

## 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

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- **PBT scheme**
  - **Background**
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# 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	$BOD \leq 30\%$	REACH Annex XIII [1]	Experimental data only
P	$30\% < BOD \leq 40\%$ or biodegradation probability $< 0.5$	REACH Annex XIII [1]	Experimental data and BIOWIN 5 and 6 models
vB	$BCF \geq 3.699 \log(L/kg \text{ wet})$	REACH Annex XIII [1]	Experimental data and BCFWIN model
B	$3.301 \leq BCF < 3.699 \log(L/kg \text{ wet})$ or $\log Kow > 4.5$	REACH Annex XIII [1]	Experimental data and BCFWIN and KOWWIN models
vT	$LC50 \leq 1 \text{ mg/l}$	GHS classification [2]	Experimental data only
T	$1 \text{ mg/l} < LC50 \leq 10 \text{ mg/l}$	GHS classification [2]	Experimental data only

[1] [https://echa.europa.eu/documents/10162/13632/information\\_requirements\\_r11\\_en.pdf](https://echa.europa.eu/documents/10162/13632/information_requirements_r11_en.pdf)

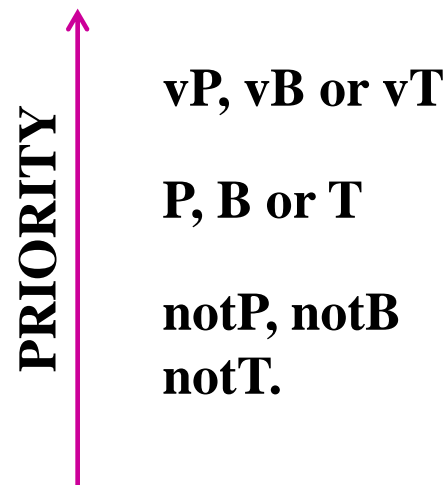
[2] [https://www.unece.org/fileadmin/DAM/trans/danger/publi/ghs/ghs\\_rev04/English/ST-SG-AC10-30-Rev4e.pdf](https://www.unece.org/fileadmin/DAM/trans/danger/publi/ghs/ghs_rev04/English/ST-SG-AC10-30-Rev4e.pdf)

