QSAR TOOLBOX

The OECD QSAR Toolbox for Grouping Chemicals into Categories

OECD (Q)SAR Toolbox v.4.4.1

Examples illustrating customized search (Query Tool) in Toolbox

Outlook

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

Background

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

Outlook

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

Objectives

In this presentation we will use functionalities of the QT to identify:

1) chemicals having specific structural fragments in their molecules

2) chemicals answering specific structural and parametric criteria

3) chemicals answering specific combinations of data, structural and parametric criteria

Outlook

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

Overview of Query tool

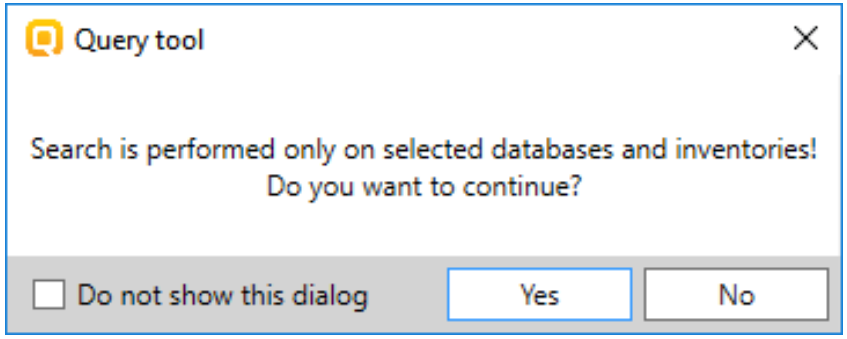
Goal: Query tool allows searching for chemicals by structure, sub fragments, phys-chem properties and experimental data

- **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

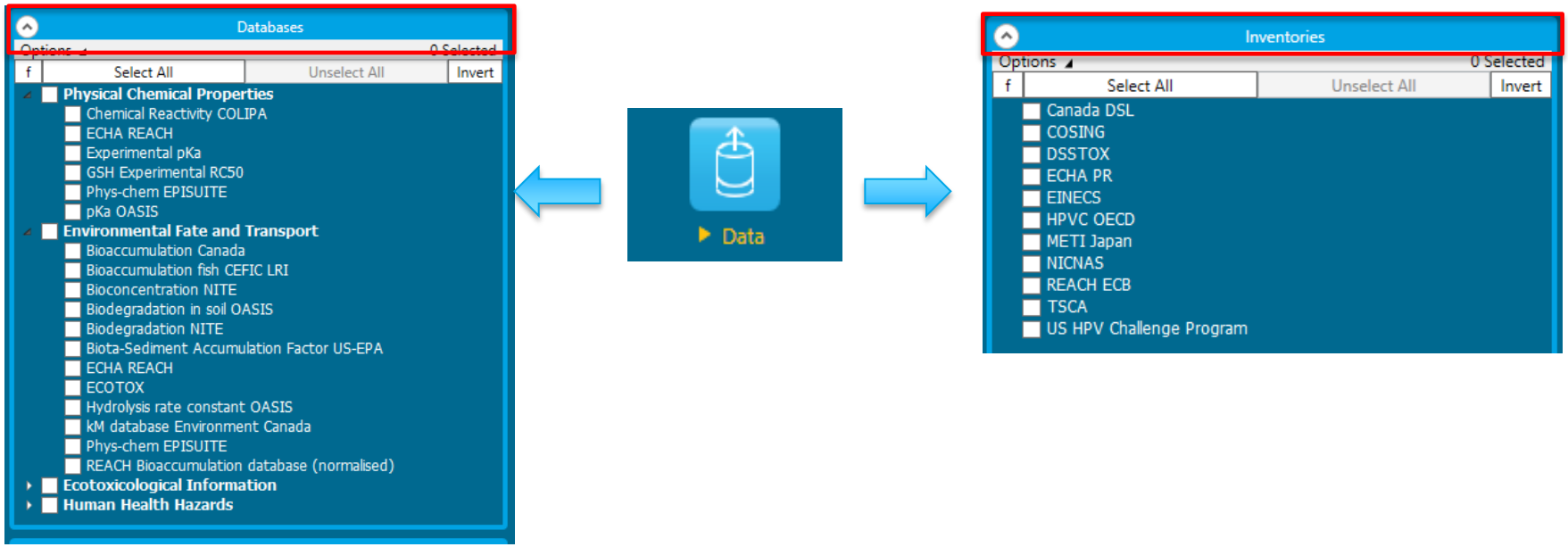
•The Query tool functionality searches for single structures matching desired criteria.

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

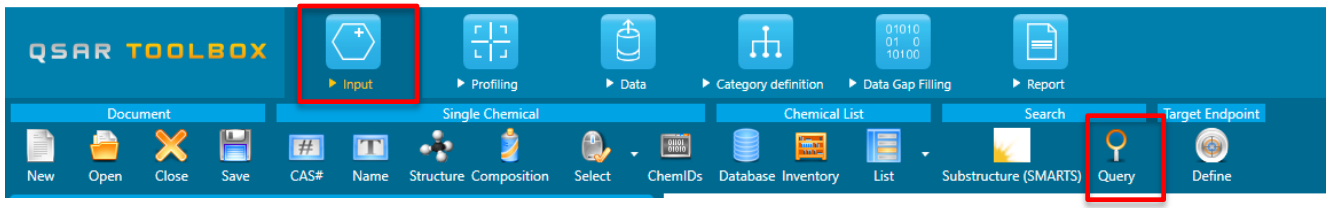


Overview of Query tool
Procedure for defining query

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



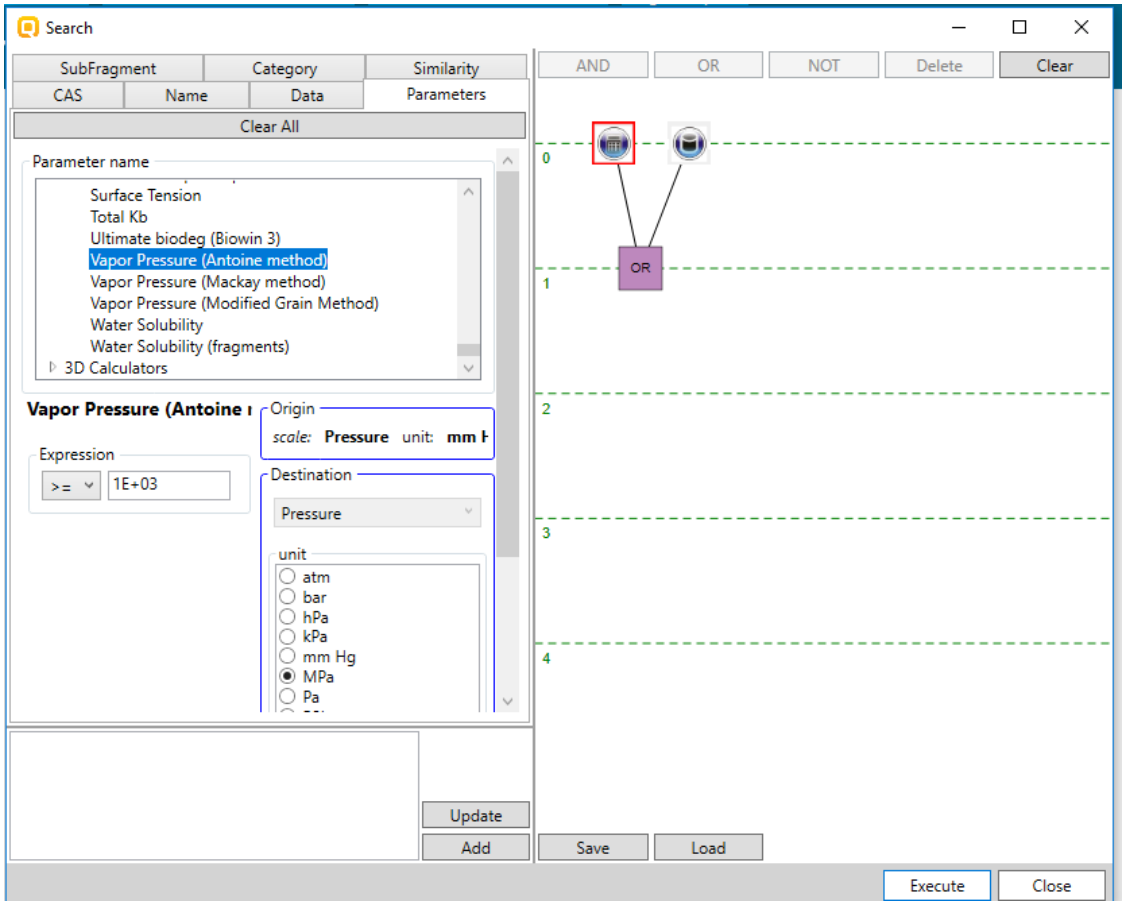
Step 2: Click *Query* button



Overview of Query tool

Procedure for defining query

Step 3: Specify criteria for searching structures

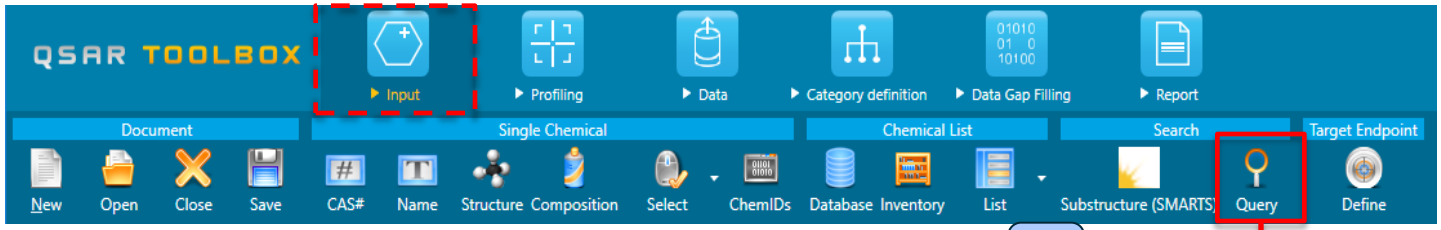


Outlook

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

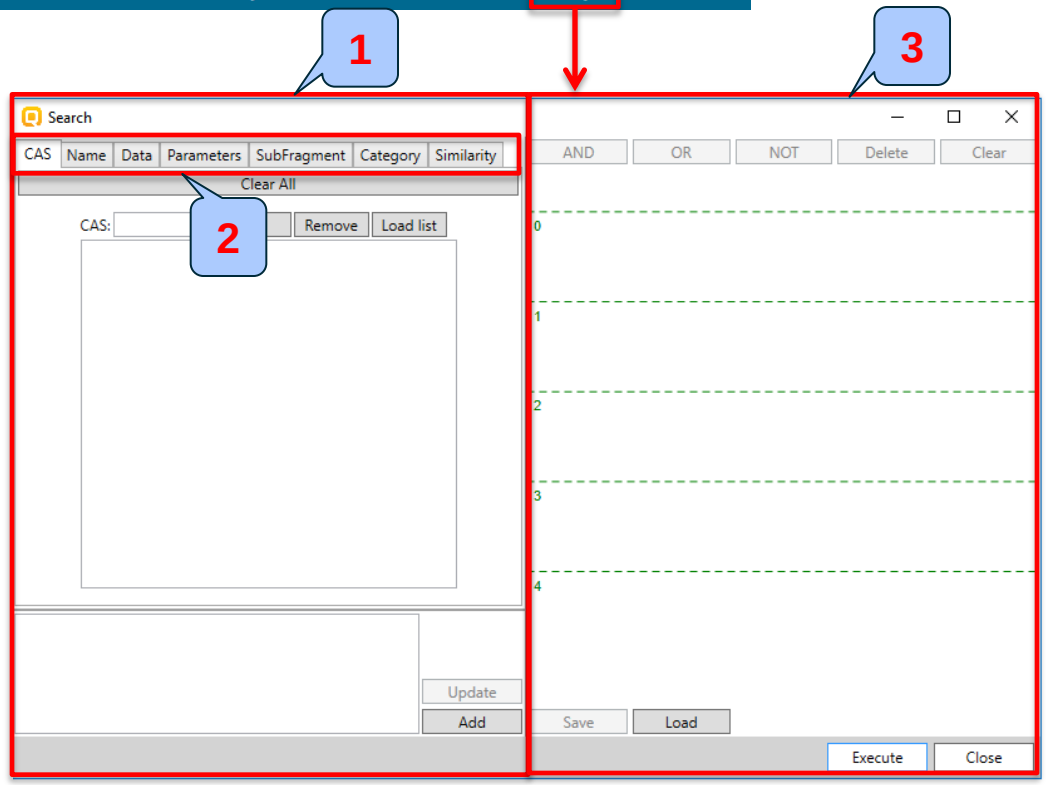
Query tool window

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



The main components of Query tool window includes:

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



Outlook

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

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 queries with Environmental Data (BCF) and 3D parameters (D*max*) *(Example 3)*
  - Combination of queries with predefined category (Aldehydes) and ecotox data (LC50<1mg/l) *(Example 4)*
  - Combination of queries with positive Ames; positive Carcinogenicity data and Subfragment search (*Epoxides*) *(Example 5)*
  - Combination of Skin sensitization data (EC3) and predefined category (*Aldehydes*) queries *(Example 6)*

Outlook

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

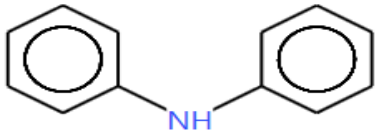
Subfragment search for identifying chemicals

Substituted diphenyl amine

Example 1

Search for structures that meet the following structural requirements:

- *Substituted diphenyl amine*



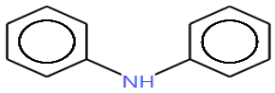
N(c1ccccc1)c1ccccc1

Subfragment search for identifying chemicals

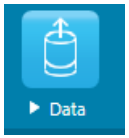
Procedure for defining

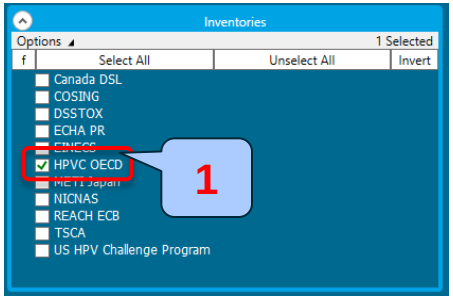
Example 1

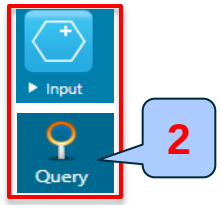
Substituted diphenyl amine

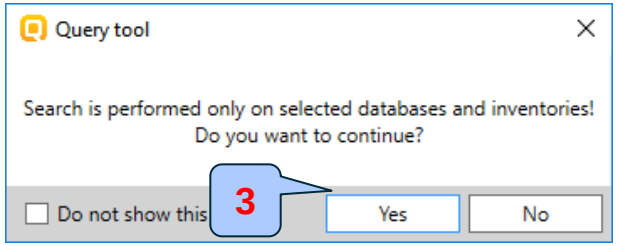


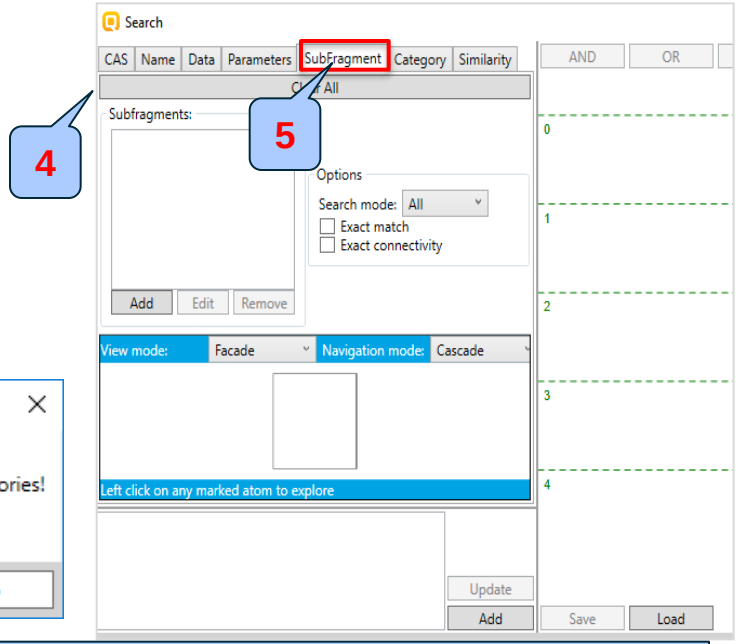
N(c1ccccc1)c1ccccc1











QT procedure starts with selecting databases/inventories used for searching the desired criteria:

1. **Select** HPVC OECD inventory located under **Data** module. No databases have been selected in this exercise;
2. Click **Query** button located under **Input** module; 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;

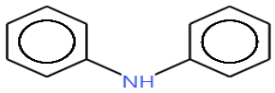
Continued on the next slide

Subfragment search for identifying chemicals

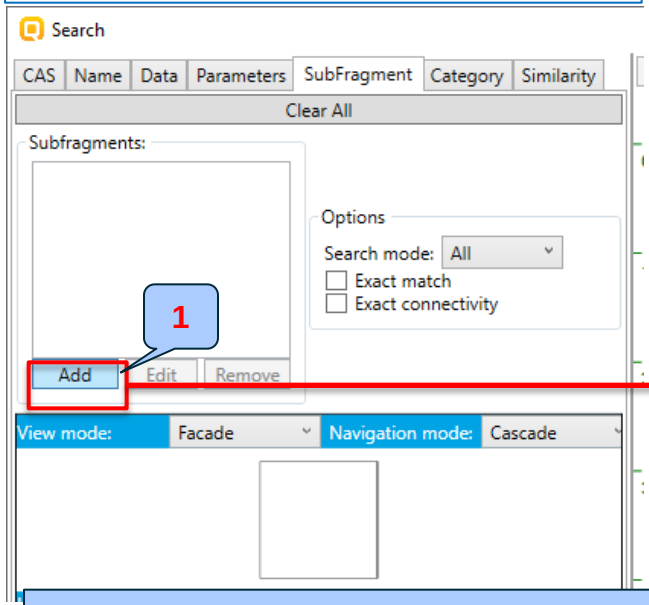
Procedure for defining

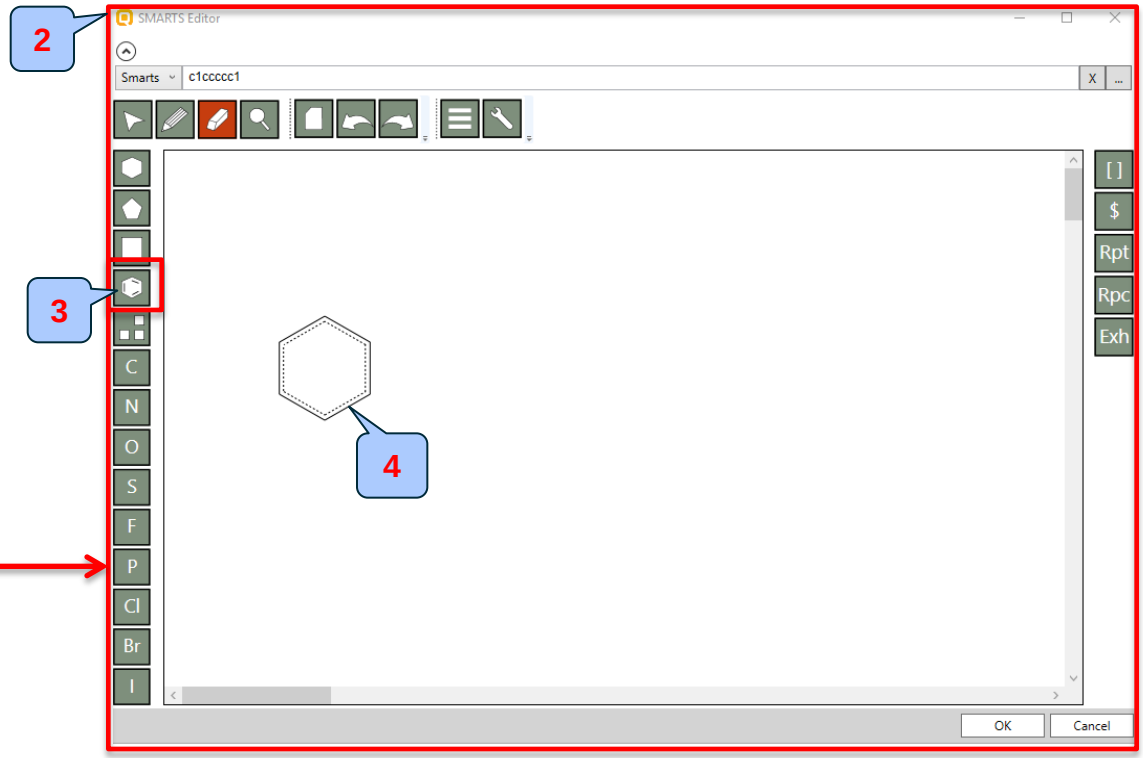
Example 1

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;

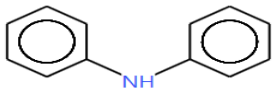
Continued on the next slide

Subfragment search for identifying chemicals

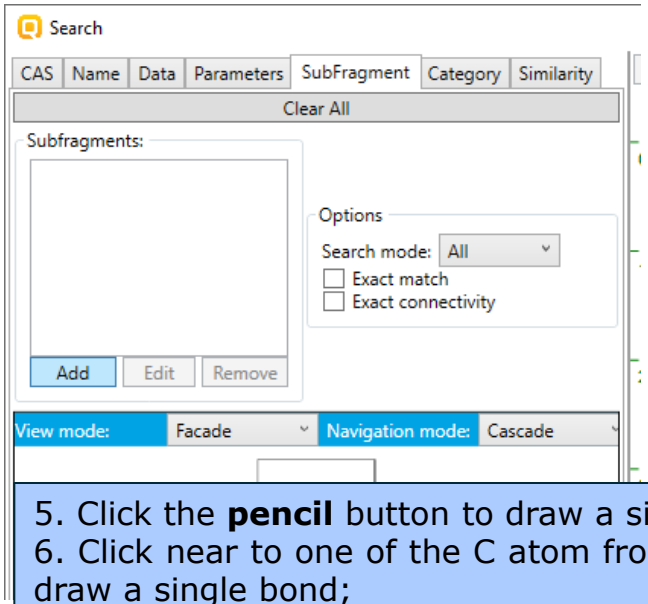
Procedure for defining

Example 1

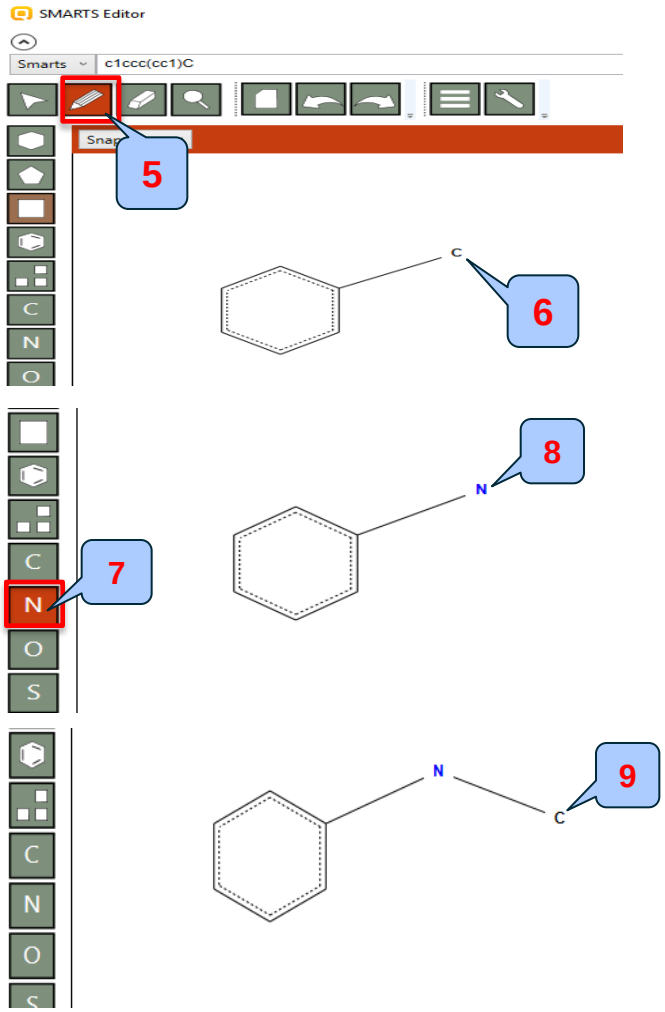
Substituted diphenyl amine



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;



