QSAR TOOLBOX

The OECD QSAR Toolbox for Grouping Chemicals into Categories

OECD QSAR Toolbox v.4.1

Tutorial for using the PBT prioritization scheme

Outlook

- **Aim**
- PBT scheme
- Workflow of the prediction
- Export of the results

Aim

This is a step-by-step presentation designed to take the user of Toolbox through the PBT prioritization scheme implemented in the software.

Outlook

- Aim
- **PBT scheme**
  - **Background**
- Workflow of the prediction
- Export of the results

Background: PBT prioritization scheme

• PBT prioritization scheme is based on experimental data and QSAR models.

- A substance is classified based on thresholds for persistence, bioaccumulation and toxicity, and the following classifications could be given:
  - very persistent (**vP**),
  - persistent (**P**),
  - very bioaccumulative (**vB**),
  - bioaccumulative (**B**),
  - very toxic (**vT**),
  - toxic (**T**).

- The thresholds are illustrated in the table on the next slide.

Background: PBT assessment criteria

Classification	Criteria	Guidance	Data and models
vP	BOD ≤ 30%	REACH Annex XIII [1]	Experimental data only
P	30% < BOD ≤ 40% or biodegradation probability < 0.5	REACH Annex XIII [1]	Experimental data and BIOWIN 5 and 6 models
vB	BCF ≥ 3.699 log(L/kg wet)	REACH Annex XIII [1]	Experimental data and BCFWIN model
B	3.301 ≤ BCF < 3.699 log(L/kg wet) or log Kow > 4.5	REACH Annex XIII [1]	Experimental data and BCFWIN and KOWWIN models
vT	LC50 ≤ 1 mg/l	GHS classification [2]	Experimental data only
T	1 mg/l < LC50 ≤ 10 mg/l	GHS classification [2]	Experimental data only

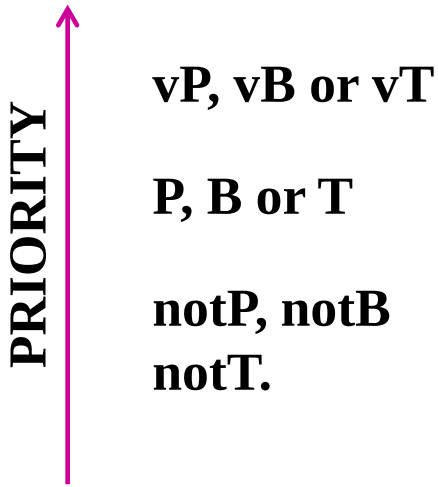
[1] https://echa.europa.eu/documents/10162/13632/information_requirements_r11_en.pdf
[2] https://www.unece.org/fileadmin/DAM/trans/danger/publi/ghs/ghs_rev04/English/ST-SG-AC10-30-Rev4e.pdf

Background: PBT assessment criteria

PBT priority grouping:

Based on the collected experimental data and results provided by QSAR models, the system applies the worst case scenario to categorize chemicals using the following priority:

- With the **highest priority** are chemicals **with available experimental data** for P, B or T assessment.
- In case of unavailable experimental data for P, B or T, QSAR models are applied for making predictions.

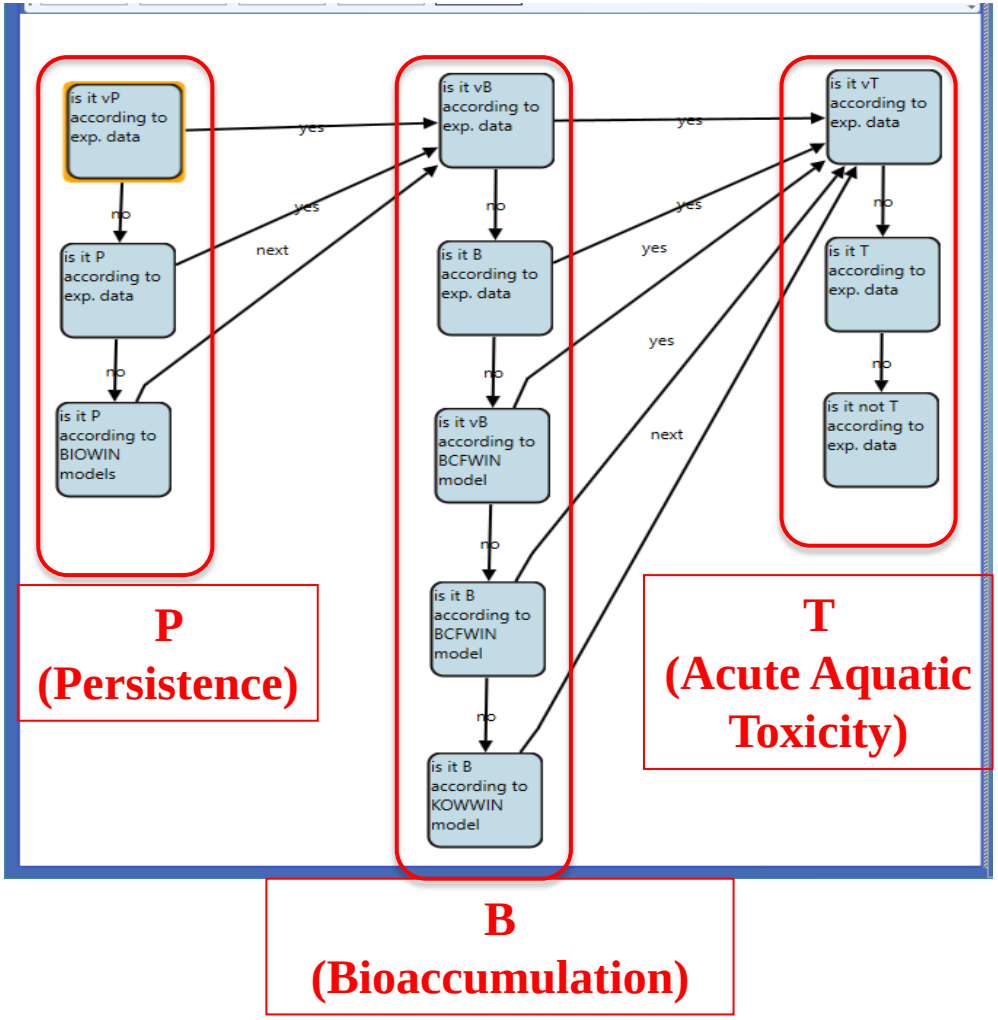


Outlook

- Aim
- **PBT scheme**
  - Background
  - **Implementation**
- Workflow of the prediction
- Export of the results

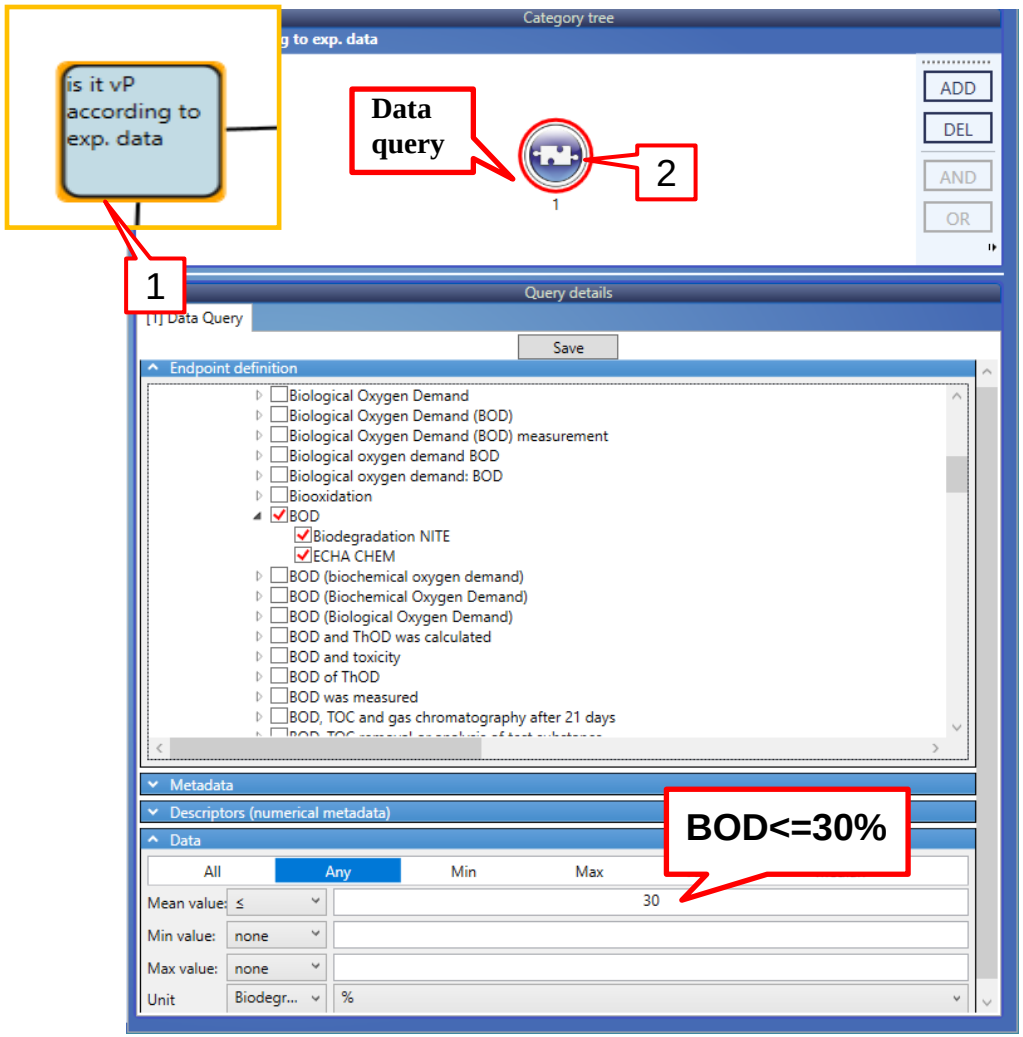
Implementation of PBT prioritization scheme

- PBT prioritization scheme is a graph of logically connected nodes.
- The nodes are divided into three groups based on the P, B or T classification for hazard assessment.