# 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.



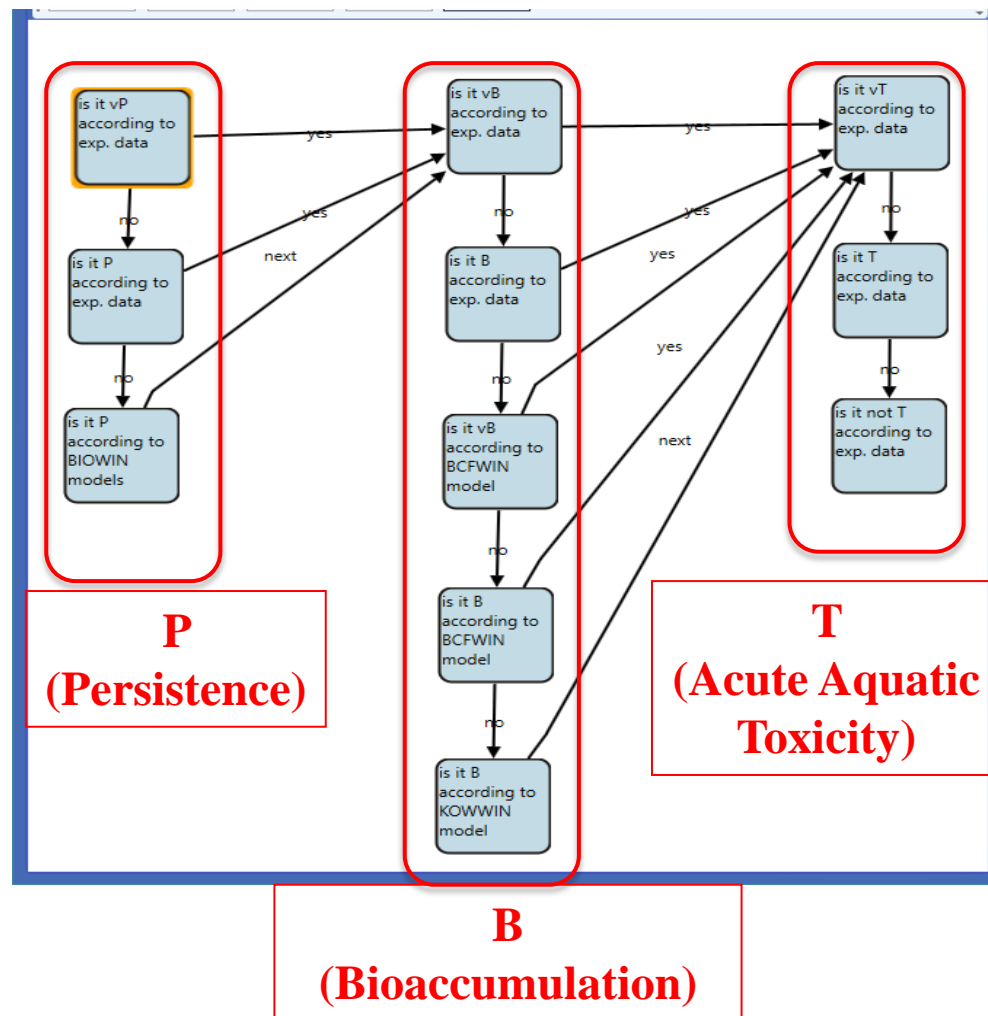
# Outlook

- 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.

The screenshot displays the 'Category tree' and 'Query details' windows. A callout box labeled '1' points to a node in the category tree with the text 'is it vP according to exp. data'. Another callout box labeled '2' points to a query icon in the tree. The 'Query details' window shows a tree of endpoint definitions with 'BOD' selected. Below, the 'Data' section shows a filter for 'BOD <= 30%'.

# Outlook

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# Workflow of the prediction: Steps

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

# Outlook

- Aim
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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:

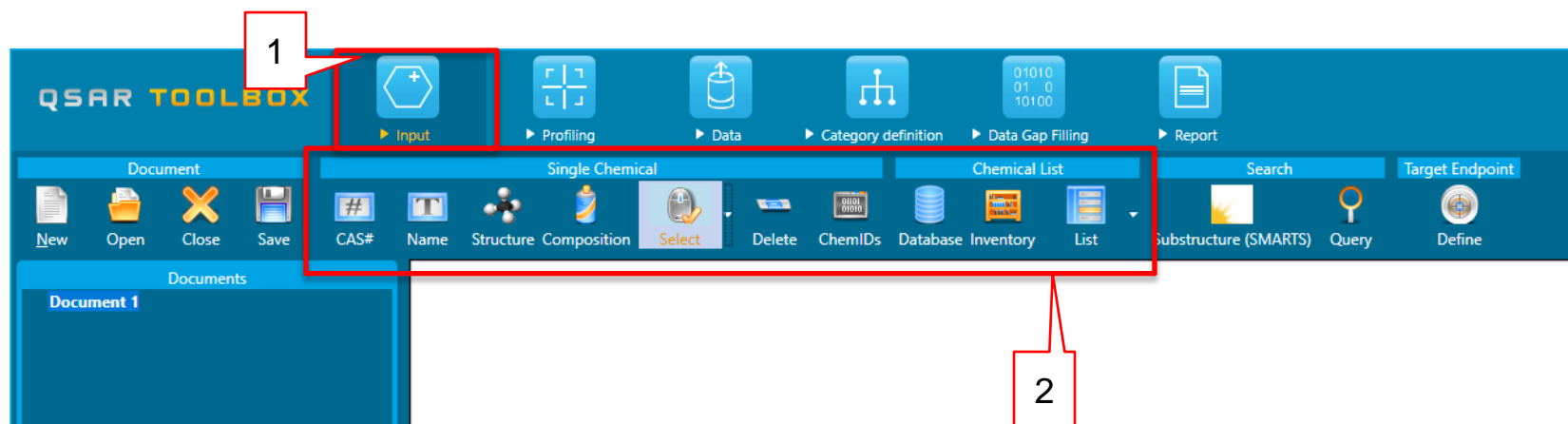
- User's List
- Inventory/Database

## 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).

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 screenshot shows the QSAR Toolbox interface with the 'Single Chemical' tab selected. The 'Filter endpoint tree...' panel is open, displaying a chemical structure and its properties. A red box highlights the '1 [target]' entry in the data matrix, with a callout box containing the number '1'.

1 [target]

57-74-9
High
1,2,4,5,6,7,8,8-tetrachloro-2,3-dibromodibenzofuran
C <sub>10</sub> H <sub>6</sub> Cl <sub>8</sub>
Mono constituent
<chem>C1C1CC2C(C1C1)C1(CI)C(CI)=C(CI)C1</chem>

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

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# 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.

The screenshot shows the QSAR Toolbox Profiling interface. The 'Profiling' tab is selected in the top menu bar (1). In the 'Documents' section, the 'Unselect All' button is highlighted (2). In the 'Profiling methods' list, the 'Example Prioritization Scheme (PBT)' checkbox is checked (3). The 'Apply' button is highlighted (4). On the right, the 'Filter endpoint tree...' panel shows the 'Example Prioritization Scheme (PBT)' expanded, displaying the results 'P', 'vB', and 'vT' (5). A chemical structure is also visible in the 'Structure' panel.

# 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)

The screenshot illustrates the steps for explaining a "P" prediction in the QSAR Toolbox. The main window shows a "Filter endpoint tree..." with a "Structure" field. A "Profiling results" window is open, displaying a tree view for "Chemical 1" with a "P" prediction highlighted. A "Details" button is visible at the bottom of this window. A pop-up window labeled "Explain" is shown over the "P" prediction, with a chemical structure of the target displayed above it. Red callout boxes with numbers 1 through 5 indicate the sequence of actions: 1. Clicking on the "P" prediction; 2. Clicking the "Explain" button; 3. The "Profiling results" window appearing; 4. Selecting the "P" prediction; 5. Clicking the "Details" button.

# 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).

The screenshot displays the QSAR Toolbox interface. On the left, a decision tree titled 'Categories' shows three nodes. The top two nodes, 'is it vP according to exp. data', are red with an 'X' and labeled '2'. The bottom node, 'is it P according to BOWIN models', is green with a checkmark and labeled '1'. A yellow border surrounds this node. On the right, the 'Definition' panel shows a logic diagram for '[32] is it P according to BOWIN models'. The diagram consists of several nodes connected by arrows. One node is circled in red and labeled '3'. Below the diagram, the 'Explanation' panel shows the parameter name 'Biodeg probability (Biowin 5)' and an expression '<' with a value of '0.5'. At the bottom of the interface, the calculated value is shown as '-0.2259'.



# 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.

The screenshot displays the QSAR Toolbox interface. On the left, a decision tree under the 'Categories' tab shows a flow from 'is it vP according to exp. data' to 'is it P according to exp. data', and finally to 'is it P according to BIOWIN models'. The final node is highlighted with a green border and a checkmark. A red circle highlights the 'is it P according to exp. data' node. A red arrow points from this node to the 'is it P according to BIOWIN models' node. The 'Explanation' tab at the bottom shows 'Biodeg probability = -0.23' in a red callout box, with the calculated value '-0.2259' below it.

