

## 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.

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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
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- 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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  - 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
- Examples

## 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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  - **Implementation in Toolbox**
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# 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)

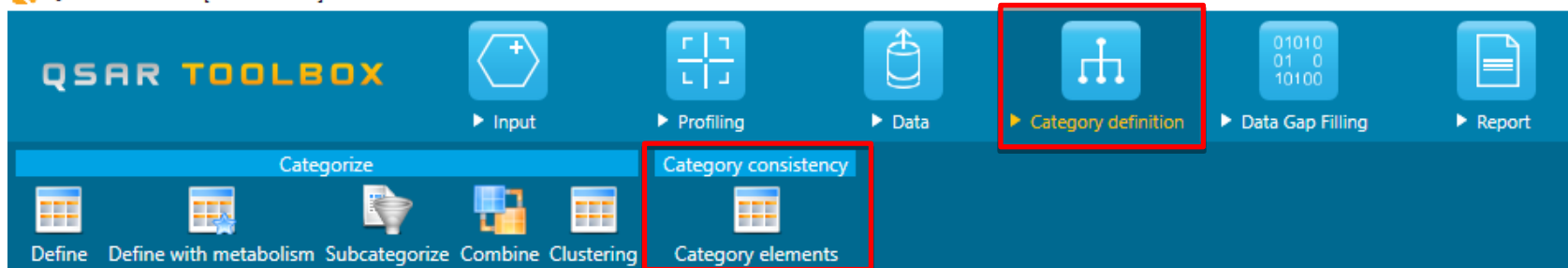
- **(Eco)toxicological experimental data** – depends on the pre-defined target endpoint
- Different selection of the category consistency elements than the default one is allowed

# 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

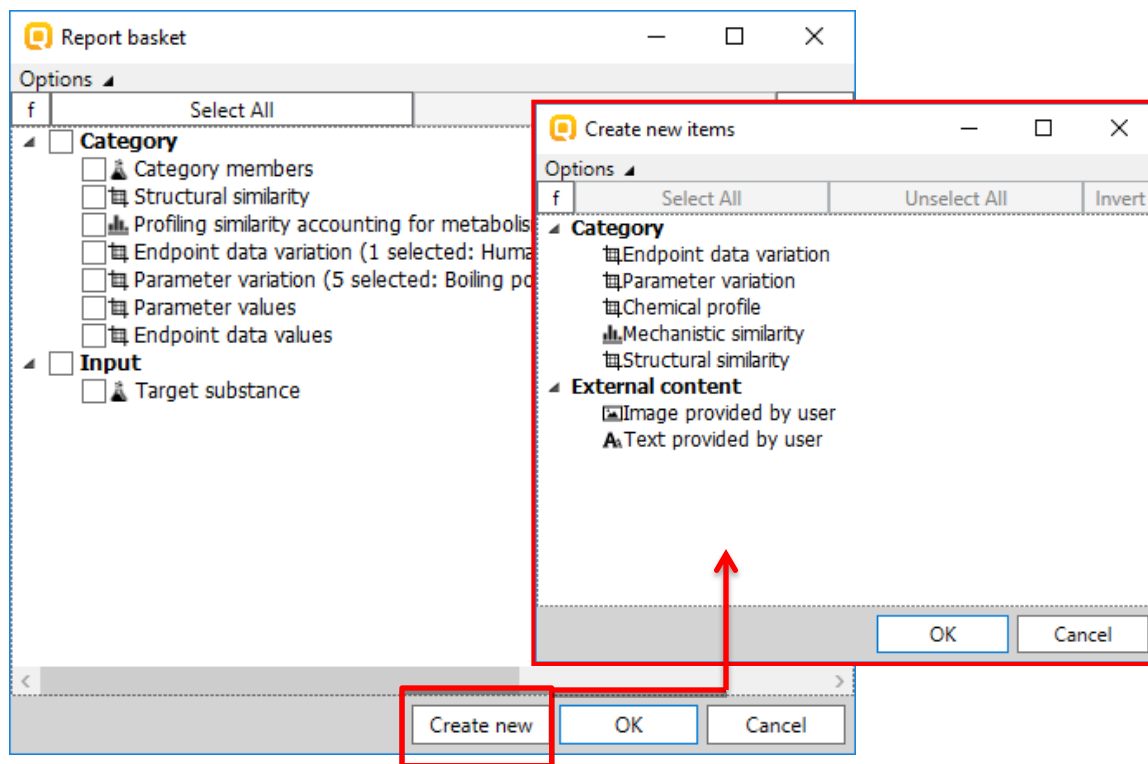
QSAR Toolbox 4.2 [Document 2]





