QSAR TOOLBOX

The OECD QSAR Toolbox for Grouping Chemicals into Categories

OECD QSAR Toolbox v.3.4

Illustrating functionalities of Query tool

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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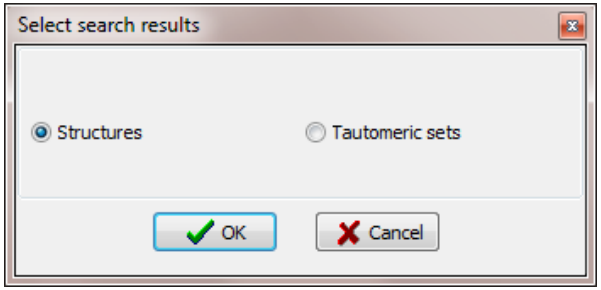
Overview of Query tool

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

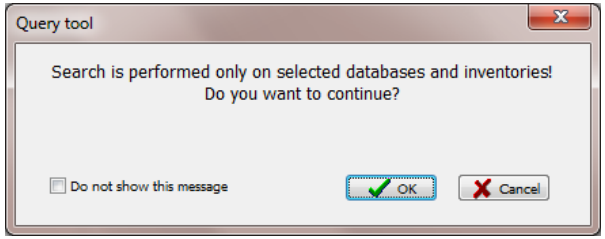
- **Chemical identifier search**
  - CAS
  - Name
  - Molecular structures
  - Tautomeric number
- **Parameter search**
  - Calculated 2D parameters
  - Calculated 3D parameters
- **Data search**
  - Search for data and metadata within imported databases
- **Extended search**
  - Profiling
  - Substructure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

Overview of Query tool
Prerequisites

•The Query tool functionality search for single structures or tautomeric sets matching desired criteria. The user should select one of the proposed options

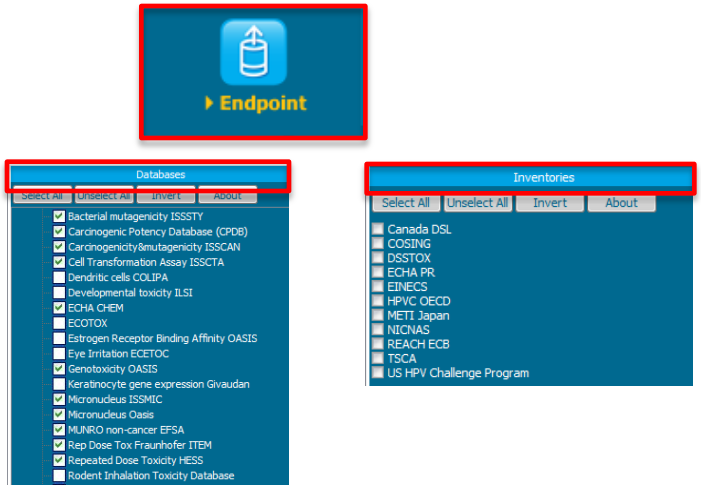


•The Query tool functionality search for chemicals within the selected databases and inventories only

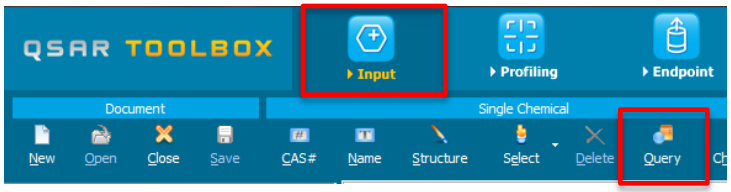


Overview of Query tool
Procedure for defining query

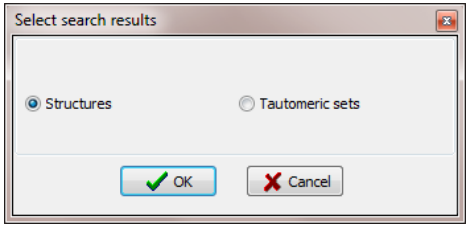
Step 1: Select databases/inventories of interest



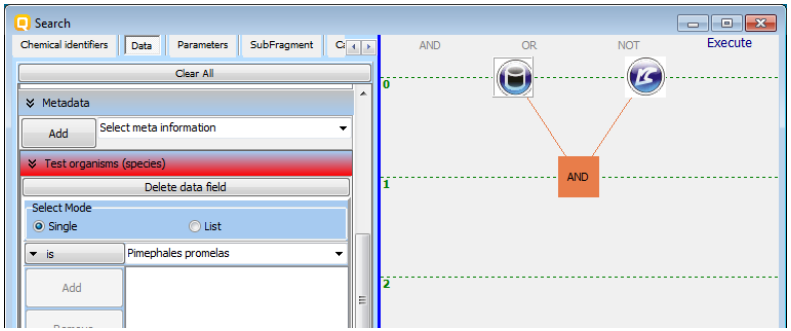
Step 2: Click on Query button



Step 3: Select structures/tautomeric sets



Step 4: Specify criteria for searching structures



Outlook

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- Overview of Query tool
- **Query tool window**
- The exercise
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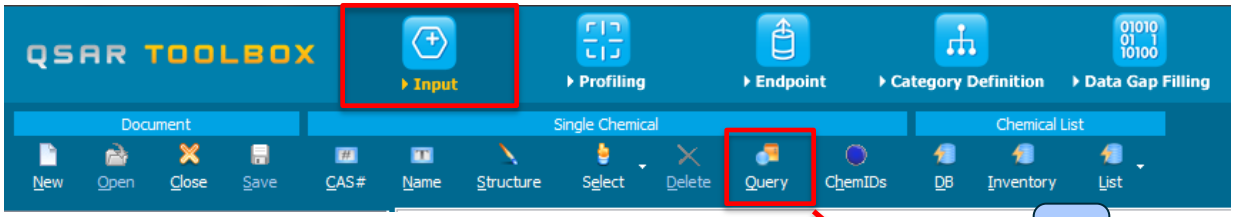
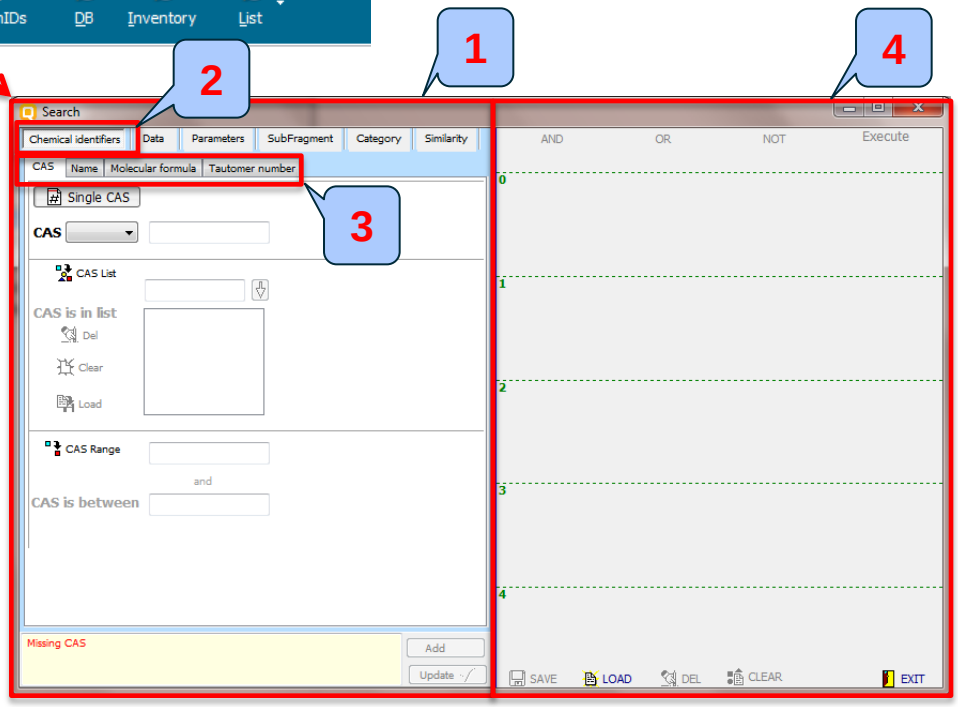
Query tool window

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



- Query tool main components
  - Query edit panel (1)
    - search group panel (2)
    - available searches for selected group (3)
  - Query tree logic panel (4)



Outlook

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- Query tool window
- **The exercise**
- Workflow process
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The Exercise

- In this exercise we will demonstrate the following queries:
  - Sub fragment 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 sub fragment search (*Epoxides*) *(Example 5)*
  - Combination of Skin sensitization data (EC 3) and predefined category (*Aldehydes*) *(Example 6)*

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- **Workflow process**
- Save QT searches

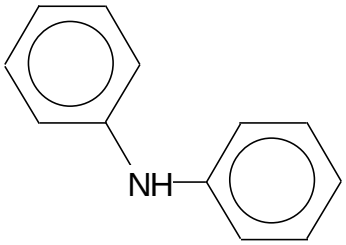
Sub fragment search for identifying chemicals

Substituted diphenyl amine

Example 1

Search for structures that meet the structural requirements:

- *Substituted diphenyl amine*



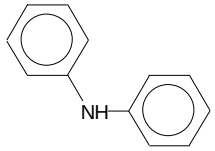
c1ccc(Nc2ccccc2)cc1

Sub fragment search for identifying chemicals

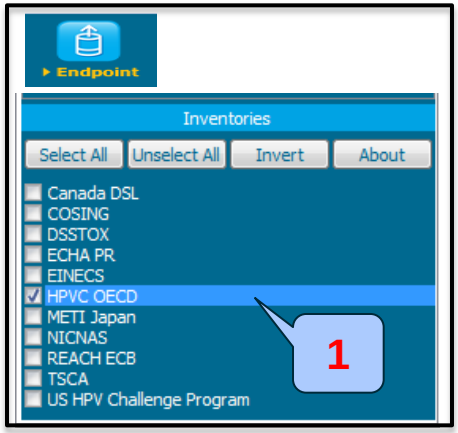
Procedure for defining

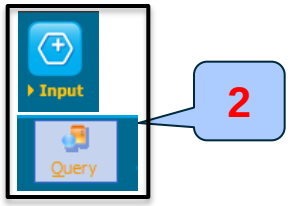
Example 1

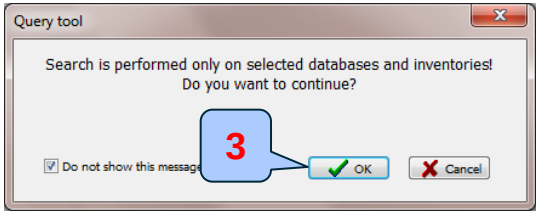
- *Substituted diphenyl amine*

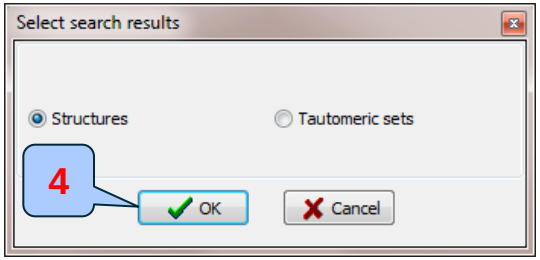


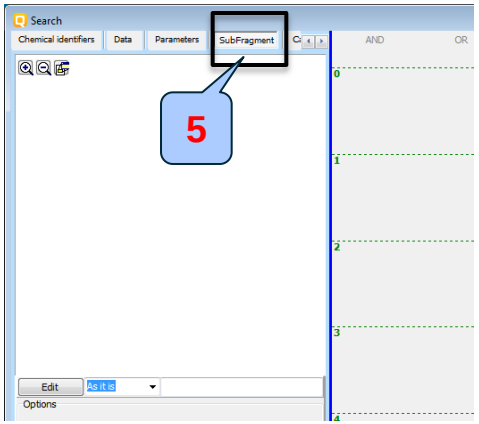
c1ccc(Nc2ccccc2)cc1











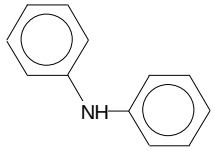
QT procedure starts with selecting databases/inventories used for searching the desired criteria:
1. **Select** HPVC OECD inventory located under **Endpoint section.** No databases have been selected in this excirsize; 2. **Click** on Query button located under **Input** section; The message informs the user that search will be performed on selected databases or inventories only 3. **Click** OK. The window proposing two different options for searching (discrete or tautomeric sets) appears. By default "structures" is selected. In our case we are searching for single structures 4. **Click** OK 5. Query panel appears; 6. **Select** "Sub Fragment" panel

Sub fragment search for identifying chemicals

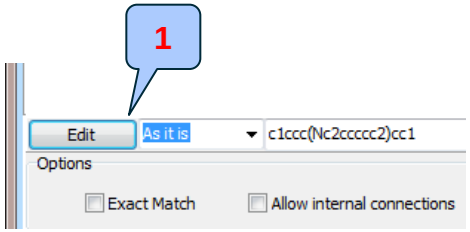
Procedure for defining

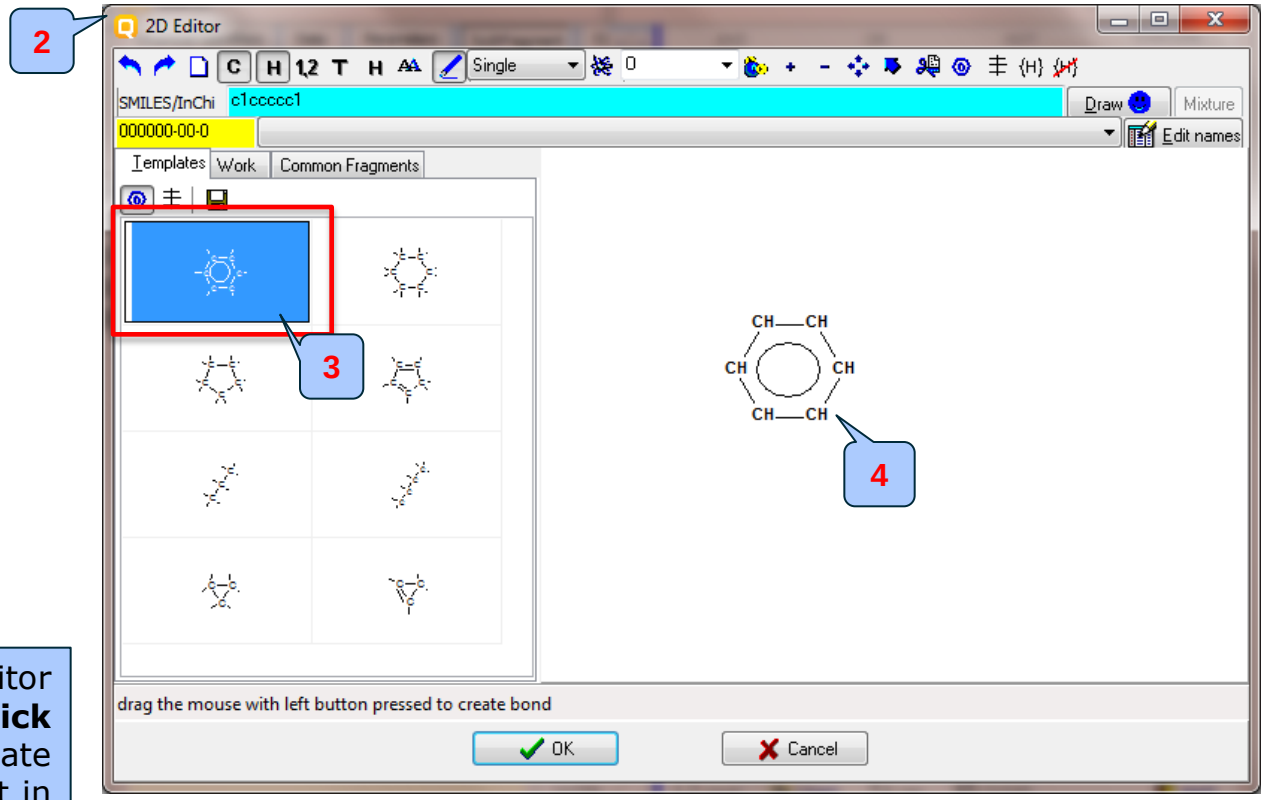
Example 1

- *Substituted diphenyl amine*



c1ccc(Nc2ccccc2)cc1





1. **Click** Edit button; 2. The 2D 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 generate benzene fragment;

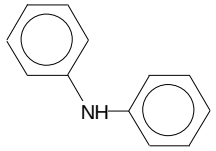
Continued on the next slide

Sub fragment search for identifying chemicals

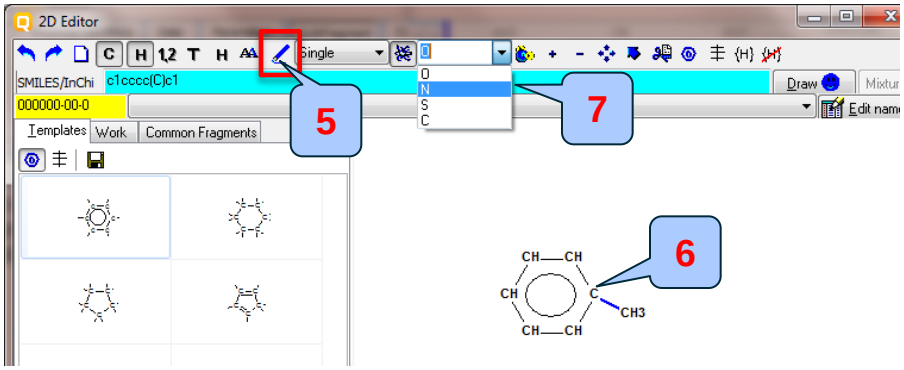
Procedure for defining

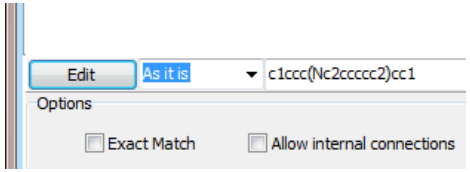
Example 1

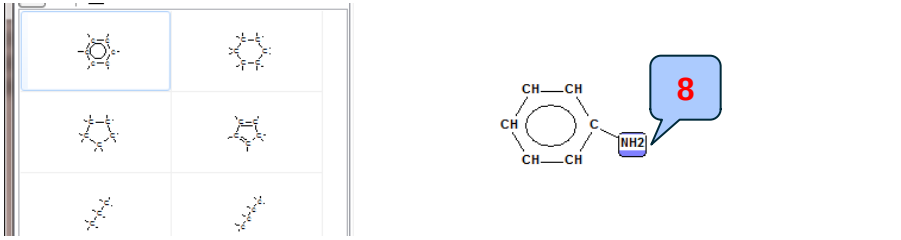
- *Substituted diphenyl amine*



c1ccc(Nc2ccccc2)cc1







5. **Click** on the button of Single bond; 6. **Highlight** one of the C atom from the benzene ring and **drag** to generate single bond; 7. **Select** N atom from the list; 8. **Put** the selected N atom over the C atom from the single bond; 9. **Repeat** step 5 and **Draw** single bond to the N atom from NH2 group;

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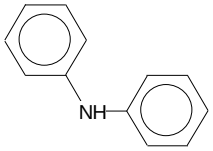
Sub fragment search for identifying chemicals

Procedure for defining

Example 1

- *Substituted diphenyl amine*



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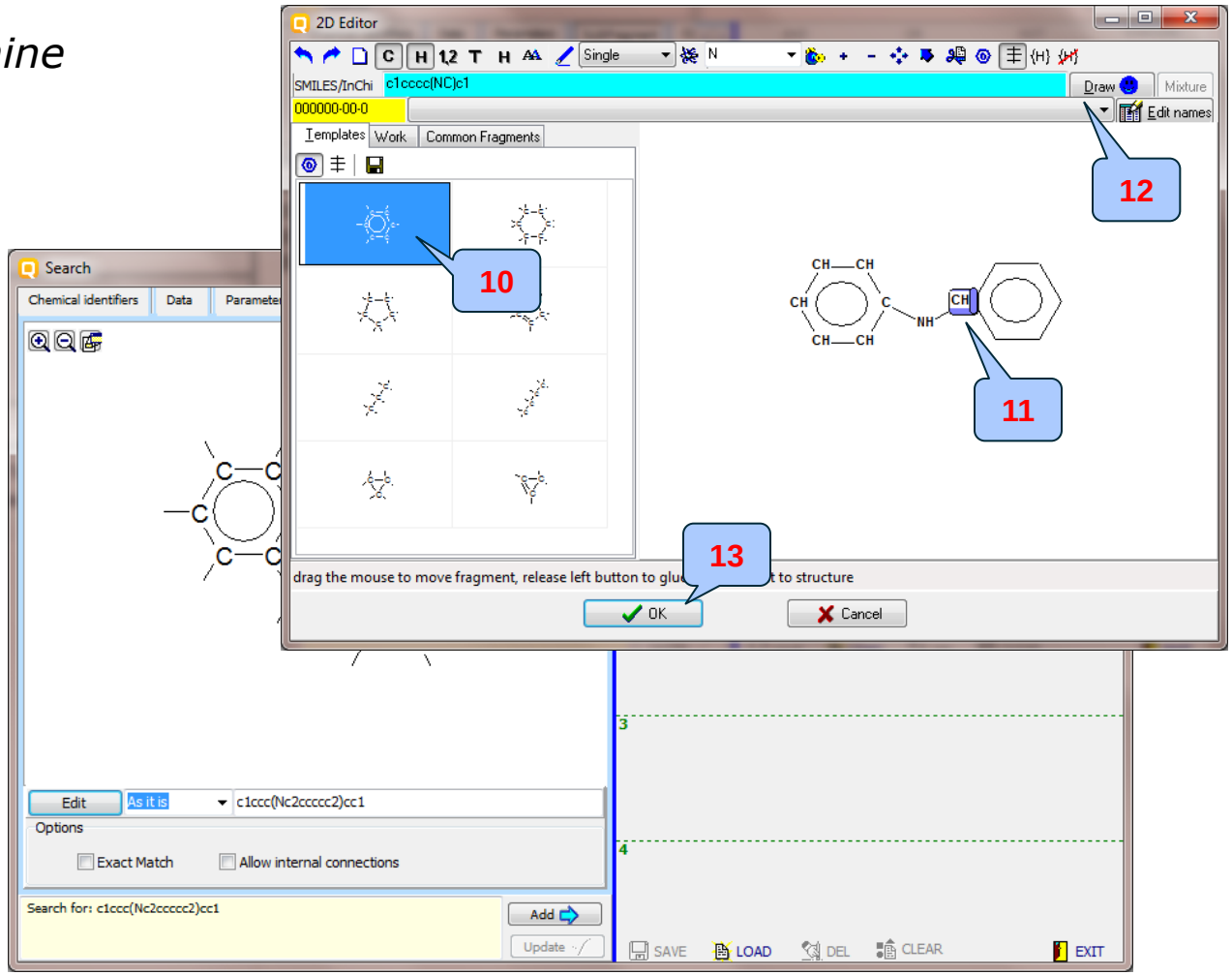


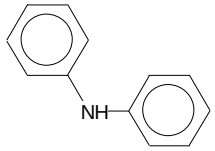
10. **Left click** over benzene ring from the template in order to take benzene ring 11. **Left lick** over the C atom in order to define second benzene ring to the NH group 12. **Click Draw**; 13. **Click OK**

Sub fragment search for identifying chemicals

Procedure for defining

Example 1

- *Substituted diphenyl amine*



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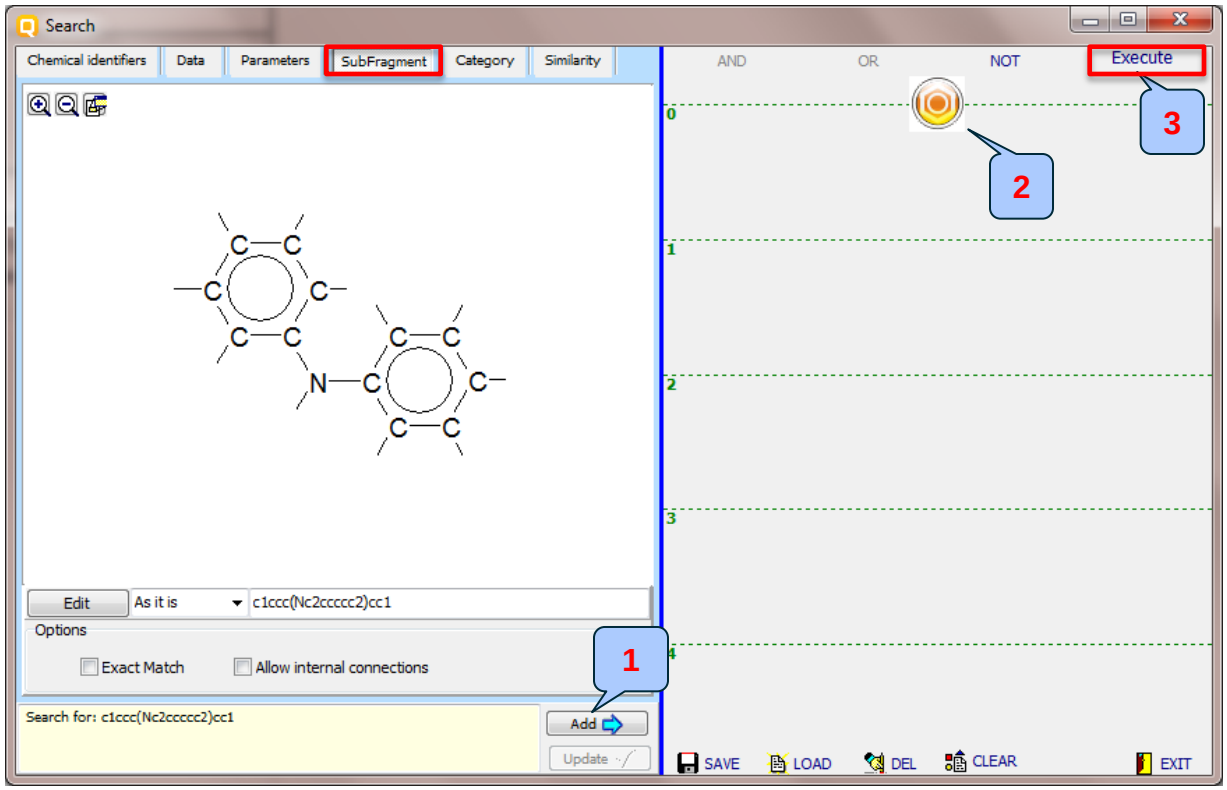