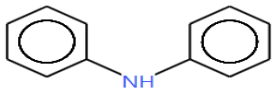
Continued on the next slide

Subfragment search for identifying chemicals

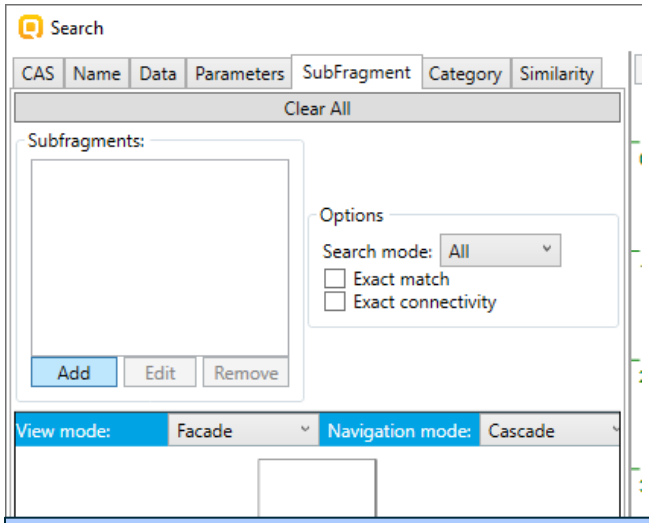
Procedure for defining

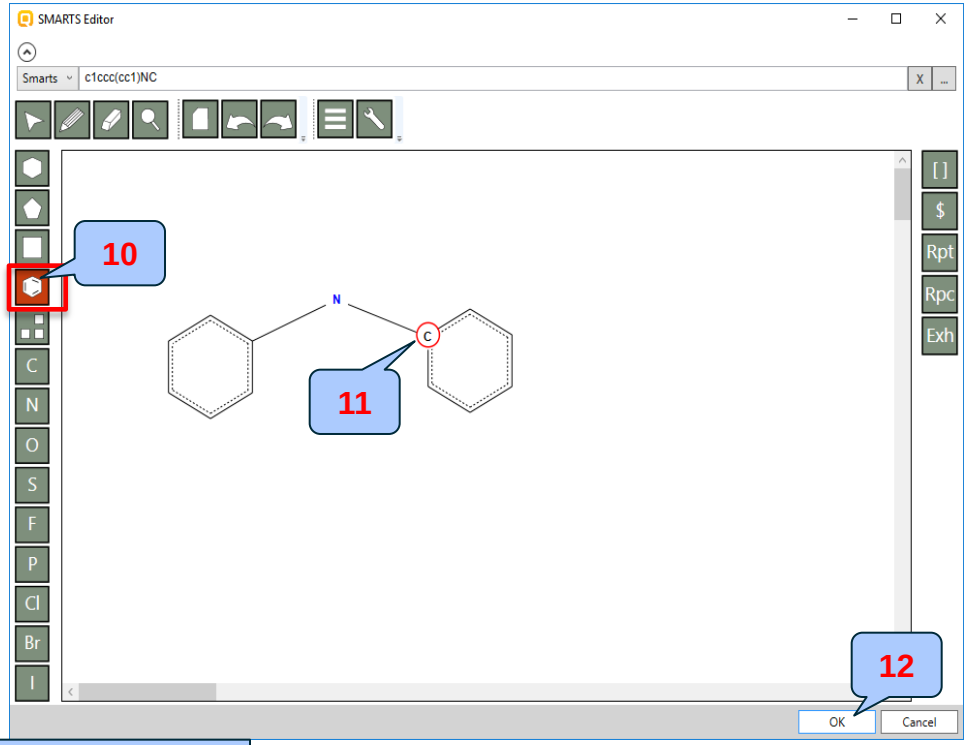
Example 1

Substituted diphenyl amine



N(c1ccccc1)c1ccccc1





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**.

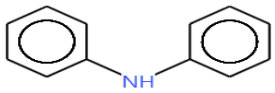
Continued on the next slide

Subfragment search for identifying chemicals

Procedure for defining

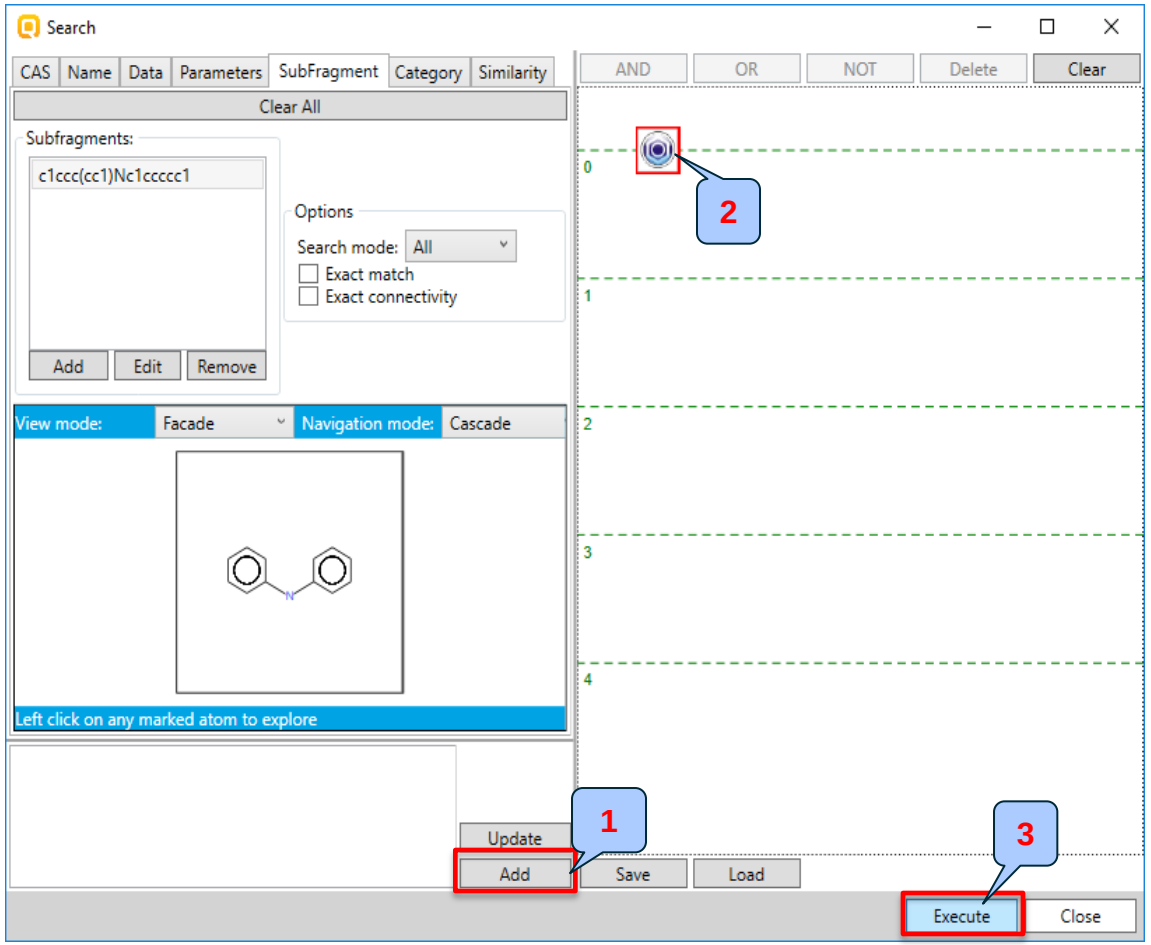
Example 1

Substituted diphenyl amine



N(c1ccccc1)c1ccccc1

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

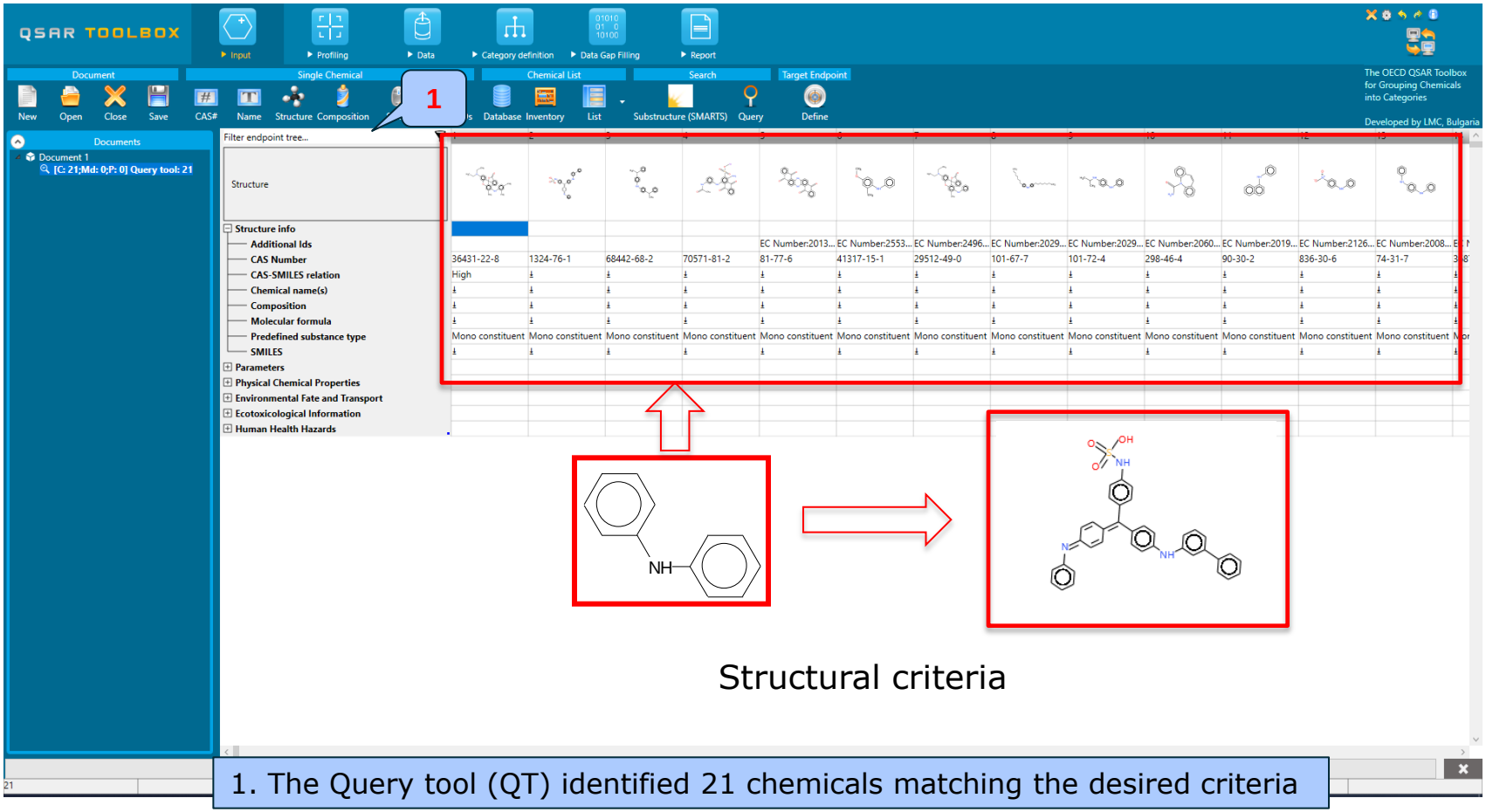


Subfragment search for identifying chemicals

Procedure for defining

Example 1

Substituted diphenyl amine



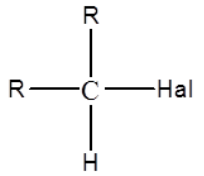
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

Search for structures that meet the structural requirements:

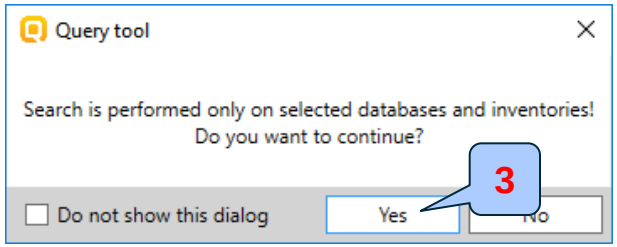
- *Aliphatic halogens*



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*** module;
3. Click **Yes**

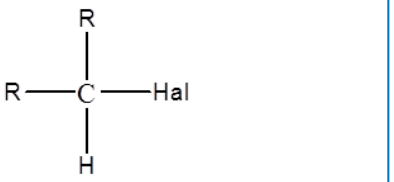
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

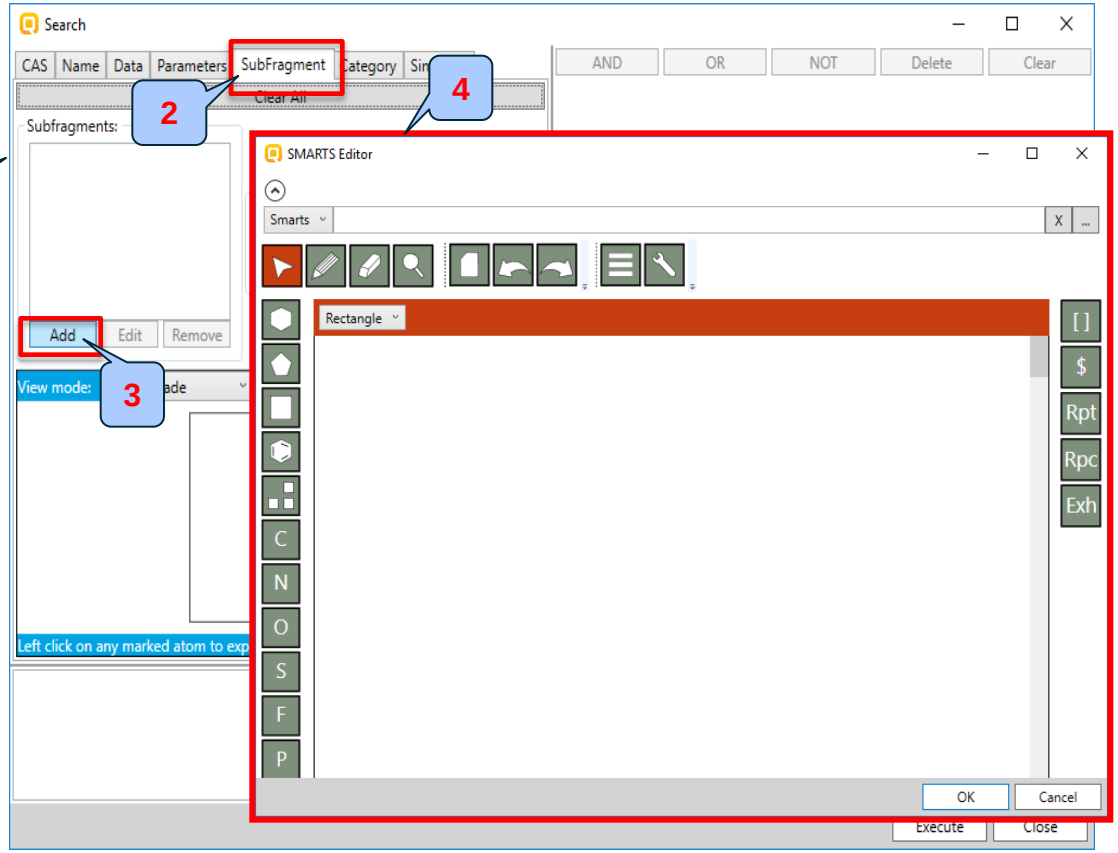
Search for structures that meet the structural requirements:

- *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;

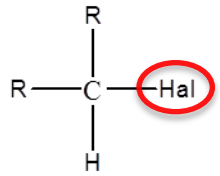
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

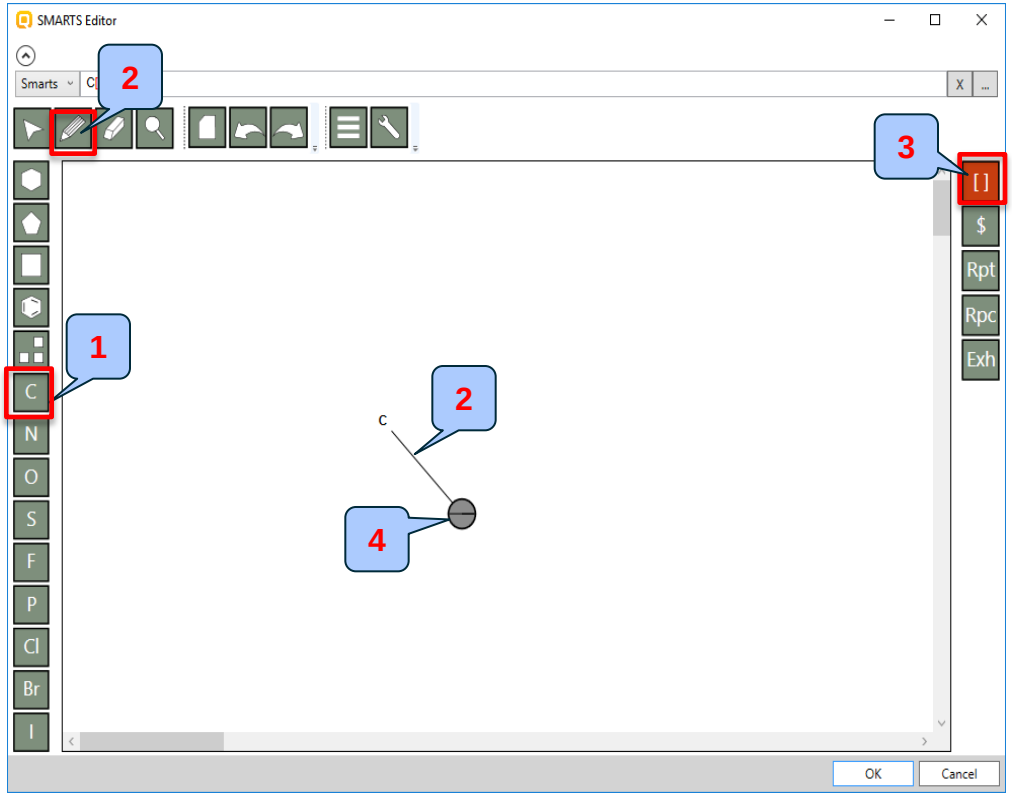
Search for structures that meet the structural requirements:

- *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;

Continued on the next slide

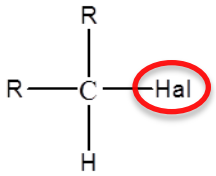
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

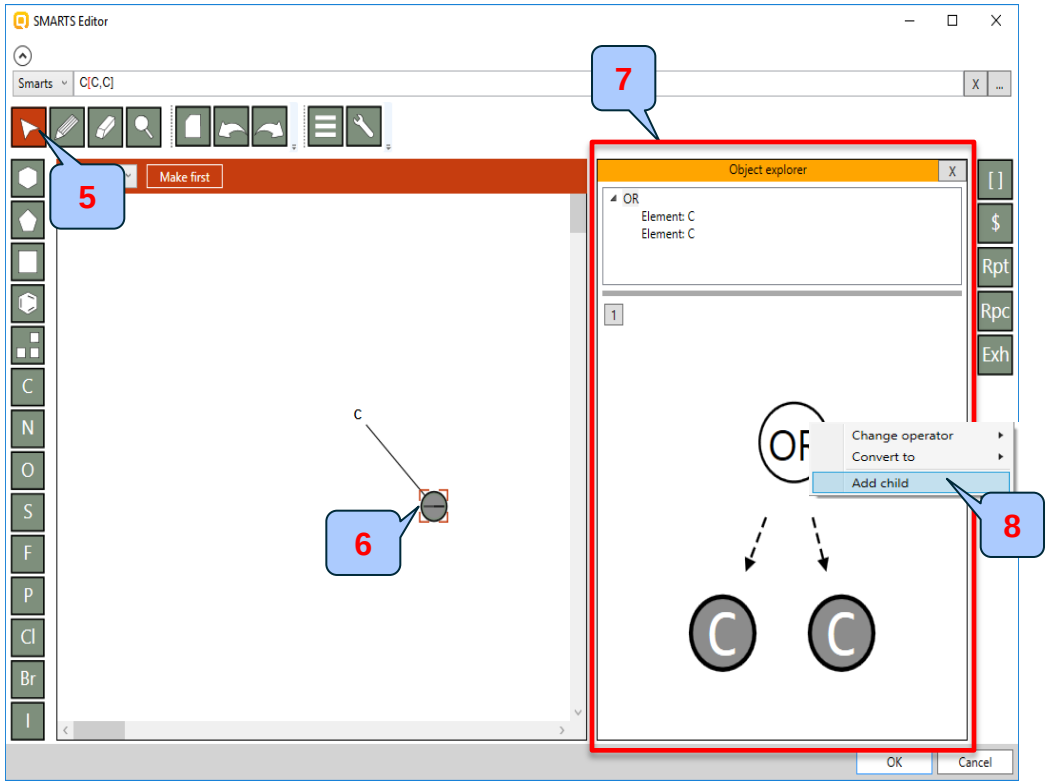
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define **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**;

Continued on the next slide

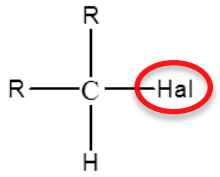
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

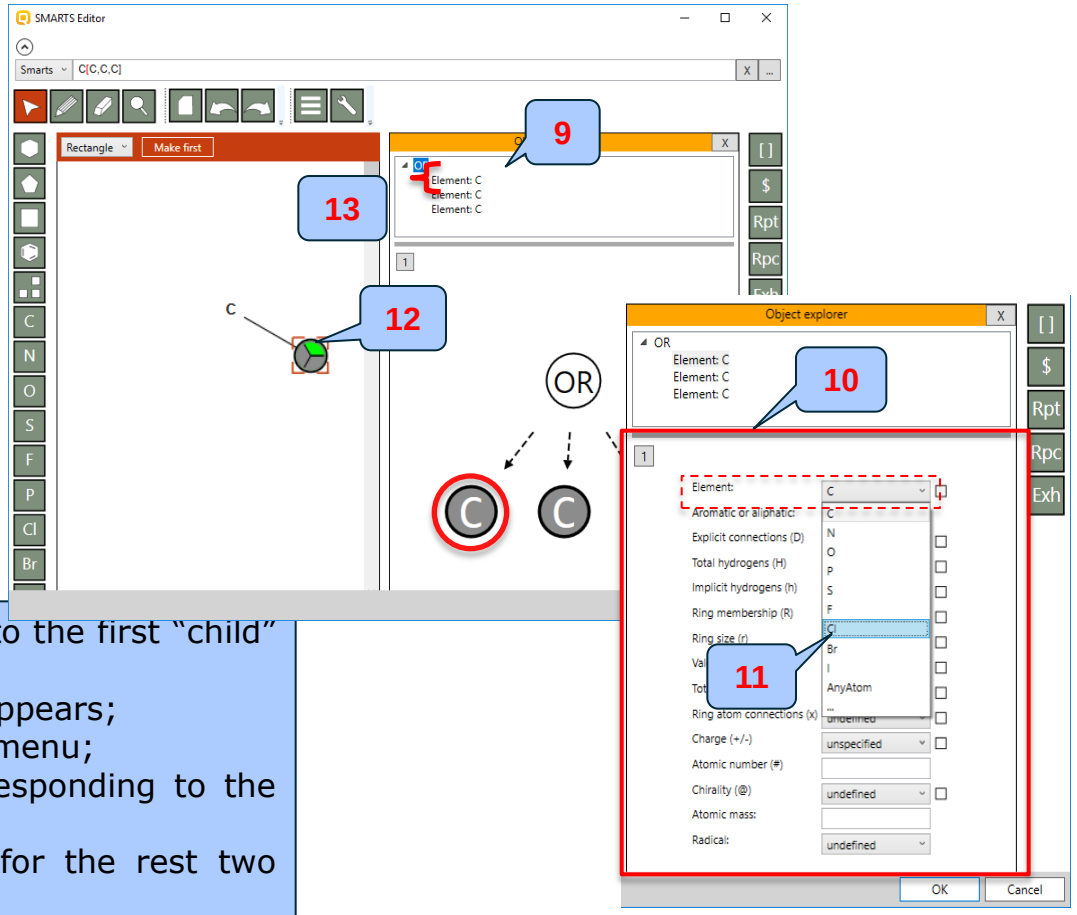
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define **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 been colored in green.
13. Select "**Br**" and "**I**" in the same way for the rest two elements , successively.