Implementation of PBT prioritization scheme

- Each node (1) contains a data or parametric (model) boundary (2) where the criteria for PBT assessment are set.
- Data query is depicted here.



Outlook

- Aim
- PBT scheme
  - Background
  - Implementation
- **Workflow of the prediction**
- Export of the results

Workflow of the prediction: Steps

- Input of target chemical(s)
- Profiling: Example prioritization scheme (PBT)
- Report

Outlook

- Aim
- PBT scheme
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  - Implementation
- **Workflow of the prediction**
  - **Chemical input**
- Export of the results

Chemical Input

- This module provides the user with several means of entering the chemical of interest or the target chemical.
- Since all subsequent functions are based on chemical structure, the goal here is to make sure the molecular structure assigned to the target chemical is the correct one.

Chemical Input
Ways of Entering a Chemical

I. Single target chemical:

- Chemical Name
- Chemical Abstract Services (CAS) number (#)
- SMILES (simplified molecular information line entry system) notation
- Chemical with defined composition
- Drawing chemical structure
- Select from User List/Inventory/Databases

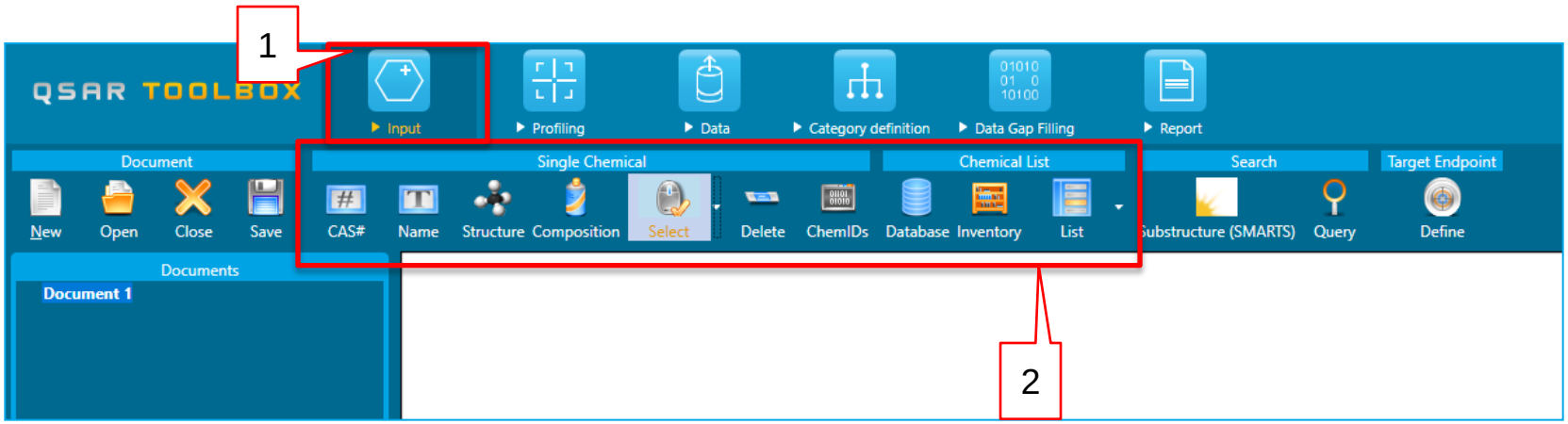
II. Group of chemicals:

- User's List
- Inventory/Database

Chemical Input: Single chemical

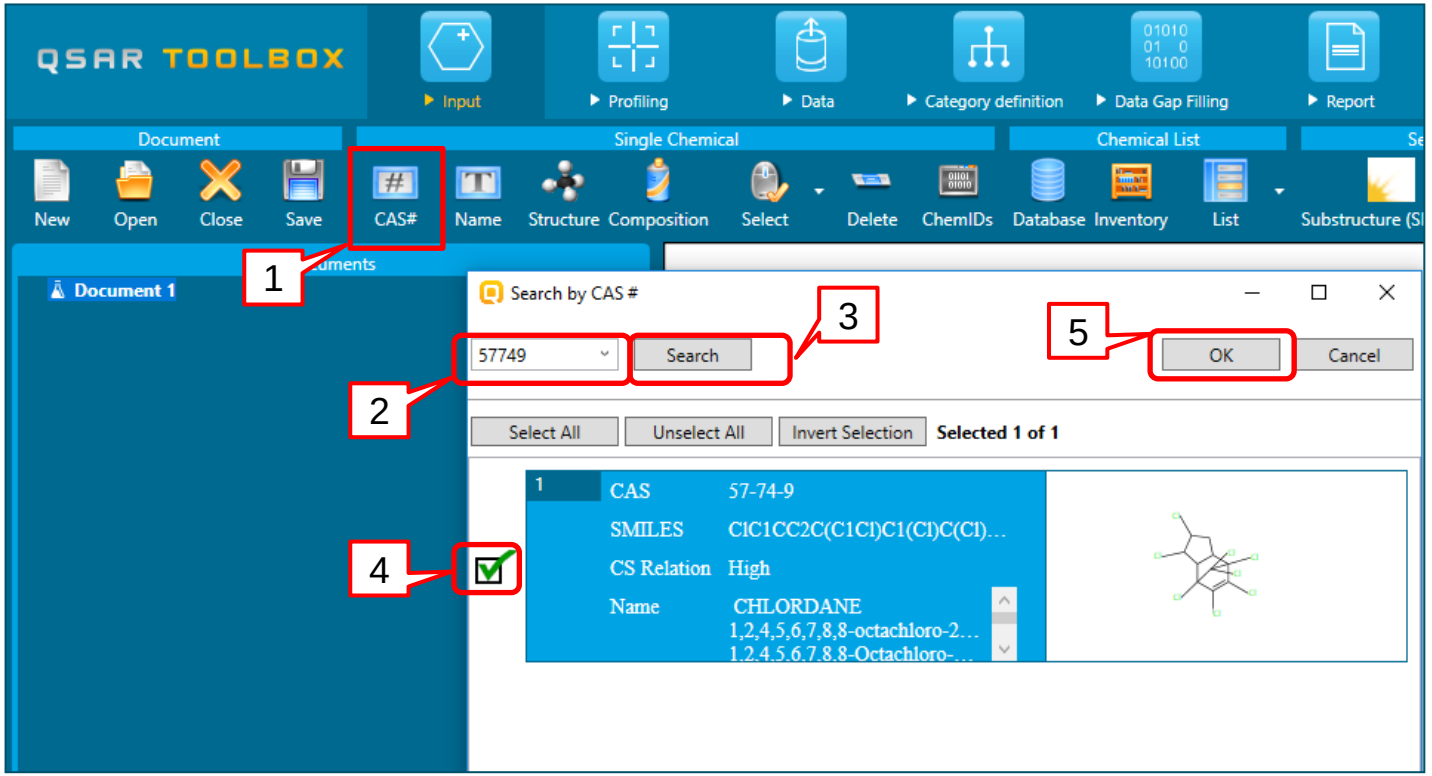
- Open the Toolbox.
- Click on “Input” (see next screen shot).

Chemical Input
Single chemical



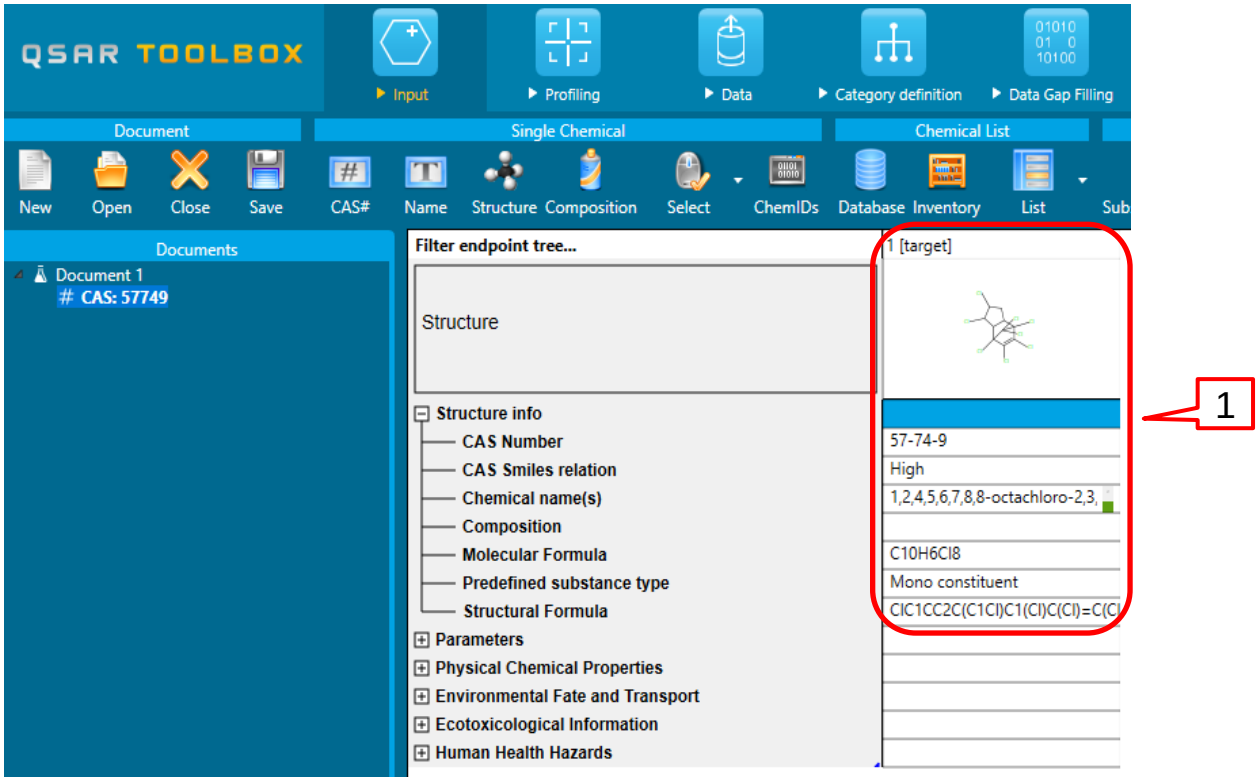
1. Click on *Input (1)* to display the main Input section (2).