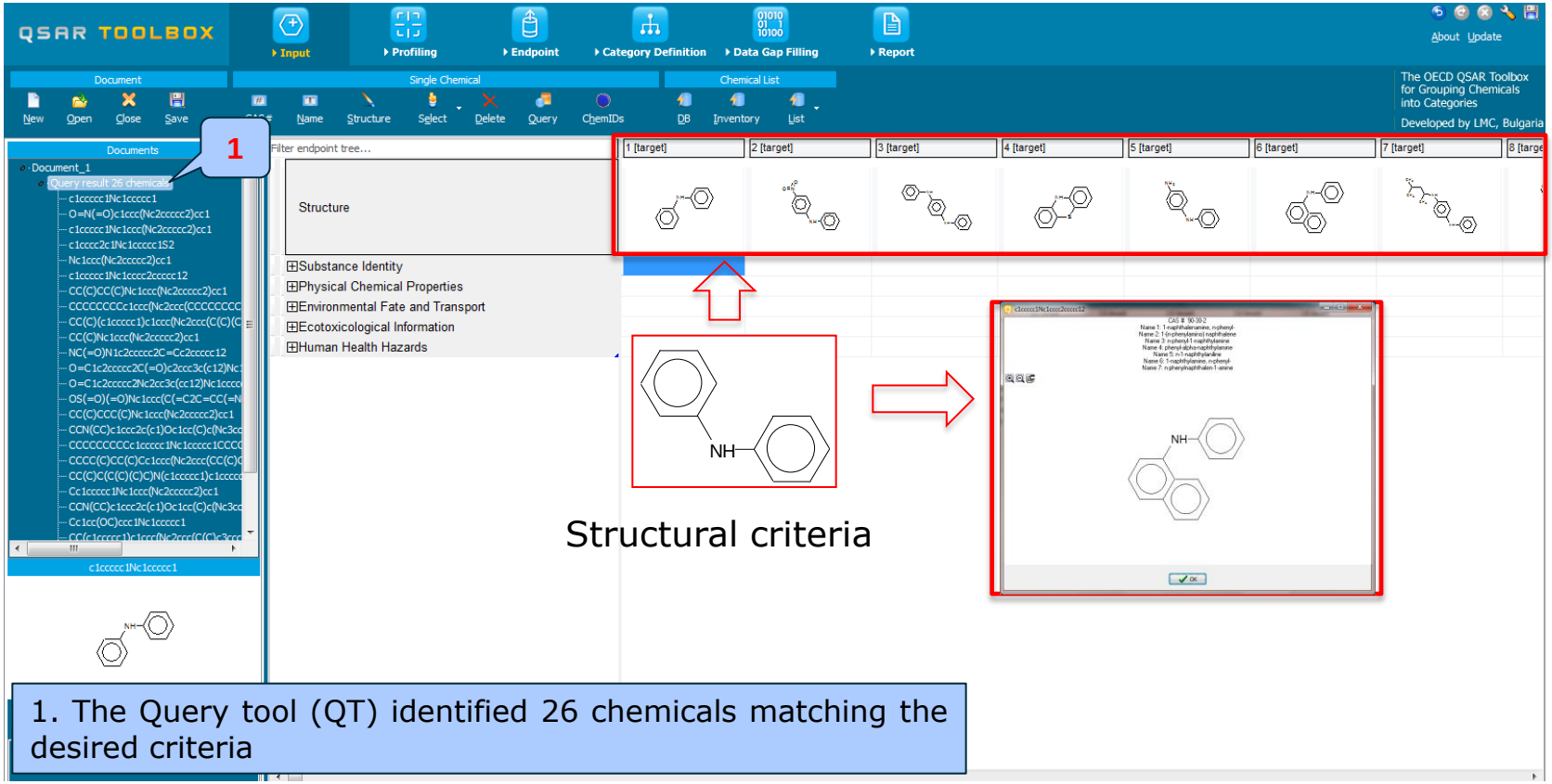
1. **Click** Add button; 2. The defined query appears on logic panel; 3. **Double click** over the query to execute it or **click** Execute button.

Sub fragment search for identifying chemicals

Procedure for defining

Example 1

- *Substituted diphenyl amine*



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

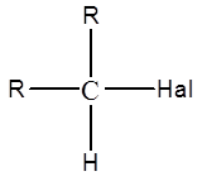
Sub fragment search for identifying chemicals

Aliphatic halogens

Example 2

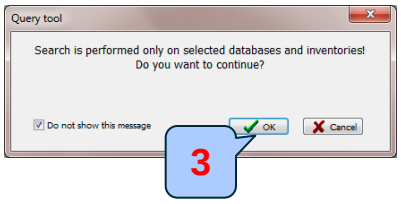
Search for structures that meet the structural requirements:

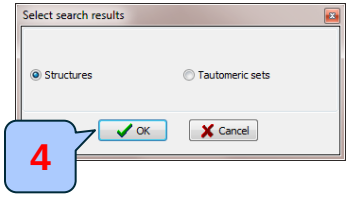
- *Aliphatic halogens*



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 Endpoint section; 2. **Click** on Query button under Input section; 3. **Click** OK 4. **Click** OK in order to search for discrete chemicals

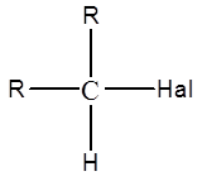
Sub fragment search for identifying chemicals

Aliphatic halogens

Example 2

Search for structures that meet the structural requirements:

- *Aliphatic halogens*



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- **HPVC OECD** inventory has been selected
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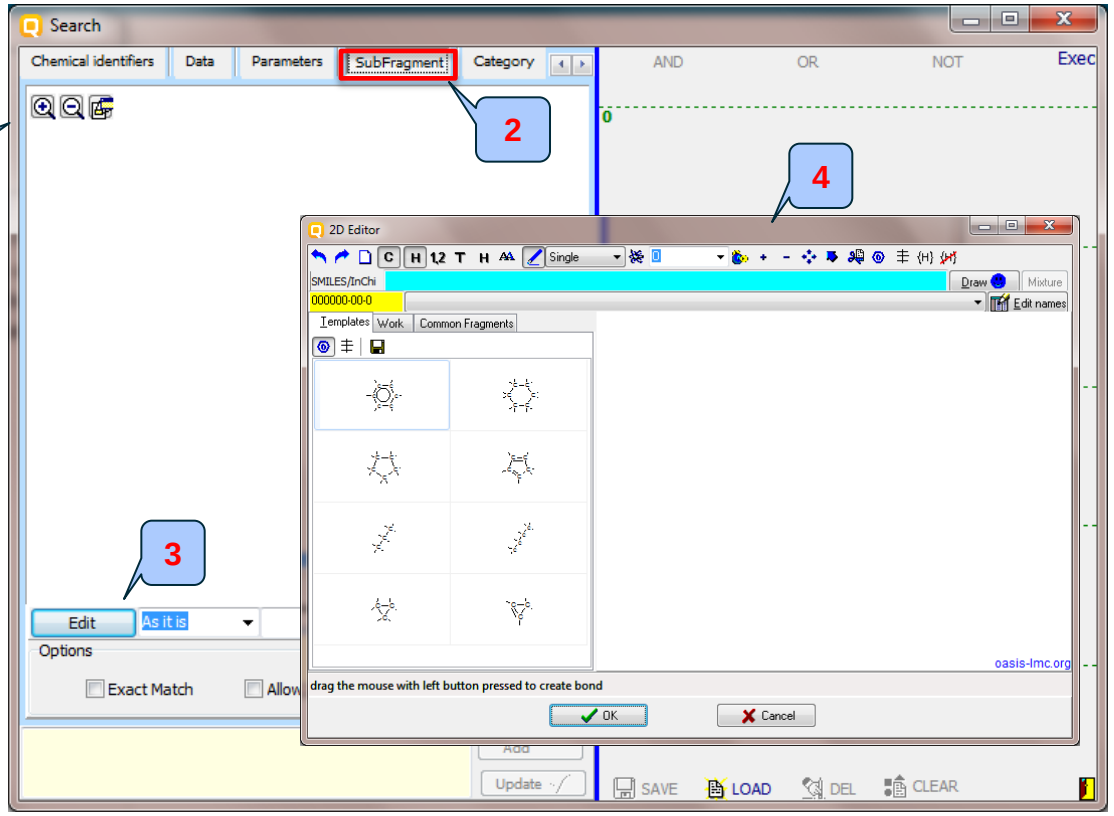


1. Query panel appears; 2. **Go** to SubFragment panel; 3. **Click** Edit button; 4. 2D Editor window appears

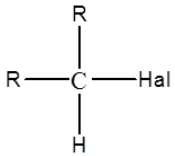
Sub fragment search for identifying chemicals

Aliphatic halogens

Example 2

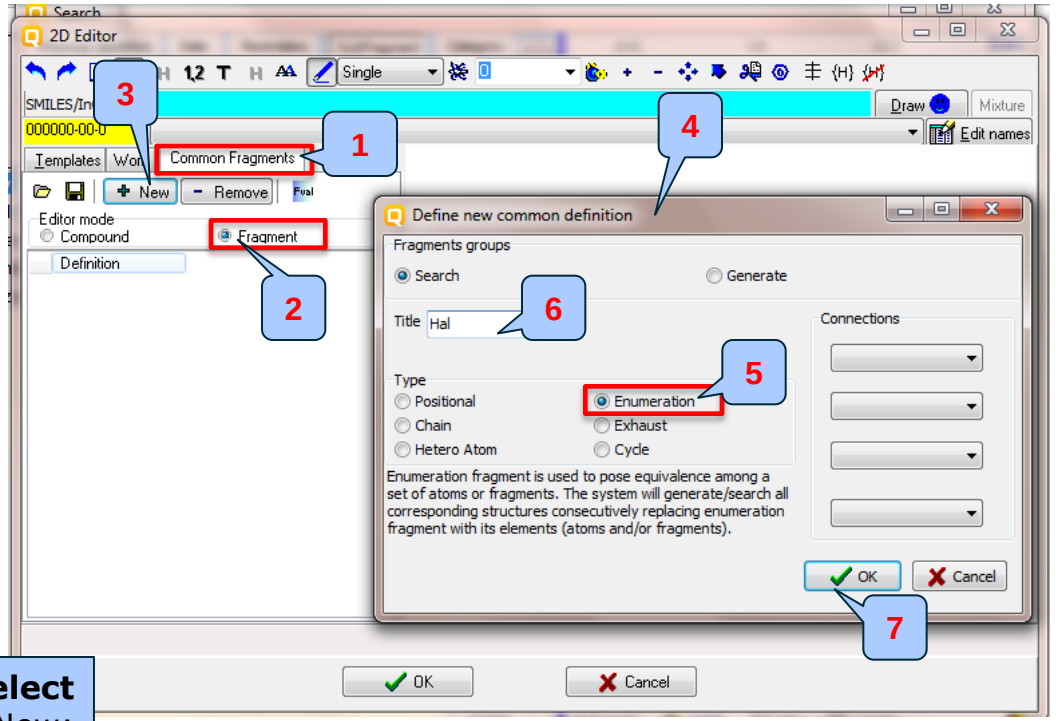
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define common fragment Hal with three members (halogen atoms)



1.**Click** on Common fragments panel; 2. **Select** Fragment radio button; 3. **Click** New; 4.Additional window appears; 5. **Select** Enumeration type fragment; 6. **Define name** of the fragment (e.g. Hal); 7. **Click** OK

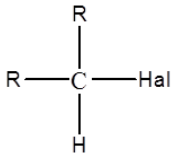
Sub fragment search for identifying chemicals

Aliphatic halogens

Example 2

Search for structures that meet the structural requirements:

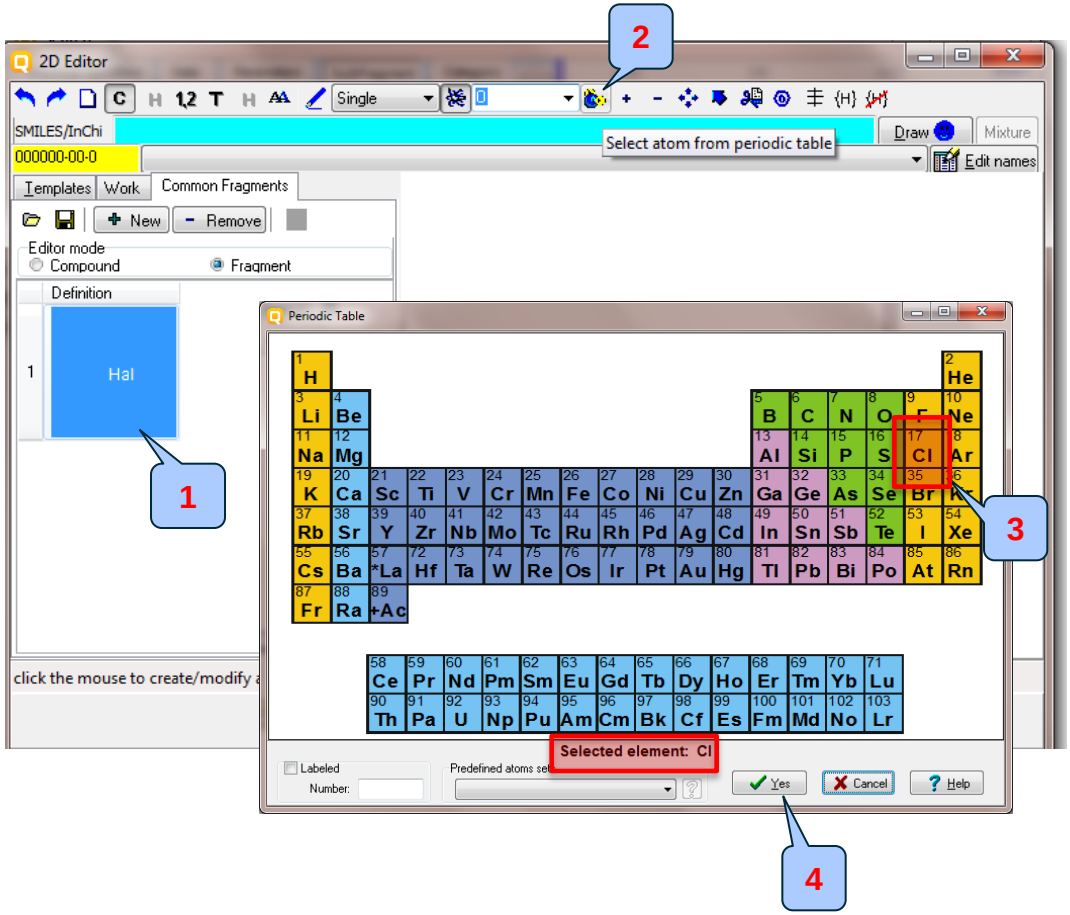
- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define common fragment Hal with three members (halogen atoms)

1. The common fragment definition appears in the library with fragments;
2. **Click** on button with periodic table;
3. **Select** Cl atom; 4. **Click** Yes



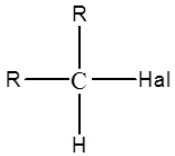
Sub fragment search for identifying chemicals

Aliphatic halogens

Example 2

Search for structures that meet the structural requirements:

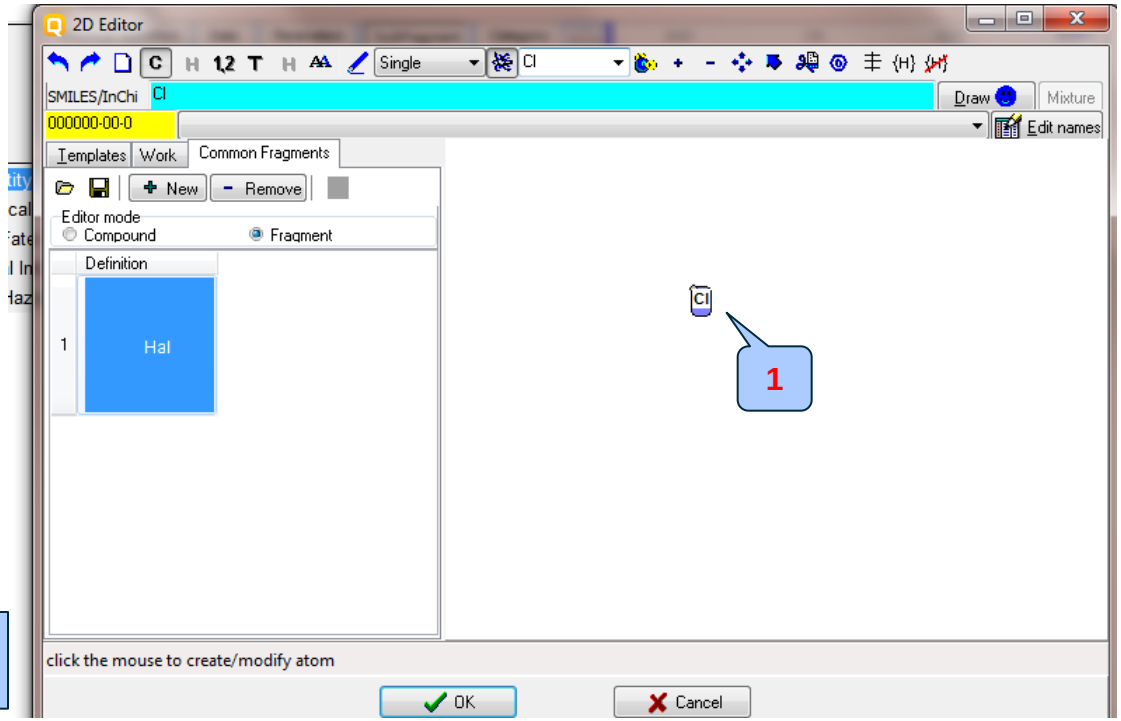
- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define common fragment Hal with three members (halogen atoms)

1. **Click** on the plot area in order to create Cl atom



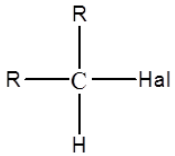
Sub fragment search for identifying chemicals

Aliphatic halogens

Example 2

Search for structures that meet the structural requirements:

- *Aliphatic halogens*



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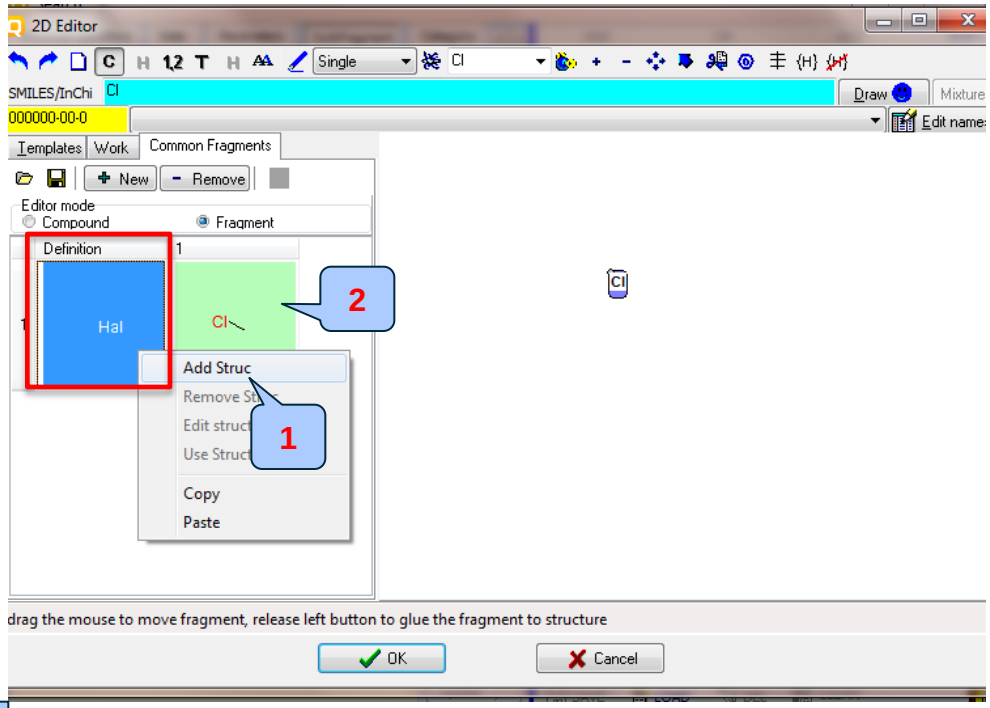
•Define common fragment Hal with three members (halogen atoms)



1. **Right click** over the library with fragments and select "Add Struc"
2. The Cl atom appears on the right

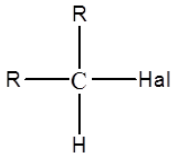
Sub fragment search for identifying chemicals

Aliphatic halogens

Example 2

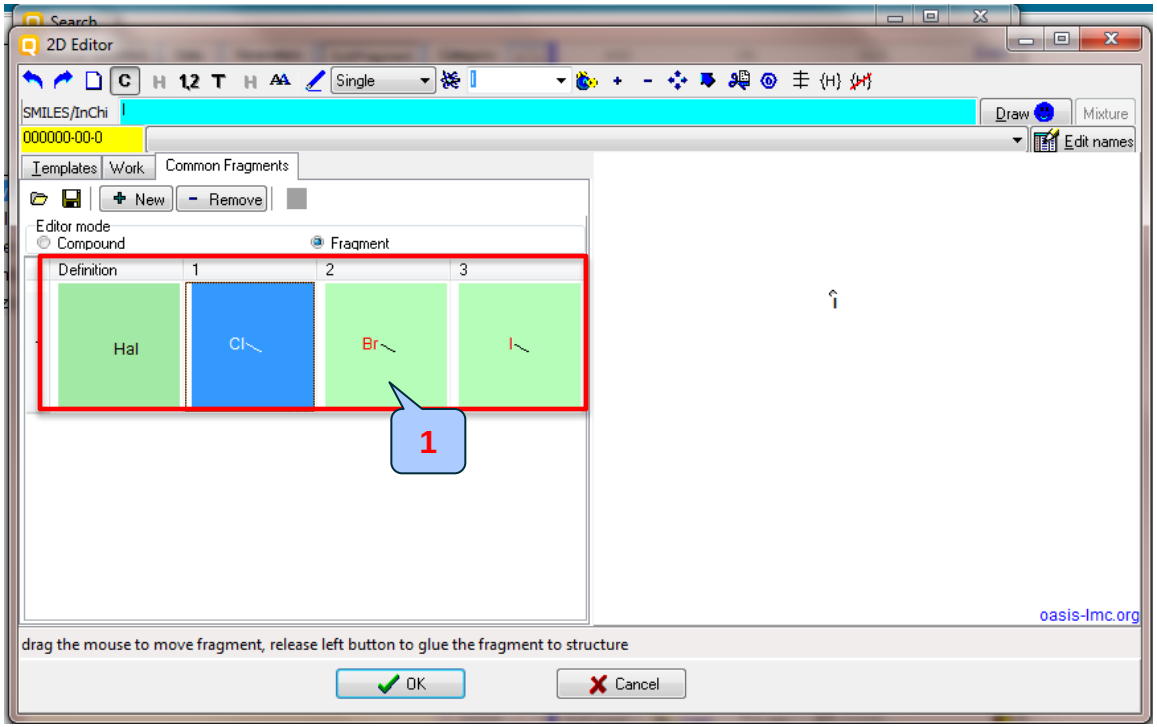
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define common fragment Hal with three members (halogen atoms)



1. Add the other two halogen atoms (Br and I) following steps shown on slides (#25-27)

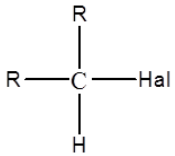
Sub fragment search for identifying chemicals

Aliphatic halogens

Example 2

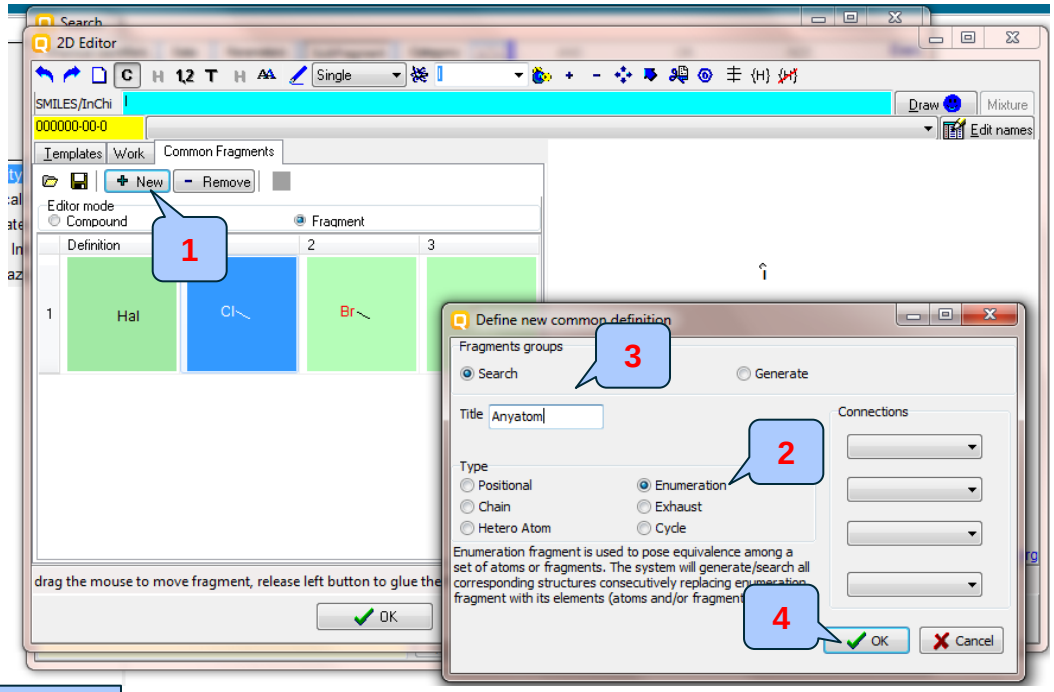
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define fragment R including any type atom except H atom