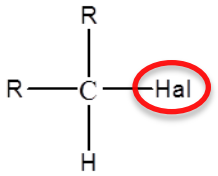
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

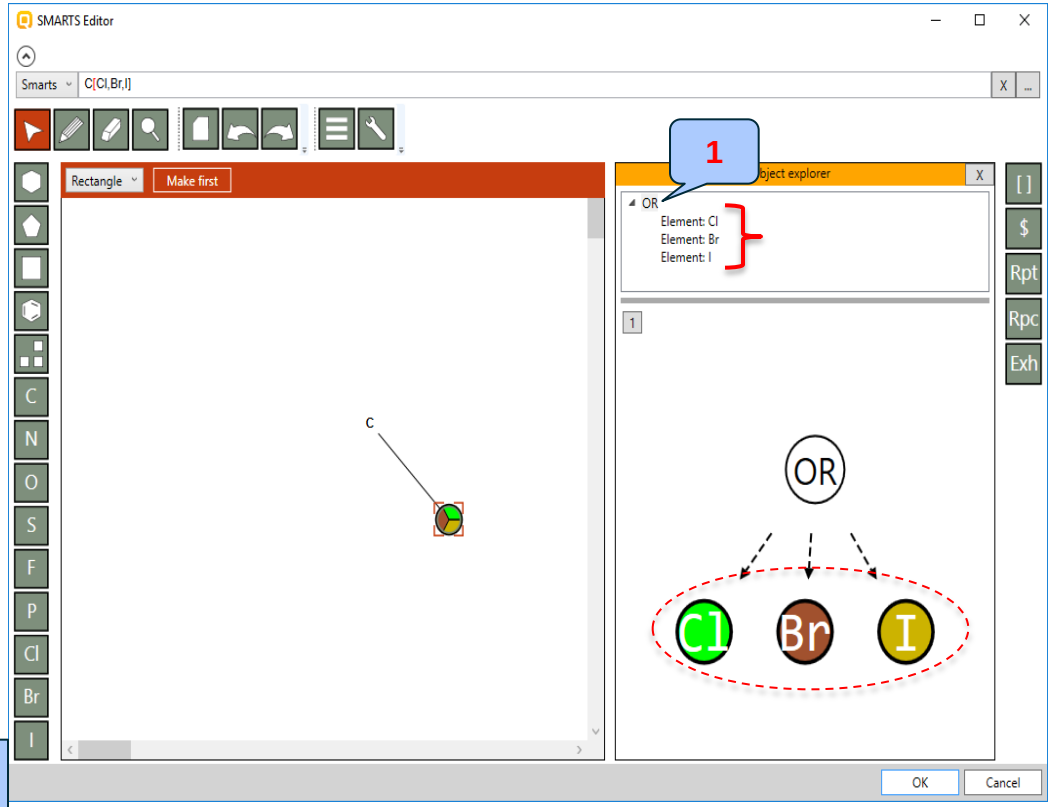
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

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



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

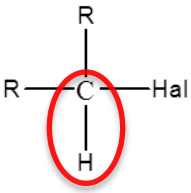
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

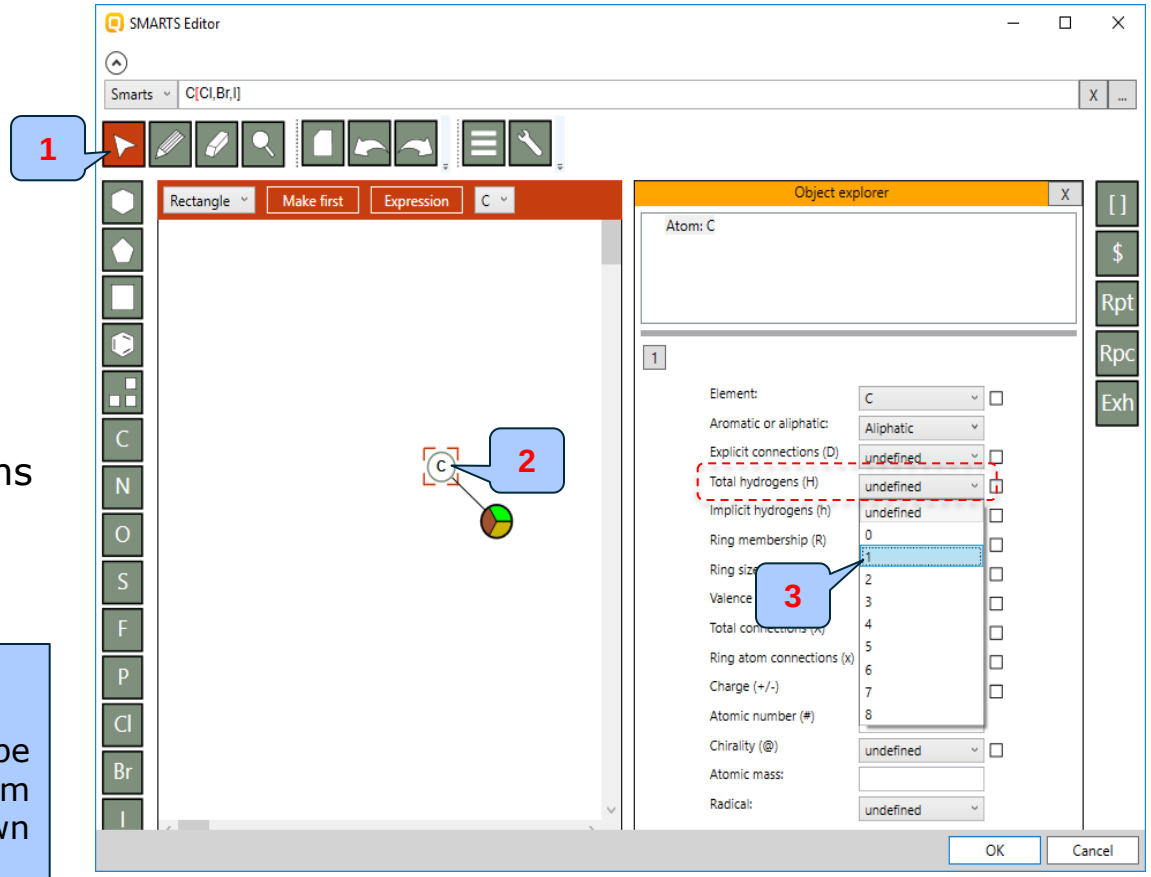
Search for structures that meet the structural requirements:

- *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

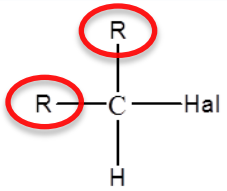
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

Search for structures that meet the structural requirements:

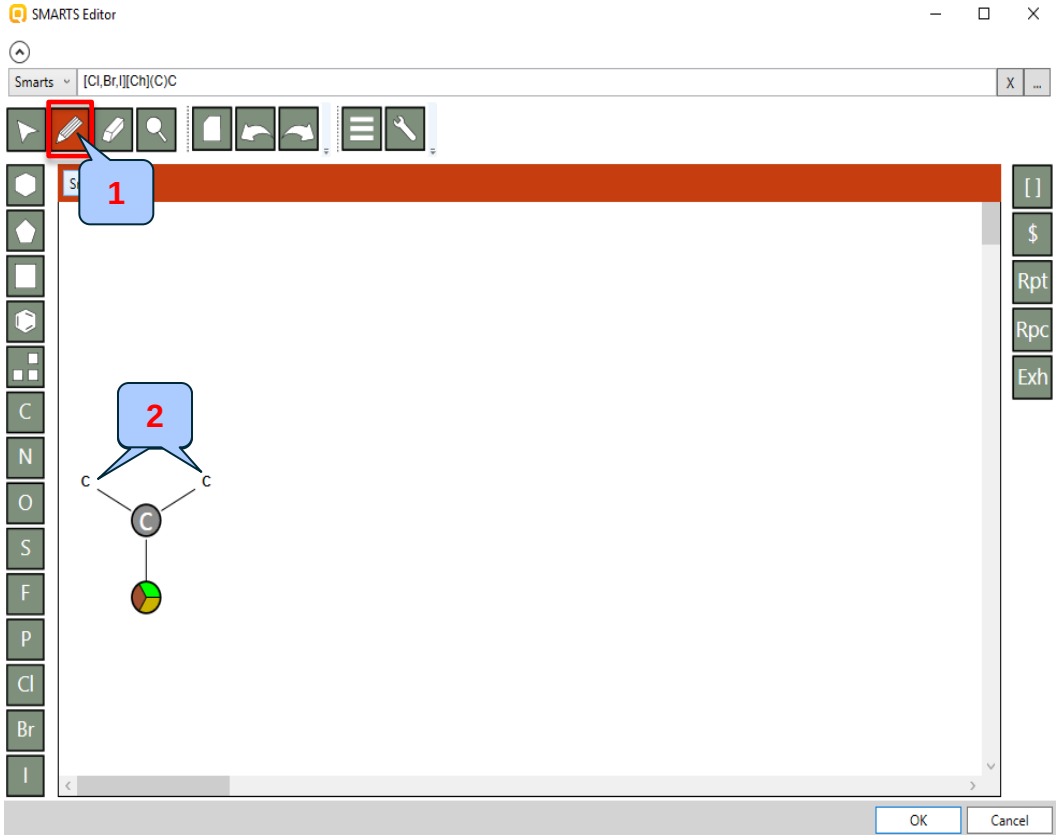
- *Aliphatic halogens*



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

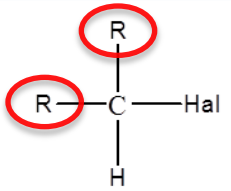
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

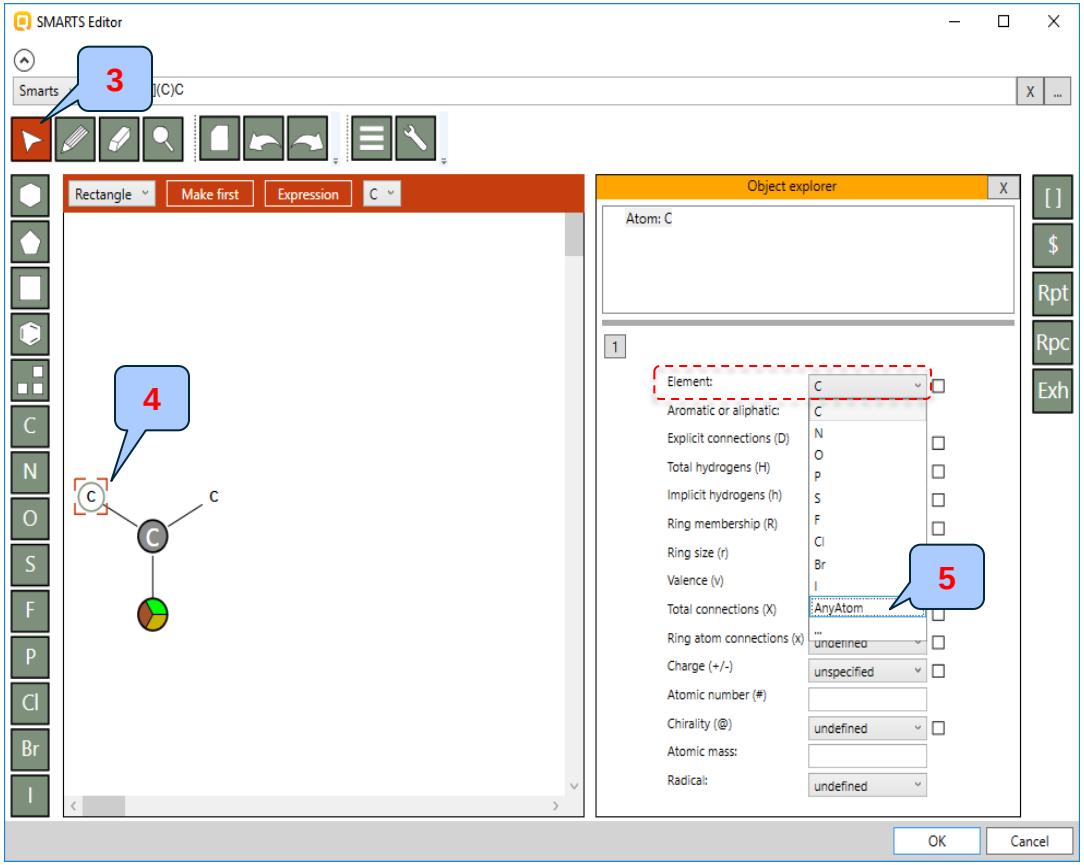
Search for structures that meet the structural requirements:

- *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

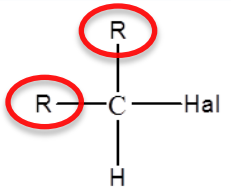
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

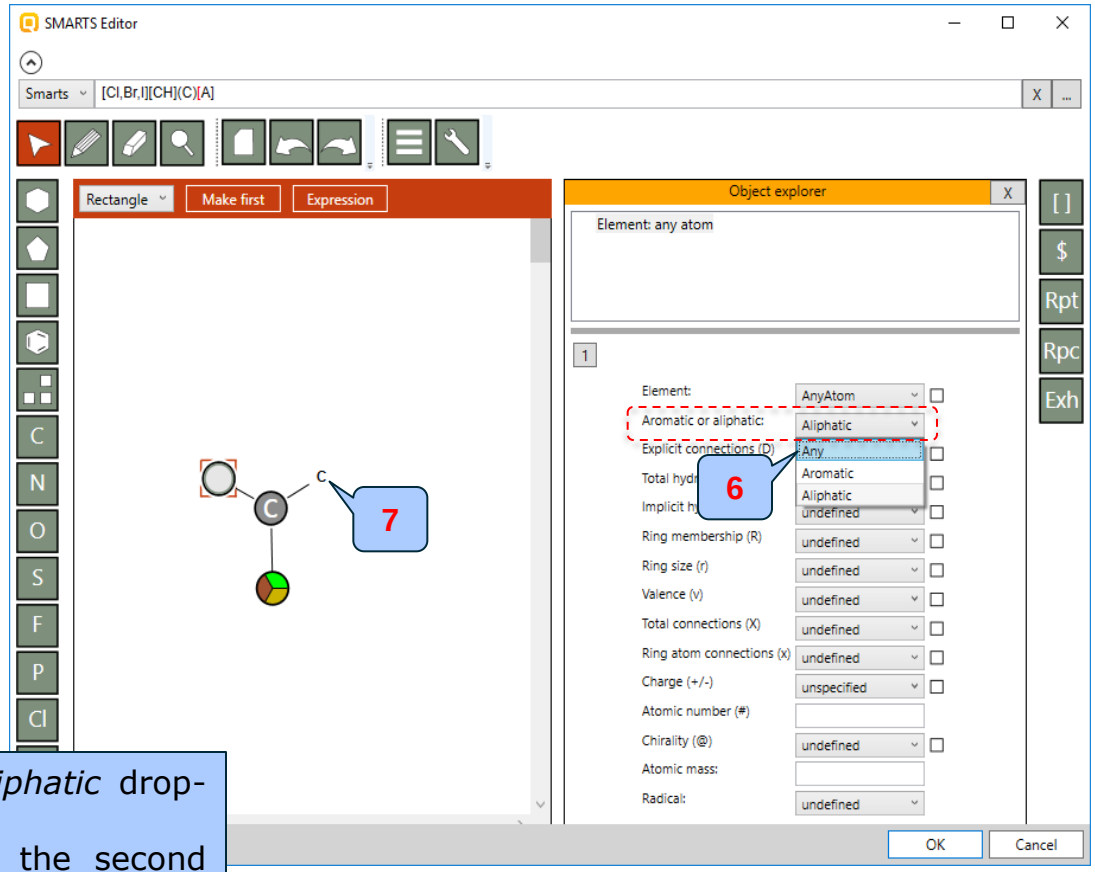
Search for structures that meet the structural requirements:

- *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

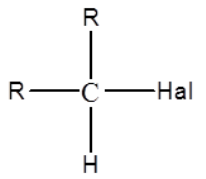
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

Search for structures that meet the structural requirements:

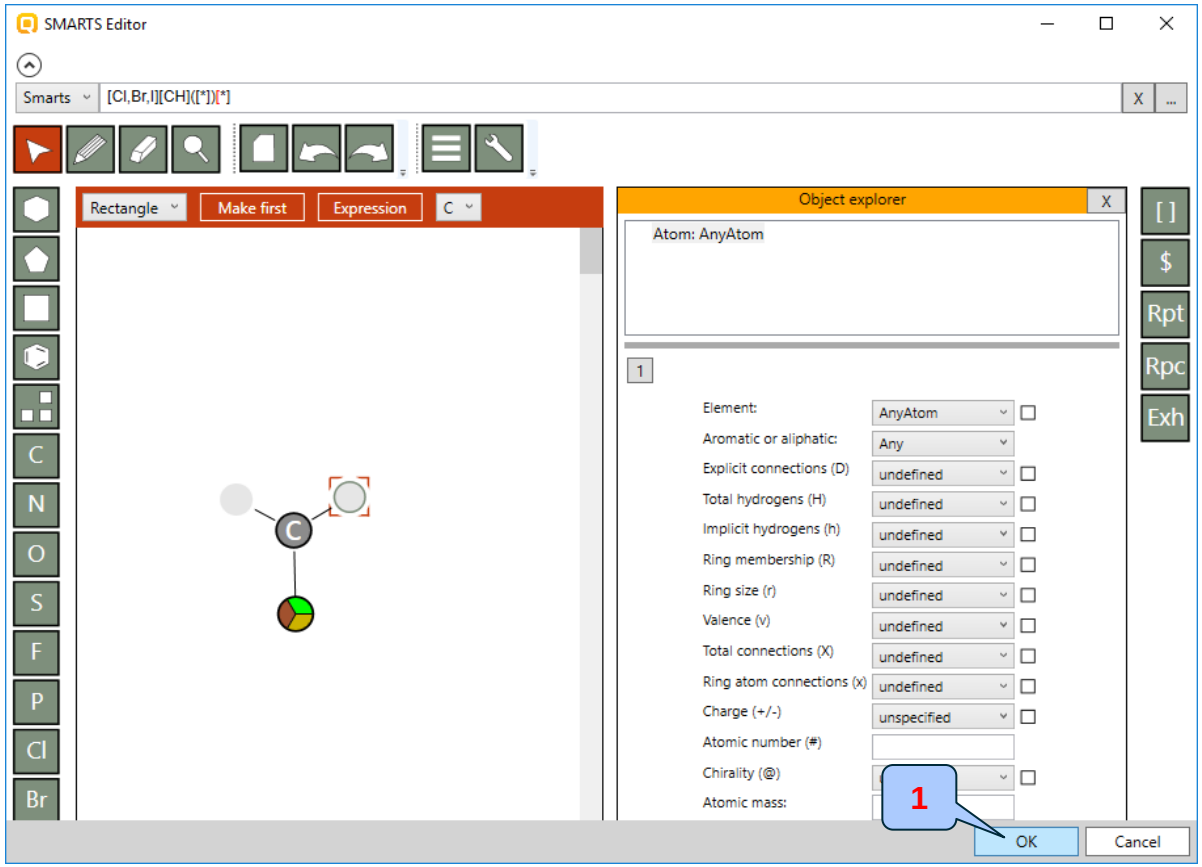
- *Aliphatic halogens*



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).