Chemical Input
Single chemical: CAS RN



1. Press CAS# (1); 2. Type in the CAS # (2) ; 3. Click on *Search* (3);
4. Select the chemical (4); 5. Press *OK* (4).

Chemical Input
Single chemical: CAS RN



The chemical is displayed in the data matrix (1).

Outlook

- Aim
- PBT scheme
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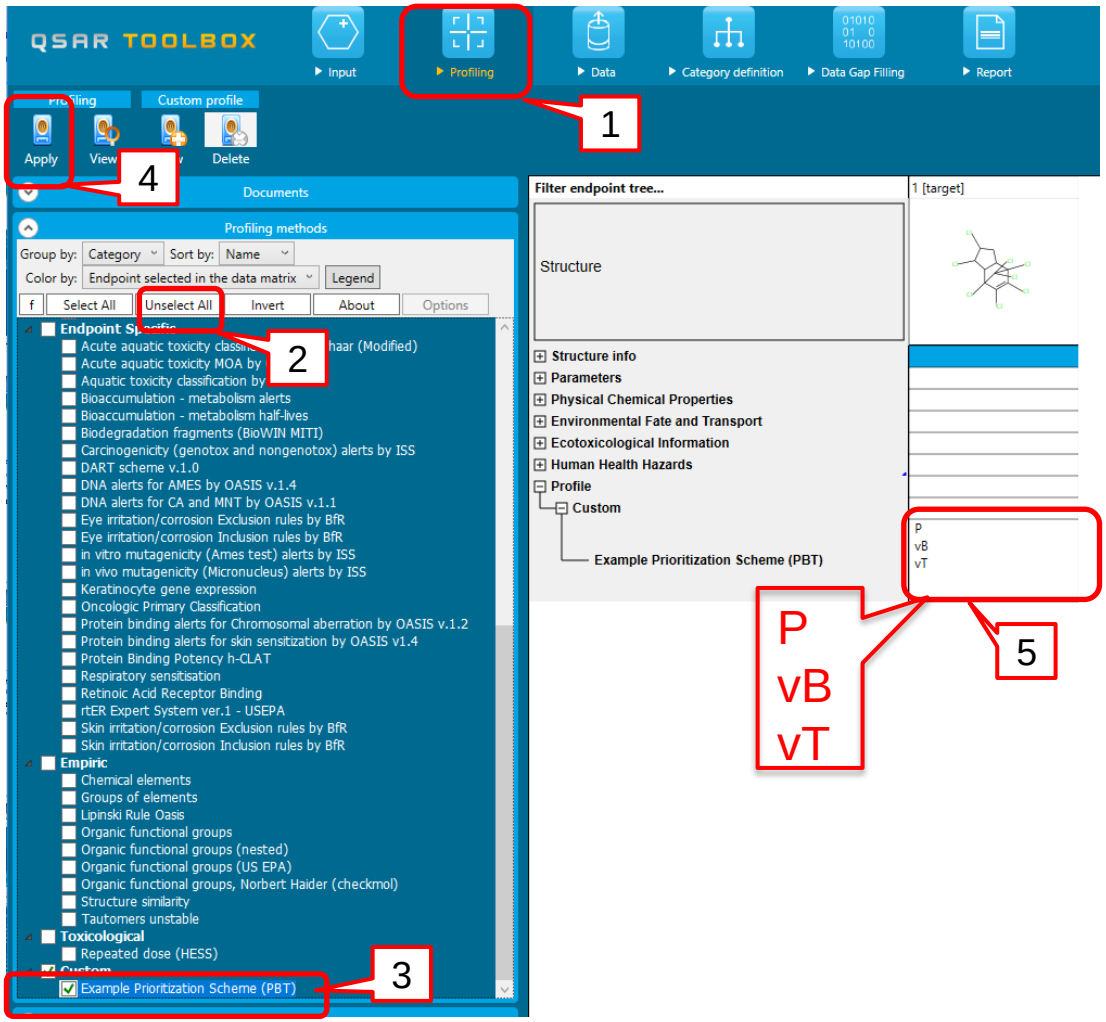
  - Implementation
- **Workflow of the prediction**
  - Chemical input
  - **Profiling**
- Export of the results

Profiling
Overview

- "Profiling" refers to the electronic process of retrieving relevant information on a compound which is stored in the Toolbox, other than its fate and (eco)toxicity data.
- Toolbox has many predefined profilers but it also allows the user to develop new profilers.

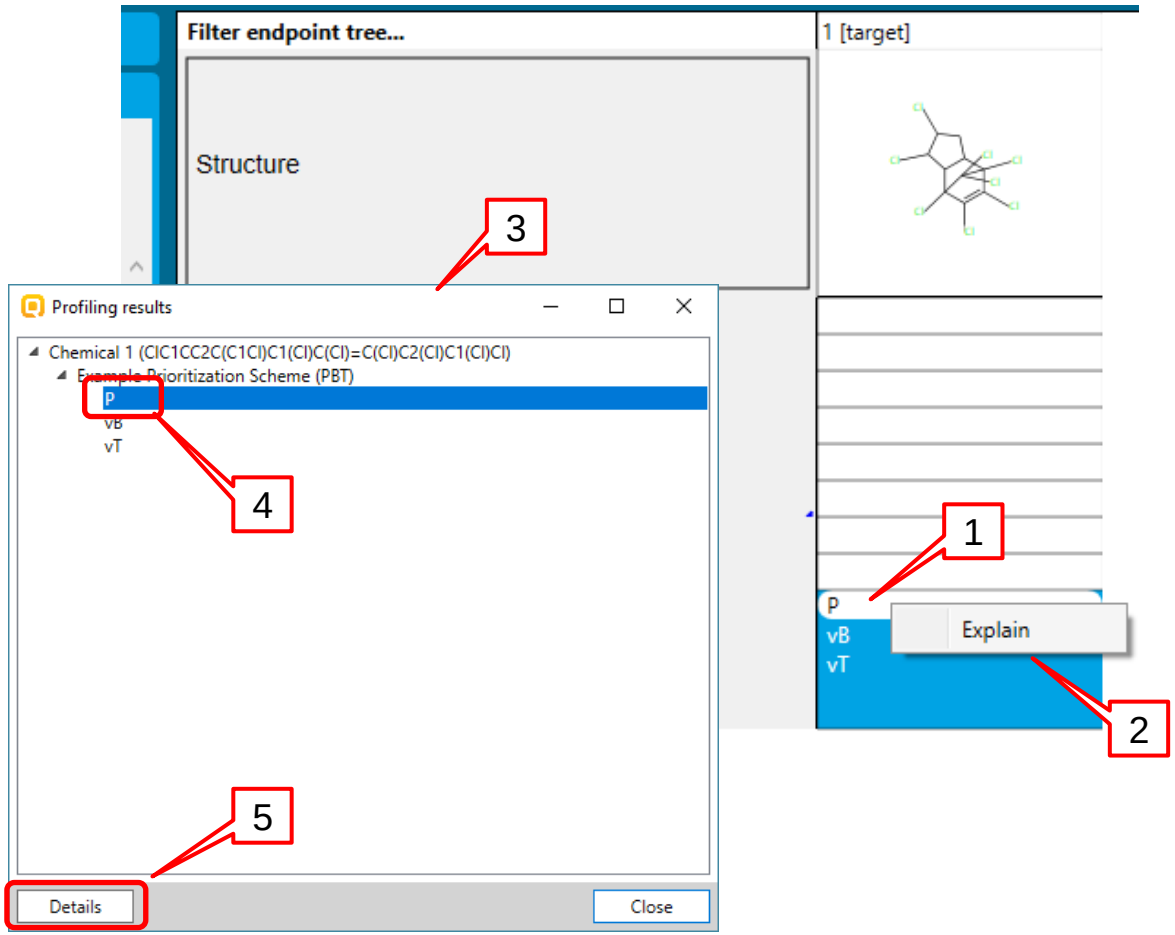
Profiling

1. Select *Profiling tab* (1);
2. Click on *Unselect All (2);*
3. Tick *Example prioritization Scheme (PBT)* (3);
4. Click on *Apply (4).*
5. Expand the cell to see the results: P, vB, vT.
6. The results are explained in the next slides.