1. **Click** New; 2. **Select** Enumeration type fragment; 3. **Define name** of the fragment (e.g. Any atom); 4. **Click** OK

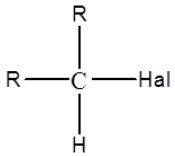
Sub fragment search for identifying chemicals

Aliphatic halogens

Example 2

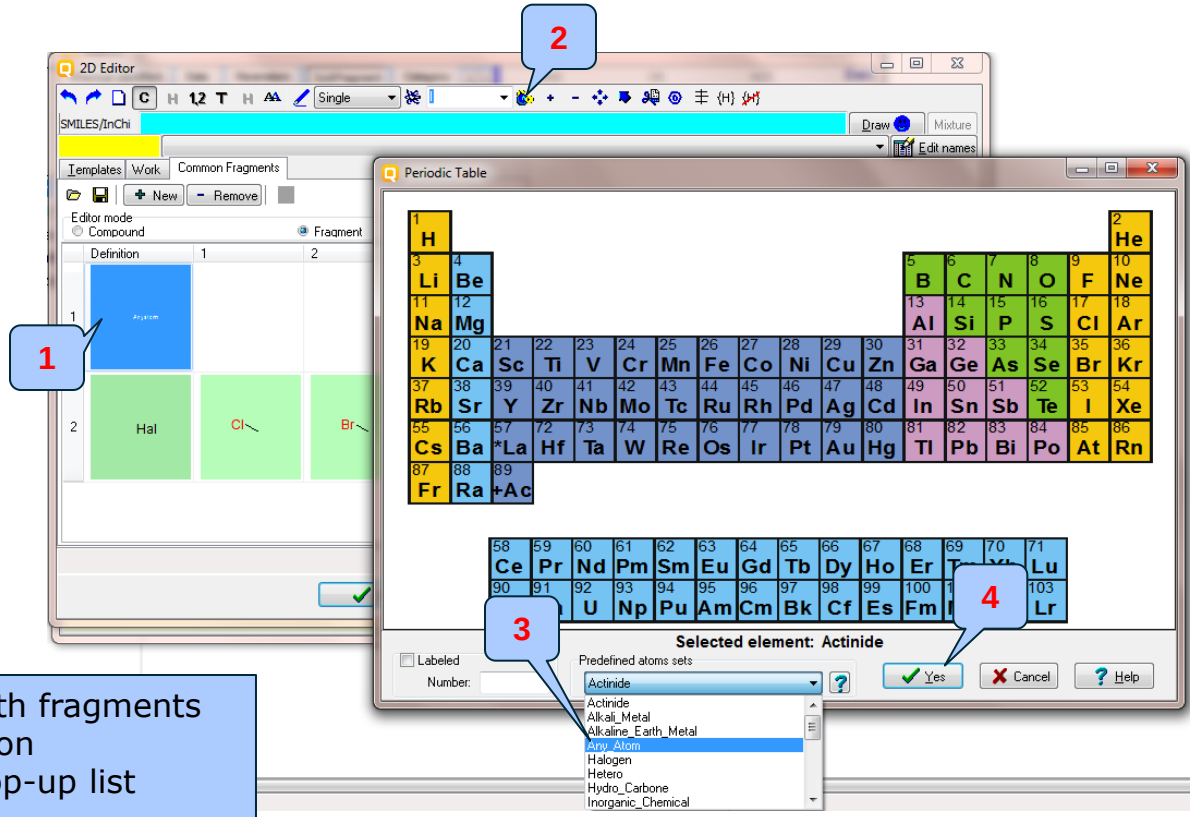
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define fragment R including any type atom except H atom



1. The definition appears in list with fragments
2. **Click** on the periodic table button
3. **Select** "Any Atom" from the pop-up list
4. **Click** Yes

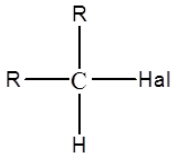
Sub fragment search for identifying chemicals

Aliphatic halogens

Example 2

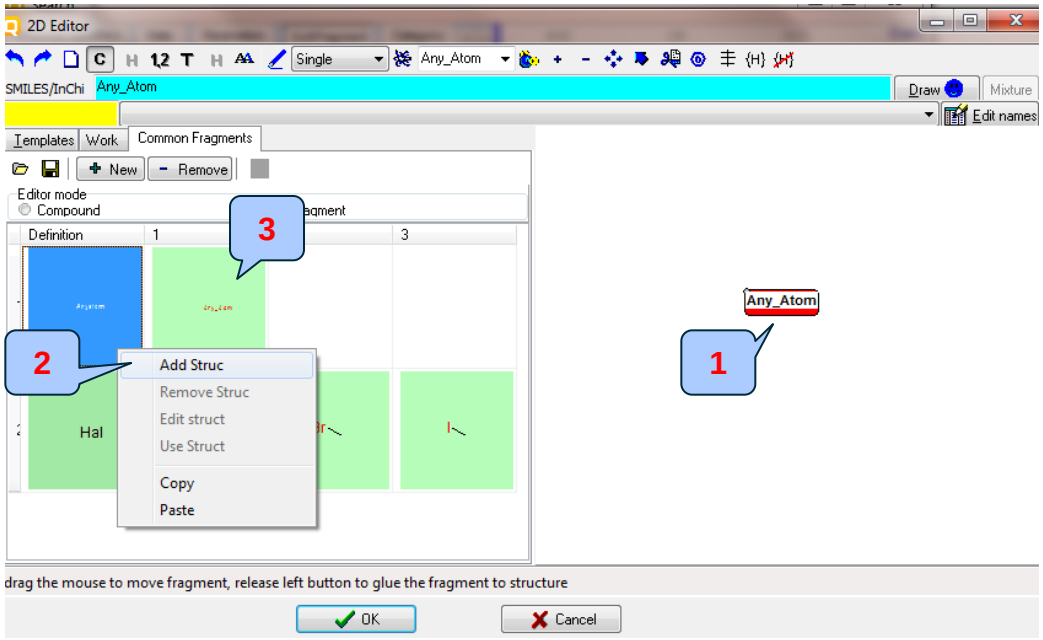
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define fragment R including any type atom except H atom



1. **Click** on the plot in order to create the fragment
2. **Right click** over the definition and select "Add Struc"
3. The fragment appears on the right

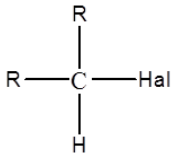
Sub fragment search for identifying chemicals

Aliphatic halogens

Example 2

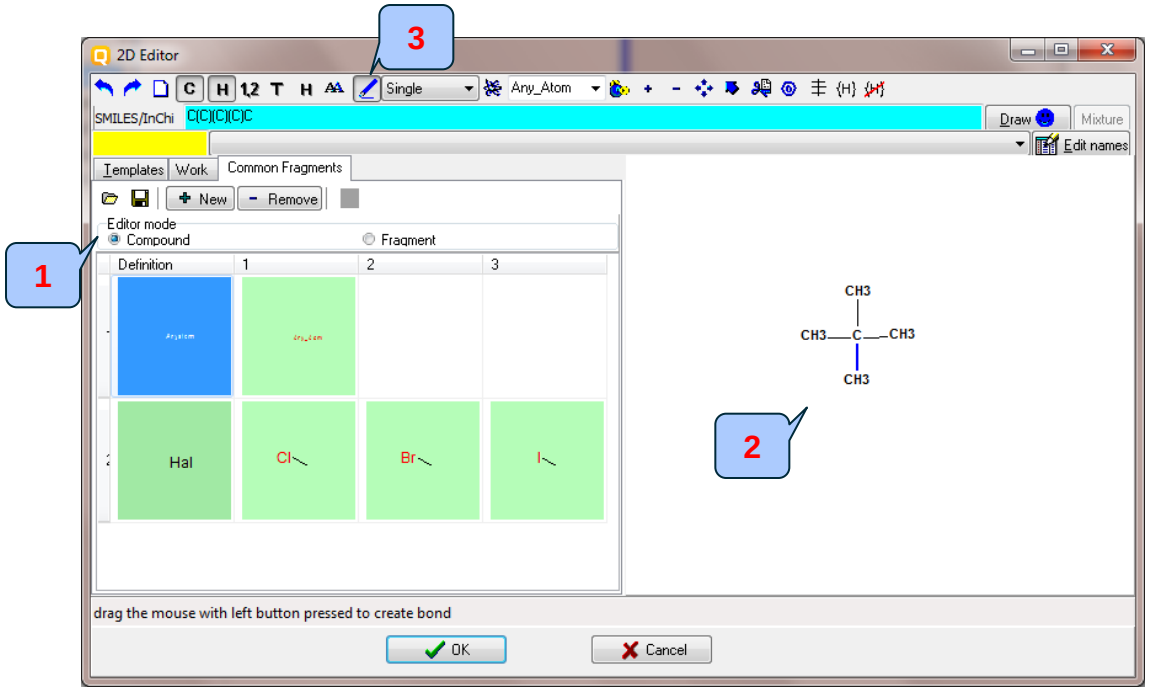
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define skeleton of target compound



1. **Click** on Compound radio button
2. **Define** the carbon skeleton of the defined query
3. **Use** single bond button (help explanation is provided on slide #18)

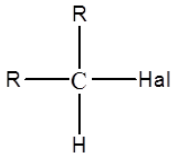
Sub fragment search for identifying chemicals

Aliphatic halogens

Example 2

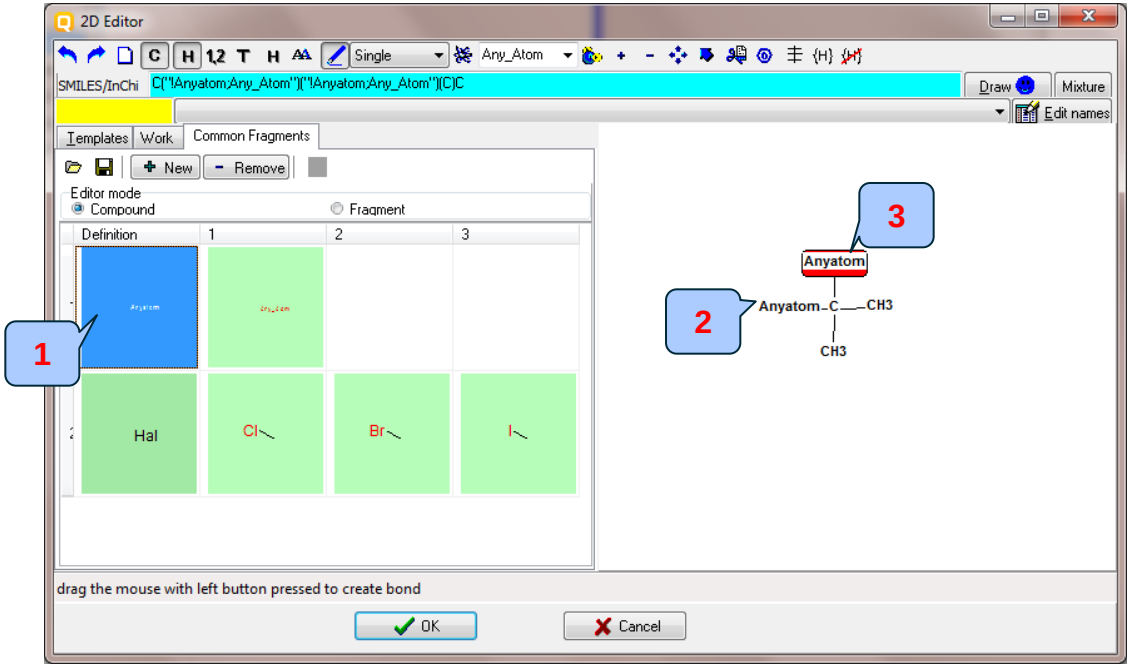
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define skeleton of target compound



1. **Left click** over the definition of Any atom fragment (the fragment is selected)
2. **Put** it over CH_3 group
3. **Repeat** again for the second CH_3 group

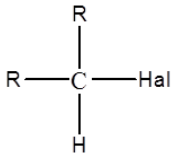
Sub fragment search for identifying chemicals

Aliphatic halogens

Example 2

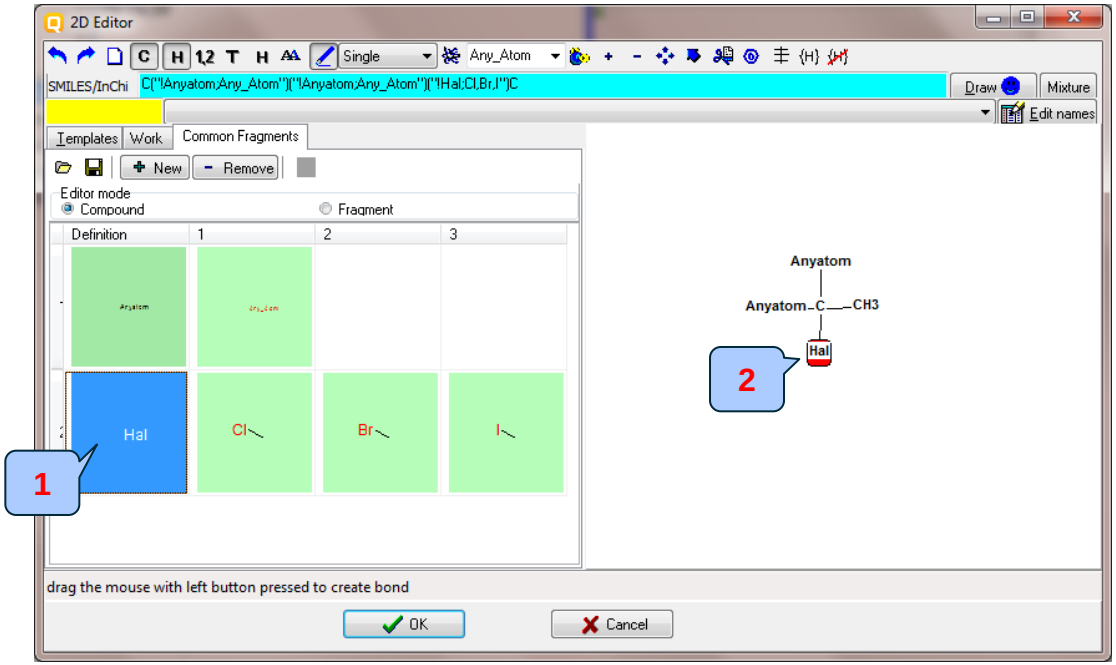
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define skeleton of target compound



1. **Left click** over the Hal fragment
2. **Put** it over CH_3 group in order to replace CH3 group with Hal atoms

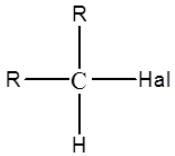
Sub fragment search for identifying chemicals

Aliphatic halogens

Example 2

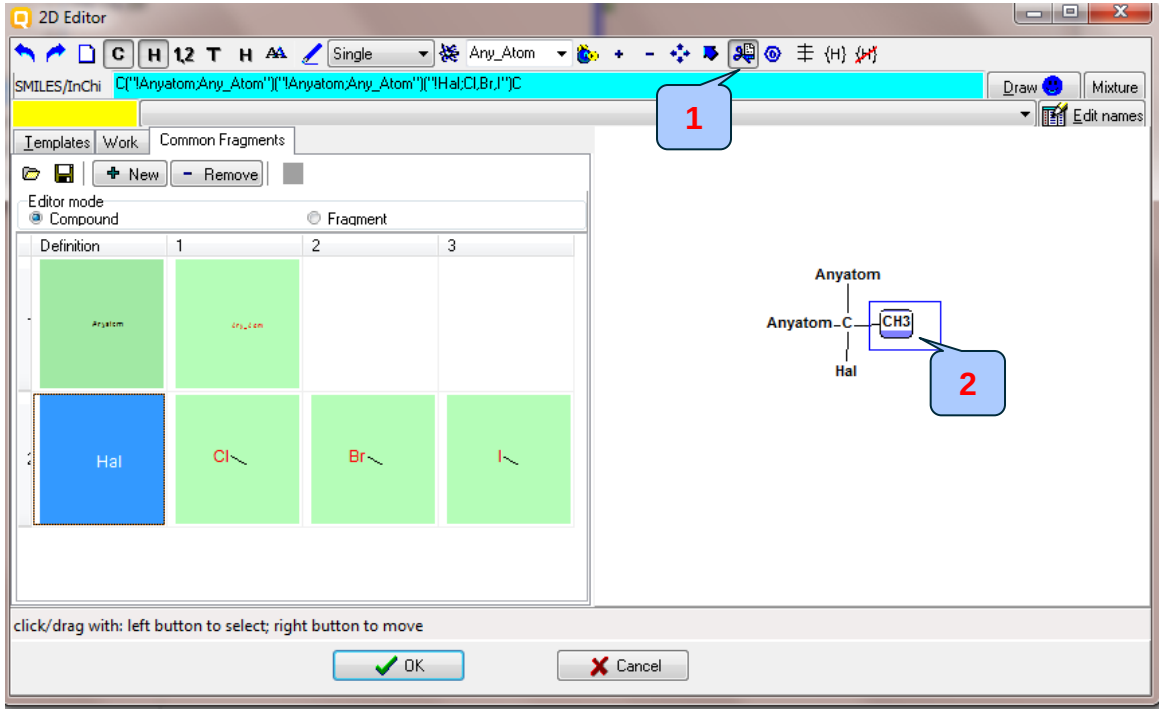
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define skeleton of target compound



1. **Click** on the scissors button
2. **Erase** the free CH_3 group (by left button and drag)

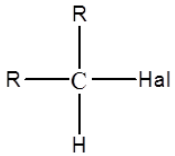
Sub fragment search for identifying chemicals

Aliphatic halogens

Example 2

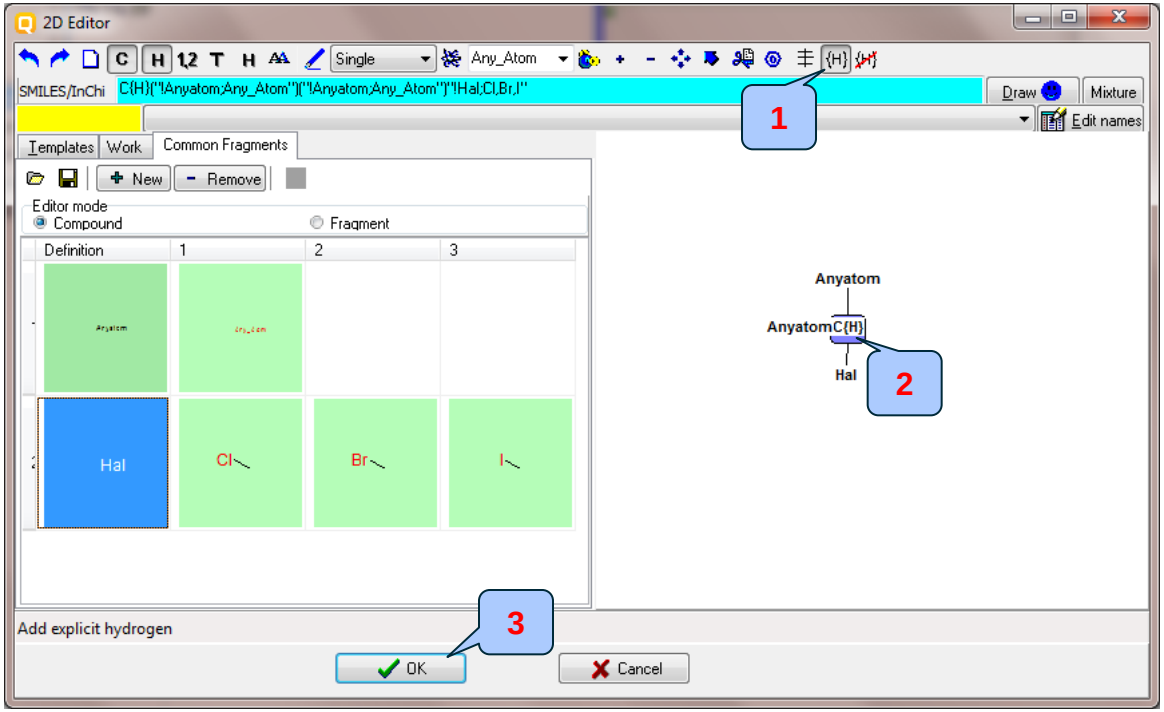
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define skeleton of target compound



1. **Click** on the {H} button in order to make the H atom connected to C-atom explicit
2. **Click** over the C atom
3. **Click** OK

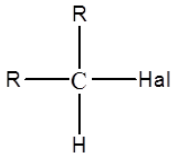
Sub fragment search for identifying chemicals

Aliphatic halogens

Example 2

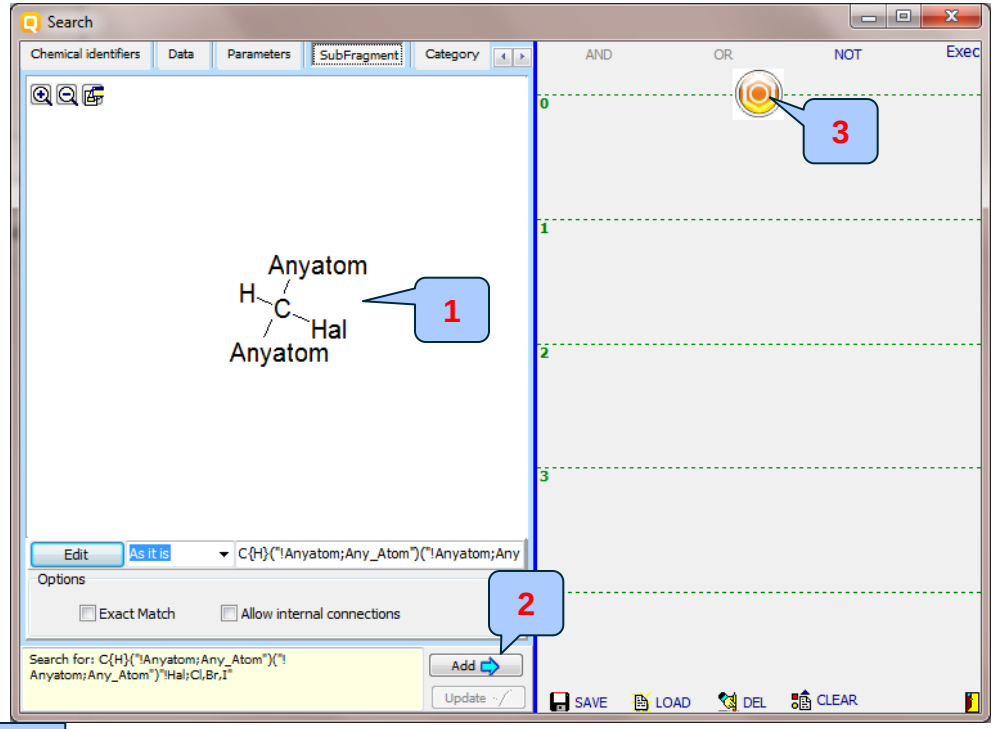
Search for structures that meet the structural requirements:

- *Aliphatic halogens*



R – Any atom except H
Hal – Cl, Br, I

•Define skeleton of target compound



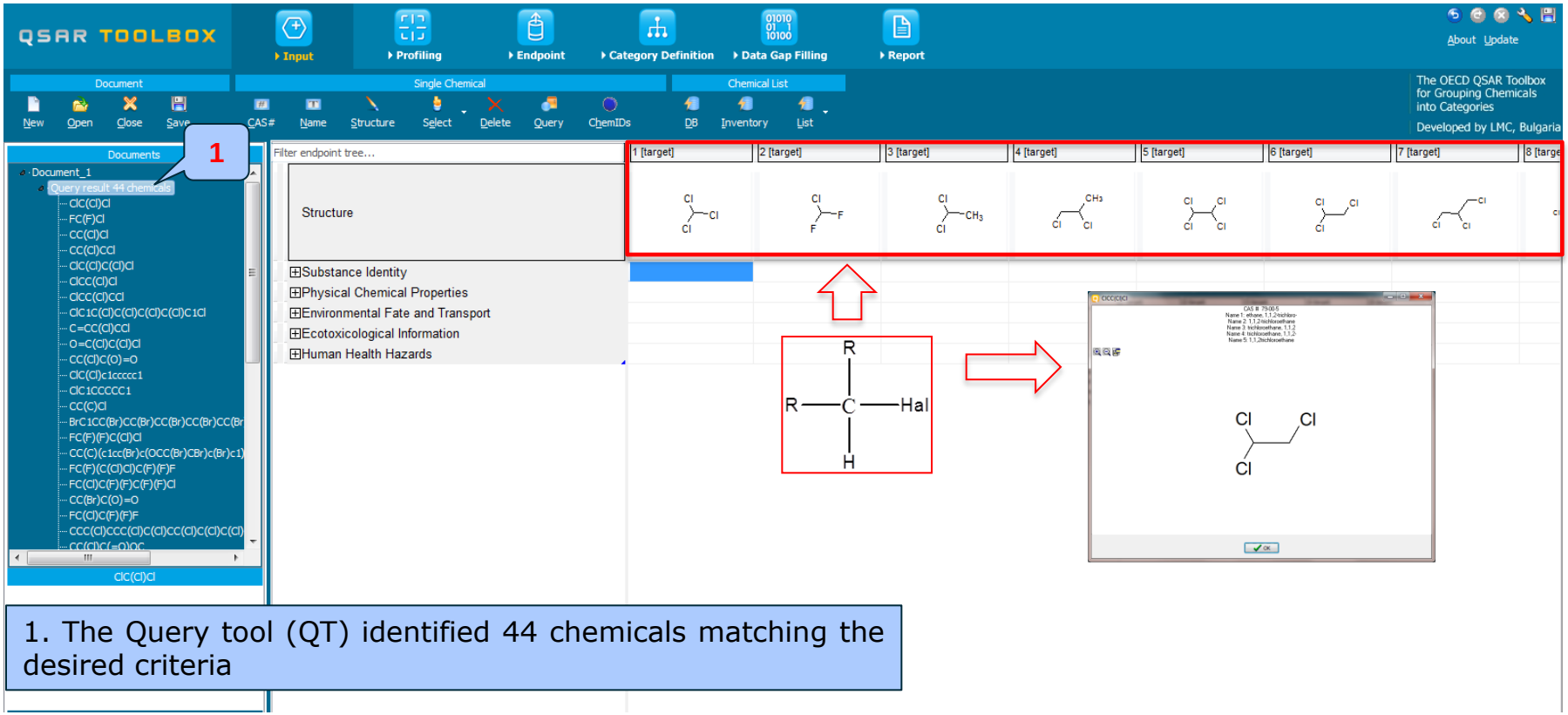
1. The definition of aliphatic halogens appears on the blank plot
2. **Click** Add button
3. **Double click** on the query to execute it