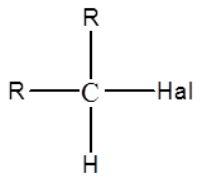
Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

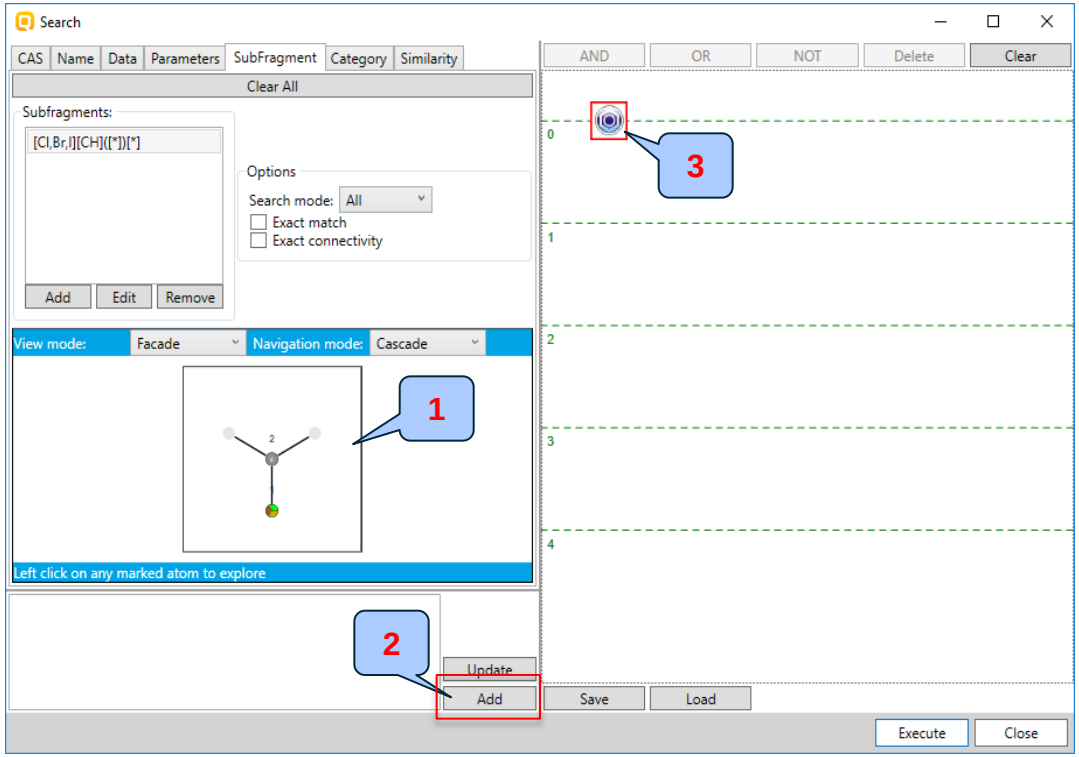
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define skeleton of target compound



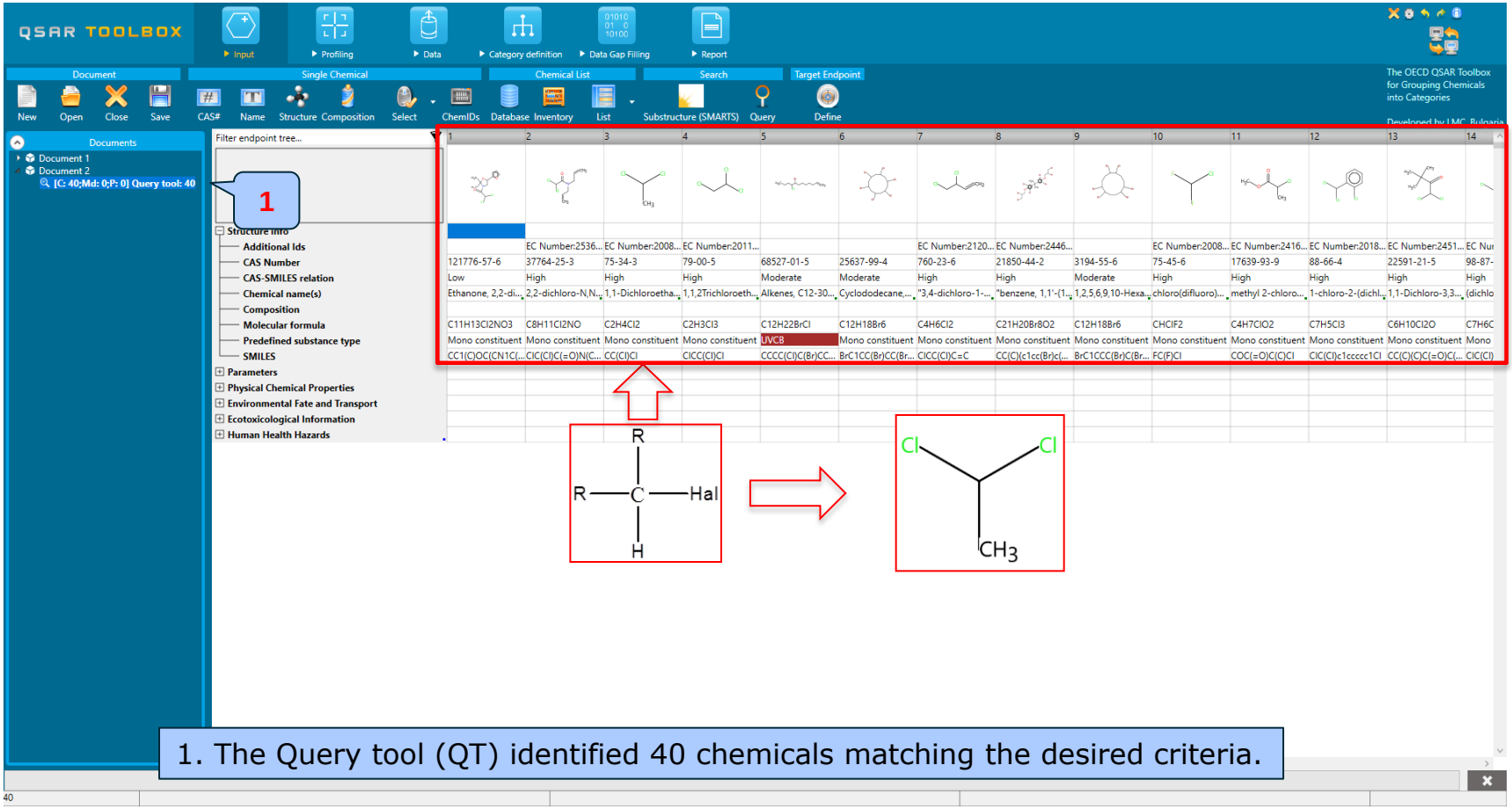
1. The defined general structure of the aliphatic halogens appears on the separate plot;
2. Click **Add** button;
3. Double click the query to perform the search

Subfragment search for identifying chemicals

Aliphatic halogens

Example 2

- *Aliphatic halogens*



1. The Query tool (QT) identified 40 chemicals matching the desired criteria.

Subfragment search for identifying chemicals

BCF and (Dmax)

Example 3

Search for structures that meet the structural requirements:

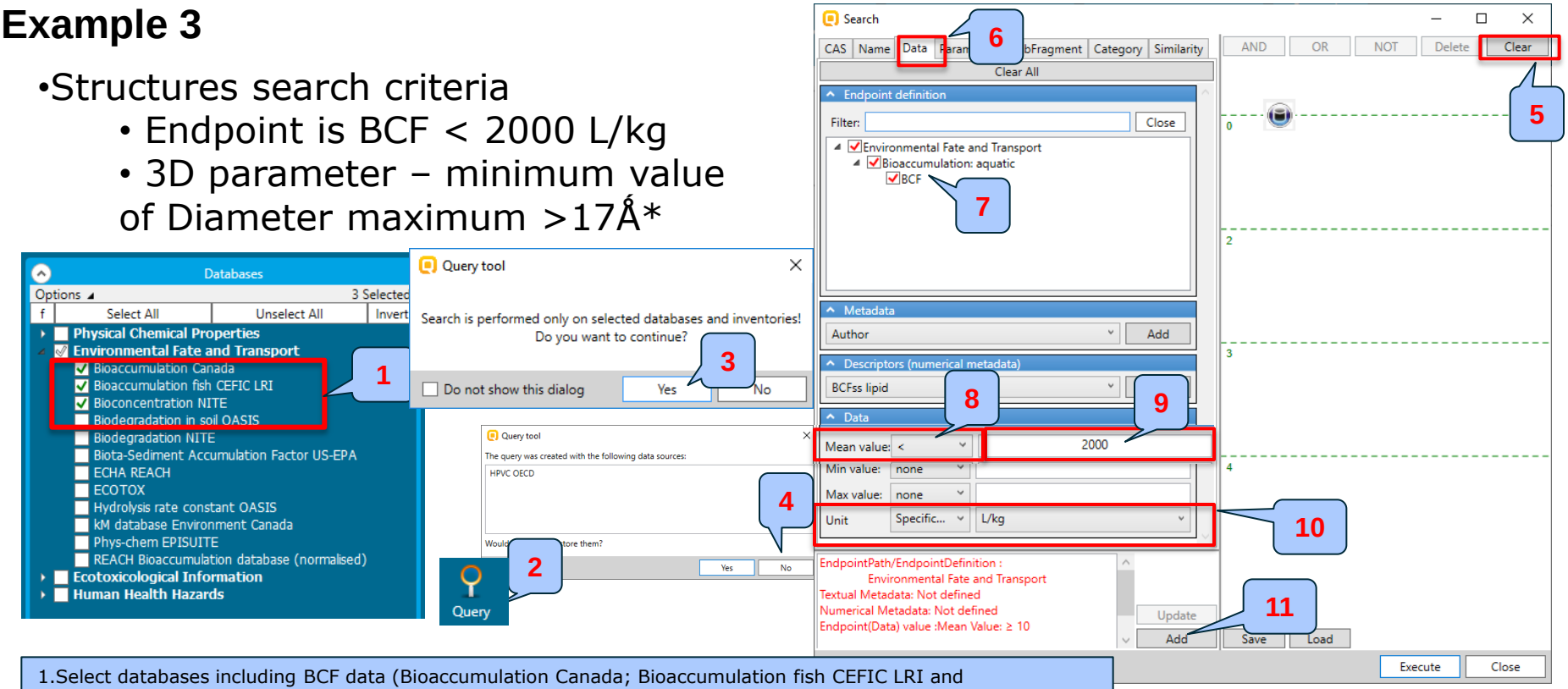
- Endpoint is BCF <2000 L/kg
- 3D parameter – minimum value of Diameter maximum >17 Å

Subfragment search for identifying chemicals

BCF and (Dmax)

Example 3

- Structures search criteria
  - Endpoint is BCF < 2000 L/kg
  - 3D parameter – minimum value of Diameter maximum >17Å*



1.Select databases including BCF data (Bioaccumulation Canada; Bioaccumulation fish CEFIC LRI and Bioconcentration NITE). No inventory has been selected in this exercise (keep them unselected);
2. Click **Query** button;
3. Confirm that the searches will be performed on selected databases and inventories;
4. Click **No** on the message asking to restore source (HPVC OECD inventory) used in the previous example.
5. Click **Clear** button to clean the desk from previous exercise;
6. Go to **Data** panel;
7. Expand the endpoint tree and select BCF;
8. Specify qualifier "**<**" and add 2000 in the *Mean value* field (9);
10. Select scale **"Specific volume"** and select the appropriate unit (**L/kg**);
11. Click **Add** button;

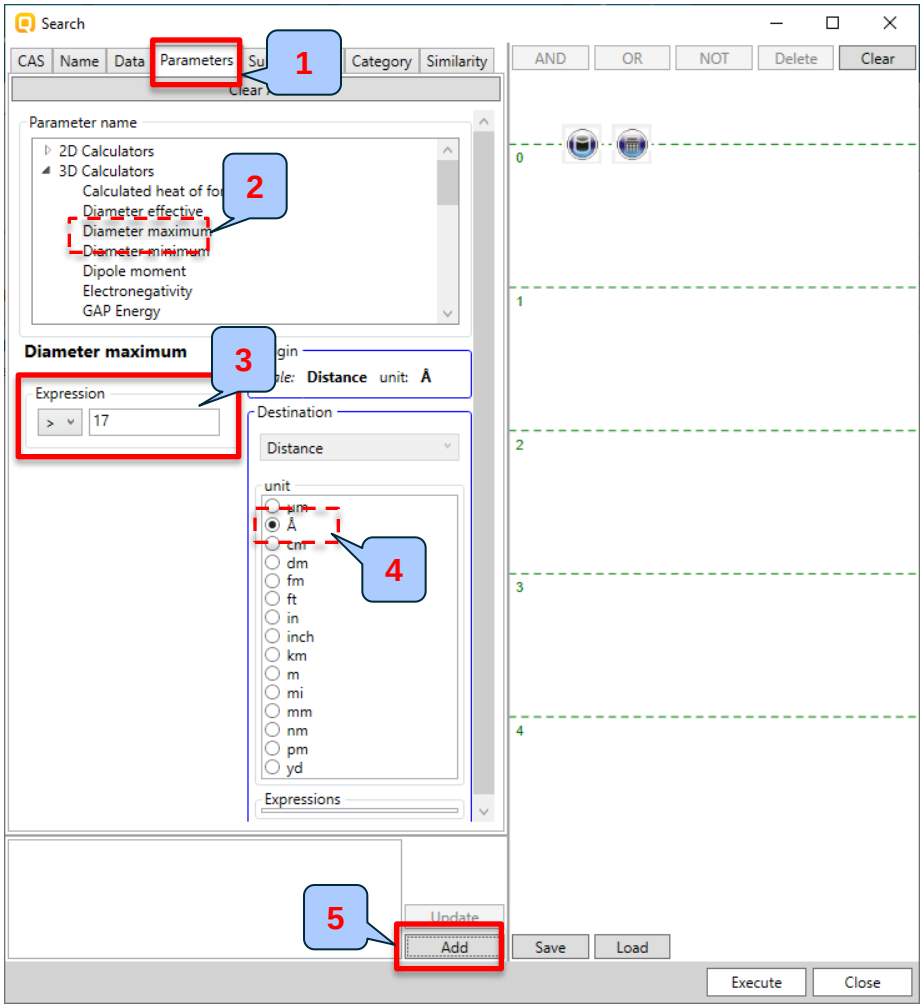
According to the European authorities $D_{MAX\ AVER}$ larger than 1.7 nm (or 17.4 Å) is considered as a threshold for not very bioaccumulative (not vB) and not bioaccumulative (not B) chemicals (i.e., *BCF* < 2000 L/kg): https://echa.europa.eu/documents/10162/13632/information_requirements_r11_en.pdf

Subfragment search for identifying chemicals

BCF and (Dmax)

Example 3

- Structures search criteria
  - Endpoint is BCF < 2000 L/kg
  - 3D parameter – minimum value of Diameter maximum >17 Å



1. Click on **Parameters** panel;
2. Select ***Diameter maximum*** from the list;
3. Select qualifier "**≥**" from the drop down list and add **"17"** in the *Expression* field;
4. Unit of the Dmax parameter is "A", it is selected by default;
5. Click **Add** button.

Subfragment search for identifying chemicals

BCF and (Dmax)

Example 3

- Structures search criteria
  - Endpoint is BCF < 2000 L/kg
  - 3D parameter – minimum value of Diameter maximum >17 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);

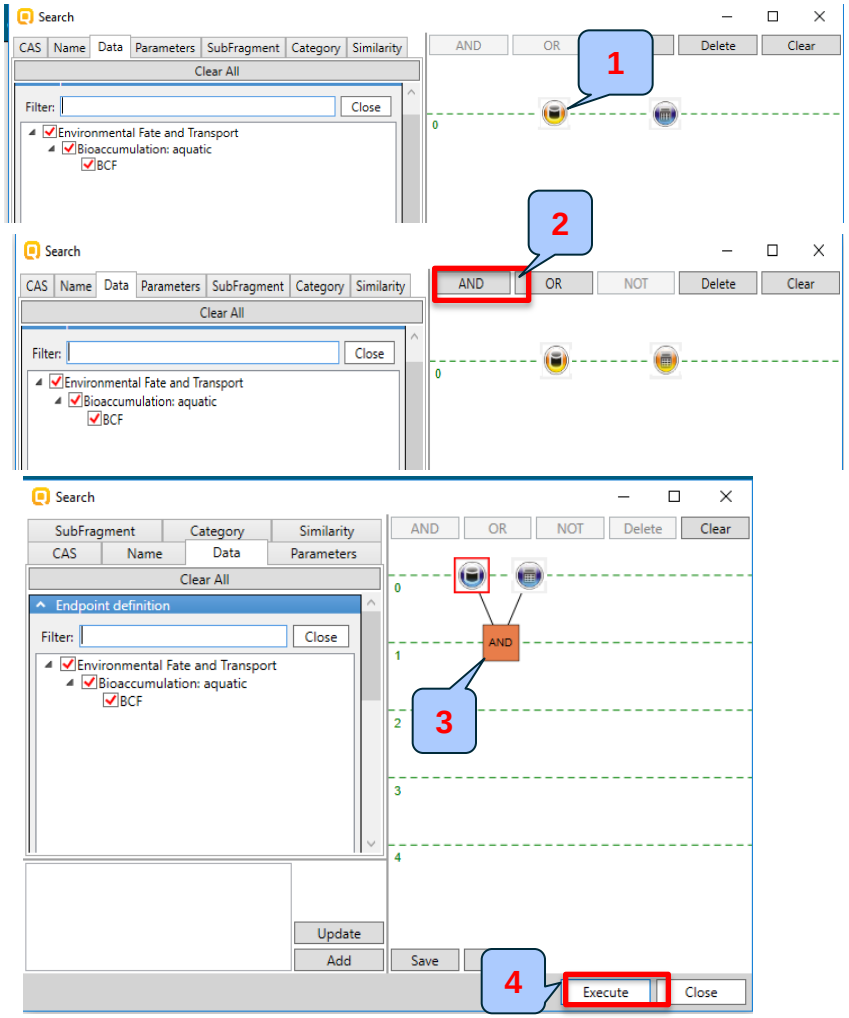
Selected query

Not selected query

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

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

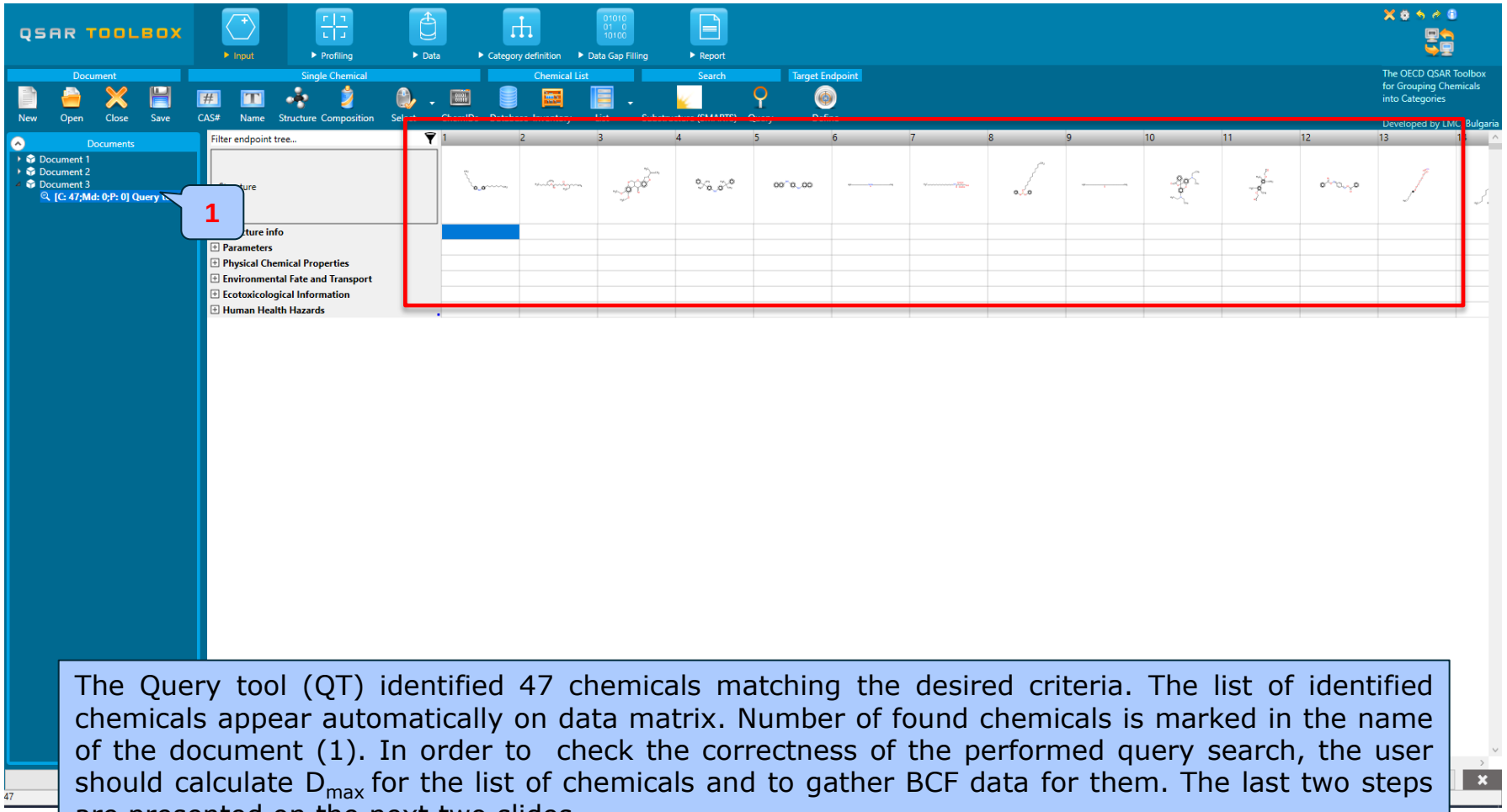
4. Double click "**AND**" query or click "**Execute**" button to execute the search;



Subfragment search for identifying chemicals

BCF and (Dmax)

Example 3

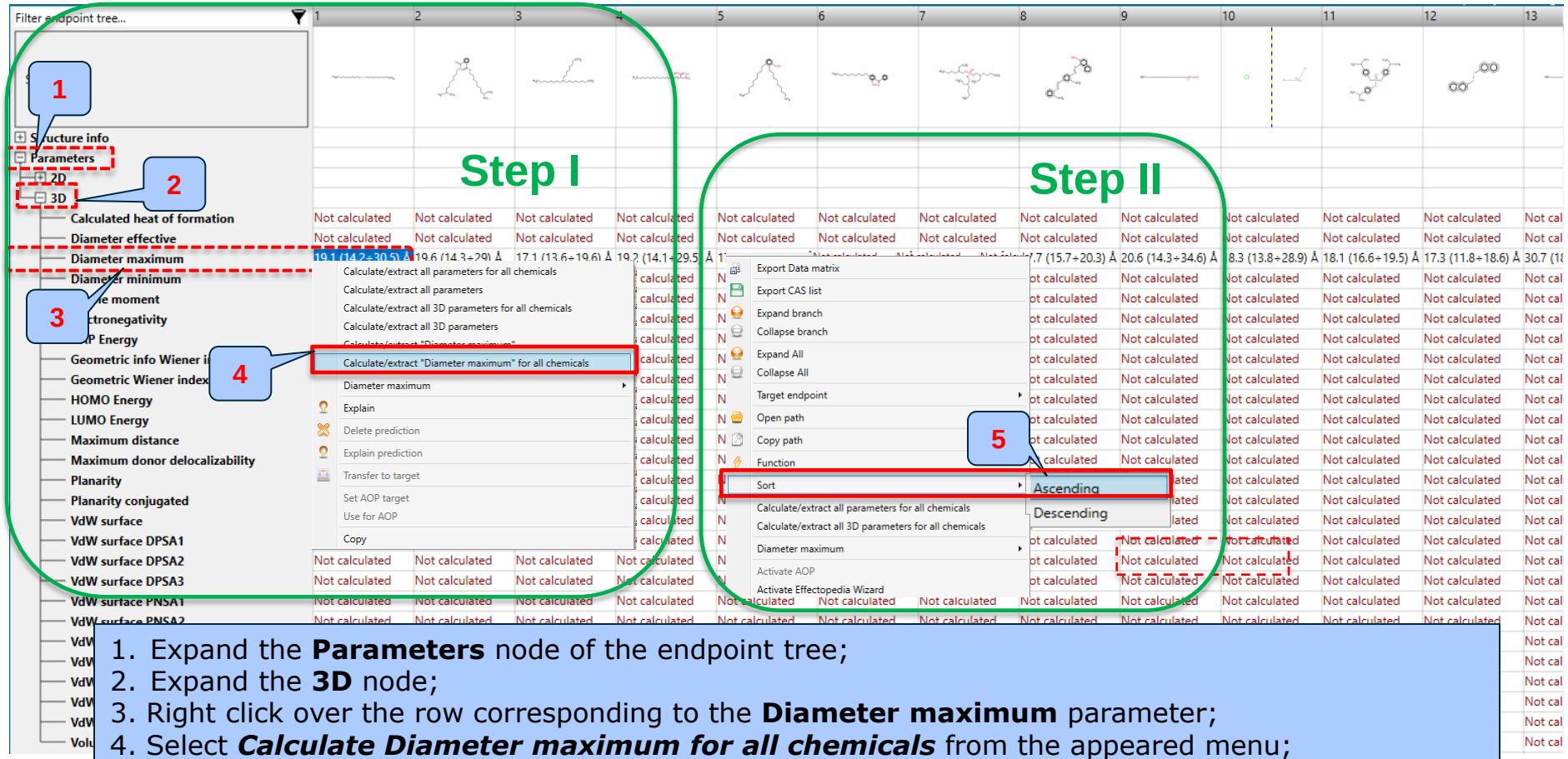


The Query tool (QT) identified 47 chemicals matching the desired criteria. The list of identified chemicals appear automatically on data matrix. Number of found chemicals is marked in the name of the document (1). In order to check the correctness of the performed query search, the user should calculate 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

