QSAR TOOLBOX

The OECD QSAR Toolbox for Grouping Chemicals into Categories

OECD QSAR Toolbox v.4.1

Examples illustrating customized search (Query Tool) in Toolbox

Outlook

- **Background**
- Objectives
- Overview of Query tool
- Query tool window
- The exercise
- Workflow process
- Save QT searches

Background

- This is a step-by-step presentation designed to take the user through the functionalities of Query tool (QT) engine implemented in Toolbox

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Objectives

This presentation demonstrates a number of functionalities of the Query tool (QT):

- Identifying chemicals with specified structural fragments
- Identifying chemicals answering specific structural fragment criteria combined with parametric ranges
- Identifying chemicals answering specific combination of data, structural fragments and parametric data

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Overview of Query tool

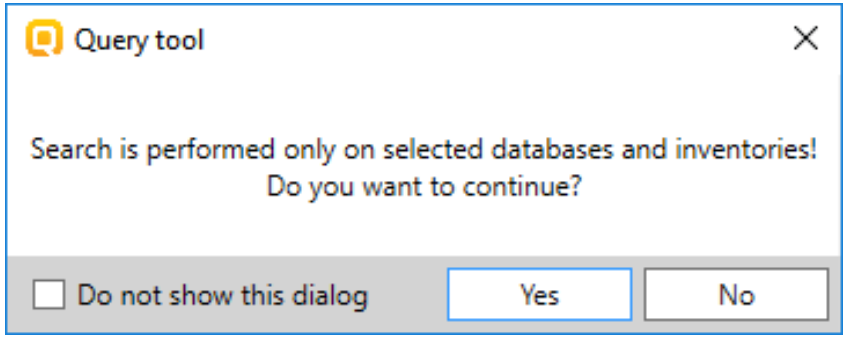
Goal: Searching for chemicals by structure, sub fragments, phys-chem properties and experimental data

- **Chemical identifier search**
  - CAS
  - Name
  - Molecular structures
- **Parameter search**
  - Calculated 2D parameters
  - Calculated 3D parameters
- **Data search**
  - Search for data and metadata within imported databases
- **Extended search**
  - Profiling
  - Substructure
  - Similarity

Overview of Query tool
Prerequisites

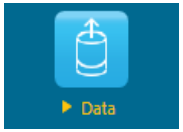
•The Query tool functionality search for single structures matching desired criteria.

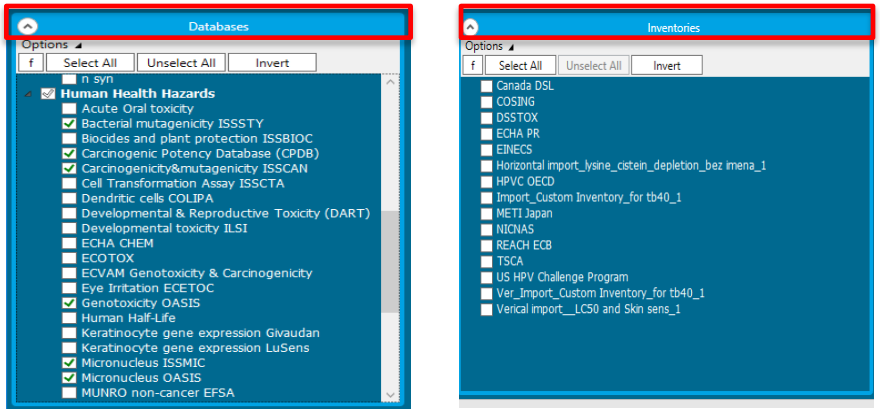
•The Query tool functionality search for chemicals within the selected databases and inventories only



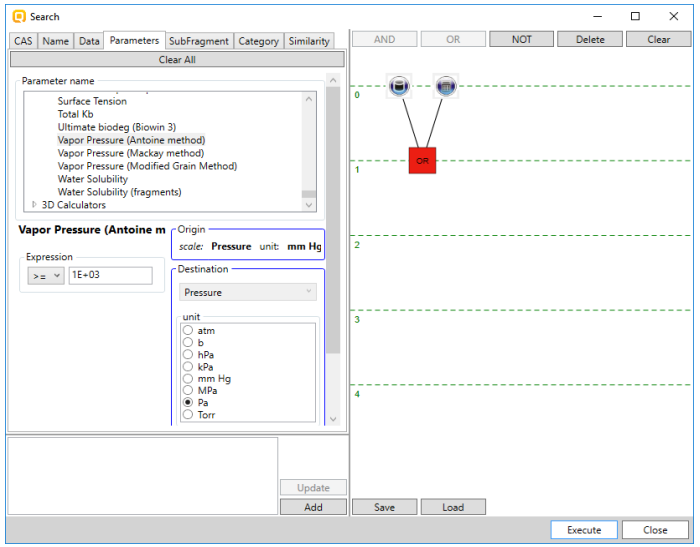
Overview of Query tool
Procedure for defining query

Step 1: Select databases/inventories of interest in the *Data* module

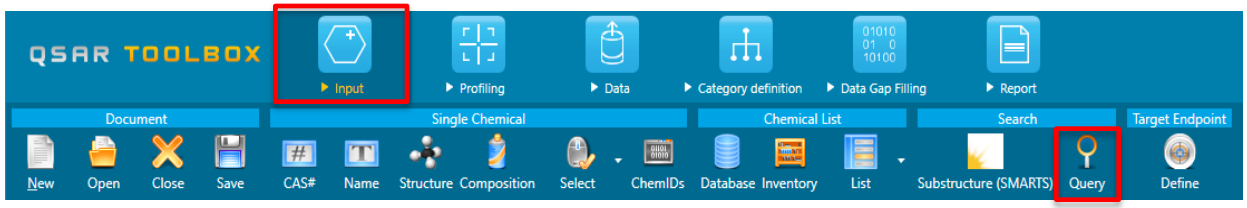




Step 3: Specify criteria for searching structures



Step 2: Click *Query* button



Outlook

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- **Query tool window**
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- Workflow process
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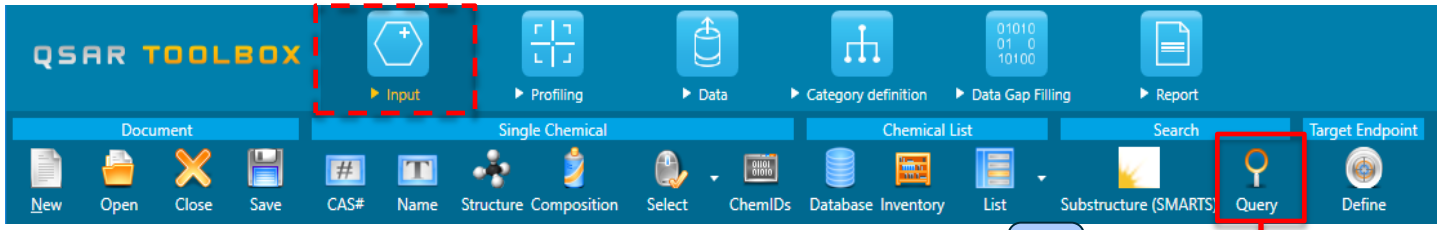
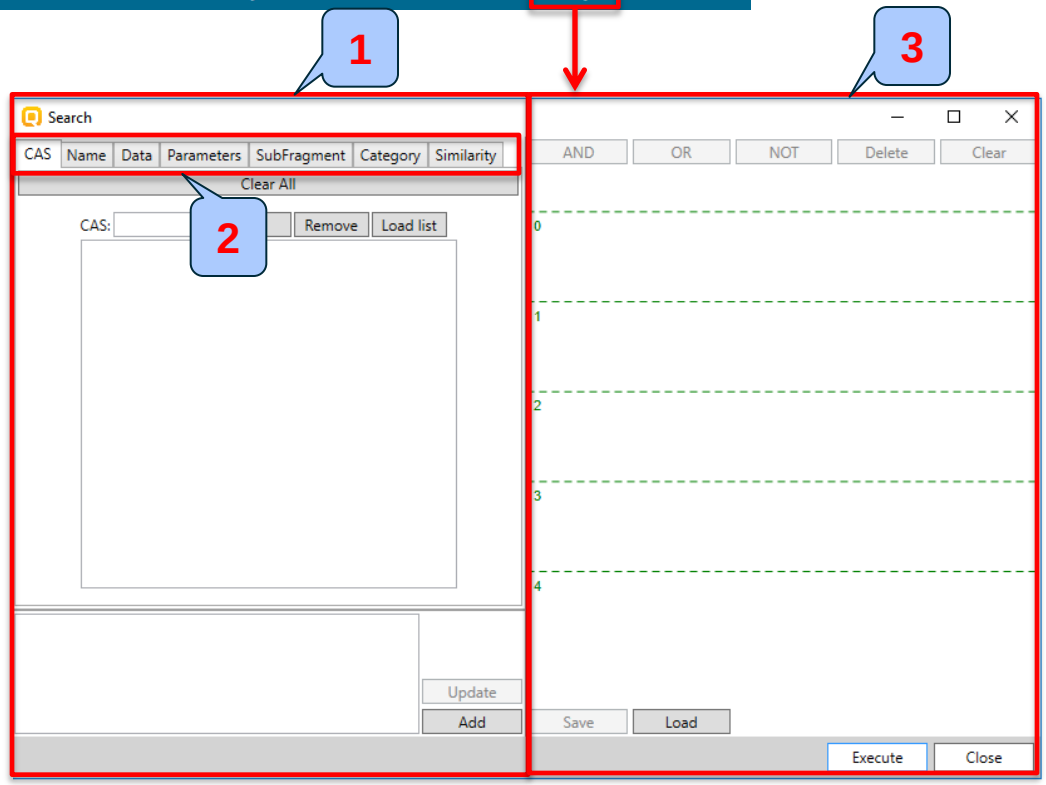
Query tool window

- The Query tool is easily accessible on the Toolbox input panel



The main components of Query tool include:

- Query edit panel (1)
  - search group panel (2)
- Query tree logic panel (3)



Outlook

- Background
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- Overview of Query tool
- Query tool window
- **The exercise**
- Workflow process
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The Exercise

- In this exercise we will demonstrate the following queries:
  - Subfragment search for:
    - *Substituted diphenyl amine (Example 1)*
    - *Aliphatic halogens (Example 2)*
  - Combination of Environmental Data (BCF) and 3D parameters (D*max*) *(Example 3)*
  - Combination of predefined category (Aldehydes) and ecotox data (LC50<1mg/l) *(Example 4)*
  - Combination of positive Ames; positive Carcinogenicity data and Subfragment search (*Epoxides*) *(Example 5)*
  - Combination of Skin sensitization data (EC3) and predefined category (*Aldehydes*) *(Example 6)*

Outlook

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- The exercise
- **Workflow process**
- Save QT searches

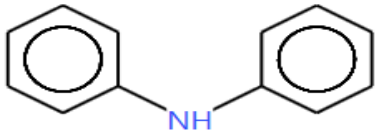
Subfragment search for identifying chemicals

Substituted diphenyl amine

Example 1

Search for structures that meet the structural requirements:

- *Substituted diphenyl amine*



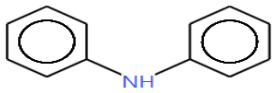
N(c1ccccc1)c1ccccc1

Subfragment search for identifying chemicals

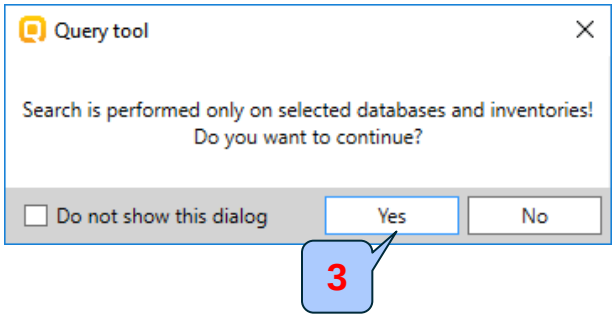
Procedure for defining

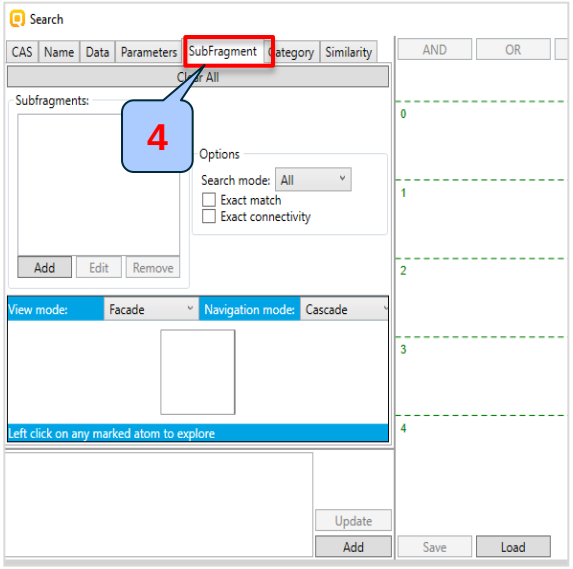
Example 1

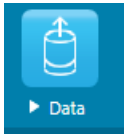
Substituted diphenyl amine

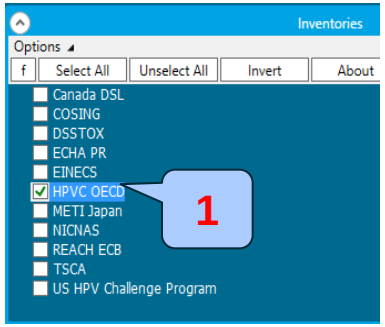


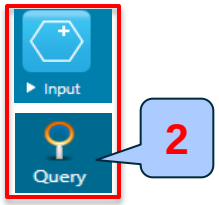
N(c1ccccc1)c1ccccc1











QT procedure starts with selecting databases/inventories used for searching the desired criteria:
1. **Select** HPVC OECD inventory located under Data section**.** No databases have been selected in this exercise; 2. Click **Query** button located under **Input** section; The message informs the user that search will be performed on selected databases or inventories only 3. Click **Yes**; 4. Query panel appears; 5. Select **SubFragment** panel;

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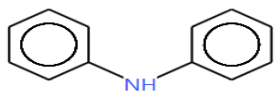
Subfragment search for identifying chemicals

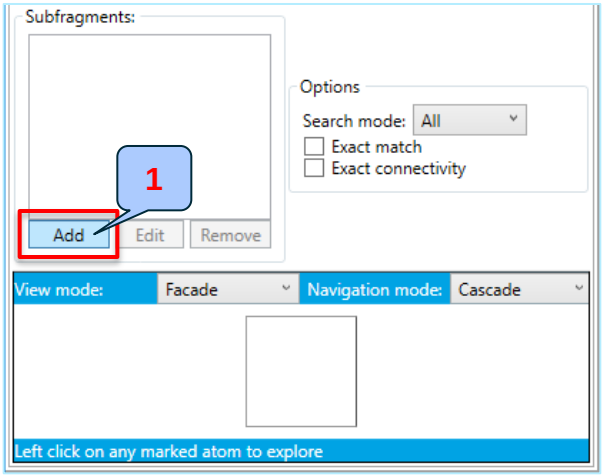
Procedure for defining

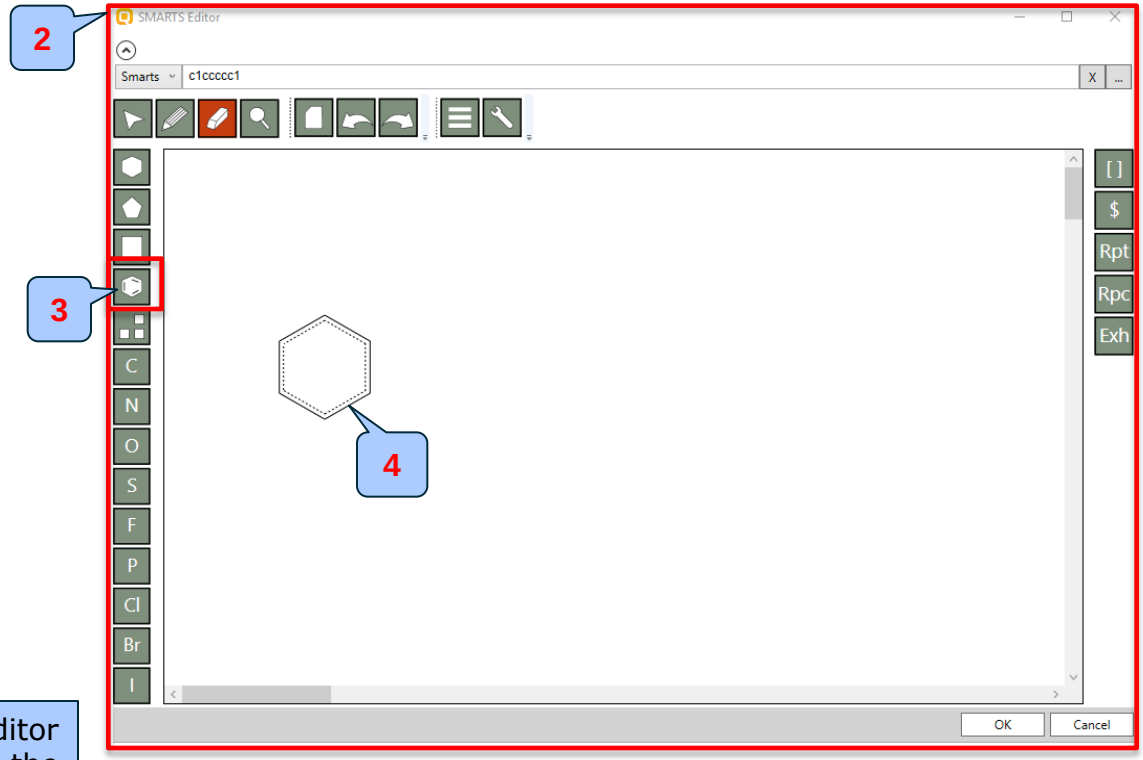
Example 1

Substituted diphenyl amine



N(c1ccccc1)c1ccccc1





1. Click **Add** button; 2. The SMARTS Editor window appears; 3. Perform **left click** on the benzene ring from the Template panel 4. **Left click** on the blank plot in order to put benzene fragment;

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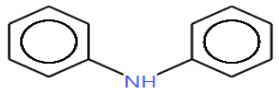
Subfragment search for identifying chemicals

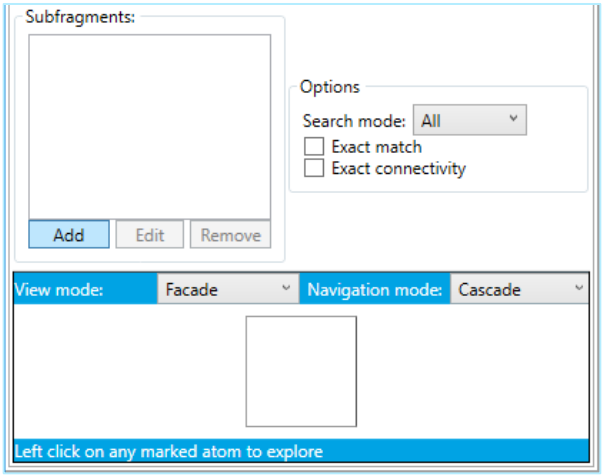
Procedure for defining

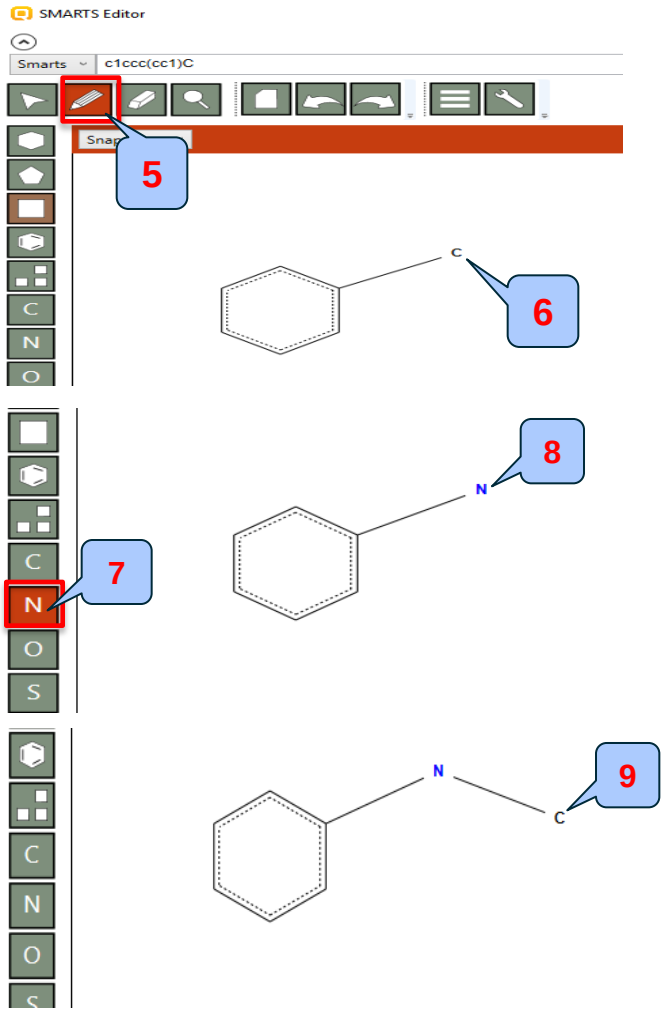
Example 1

Substituted diphenyl amine



N(c1ccccc1)c1ccccc1





5. Click the pencil button to draw a single bond; 6. Click near to one of the C atom from the benzene ring to draw a single bond; 7.Click **N** atom from the templates; 8. Put the selected N atom over the C atom from the single bond; 9. Repeat step 5 and draw a single bond to the N atom from NH2 group;

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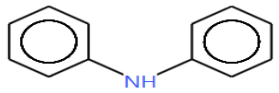
Subfragment search for identifying chemicals

Procedure for defining

Example 1

Substituted diphenyl amine



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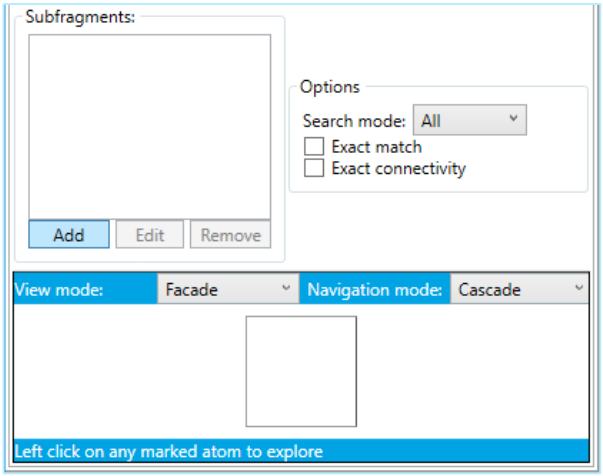

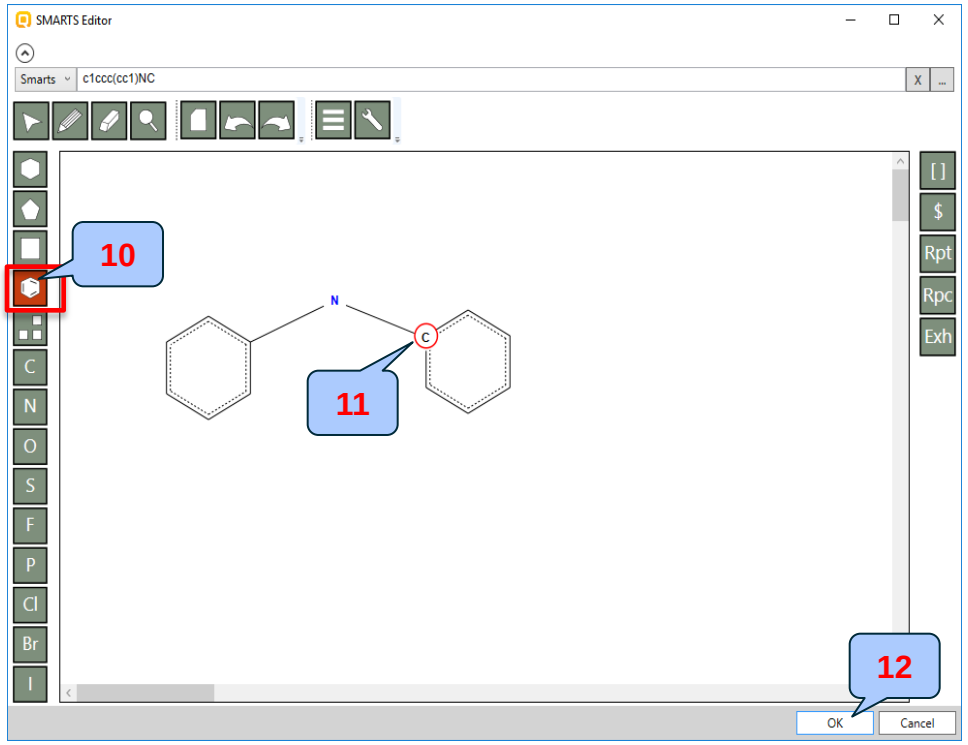

10. Left click over benzene ring from the template in order to take benzene ring 11. Left click over the C atom in order to define second benzene ring to the NH group 12. Click **OK**.