Sub fragment search for identifying chemicals

Aliphatic halogens

Example 2

- *Aliphatic halogens*



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

Sub fragment search for identifying chemicals

BCF and (Dmax)

Example 3

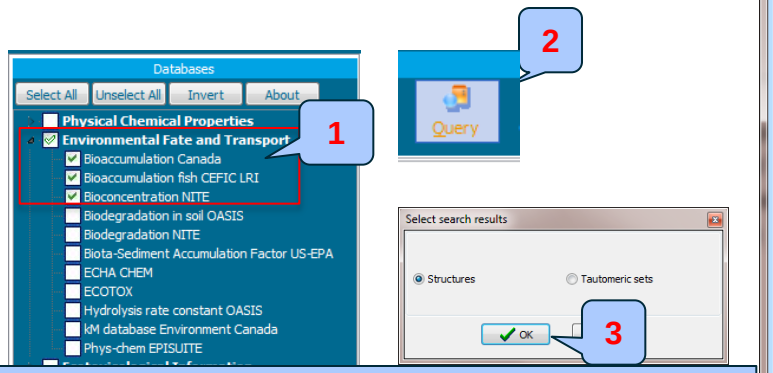
- Structures search criteria
  - Endpoint is BCF
  - 3D parameter – minimum value of Diameter maximum >15 Å

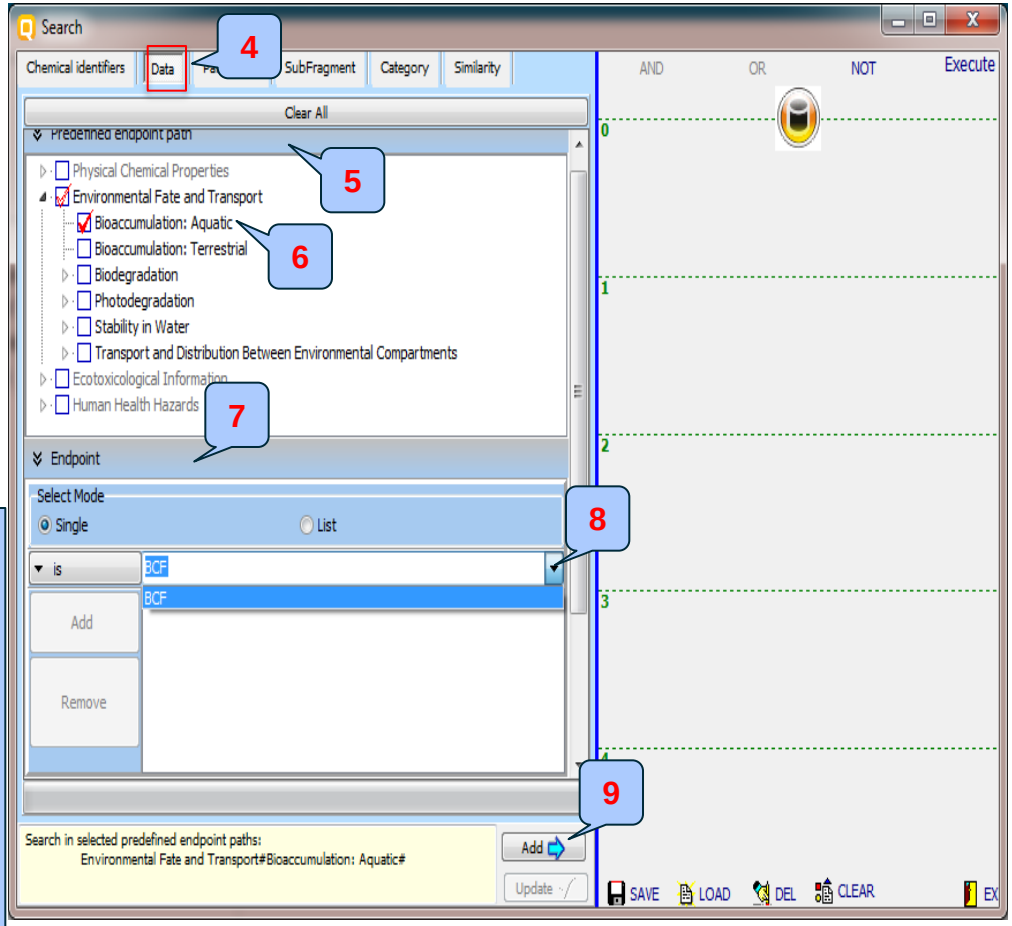
Sub fragment search for identifying chemicals

BCF and (Dmax)

Example 3

- Structures search criteria
  - Endpoint is BCF
  - 3D parameter – minimum value of Diameter maximum >15 Å





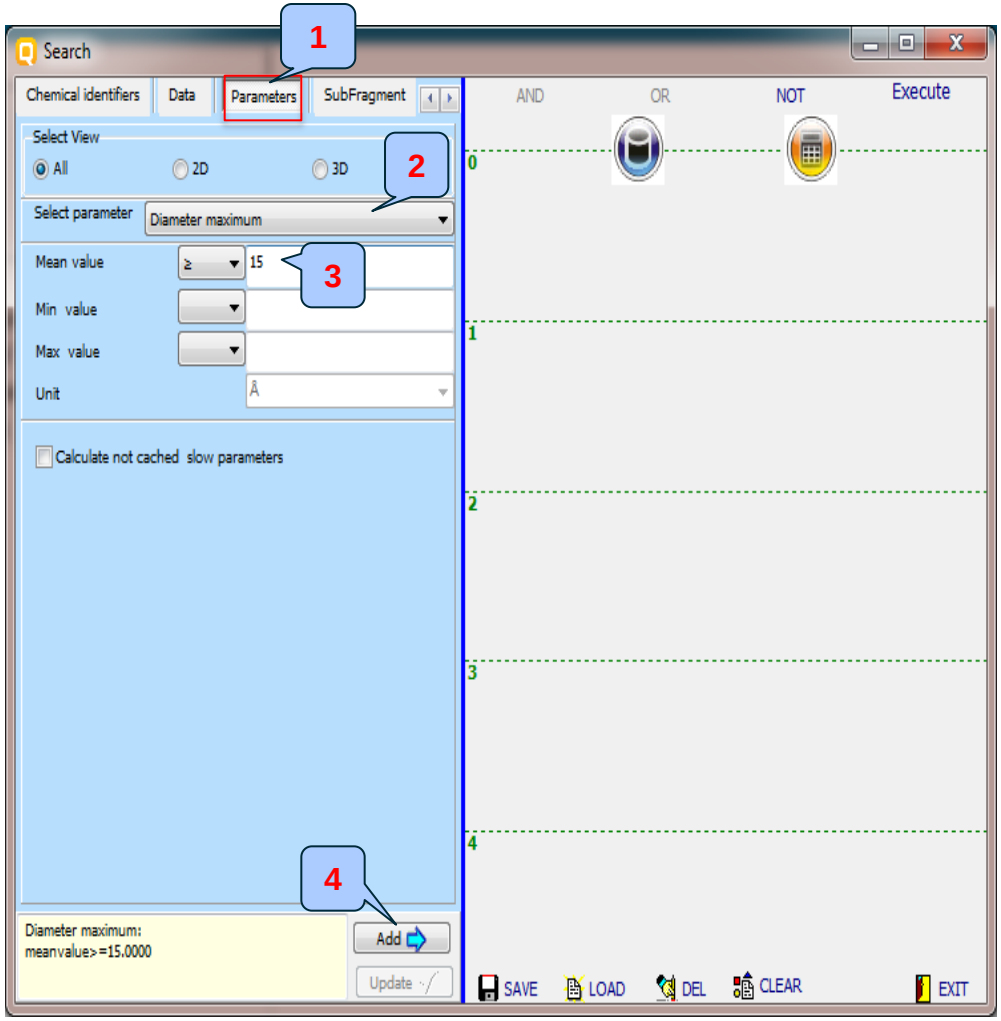
1. **Select** databases including BCF data (Bioaccumulation Canada; Bioaccumulation fish CEFIC LRI and Bioconcentration NITE). No inventory has been selected in this exercise
2. **Click** on Query button
3. **Select** Structures
4. **Go** to Data panel
5. **Click on** Predefined endpoint path in order to expand it
6. **Select** Bioaccumulation: Aquatic
7. **Click** Endpoint tab in order to expand it
8. **Select** BCF from the appeared popup menu
9. **Click** Add button

Sub fragment search for identifying chemicals

BCF and (Dmax)

Example 3

- Structures search criteria
  - Endpoint is BCF
  - 3D parameter – minimum value of Diameter maximum >15 Å



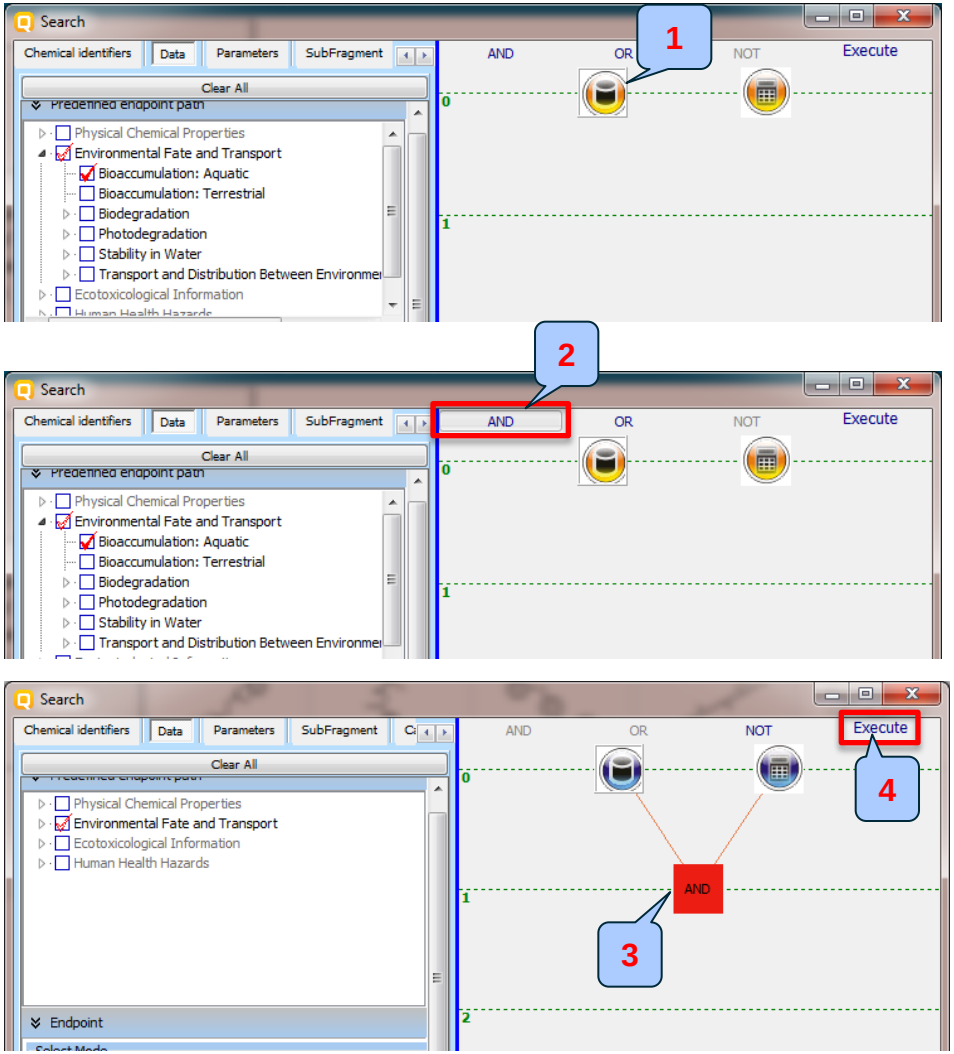
1. **Open** Parameters panel
2. **Select** Diameter maximum from the po-up list
3. **Specify qualifier "≥"** 15 in the Mean value field
4. **Click** Add button

Sub fragment search for identifying chemicals

BCF and (Dmax)

Example 3

- Structures search criteria
  - Endpoint is BCF
  - 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

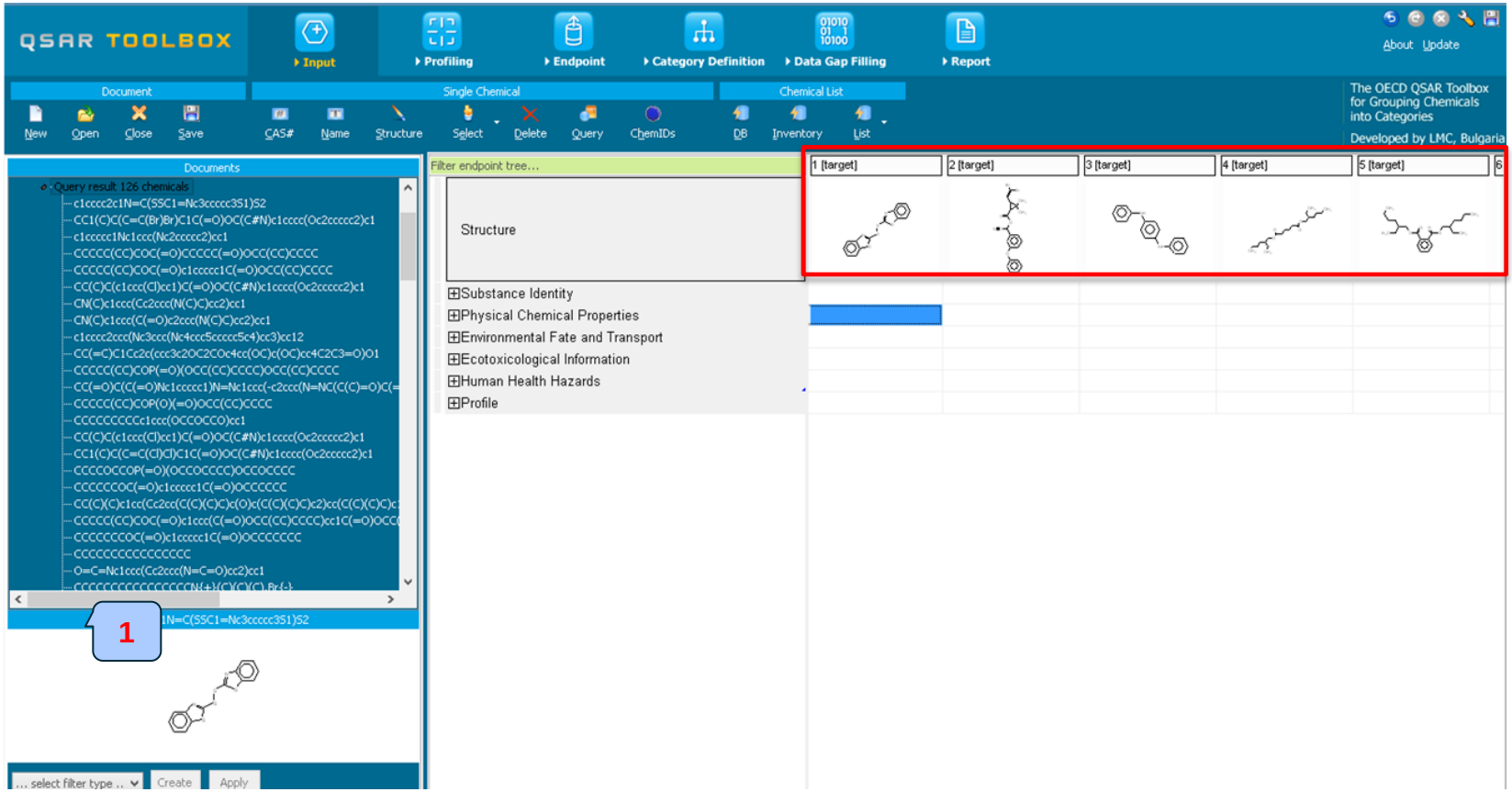
Not selected query

2. When the both queries are selected, **click** AND button
3. The two queries are combined by logical AND
4. **Execute** the AND query

Sub fragment search for identifying chemicals

BCF and (Dmax)

Example 3

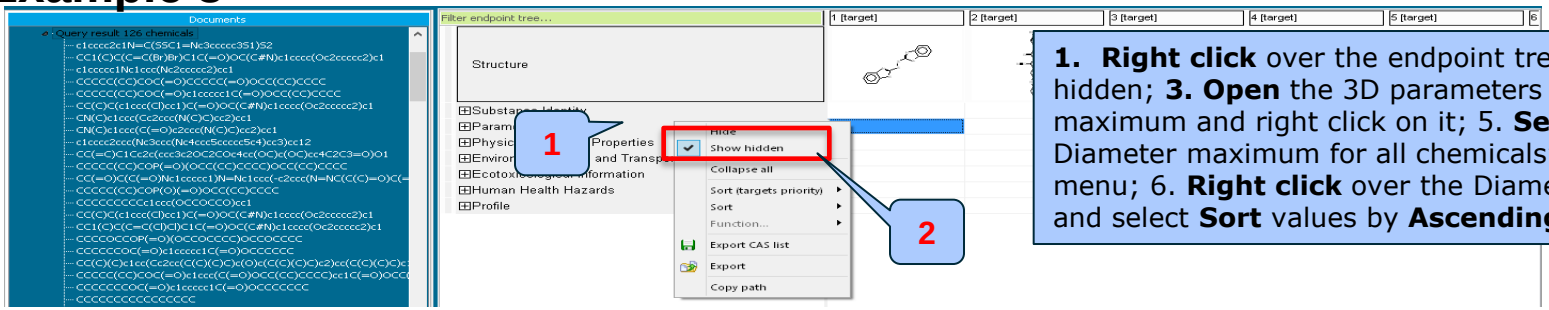


The Query tool (QT) identified 127 chemicals matching the desired criteria. The list of identified chemicals appear automatically on data matrix. Number of found chemicals is marked in the name of the document (1). In order to check the correctness of the performed query search, the user should calculate 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

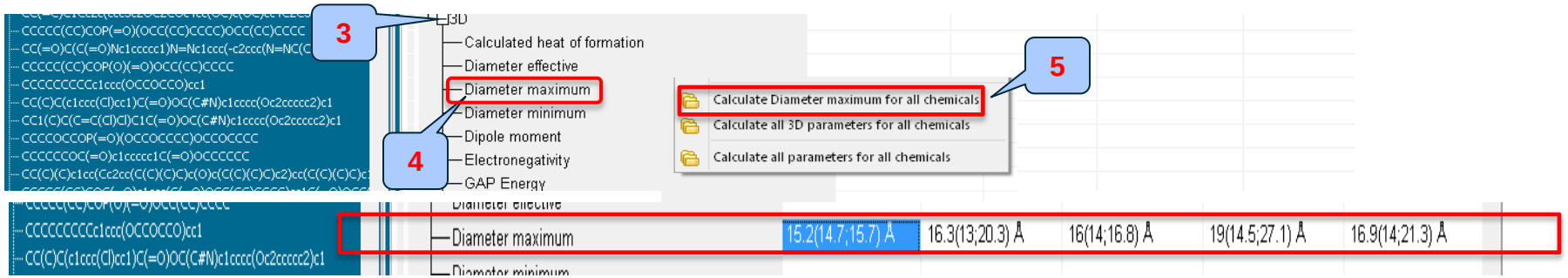
Sub fragment search for identifying chemicals

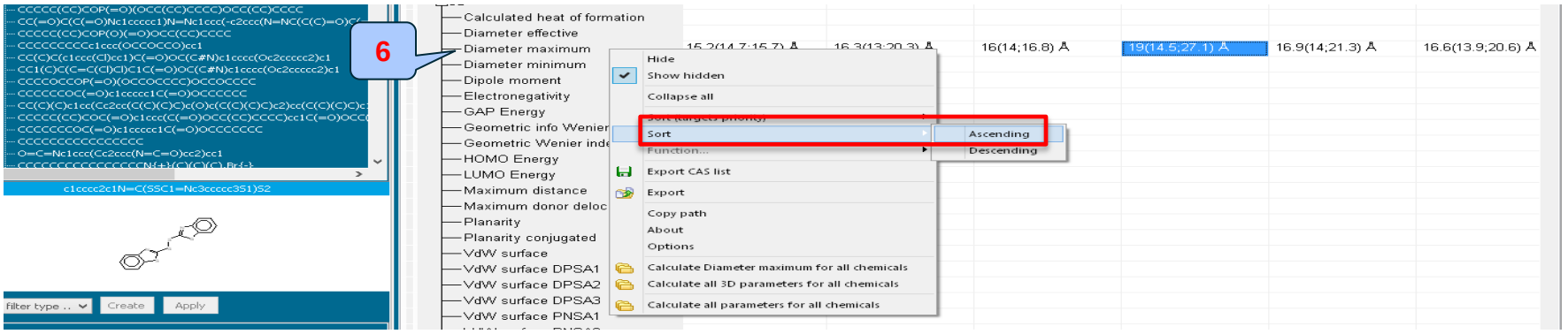
BCF and (Dmax)

Example 3



1. Right click over the endpoint tree; 2. **Select** Show hidden; **3. Open** the 3D parameters **4. Find** Diameter maximum and right click on it; 5. **Select** "Calculate Diameter maximum for all chemicals" from the appeared menu; 6. **Right click** over the Diameter maximum row and select **Sort** values by **Ascending** order.