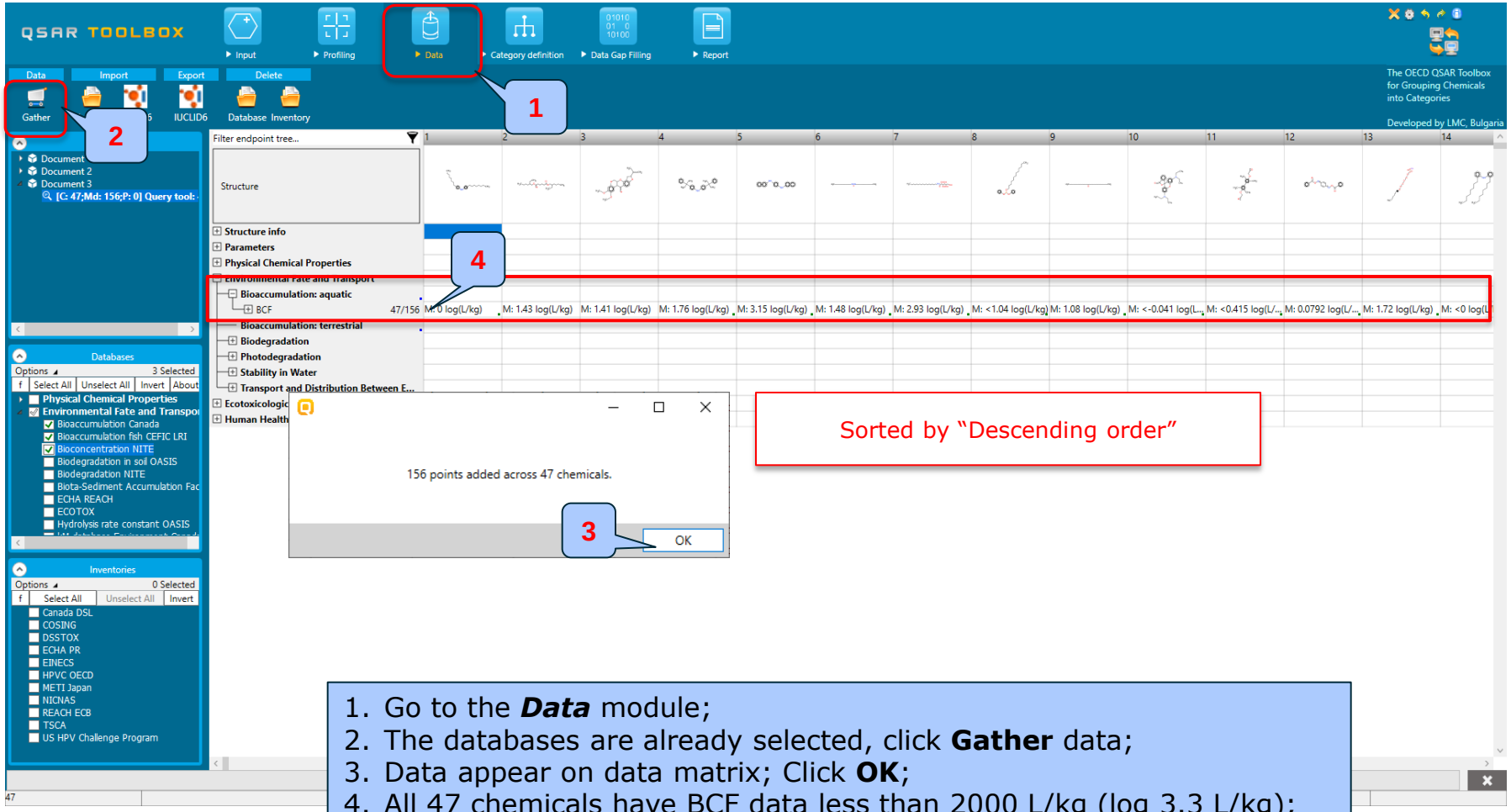


1. Expand the **Parameters** node of the endpoint tree;
2. Expand the **3D** node;
3. Right click over the row corresponding to the **Diameter maximum** parameter;
4. Select ***Calculate Diameter maximum for all chemicals*** from the appeared menu;
5. Once the values are calculated right click over the 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. Data appear on data matrix; Click **OK**;
4. All 47 chemicals have BCF data less than 2000 L/kg (log 3.3 L/kg);

Subfragment search for identifying chemicals

LC 50 and predefined category (Aldehydes)

Example 4

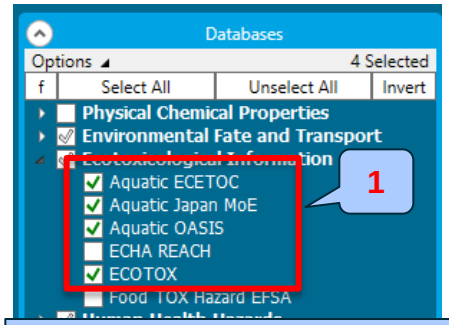
- Structures search criteria
  - Endpoint: LC 50 <1 mg/l
  - Fish: *P.promelas*
  - Effect: *Mortality*
  - Predefined category: *aldehydes*

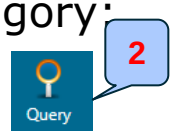
Subfragment search for identifying chemicals

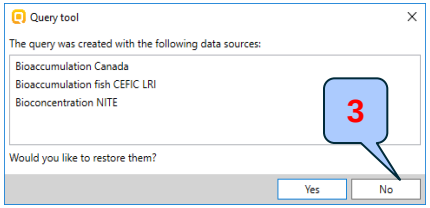
LC 50 and predefined category (Aldehydes)

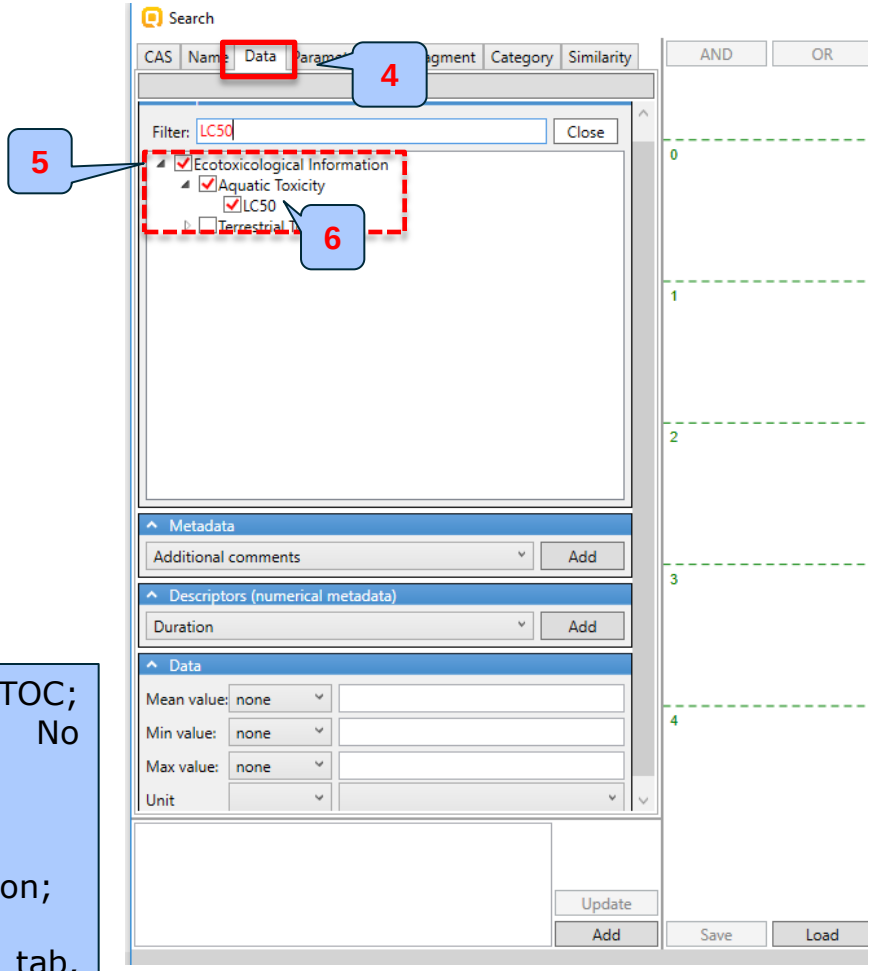
Example 4

- 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, but before that click on **Clear** button;
5. Type in filter the name of searched endpoint (**LC50**);
6. Select **Aquatic Toxicity** and expand the endpoint tab, check **LC50**

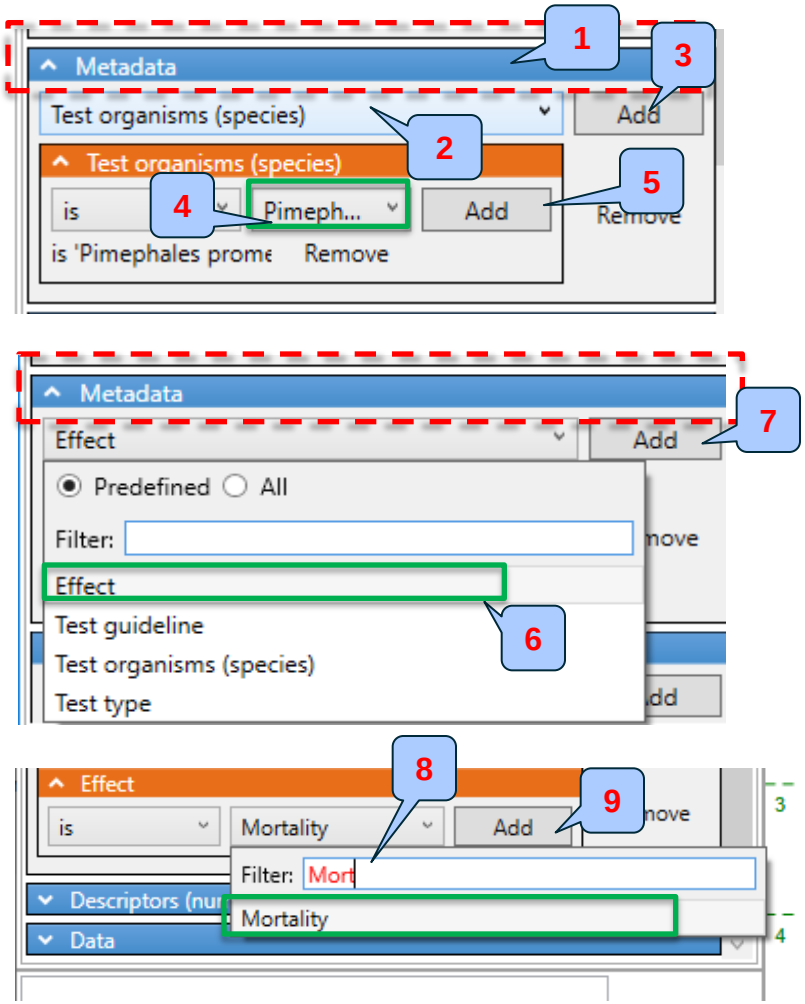
Subfragment search for identifying chemicals

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 the drop-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**

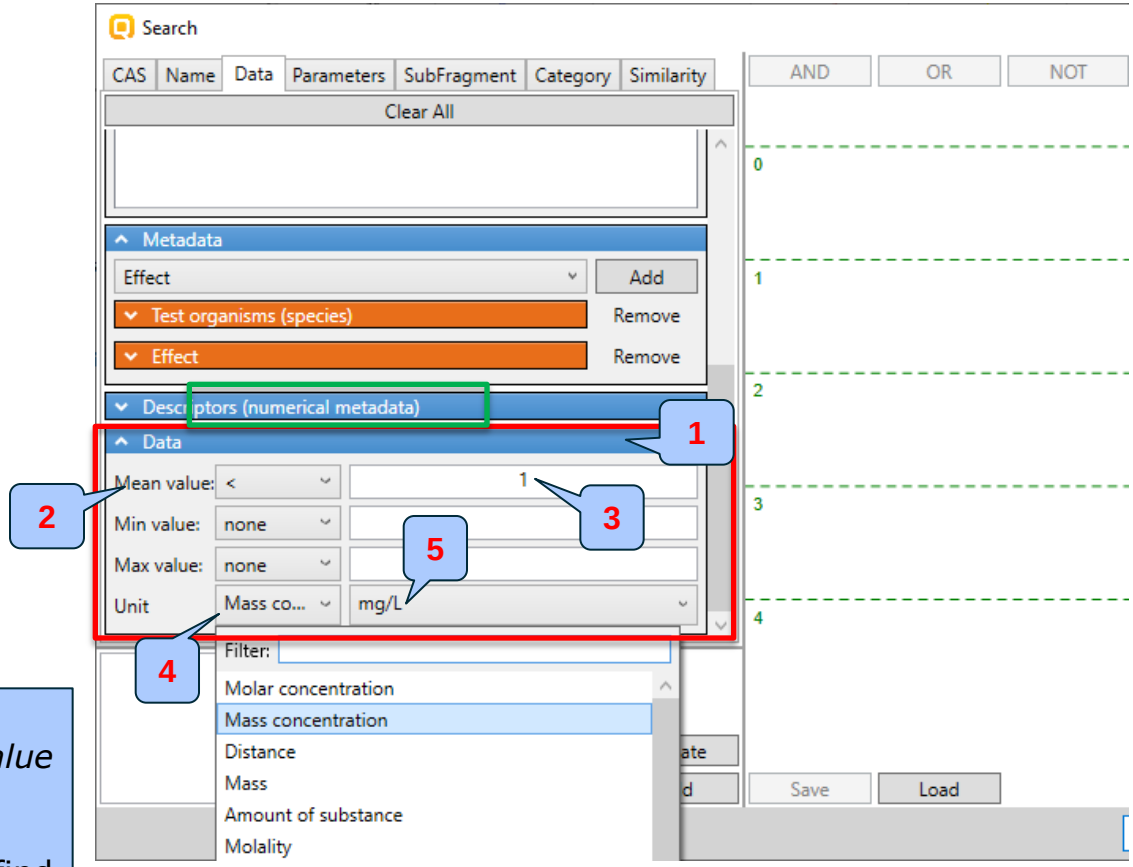


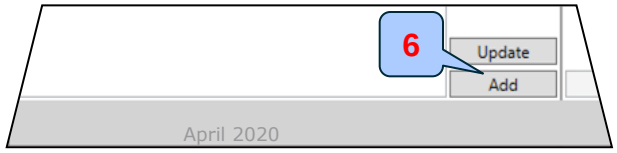
Subfragment search for identifying chemicals

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*





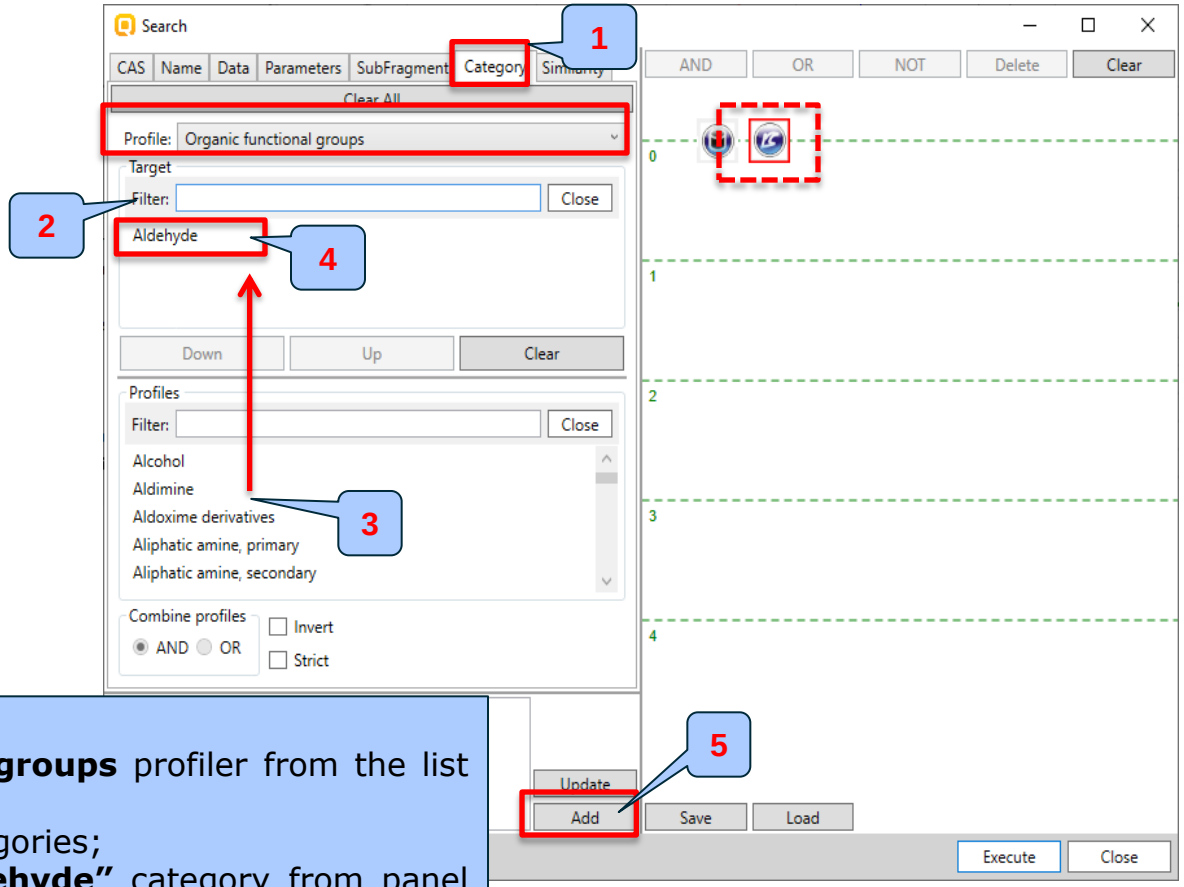
1. Open **Data** panel;
2. Open qualifiers from *Mean value* section and select "**<**";
3. Type "**1**" in the blank field;
4. From the *Unit* section use Filter to find "**Mass concentration**";
5. Select "**mg/l**" from the list with units;
6. Click **Add**;

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*



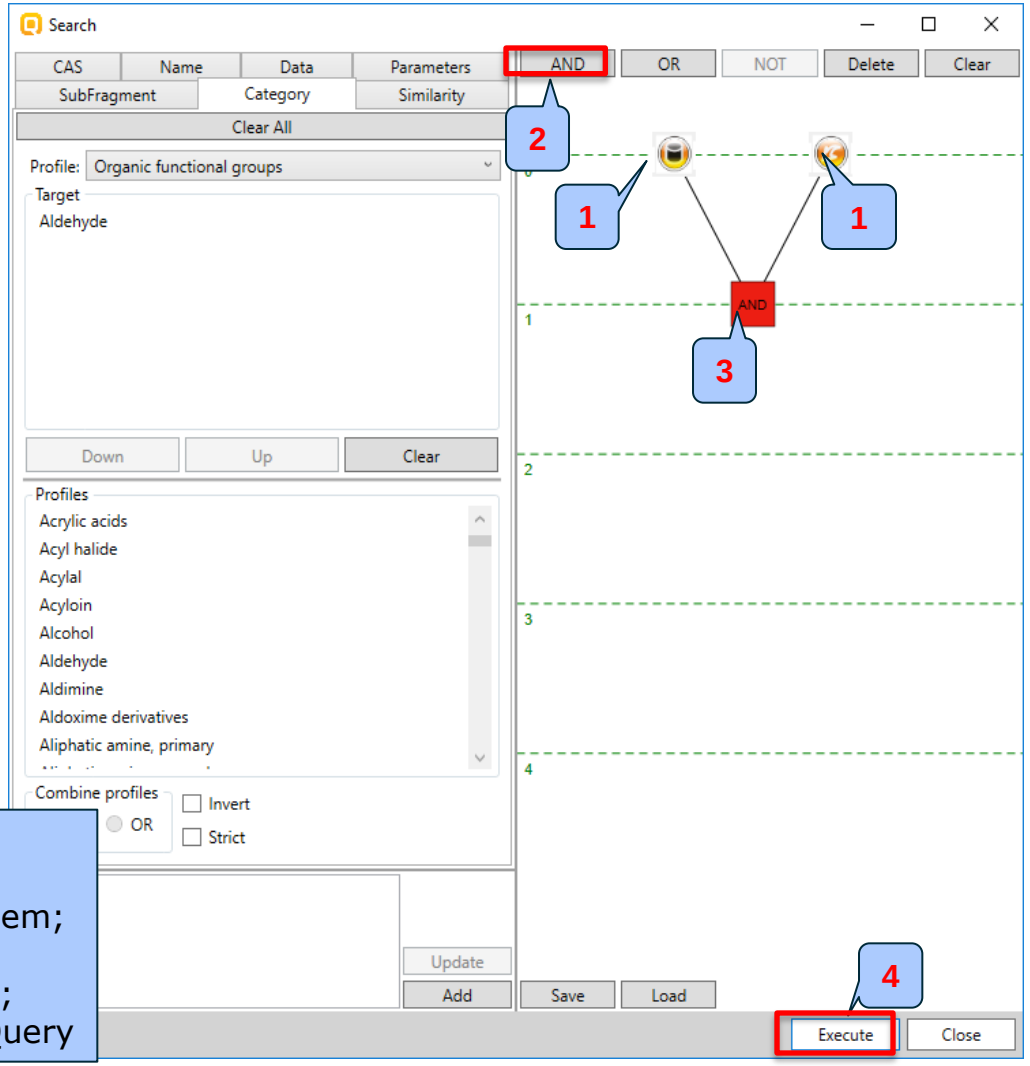
1. Open **Category** panel;
2. Use *Filter* to find **Organic functional groups** profiler from the list with profilers and select it;
3. Find **"Aldehyde"** from the list with categories;
4. Click "**Up**" to move the selected **"Aldehyde"** category from panel "*Profilers*" to the panel "*Target*"
5. The selected category appears in the panel "Target" and finally click **Add** button. The query with predefined category appears on the logic panel.