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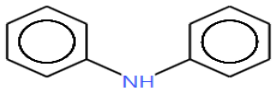
Subfragment search for identifying chemicals

Procedure for defining

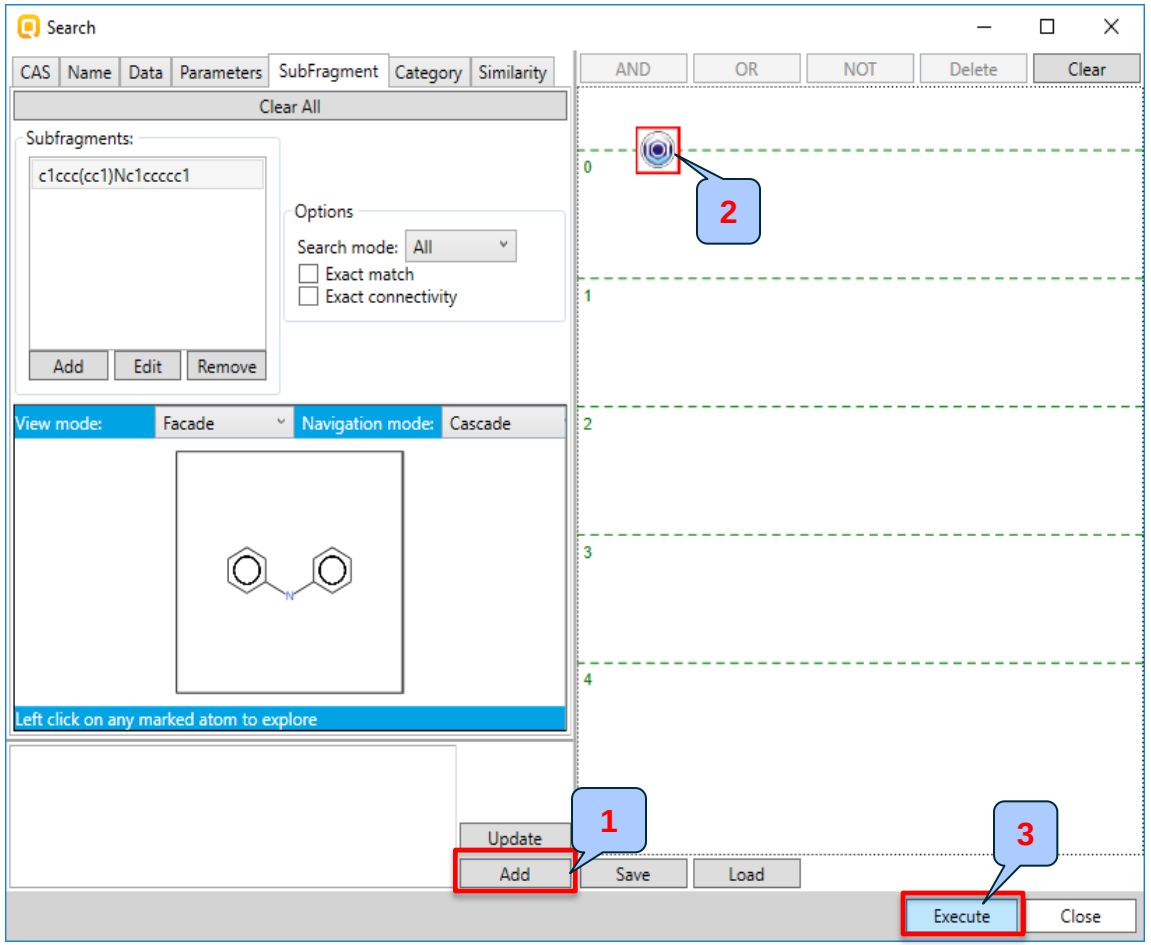
Example 1

Substituted diphenyl amine



N(c1ccccc1)c1ccccc1

1. Click **Add** button; 2. The defined query appears on logic panel; 3. Double click over the query or click **Execute** button to execute it.

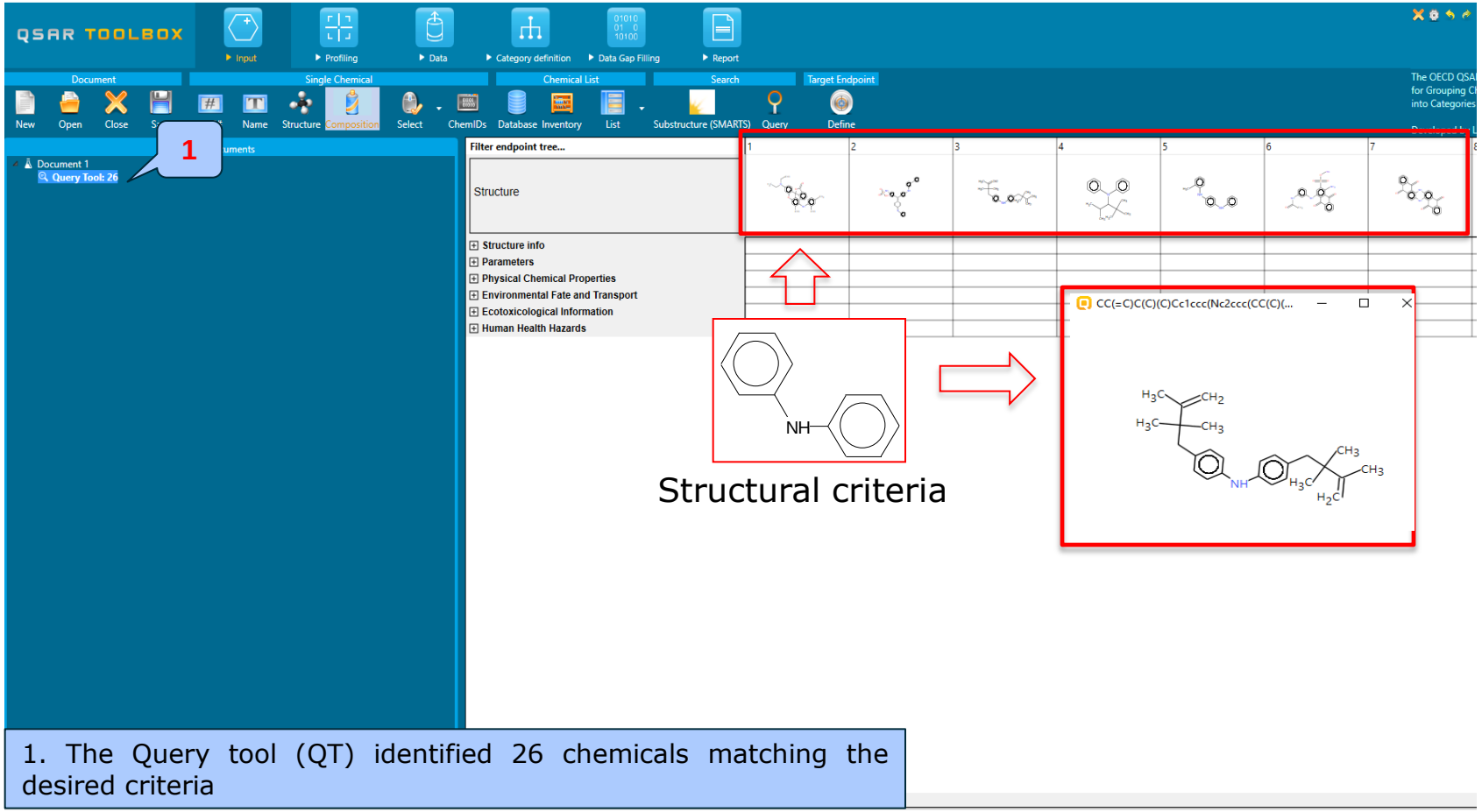


Subfragment search for identifying chemicals

Procedure for defining

Example 1

Substituted diphenyl amine



1. The Query tool (QT) identified 26 chemicals matching the desired criteria

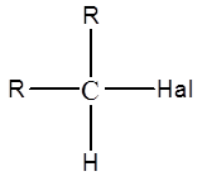
Subfragment search for identifying chemicals

Aliphatic halogens

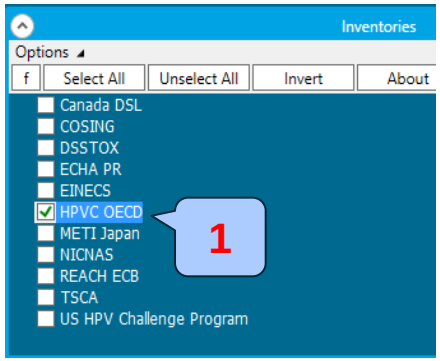
Example 2

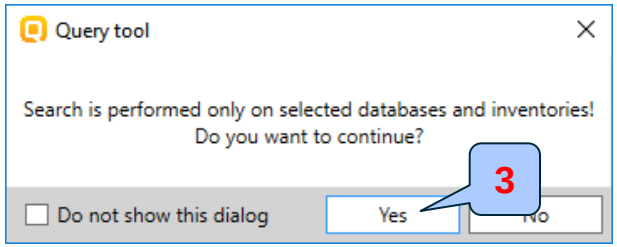
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I





- **HPVC OECD** inventory has been selected
- Search for discrete chemicals

1. Select the **HPVC OECD** inventory (no database has been selected in this case, only HPVC OECD) located under *Data* section; 2. Click **Query** button under *Input* section; 3. Click **Yes**

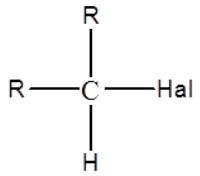
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

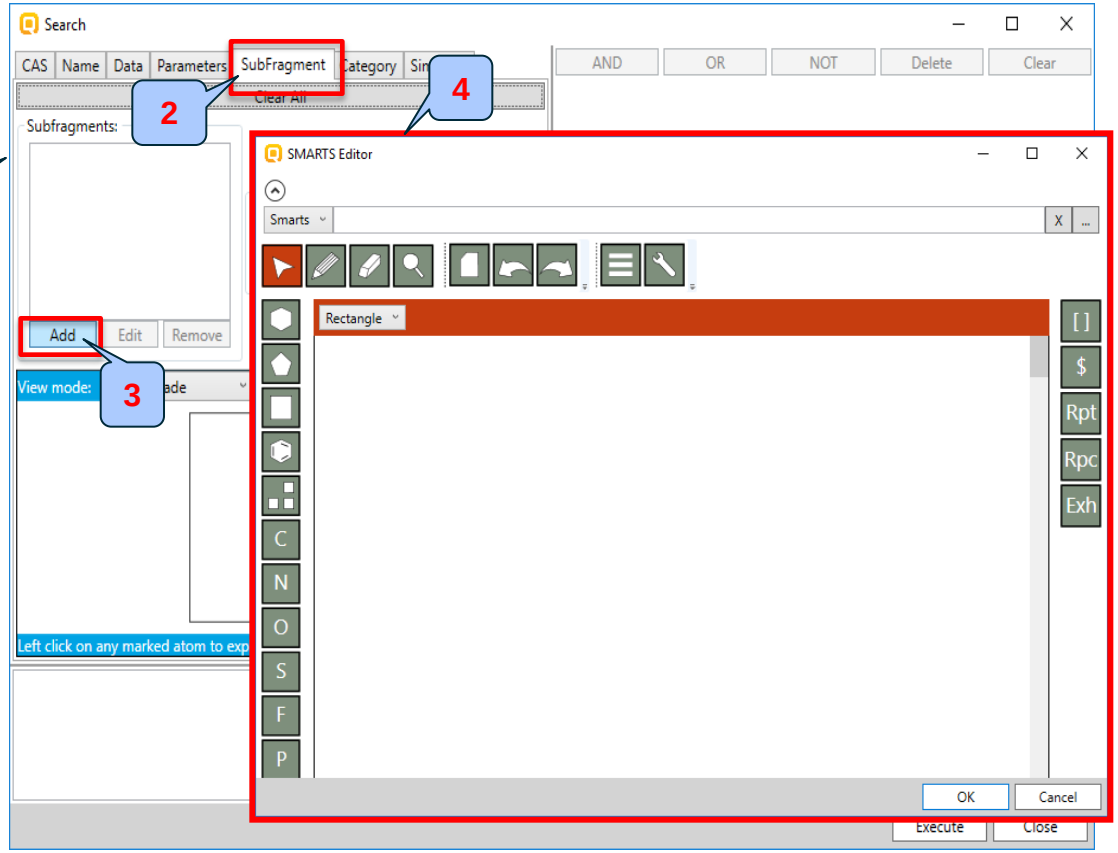
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

- **HPVC OECD** inventory has been selected
- Search for discrete chemicals



1. Query panel appears; 2. **Go** to SubFragment panel; 3. **Click** "Add" button; 4. "SMARTS Editor" window appears;

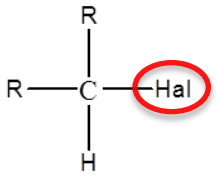
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

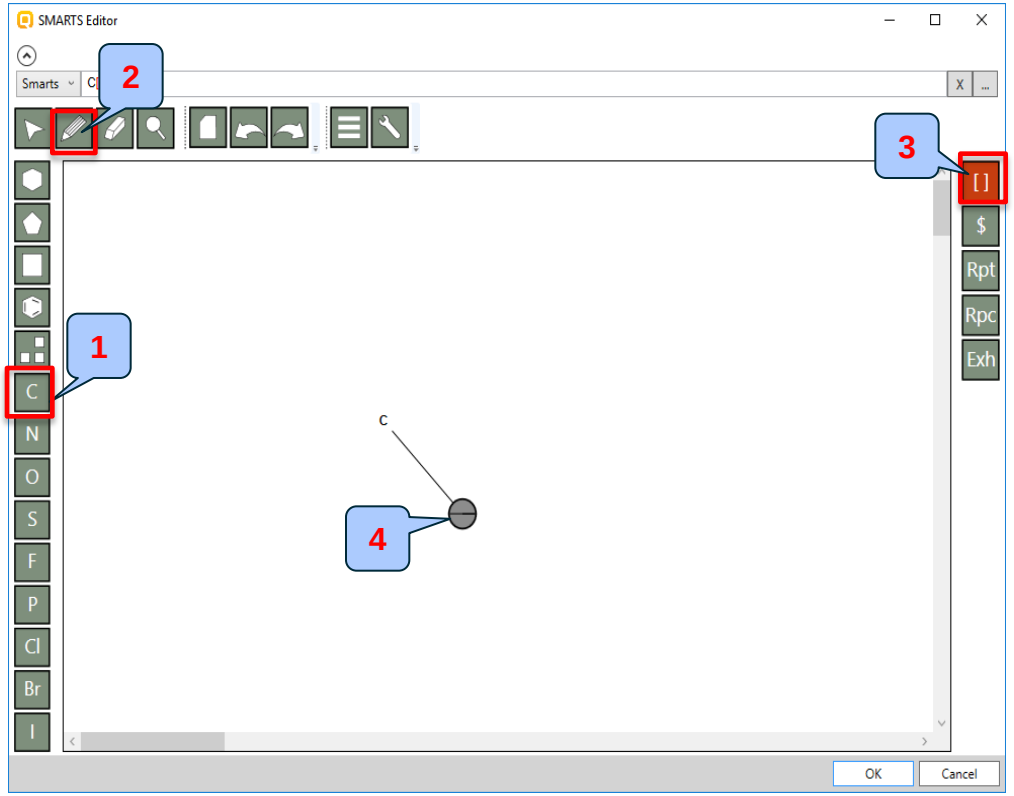
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define **Enumeration** fragment with three members (halogen atoms)



1. Left click the **C** symbol from the template and then left click in the drawing panel;
2. Left click the **pencil** button and draw a single bond;
3. Select the "**[ ]**" (enumeration) button;
4. Click over one of the carbon atoms;

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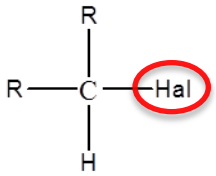
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

Search for structures that meet the structural requirements:

- *Aliphatic halogens*



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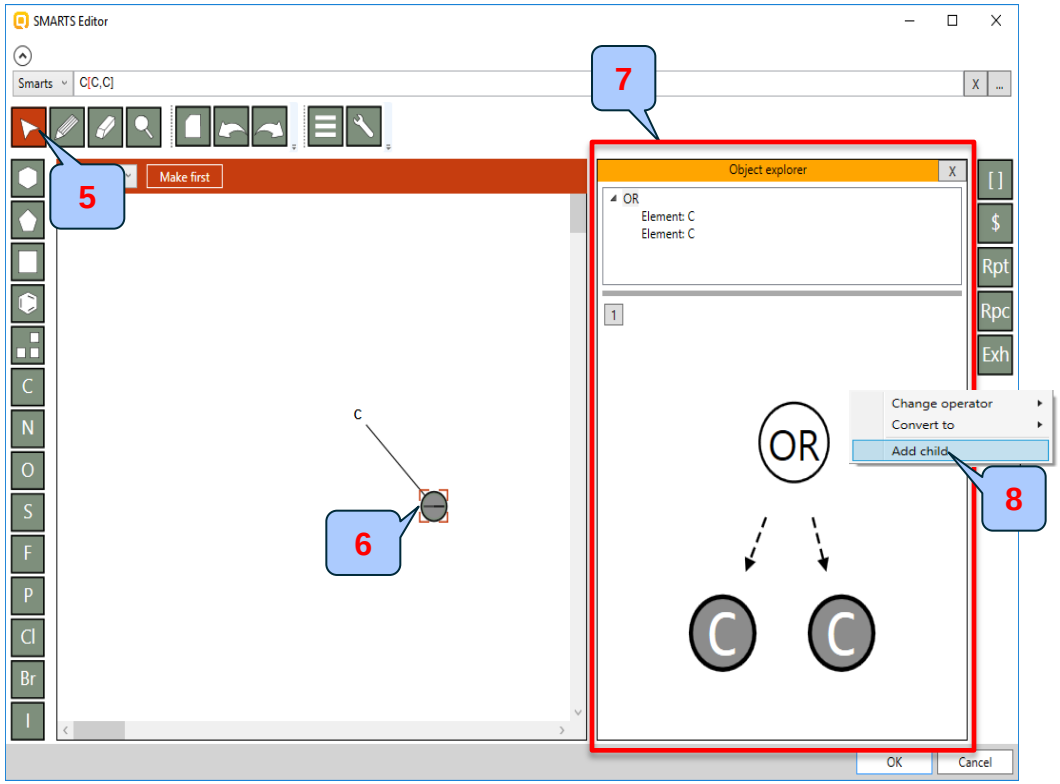
•Define **Enumeration** fragment with three members (halogen atoms)



5. Click the **selection tool**; 6. Click the new object; 7. *Object explorer* panel appears; 8. Right click over the ***OR*** expression node and select **Add child**;

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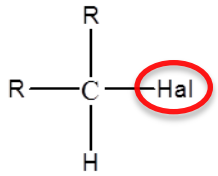
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

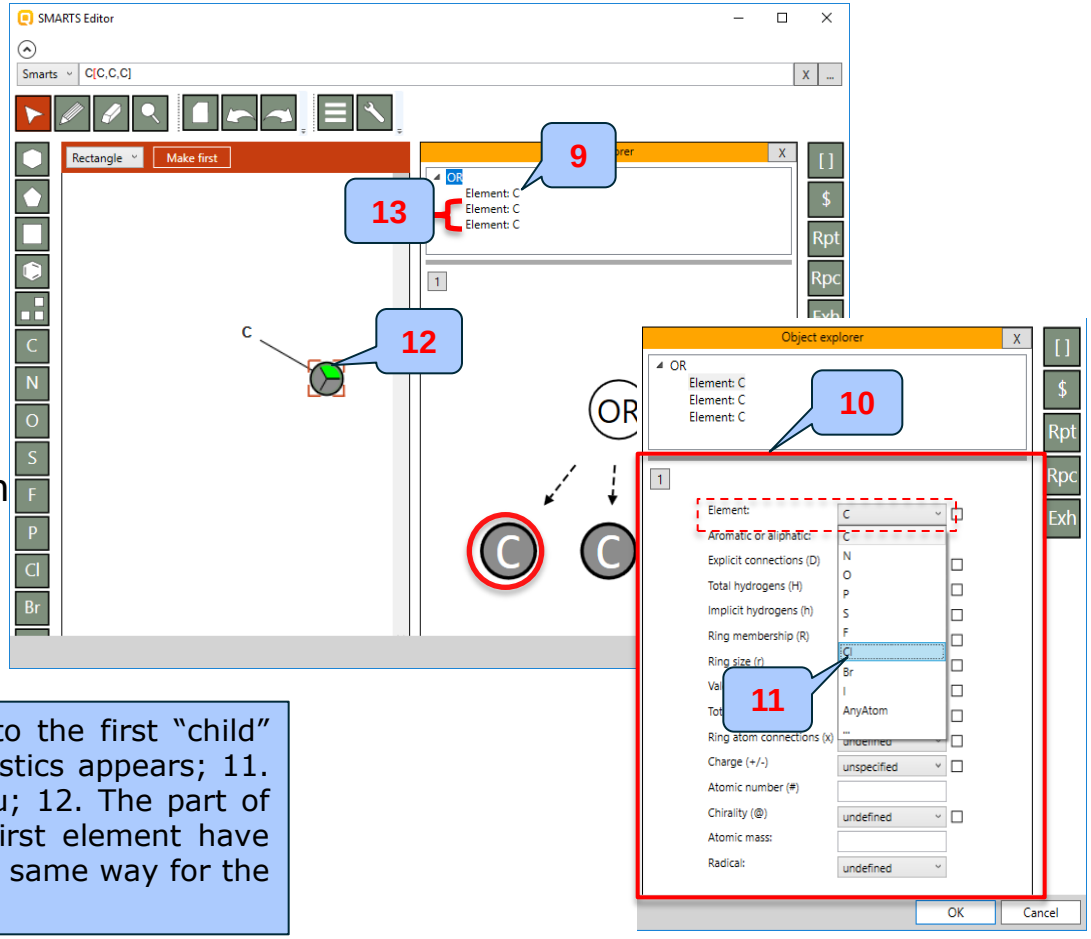
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define **Enumeration** fragment with three members (halogen atoms)



9. Click the first element which corresponds to the first "child" query; 10. The panel with the atom characteristics appears; 11. Select "***Cl***" from the *Element* drop-down menu; 12. The part of the SMARTS fragment corresponding to the first element have colored in green. 13. Select "**Br**" and "**I**" in the same way for the rest two elements , successively.