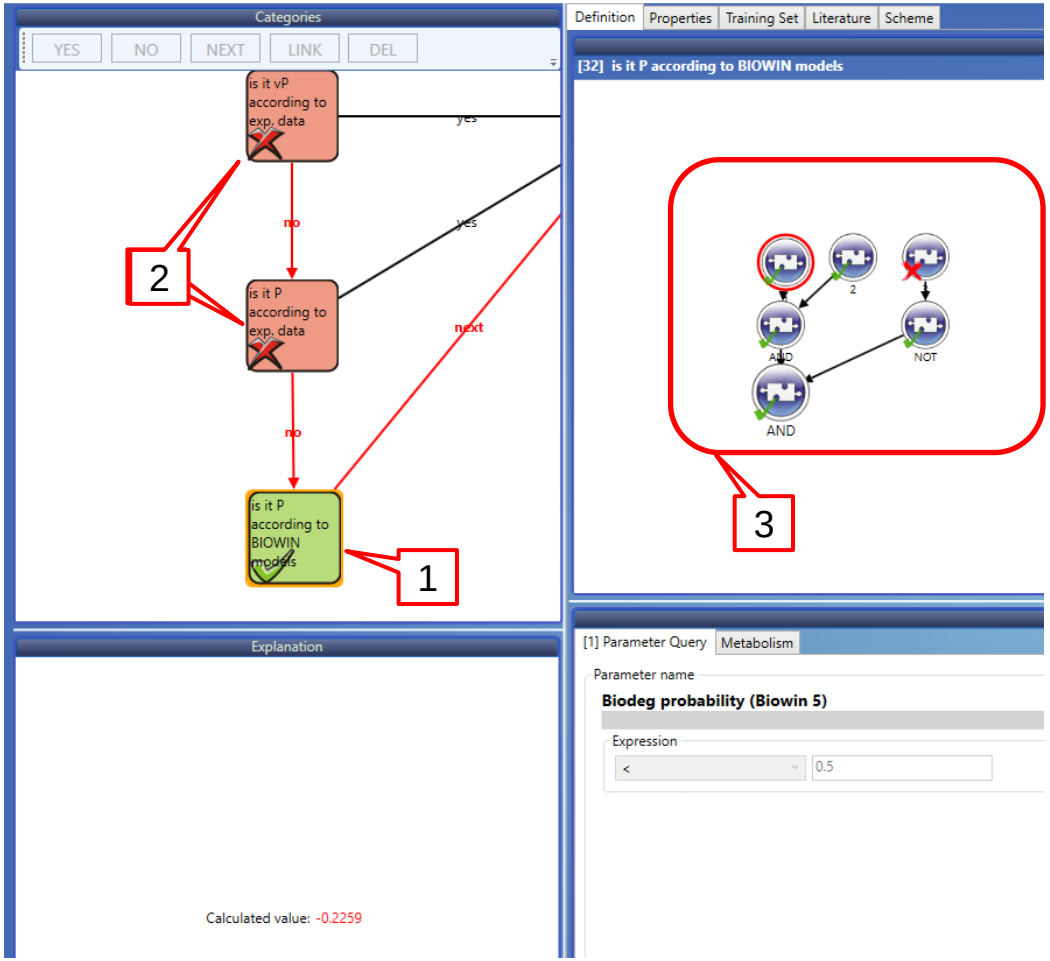
Profiling: explanation of "P" prediction

1. Left click on *"P"* (1)
2. Click *on the pop-up window* *Explain* (2)
3. The *Profiling results* window is displayed (3)
4. Select *"P"* (4)
5. Click on the *Details* (5)
6. The PBT scheme is displayed and the query, which gives the prediction is shown (see next slide)



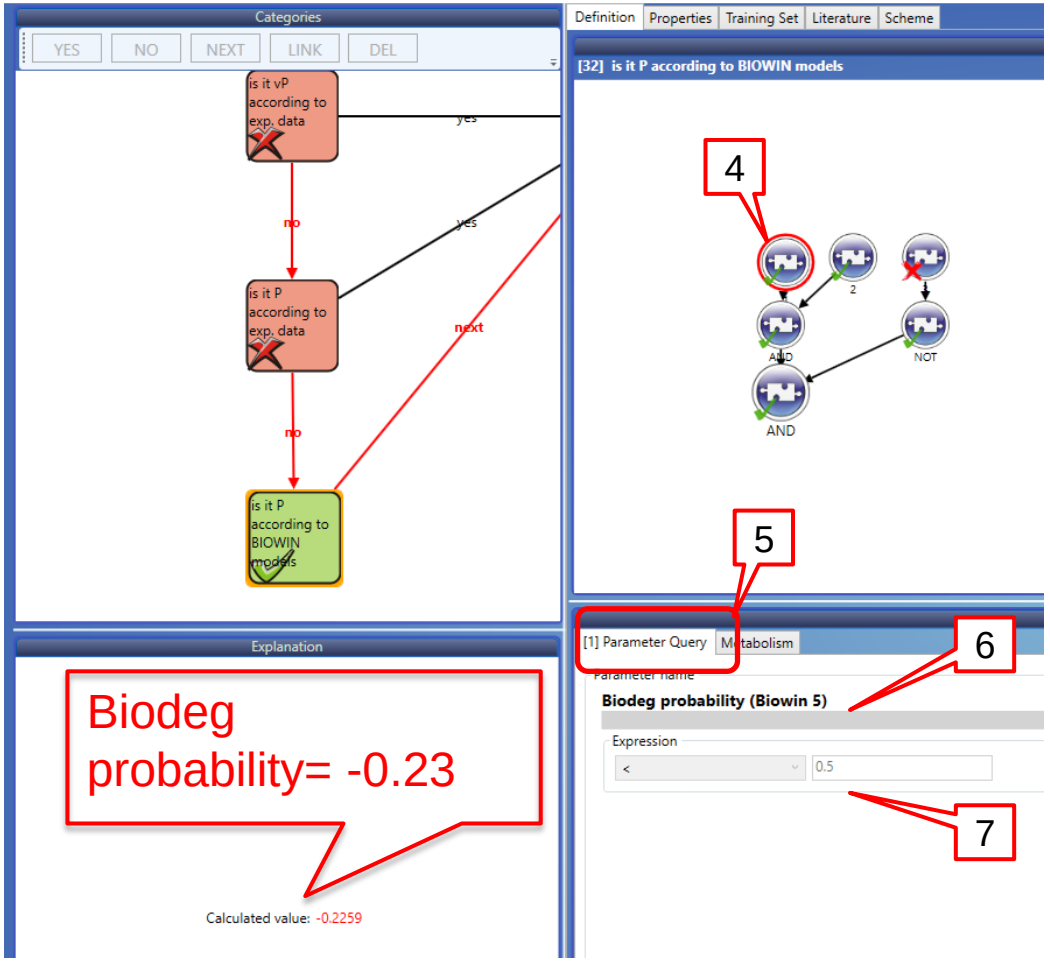
Profiling: explanation of "P" prediction

1. The node, which criteria are fulfilled is colored green and marked with "V" sign (1).
2. The nodes, which criteria are not fulfilled are colored in red and marked with "X" sign (2).
3. A yellow border around the node (1) indicates that it is selected and its queries are displayed in the definition panel (3).



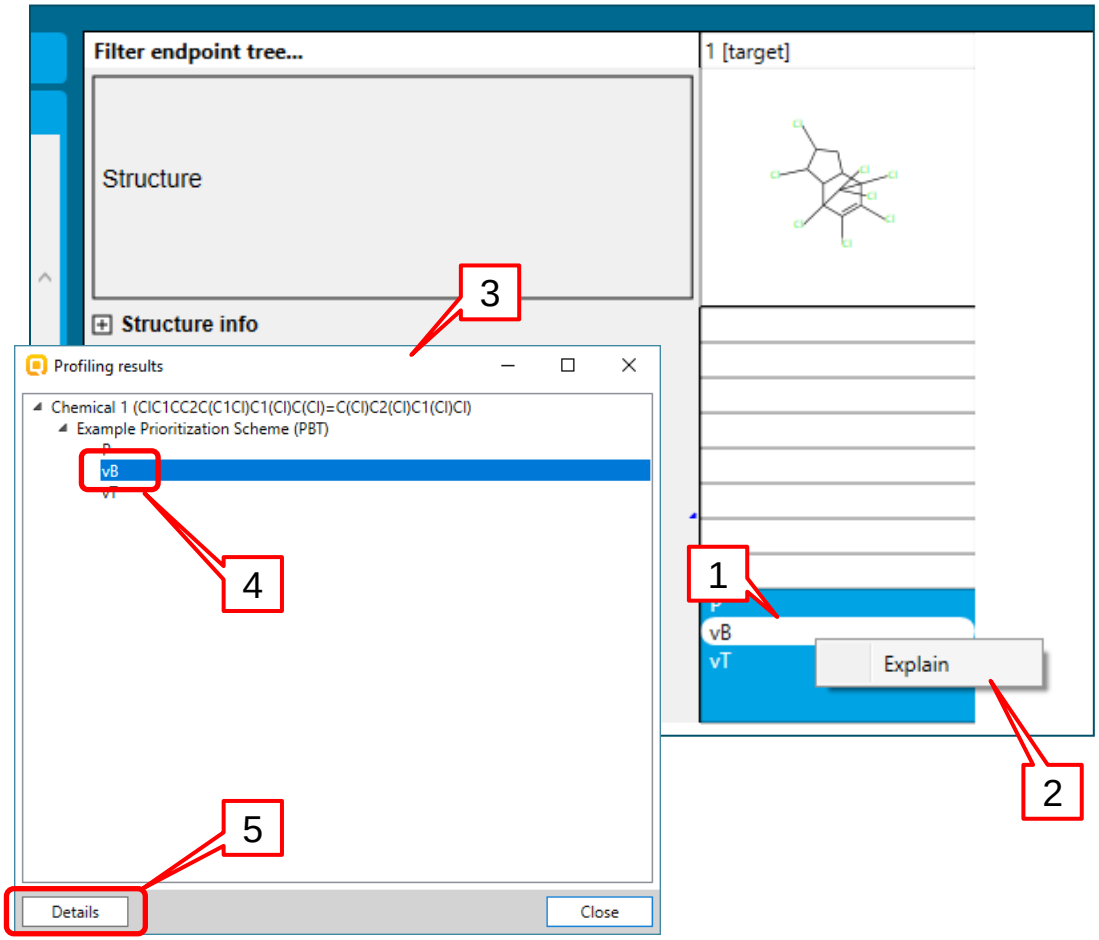
Profiling: explanation of "P" prediction

4. A red circle around the query indicates that it is selected (4).
5. Here it is a parameter query (5), which content is shown in the Parameter query tab (5)
6. Biodegradation probability (Biowin 5 model) is implemented (6). The predicted outcome has to be below 0.5 (7) in order for the requirements to be fulfilled.
7. The calculated biodegradation probability for the target chemical, by Biowin 5 model, is -0.23.