# Category consistency elements

## Report basket

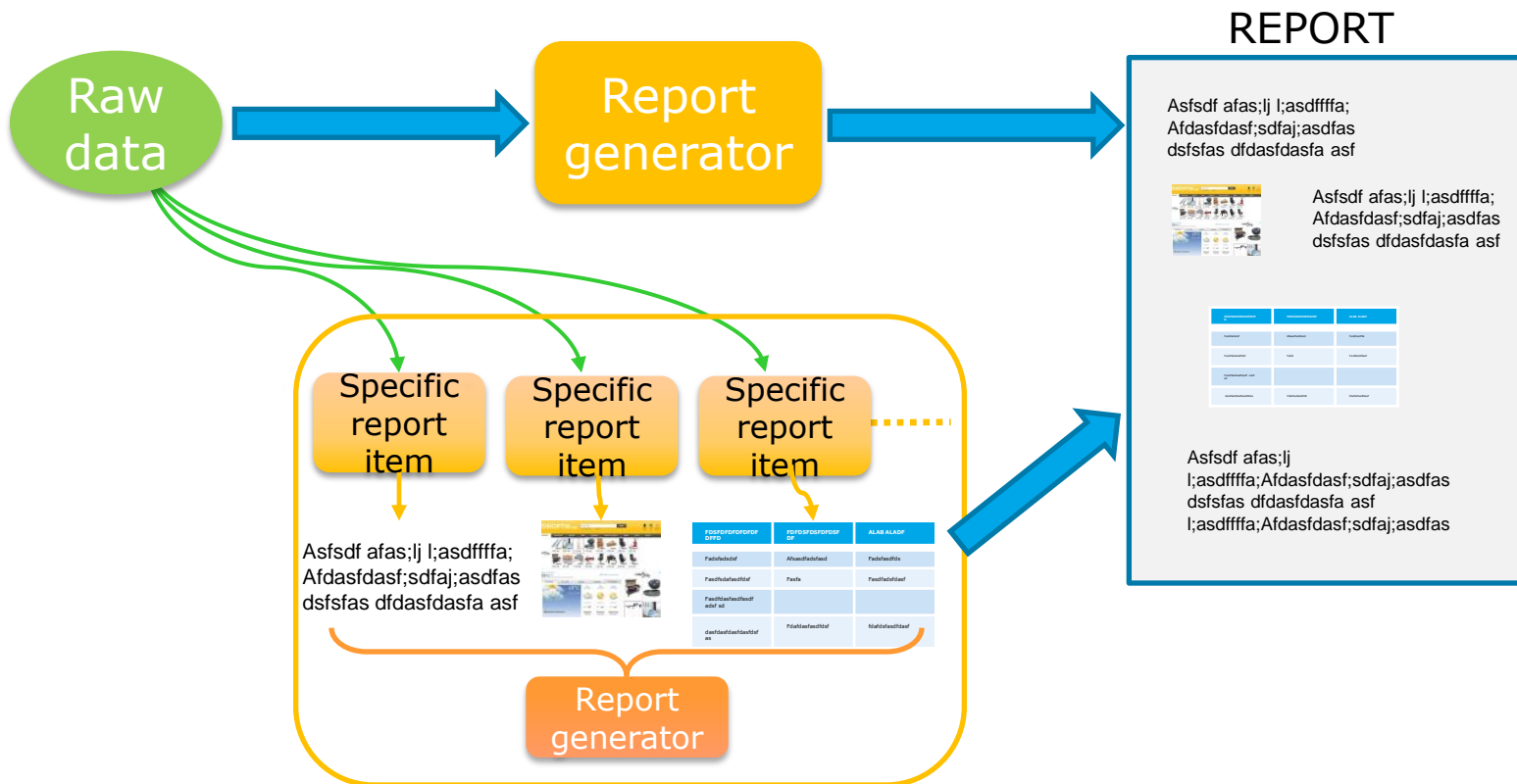


- The selected category elements are automatically stored in the so-called "Report basket"
- Additional report items (such as parameter variation for the closest analogues, text, pictures etc.) could be added.

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

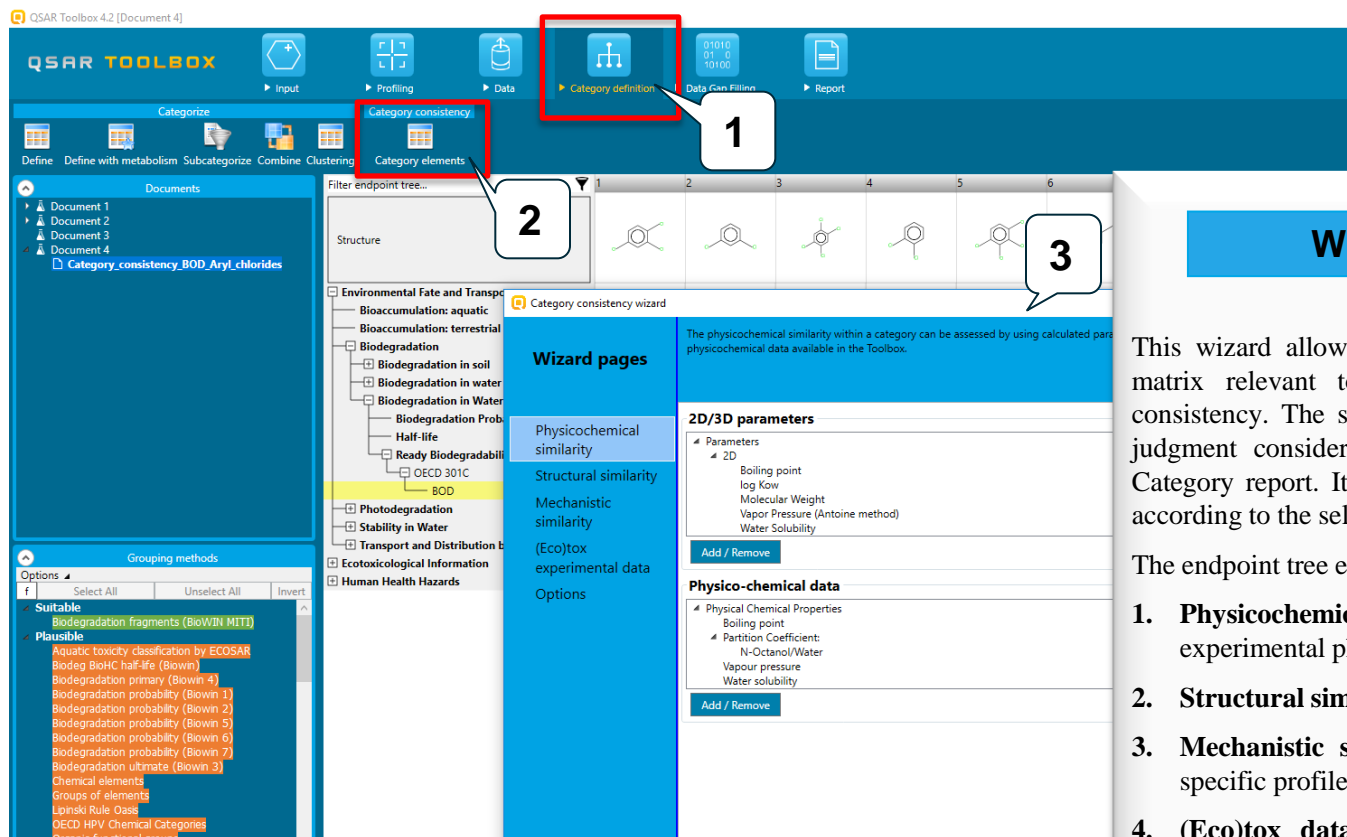
- A list of 7 aromatic halogens is submitted as a category
- The defined target endpoint is: **Ready Biodegradability/BOD/OECD 301C**

The screenshot shows the QSAR Toolbox 4.2 interface. The 'List' menu item is highlighted with a red box and callout '1'. Below it, the 'From examples folder' option is also highlighted with a red box. The 'Define' button in the 'Target Endpoints' section is highlighted with a red box and callout '2'. The 'Select endpoint' dialog box is open, showing a tree view of endpoints. The 'Ready Biodegradability' endpoint is selected in the tree, and 'BOD' is selected in the 'Endpoint' dropdown. The 'Test guideline' is set to 'OECD 301C'. Callout '3' points to the 'Finish' button in the dialog box.