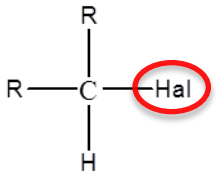
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

Search for structures that meet the structural requirements:

- *Aliphatic halogens*



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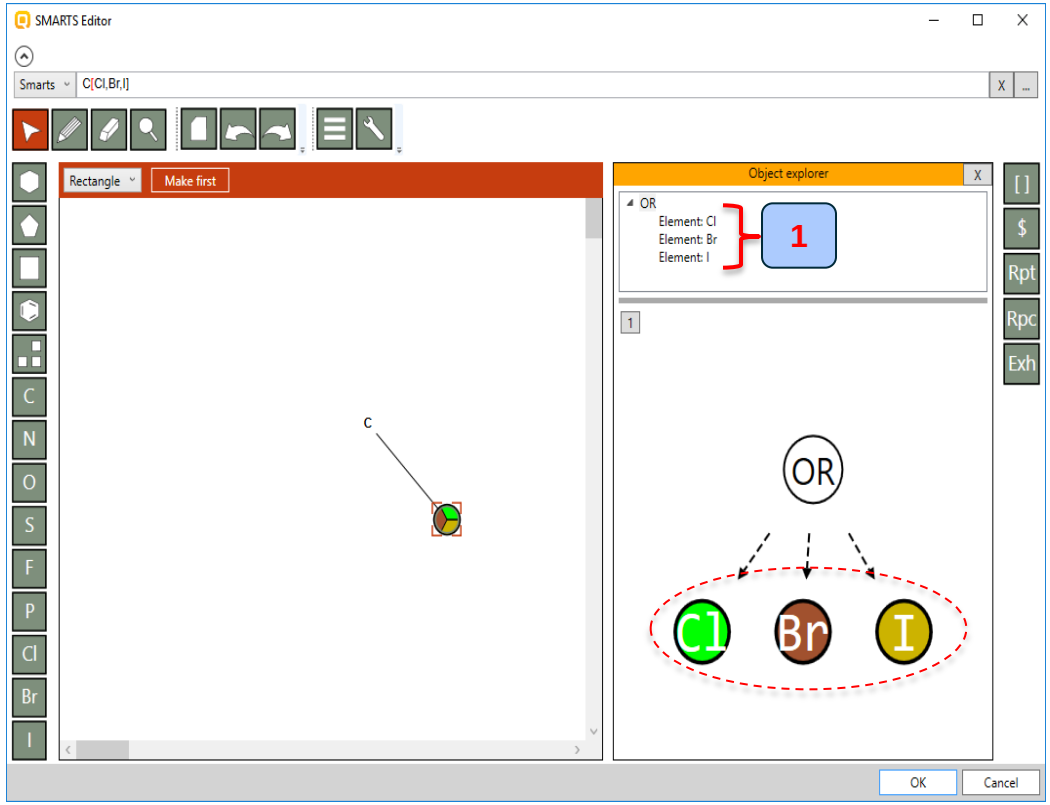
Hal – Cl, Br, I

•Define **Enumeration** fragment with three members (halogen atoms)



Hal substituent is ready when all elements are selected (1). Now we can continue with defining of the rest substituents of the carbon atom (see the general structure above).

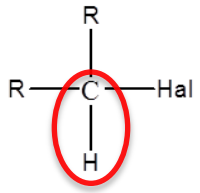
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

Search for structures that meet the structural requirements:

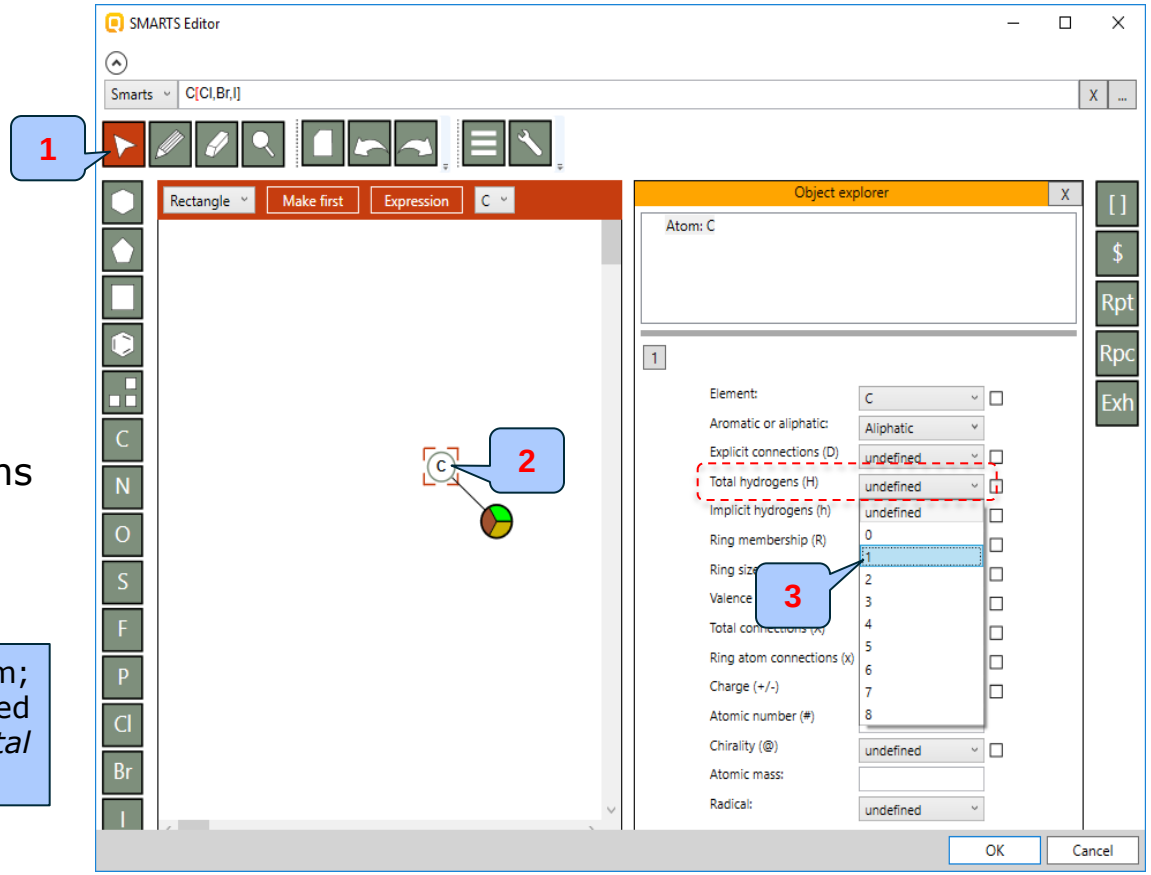
- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define the number of hydrogens bonded to **C atom**

1. Click *Selection tool*; 2. Click *C* atom; 3. Define this carbon atom to be bonded with total one H atom from the *Total hydrogens* drop-down menu



Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

Search for structures that meet the structural requirements:

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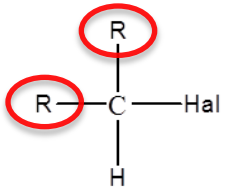
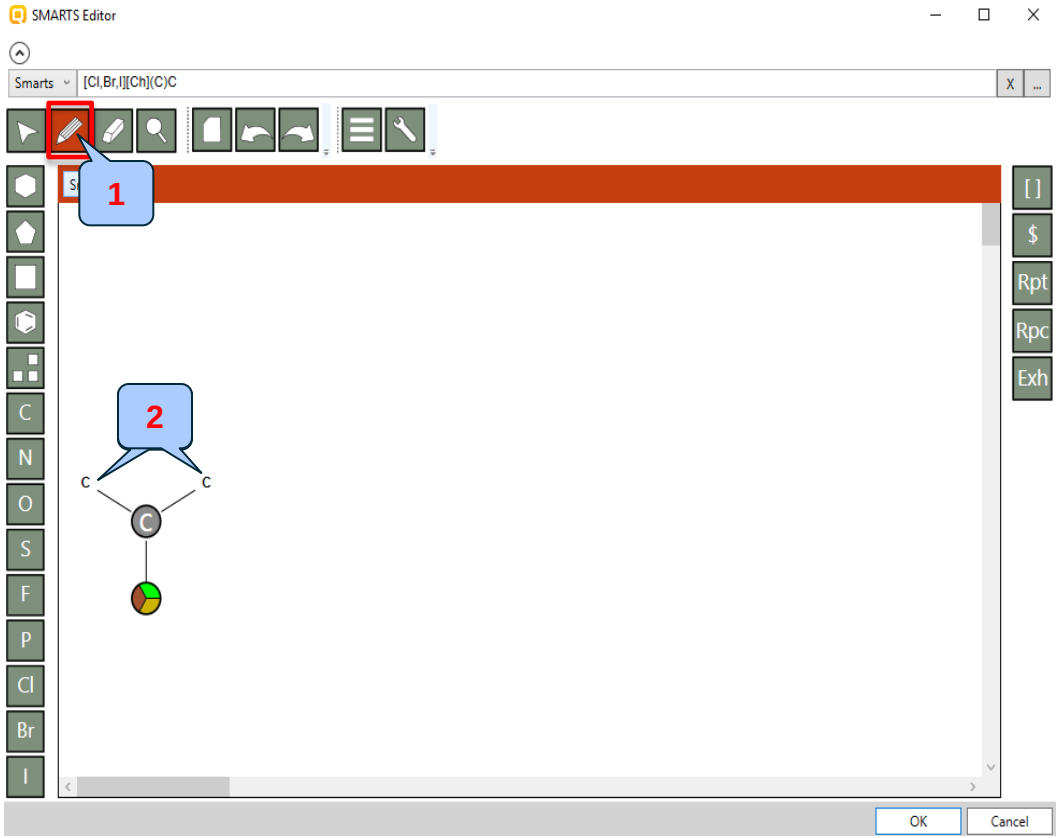


R – Any atom except H
Hal – Cl, Br, I

•Define fragment R including any type atom except H atom

1. Select the pencil button; 2. Draw two single bonds to the C atom;



Continued on the next slide

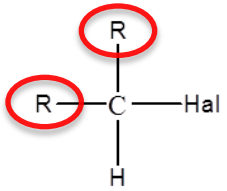
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

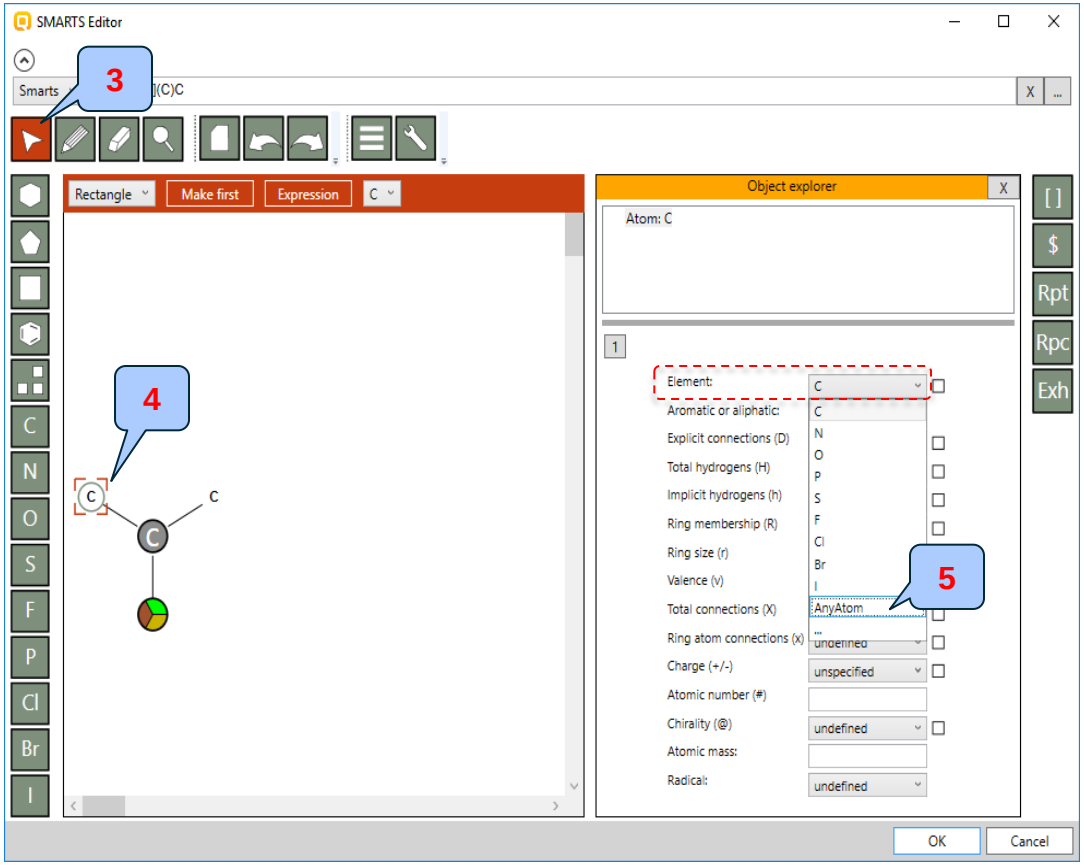
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define fragment R including any type atom except H atom



3. Click *Selection tool*; 4. Select C atom**;**
5. Select "***Any atom***" from the *Element* drop-down menu;

Continued on the next slide

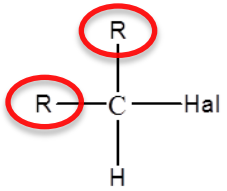
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

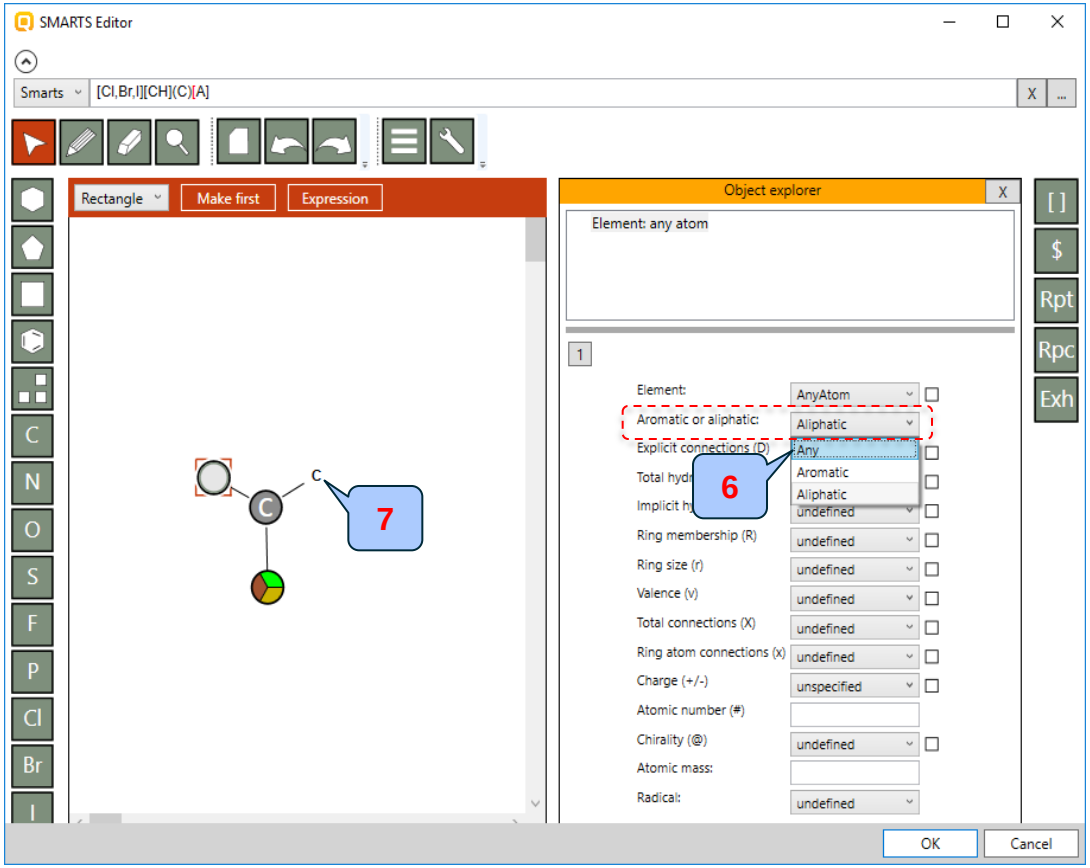
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define fragment R including any type atom except H atom



6. Select **Any** from the *Aromatic or aliphatic* drop-down menu; 7.Repeat the steps from 3 to 6 for the second carbon atom

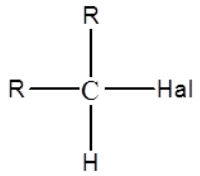
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

Search for structures that meet the structural requirements:

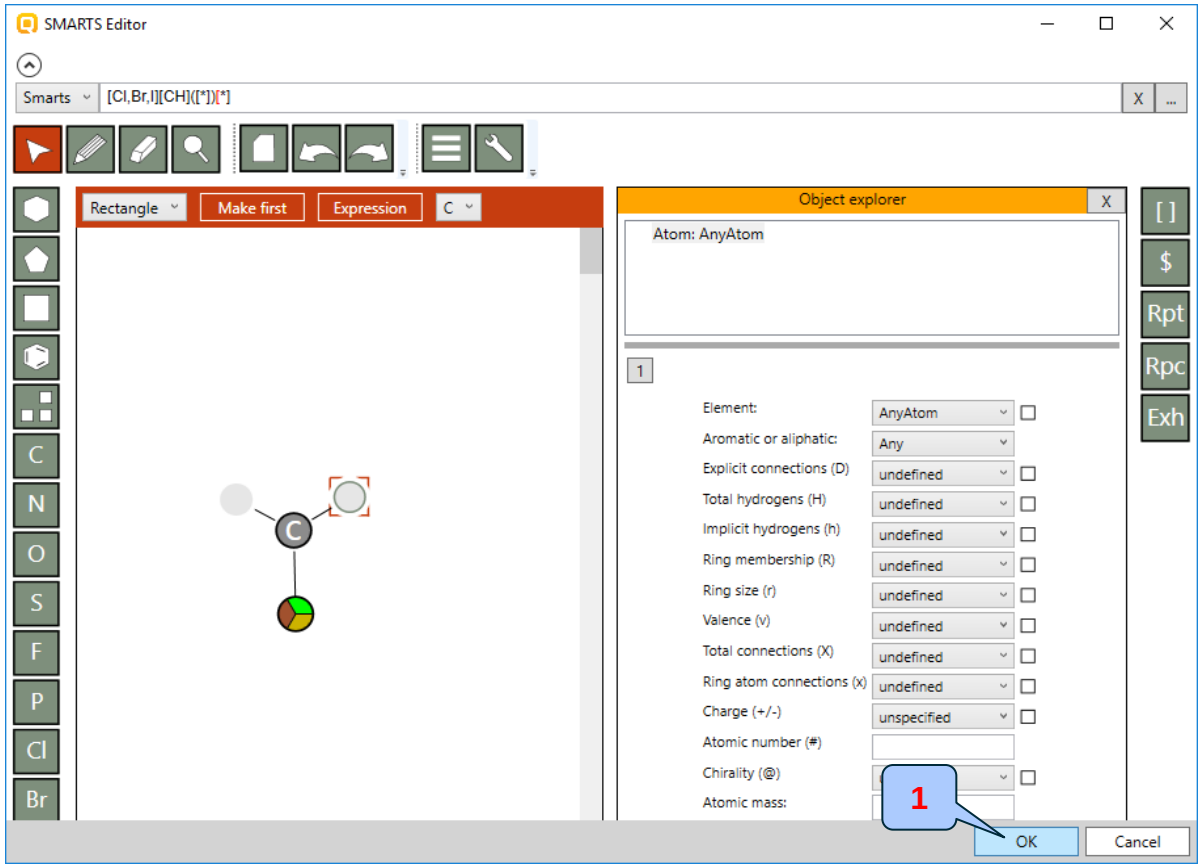
- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define skeleton of target compound

When all substituents of the carbon atom are defined (Hal, H, R) click on **OK** (1).



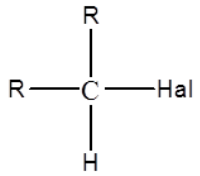
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

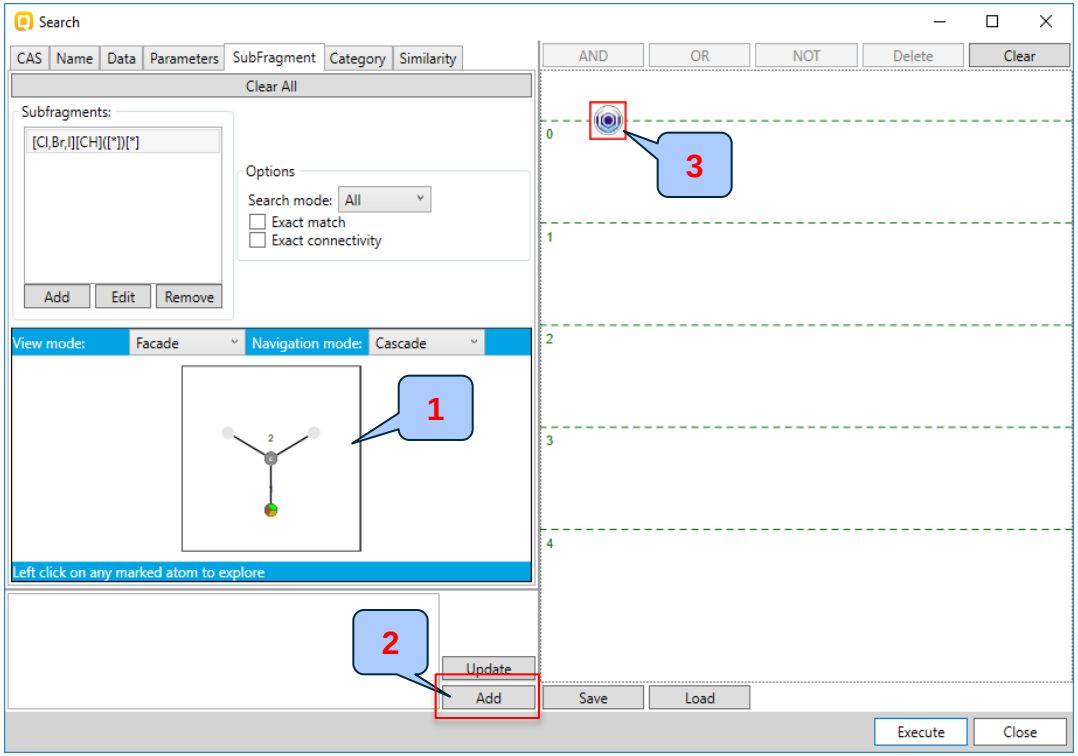
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define skeleton of target compound



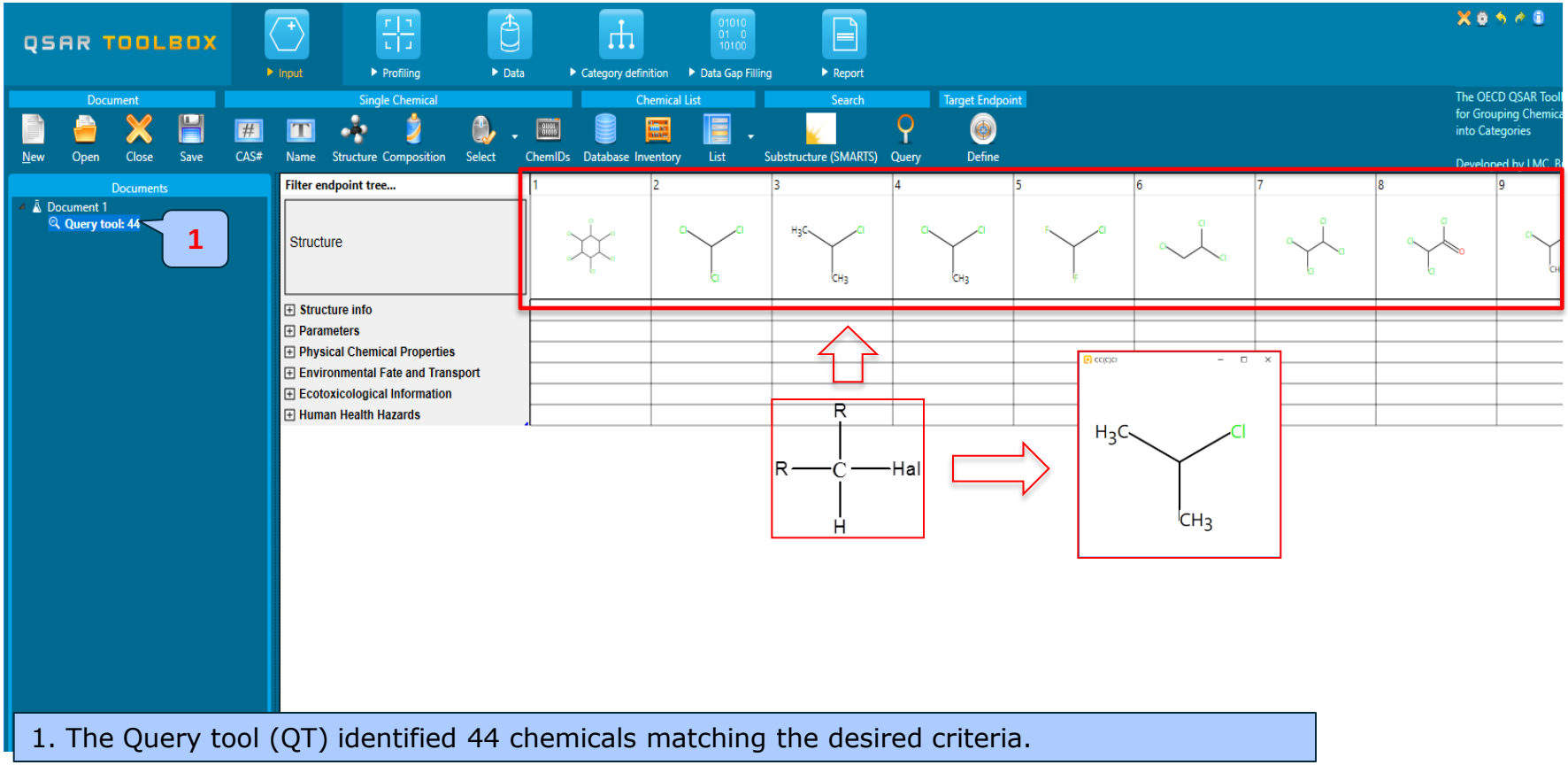
1. The defined general structure of the aliphatic halogens appears on the separate plot; 2. Click **Add** button; 3. Double click the query to perform the search

Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

- *Aliphatic halogens*



1. The Query tool (QT) identified 44 chemicals matching the desired criteria.

Subfragment search for identifying chemicals

BCF and (Dmax)

Example 3

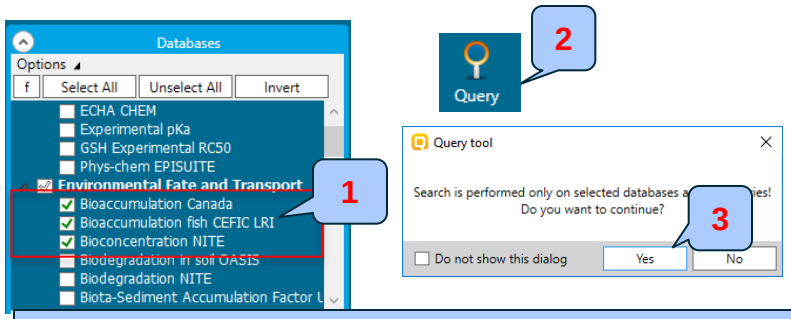
- Structures search criteria
  - Endpoint is BCF ≥ 10 L/kg bdwt
  - 3D parameter – minimum value of Diameter maximum >15 Å

Subfragment search for identifying chemicals

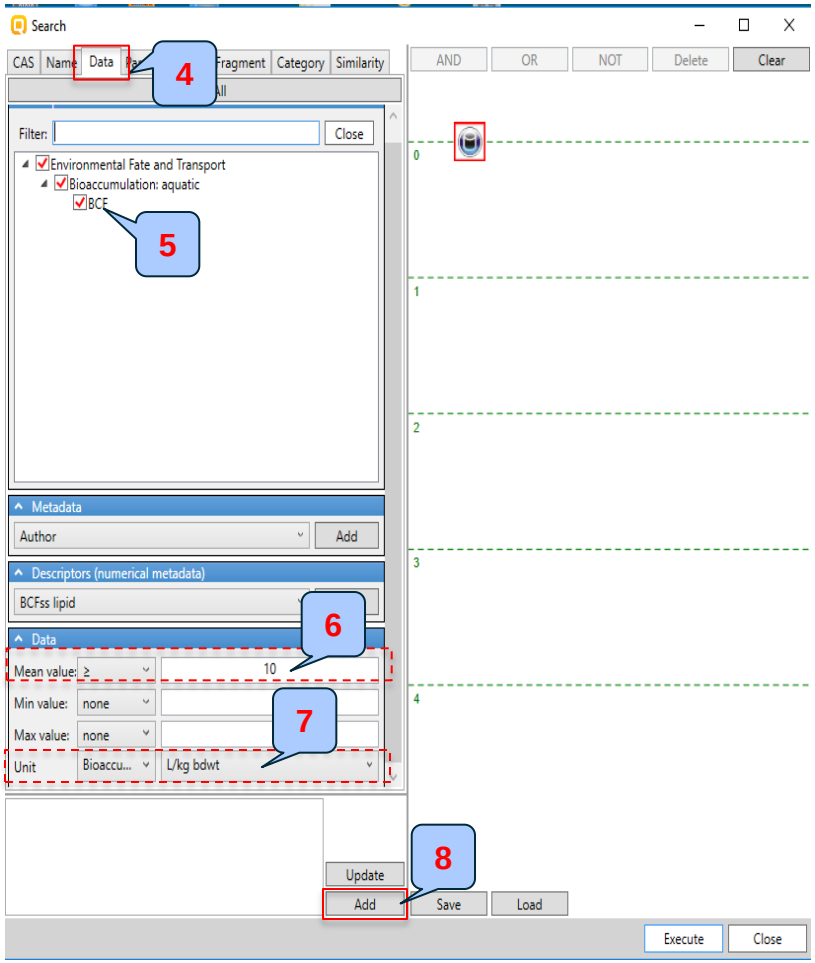
BCF and (Dmax)

Example 3

- Structures search criteria
  - Endpoint is BCF ≥ 10 L/kg bdwt
  - 3D parameter – minimum value of Diameter maximum >15 Å



1. Select databases including BCF data (Bioaccumulation Canada; Bioaccumulation fish CEFIC LRI and Bioconcentration NITE). No inventory has been selected in this exercise;
2. Click **Query** button;
3. Confirm that the searches perform on selected databases and inventories;
4. Go to **Data** panel;
5. Expand the endpoint tree and select BCF;
6. Specify qualifier "**≥**" 10 in the *Mean value* field;
7. Define the scale "**Bioaccumulation**" and appropriate unit (**L/kg bdwt**) ;
8. Click **Add** button;



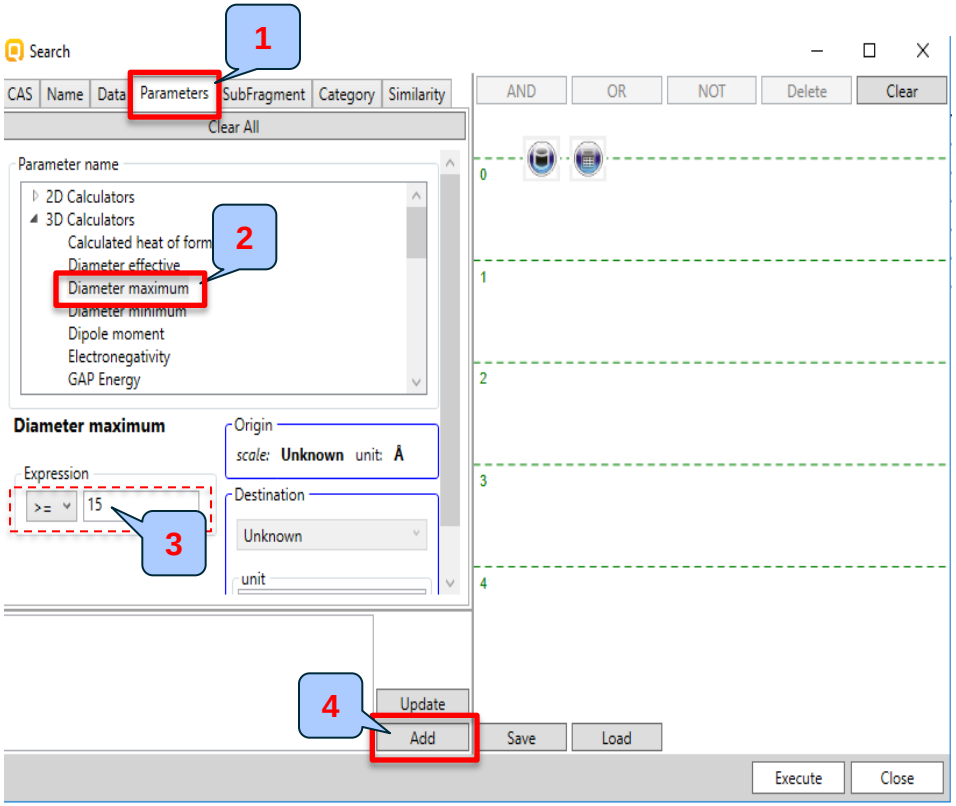
Subfragment search for identifying chemicals

BCF and (Dmax)

Example 3

- Structures search criteria
  - Endpoint is BCF ≥ 10 L/kg bdwt
  - 3D parameter – minimum value of Diameter maximum >15 Å

1. Open Parameters panel;
2. Select ***Diameter maximum*** from the pop-up list;
3. Specify qualifier "**≥**" **15** in the *Expression* field;
4. Click **Add** button;



Subfragment search for identifying chemicals

BCF and (Dmax)

Example 3

- Structures search criteria
  - Endpoint is BCF ≥ 10 L/kg bdwt
  - 3D parameter – minimum value of Diameter maximum >15 Å

Both queries should be linked together by logical **AND**. For this purpose both queries should be selected first. How to do this:

1. **Right click** over the first query to select it (the selected boundary should become orange colored);

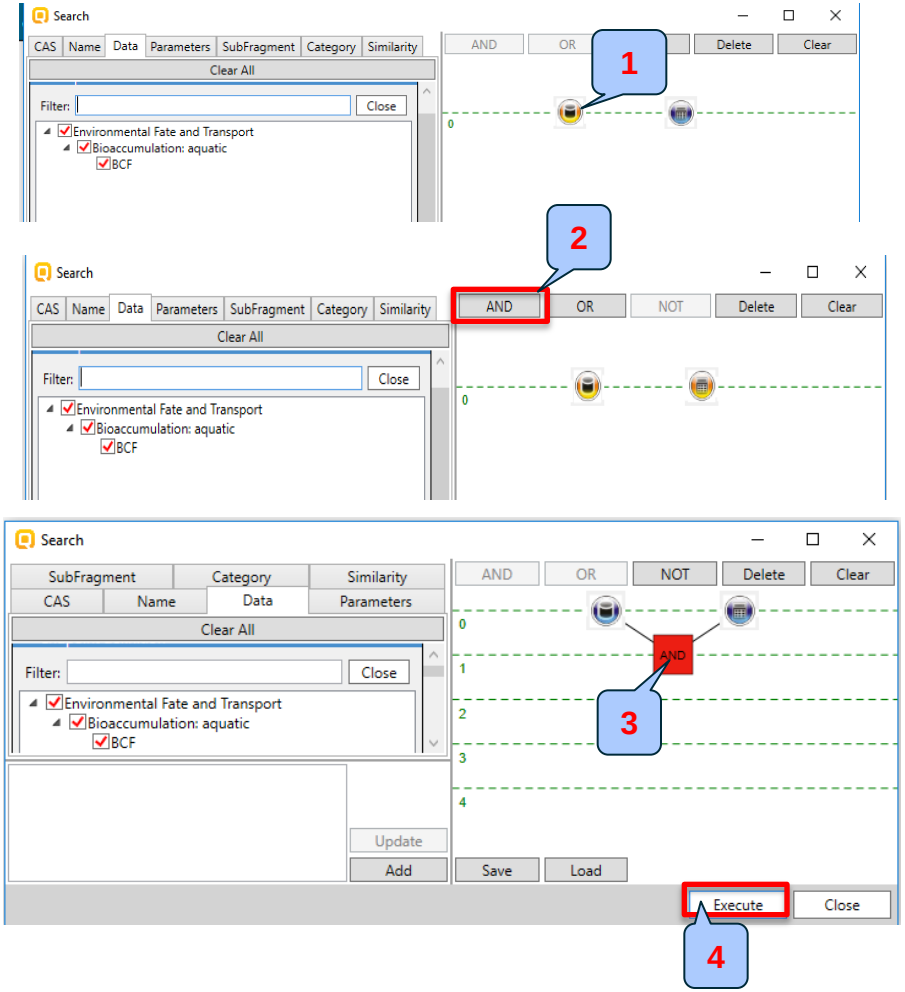
   Selected query

   Not selected query

2. When the both queries are selected, **click** "AND" button;

3. The two queries are combined by logical "AND";

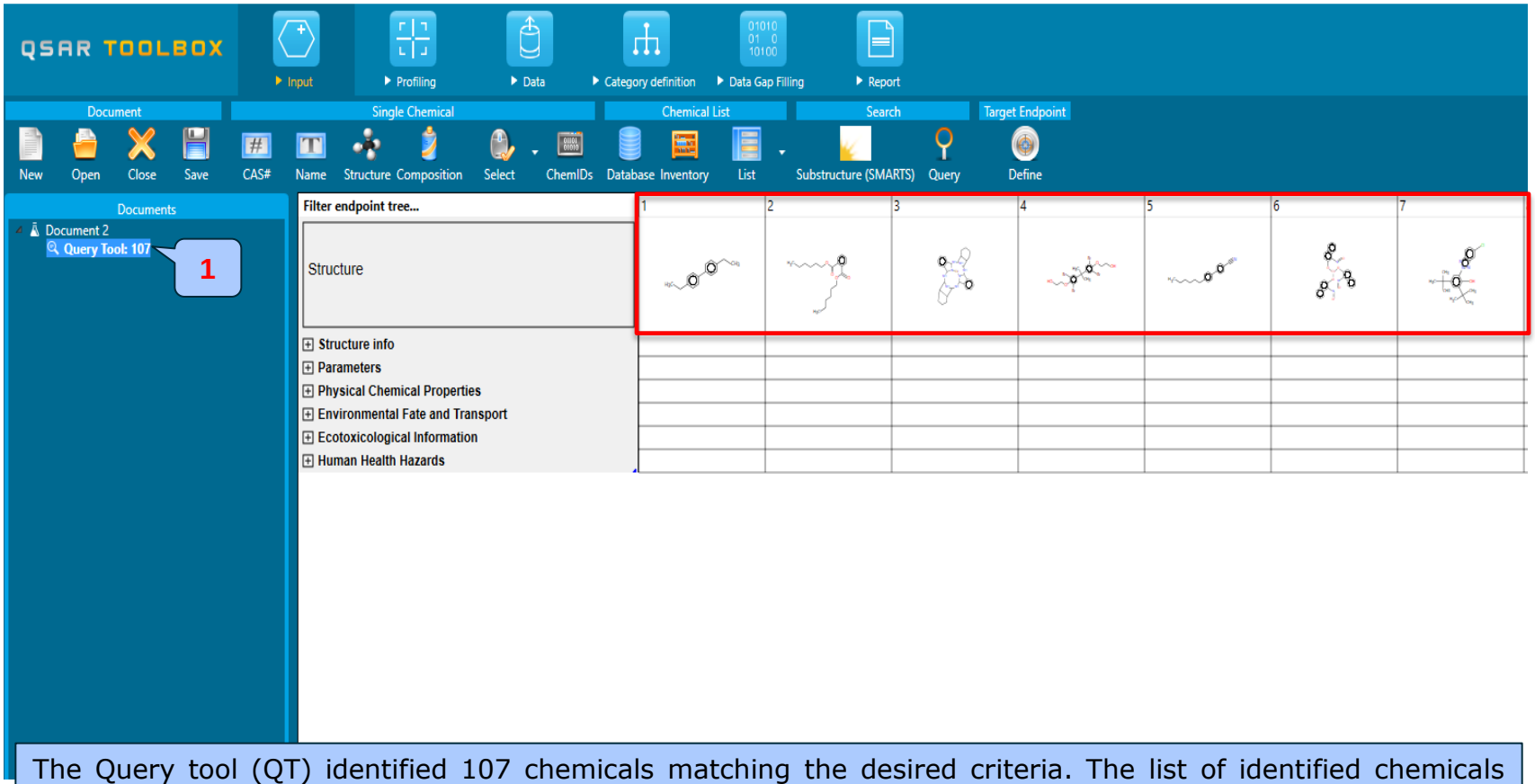
4. Double click "**AND**" query or click "**Execute**" button to execute the search;



Subfragment search for identifying chemicals

BCF and (Dmax)

Example 3

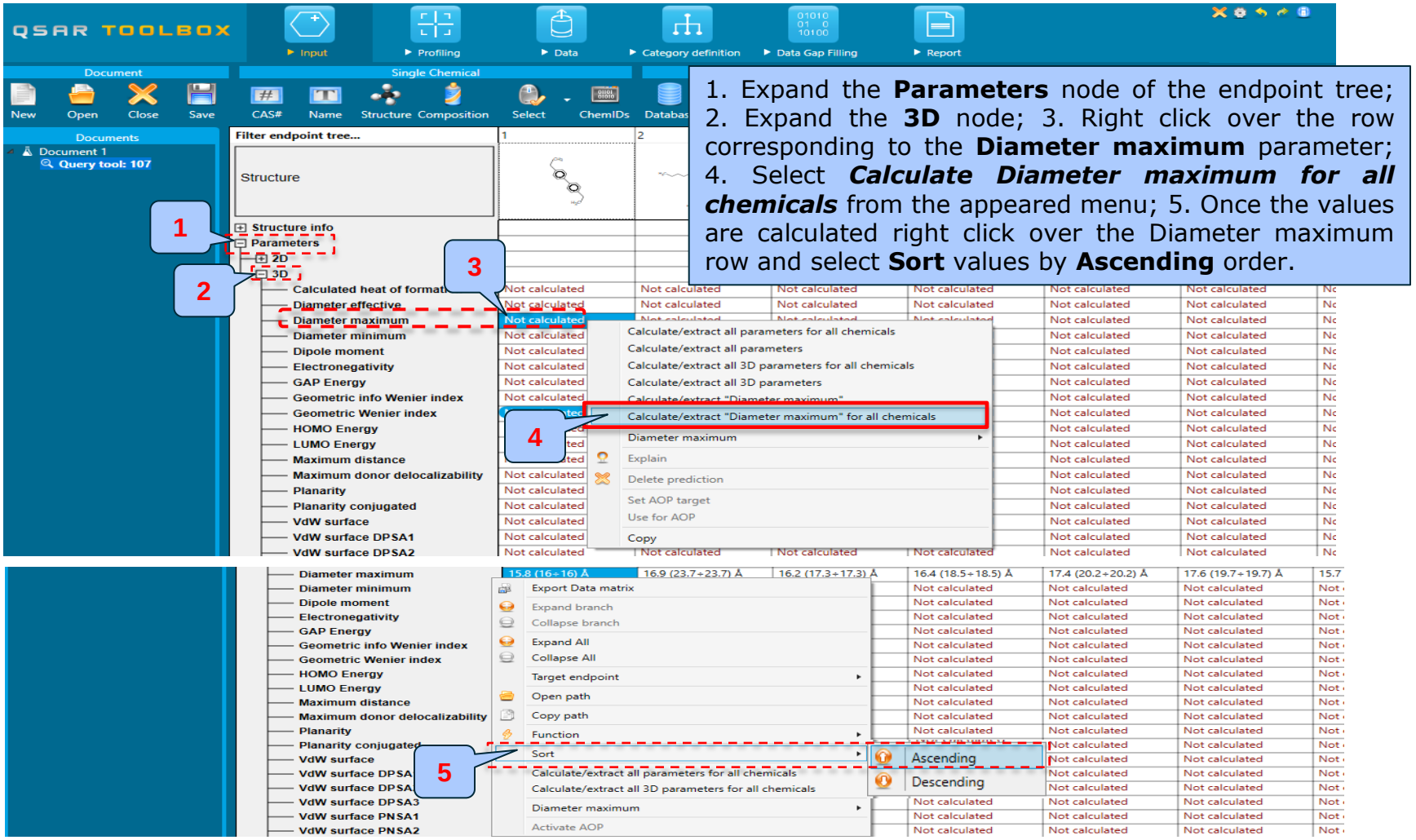


The Query tool (QT) identified 107 chemicals matching the desired criteria. The list of identified chemicals appear automatically on data matrix. Number of found chemicals is marked in the name of the document (1). In order to check the correctness of the performed query search, the user should calculate D_{max} for the list of chemicals and to gather BCF data for them. The last two steps are presented on the next two slides.

Subfragment search for identifying chemicals

BCF and (Dmax)

Example 3

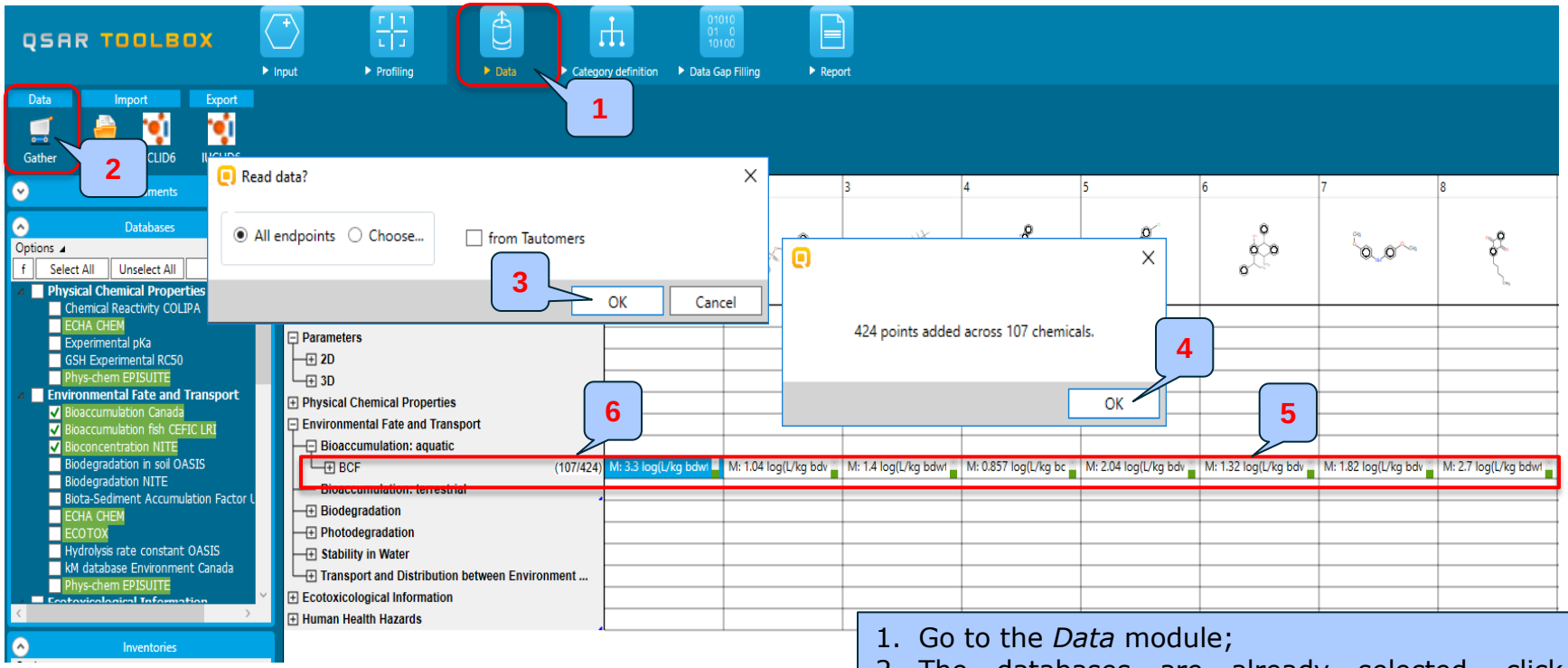


1. Expand the **Parameters** node of the endpoint tree; 2. Expand the **3D** node; 3. Right click over the row corresponding to the **Diameter maximum** parameter; 4. Select ***Calculate Diameter maximum for all chemicals*** from the appeared menu; 5. Once the values are calculated right click over the Diameter maximum row and select **Sort** values by **Ascending** order.