On the right, the 'Definition' tab shows a logic diagram for '[32] is it P according to BIOWIN models'. A red circle highlights a node in the diagram. A red arrow points from this node to the 'Parameter Query' tab, which shows the configuration for 'Metabolism'. The 'Parameter name' is 'Biodeg probability (Biowin 5)'. The 'Expression' is set to '<' and the value is '0.5'. A red callout box highlights the value '0.5'.

# 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)

The screenshot shows the QSAR Toolbox interface. At the top, there is a 'Filter endpoint tree...' window with a 'Structure' field and a 'Structure info' button. To the right, a '1 [target]' window displays a chemical structure. Below these, a 'Profiling results' window is open, showing a list of results for 'Chemical 1'. The 'vB' result is selected and highlighted in blue. A red callout '1' points to the 'vB' entry. A red callout '2' points to an 'Explain' button that appears over the 'vB' entry. A red callout '3' points to the 'Structure info' button in the 'Filter endpoint tree...' window. A red callout '4' points to the 'vB' entry in the 'Profiling results' window. A red callout '5' points to a 'Details' button at the bottom of the 'Profiling results' window. The 'Profiling results' window also shows a chemical structure and a 'Close' button.

# 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.

The screenshot displays the QSAR Toolbox interface. The top window shows a decision tree with three nodes. The first node, 'is it vB according to exp. data', is highlighted in green and contains a checkmark, with a red callout '1' pointing to it. The second node, 'is it B according to exp. data', is greyed out, with a red callout '2' pointing to it. The third node, 'is it vB according to BCFWIN model', is also greyed out, with a red callout '3' pointing to it. Below the decision tree is the 'Explanation' panel, which shows the result 'True' and a table of values. The table has columns for 'All values', 'Mean value', 'Min value', 'Max value', and 'Unit (Scale)'. The values listed are 10.8, 12, 970, 21, 559, 448, 31, 4.16, 2.44, and 6.26, all with the unit 'L/kg bdwt'. To the right, the 'Endpoint definition' panel shows a tree structure with 'Bioaccumulation: aquatic' selected, and 'BCF' checked. The 'Test organisms (species)' panel at the bottom shows 'Abarenicola pacifica' and 'Pimephales promelas'.

All values	Mean value	Min value	Max value	Unit (Scale)
10.8				L/kg bdwt
12				L/kg bdwt
970				L/kg bdwt
21				L/kg bdwt
559				L/kg bdwt
448				L/kg bdwt
31				L/kg bdwt
4.16				L/kg bdwt
2.44				L/kg bdwt
6.26				L/kg bdwt

# Profiling: explanation of "vB" prediction

The image shows two screenshots of the QSAR Toolbox interface. The left screenshot displays a list of values under the 'All values' section. The values are: 322, 1.6E+04, 2.8E+04 (highlighted with callout 1), 1.4E+04, 7.5E+03, 1.3E+04 (highlighted with callout 3), and 5.9E+03. Callout 2 points to the expansion arrow next to the 2.8E+04 value. Below the list is a 'Complete data' section with a table. The right screenshot shows the expanded details for the 2.8E+04 value, with callout 4 pointing to the table. The table has columns: Created date, Database, Duration, Effect, Endpoint, Endpoint assigned, and Exposure. The data row shows: 09/08/1998, ECOTOX, Min, Accumulation, BCF, and Publication reported endpoint.

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)

The screenshot displays the QSAR Toolbox interface. At the top, there is a 'Filter endpoint tree...' window with a 'Structure' field. Below it is the 'Structure info' window. The main 'Profiling results' window is open, showing a tree view with 'Chemical 1 (C1C1CC2C(C1Cl)C1(Cl)C(Cl)=C(Cl)C2(Cl)C1(Cl)Cl)' and 'Example Prioritization Scheme (PBT)'. Under 'PBT', there are three items: 'P', 'vB', and 'vT'. The 'vT' item is highlighted in blue and has a red box around it with a callout '4'. Below the 'vT' item is an 'Explain' button with a red box around it and a callout '2'. At the bottom of the 'Profiling results' window, there is a 'Details' button with a red box around it and a callout '5', and a 'Close' button. In the background, there is a '1 [target]' window showing a chemical structure and a list of endpoints: 'P', 'vB', and 'vT'. The 'vT' endpoint is highlighted in blue and has a red box around it with a callout '1'.