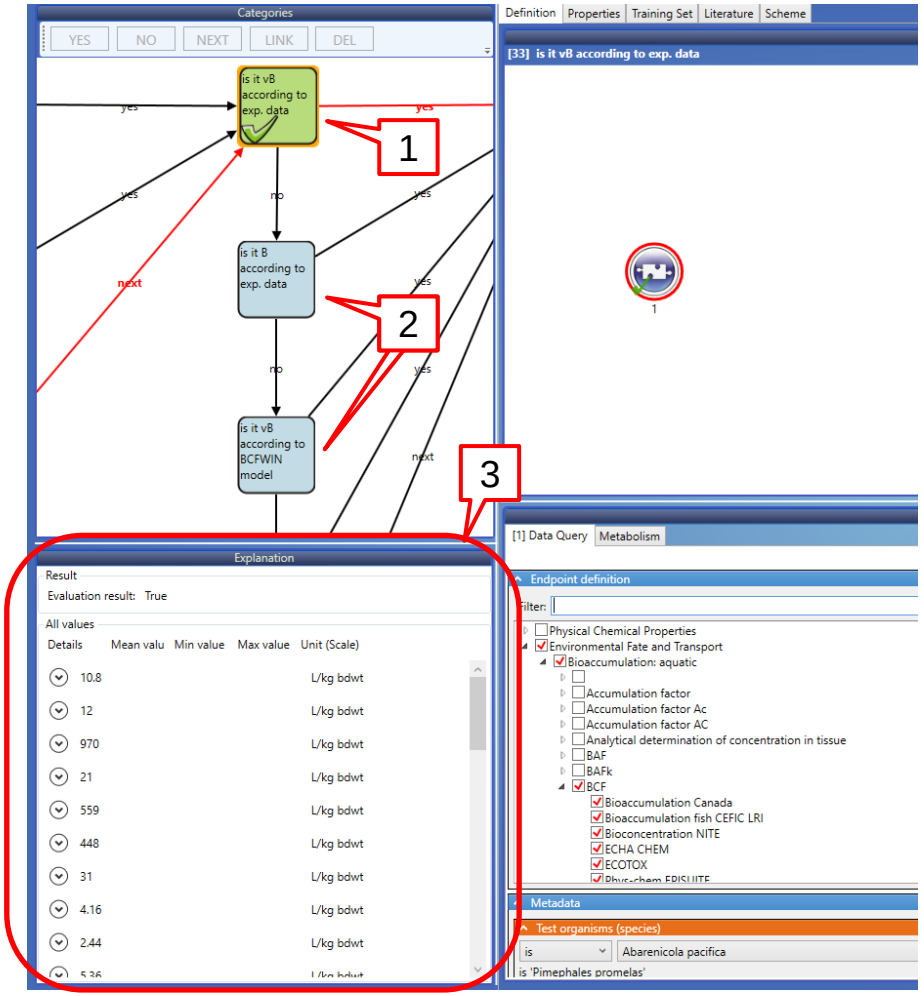
Profiling: explanation of "vB" prediction

1. Left click on "*vB*"(1)
2. Click *on the pop-up window Explain (2)*
3. The *Profiling results* window is displayed (3)
4. Select "*vB*" (4)
5. Click on the *Details* (5)
6. The PBT scheme is displayed and the query, which gives the prediction is shown (see next slide)

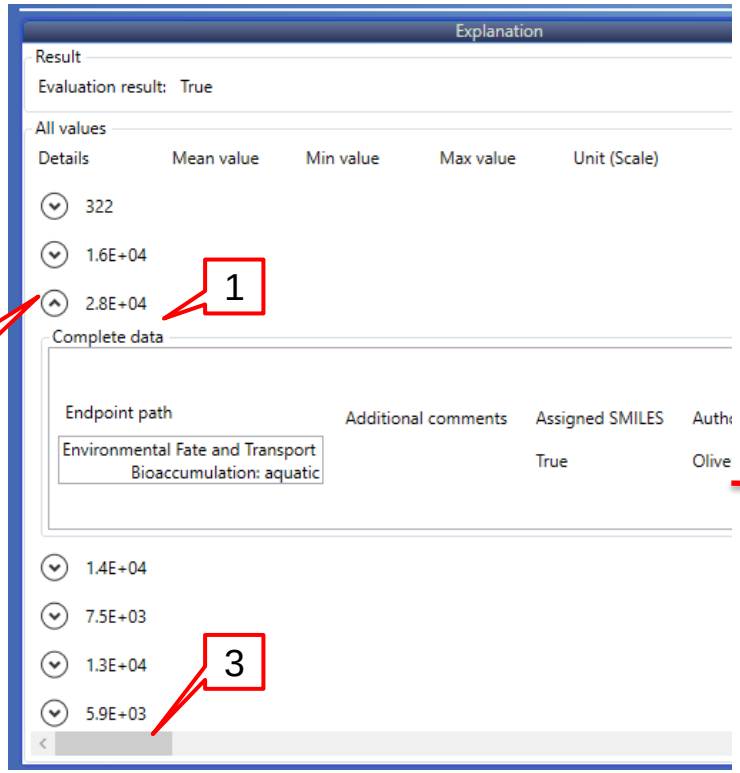


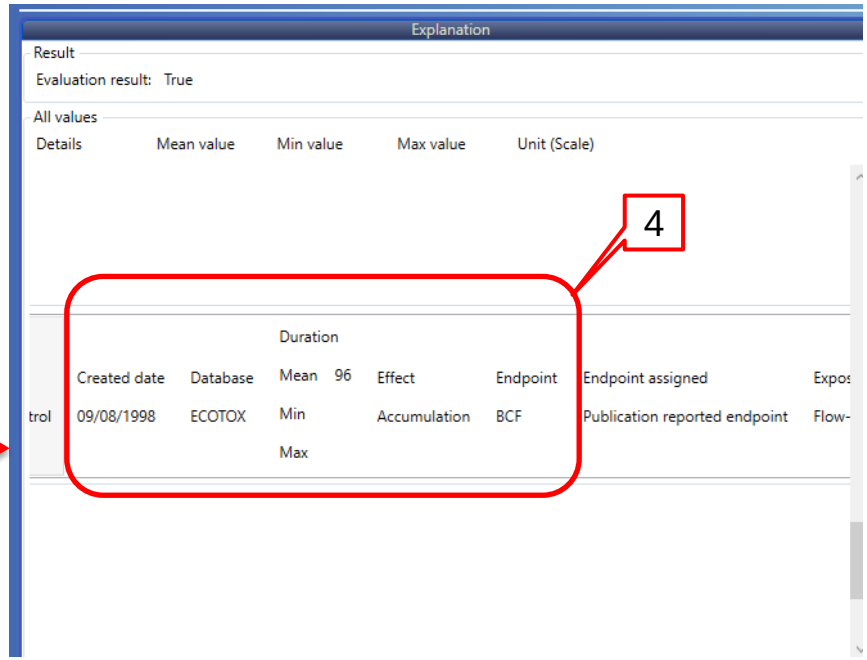
Profiling: explanation of "vB" prediction

1. The node, which criteria are fulfilled is colored green and marked with "V" sign (1).
2. Here it is a node with experimental data. The logic implemented in the PBT scheme implies that if the target chemical has experimental data (in this case vB) then the consecutive nodes from the bioaccumulation assessment are not run. Hence they are colored in grey (2).
3. All experimental data available for the target chemical is listed in the *Explanation* panel(3). The unit is L/kg bdwt.



Profiling: explanation of "vB" prediction

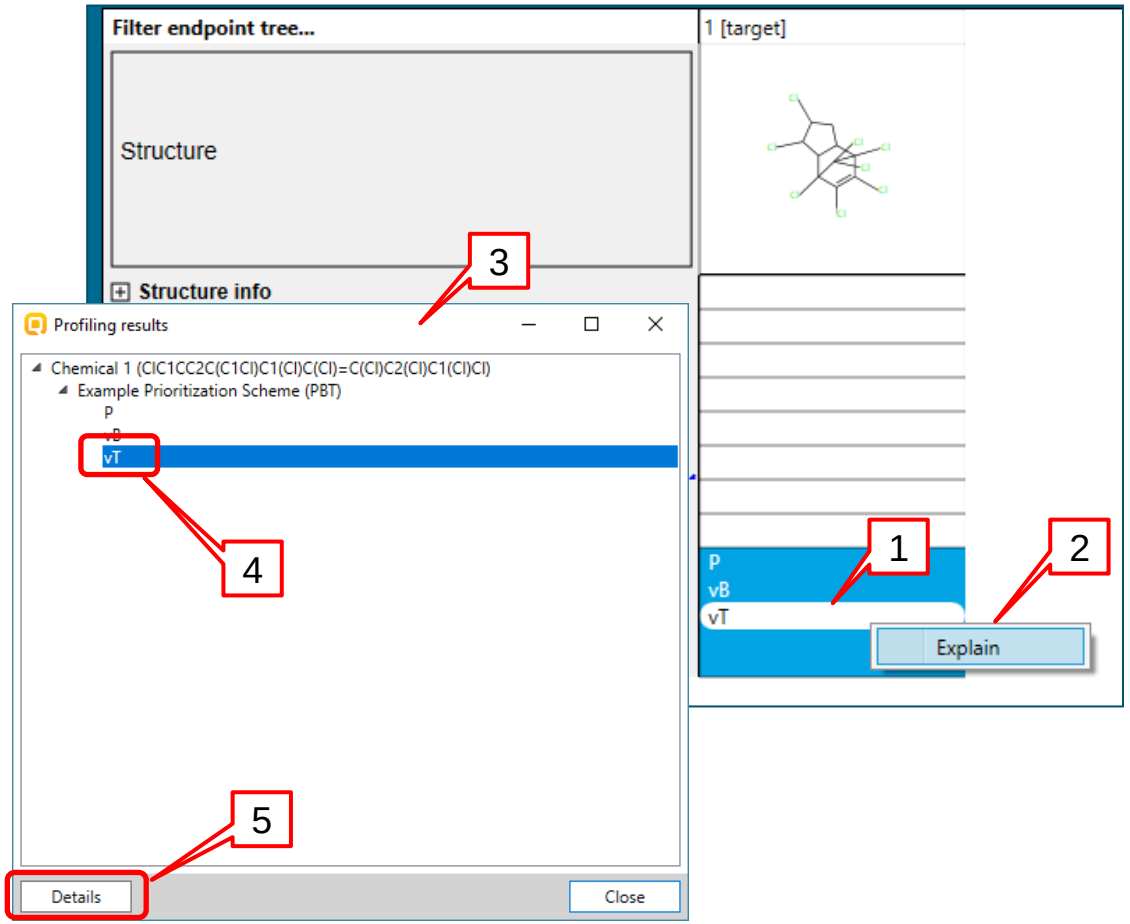




1. As the endpoint is bioaccumulation, the highest value is taken into account(1).
2. Expand the prediction from the arrow next to the digits (2).
3. By moving the scroll bar (3) , you can see all details of the measured data (4).