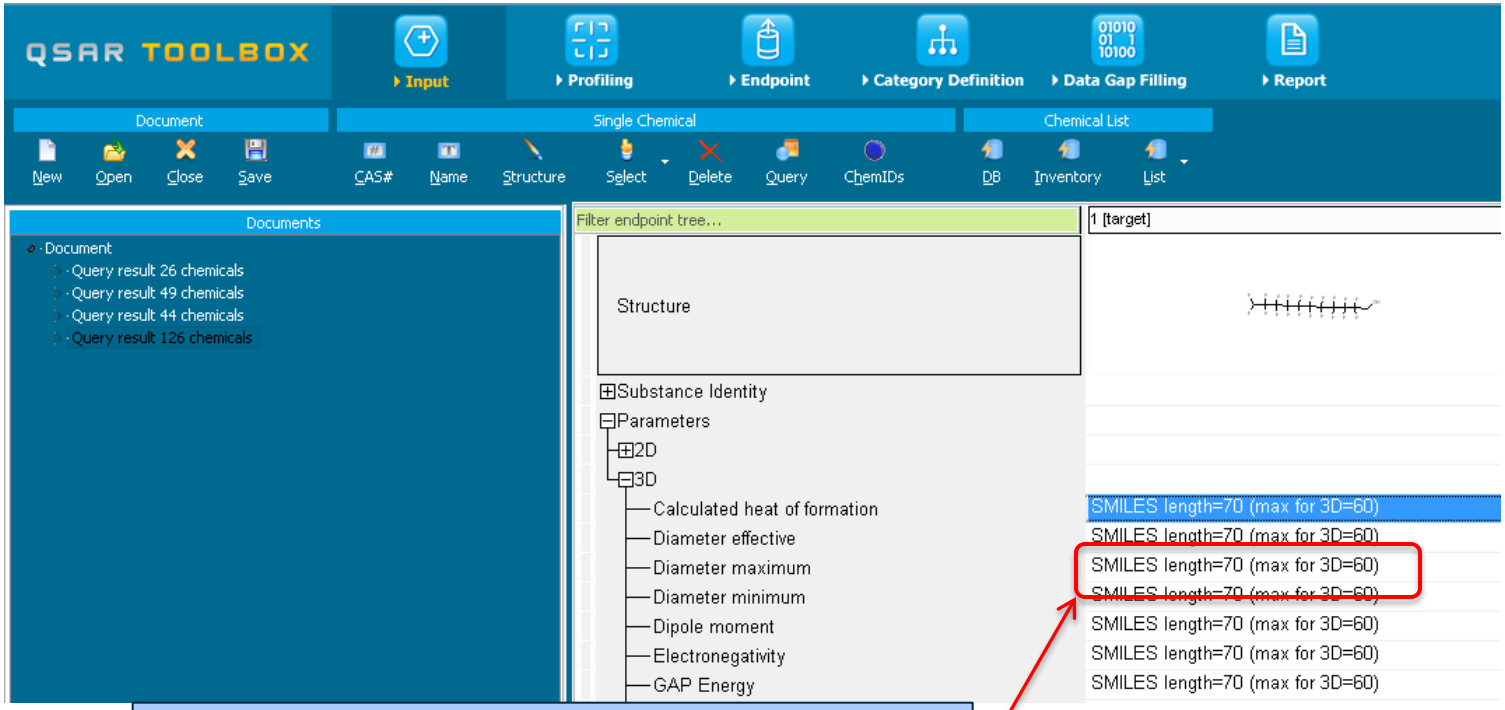




Sub fragment search for identifying chemicals

BCF and (Dmax)

Example 3



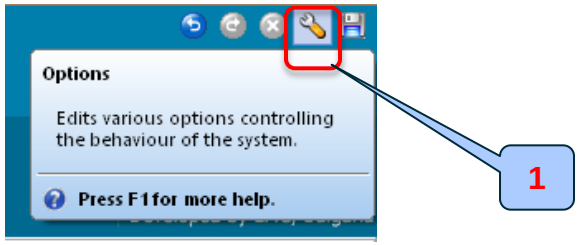
The following message could be displayed if the SMILES of a chemical has length higher than 60 symbols. This could be resolved by changing the Calculation options (see next slide)

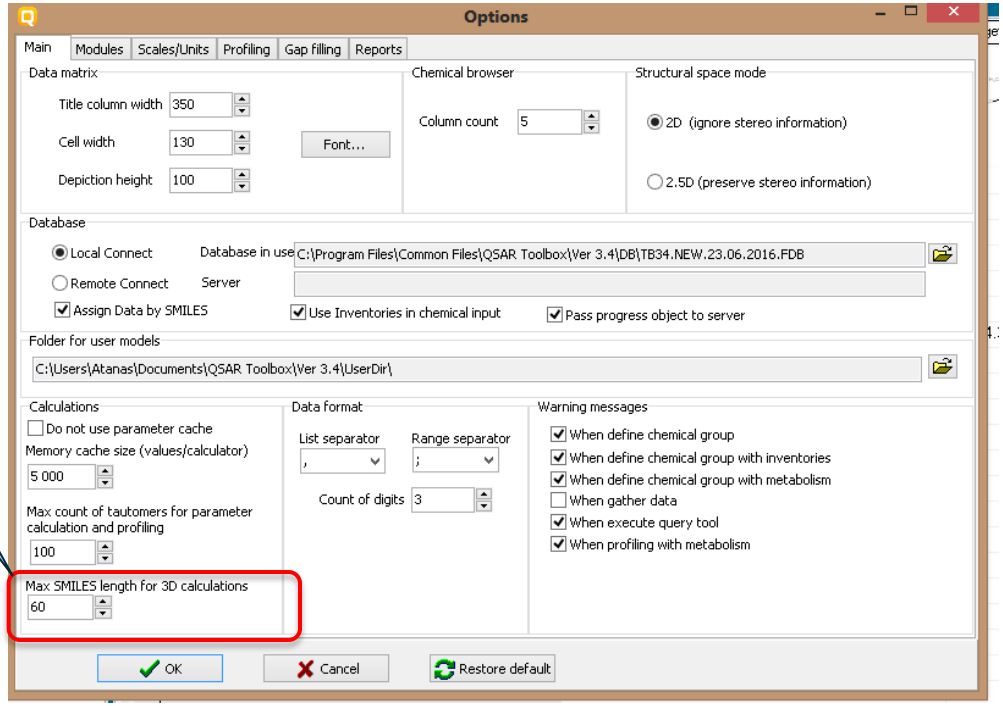
Sub fragment search for identifying chemicals

BCF and (Dmax)

Example 3

1. Press **Options** button.



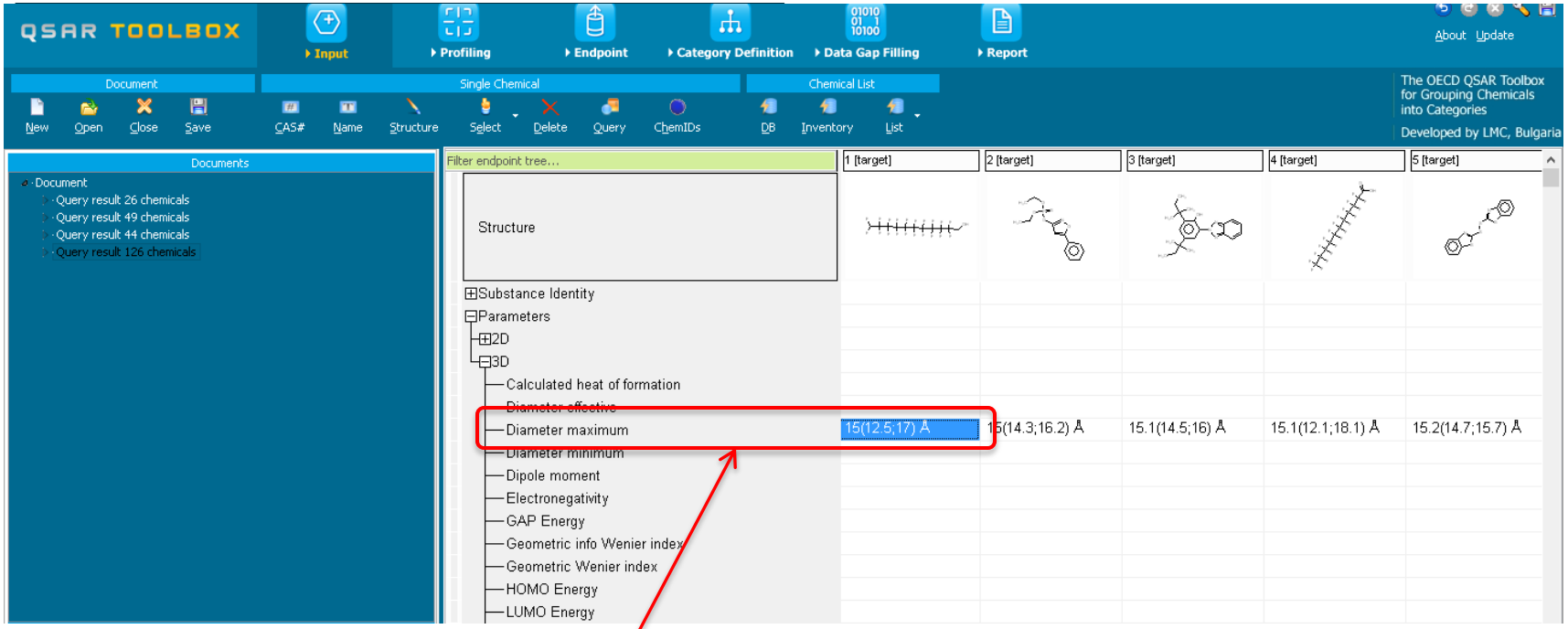


2. Change the **max SMILES length for 3D calculations** from 60 to 100.

Sub fragment search for identifying chemicals

BCF and (Dmax)

Example 3

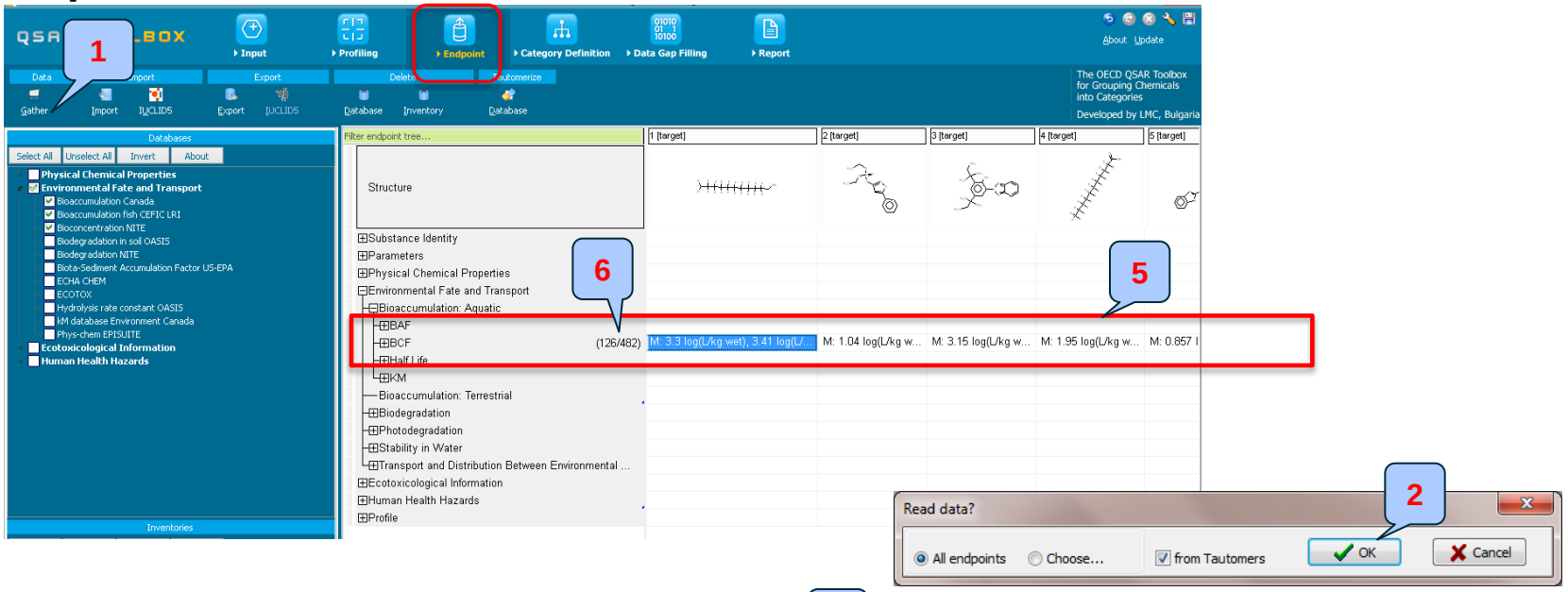


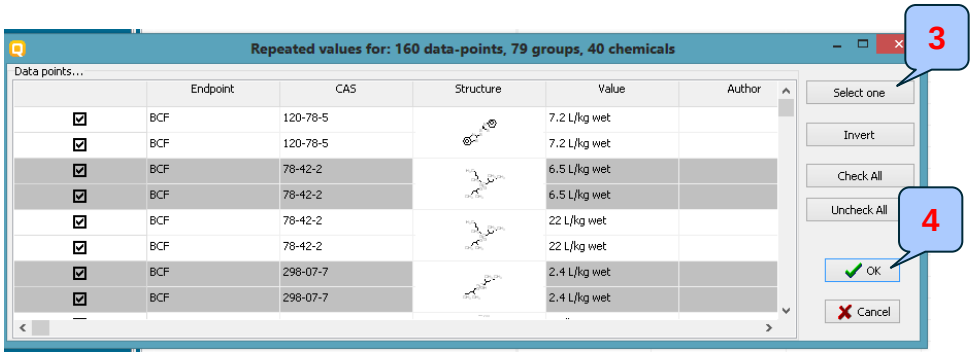
Recalculate **the diameter maximum** as done in the previous slides.

Sub fragment search for identifying chemicals

BCF and (Dmax)

Example 3





1. Databases are already selected, **Click** gather data
2. **Click** OK
3. **Click** Select one
4. **Click** OK
5. Data appear on data matrix
6. All 127 chemicals have BCF data

Sub fragment search for identifying chemicals

LC 50 and predefined category (Aldehydes)

Example 4

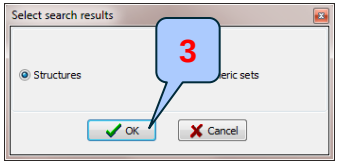
- Structures search criteria
  - Endpoint: LC 50 <1 mg/l
  - Fish: *P.promelas*
  - Effect: *Mortality*
  - Predefined category: *aldehydes*

Sub fragment search for identifying chemicals

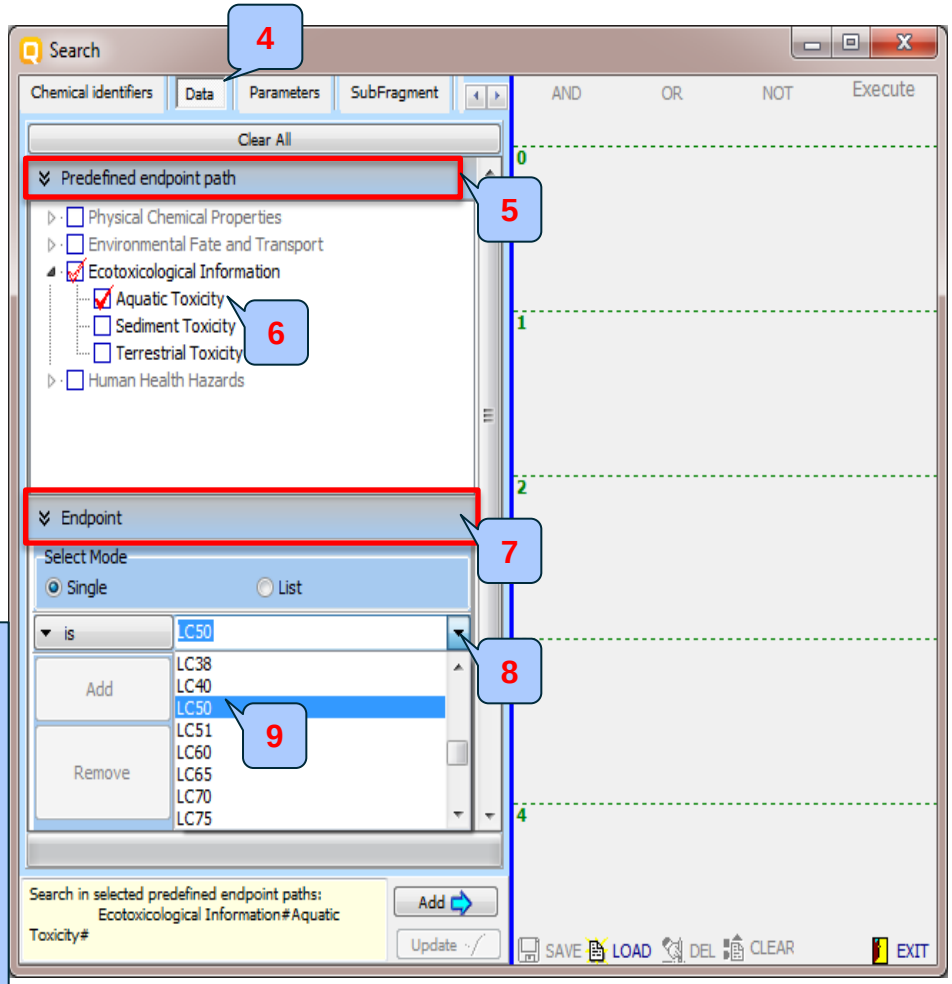
LC 50 and predefined category (Aldehydes)

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** on Query tool button
3. **Select** Structures
4. **Go** to Data panel
5. **Open** Predefined endpoint path in order to expand it
6. **Open** Ecotoxicological Information and **select** Aquatic Toxicity
7. **Open** Endpoint tab
8. **Open** pop-up menu
9. **Select** LC50



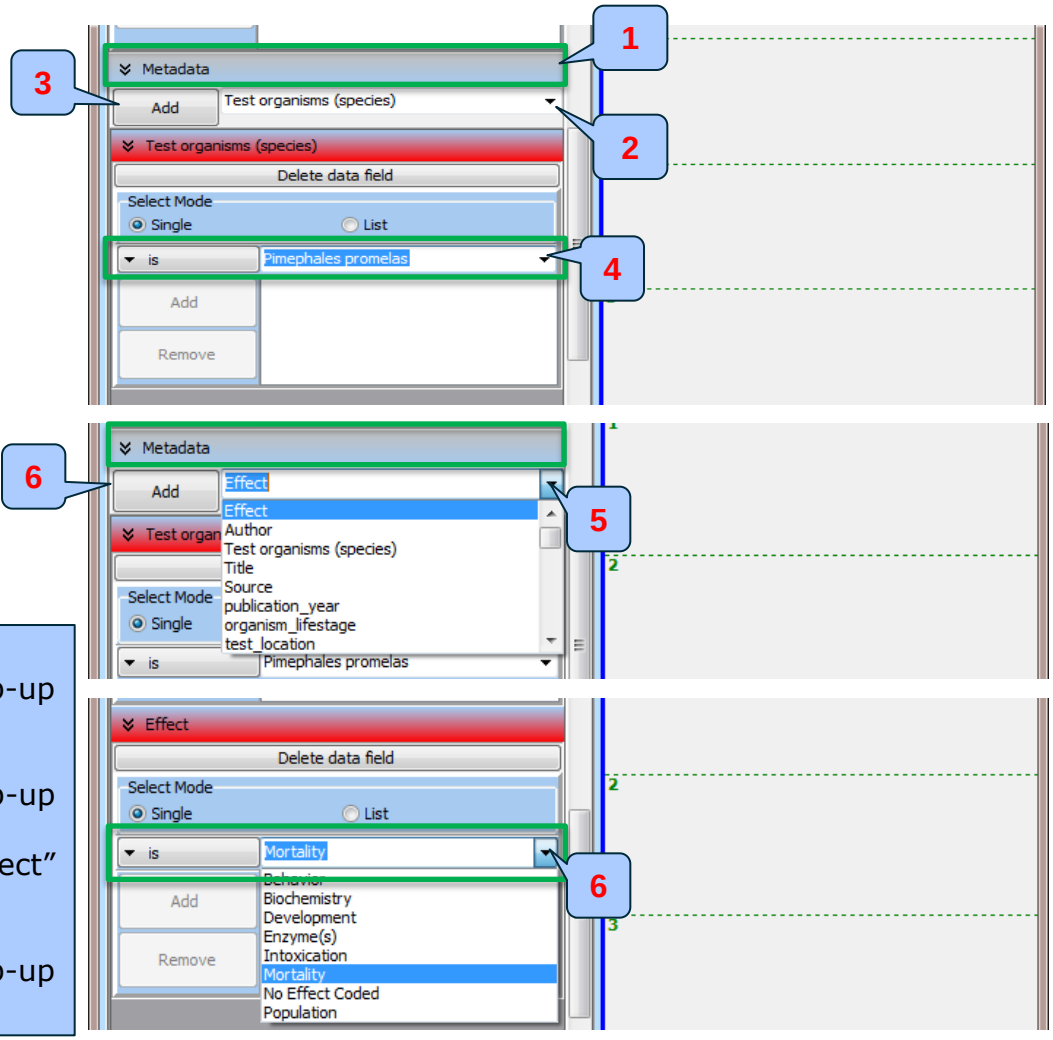
Continued on next slide

Sub fragment 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*



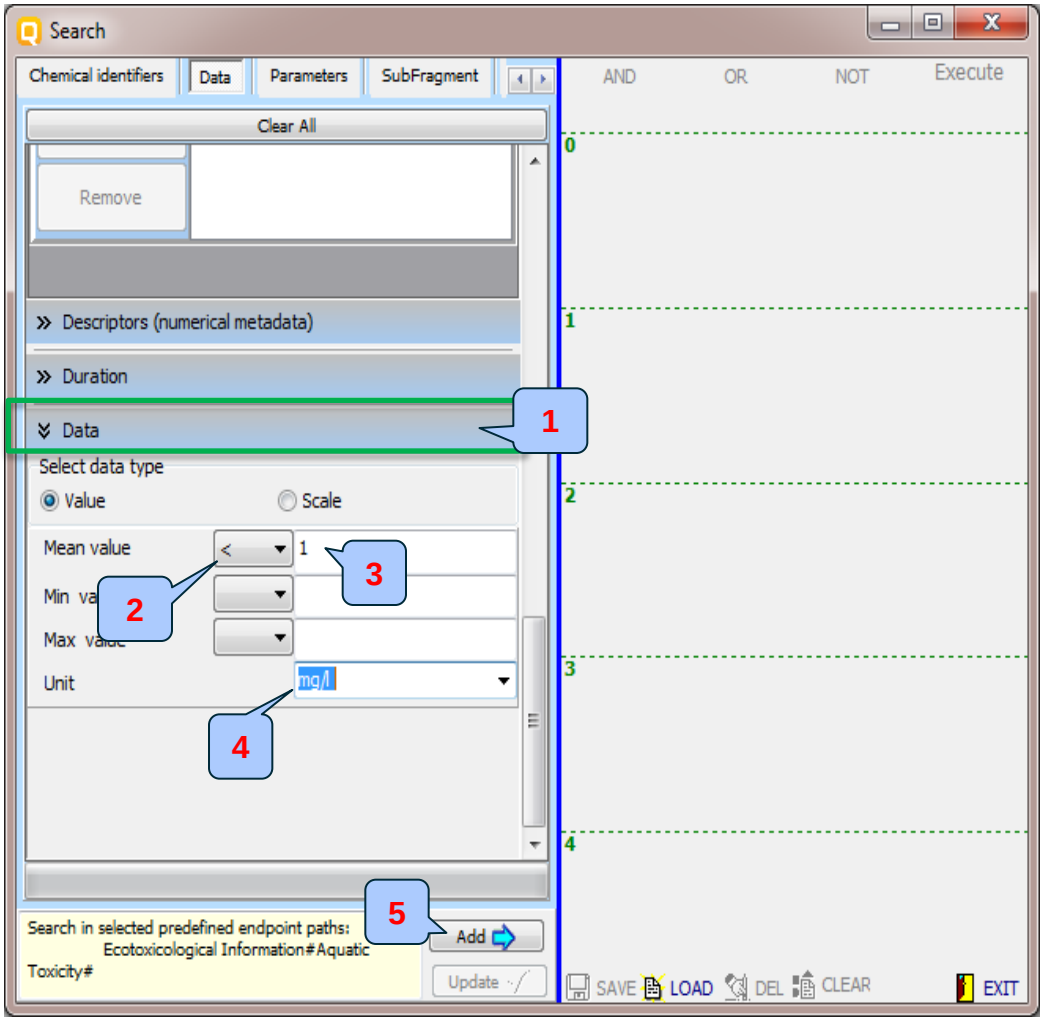
1. **Open** Metadata field
2. **Select** "Test organism (species)" from pop-up menu
3. **Click** Add
4. **Select** *Pimephales promelas* from pop-up menu
5. **Go back** to Metadata field and select "Effect" from the pop-up menu
6. **Click** Add
7. **Select** Mortality from the appeared pop-up menu

Sub fragment 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*



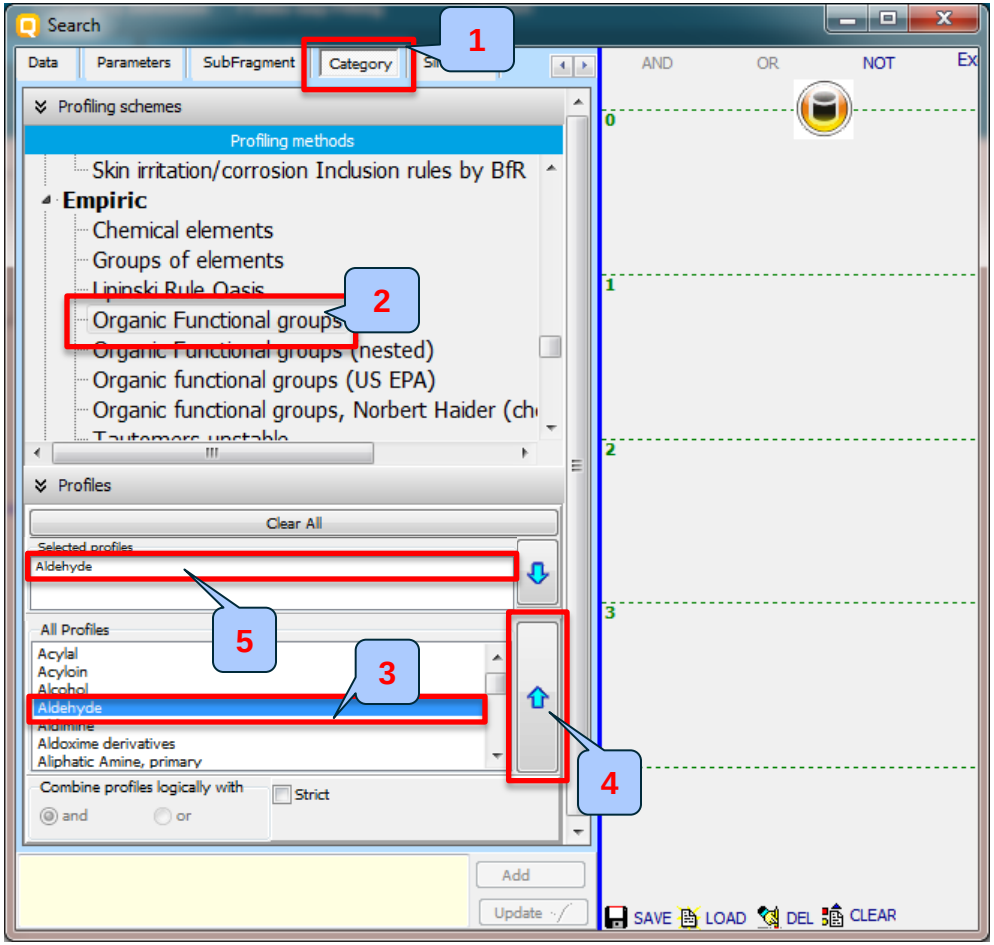
1. **Open** Data panel
2. **Open** qualifiers from Mean value and select <
3. **Type** 1 in the blank field
4. **Select** mg/l from the list with units
5. **Click** Add