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



### 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.

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

# Category consistency elements

## Example 1 – Fate endpoint

### Category element: **Physicochemical similarity**

The screenshot displays the QSAR Toolbox interface. The 'Category definition' tab is active, and the 'Category consistency' wizard is open. The wizard is titled 'Category consistency wizard' and contains the following sections:

- Wizard pages:** A list of pages including 'Physicochemical similarity', 'Structural similarity', 'Mechanistic similarity', '(Eco)tox experimental data', and 'Options'. 'Physicochemical similarity' is the current page.
- 2D/3D parameters:** A section for selecting parameters. Under '2D', the following parameters are listed: Boiling point, log Kow, Molecular Weight, Vapor Pressure (Antoine method), and Water Solubility. There is an 'Add / Remove' button below this list.
- Physico-chemical data:** A section for selecting physical chemical properties. Under 'Physical Chemical Properties', the following are listed: Boiling point, Partition Coefficient: N-Octanol/Water, Vapour pressure, and Water solubility. There is an 'Add / Remove' button below this list.

A text box within the wizard states: 'The physicochemical similarity within a category can be assessed by using calculated parameters and experimental physicochemical data available in the Toolbox.'

**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**

QSAR Toolbox 4.2 [Document 4]

**User can select other parameters or experimental phys-chem data for the analysis from the lists**

The physicochemical similarity within a category can be assessed by using calculated parameters and experimental physicochemical data available in the Toolbox.

**1** 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)

**Select**

- Parameters
  - 2D
    - (Q) Acidic pKa (Chemaxon)
    - (Q) Basic pKa (Chemaxon)
    - BAF
    - BAF (lower trophic)
    - BAF (mid trophic)
    - BAF (upper trophic)
    - BAF (upper trophic, biotransformation rate is zero)
    - BCF
    - BCF (lower trophic)
    - BCF (mid trophic)

**Select**

- Physical Chemical Properties
  - Autoflammability / Self-ignition temperature
  - Boiling point
  - Chemical reactivity
  - Density
  - Dissociation Constant (pKa)
  - Explosive properties
  - Flammability
  - Flash point
  - Melting / freezing point
  - Oxidation reduction potential
  - Oxidising properties
  - Particle size
  - Partition Coefficient:
    - Solubility in organic solvents / fat solubility
    - Stability in organic solvents and identity of relevant degrad
    - Surface tension

biotransformation rate is zero)

Biowin 1)  
Biowin 2)  
Biowin 5)

OK Cancel

OK Cancel

The OECD QSAR Toolbox for Grouping Chemicals into Categories

# Category consistency elements

## Example 1 – Fate endpoint

### Category element: **Structural similarity**

QSAR Toolbox 4.2 [Document 4]

**Wizard pages**

- Physicochemical similarity
- Structural similarity**
- Mechanistic similarity (Eco)tox experimental data
- Options

The structural similarity within a category can be assessed by using the empirical profilers available in the Toolbox.

**Empiric profiles**

Options

- Plausible
  - Chemical elements
  - Groups of elements
  - Lipinski Rule Oasis
  - Organic functional groups
  - Organic functional groups (nested)
  - Organic functional groups (US EPA)
  - Organic functional groups, Norbert Haider (checkmol)
  - Structure similarity
- Unclassified
  - Tautomers unstable

**Default selection of profilers related to structural similarity:**

- ✓ Organic functional groups
- ✓ Structure similarity

1. Select **Structural similarity** section

2. Keep the default selections.

3. Move to **Mechanistic similarity**

Back Next Cancel OK

# Category consistency elements

## Example 1 – Fate endpoint

### Category element: **Mechanistic similarity**

QSAR Toolbox 4.2 [Document 4]

**Wizard pages**

The mechanistic similarity within a category can be assessed by using mechanistic and endpoint specific profilers, and metabolic simulators available in the Toolbox.

**1**

**2**

**You can select other profilers or metabolic simulators from the plausible list for example**

**Default selection of endpoint specific profilers and simulators depend on defined target endpoint:**

- ✓ **Biodegradation fragments (BioWIN MITI)**

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

QSAR Toolbox 4.2 [Document 4]

The screenshot shows the QSAR Toolbox interface. The 'Category consistency wizard' is the central window. On the left, the 'Wizad pages' tree has 'Options' selected. The 'Experimental data' page is active, showing a tree view of 'Environmental Fate and Transport' with 'Bioaccumulation: aquatic' selected. A 'Select' dialog box is open, showing a tree view of 'Experimental data' with 'Environmental Fate and Transport' and 'Bioaccumulation: aquatic' selected. The 'OK' button in the 'Select' dialog is highlighted with a red box. The 'OK' button in the 'Category consistency wizard' is also highlighted with a red box. Numbered callouts (1-5) point to these elements.

Additional experimental data to support the consistency of the category could be selected

Data related to the defined target endpoint is selected by default

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

Filter endpoint tree...	1	2	3	4	5	6	7
Structure							
<b>Structure info</b>	<b>Selected calculated parameters and experimental data appear on DM</b>						
<b>Parameters</b>							<u>Calculated values</u>
2D							
Boiling point	207 °C	175 °C	238 °C	175 °C	238 °C	175 °C	266 °C
log Kow	3.93	3.28	4.57	3.28	4.57	3.28	5.22
Molecular Weight	181 Da	147 Da	216 Da	147 Da	216 Da	147 Da	250 Da
Vapor Pressure (Antoine method)	0.196 mm Hg	1.48 mm Hg	0.00264 mm Hg	1.05 mm Hg	0.0139 mm Hg	0.793 mm Hg	0.00156 mm Hg
Water Solubility	20 mg/L	75.6 mg/L	3.94 mg/L	92 mg/L	4.27 mg/L	90.2 mg/L	0.906 mg/L
<b>Physical Chemical Properties</b>							<u>Exp. data values</u>
Boiling point	7/32 M: 213 °C	M: 173 °C	M: 245 °C	M: 180 °C	M: 254 °C		
+ Partition Coefficient:	7/30 M: 4.02	M: 2.75E+03	M: 4.64	M: ≥3.18÷4.36	M: 4.6	M: 3.37	M: 5.17
Vapour pressure	7/55 M: 0.13 Pa	M: 0.44 Pa	M: 0.0054 mm Hg	M: 1.36 mm Hg	M: 0.039 mm Hg	M: 0.53 Pa	M: 0.00101 mm...
Water solubility	7/42 M: 19 mg/L	M: 111 mg/L	M: 0.595 mg/L	M: 156 mg/L	M: 5.92 mg/L	M: 31.7 mg/L	M: 0.831 mg/L