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*



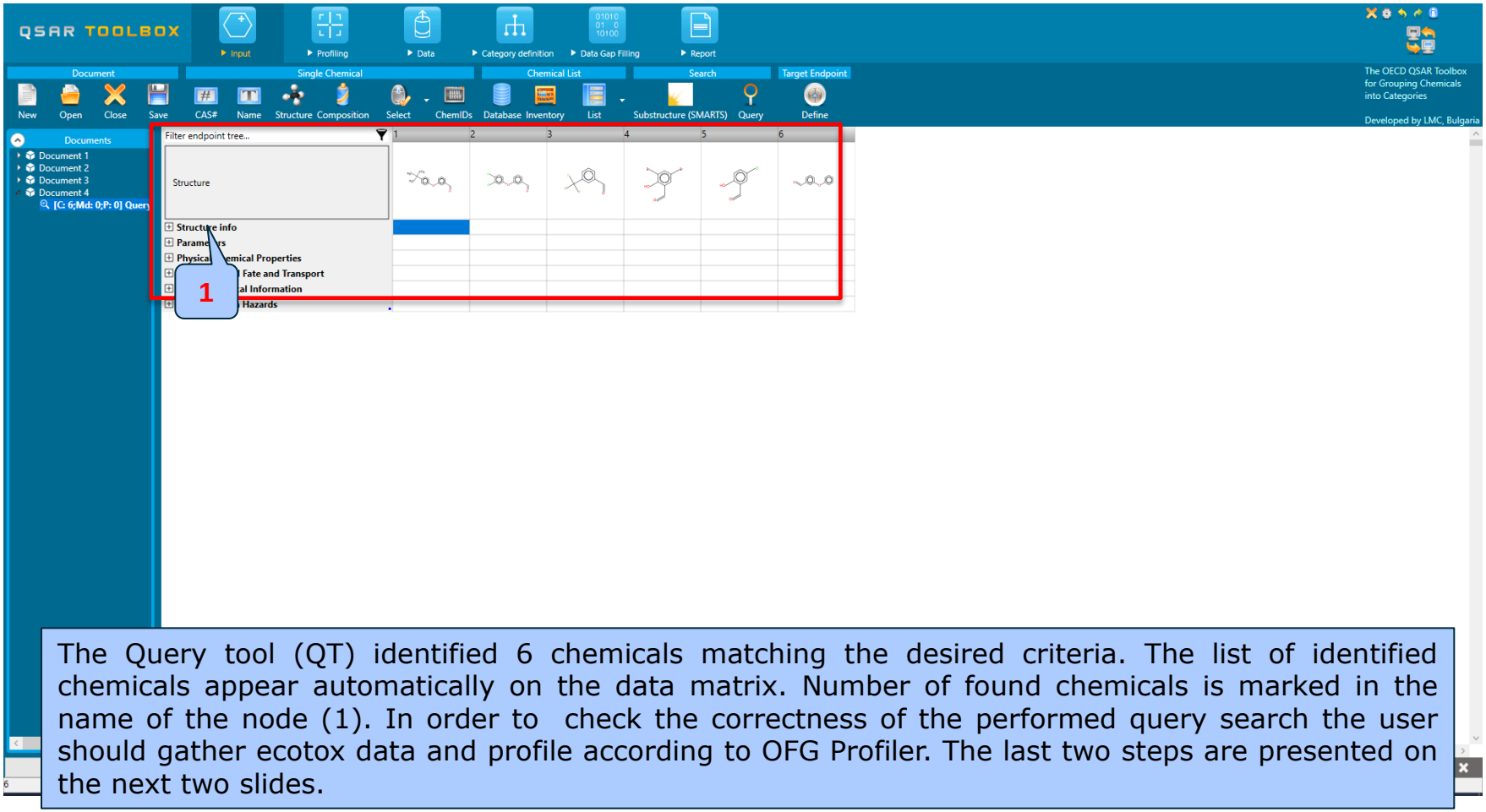
The both queries should be combined by logical "AND". Follow the steps explained on slide # 39

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

Subfragment search for identifying chemicals

LC 50 and predefined category (Aldehydes)

Example 4

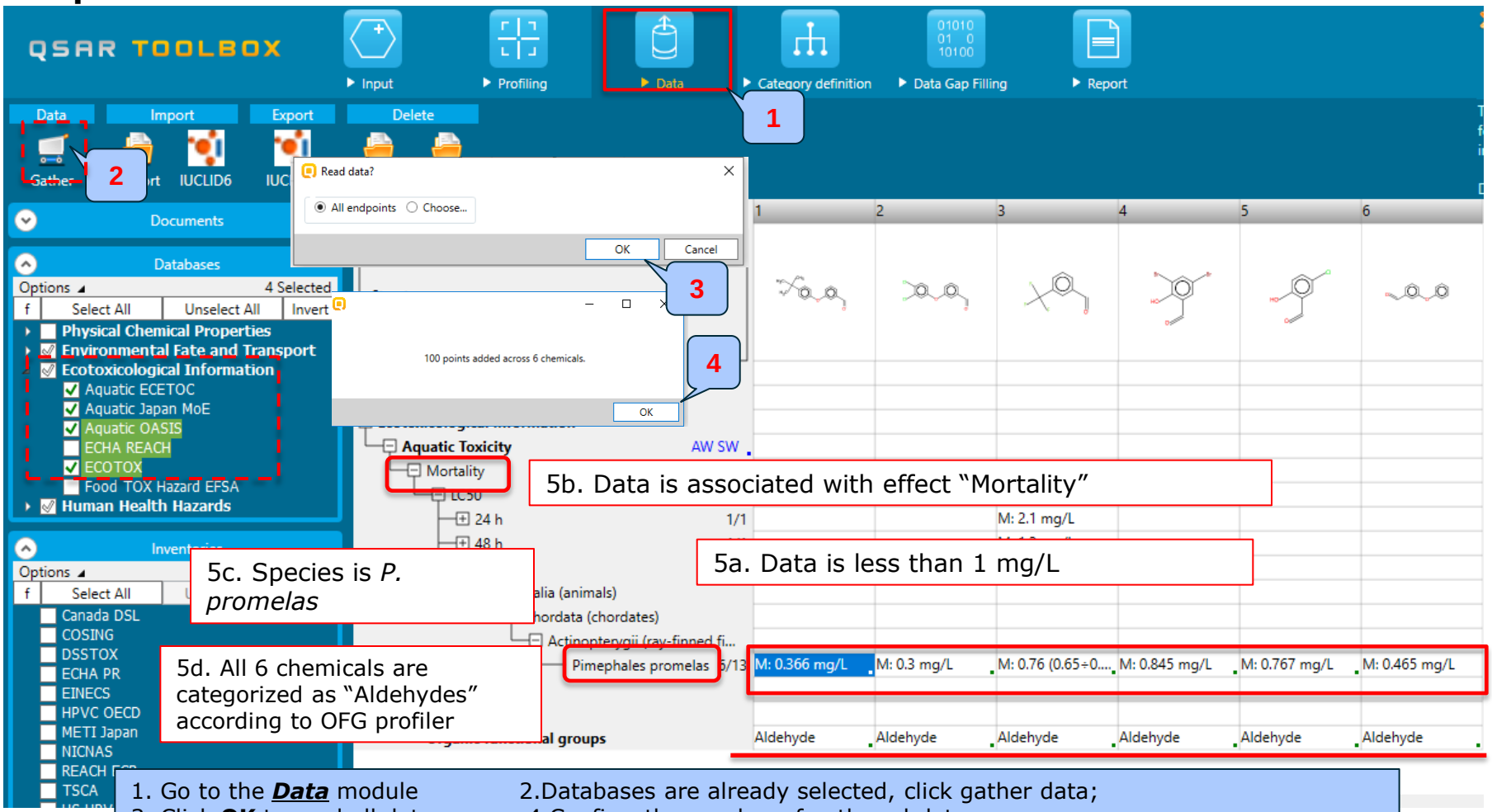


The Query tool (QT) identified 6 chemicals matching the desired criteria. The list of identified chemicals appear automatically on the data matrix. Number of found chemicals is marked in the name of the node (1). In order to check the correctness of the performed query search the user should gather ecotox 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 criteria:
5a. *LC50 < 1mg/l* *5b.Effect: Mortality* *5c. Species: P.promelas.*
Go to Profiling, unselect all profilers and select Organic functional group and click Apply (Not illustrated here).

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

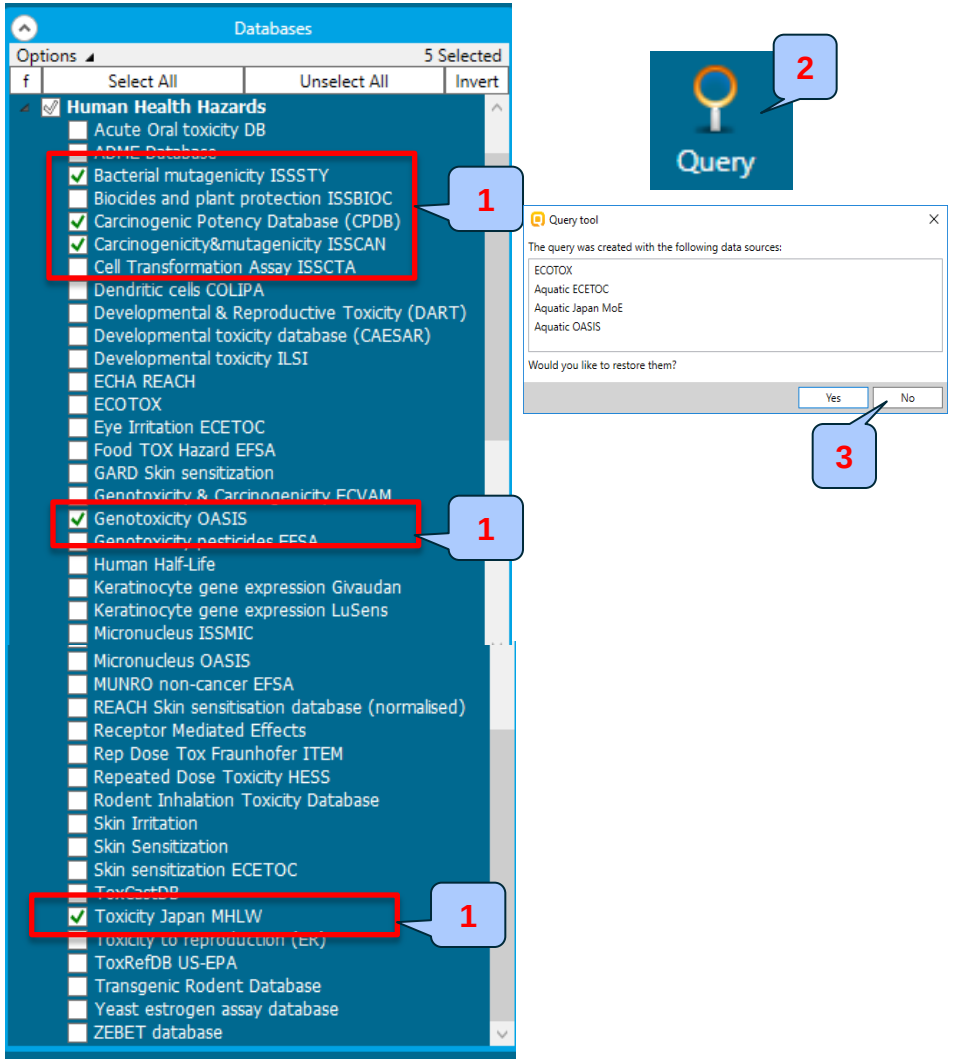
- Structures search criteria
  - Endpoint: Gene mutation
  - Species: *S.thyphimurium*
  - Data: *Positive*

  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 mutagenicity 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

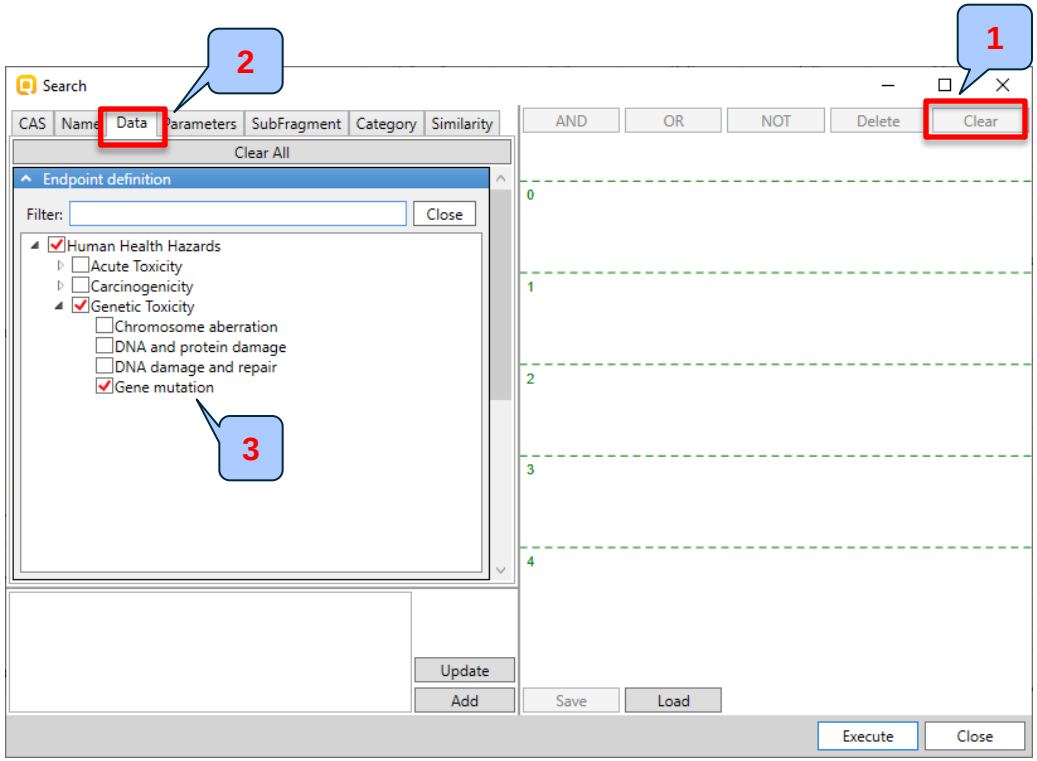
Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

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. First click on **Clear** button
2. Click on the **Data** panel;
3. Open Human health hazard>>Genetic Toxicity and select **Gene mutation**;

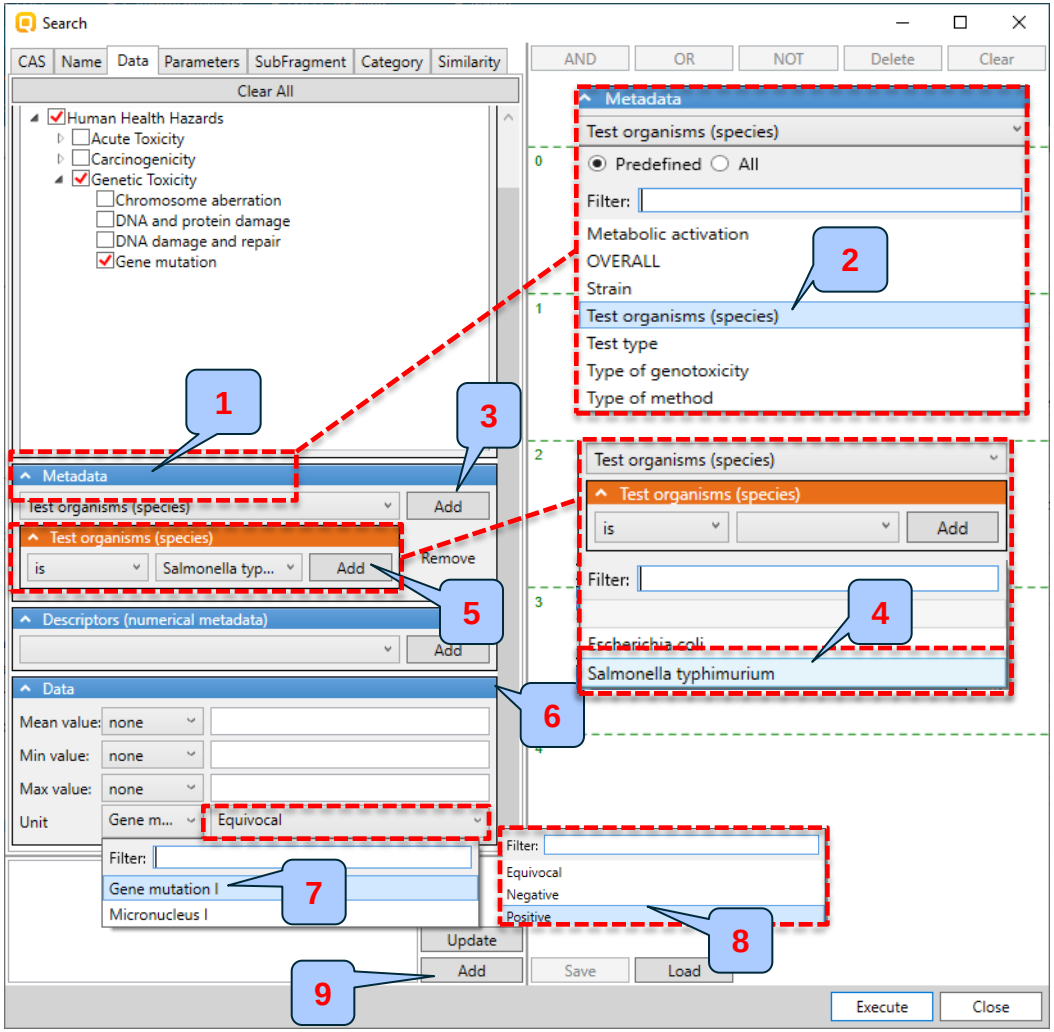
Subfragment search for identifying chemicals

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. In a newly appeared field 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;

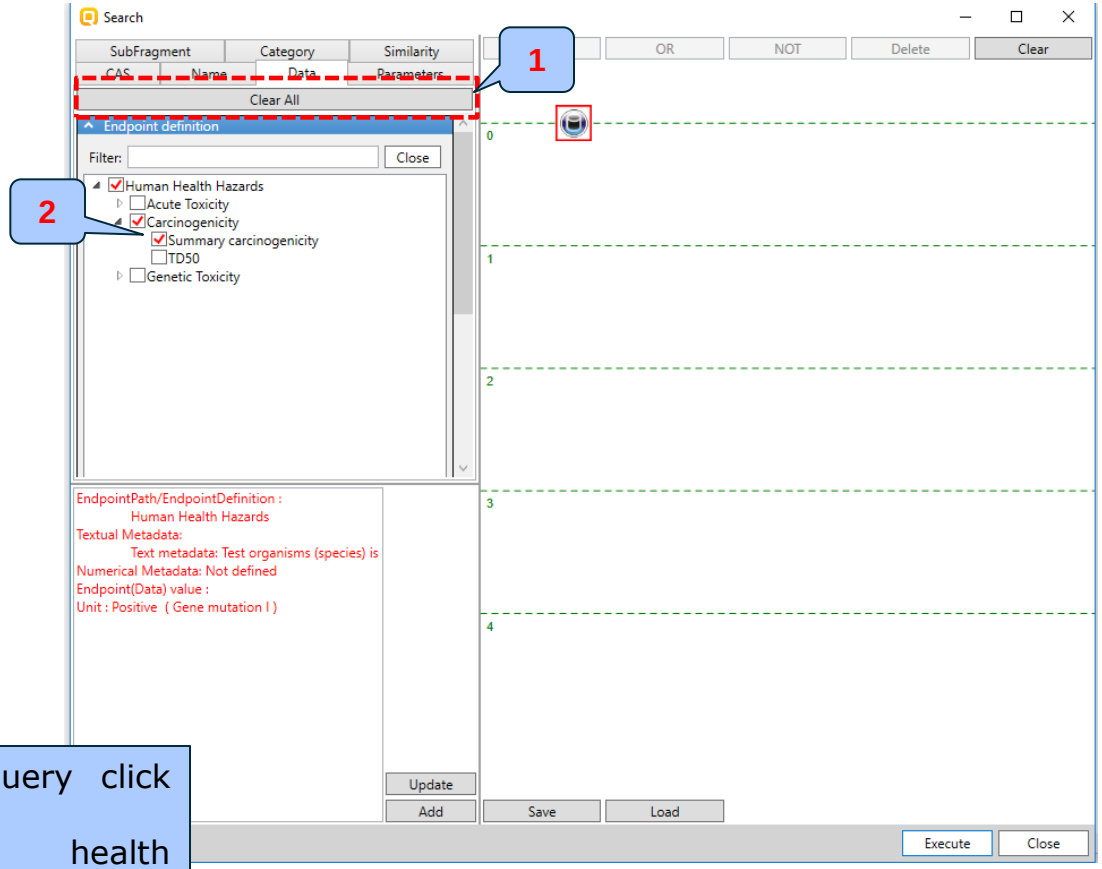


Subfragment search for identifying chemicals

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*



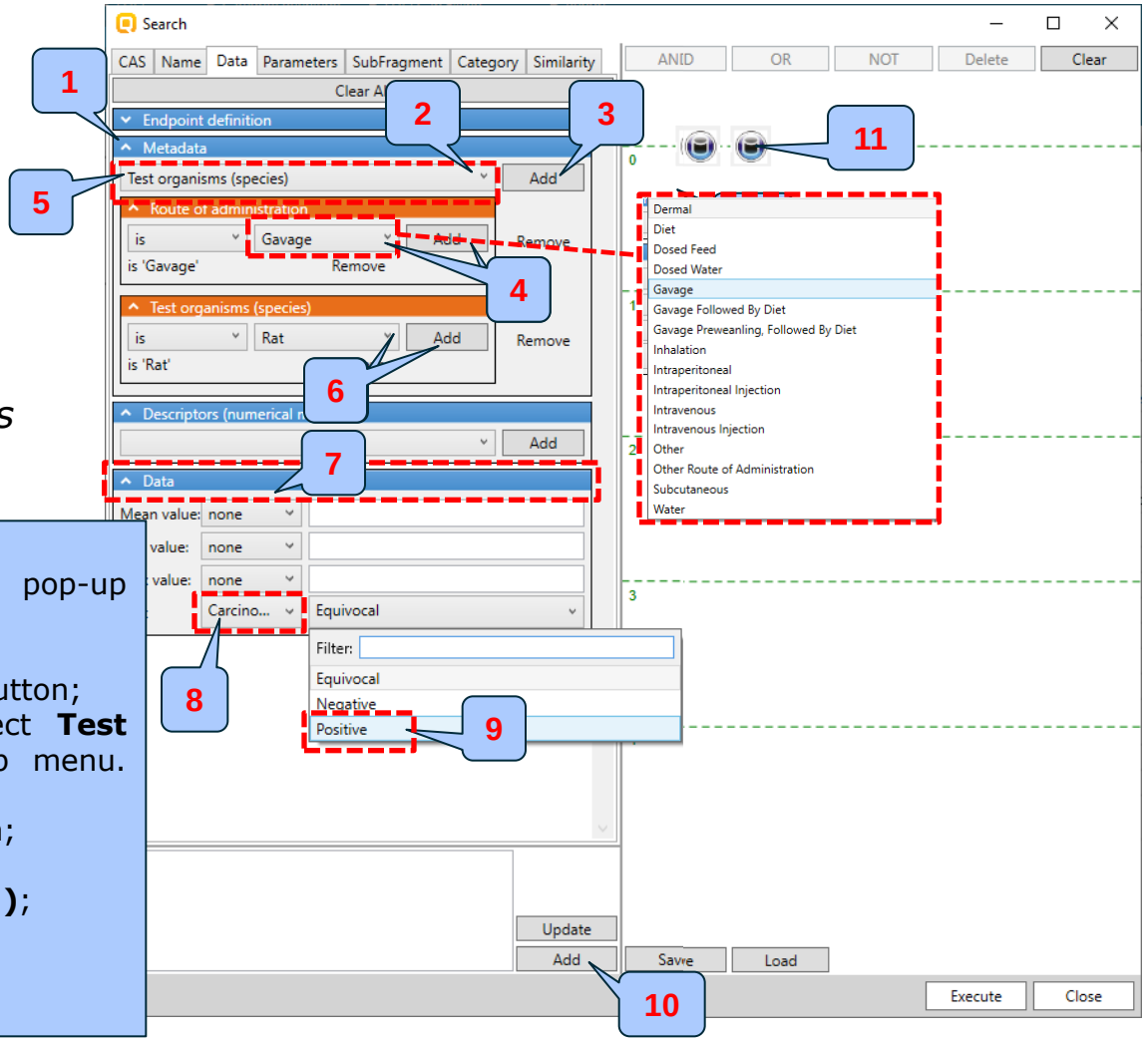
1. Before defining the second query click **Clear All** button;
2. Open path: Human health hazard>>Carcinogenicity and select *Summary carcinogenicity* node