# 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).

The screenshot displays the QSAR Toolbox interface. At the top, a decision tree shows a green node 'is it vT according to exp. data' (callout 1) with a checkmark and 'V' sign. Below it are grey nodes 'is it T according to exp. data' (callout 2) and 'is it not T according to exp. data' (callout 3). The 'Explanation' panel (callout 3) shows the following table:

Details	Mean value	Min value	Max value	Unit (Scale)
0.115				mg/L
0.038				mg/L
0.18				mg/L
0.04				mg/L
0.0029				mg/L
0.022				mg/L
0.022				mg/L
0.045				mg/L
0.341	0.298	0.384		mg/L
44				ppb

The right panel shows a 'Data Query' for 'Metabolism' with a filter for 'Ecotoxicological Information' and 'Aquatic Toxicity' checked.

# 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)

The screenshot displays the 'Category tree' window with the title '[38] is it vT according to exp. data'. It features a toolbar with buttons for ADD, DEL, AND, OR, NOT, Copy, Paste, and Redraw. A query icon is highlighted with a red box and the number '1'. Below it, the 'Query details' panel is shown, containing a 'Data Query' section with a 'Save' button and a list of species: 'is 'Oryzias latipes'', 'is 'Cyprinus carpio'', 'is 'Lepomis macrochirus'', and 'is 'Danio rerio''. The 'Descriptors (numerical metadata)' section is expanded to show a table for 'Duration' with fields for Mean value, Min value, Max value, and Unit. A red box highlights this table, with a callout '3' pointing to the 'Unit' field. A red line connects the '1' callout to the 'Query details' panel, with a callout '2' pointing to the panel.

Duration	
Mean value: =	96
Min value: none	
Max value: none	
Unit: Time	h

Data						
	All	Any	Min	Max	Average	Median
Mean value: ≤						1
Min value: none						
Max value: none						
Unit: Mass co...		mg/L				

# 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

Explanation

Result  
Evaluation result: True

All values

Details	Mean value	Min value	Max value	Unit (Scale)
0.115				
0.038				
0.18				
0.04				
0.0029				
0.022				