# 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

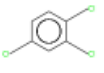
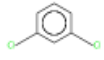
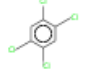
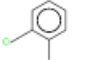
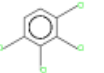
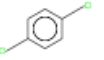
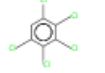
	Chemical 1	Chemical 2	Chemical 3	Chemical 4	Chemical 5	Chemical 6	Chemical 7
Chemical 1	100%	70.6 %	63.2 %	70.6 %	73.7 %	58.8 %	60 %
Chemical 2	70.6 %	100%	33.3 %	62.5 %	44.4 %	75 %	31.6 %
Chemical 3	63.2 %	33.3 %	100%	44.4 %	60 %	22.2 %	66.7 %
Chemical 4	70.6 %	62.5 %	44.4 %	100%	66.7 %	50 %	42.1 %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

Filter endpoint tree...	1	2	3	4	5	6	7	
Structure								
<b>Environmental Fate and Transport</b>								
<b>Bioaccumulation: aquatic</b>								
+ BCF	7/571	M: >2.3+2.48 lo...	M: 1.82 log(L/kg...	M: 3.44 log(L/kg...	M: >4.4+4.48 lo...	M: >4.9+5 log(L/...	M: >45+63	M: >5.3+5.48 lo...
+ BCF/	1/1				M: 1.35E+05 RA			
+ BCFD	2/15				M: 3.69 log(L/kg...		M: 3 log(L/kg bd...	
+ BSAF	4/11	M: 0.00893 kg or...	M: 0.00101 kg or...		M: 0.00598 kg or...	M: 0.000878 kg...		
+ kM	7/39	M: 0.00881 1/Days	M: 0.0437 1/Days	M: 0.00229 1/Days	M: 0.0624 1/Days	M: 0.00197 1/Days	M: 0.0341 1/Days	M: 0.00172 1/Days
+ kM Half-Life	7/7	M: 1.2 log(Days)	M: -0.214 log(Da...	M: 1.79 log(Days)	M: 0.504 log(Days)	M: 0.691 log(Days)	M: 1.1 log(Days)	M: 1.87 log(Days)
<b>Biodegradation</b>								
<b>Biodegradation in Water: Screening Te...</b>								
<b>Ready Biodegradability</b>								
+ According to Bunch and Cham...	1/2							
+ OECD 301C								
+ BOD	6/6	M: 0 %	M: 0 %	M: 0 %	M: 0 %	M: 0 %	M: 0 %	
+ OECD Guideline 301 C (Ready...	4/6	M: 0	M: 0	M: 0		M: 0		
+ OECD Guideline 301 D (Ready...	1/3					M: 1.4		
+ Undefined Test guideline	2/11		M: 77			M: >95		
<b>Profile</b>								

BOD and BCF data are filtered and appeared on DM if available

# 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

2

3

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*

The screenshot displays the QSAR Toolbox 4.2 interface. The 'Category definition' module is active, showing a 'Filter endpoint tree...' on the left and a grid of chemical structures on the right. A 'Category consistency wizard' dialog is open in the foreground, showing 'Wizard pages' and '2D/3D parameters' sections. The wizard is labeled '3'. The 'Category consistency' button is highlighted with a red box and labeled '1'. The 'Category elements' button is highlighted with a red box and labeled '2'.

**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

The screenshot displays the QSAR Toolbox 4.2 interface with the 'Category consistency wizard' dialog box open. The wizard is currently on the 'Mechanistic similarity' page. The 'Empiric profiles' section is expanded, showing 'Plausible' and 'Unclassified' categories. The 'Plausible' category is selected, and several options are checked, including 'Organic functional groups (nested)', 'Organic functional groups (US EPA)', and 'Structure similarity'. The 'Suitable' category is also expanded, showing 'Acute aquatic toxicity classification by Verhaar (Modified)', 'Acute aquatic toxicity MOA by OASIS', 'Aquatic toxicity classification by ECOSAR', and 'US-EPA New Chemical Categories'. The 'Options' section is also expanded, showing 'Hydrolysis half-life (Ka, pH 7)(Hydrowin)', 'Hydrolysis half-life (Ka, pH 8)(Hydrowin)', 'Hydrolysis half-life (Kb, pH 7)(Hydrowin)', 'Hydrolysis half-life (Kb, pH 8)(Hydrowin)', 'Hydrolysis half-life (pH 6.5-7.4)', 'Ionization at pH = 1', 'Ionization at pH = 4', 'Ionization at pH = 7.4', 'Ionization at pH = 9', 'OECD HPV Chemical Categories', 'Protein binding by OASIS', 'Protein binding by OECD', 'Protein binding potency GSH', and 'Substance type'. The 'Wizard pages' sidebar on the left shows 'Mechanistic similarity' selected. The 'Category consistency wizard' title bar is visible at the top of the dialog box. Three callout boxes with numbers 1, 2, and 3 are overlaid on the image. Callout 1 points to the 'Mechanistic similarity' page. Callout 2 points to the 'Empiric profiles' section. Callout 3 points to the 'OK' button.