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*



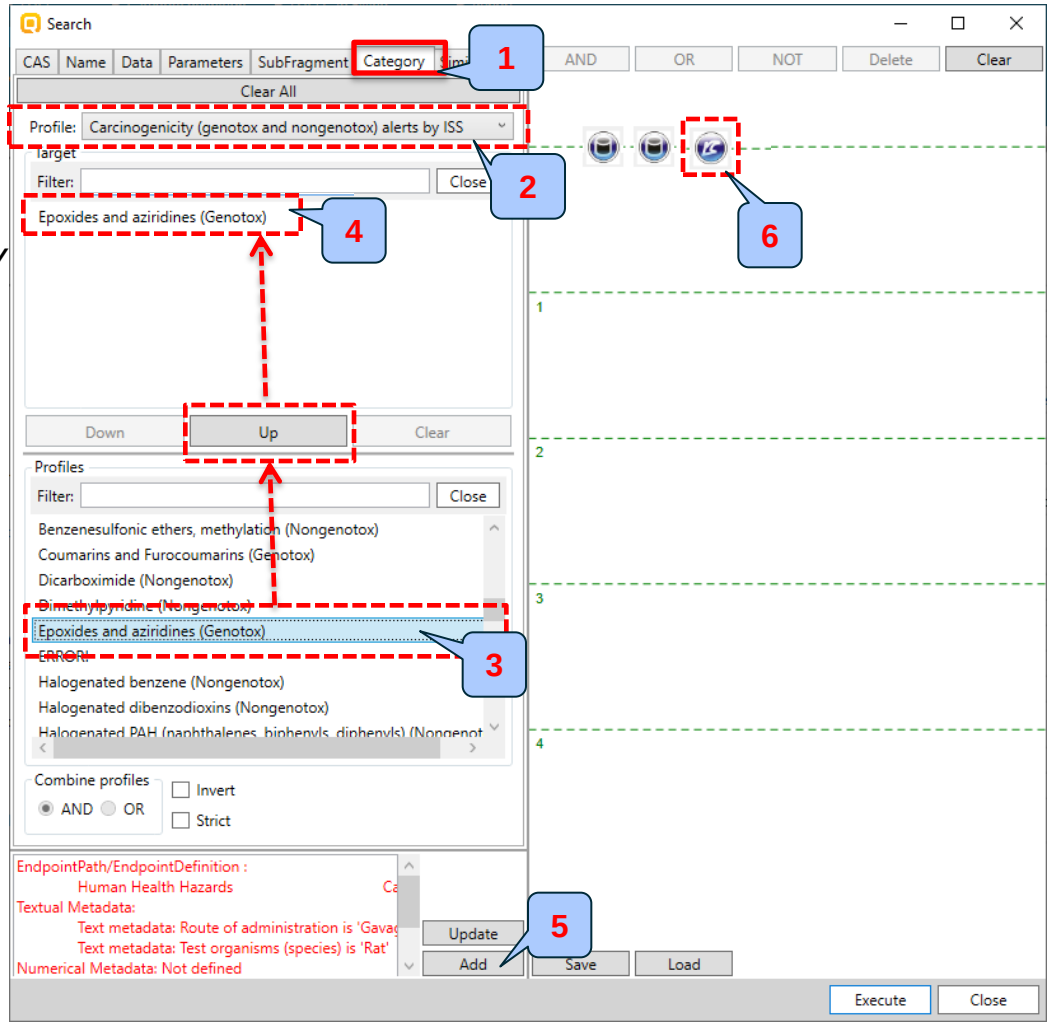
1. Open *Metadata* panel;
2. Select ***Route of administration*** from pop-up menu;
3. Click **Add** button;
4. Select **Gavage** from the list. Click **Add** button;
5. Go back to *Metadata* panel and select **Test organism (species)** from the pop-up menu. Click **Add** button;
6. Select **Rat** from 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*



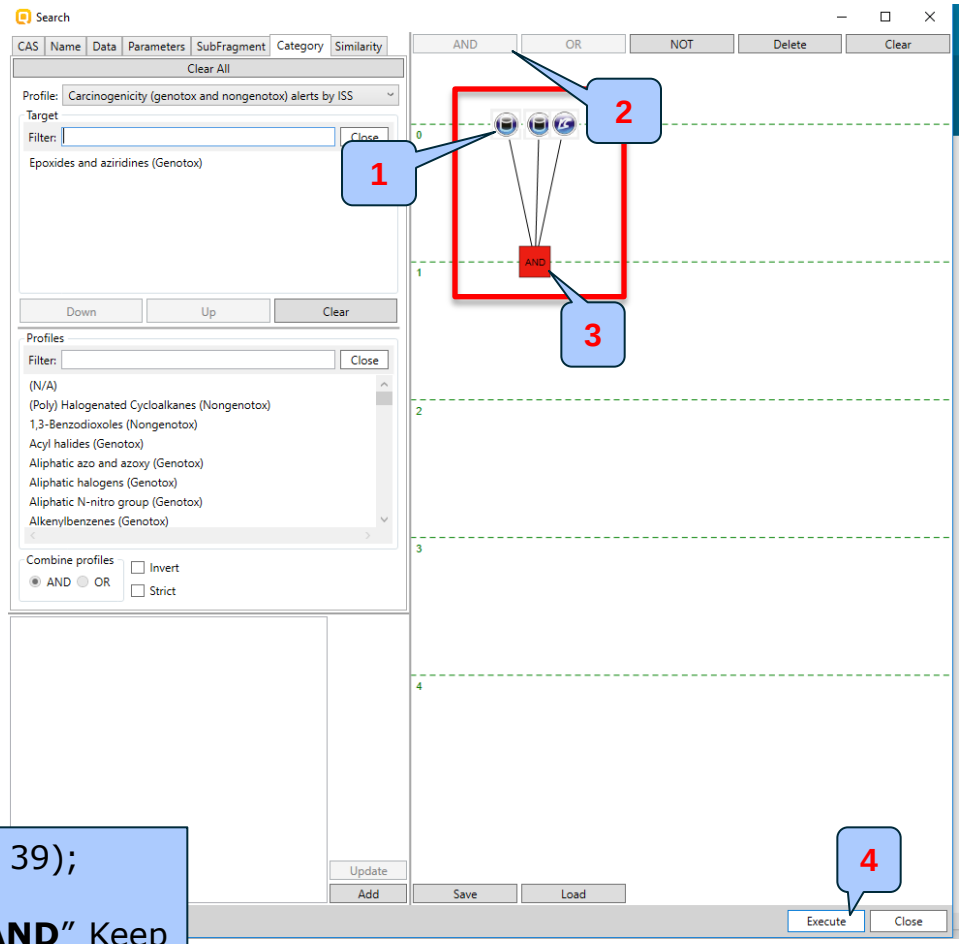
1. Click ***Category*** panel;
2. Select **Carcinogenicity (genotox and nongenotox) alerts by ISS**;
3. Select category **Epoxides and aziridines (Genotox)**;
4. Click **Up** to move the selected category to the panel Target;
5. Click **Add** button;
6. The query appears on the logic panel;

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*

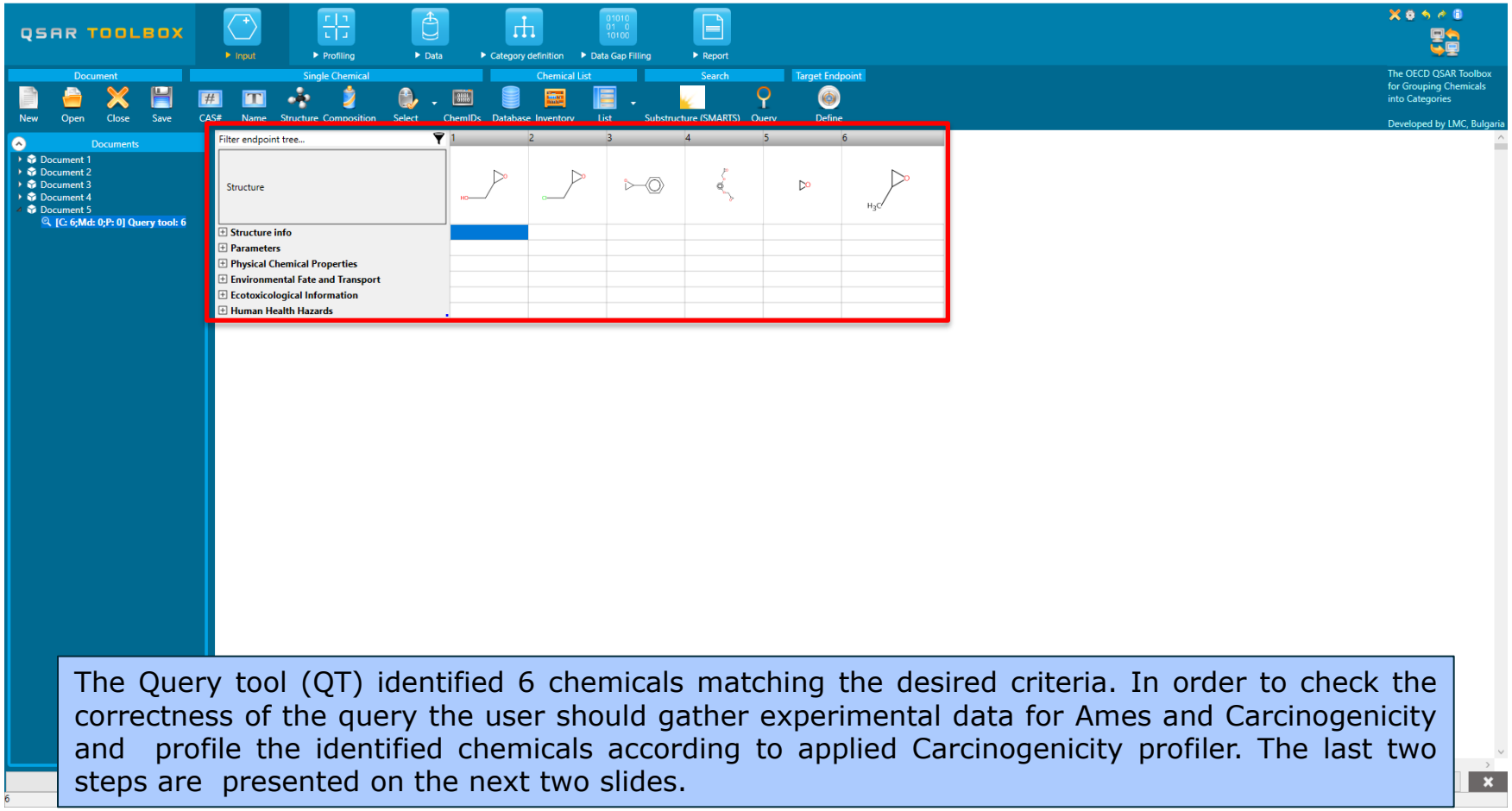


1. Right click over the three queries (see slide # 39);
2. Click **AND** button;
3. The three queries are combined by logical "**AND**" Keep the "AND" selected (clicked);
4. Click **Execute** button;

Subfragment search for identifying chemicals

Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

Example 5

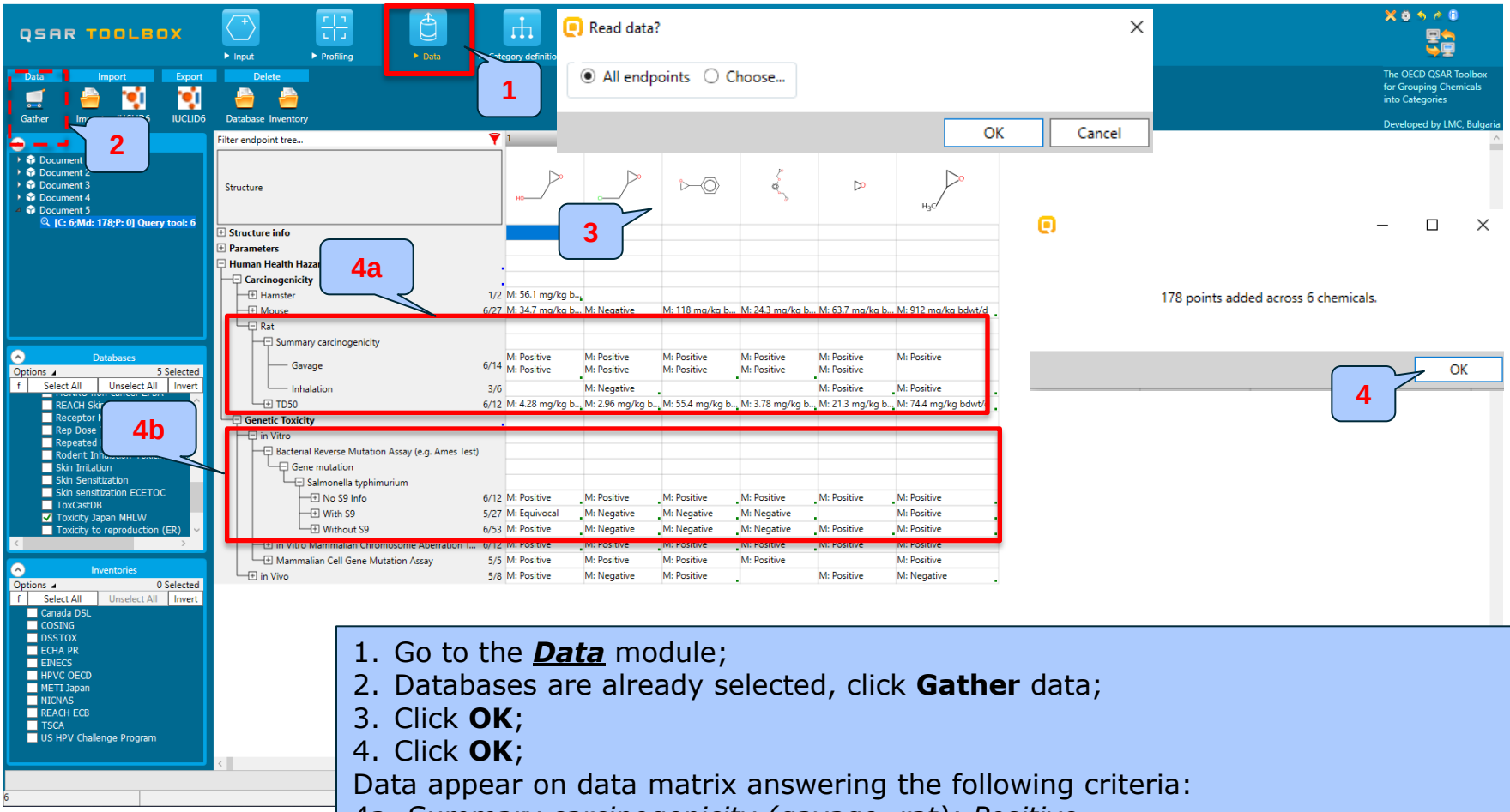


The Query tool (QT) identified 6 chemicals matching the desired criteria. In order to check the correctness of the query the user should gather experimental data for Ames and Carcinogenicity and profile the identified chemicals according to applied Carcinogenicity profiler. The last two steps are presented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

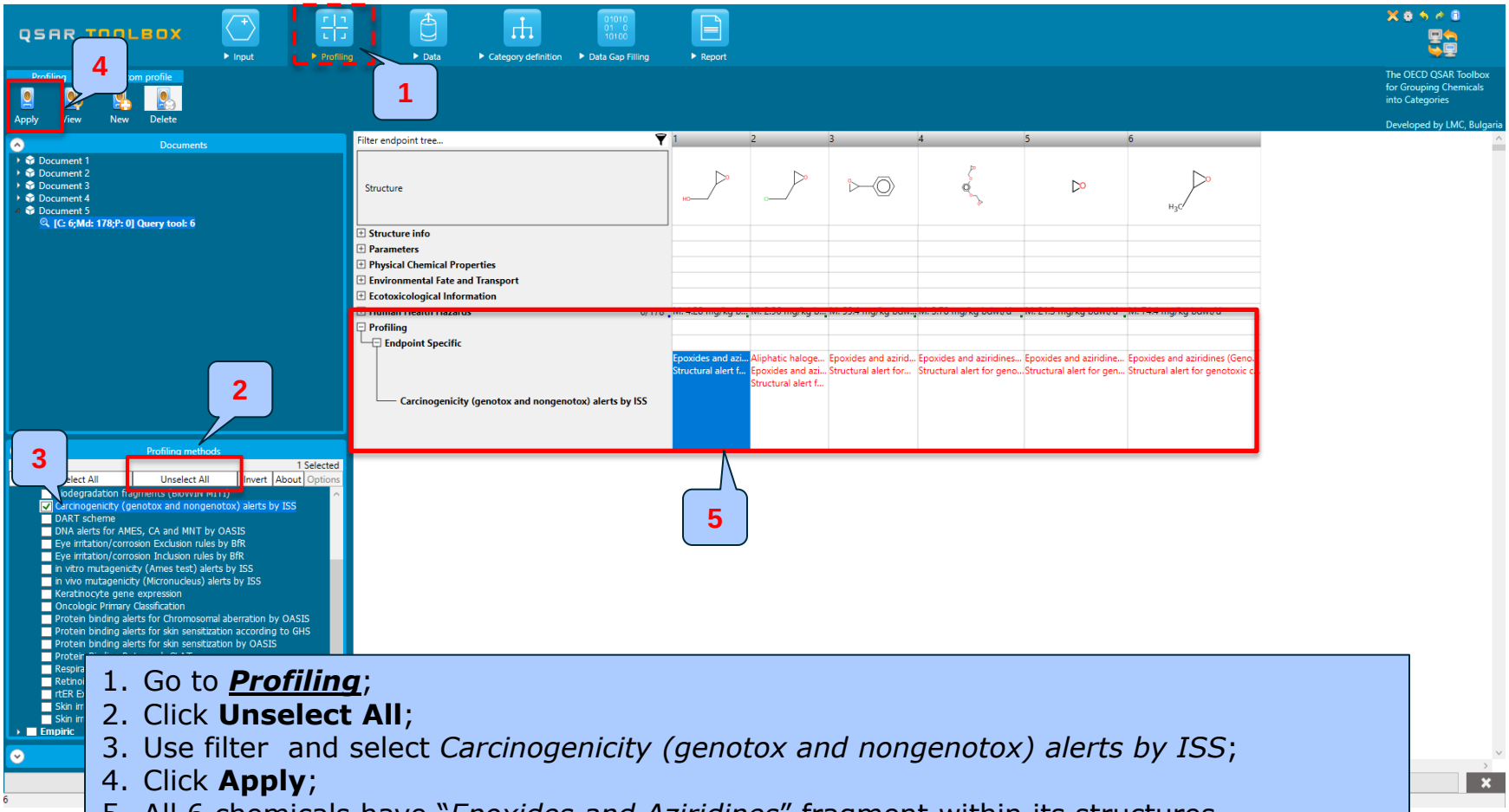
4a. *Summary carcinogenicity (gavage, rat): Positive*

4b. Ames mutagenicity (S. thuphimurium): Positive

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 structures.

Subfragment search for identifying chemicals

Chemicals with Skin sensitization positive data including Aldehyde fragment

Example 6

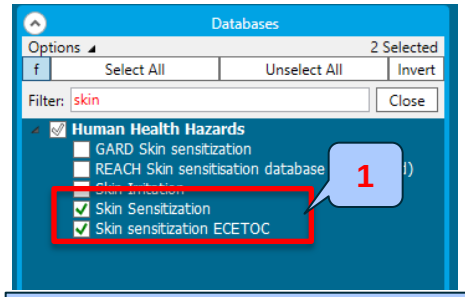
- Structures search criteria
  - Endpoint: *EC3*
  - Data: *Positive*
  - *SubFragment: Aldehyde*

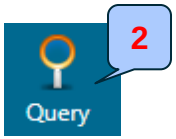
Subfragment search for identifying chemicals

Chemicals with Skin sensitization positive data including Aldehyde fragment

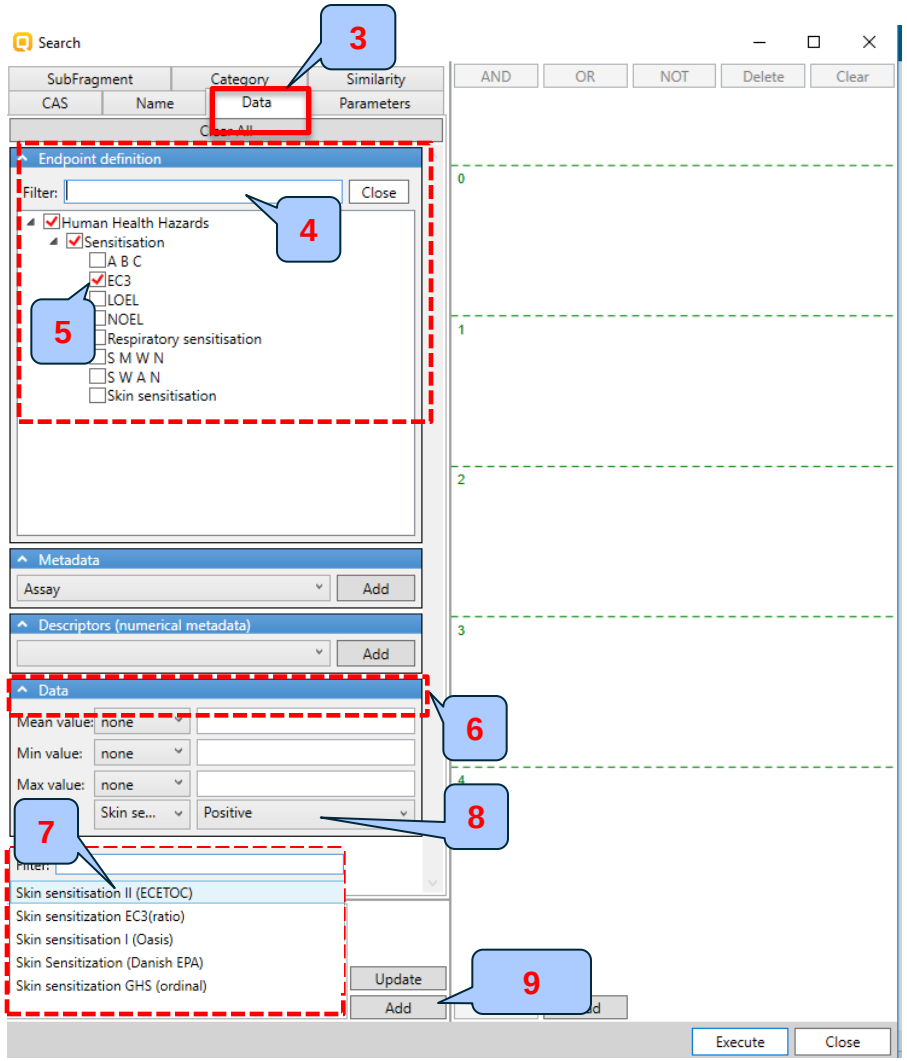
Example 6

- Structures search criteria
  - Endpoint: *EC3*
  - Data: *Positive*
  - SubFragment: Aldehydes





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

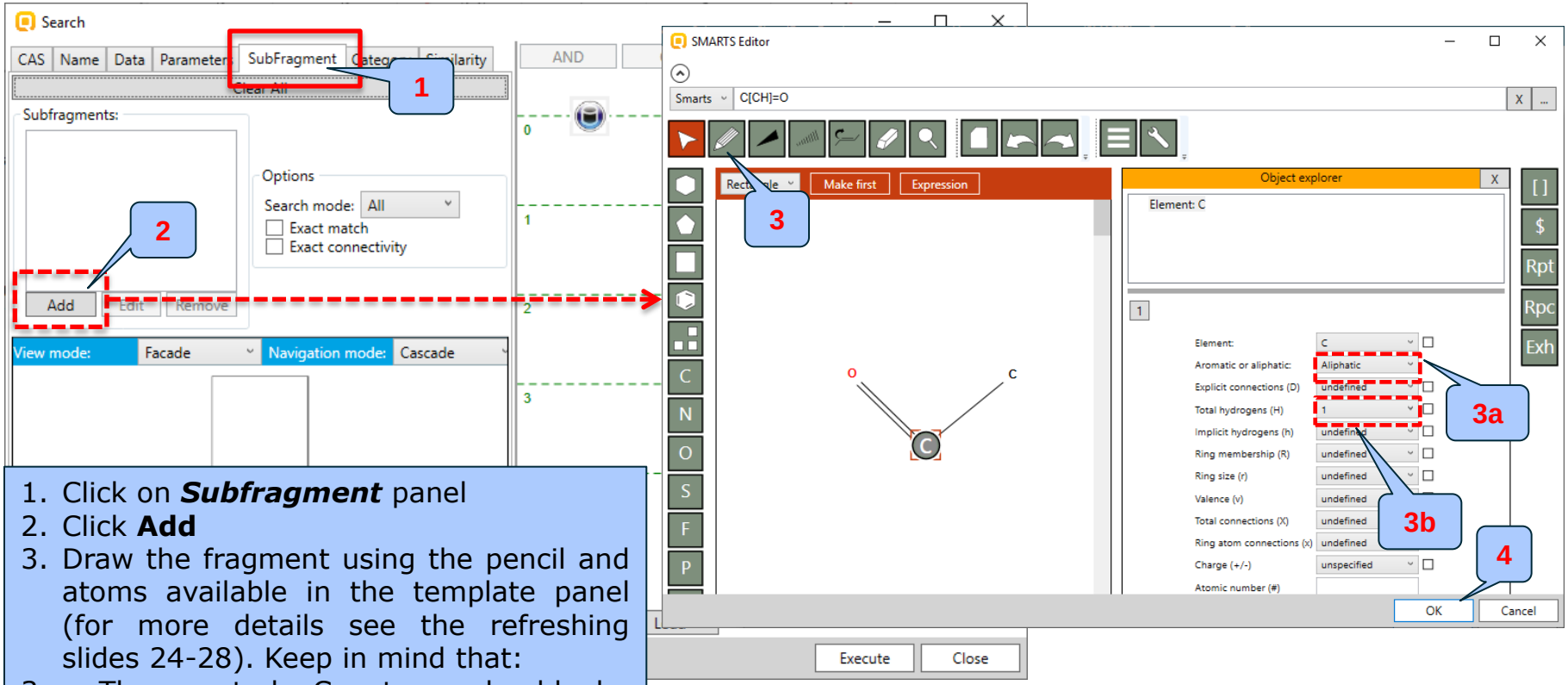


Subfragment search for identifying chemicals

Chemicals with Skin sensitization positive data including Aldehyde fragment

Example 6

•SubFragment: Aldehydes



1. Click on ***Subfragment*** panel
2. Click **Add**
3. Draw the fragment using the pencil and atoms available in the template panel (for more details see the refreshing slides 24-28). Keep in mind that:

3a. The central C atom should be "aliphatic" 3b. The central C atom should have one H atom;

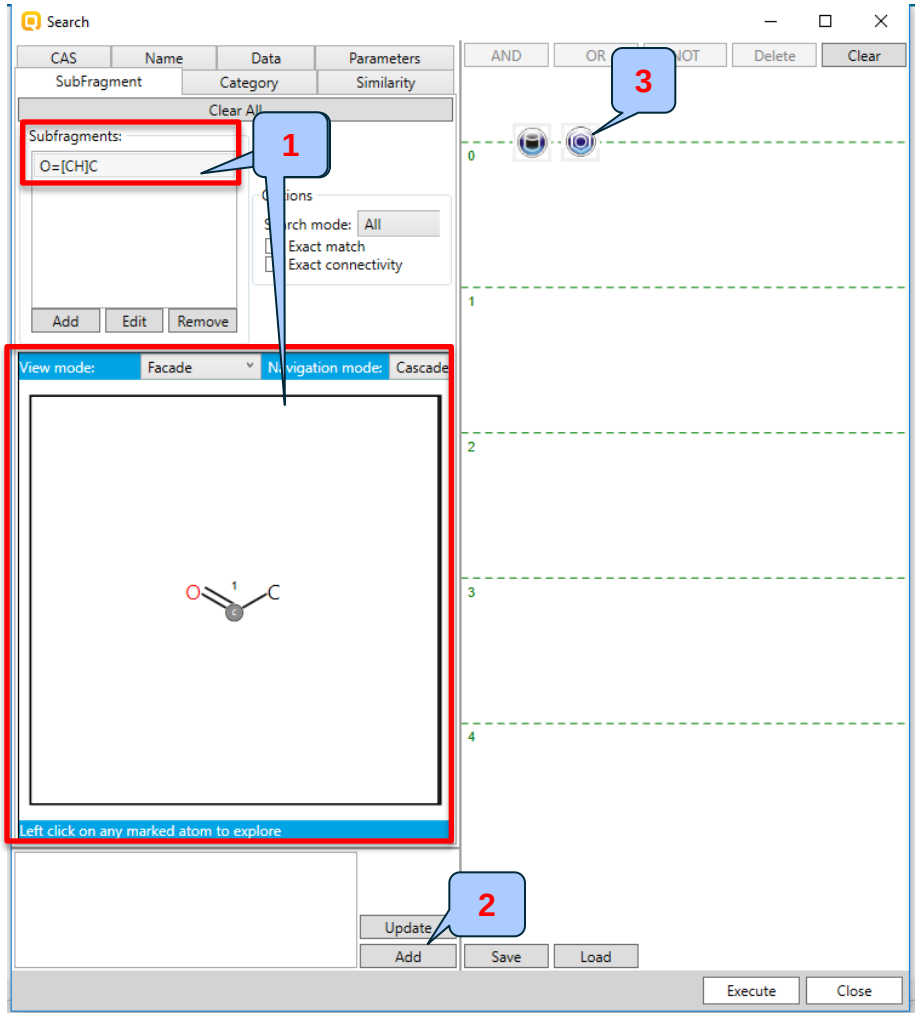
4. Click **OK**.

Subfragment search for identifying chemicals

Chemicals with Skin sensitization positive data including Aldehyde fragment

Example 6

- Structures search criteria
  - Endpoint: *EC3*
  - Data: *Positive*
  - SubFragment: Aldehydes



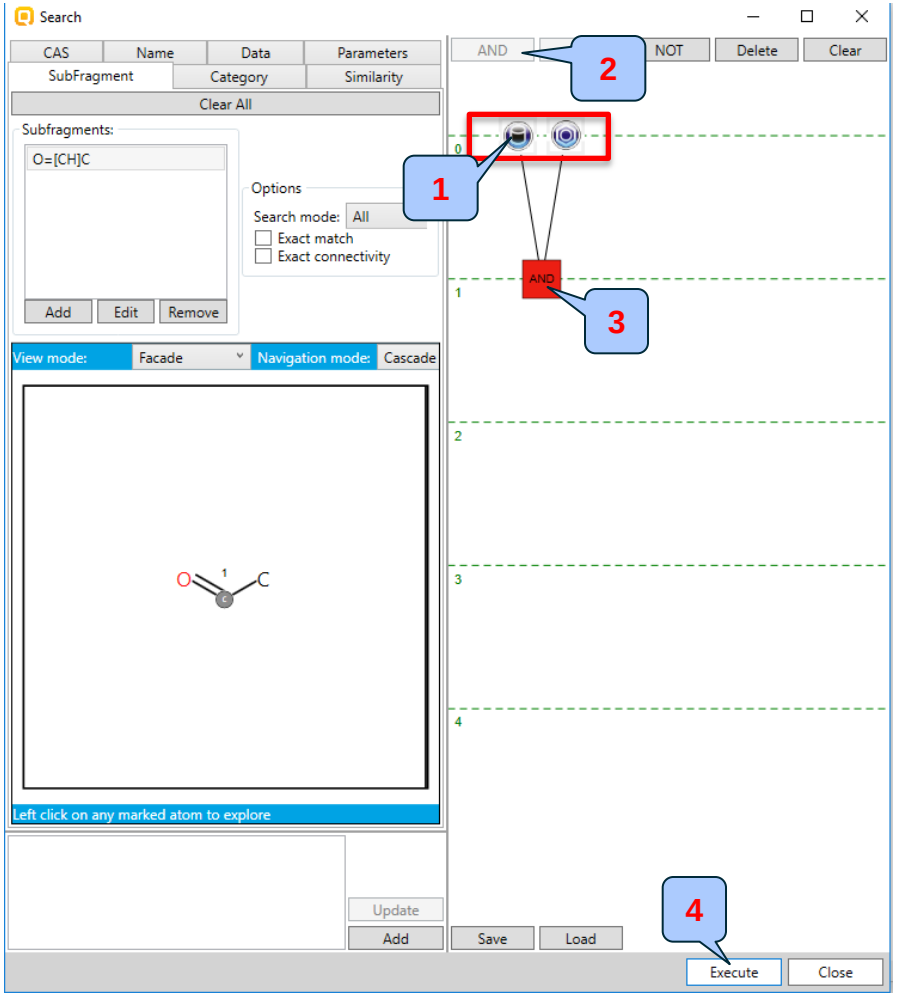
1. The drawn fragment appears in a new panel
2. Click **Add** button;
3. The query appears on the logic panel.

Subfragment search for identifying chemicals

Chemicals with Skin sensitization positive data including Aldehyde fragment

Example 6

- Structures search criteria
  - Endpoint: *EC3*
  - Data: *Positive*
  - SubFragment: Aldehydes

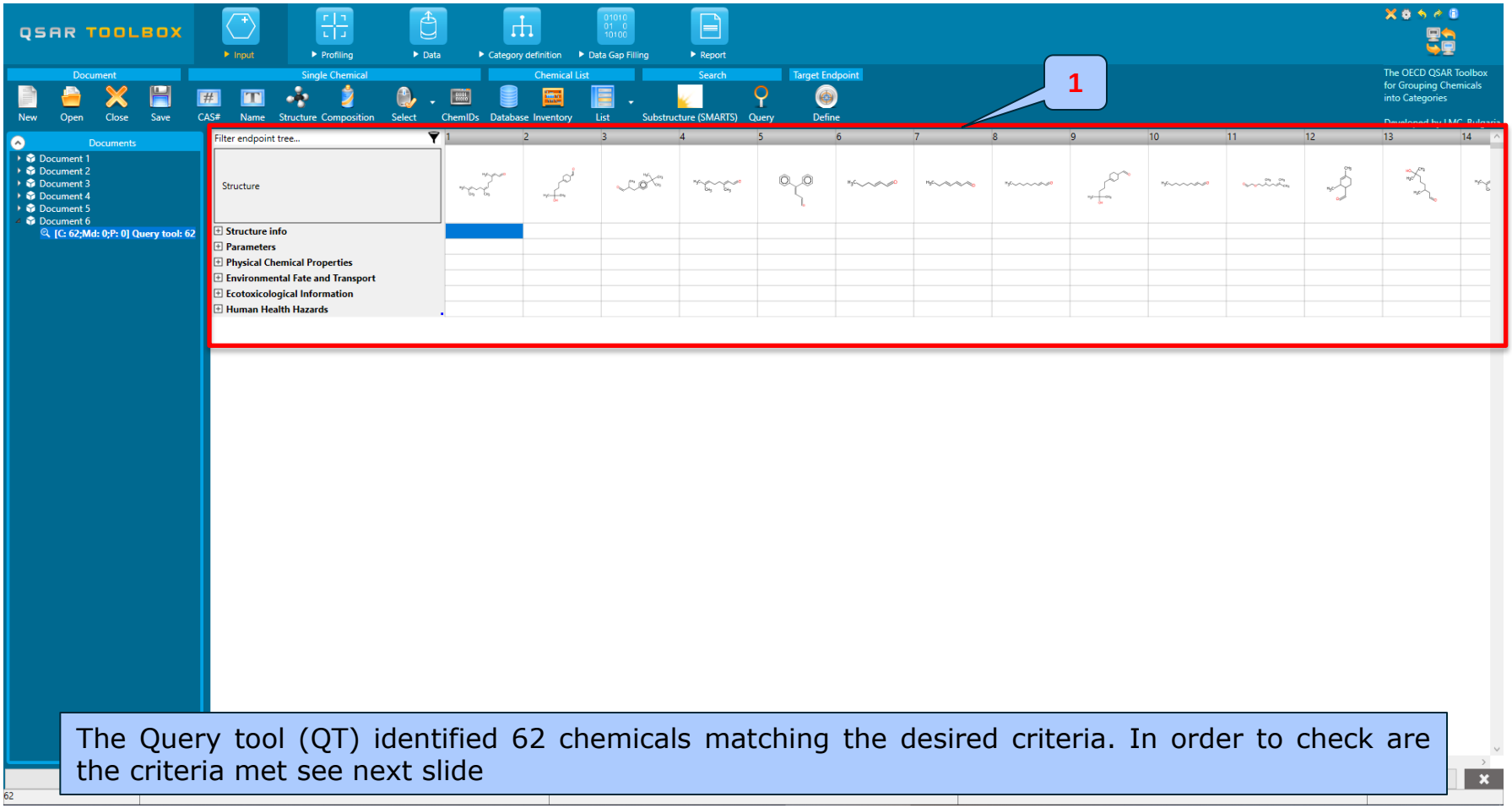


1. Right click over the queries in order to select them;
2. Click **AND** button;
3. The two queries are combined together by logical "*AND*";
4. Click **Execute** button or double click *And*;

Subfragment search for identifying chemicals

Chemicals with Skin sensitization positive data including Aldehyde fragment

Example 6

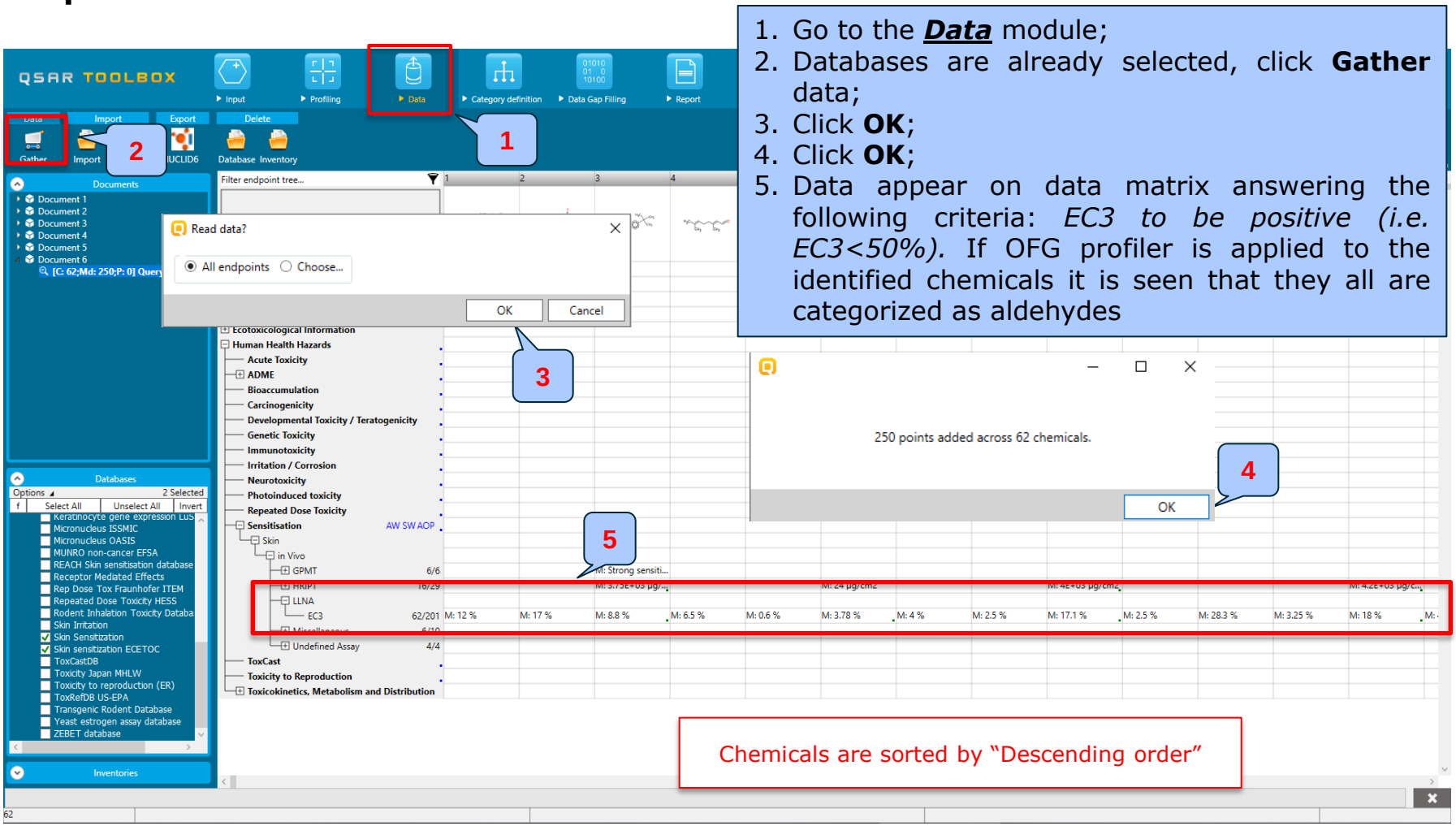


The Query tool (QT) identified 62 chemicals matching the desired criteria. In order to check are the criteria met see next slide

Subfragment search for identifying chemicals

Chemicals with Skin sensitization positive data including Aldehyde fragment

Example 6



Outlook

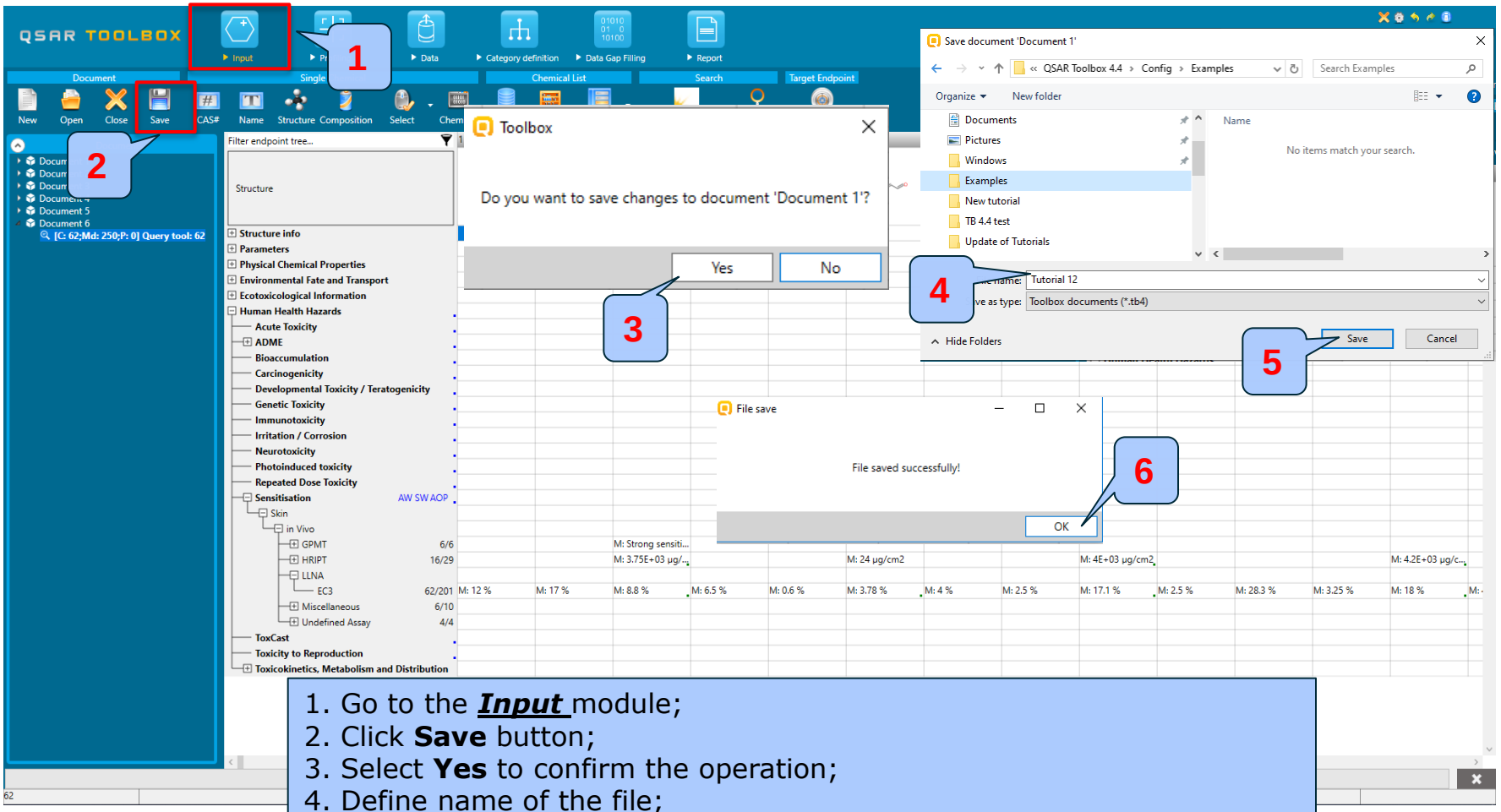
- Background
- Objectives
- Overview of Query tool
- Query tool window
- The exercise
- Workflow process
- **Save QT searches**

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).

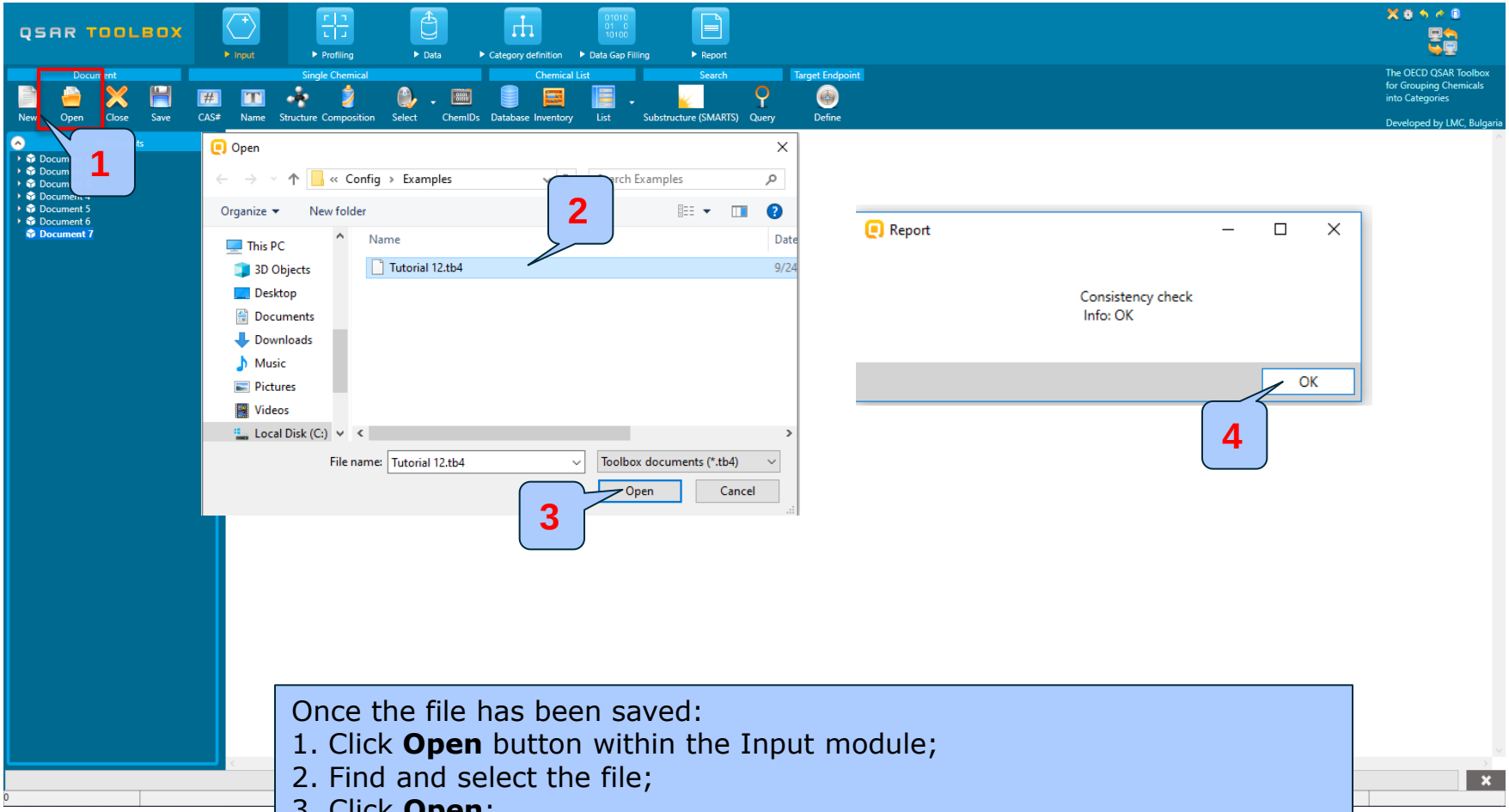
- Saving/Loading the file with TB prediction is shown on the next screenshots

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**.