (1980). Acute toxicological properties and skin sensitization potential of aminoethylethanolamine. R+D report, TXT: K-4409-(3), 13 Nov 1980, as cited in	99.5	µM	in Vitro KeratinoSens 2015 Arch Toxicol Joanna S. Jaworska et all Bayesian integrated testing strategy (ITS) for skin sensitization potency assessment: a decision support system for quantitative weight of	Negative		in Vitro Dendritic Cell Activity (h-CLAT) 2012 Nukada

Measured data for the chemicals in the category

Congratulation

- You have now been introduced to the defining of a target endpoint;
- You have now been introduced to the elements of the category consistency;
- You have now been introduced to the Report basket;
- Note proficiency comes with practice.