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

Filter endpoint tree...	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Structure															
Structure info	<b>Calculated and experimental data</b>														
Parameters	<b>Calculated phys-chem values</b>														
2D															
Boiling poi...					271 °C	199 °C	178 °C	103 °C	112 °C	218 °C	157 °C	192 °C	87.7 °C	135 °C	62.7 °C
log Kow	-1.13	-0.15	4.27	4.76	5.25	3.29	2.8	-1.62	1.33	3.78	2.31	0.35	0.83	1.82	0.34
Molecular Weight	74.1 Da	45.1 Da	171 Da	185 Da	199 Da	143 Da	129 Da	60.1 Da	87.2 Da	157 Da	115 Da	116 Da	73.1 Da	101 Da	59.1 Da
Vapor Pressure (Antoine...)	6.93 mm Hg	153 mm Hg	0.0432 mm Hg	0.00642 mm Hg	0.00613 mm Hg	0.35 mm Hg	1.07 mm Hg	19 mm Hg	32.8 mm Hg	0.136 mm Hg	3.3 mm Hg	0.215 mm Hg	97.6 mm Hg	9.49 mm Hg	313 mm Hg
Water Solubility	1E+06 mg/L	1E+06 mg/L	139 mg/L	45.1 mg/L	14.6 mg/L	1.28E+03 mg/L	3.15E+03 mg/L	1E+06 mg/L	6.88E+04 mg/L	423 mg/L	6.79E+03 mg/L	5.34E+05 mg/L	2.03E+05 mg/L	2.06E+04 mg/L	5.44E+05 mg/L
Physical Chemical Properties															
Boilir			M: 242 °C	M: >348+352 °C	M: 276 °C	M: 202 °C	M: 178 °C	M: 116+117 NO...	M: 104 °C	M: 221 °C	M: 156 °C	M: 154 °C	M: 77 °C	M: 128+130 °C	M: 46+48 °C
Partit							M: 2.9	M: -2.04	M: 1.49		M: 2.57		M: 0	M: 1.68	M: 0.28
Vapo				M: 0.0079 Pa		M: 0.278 mm Hg	M: +1 bar	M: 1.25E+03 Pa	M: 30 mm Hg	M: 0.1 mm Hg	M: 2.74 mm Hg	M: 0.118 mm Hg	M: 102 Pa	M: 10.6 Pa	M: 1.06E+03
Water solubility	10/27		M: 1E+06 mg/L		M: 0.0488 mg/L		M: 0.15 (mass %)	M: 1E+06 mg/L	M: 1E+06 mg/L	M: 550 mg/L		M: 2.46E+06 mg/L	M: ≥50 % (w/w)	M: 1.2E+04 mg/L	M: 1E+06 mg/L
Ecotoxicological Information															
Aquatic Toxicity AW SW 15/487	M: >10 mg/L	M: >500 mg/L	M: 0.21 mg/L	M: 0.02 mg/L	M: 0.015 (0.011+...)	M: 1.6 (1.2+2) m...	M: >100 mg/L	M: >10 mg/L	M: 1.9E-08 ug/cell	M: >0.75+1.5 m...	M: >20	<b>Experimental endpoint data</b>			
Predefined															
US-EPA New Chemical Cat...	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Ami
Endpoint Specific															
Acute aquatic toxicity clas...	Class 5 (Not pos...	Class 5 (Not pos...	Class 2 (less inert...	Class 2 (less inert...	Class 2 (less inert...	Class 2 (less inert...	Class 2 (less inert...	Class 5 (Not pos...	Class 2 (less inert...	Class 2 (less inert...	Class 2 (less inert...	Class 2 (less inert...	Class 2 (less inert...	Class 2 (less inert...	Class 2 (less i
Acute aquatic toxicity MO...	Narcotic Amine	Narcotic Amine	Narcotic Amine	Narcotic Amine	Narcotic Amine	Narcotic Amine	Narcotic Amine	Narcotic Amine	Narcotic Amine	Narcotic Amine	Narcotic Amine	Narcotic Amine	Narcotic Amine	Narcotic Amine	Narcotic Ami
Aquatic toxicity classificat...	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Amines	Aliphatic Ami
Empiric															
Organic functional groups	Aliphatic amine...	Aliphatic amine...	Aliphatic amine...	Aliphatic amine...	Aliphatic amine...	Aliphatic amine...	Aliphatic amine...	Aliphatic amine...	Aliphatic amine...	Aliphatic amine...	Aliphatic amine...	Aliphatic amine...	Aliphatic amine...	Aliphatic amine...	Aliphatic ami
Structure similarity	25+88.9 %	18.2+57.1 %	25+96 %	23.5+96.3 %	22.2+96.3 %	28.6+95.2 %	30.8+94.7 %	22.2+88.9 %	40+92.3 %	26.7+95.7 %	33.3+94.1 %	18.2+76.9 %	44.4+90.9 %	36.4+93.3 %	33.3+88.9 %

**Mechanistic and structure-based profiling results**

# 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**

The screenshot shows the QSAR Toolbox 4.2 interface. The main window displays a list of chemical structures and a tree view of hazard categories. A 'Select endpoint' dialog box is open, showing the selection of 'Human Health Hazards Sensitisation' and 'EC3' as the target endpoint. Red boxes and arrows highlight the 'List' and 'Define' buttons, and the 'EC3' selection in the dialog.

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

The screenshot displays the QSAR Toolbox 4.2 interface. The top menu bar includes 'Input', 'Profiling', 'Data', 'Category definition', 'Data Gap Filling', and 'Report'. The 'Category definition' module is active, showing a 'Filter endpoint tree' on the left and a 'Category consistency wizard' window on the right. The wizard window is divided into 'Wizard pages' (Physicochemical similarity, Structural similarity, Mechanistic similarity, (Eco)tox experimental data, Options) and a main content area. The main content area shows '2D/3D parameters' (Boiling point, log Kow, Molecular Weight, Vapor Pressure, Water Solubility) and 'Physico-chemical data' (Boiling point, Partition Coefficient, Vapour pressure, Water solubility). Three callouts are present: '1' points to the 'Category consistency' button in the top toolbar; '2' points to the 'Sensitisation' and 'Skin' endpoints in the filter tree; '3' points to the 'Category consistency wizard' window.

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

The screenshot displays the QSAR Toolbox 4.2 interface with the 'Category consistency wizard' open. The wizard is titled 'Category consistency wizard' and is used to define the consistency of categories. The interface is divided into several sections:

- Wizard pages:** A vertical sidebar on the left lists the wizard pages: Physicochemical similarity, Structural similarity, Mechanistic similarity, (Eco)tox experimental data, and Options. The 'Structural similarity' page is currently selected.
- 2D/3D parameters:** A section for selecting parameters for physicochemical similarity, including Boiling point, log Kow, Molecular Weight, Vapor Pressure (Antoine), and Water Solubility.
- Physico-chemical data:** A section for selecting physical chemical properties, including Boiling point, Partition Coefficient, N-Octanol/Water, Vapour pressure, and Water solubility.
- Empiric profiles:** A section for selecting empiric profiles, divided into 'Plausible' and 'Unclassified' categories. The 'Plausible' category includes options like Chemical elements, Groups of elements, Lipinski Rule Oass, Organic functional groups (nested), Organic functional groups (US EP), Organic functional groups, Norber, and Structure similarity. The 'Unclassified' category includes Taxtomers unstable.
- Mechanistic profiles:** A section for selecting mechanistic profiles, divided into 'Suitable' and 'Plausible' categories. The 'Suitable' category includes Protein binding alerts for skin sensitization according to GHS, Protein binding alerts for skin sensitization by OASIS, and Protein binding by OASIS. The 'Plausible' category includes Aquatic toxicity classification by ECOSAR, Keratinocyte gene expression, OECD HPV Chemical Categories, Protein binding by OECD, Protein binding potency Cys (DPRA 13%), Protein binding potency GSH, Protein Binding Potency h-CLAT, Protein binding potency Lys (DPRA 13%), Respiratory sensitisation, Substance type, and US-EPA New Chemical Categories.
- Metabolisms:** A section for selecting metabolisms, divided into 'Suitable' and 'Plausible' categories. The 'Suitable' category includes Autoxidation simulator and Skin metabolism simulator. The 'Plausible' category includes Autoxidation simulator (alkaline medium), Dissociation simulator, and Hydrolysis simulator (neutral).
- Options:** A section for selecting options, including Select All, Unselect All, and Invert.