Subfragment search for identifying chemicals

BCF and (Dmax)

Example 3



1. Go to the *Data* module;
2. The databases are already selected, click **Gather** data;
3. Click **OK**;
4. Click **OK**;
5. Data appear on data matrix;
6. All 107 chemicals have BCF data;

Subfragment search for identifying chemicals

LC 50 and predefined category (Aldehydes)

Example 4

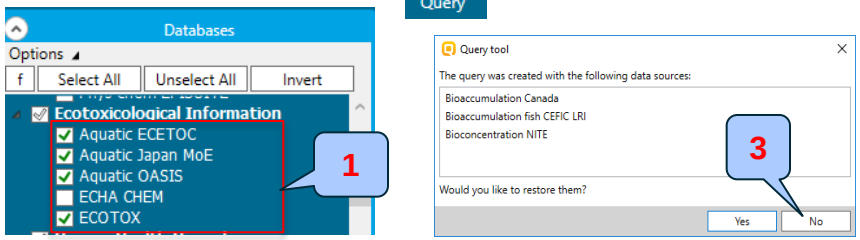
- Structures search criteria
  - Endpoint: LC 50 <1 mg/l
  - Fish: *P.promelas*
  - Effect: *Mortality*
  - Predefined category: *aldehydes*

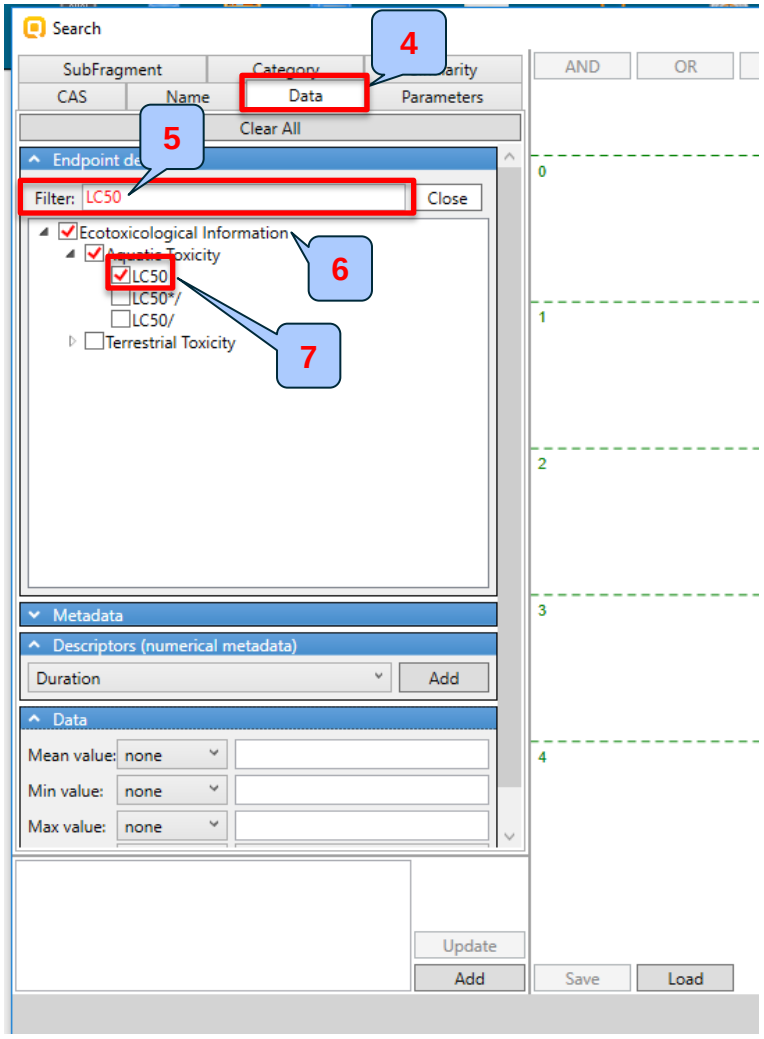
Subfragment search for identifying chemicals

LC 50 and predefined category (Aldehydes)

Example 4

- Structures search criteria
  - Endpoint: LC 50 <1 mg/l
  - Fish: *P.promelas*
  - Effect: *Mortality*
  - Predefined category: *aldehydes*





1. Select databases related to LC50 data (Aquatic ECETOC; aquatic Japan MoE; Aquatic OASIS; ECOTOX). No inventories has been selected in this case;
2. Click **Query** tool button;
3. Select "**No**";
4. Go to **Data** panel;
5. Type in filter the name of searched endpoint (**LC50**);
6. Select **Aquatic Toxicity** and expand the endpoint tab;
7. Check **LC50**

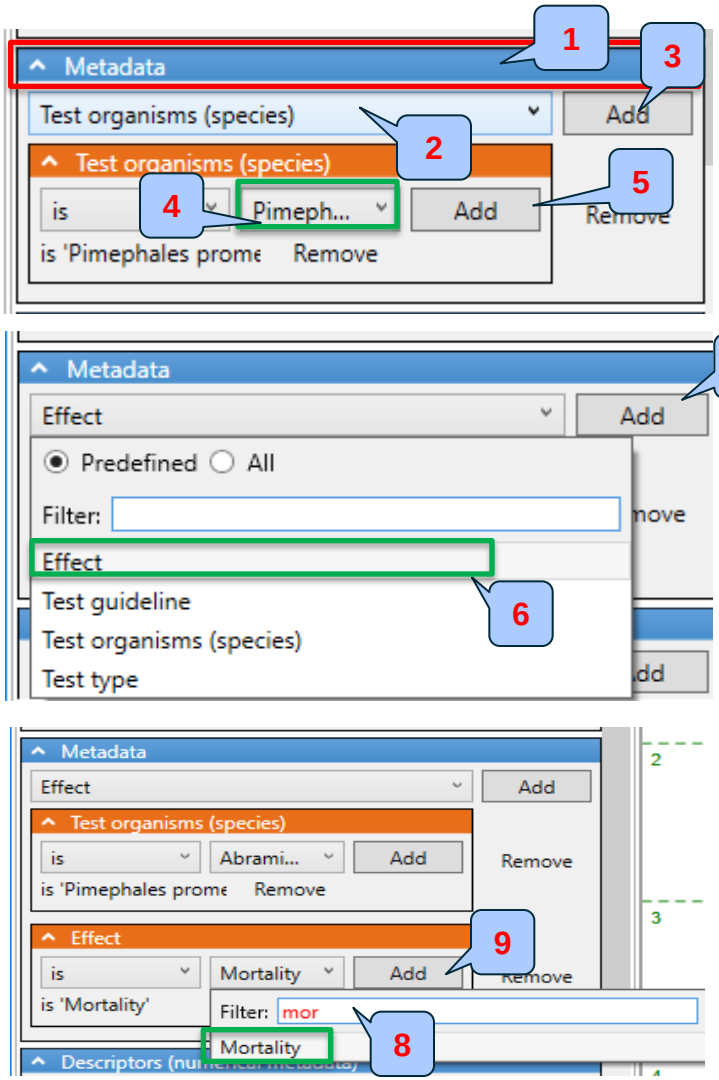
Subfragment search for identifying chemicals

LC 50 and predefined category (Aldehydes)

Example 4

- Structures search criteria
  - Endpoint: LC 50 <1 mg/l
  - Fish: *P.promelas*
  - Effect: *Mortality*
  - Predefined category: *aldehydes*

1. Open **Metadata** field
2. Select "**Test organism (species)**" from thedrop-down menu;
3. Click **Add**;
4. Select ***Pimephales promelas*** from the drop-down menu;
5. Click **Add**;
6. Go back to **Metadata** field and select **Effect** from the drop-down menu;
7. Click **Add**;
8. Use filter to find **"Mortality"** from the appeared drop-down menu;
9. Click **Add**

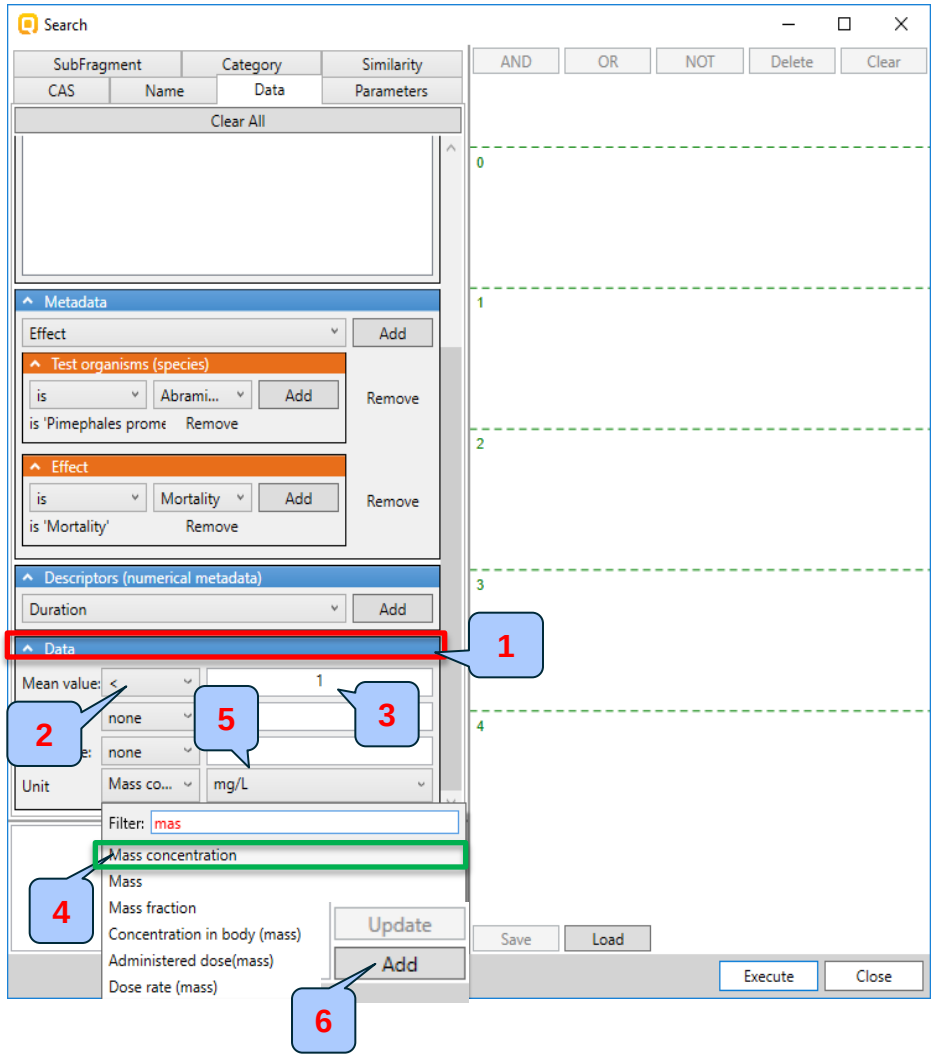


Subfragment search for identifying chemicals

LC 50 and predefined category (Aldehydes)

Example 4

- Structures search criteria
  - Endpoint: LC 50 <1 mg/l
  - Fish: *P.promelas*
  - Effect: *Mortality*
  - Predefined category: *aldehydes*



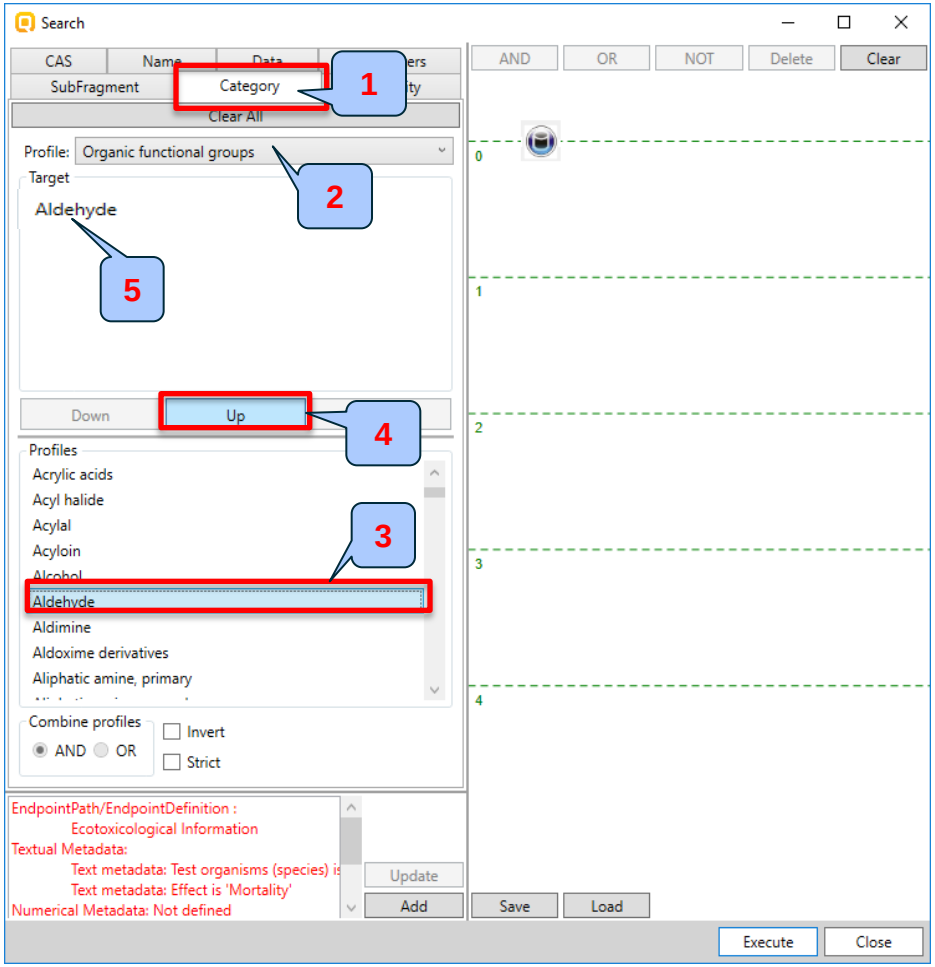
1. Open **Data** panel;
2. Open qualifiers from Mean value and select "**<**";
3. Type "**1**" in the blank field;
4. Use Filter to find "**Mass concentration**";
5. Select "**mg/l**" from the list with units;
6. Click **Add**;

Subfragment search for identifying chemicals

LC 50 and predefined category (Aldehydes)

Example 4

- Structures search criteria
  - Endpoint: LC 50 <1 mg/l
  - Fish: *P.promelas*
  - Effect: *Mortality*
  - Predefined category: *aldehydes*



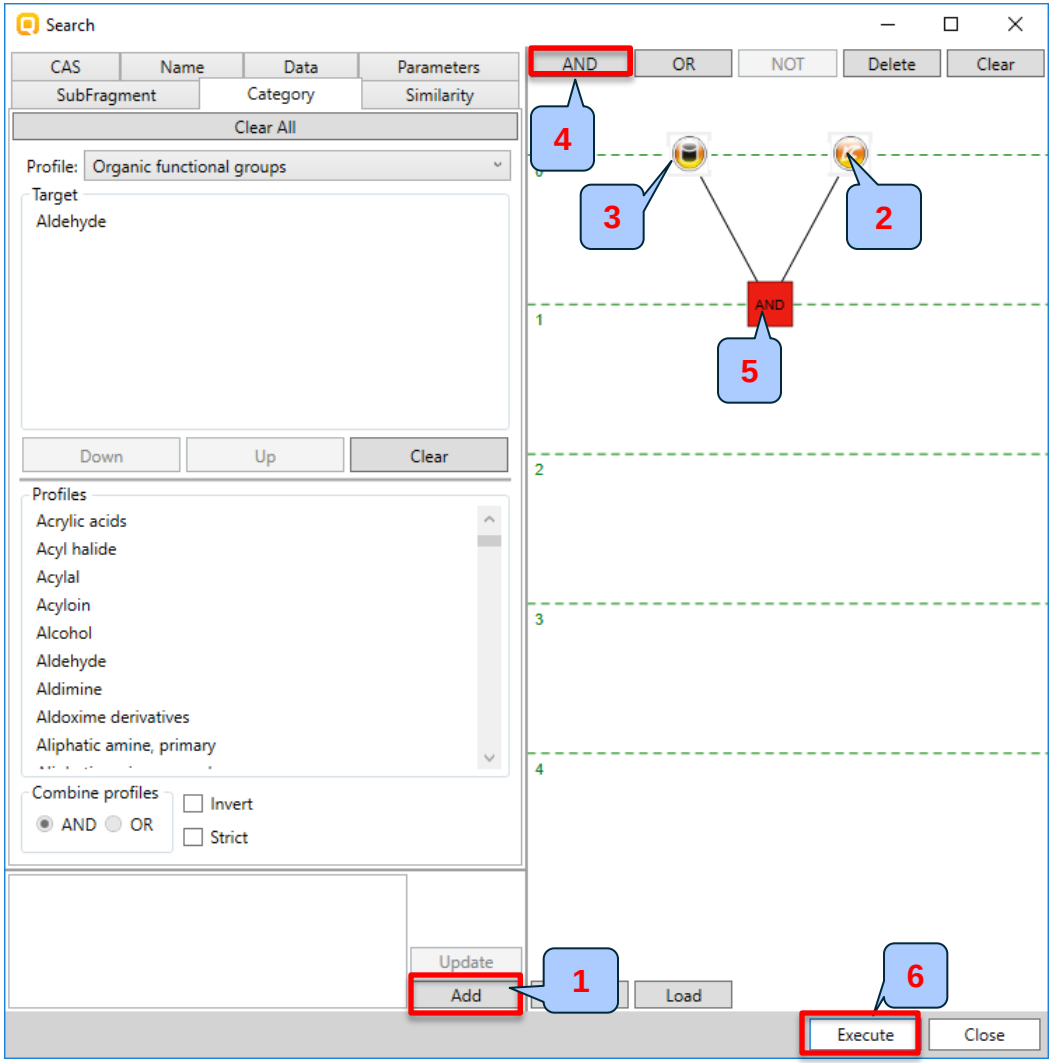
1. Open **Category** panel;
2. Use *Filter* to find **Organic functional groups** profiler from the list with profilers;
3. Find **"Aldehyde"**;
4. Click "**Up**" to move the selected category from panel "*Profilers*" to the panel "*Target*"
5. The selected category appears in the panel "Target"

Subfragment search for identifying chemicals

LC 50 and predefined category (Aldehydes)

Example 4

- Structures search criteria
  - Endpoint: LC 50 <1 mg/l
  - Fish: *P.promelas*
  - Effect: *Mortality*
  - Predefined category: *aldehydes*



1. Click **Add** button;
2. The query with predefined category appears on the logic panel.

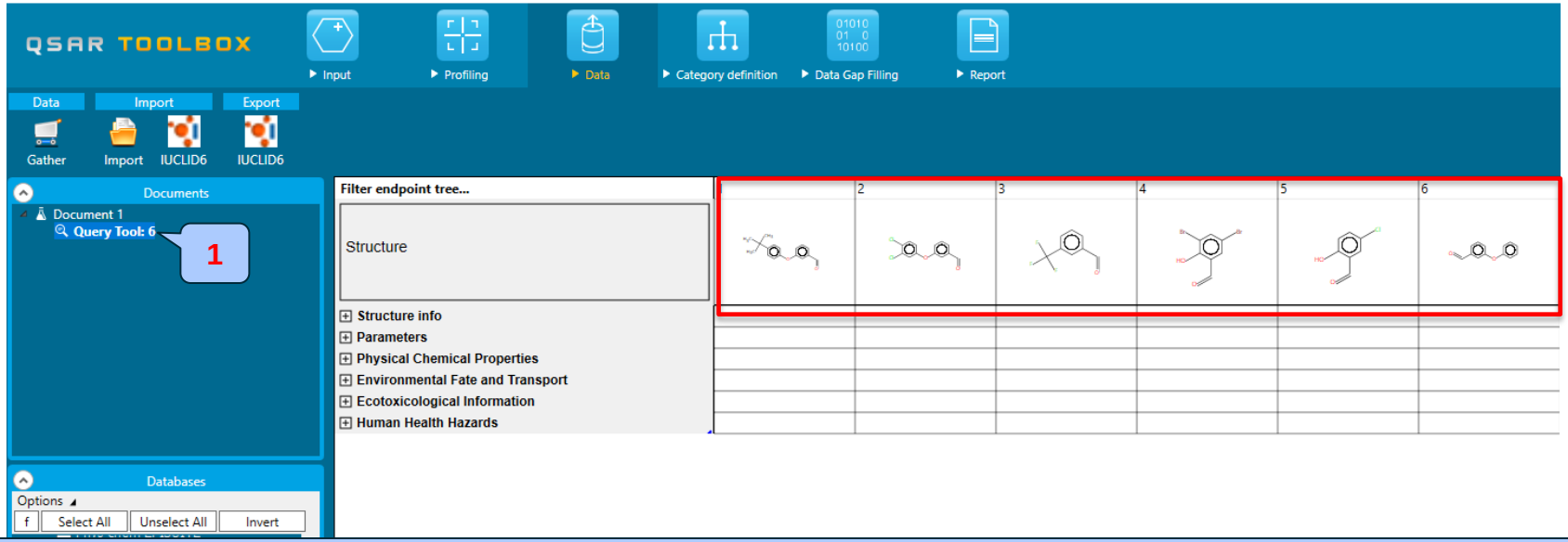
The both queries should be combined by logical "AND". Follow the steps explained on slide # 39

3. Right click over the both queries to highlight them;
4. Click **AND** button;
5. The two queries are combined by logical "AND";
6. Click **Execute** button in order to execute the Query

Subfragment search for identifying chemicals

LC 50 and predefined category (Aldehydes)

Example 4

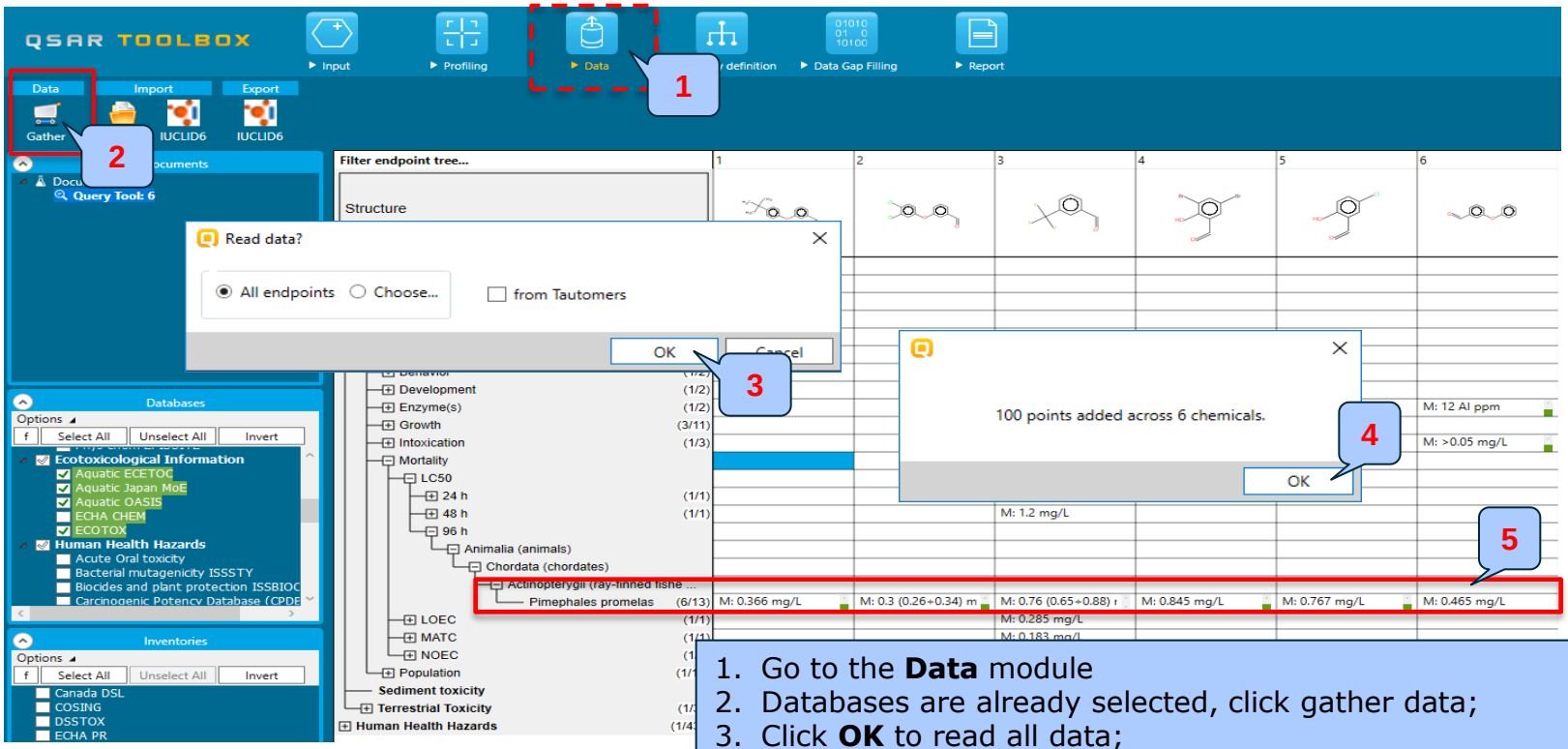


The Query tool (QT) identified 6 chemicals matching the desired criteria. The list of identified chemicals appear automatically on the data matrix. Number of found chemicals is marked in the name of the node (1). In order to check the correctness of the performed query search the user should gather ecotox data and profile according to OFG Profiler. The last two steps are presented on the next two slides.