Sub fragment 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*



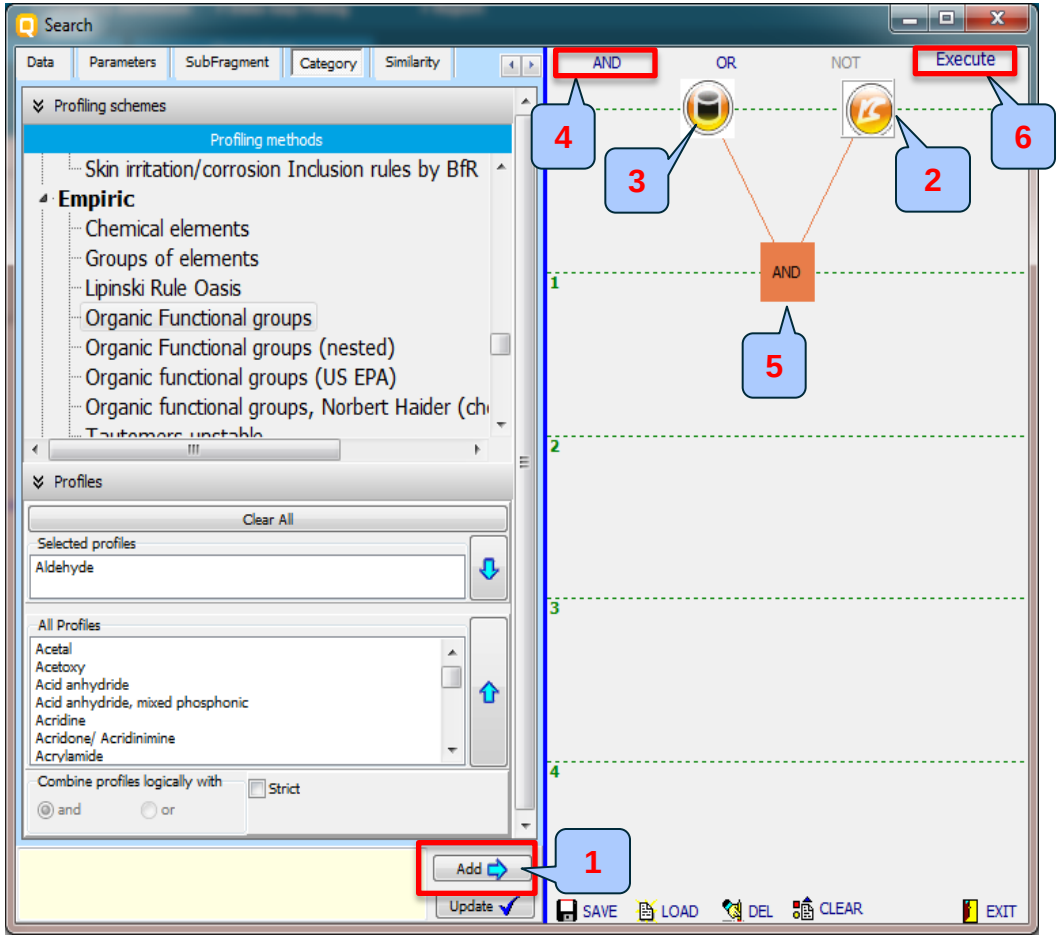
1. **Open** Category panel
2. **Find** Organic functional groups profiler from the list with profilers
3. **Find** Aldehyde
4. **Move** the selected category from panel "All profilers" to the panel "Selected profiles"
5. The selected category appears in the panel "Selected profiles"

Sub fragment 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 # 44

3. Right click over first query to select it (slide # 42)

4. Click AND button

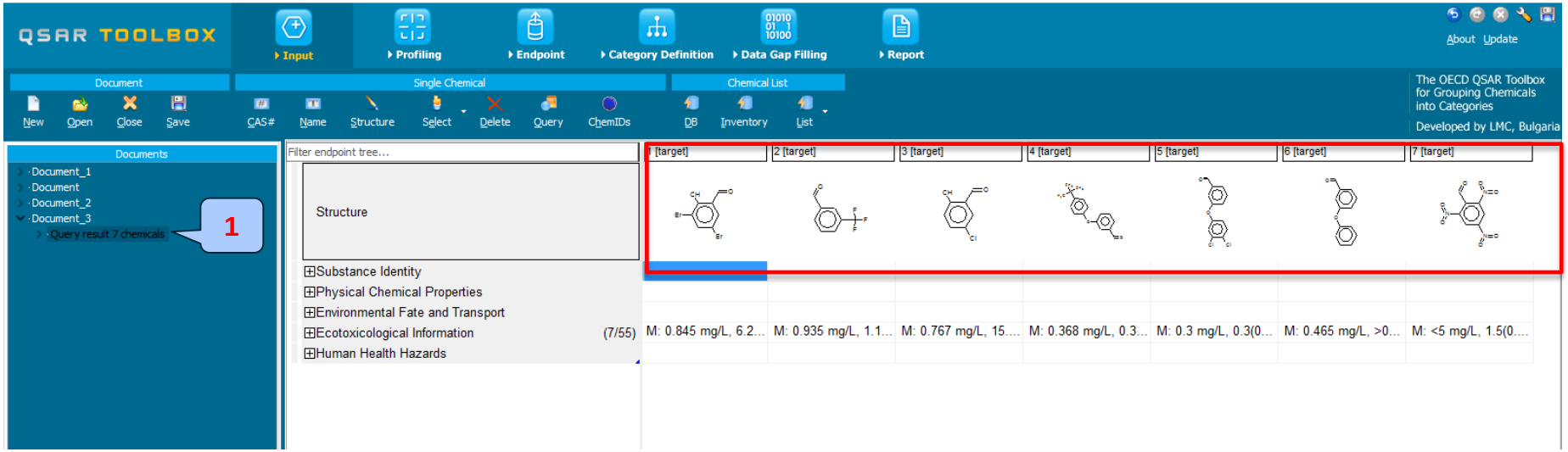
5. The two queries are combined by logical AND

6. Click Execute button in order to execute the query

Sub fragment search for identifying chemicals

LC 50 and predefined category (Aldehydes)

Example 4

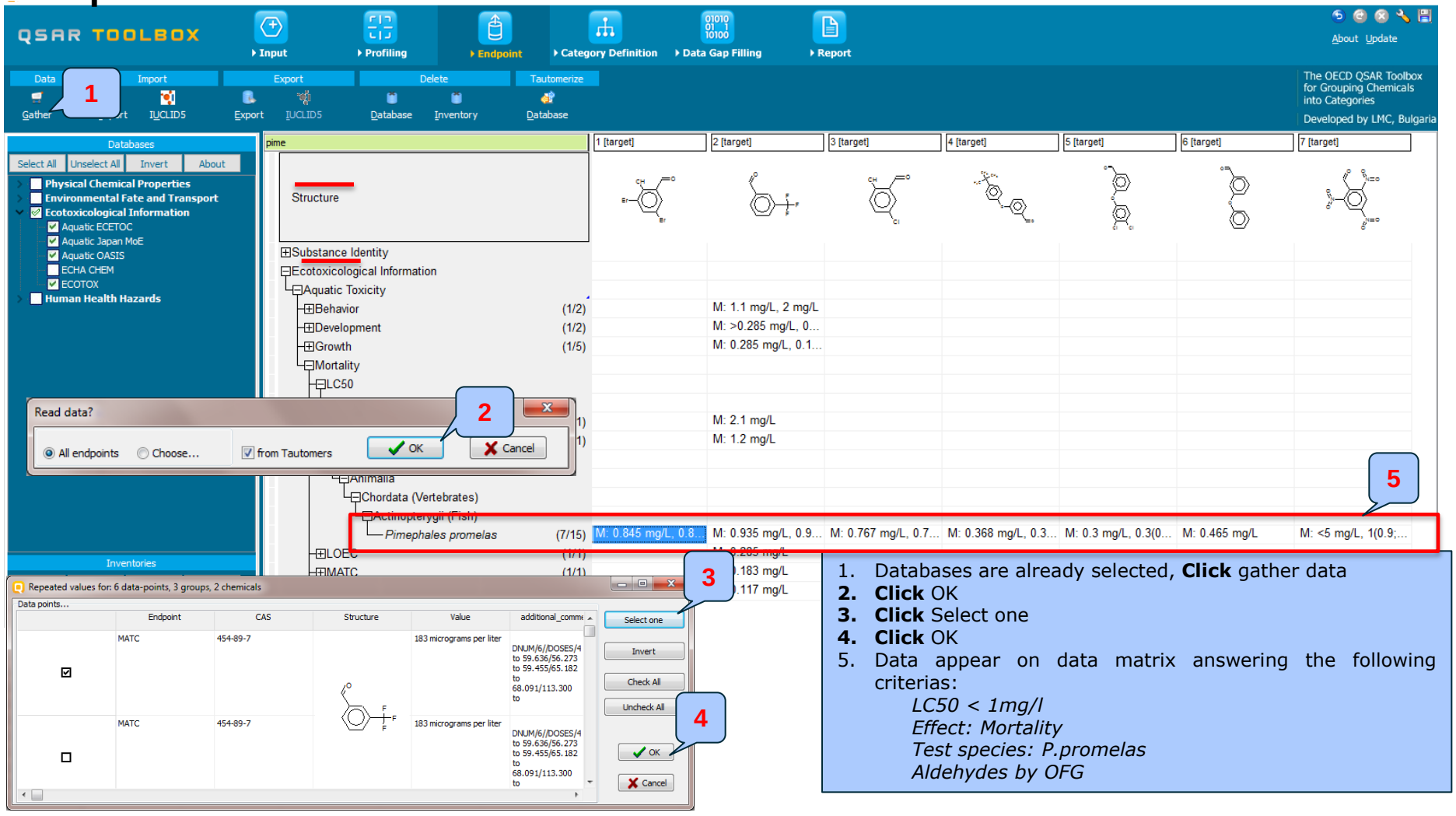


The Query tool (QT) identified 7 chemicals matching the desired criteria. The list of identified chemicals appear automatically on the data matrix. Number of found chemicals is marked in the name of the document (1). In order to check the correctness of the performed query search the user should gather ecotox data and profile according to OFG Profiler. The last two steps are presented on the next two slides

Sub fragment search for identifying chemicals

LC 50 and predefined category (Aldehydes)

Example 4

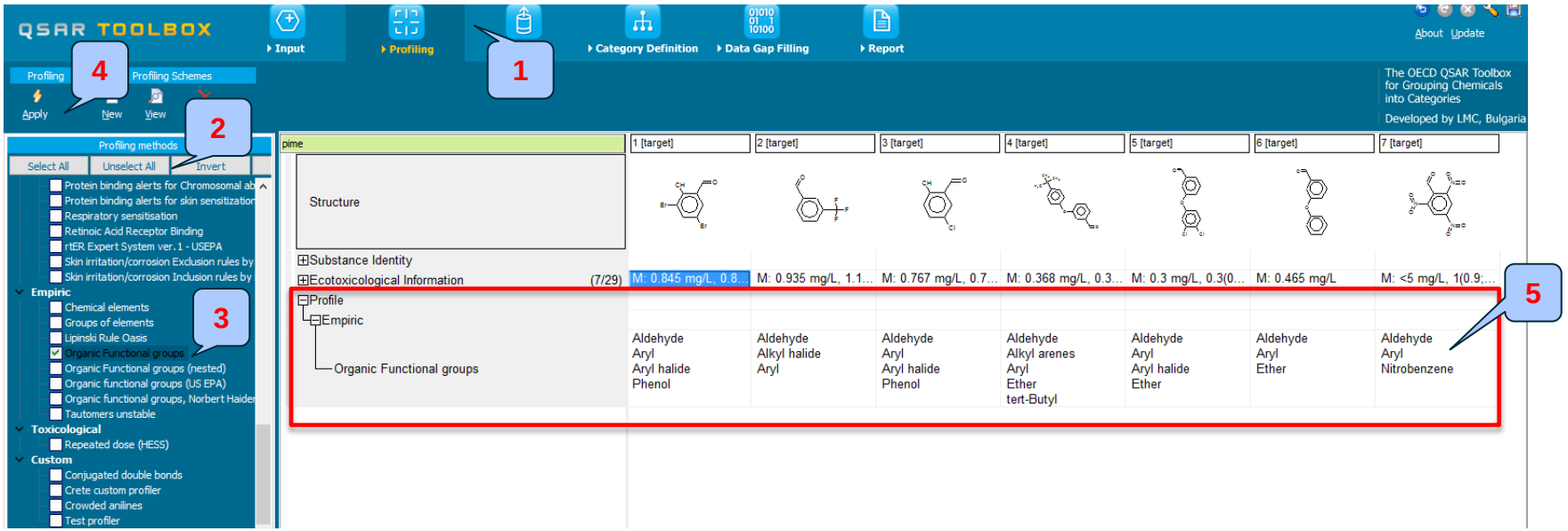


1. Databases are already selected, **Click** gather data
2. **Click** OK
3. **Click** Select one
4. **Click** OK
5. Data appear on data matrix answering the following criterias:
   - *LC50 < 1mg/l*
   - *Effect: Mortality*
   - *Test species: P.promelas*
   - *Aldehydes by OFG*

Sub fragment search for identifying chemicals

LC 50 and predefined category (Aldehydes)

Example 4



1. **Go** to Profiling
2. **Unselect All**
3. **Select** Organic functional group
4. **Click** Apply
5. All7 chemicals have “Aldehyde” fragment within its structure

Sub fragment 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*

Sub fragment search for identifying chemicals

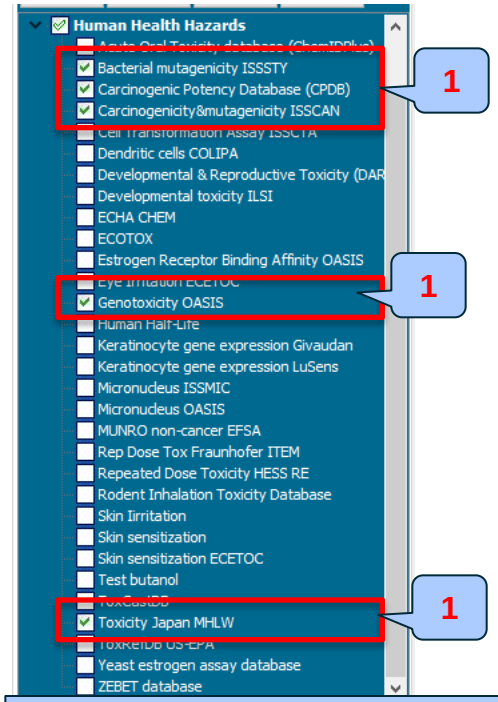
Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

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** on Query button
3. **Select** Structures

Sub fragment search for identifying chemicals

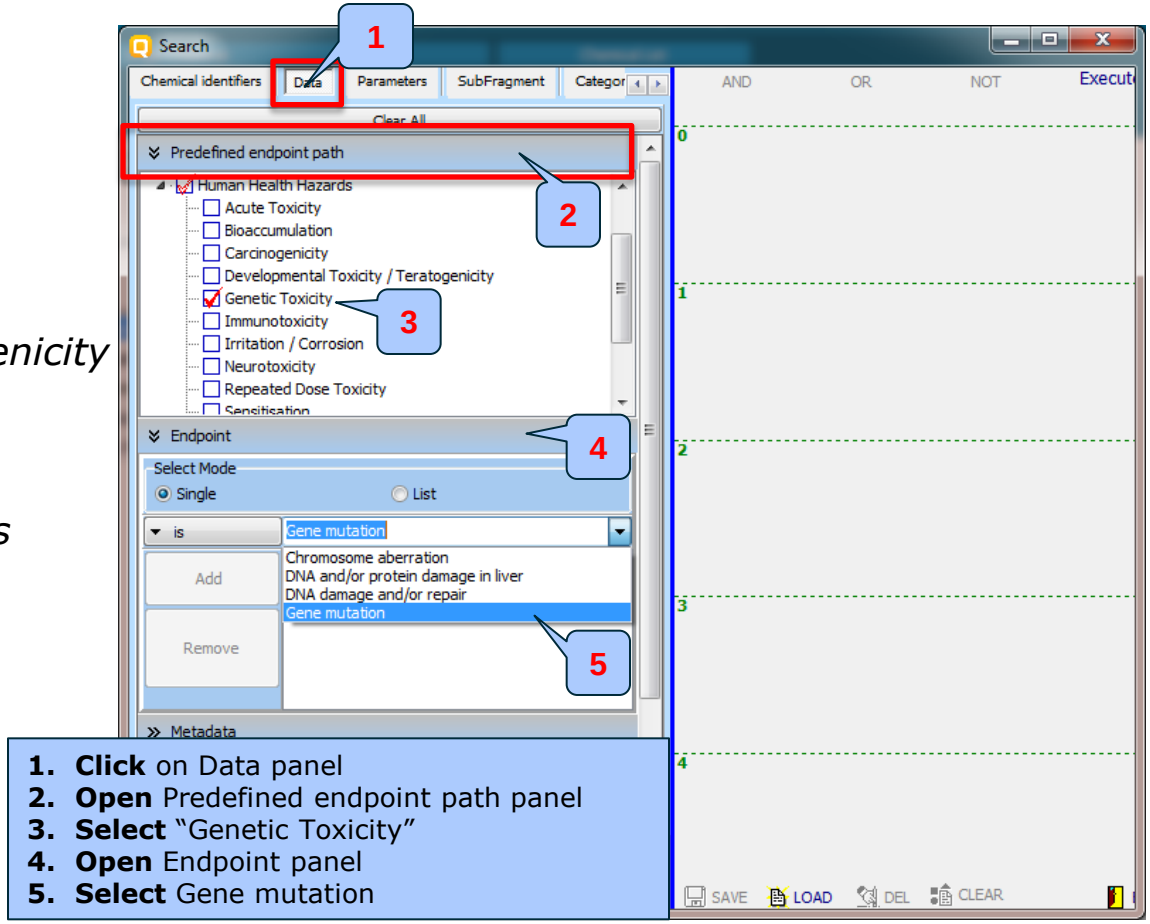
Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

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 Data panel
2. **Open** Predefined endpoint path panel
3. **Select** "Genetic Toxicity"
4. **Open** Endpoint panel
5. **Select** Gene mutation

Sub fragment search for identifying chemicals

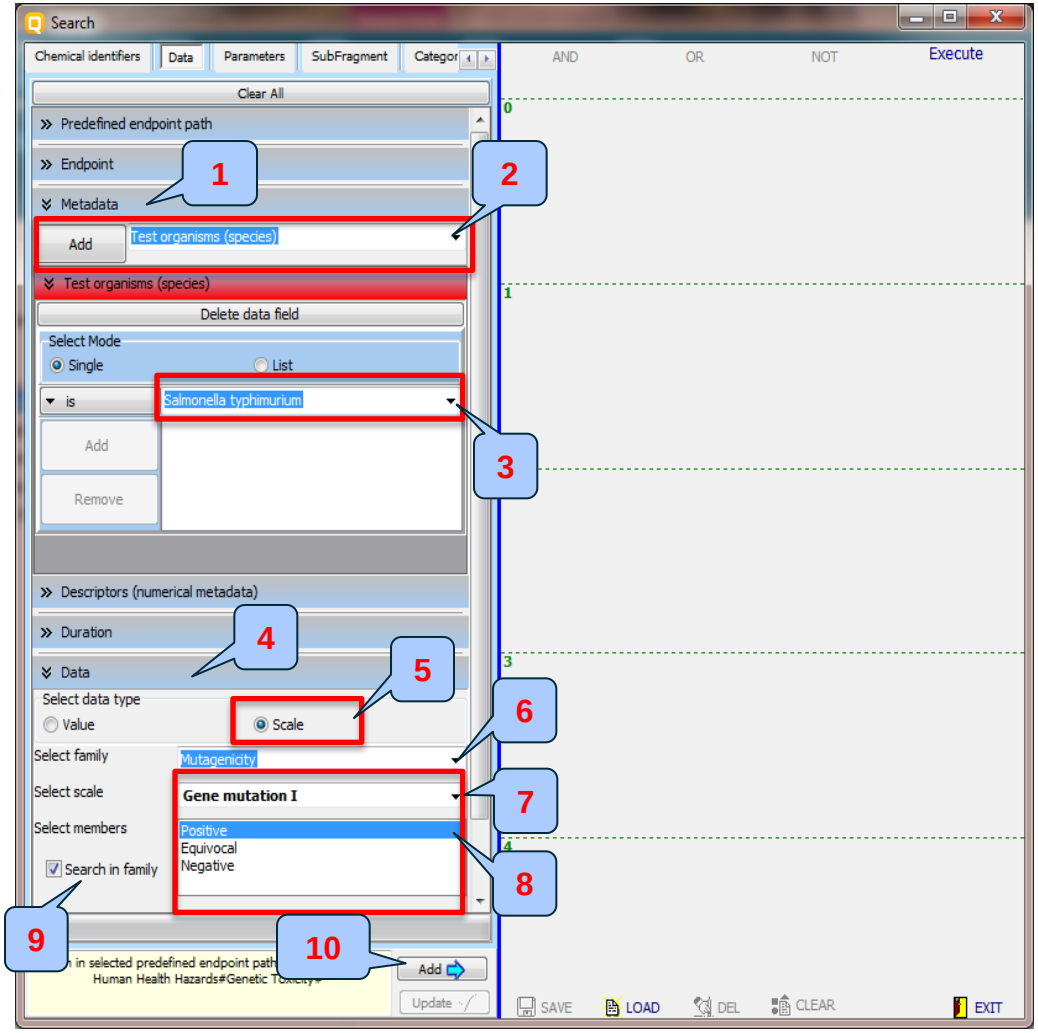
Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

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. **Open** Data panel
6. **Select** Scale radio button
7. **Select** Mutagenicity family
8. **Select** scale Gene mutation I
9. **Select** Positive from the list with scale members
10. Search in family* option is selected by default (remain it as it is)
11. **Click** Add button

- **Search in family** option allows to find data pertaining to different scales within one family (e.g. find positive data belonging to scale Gene mutation I and Chromosomal aberration I (OASIS) part of family Mutagenicity). The latter is possible due to the implemented scale conversions.



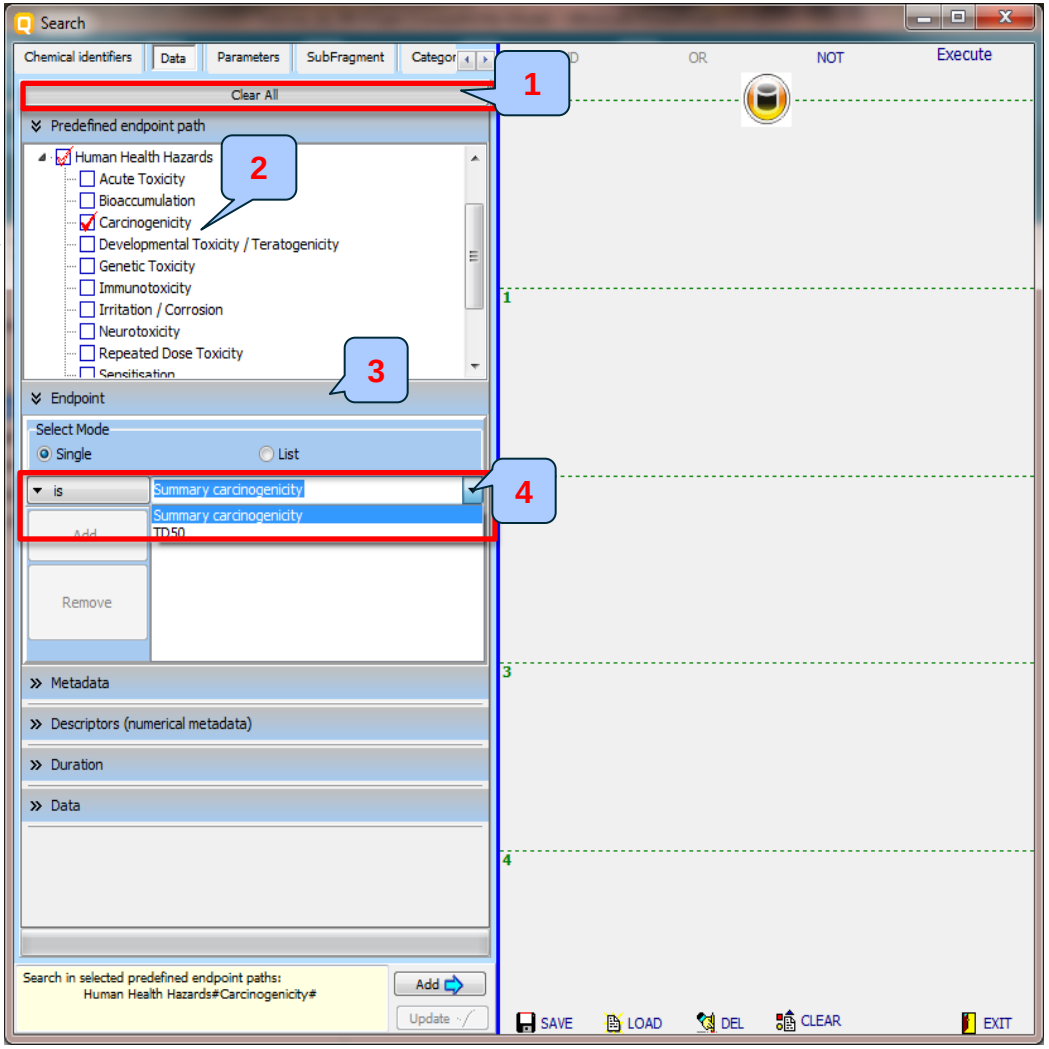
Sub fragment search for identifying chemicals

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** on Clear All button
2. **Open** Predefined endpoint path and select "Carcinogenicity" node
3. **Open** Endpoint tab
4. **Select** Summary carcinogenicity from the appeared pop-up list