Callouts 1, 2, and 3 are used to highlight specific elements in the wizard:

1. Points to the 'Structure' parameter in the '2D/3D parameters' section.
2. Points to the 'Protein binding alerts for skin sensitization according to GHS' and 'Skin metabolism simulator' options.
3. Points to the 'OK' button.

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				
<b>Parameters</b>				
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
Water solubility	1E+06 mg/L	1E+06 mg/L	1E+06 mg/L	1E+06 mg/L
<b>Physical Chemical Properties</b>				
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: 0.00819 mm Hg
Water solubility	3/5	M: 1E+06 mg/L	M: 1E+06 mg/L	M: 1E+06 mg/L
<b>Human Health Hazards</b>				
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
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 %
Miscellaneous	4/27	M: Category C	M: Ambiguous	M: Ambiguous
Mouse Local Lymphnode Assay (LLNA)	2/3	M: sensitising	M: sensitising	M: sensitising
Undefined Assay	1/1	M: Positive		
<b>Profile</b>				
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 Cat...	1 x Skin sensitization Category...	1 x Skin sensitization...
Protein binding alerts for skin sensitization by OASIS	1 x Skin sensitization Ca...	1 x Skin sensitization Cat...	1 x Skin sensitization Category...	1 x Skin sensitization...
Schiff base formatio...	1 x Schiff base formatio...	1 x Schiff base formatio...	1 x Schiff base formation >> S...	1 x Schiff base forma...
Protein binding alerts for skin sensitization by OASIS	2 x No alert found	1 x Schiff base formatio...	2 x No alert found	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

The screenshot shows the QSAR Toolbox 4.2 interface. The 'Reports' menu is open, with 'Category' highlighted. A red box highlights the 'Report' button in the top toolbar. Another red box highlights the 'Category' option in the 'Reports' menu. A callout box with the number '1' points to the 'Category' option, and another callout box with the number '2' points to the 'Documents' pane showing a file named 'consistency\_SS\_list\_of\_amines'.

Filter endpoint tree...	1	2	3	4
Structure	<chem>NCCCCN</chem>	<chem>NCCCN</chem>	<chem>NCCCN</chem>	<chem>NCCCN</chem>
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				
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		

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 appear automatically in the report if available.
- Table with category members is also available.

Keep the default settings

# Category consistency elements Report

QSAR Toolbox 4.2 [Document 2] - Customize report content and appearance

**Wizard pages**

- Customization
  - Customize report
- Category
  - Category definition and members
  - Consistency check**
    - Options
- Data matrix
  - Options

**Reports**

- Prediction
- Data Matrix
- Category**
- QMF

**Documents**

- Document 1
- Document 2
- Category\_consistency\_SS\_lis

**Customization**

- Physicochemical similarity based on calculated parameter:**
  - Boiling point
  - log Kow
  - Molecular Weight
  - Vapor Pressure (Antoine method)
  - Water Solubility
- Physicochemical similarity based on experimental data:**
  - Tree position: Physical Chemical Properties#Boiling point
  - Tree position: Physical Chemical Properties#Partition Coefficient#N-Octanol/Water
- Structural similarity:**
  - Justification for selected structure similarity promoters
  - Comments on structural similarity
- Mechanistic similarity:**
  - Justification for selected mechanistic similarity promoters/metabolisms
  - Comments on mechanistic similarity
- Additional endpoints:**
  - Tree position: Human Health Hazards#Sensitisation

**Report**

	3	4
<chem>NCCCN</chem>	<chem>NCCCN</chem>	<chem>NCCCN</chem>
-2.04	M: -1.46	M: -1.46
1.25E+03 Pa	M: 0.232 mm Hg	M: 0.00819 mm Hg
1E+06 mg/L	M: 1E+06 mg/L	M: 1E+06 mg/L
>750 µg/L		
2.2 %	M: 1.85 %	M: 15.2 %
Ambiguous	M: Category A	M: Ambiguous
Positive		M: sensitising

**The category consistency elements are part from the "Consistency check" section in the wizard**

**Keep the default settings**

# Category consistency elements

## Report

QSAR Toolbox 4.2 [Document 2]

**Report**

**Wizard pages**

- Customization
- Customize report
- Category
- Category definition and members
- Consistency check**
- Options
- Data matrix
- Options

**Physicochemical similarity based on calculated parameters**

- Boiling point
- log Kow
- Molecular Weight
- Vapor Pressure (Antoine method)
- Water Solubility

Selected 2D/3D parameters for category members

Add / Remove

Parameter values Preview

**Physicochemical similarity based on experimental data**

- Tree position: Physical Chemical Properties#Boiling point  
Data filters:
- Tree position: Physical Chemical Properties#Partition Coefficient#N-Octanol/Water  
Data filters:
- Tree position: Physical Chemical Properties#Vapour pressure  
Data filters:
- Tree position: Physical Chemical Properties#Water solubility  
Data filters:

**Comments on physicochemical similarity**

Back Next Cancel Create report

The physicochemical **calculated parameters** selected in the Category consistency appear here

The physicochemical **experimental parameters** selected in the Category consistency appear here

Text justifying the selected parameters should be added by user

Keep the default settings

# Category consistency elements

## Report

QSAR Toolbox 4.2 [Document 2]

**Wizard pages**

- Customize report
- Category**
  - Category definition and members
  - Consistency check
- Options
- Data matrix
- Options

**Structural similarity**

Structure similarity profilers

Options: Select All, Unselect All, Invert

- Plausible
  - Chemical elements
  - Groups of elements
  - Lipinski Rule Oass
  - Organic functional groups
  - Organic functional groups (nested)
  - Organic functional groups (US EPA)
  - Organic functional groups, Norbert Haider (checkmol)
  - Structure similarity
- Unclassified
  - Tautomers unstable