Subfragment search for identifying chemicals

LC 50 and predefined category (Aldehydes)

Example 4

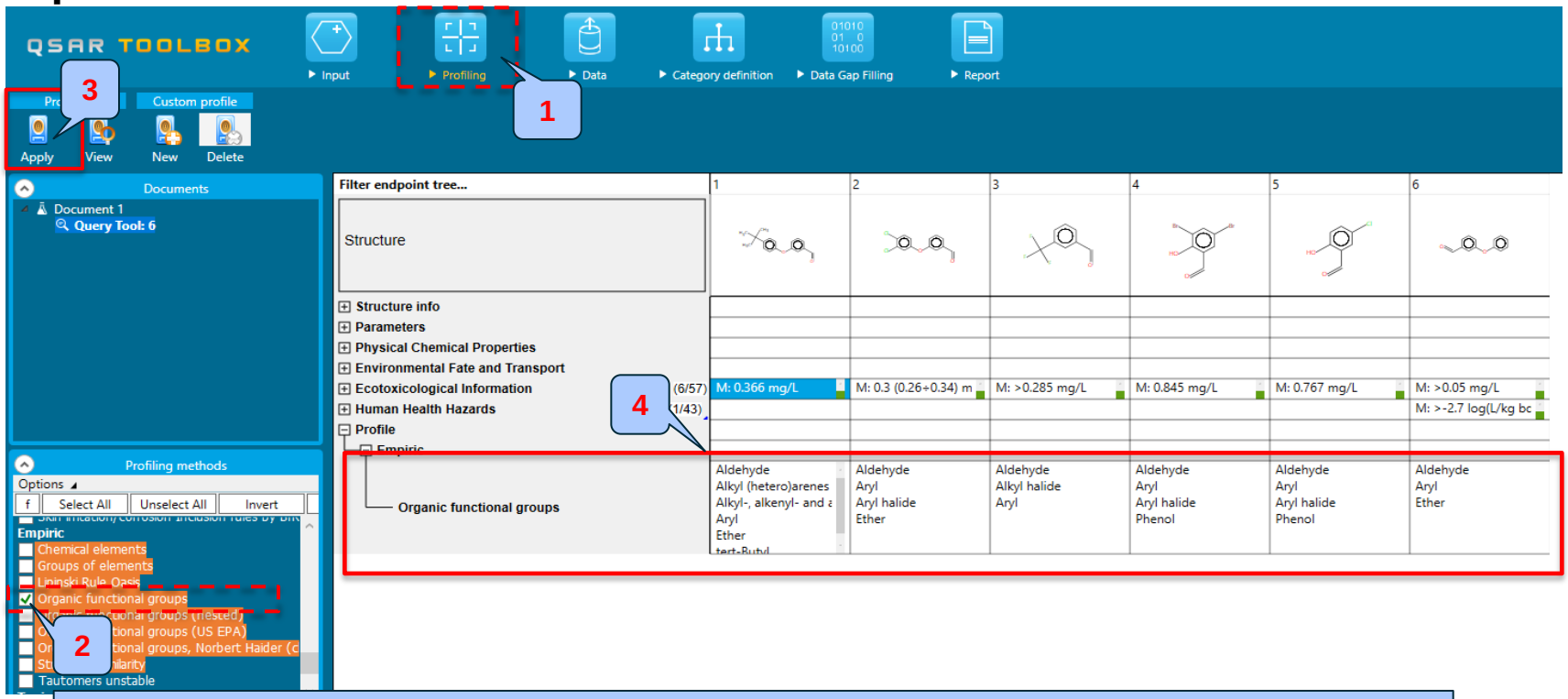


1. Go to the **Data** module
2. Databases are already selected, click gather data;
3. Click **OK** to read all data;
4. Confirm the number of gathered data:
5. Data appear on data matrix answering the following criterias:
   - *LC50 < 1mg/l*
   - *Effect: Mortality*
   - *Test species: P.promelas*
   - *Aldehydes by OFG*

Subfragment search for identifying chemicals

LC 50 and predefined category (Aldehydes)

Example 4



1. Go to the *Profiling* module;
2. Check **Organic functional group** profile;
3. Click **Apply**;
4. All 6 chemicals have "*Aldehyde*" fragment within its structure;

Subfragment search for identifying chemicals

Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

Example 5

- Structures search criteria
  - Endpoint: Gene mutation
  - Species: *S.thyphimurium*
  - Data: *Positive*

  AND

  - Endpoint: *Summary carcinogenicity*
  - Species: *Rat*
  - Route: *gavage*
  - Data: *Positive*
  - Predefined category: *Epoxides*

Subfragment search for identifying chemicals

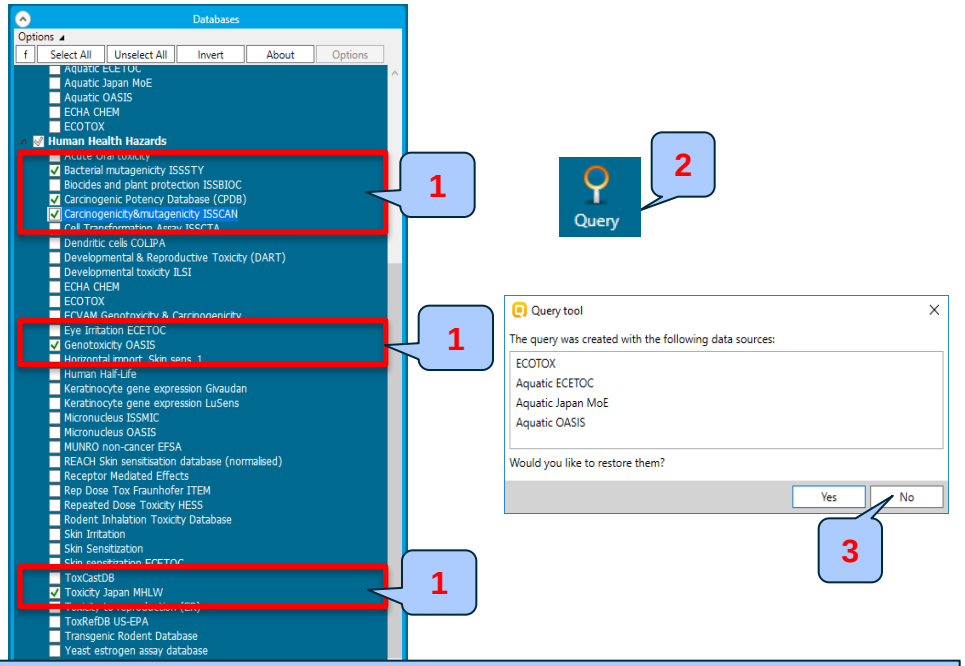
Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

Example 5

- Structures search criteria
  - Endpoint: Gene mutation
  - Species: *S.thyphimurium*
  - Data: *Positive*

  AND

  - Endpoint: *Summary carcinogenicity*
  - Species: *Rat*
  - Route: *gavage*
  - Data: *Positive*
  - Predefined category: *Epoxides*



Before application of Query tool, the user should select databases which includes required data. Inventories are not selected in this particular case.

1. Select the following databases:
   - Bacterial mutagenity ISSSTY
   - Carcinogenicity potency Database (CPDB)
   - Carcinogenicity&mutagenicity ISSCAN
   - Genotoxicity OASIS
   - Toxicity Japan MHLW
2. Click **Query** button;
3. Select **No** to not restore the databases used in the previous example.

Subfragment search for identifying chemicals

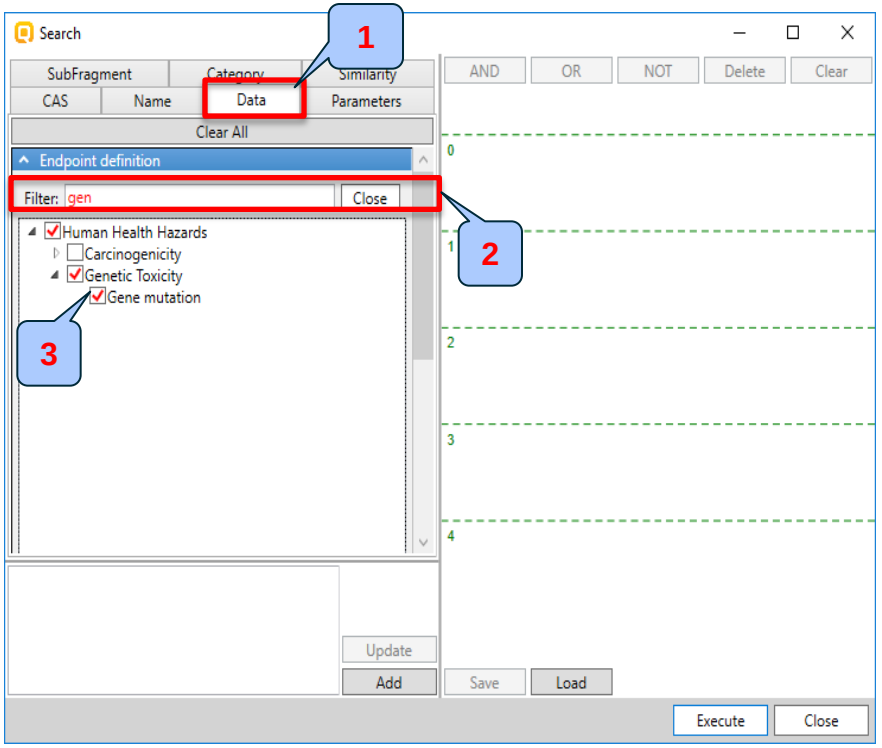
Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

Example 5

- Structures search criteria
  - Endpoint: Gene mutation
  - Species: *S.thyphimurium*
  - Data: *Positive*

  AND

  - Endpoint: *Summary carcinogenicity*
  - Species: *Rat*
  - Route: *gavage*
  - Data: *Positive*
  - Predefined category: *Epoxides*



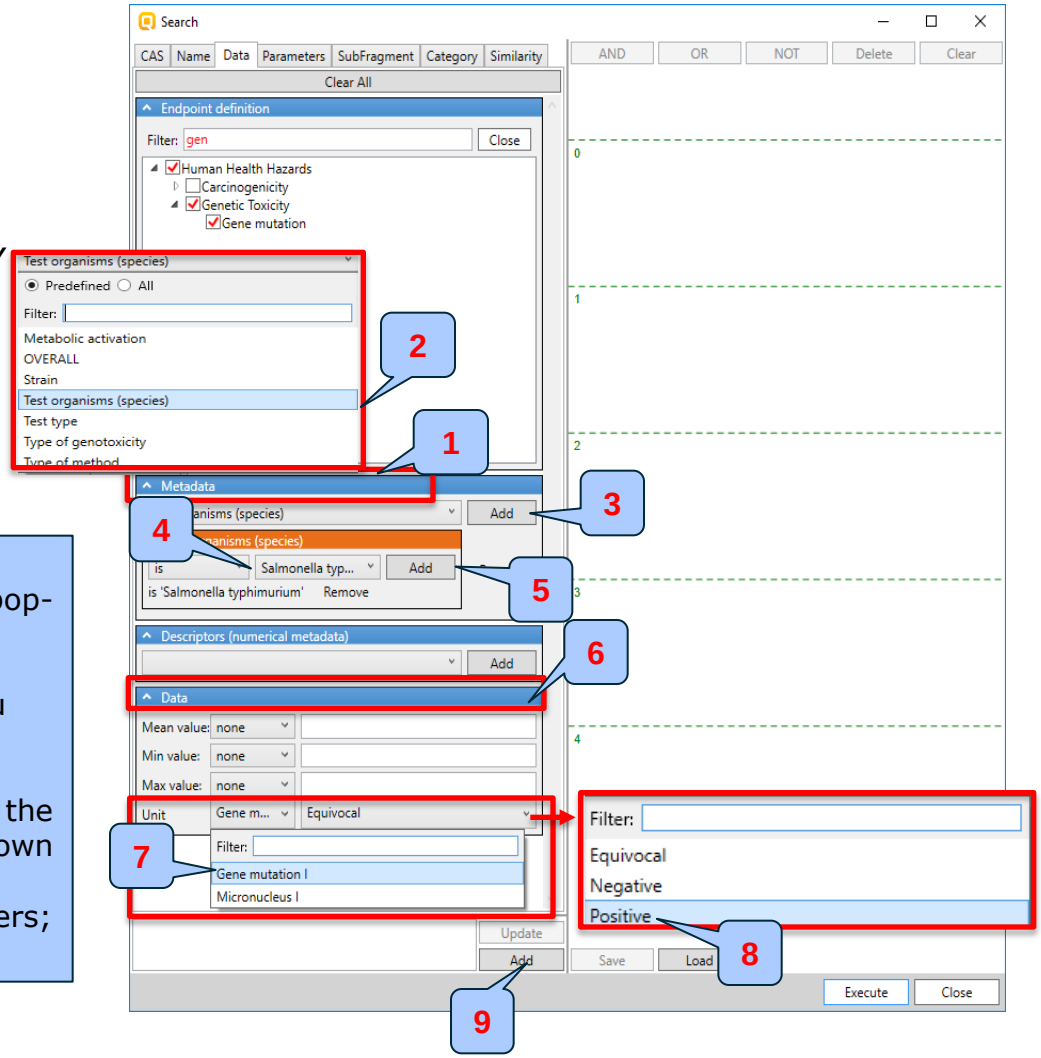
1. Click on the **Data** panel;
2. Use filter to find searched endpoint;
3. Select **Gene mutation**;

Subfragment search for identifying chemicals

Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

Example 5

- Structures search criteria
  - Endpoint: Gene mutation
  - Species: *S.thyphimurium*
  - Data: *Positive*
  - Endpoint: *Summary carcinogenicity*
  - Species: *Rat*
  - Route: gavage
  - Predefined category: *Epoxides*



1. Open Metadata panel;
2. Select **Test organism (species)** from the pop-up menu;
3. Click "Add";
4. Select **S.thyhimurium** from the pop-up-menu
5. Click **Add**;
6. Open **Data** panel;
7. Select **Gene mutation I** scale (belonging to the Mutagenicity family) from the *Units* drop-down menu;
8. Select **Positive** from the list with scale members;
9. Click **Add** button;

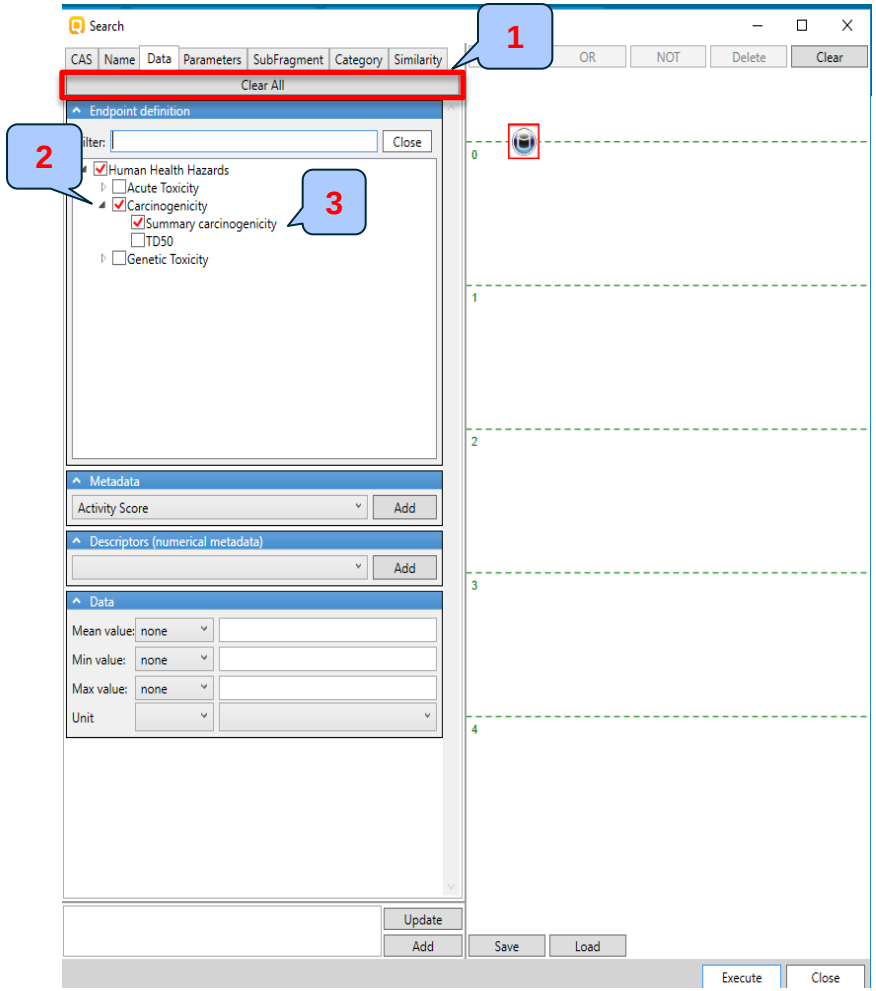
Subfragment search for identifying chemicals

Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

Example 5

- Structures search criteria
  - Endpoint: Gene mutation
  - Species: *S.thyphimurium*
  - Data: *Positive*
  - Endpoint: *Summary carcinogenicity*
  - Species: *Rat*
  - Route: gavage
  - Predefined category: *Epoxides*

1. Before defining the second query click **Clear All** button;
2. Open endpoint path and select *Carcinogenicity* node;
3. Select **Summary carcinogenicity**;



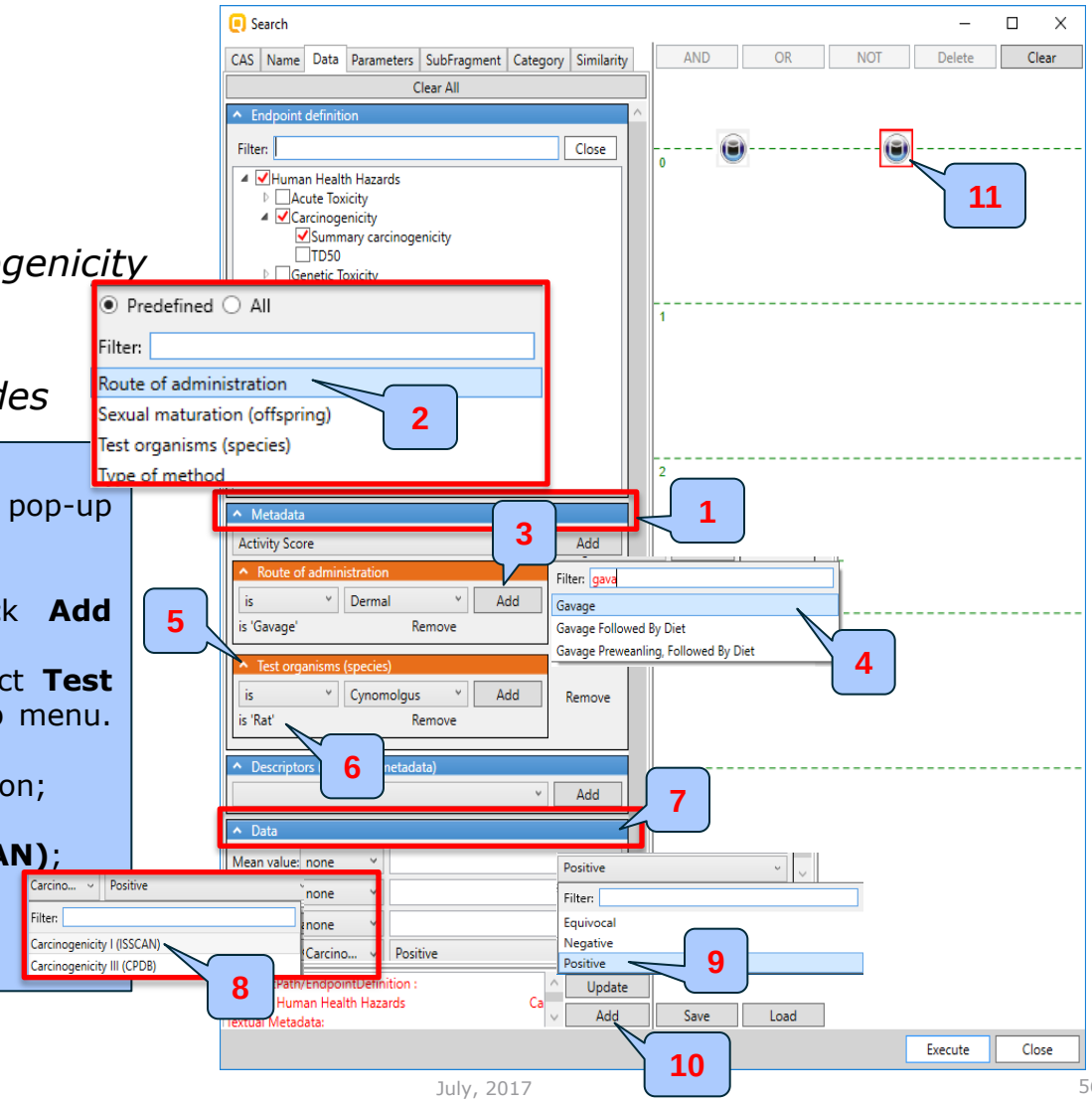
Subfragment search for identifying chemicals

Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

Example 5

- Structures search criteria
  - Endpoint: Gene mutation
  - Species: *S.thyphimurium*
  - Data: *Positive*
  - Endpoint: *Summary carcinogenicity*
  - Species: *Rat*
  - Route: gavage
  - Predefined category: *Epoxides*

1. Open *Metadata* panel;
2. Select ***Route of administration*** from pop-up menu;
3. Click **Add** button;
4. Select **Gavage** from the list. Click **Add** button;
5. Go back to *Metadata* panel and select **Test organism (species)** from the pop-up menu. Click **Add** button;
6. Select **Rat** from the list. Click **Add** button;
7. Open *Data* panel
8. Select scale **Carcinogenicity I (ISSCAN)**;
9. Select **Positive**;
10. Click **Add** button;
11. The query appears on the logic panel.