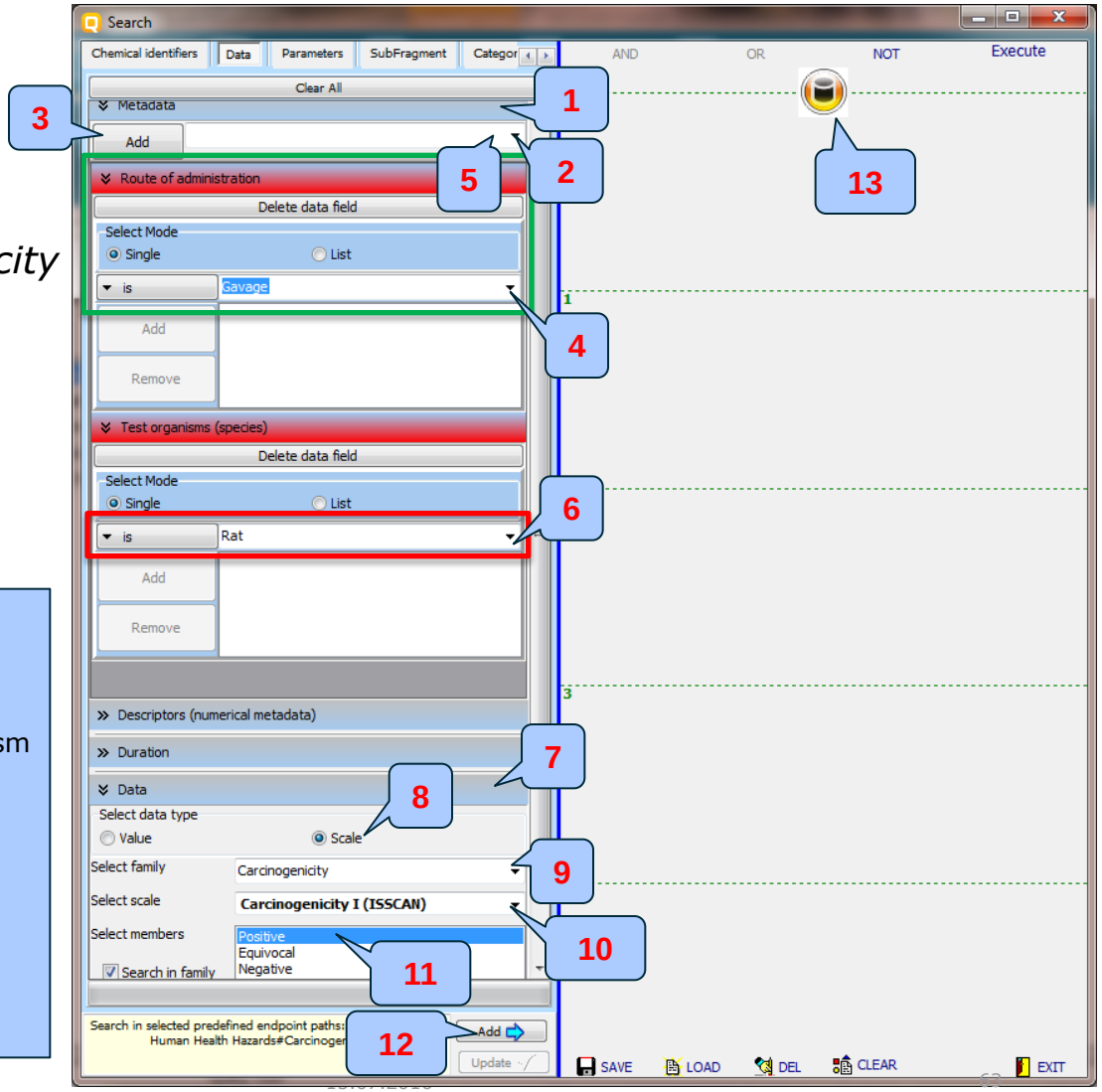


Sub fragment search for identifying chemicals

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*



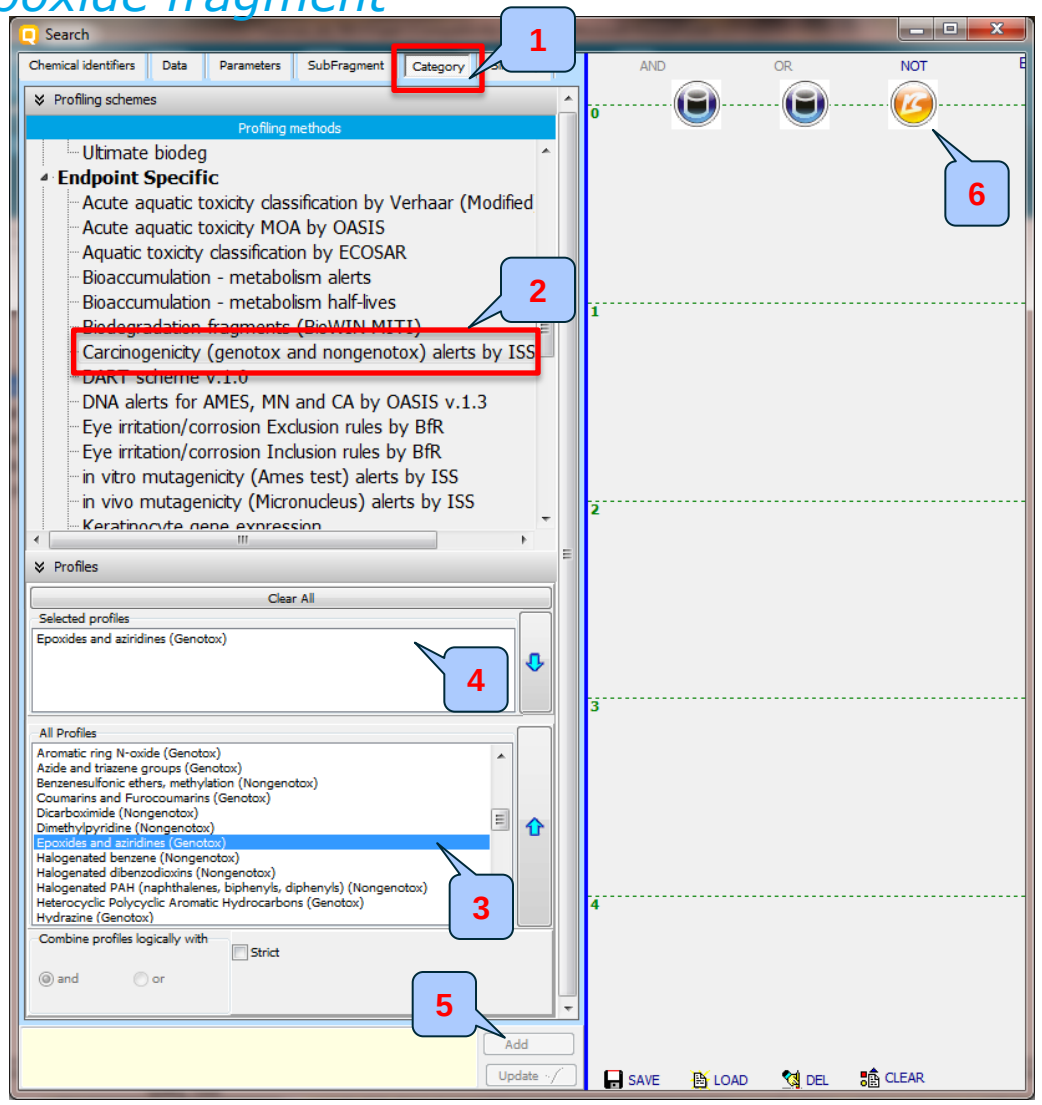
1. **Open** Metadata panel
2. **Select** Route of administration from pop-up menu
3. **Click** Add button
4. **Select** Gavage from the list
5. **Go back** to Metadata panel and select Test organism (species) from the pop-up menu. Click Add button
6. **Select** Rat from the list
7. **Open** Data panel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

Sub fragment 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*



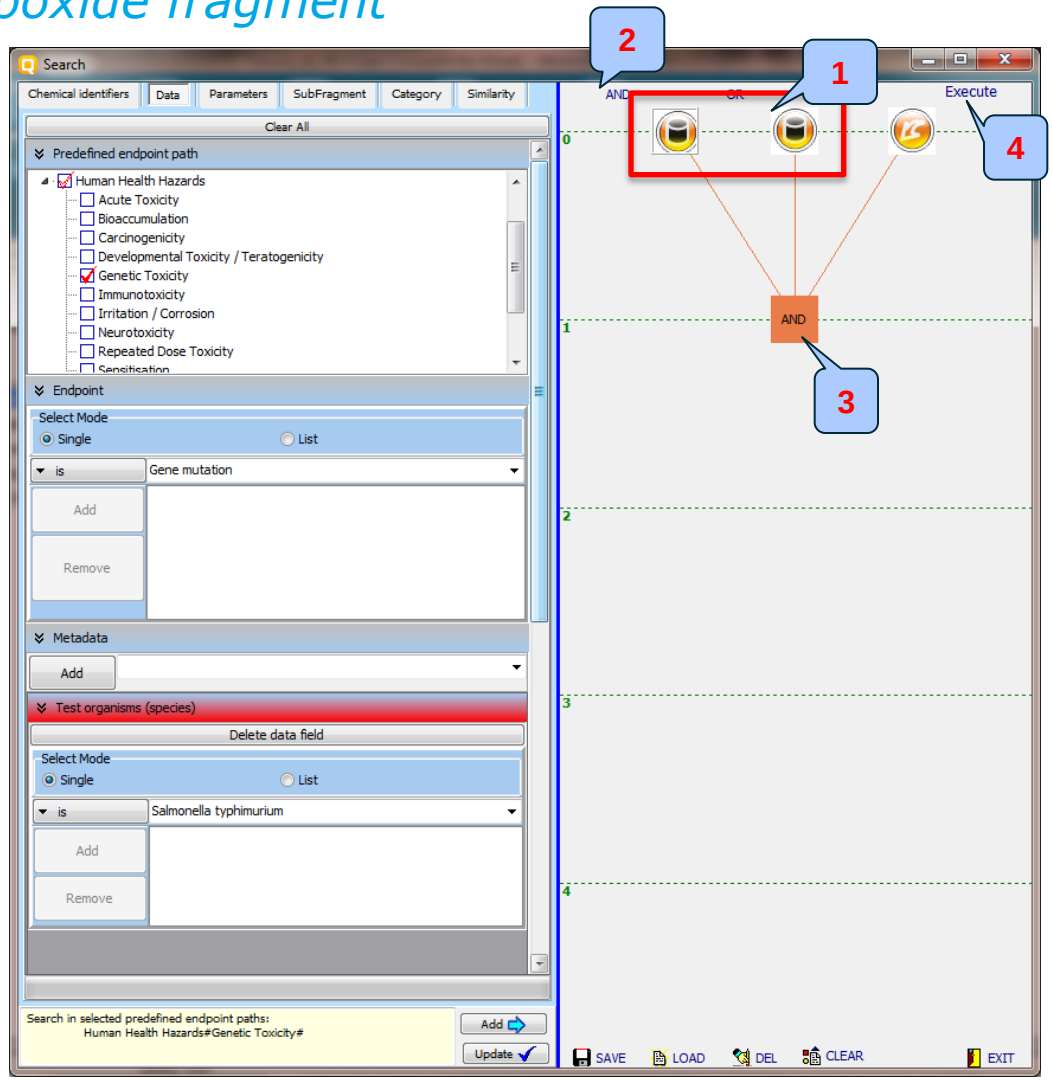
1. **Click** on Category panel
2. **Select** Carcinogenicity alerts by ISS
3. **Select** category Epoxides and aziridines (Genotox)
4. **Move** the selected category to the panel Selected profiles
5. **Click** Add button
6. The query appears on the logic panel

Sub fragment 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*

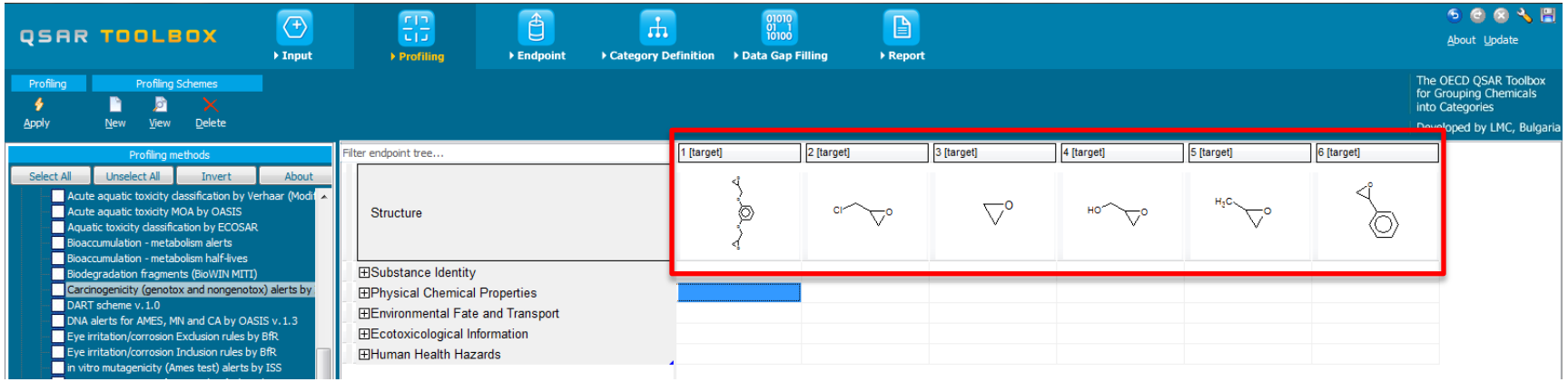


1. **Right click** over the first two queries (see slide # 42)
2. **Click** AND button
3. The three queries are combined by logical AND
4. **Click** on Execute button

Sub fragment search for identifying chemicals

Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

Example 5

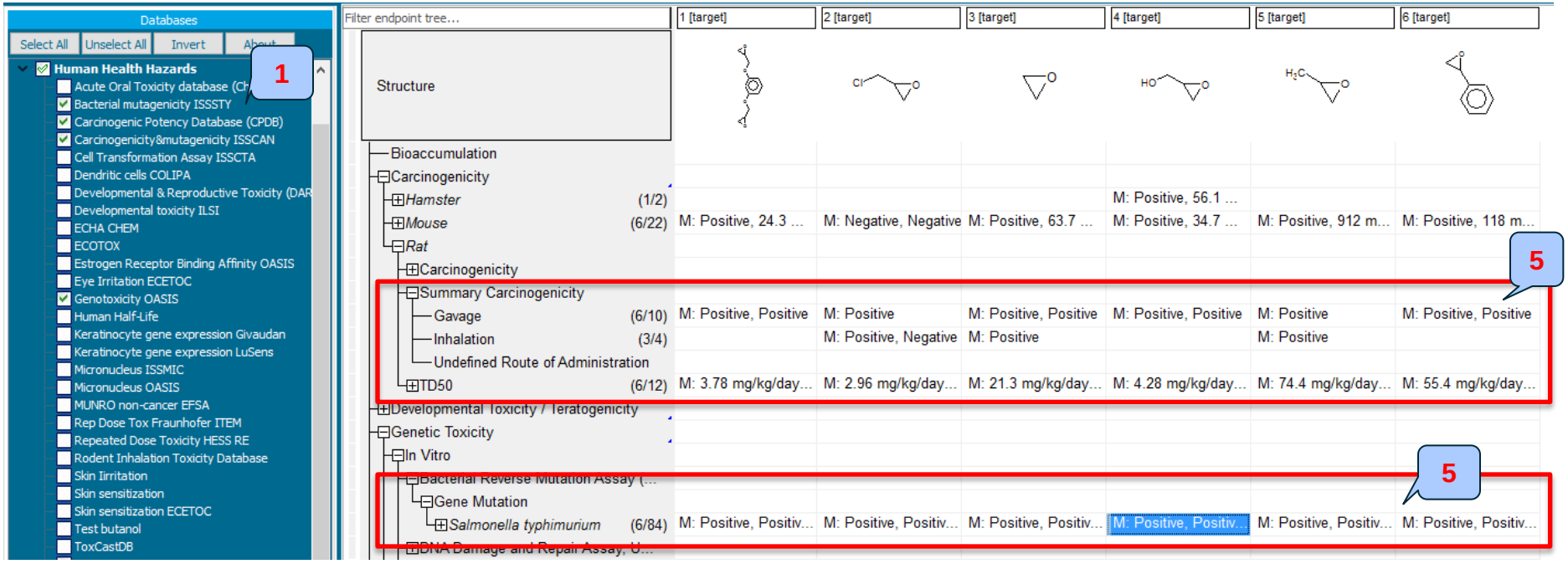


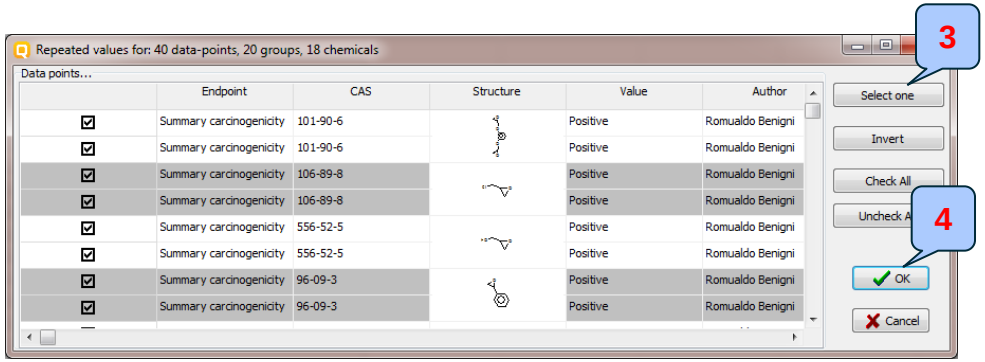
The Query tool (QT) identified 6 chemicals matching the desired criteria. In order to check the correctness of the query the user should gather experimental data for Ames and Carcinogenicity and profile the identified chemicals according to applied Carcinogenicity profiler. The last two steps are presented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

Sub fragment search for identifying chemicals

Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

Example 5



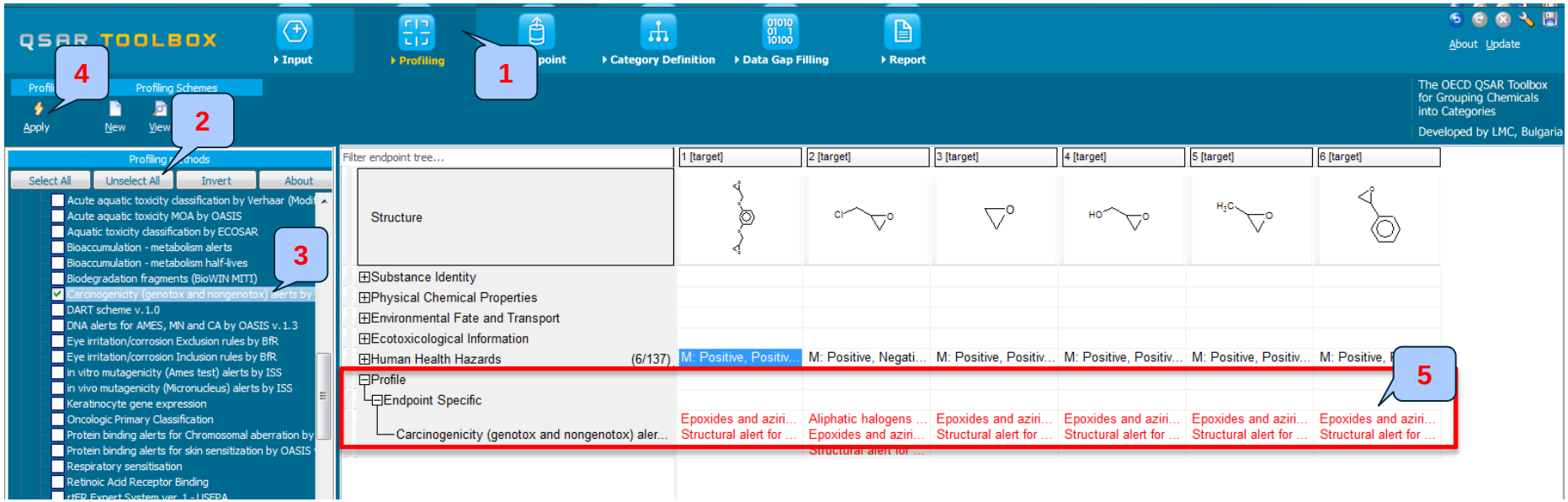


1. Databases are already selected, **Click** gather data
2. **Click** OK
3. **Click** Select one
4. **Click** OK
5. Data appear on data matrix answering the following criteria:
   Ames mutagenicity (S. thuphimurium): Positive
   Summary carcinogenicity (gavage, rat): Positive

Sub fragment search for identifying chemicals

Chemicals with Ames and Carcinogenicity positive data including Epoxide fragment

Example 5



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

Sub fragment search for identifying chemicals

Chemicals with Skin sensitization positive data including Aldehyde fragment

Example 6

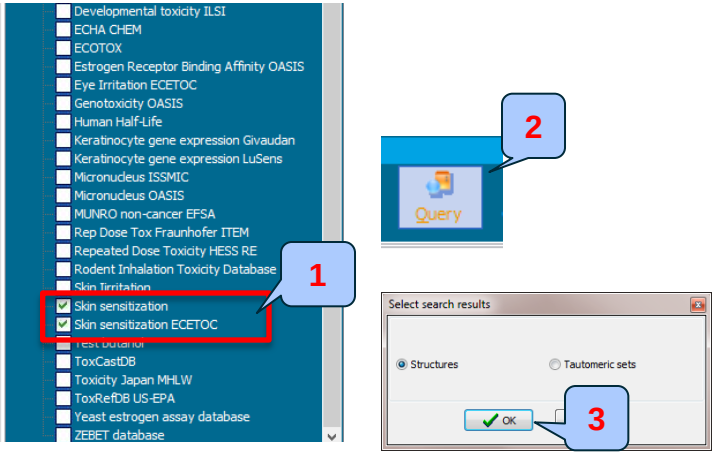
- Structures search criteria
  - Endpoint: *EC3*
  - Data: *Positive*
  - Predefined category: alpha, beta-unsaturated aldehydes

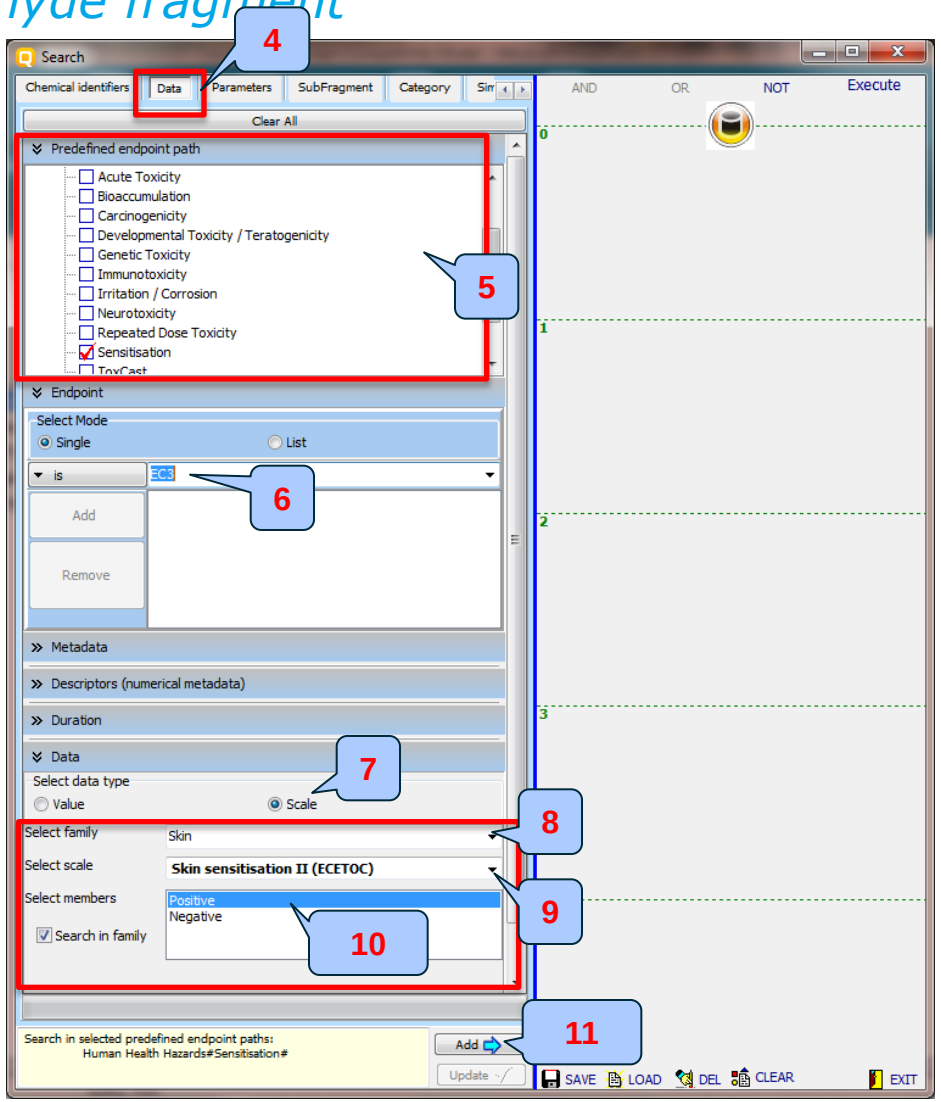
Sub fragment search for identifying chemicals

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** on Query tool button
3. **Select** Structures
4. **Click** on Data panel
5. **Open** Predefined endpoint path and **select** Sensitization
6. **Open** Endpoint panel and **select** EC3
7. **Open** Data panel and **Select** Scale
8. **Select** family Skin
9. **Scale** Skin sensitization II (ECETOC)
10. **Select** Positive
11. **Click** Add button