Justification for selected structure similarity profilers

Add / Remove

- Structural similarity [Edit] [Preview]
- Chemical profile ("Organic functional groups") [Edit] [Preview]
- Chemical profile ("Structure similarity") [Edit] [Preview]

Comments on structural similarity

**Mechanistic similarity**

Justification for selected mechanistic similarity profiles/metabolisms

Comments on mechanistic similarity

Buttons: Back, Next, Cancel, Create report

Report button in top right

The profilers selected in the Category consistency appear here

Text justifying the selected profilers should be added by user

Keep the default settings

# Category consistency elements Report

QSAR Toolbox 4.2 [Document 2]

Reports

Prediction Data Matrix **Category** QM

Documents

Document 1

Document 2

Category\_consistency\_SS\_1

Customize report content and appearance

Wizard pages

Customization

Customize report

Category

Category definition and members

**Consistency check**

Options

Data matrix

Options

Mechanistic similarity

Mechanistic similarity profilers

Options

Select All Unselect All Invert

Suitable

- Protein binding alerts for skin sensitization according to GHS
- Protein binding alerts for skin sensitization by OASIS
- Protein binding by OASIS

Plausible

Unclassified

Mechanistic similarity simulators

Options

Select All Unselect All Invert

Suitable

- Autoxidation simulator
- Skin metabolism simulator

Plausible

- Autoxidation simulator (alkaline medium)
- Dissociation simulator
- Hydrolysis simulator (neutral)

Unclassified

Justification for selected mechanistic similarity profilers/simulators

Comments on mechanistic similarity

Additional endpoints

- Tree position: Human Health Hazards#Sensitisation

Data filters:

Category values for selected additional endpoints

Comments on

Back Next Cancel Create report

Report

The profilers and simulators selected in the Category consistency appear here

Text justifying the selected mechanism-based profilers should be added by user

Keep the default settings

-2.04			M: -1.46		
1.25E+03 Pa		M: 0.232 mm Hg	M: 0.00819 mm Hg		
1E+06 mg/L		M: 1E+06 mg/L	M: 1E+06 mg/L		
>750 µl					
2.2 %		M: 1.85 %	M: 15.2 %		
Ambiguous		M: Category A	M: Ambiguous		
Positive			M: sensitising		



# Category consistency elements

## Report

QSAR Toolbox 4.2 [Document 2]

The screenshot displays the QSAR Toolbox interface with the 'Customize report content and appearance' dialog box open. The 'Wizard pages' list on the left includes 'Consistency check', which is highlighted with a red box. The main panel shows various simulation options, with 'Suitable' and 'Plausible' categories selected. A 'Report' button in the top right corner is also highlighted with a red box. In the background, a table of experimental data is visible, with chemical structures and numerical values. Two callout boxes are present: a red one pointing to a data point and a blue one pointing to a summary of experimental data.

**Experimental data for the category members supporting the consistency of the category**

	3	4
<chem>NCCCN</chem>	<chem>NCCCN</chem>	<chem>NCCCN</chem>
M: -2.04	M: -1.46	M: -1.46
M: 1.25E+03 Pa	M: 0.232 mm Hg	M: 0.00819 mm Hg
M: 1E+06 mg/L	M: 1E+06 mg/L	M: 1E+06 mg/L

**Summary of how available experimental data verify that the category is robust (i.e. category hypothesis and consistency check)**

Keep the default settings

# Category consistency elements

## Report

QSAR Toolbox 4.2 [Document 2]

Keep the default settings

“Report basket” stores automatically all category elements which have been applied by the user. It is visualized by clicking *Add/Remove* button.

New items with external content can be also included

Finally, Click *Create report*

# Category consistency elements Report

QSAR Toolbox 4.2 [Document 2]

**Wizard pages**

- Customization
  - Customize report
- Category
  - Category definition and members
  - Consistency check
  - Options
- Data matrix
  - Options

**Generated report files**

The following files were generated.

- Category report
- Data matrix

Open Save as

**Two files are generated:**

- Category report - includes all the information related to the category in \*. pdf format
- Data matrix – includes information for the category (as parameters, profilers, data) in Excel \*.xlsx format

Category 1B	M: Category 1B	M: Category 1B
sensitising	M: 1.85 %	M: sensitising
Ambiguous	M: Category A	M: Ambiguous
sensitive		M: sensitising

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

# Category consistency elements

## Report

### 1. Category definition section:

Chemicals category 1 / 28

#### QSAR Toolbox report for category

##### 1. Category definition

1.1. Category definition  
Not provided by the user

manually editable field

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)

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

manually editable field

1.3. Category hypothesis

Not provided by the user

manually editable field





Chemicals category 2 / 28

#### 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	NCCCNCN	
2	107-15-3	Ethylenediamine	NCCN	
3	111-40-0	Diethylenetriamine	NCCNCCN	
4	111-41-1	dicyclopentylsilylanedi	NCCNCCO	

Purity / Impurity

Not provided by the user

manually editable field

#### 2. Consistency check

2.1. Physicochemical similarity

Selected 2D/3D parameters for category members

manually editable field

### 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

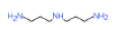

## 2. Consistency check section:

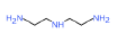
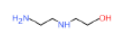
## Report

### 2. Consistency check

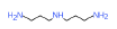

#### 2.1. Physicochemical similarity

Selected 2D/3D parameters for category members

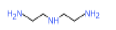
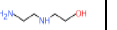
	1	2
		
Boiling point, °C	228	103
log Kow	-1.15	-1.62
Molecular Weight, Da	131	60.1
Vapor Pressure (Antoine method), mm Hg	0.0913	19
Water Solubility, mg/L	1E+06	1E+06

	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

Not provided by the user

manually edit

#### 2.2. Structural similarity

Structural similarity Options

Mode: Hologram, CombineAllFeatures



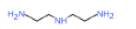
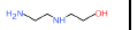
Measure:

- 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		
		

### 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")

<chem>NCCCCNCCN</chem>	<chem>NCCCCN</chem>	<chem>NCCCCNCCN</chem>
No alert found	No alert found	No alert found

<chem>NCCCCNCCO</chem>
No alert found

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

<chem>NCCCCNCCN</chem>	<chem>NCCCCN</chem>	<chem>NCCCCNCCN</chem>
No alert found	No alert found	No alert found

<chem>NCCCCNCCO</chem>
No alert found

Tables with generated metabolites for each analogue with profiling result

P1	M1 P1	M2 P1
<chem>NCCCCNCCN</chem>	<chem>N</chem>	<chem>NCCCCNCC(=O)O</chem>
No alert found	No alert found	No alert found