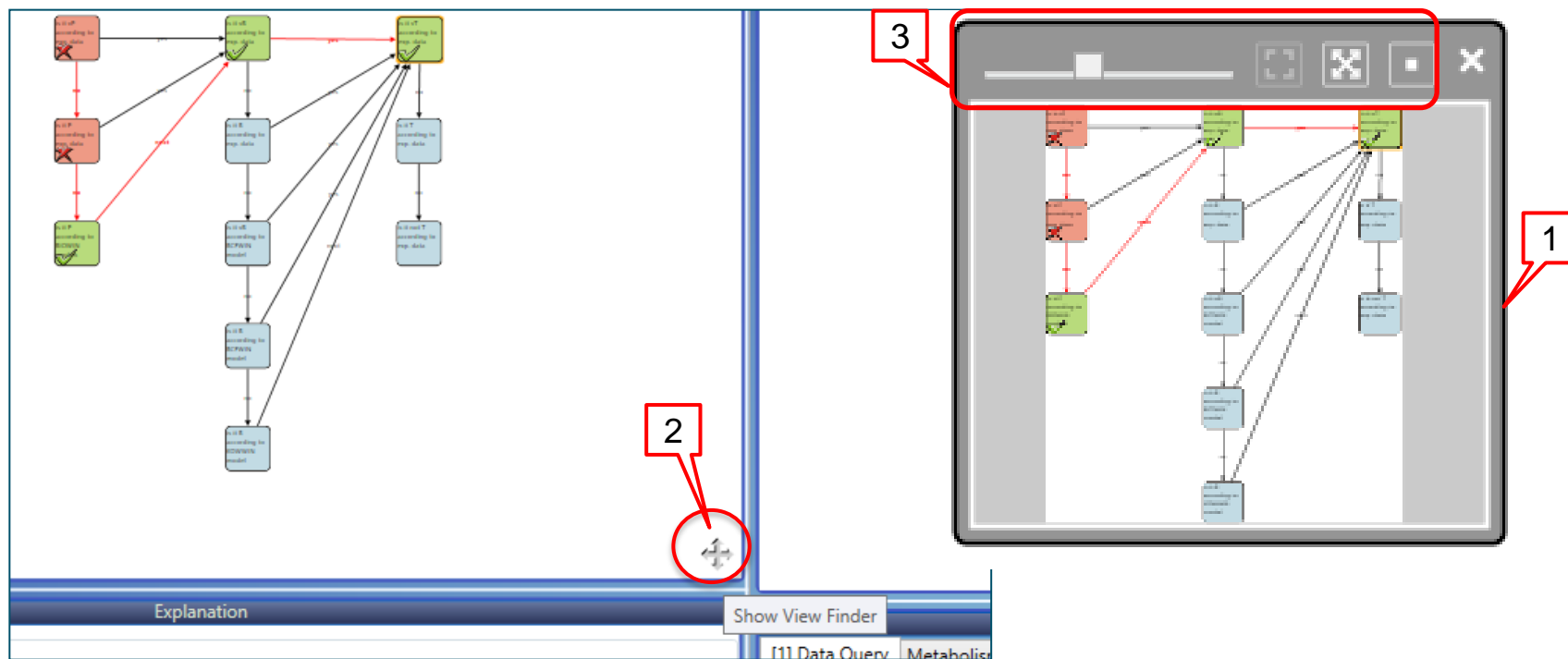
Complete data

Endpoint path: Ecotoxicological Information  
Aquatic Toxicity

Additional comments: O EFCT CONT/OF EQUILIBRIUM// CONTR/NO MORT//WQCD/THE CHD '80 WQCD DATA POI

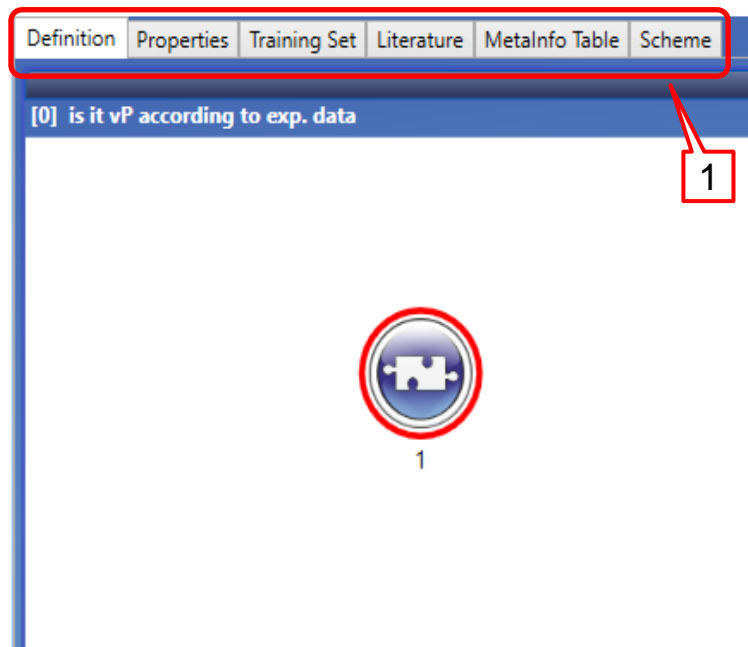


# Profiling: common features of PBT interface



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

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- Workflow of the prediction
  - Chemical input
  - Profiling
- **Export of the results**