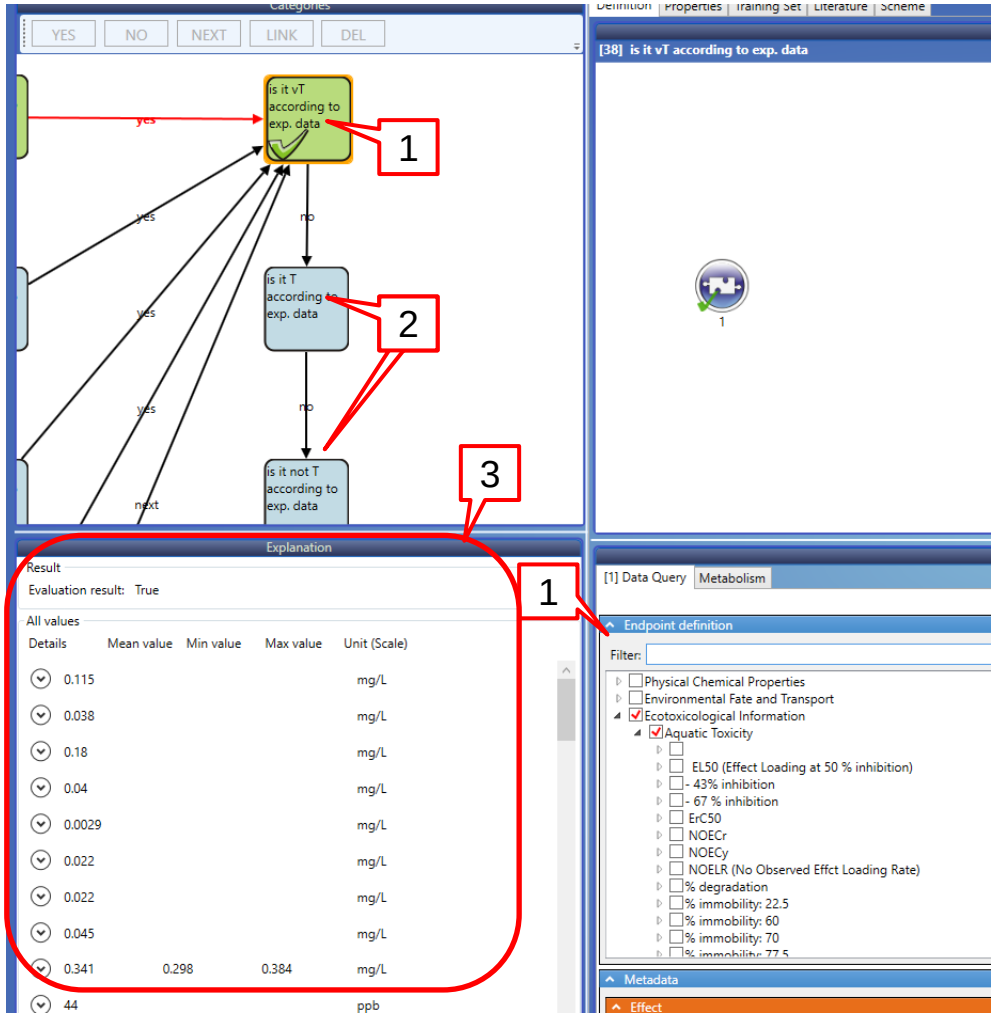
Profiling: explanation of "vT" prediction

1. Left click on "*vT*"(1)
2. Click *on the pop-up window Explain (2)*
3. The *Profiling results* window is displayed (3)
4. Select "*vT*" (4)
5. Click on the *Details* (5)
6. The PBT scheme is displayed and the query, which gives the prediction is shown (see next slide)



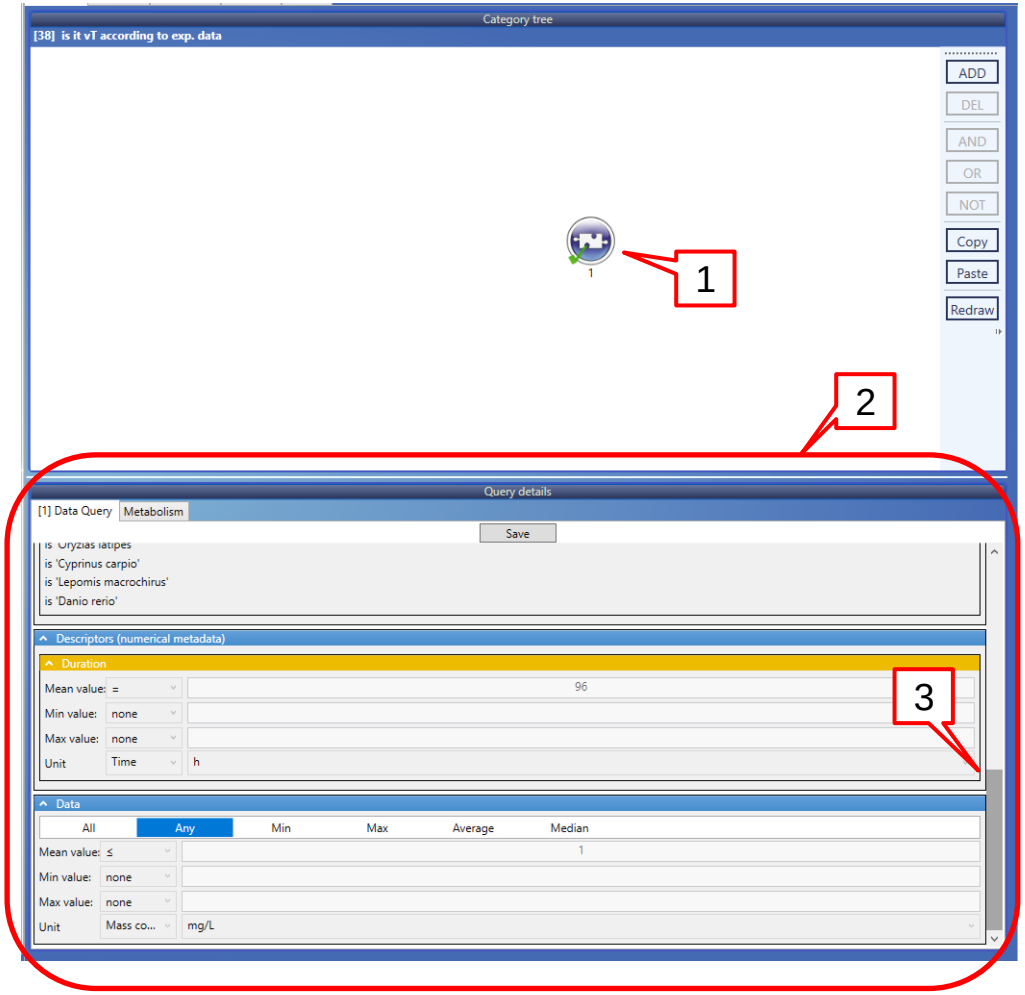
Profiling: explanation of "vT" prediction

1. The node, which criteria are fulfilled is colored green and marked with "V" sign (1).
2. Here it is a node with experimental data. The logic implemented in the PBT scheme implies that if the target chemical has experimental data (in this case vT) then the consecutive nodes from the toxicity assessment are not run. Hence they are colored in grey (2).
3. All experimental data available for the target chemical is listed in the *Explanation* panel(3). The unit is mg/L or ppb. However only mg/L is considered (see next two slides).



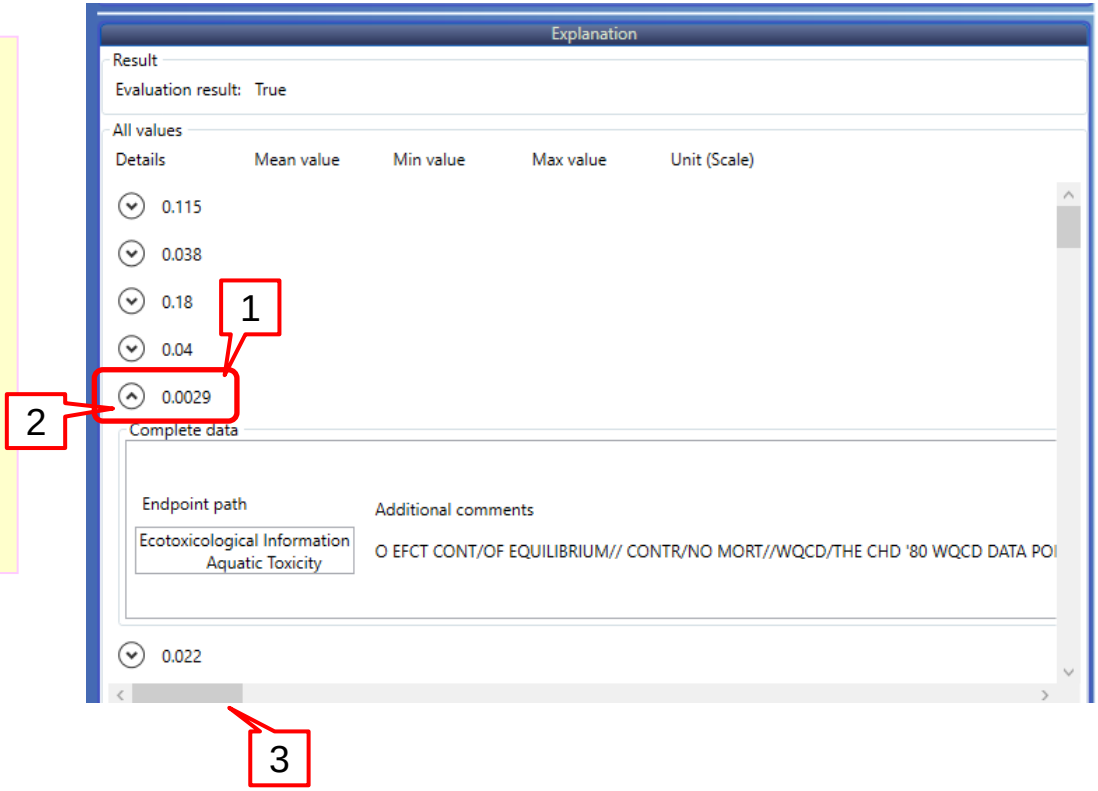
Profiling: explanation of "vT" prediction