M3 P1	M4 P1	M5 P1
<chem>NCCCCNCC=O</chem>	<chem>NCCCCN=O</chem>	<chem>NCCCCNCC=O</chem>
Aldehydes	Bis aldehydes	Aldehydes

P2	M1 P2	M2 P2
<chem>NCCCCN</chem>	<chem>N</chem>	<chem>NCCCC(=O)O</chem>
No alert found	No alert found	No alert found

Graphics with distribution of alerts across metabolites

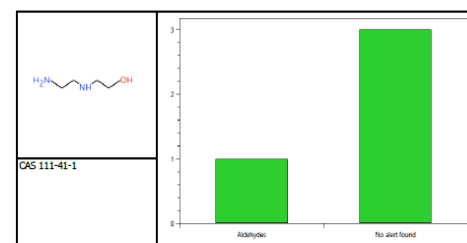
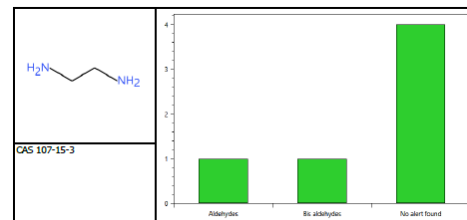
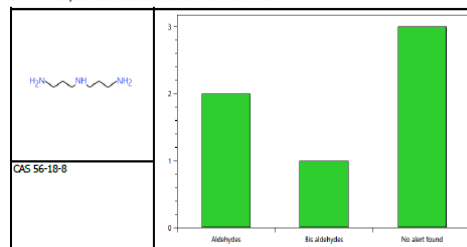


Table summarizing number of metabolites including parent with specific alerts

Protein binding alerts for skin sensitization by OASIS	P1	P2	P3	P4
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 manually editable field  
 Category values for selected additional endpoints

	1	2
	<chem>NCCCCNC</chem>	<chem>NCCCCN</chem>
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
	<chem>NCCCCN</chem>	<chem>NCCCCO</chem>
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

The screenshot shows the QSAR Toolbox 4.2 interface. The main window is titled 'Customize report content and appearance'. On the left, there is a 'Wizard pages' pane with 'Data matrix' selected under the 'Data matrix' section. The main area shows a 'Generated report files' dialog box with a list of reports: 'Category report' and 'Data matrix'. The 'Data matrix' report is highlighted with a red box and labeled '1'. Below the list, the 'Open' button is highlighted with a red box and labeled '2'. The background shows the 'Category definition' wizard page with various options and buttons.

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



# Category consistency elements

## Report

### Data matrix

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
1	Substance identity		Chemical #1		Chemical #2		Chemical #3		Chemical #4						
2	Structure		<chem>NCCNCCCN</chem>		<chem>NCCNCCO</chem>		<chem>NCCN</chem>		<chem>NCCN</chem>						
3	CAS number		56-18-8		111-41-1										
4	Chemical name		Iminobis-3-propylamine		dicyclopentylsilanediol										
5	Other identifier														
6	SMILES		NCCNCCCN		NCCNCCO										
7	Parameters		unit												
8	Vapor Pressure (Antoine method)		mm Hg		0.0913		0.00693								
9	log Kow				-1.15		-2.13								
10	Molecular Weight		Da		131.22498		104.15528		60.10352		103.17322				
11	Boiling point		°C		228.13		210.9		103.44		189.14				
12	Water Solubility		mg/L		1000000		1000000		1000000		1000000				
13	Profilers														
14	General Mechanistic														
15	Protein binding by OASIS		No alert found;		No alert found;		No alert found;		No alert found;		No alert found;		No alert found;		
16	Protein binding by OASIS, with Autoxidation		No alert found;		No alert found;		No alert found;		No alert found;		No alert found;		No alert found;		
17	Protein binding by OASIS, with Skin metabolism simulator		Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes;		Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes;		Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes;		Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes;		Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes;		Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes;		
18	Endpoint Specific														
19	Protein binding alerts for skin sensitization		No alert found;		No alert found;		No alert found;		No alert found;		No alert found;		No alert found;		
20	Protein binding alerts for skin sensitization		No alert found;		No alert found;		No alert found;		No alert found;		No alert found;		No alert found;		
21	Protein binding alerts for skin sensitization		No alert found;		No alert found;		No alert found;		No alert found;		No alert found;		No alert found;		
22	Protein binding alerts for skin sensitization		No alert found;		No alert found;		No alert found;		No alert found;		No alert found;		No alert found;		
23	Protein binding alerts for skin sensitization		No alert found;		No alert found;		No alert found;		No alert found;		No alert found;		No alert found;		
24	Protein binding alerts for skin sensitization by OASIS, with skin metabolism simulator		Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes;		Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes;		Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes;		Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes;		Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes;		Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes;		
25	Protein binding alerts for skin sensitization		Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes;		Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes;		Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes;		Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes;		Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes;		Schiff base formation >> Schiff base formation with carbonyl compounds >> Aldehydes;		
26	Protein binding alerts for skin sensitization		No alert found;		No alert found;		No alert found;		No alert found;		No alert found;		No alert found;		
27	Protein binding alerts for skin sensitization		Skin sensitization Category 1B >>		No alert found;		Skin sensitization Category 1B >>		Skin sensitization Category 1B >>		Skin sensitization Category 1B >>		Skin sensitization Category 1B >>		

Parameters values and profilers used in the workflow

Profilers accounting for metabolism if applied

	Substance identity		Chemical #1		Chemical #2		Chemical #3		Chemical #4							
33	Physical Chemical Properties#Boiling point															
34	environment	endpoint	value	unit	value	unit	value	unit	value	unit	value	unit	value	unit	value	unit
35	Boiling point	none			239	°C			117	°C	SRC		207	°C	SRC	
36	Physical Chemical Properties#Vapour															
37	environment	endpoint	value	unit	value	unit	value	unit	value	unit	value	unit	value	unit	value	unit
38	Vapour pressure	none			0.00819	mm Hg	SRC		12	mm Hg	SRC		0.232	mm Hg	SRC	
39	environment	endpoint	value	unit	value	unit	value	unit	value	unit	value	unit	value	unit	value	unit
40	N-Octanol/Water	none							-2.04		SRC					
41	Human Health Hazards#Sensitisation															
42	environment	endpoint	value	unit	value	unit	value	unit	value	unit	value	unit	value	unit	value	unit
43	Sensitisation	none							99.5	µM						
44																
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47																
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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.