# Export of the results

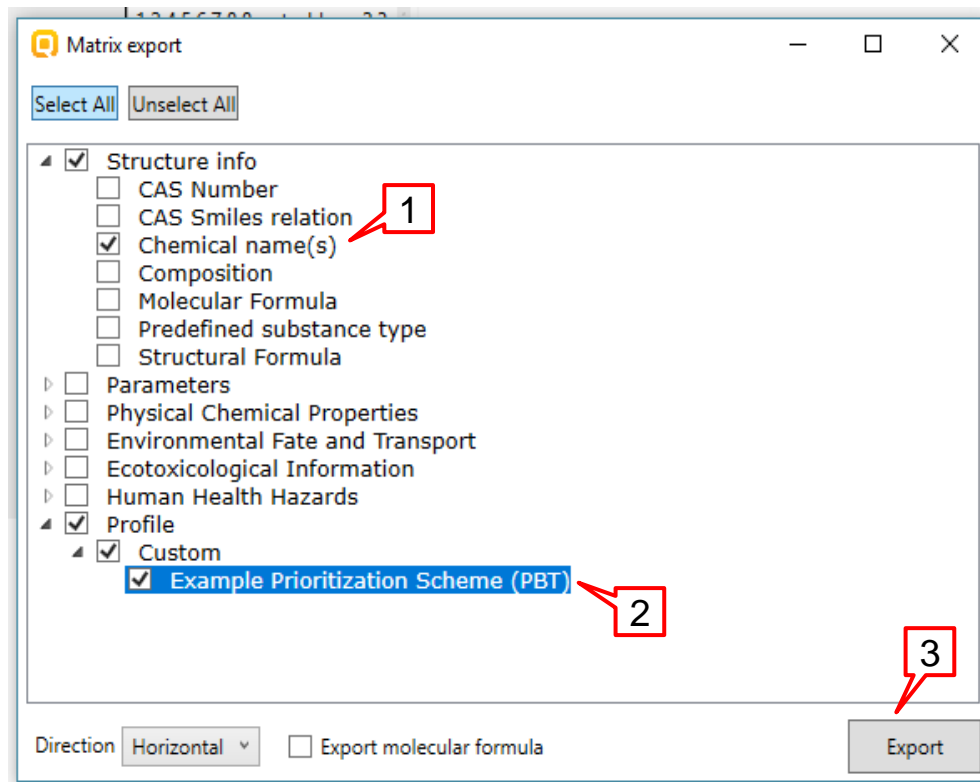
1. Right click next to the name of the scheme (1)
2. Select *Export Data matrix* (2)

The screenshot displays the 'Filter endpoint tree...' interface. On the left, a tree view shows various categories: Structure info, Parameters, Physical Chemical Properties, Environmental Fate and Transport, Ecotoxicological Information, Human Health Hazards, Profile, and Custom. Under 'Custom', 'Example Prioritization Scheme (PBT)' is selected. On the right, a table shows details for the selected scheme, including CAS Number (57-74-9), CAS Smiles relation (High), Chemical name(s) (1,2,4,5,6,7,8,8-octachloro-2,3...), Composition (C10H6Cl8), Molecular Formula (C10H6Cl8), and Predefined substance type (Mono constituent). A chemical structure is shown above the table. A right-click context menu is open over the 'Example Prioritization Scheme (PBT)' entry, with 'Export Data matrix' highlighted. Red callout boxes labeled '1' and '2' indicate the right-click action and the menu selection respectively.