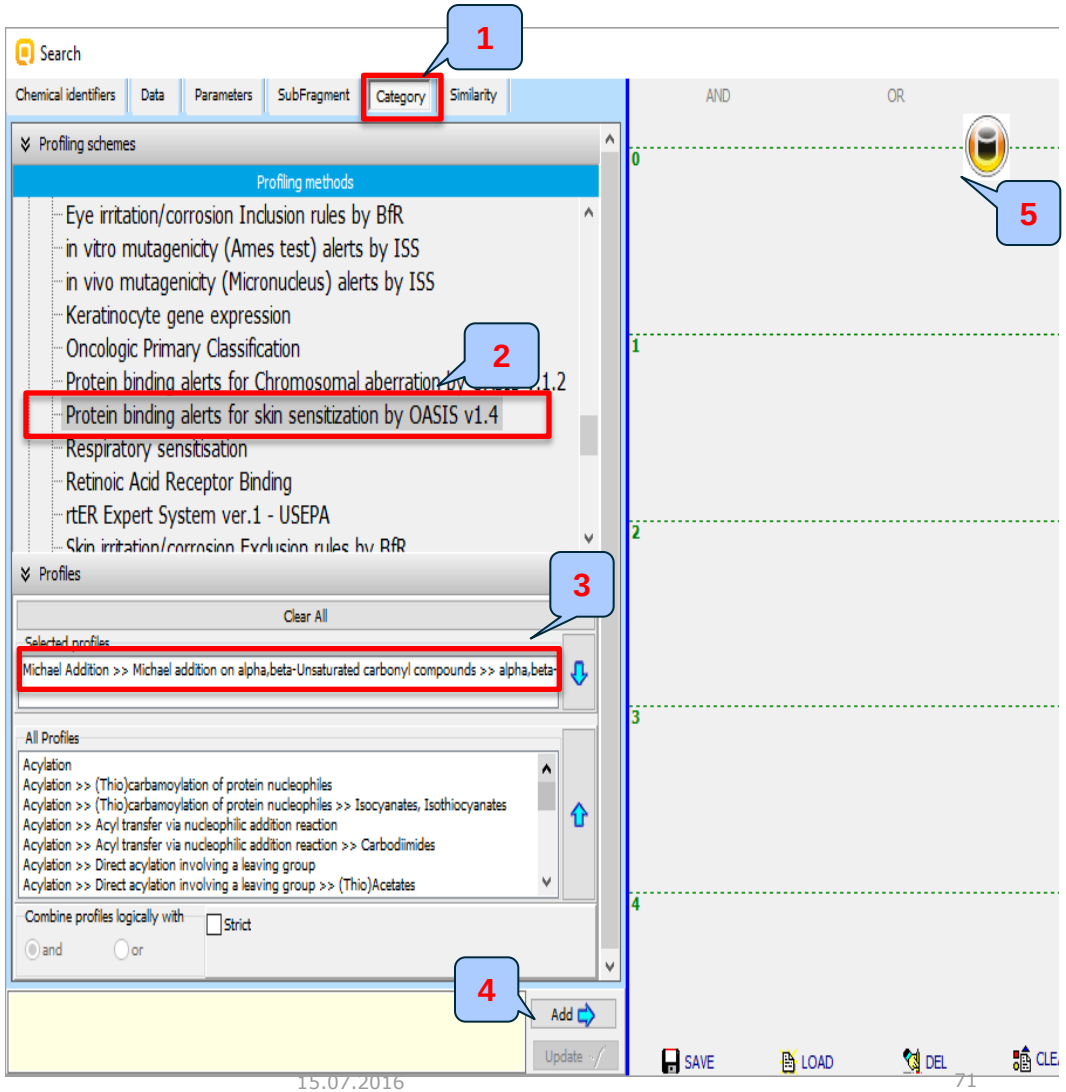
Sub fragment search for identifying chemicals

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** on Category panel
2. **Select** Protein binding alerts for skin sensitization by OASIS v1.4
3. **Select** category Michael addition >>alpha, beta-Unsaturated carbonyl compounds>>alpha, beta-Aldehydes and **Move** the selected category to the panel Selected profiles
4. **Click** Add button
5. The query appears on the logic panel

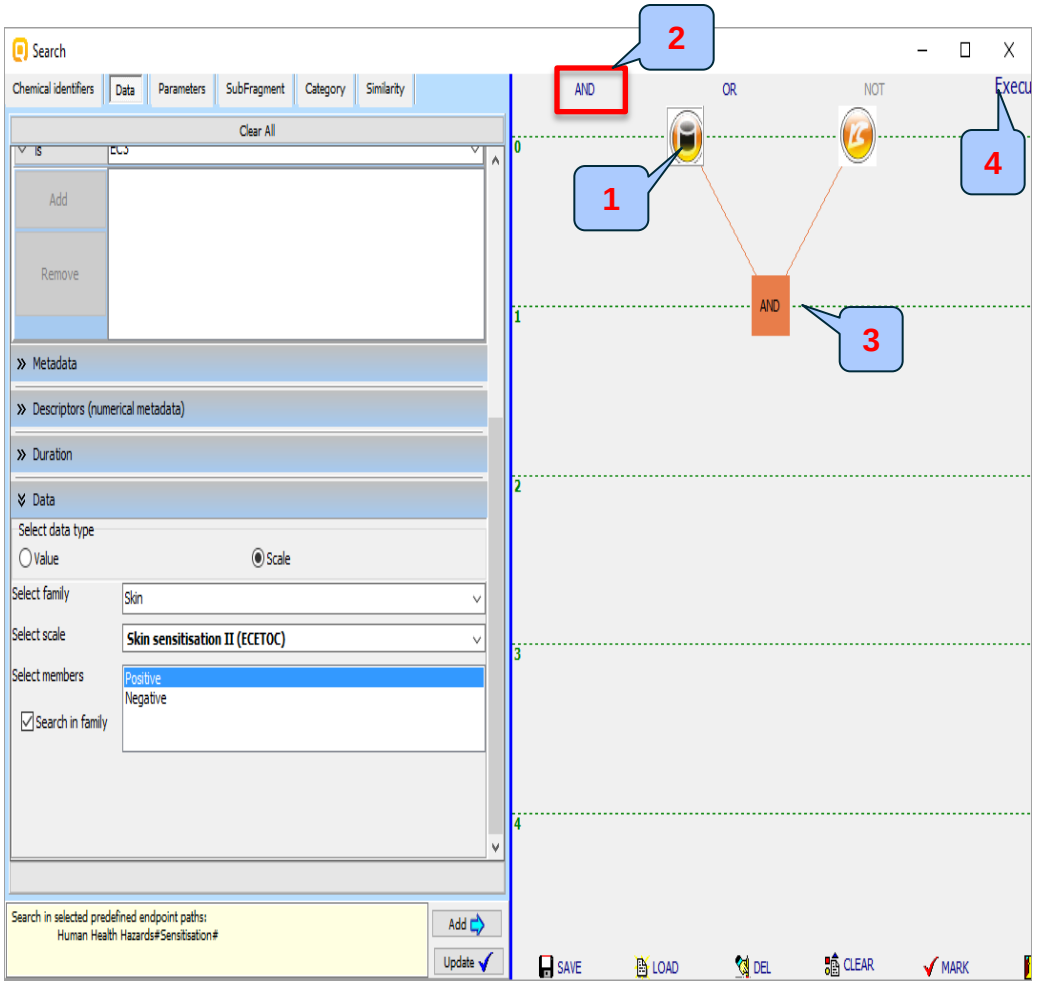


Sub fragment search for identifying chemicals

Chemicals with Skin sensitization positive data including Aldehyde fragment

Example 6

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

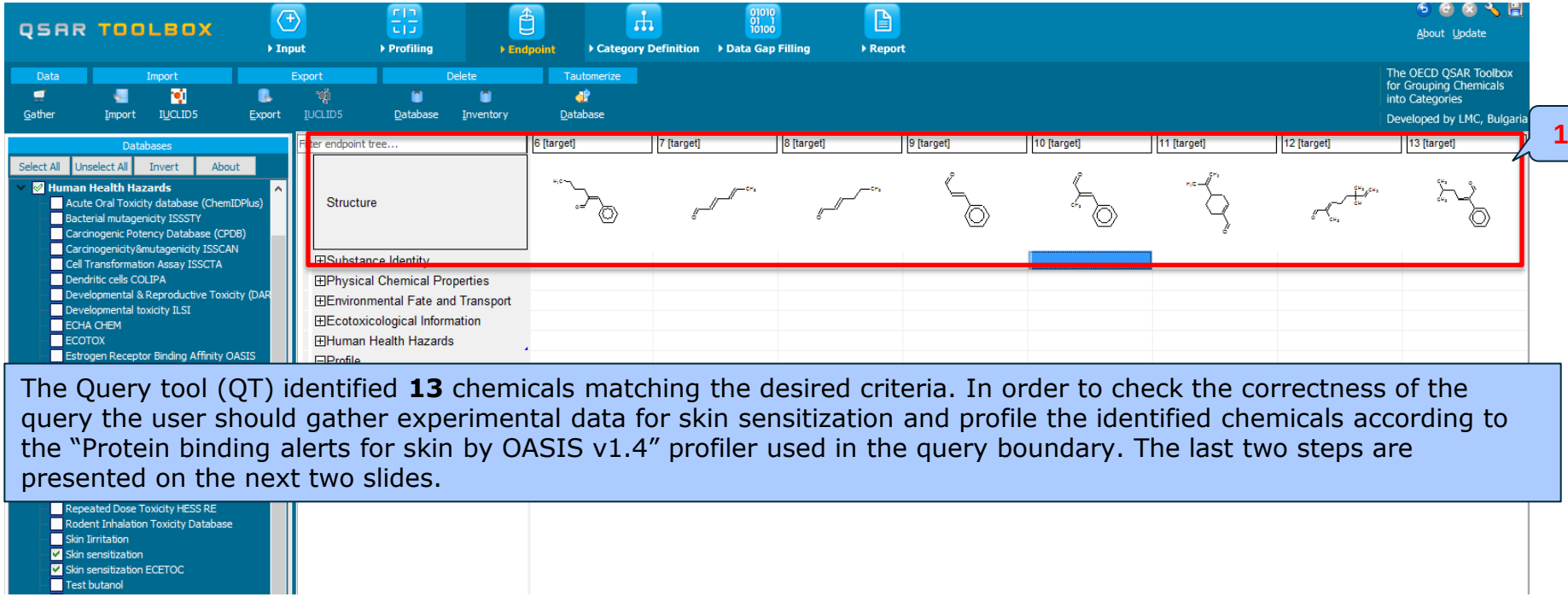


1. **Right click** over the query in order to select it
2. **Click** AND button
3. The two queries are combined together by logical AND
4. **Click** on Execute button

Sub fragment search for identifying chemicals

Chemicals with Skin sensitization positive data including Aldehyde fragment

Example 6

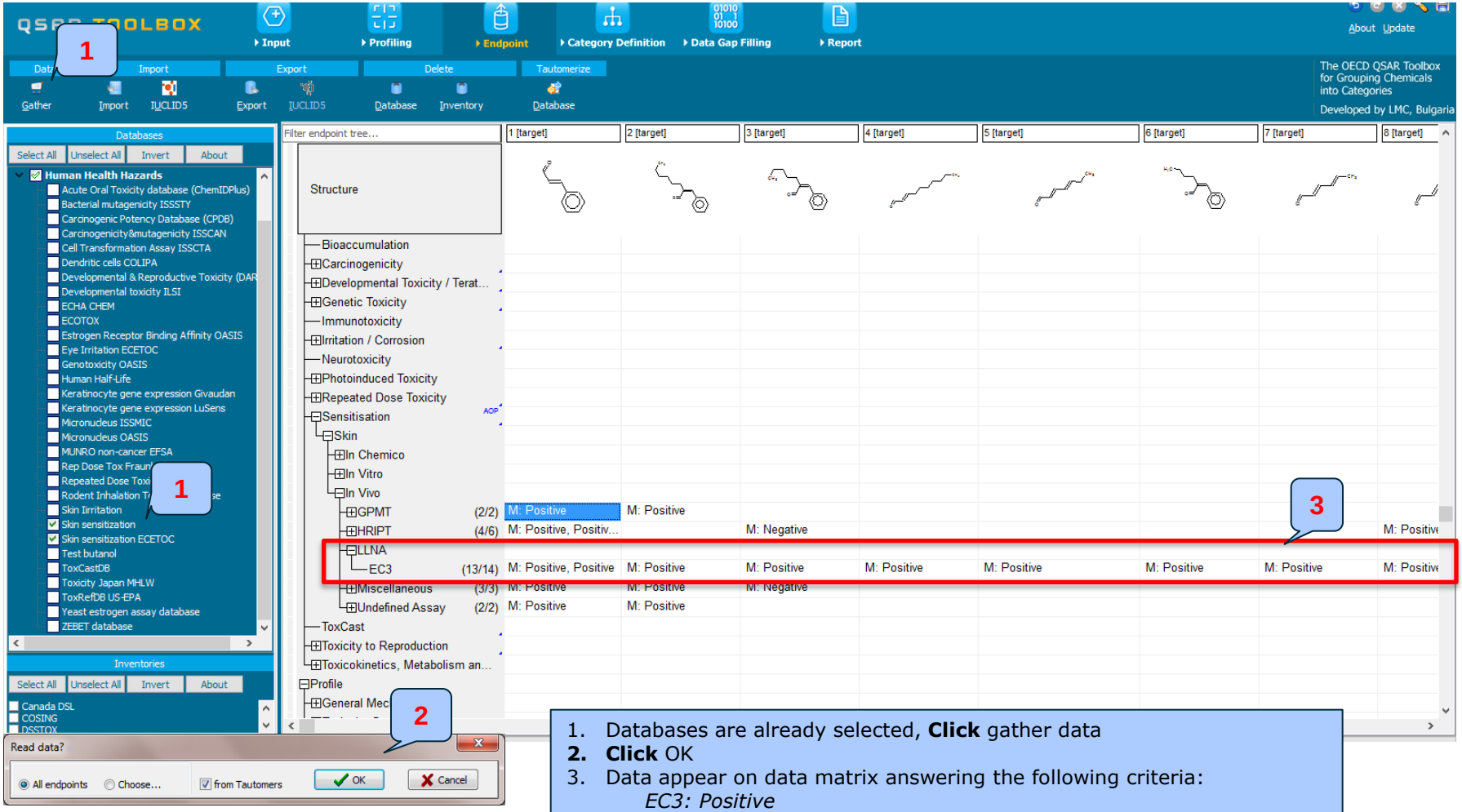


The Query tool (QT) identified **13** chemicals matching the desired criteria. In order to check the correctness of the query the user should gather experimental data for skin sensitization and profile the identified chemicals according to the "Protein binding alerts for skin by OASIS v1.4" profiler used in the query boundary. The last two steps are presented on the next two slides.

Sub fragment search for identifying chemicals

Chemicals with Skin sensitization positive data including Aldehyde fragment

Example 6

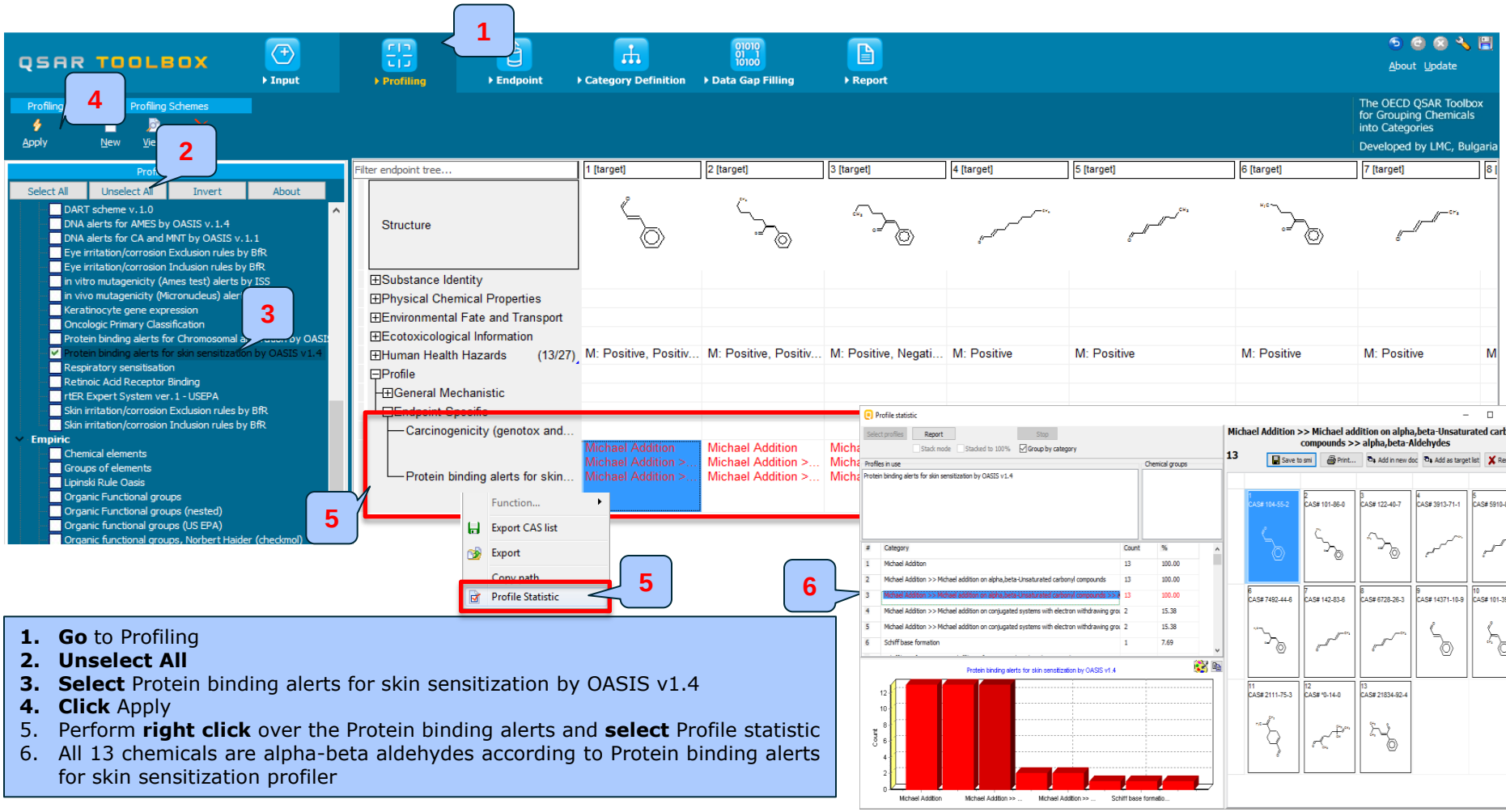


1. Databases are already selected, **Click** gather data
2. **Click** OK
3. Data appear on data matrix answering the following criteria:
   EC3: Positive

Sub fragment search for identifying chemicals

Chemicals with Skin sensitization positive data including Aldehyde fragment

Example 6



1. **Go** to Profiling
2. **Unselect All**
3. **Select** Protein binding alerts for skin sensitization by OASIS v1.4
4. **Click** Apply
5. Perform **right click** over the Protein binding alerts and **select** Profile statistic
6. All 13 chemicals are alpha-beta aldehydes according to Protein binding alerts for skin sensitization profiler

Outlook

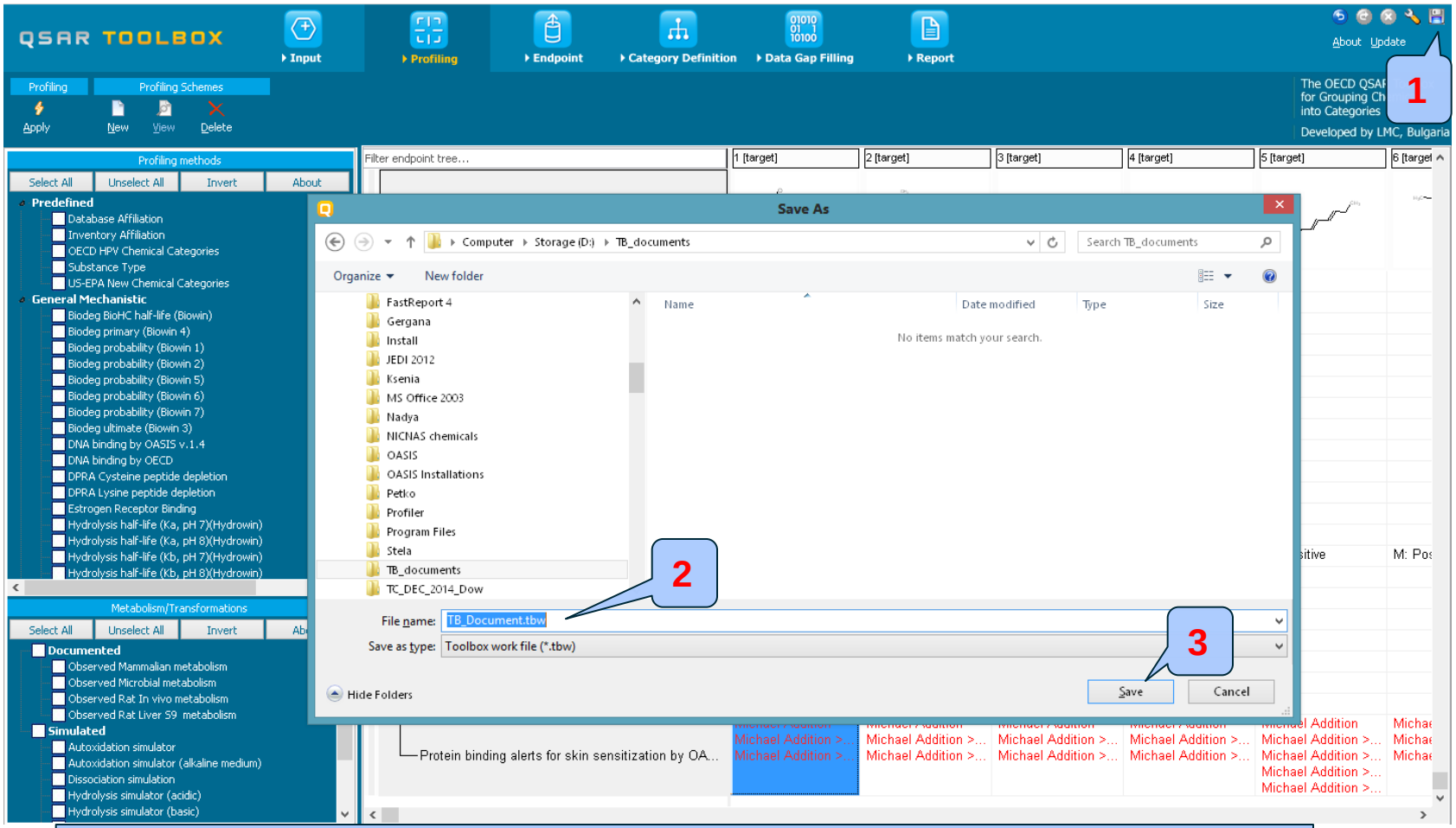
- Background
- Objectives
- Overview of Query tool
- Query tool window
- The exercise
- Workflow process
- **Save QT searches**

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).

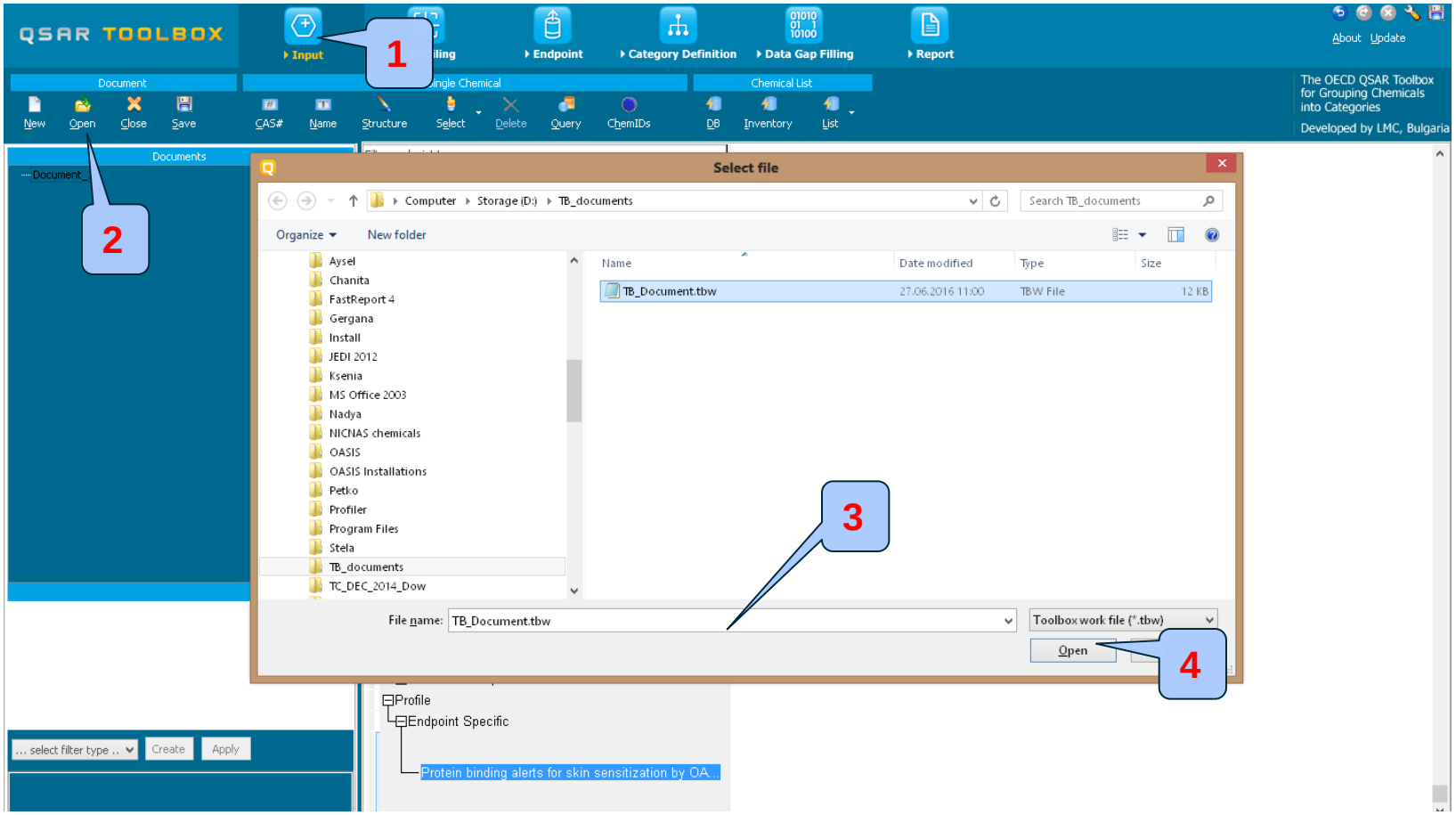
- Saving/Loading the file with TB prediction is shown on the next screenshots

Saving the QT requests



1. **Click** on Save button; **2.** **Define** name of the file; **3.** **Click** Save button

Open saved file



Once the file has been saved **1. Go** to Input; **2. Click** Open; **3. Find** and **select file**; **4. Click** Open