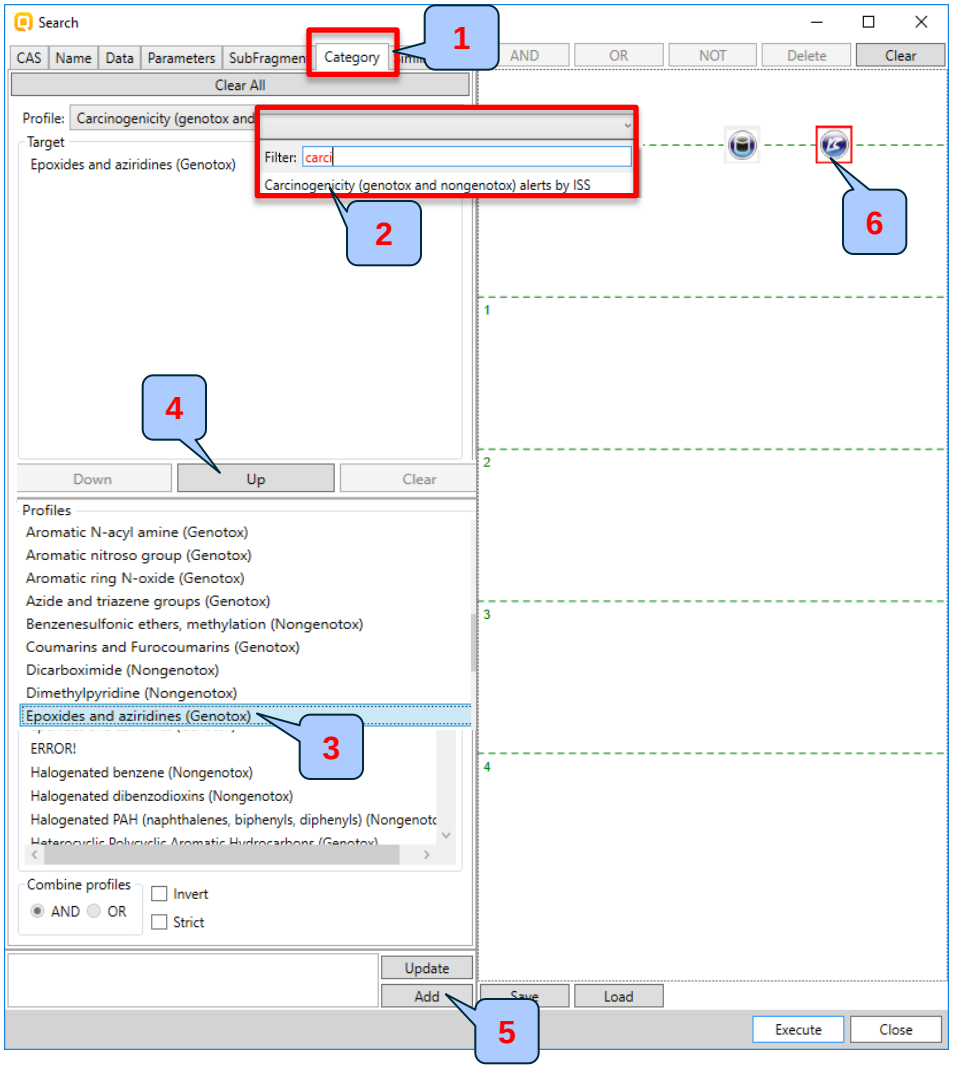


Subfragment search for identifying chemicals

Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

Example 5

- Structures search criteria
  - Endpoint: Gene mutation
  - Species: *S.thyphimurium*
  - Data: *Positive*
  - Endpoint: *Summary carcinogenicity*
  - Species: *Rat*
  - Route: gavage
  - Predefined category: *Epoxides*



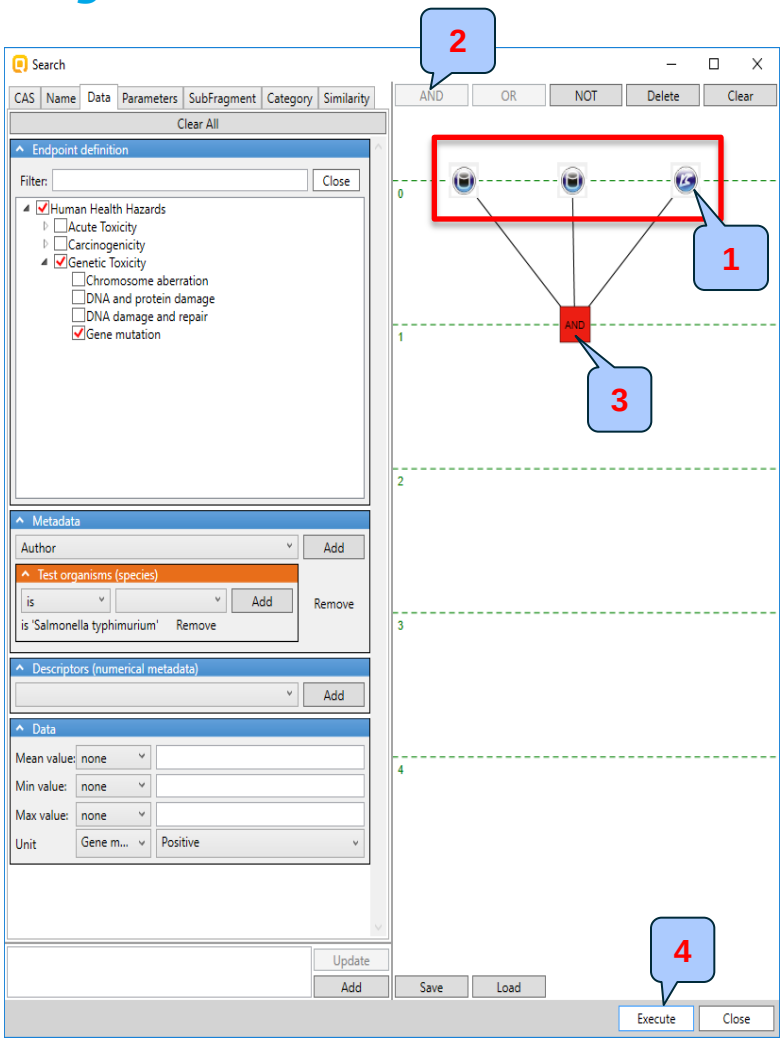
1. Click *Category* panel;
2. Select **Carcinogenicity (genotox and nongenotox) alerts by ISS**;
3. Select category **Epoxides and aziridines (Genotox)**;
4. Click **Up** to move the selected category to the panel Target;
5. Click **Add** button;
6. The query appears on the logic panel;

Subfragment search for identifying chemicals

Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

Example 5

- Structures search criteria
  - Endpoint: Gene mutation
  - Species: *S.thyphimurium*
  - Data: *Positive*
  - Endpoint: *Summary carcinogenicity*
  - Species: *Rat*
  - Route: gavage
  - Predefined category: *Epoxides*

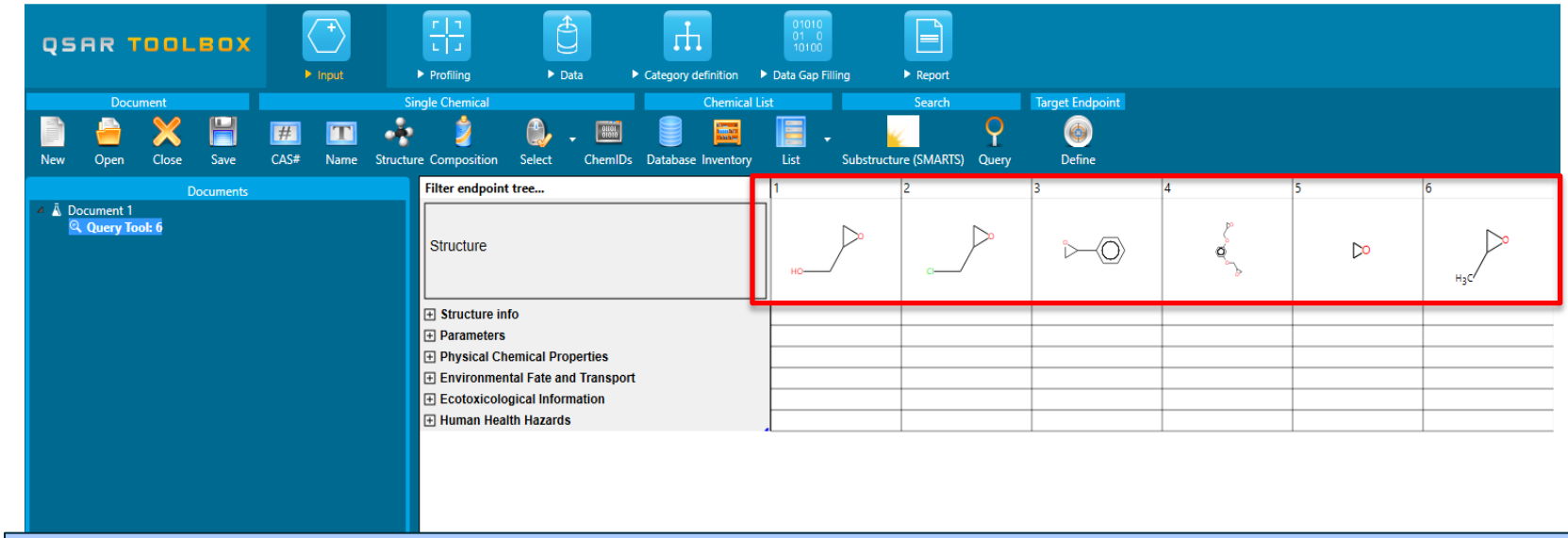


1. Right click over the three queries (see slide # 39);
2. Click **AND** button;
3. The three queries are combined by logical "**AND**";
4. Click **Execute** button;

Subfragment search for identifying chemicals

Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

Example 5

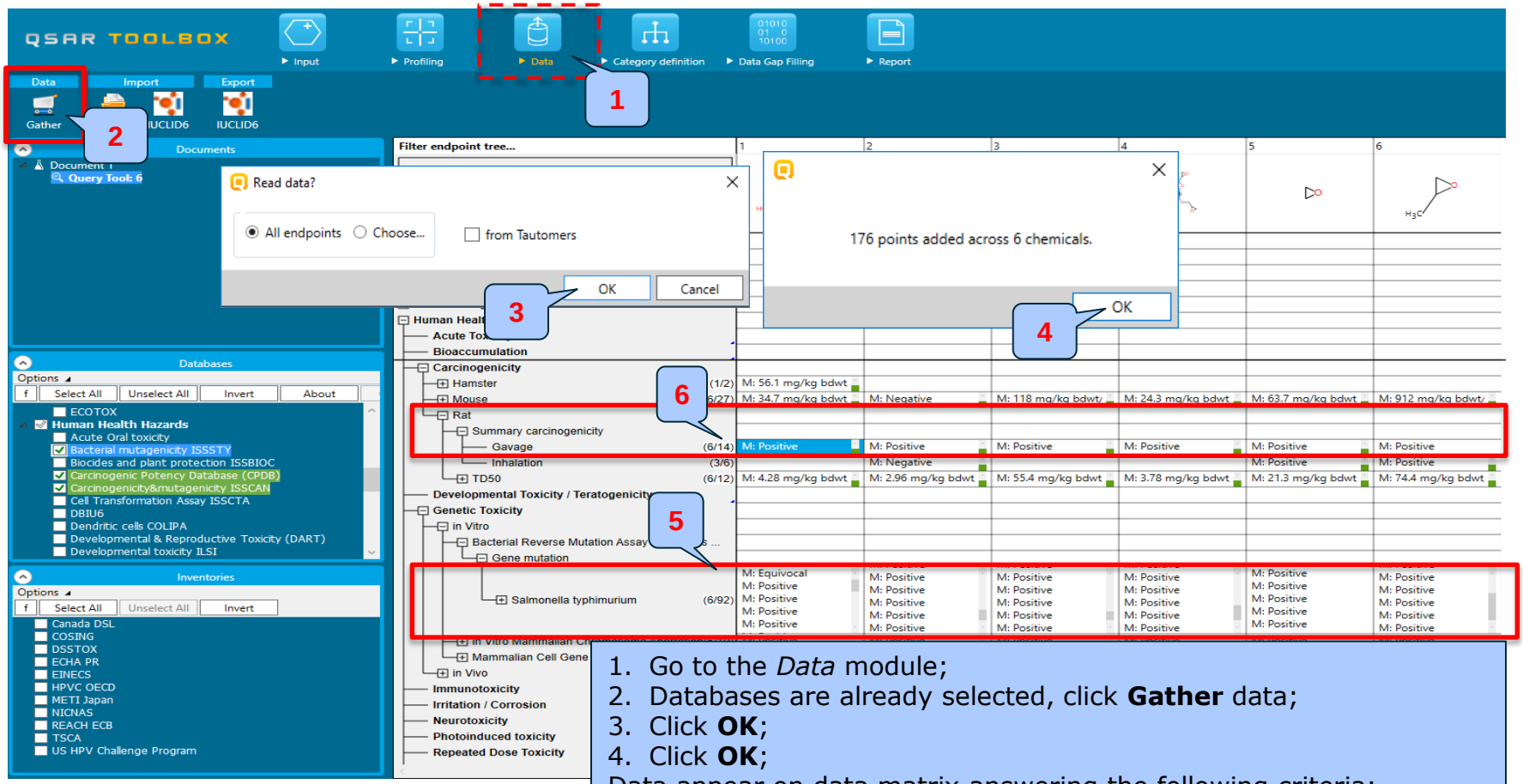


The Query tool (QT) identified 6 chemicals matching the desired criteria. In order to check the correctness of the query the user should gather experimental data for Ames and Carcinogenicity and profile the identified chemicals according to applied Carcinogenicity profiler. The last two steps are presented on the next two slides.

Subfragment search for identifying chemicals

Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

Example 5



1. Go to the *Data* module;
2. Databases are already selected, click **Gather** data;
3. Click **OK**;
4. Click **OK**;

Data appear on data matrix answering the following criteria:

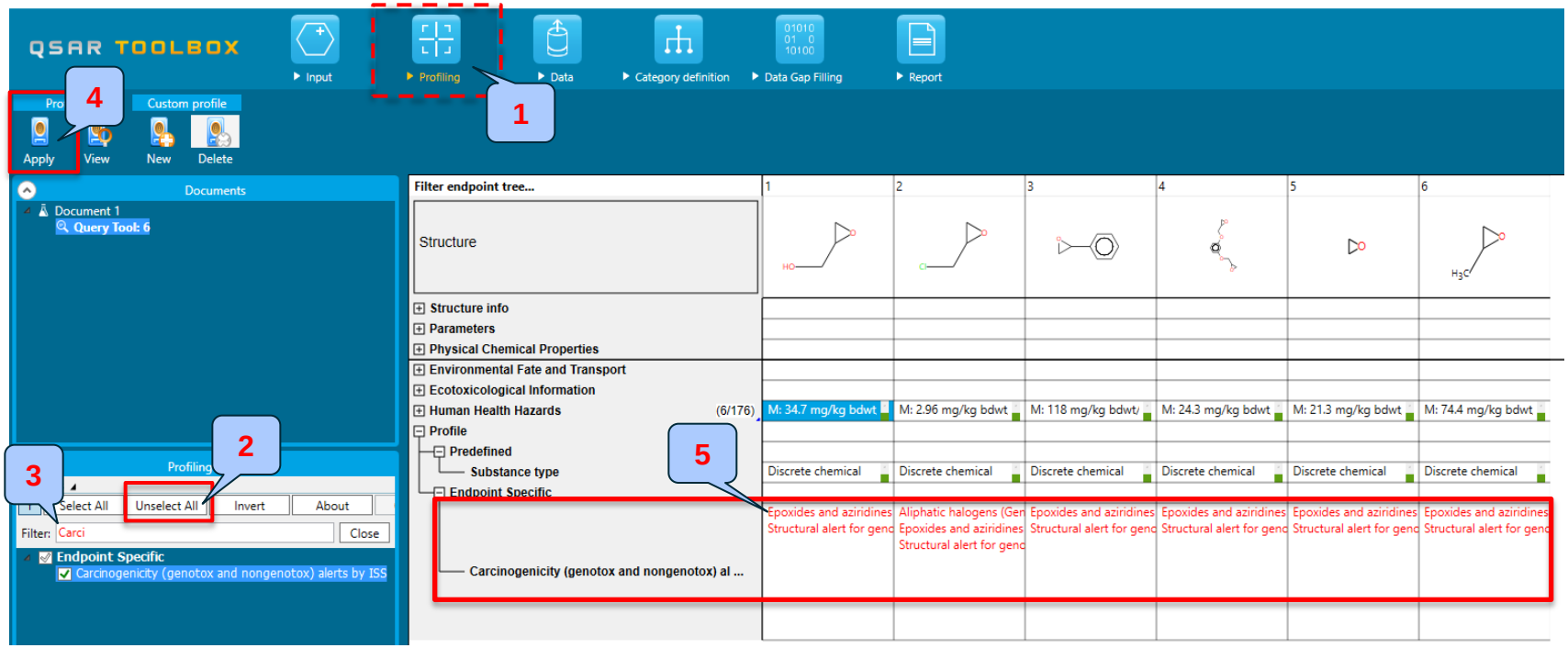
Ames mutagenicity (S. thuphimurium): Positive (5)

Summary carcinogenicity (gavage, rat): Positive (6)

Subfragment search for identifying chemicals

Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

Example 5



1. Go to *Profiling*;
2. Click **Unselect All**;
3. Use filter and select *Carcinogenicity (genotox and nongenotox) alerts by ISS*;
4. Click **Apply**;
5. All 6 chemicals have "*Epoxides and Aziridines*" fragment within its structure.

Subfragment search for identifying chemicals

Chemicals with Skin sensitization positive data including Aldehyde fragment

Example 6

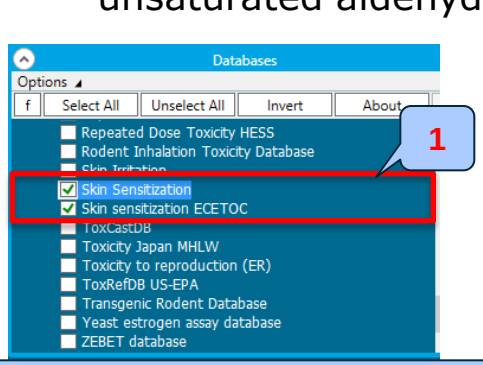
- Structures search criteria
  - Endpoint: *EC3*
  - Data: *Positive*
  - Predefined category: alpha, beta-unsaturated aldehydes

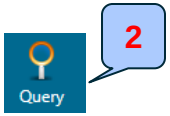
Subfragment search for identifying chemicals

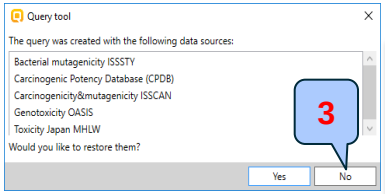
Chemicals with Skin sensitization positive data including Aldehyde fragment

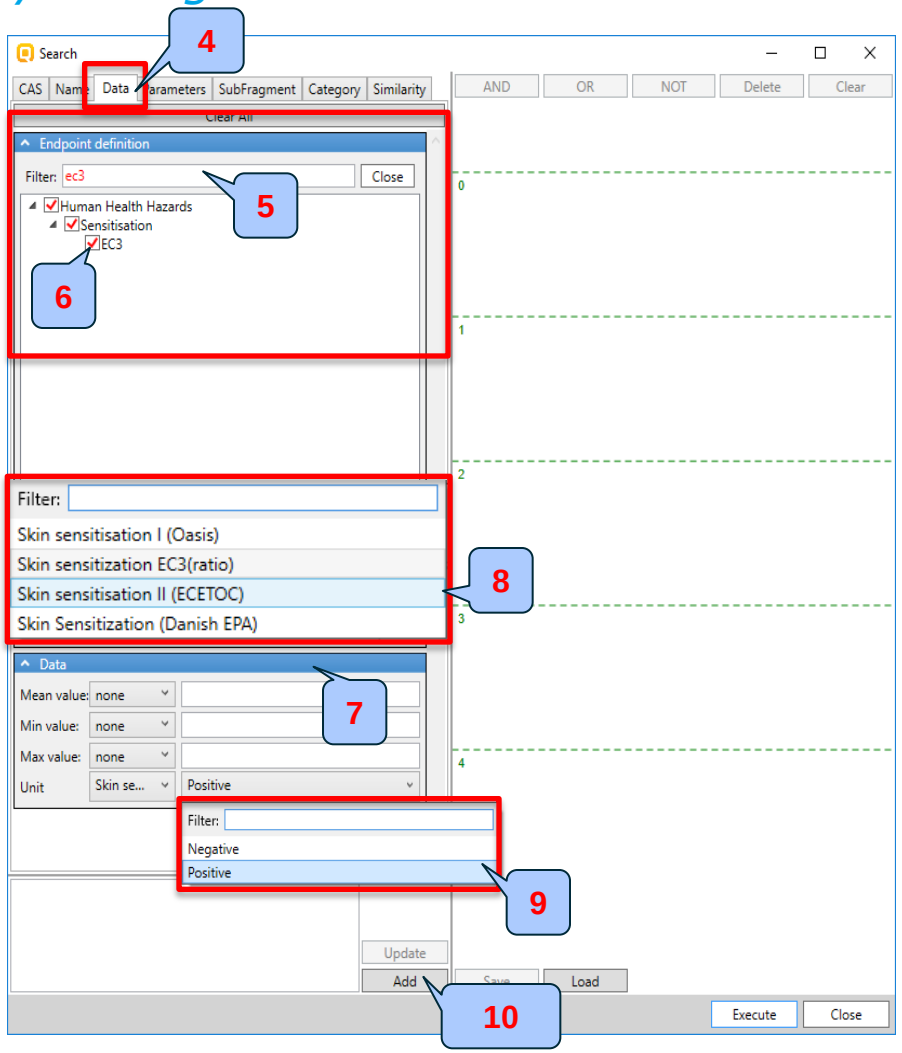
Example 6

- Structures search criteria
  - Endpoint: *EC3*
  - Data: *Positive*
  - Predefined category: alpha, beta-unsaturated aldehydes









1. Select databases including skin sensitization data. No inventories has been selected in this case;
2. Click **Query tool** button;
3. Select **No** to confirm that the databases in previous example not be used;
4. Click on *Data* panel;
5. Use filter to find searched endpoint;
6. Check **EC3**;
7. Go to *Data* panel;
8. Select scale **Skin sensitization II (ECETOC)**;
9. Select **Positive**;
10. Click **Add** button;

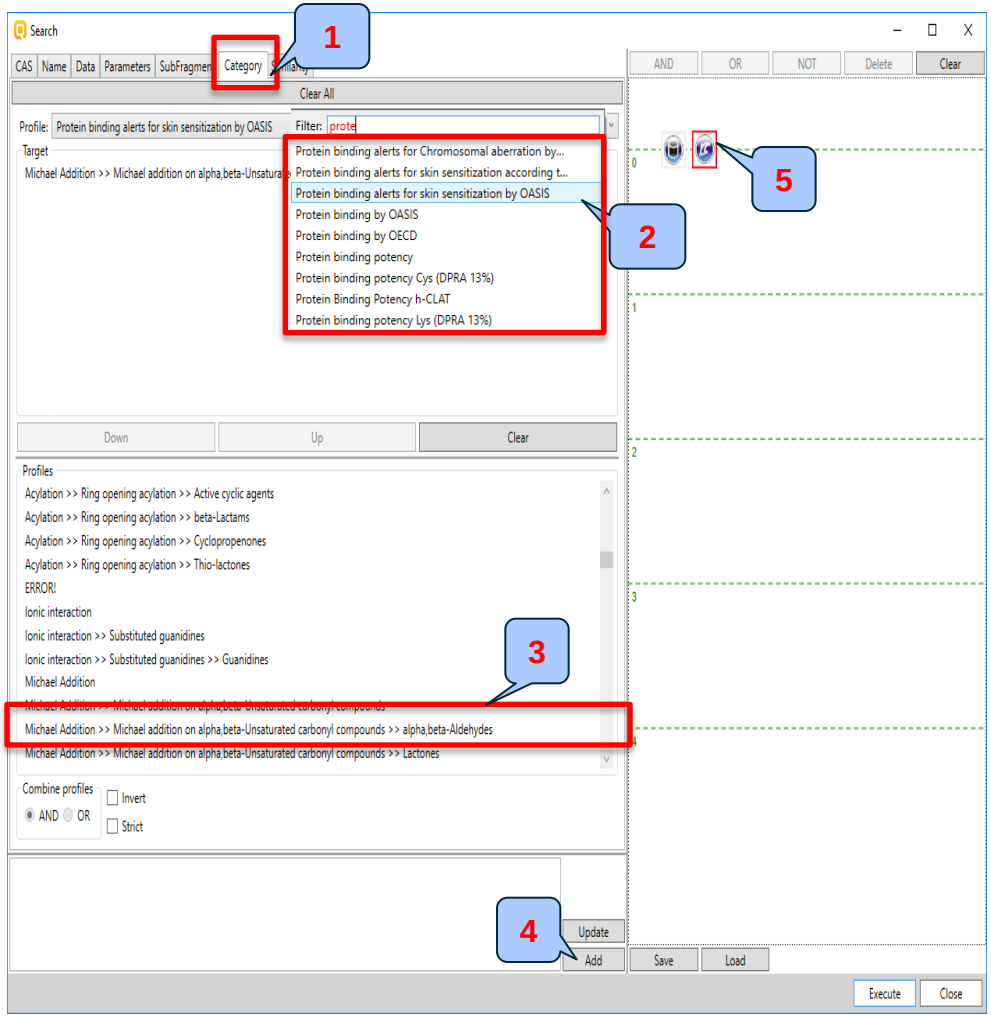
Subfragment search for identifying chemicals

Chemicals with Skin sensitization positive data including Aldehyde fragment

Example 6

- Structures search criteria
  - Endpoint: *EC3*
  - Data: *Positive*
  - Predefined category: alpha, beta-unsaturated aldehydes

1. Click *Category* panel;
2. Type in *Filter* to find the profile "***Protein binding alerts for skin sensitization by OASIS***";
3. Select category *Michael addition >>alpha, beta-Unsaturated carbonyl compounds>>alpha, beta-Aldehydes* and move the selected category to the panel Target;
4. Click **Add** button;
5. The query appears on the logic panel.