1. The details of the Data query (1), are shown in the Query details panel (2)
2. By moving the scrollbar, you can see the type of metadata included in the query
3. In this example, the type of experimental data is *Any meaning different unit/scales* are included, e.g. mg/L and ppb (see slide 30)

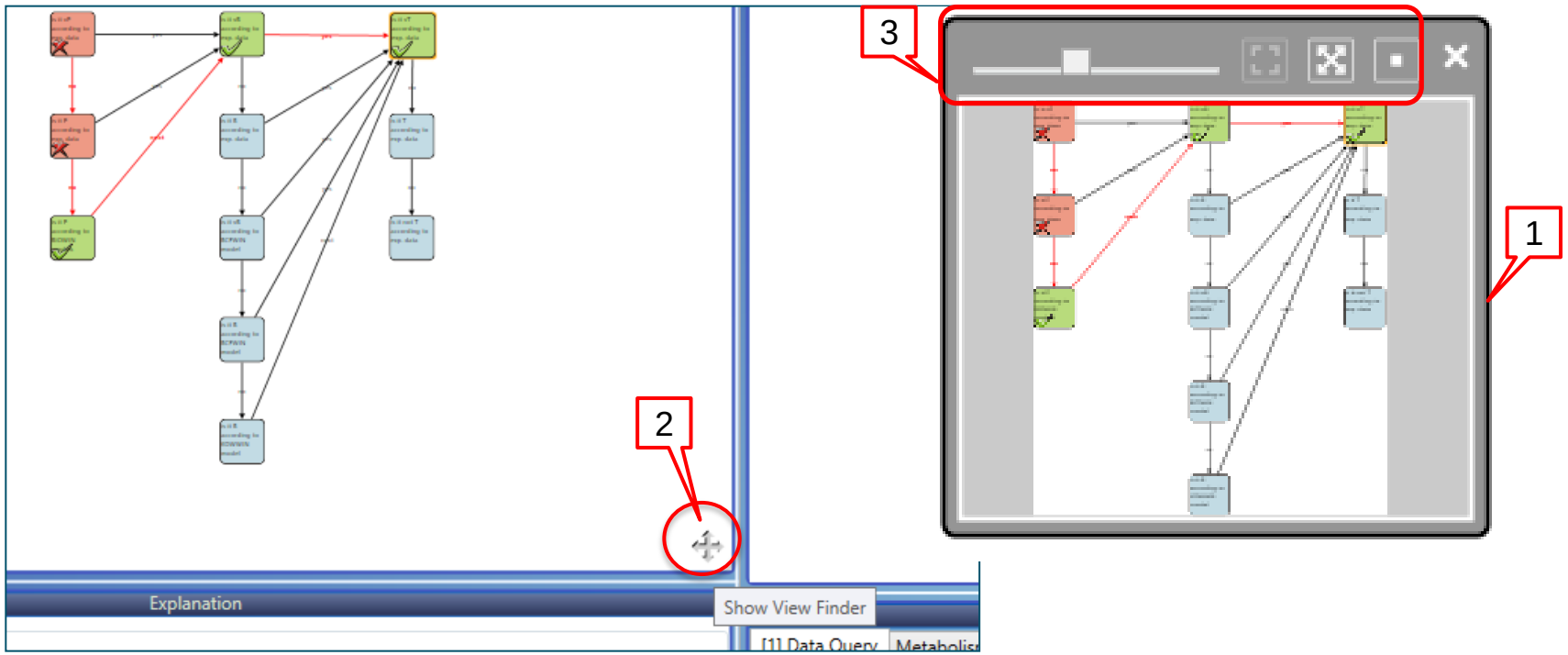


Profiling: explanation of "vT" prediction

1. As the endpoint is acute aquatic toxicity, the lowest value is taken into account (1)
2. Expand the prediction from the arrow next to the digits (2)
3. By moving the scroll bar (3), you can see all details of the measured data

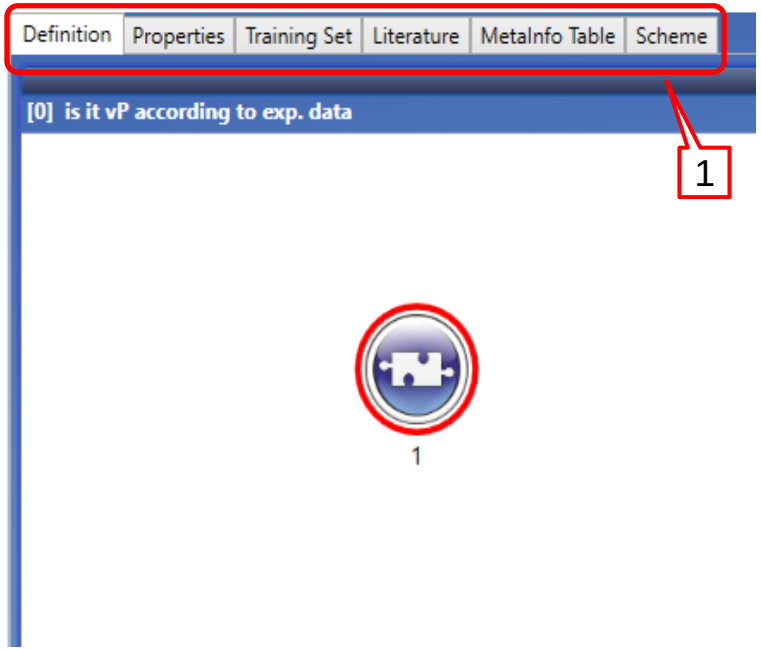


Profiling: common features of PBT interface



1. A view finder window (1) is displayed by clicking on the cross sign (2).
2. It contains navigation options for viewing the PBT scheme (3).

Profiling: common features of PBT interface



Properties, ***Literature*** and ***Scheme*** tabs gives more information about the query (properties), the node(literature) and the developer (scheme) (1).

Outlook

- Aim
- PBT scheme
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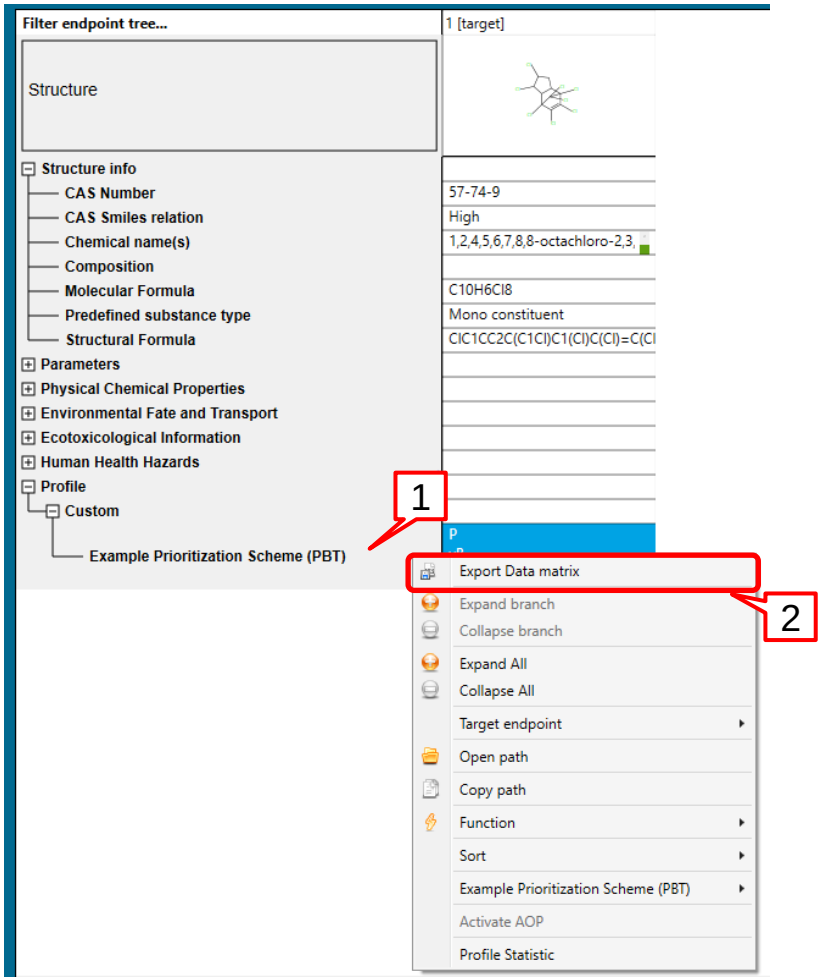
- Workflow of the prediction
  - Chemical input
  - Profiling
- **Export of the results**