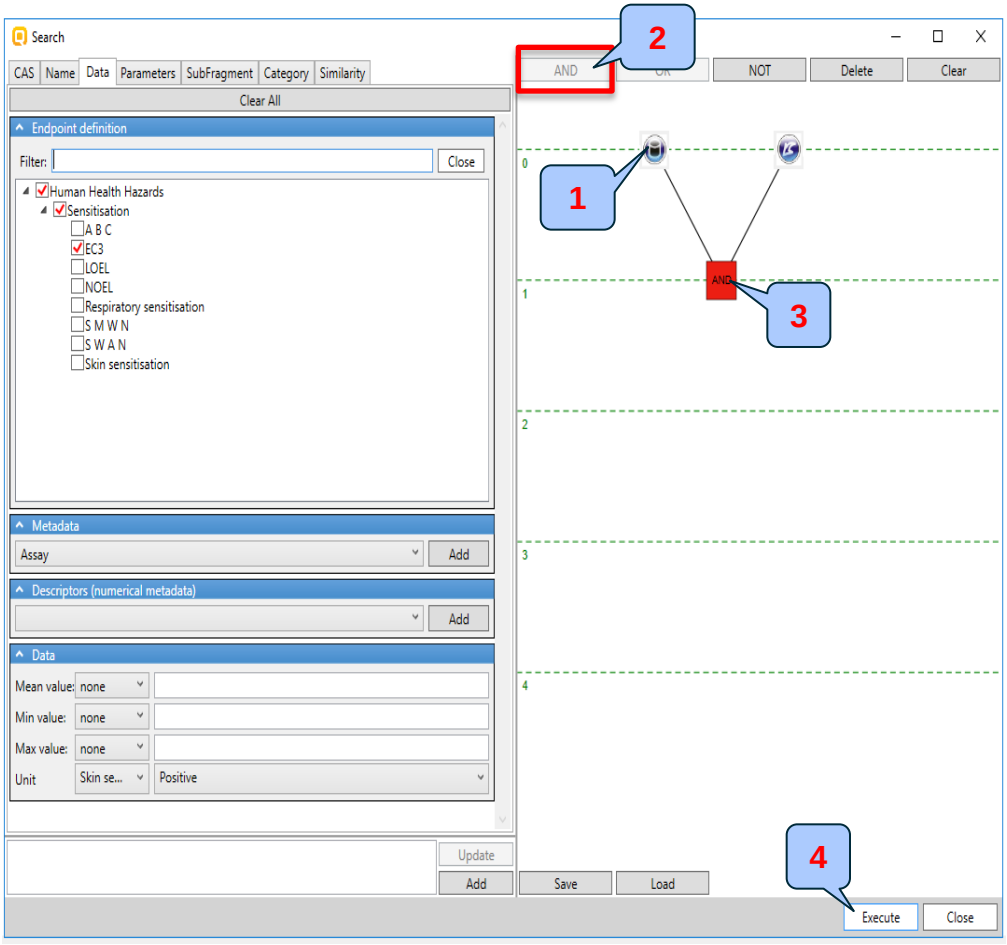


Subfragment search for identifying chemicals

Chemicals with Skin sensitization positive data including Aldehyde fragment

Example 6

- Structures search criteria
  - Endpoint: *EC3*
  - Data: *Positive*
  - Predefined category: alpha, beta-unsaturated aldehydes

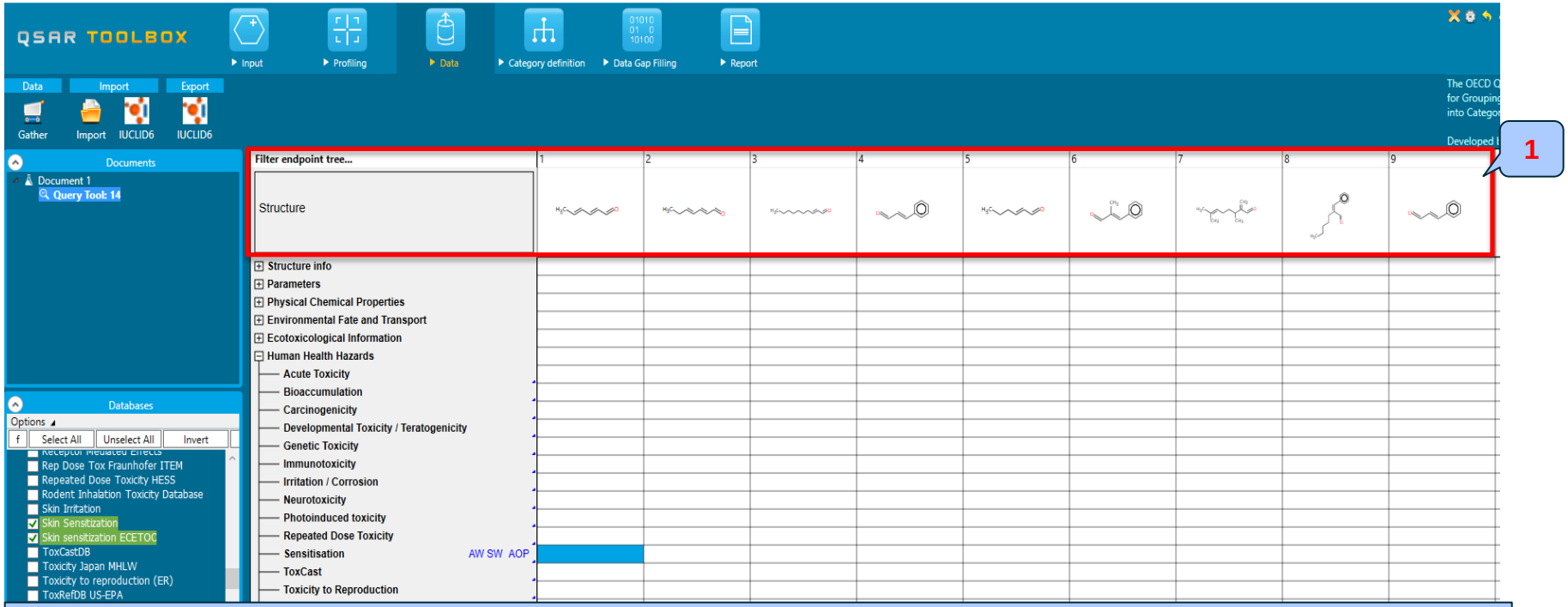


1. Right click over the queries in order to select them;
2. Click **AND** button;
3. The two queries are combined together by logical "*AND*";
4. Click **Execute** button or double click *And*;

Subfragment search for identifying chemicals

Chemicals with Skin sensitization positive data including Aldehyde fragment

Example 6

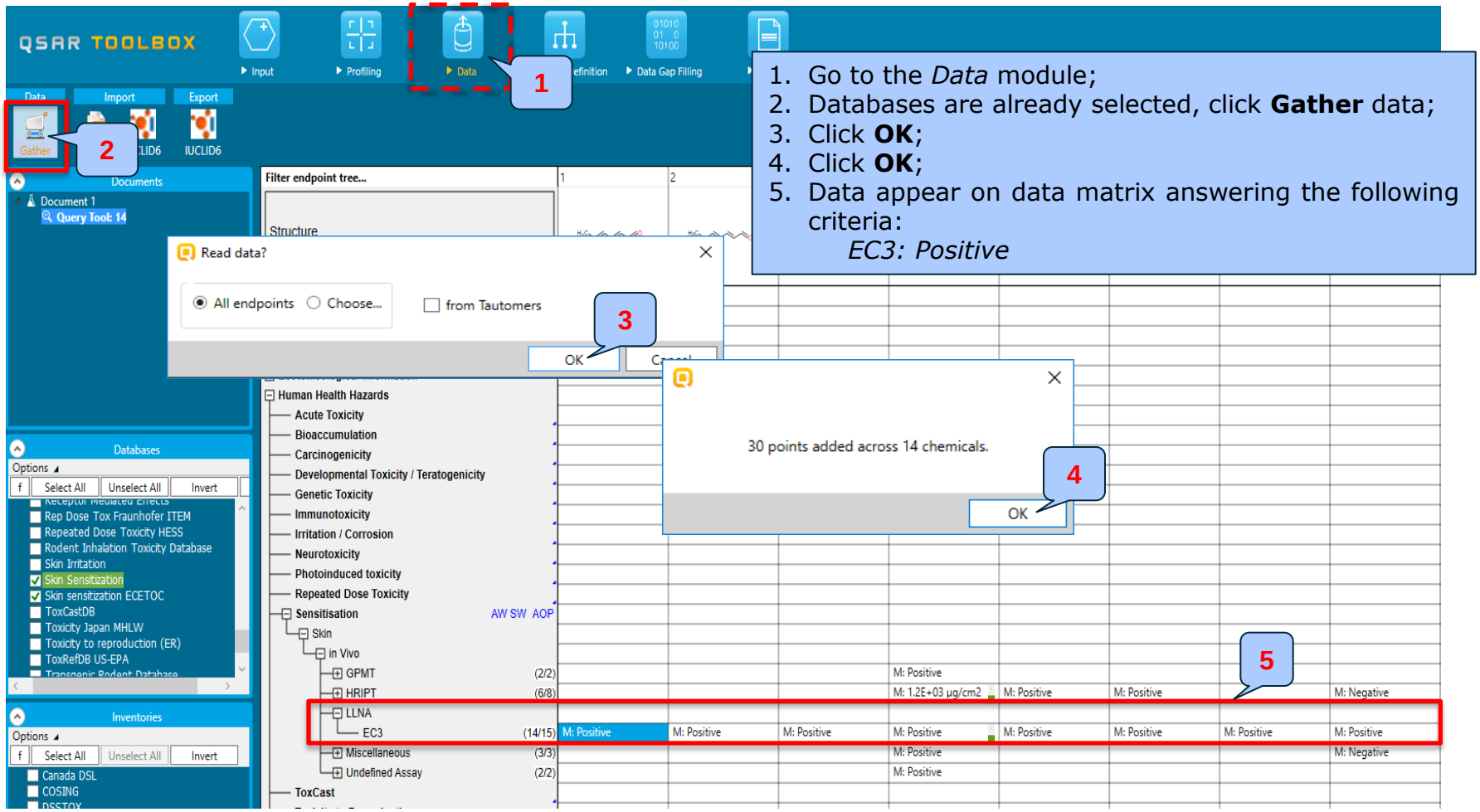


The Query tool (QT) identified 14 chemicals matching the desired criteria. In order to check the correctness of the query the user should gather experimental data for skin sensitization and profile the identified chemicals according to the "*Protein binding alerts for skin by OASIS*" profiler used in the query boundary. The last two steps are presented on the next two slides.

Subfragment search for identifying chemicals

Chemicals with Skin sensitization positive data including Aldehyde fragment

Example 6

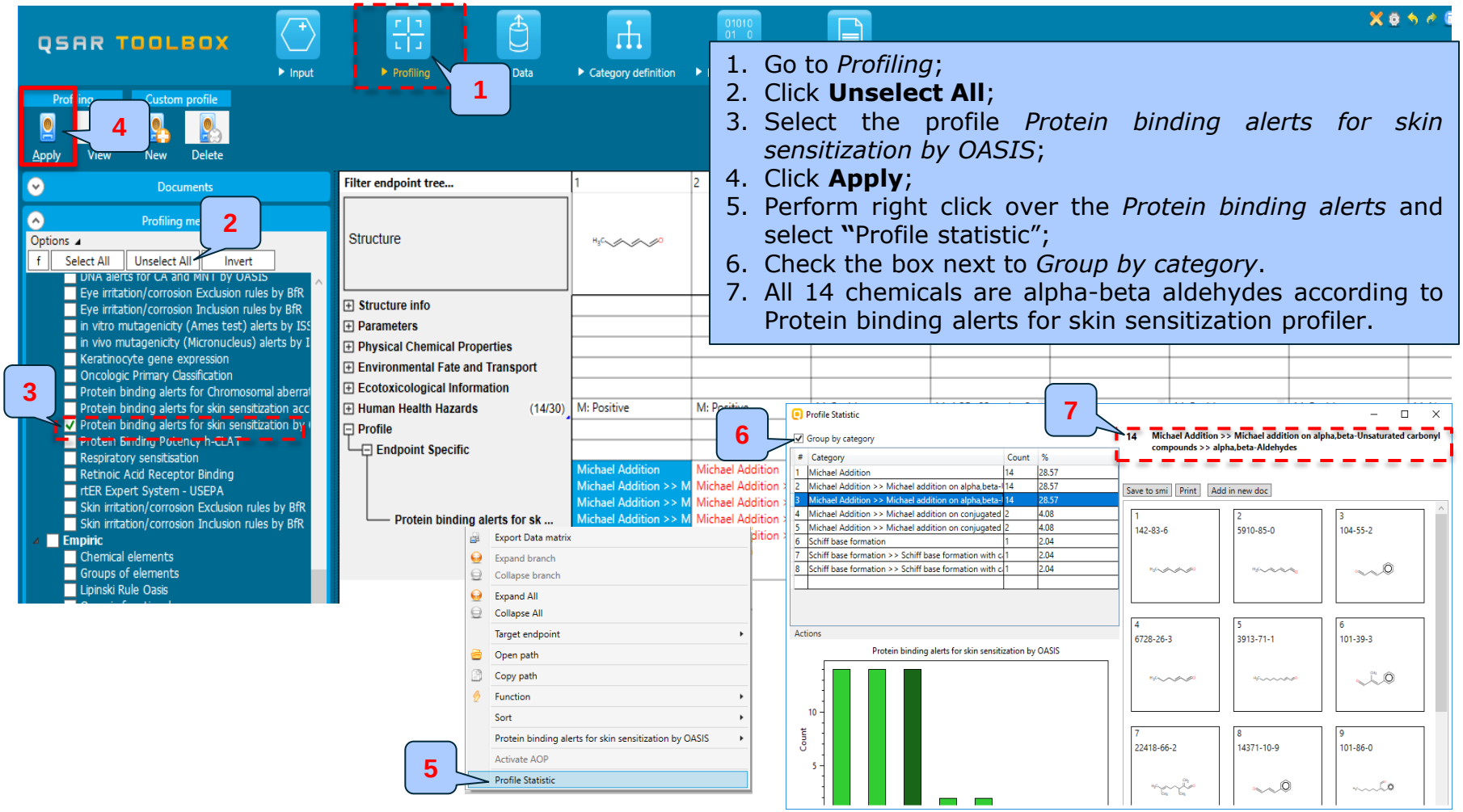


1. Go to the *Data* module;
2. Databases are already selected, click **Gather** data;
3. Click **OK**;
4. Click **OK**;
5. Data appear on data matrix answering the following criteria:
   EC3: Positive

Subfragment search for identifying chemicals

Chemicals with Skin sensitization positive data including Aldehyde fragment

Example 6



1. Go to *Profiling*;
2. Click **Unselect All**;
3. Select the profile *Protein binding alerts for skin sensitization by OASIS*;
4. Click **Apply**;
5. Perform right click over the *Protein binding alerts* and select "Profile statistic";
6. Check the box next to *Group by category*.
7. All 14 chemicals are alpha-beta aldehydes according to Protein binding alerts for skin sensitization profiler.

Outlook

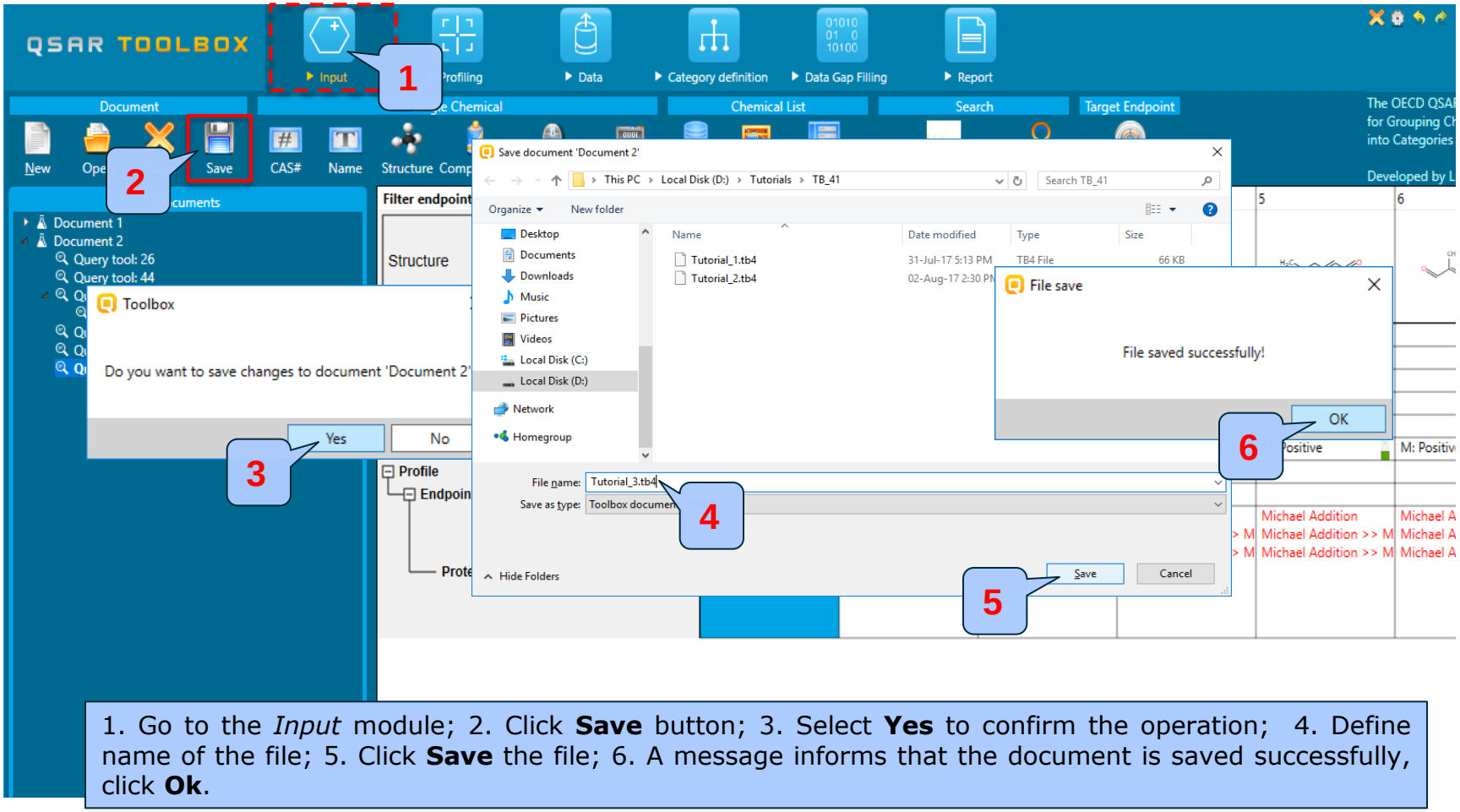
- Background
- Objectives
- Overview of Query tool
- Query tool window
- The exercise
- Workflow process
- **Save QT searches**

Saving the prediction result

- This functionality allows storing/restoring the current state of Toolbox documents including loaded chemicals, experimental data, profiles, predictions etc., on the same computer. The functionality is implemented based on saving the sequence of actions that led to the current state of the Toolbox document and later executing these actions in the same sequence in order to get the same result(s).

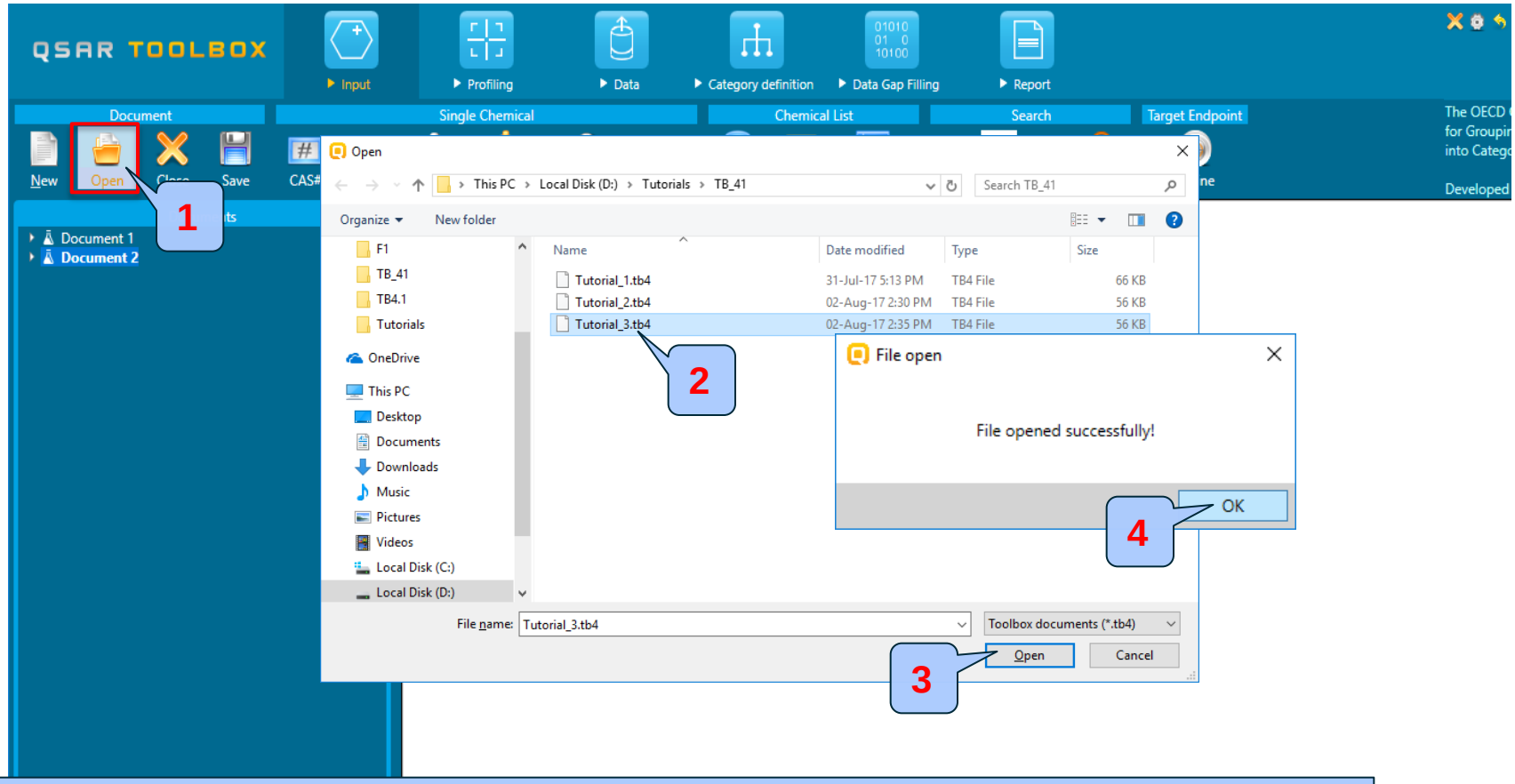
- Saving/Loading the file with TB prediction is shown on the next screenshots

Saving the QT requests



1. Go to the *Input* module; 2. Click **Save** button; 3. Select **Yes** to confirm the operation; 4. Define name of the file; 5. Click **Save** the file; 6. A message informs that the document is saved successfully, click **Ok**.

Open saved file



Once the file has been saved: 1. Click **Open** button within the Input module; 2. Find and select the file; 3. Click **Open**; 4. A message informs that the document is opened successfully, click **Ok**.