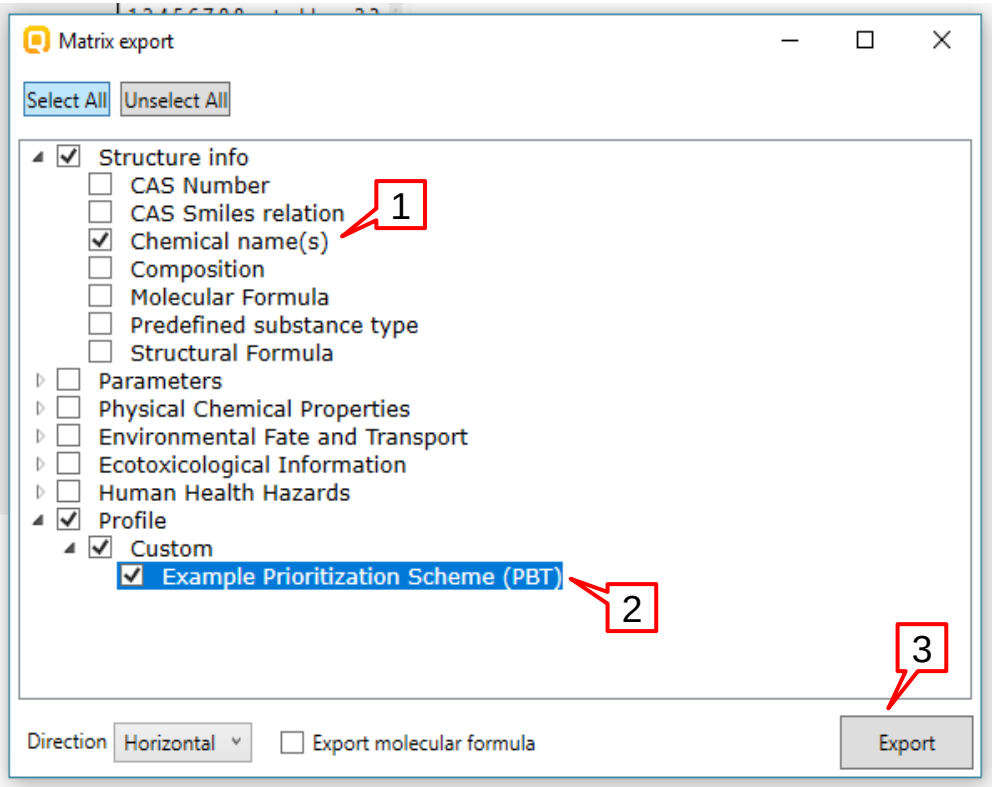
Export of the results

1. Right click next to the name of the scheme (1)
2. Select *Export Data matrix* (2)

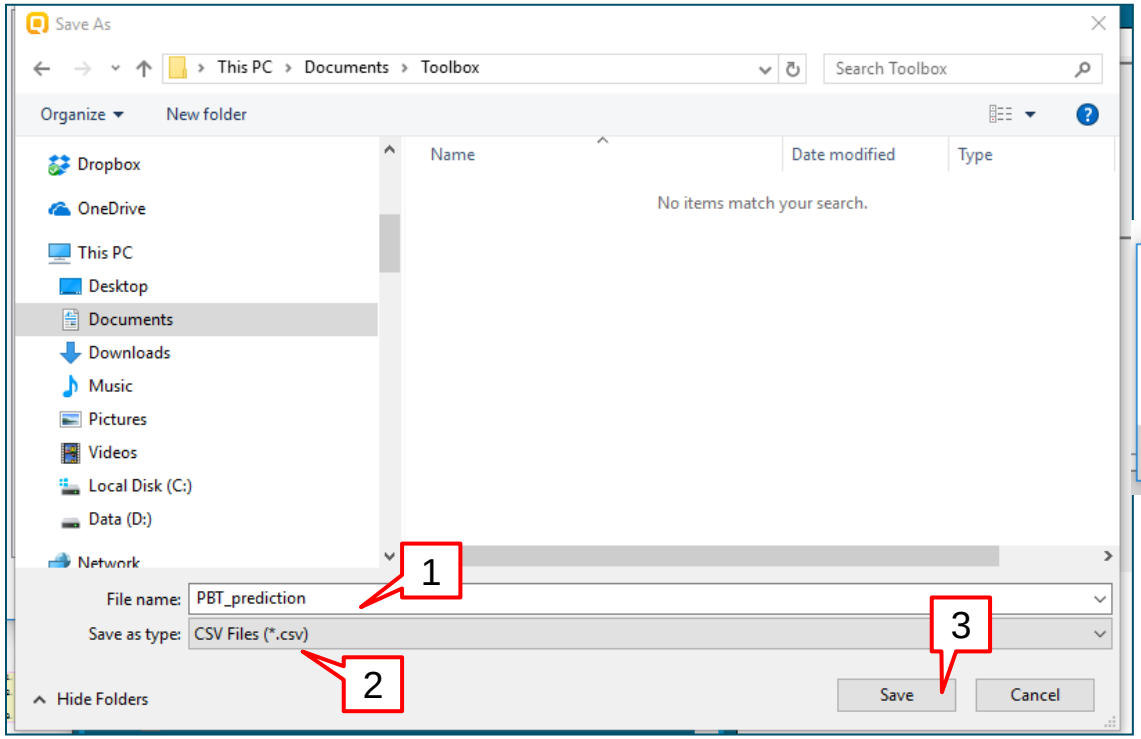


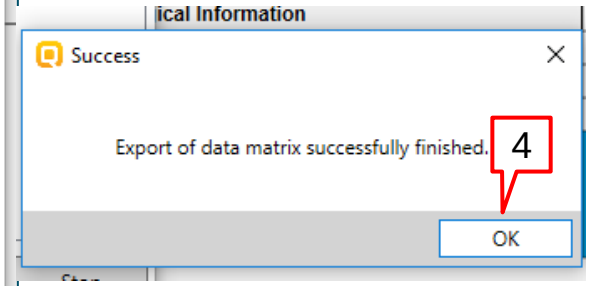
Export of the results

1. Expand structure info to add Chemical name(s) (1).
2. Example Prioritization Scheme (PBT) is selected by default (2).
3. Click on *Export* (3).



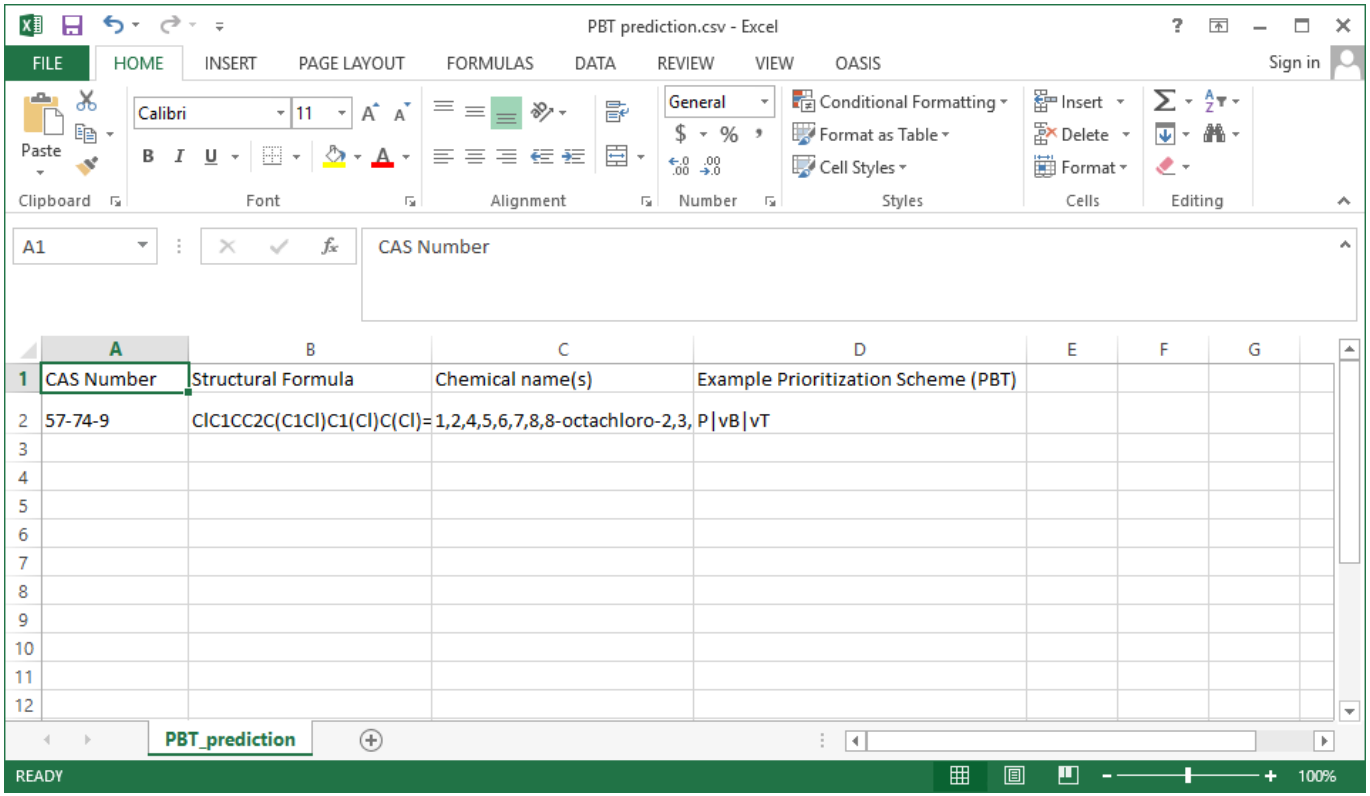
Export of the results





1. Type in the name of the file (1).
2. The files are only saved in *.csv* format(2).
3. Click on *Save* (3).
4. Click on *OK* the confirmation message (4).

Export of the results



The file can be open as an Excel sheet.