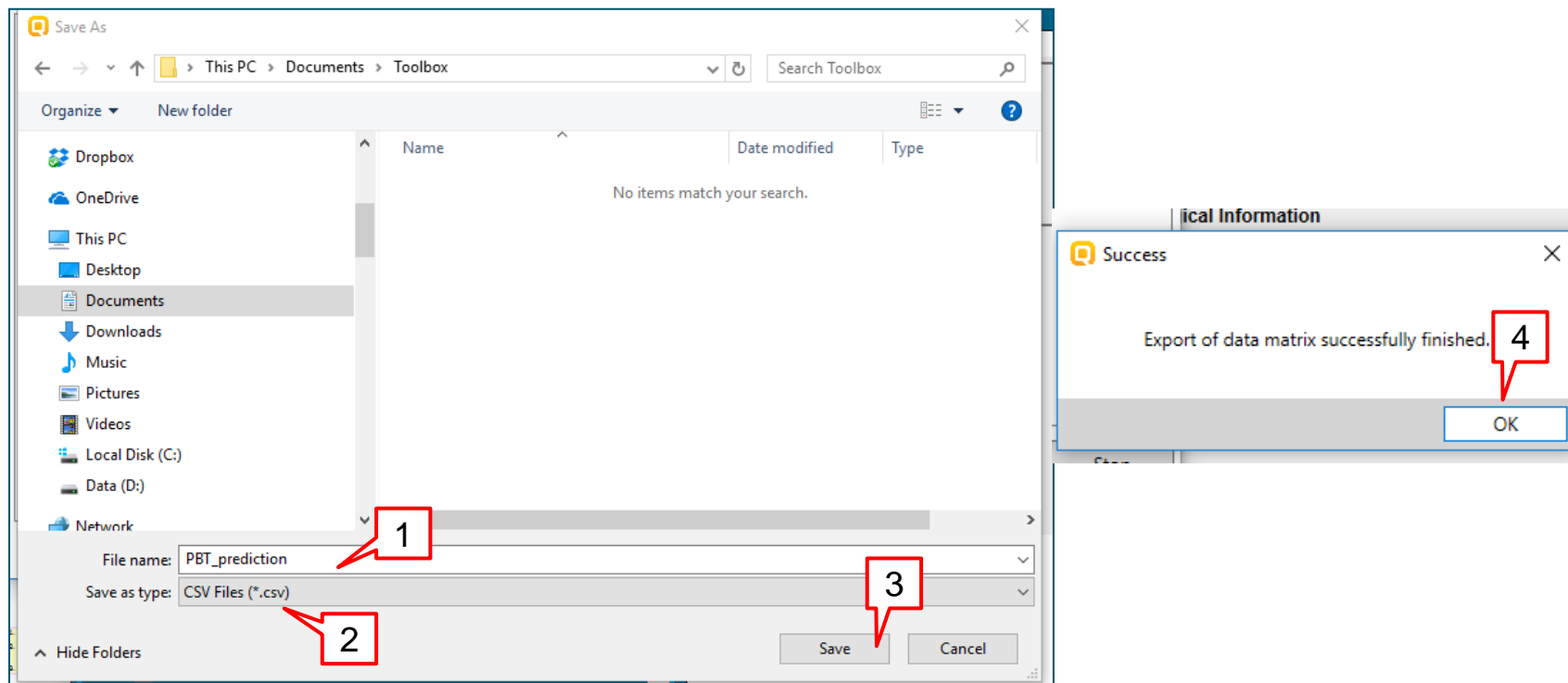
Filter endpoint tree...	1 [target]
Structure	
Structure info	
CAS Number	57-74-9
CAS Smiles relation	High
Chemical name(s)	1,2,4,5,6,7,8,8-octachloro-2,3...
Composition	
Molecular Formula	C10H6Cl8
Predefined substance type	Mono constituent
Structural Formula	C1C1CC2C(C1Cl)C1(C)C(Cl)=C(Cl)
Parameters	
Physical Chemical Properties	
Environmental Fate and Transport	
Ecotoxicological Information	
Human Health Hazards	
Profile	
Custom	
Example Prioritization Scheme (PBT)	

# 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).

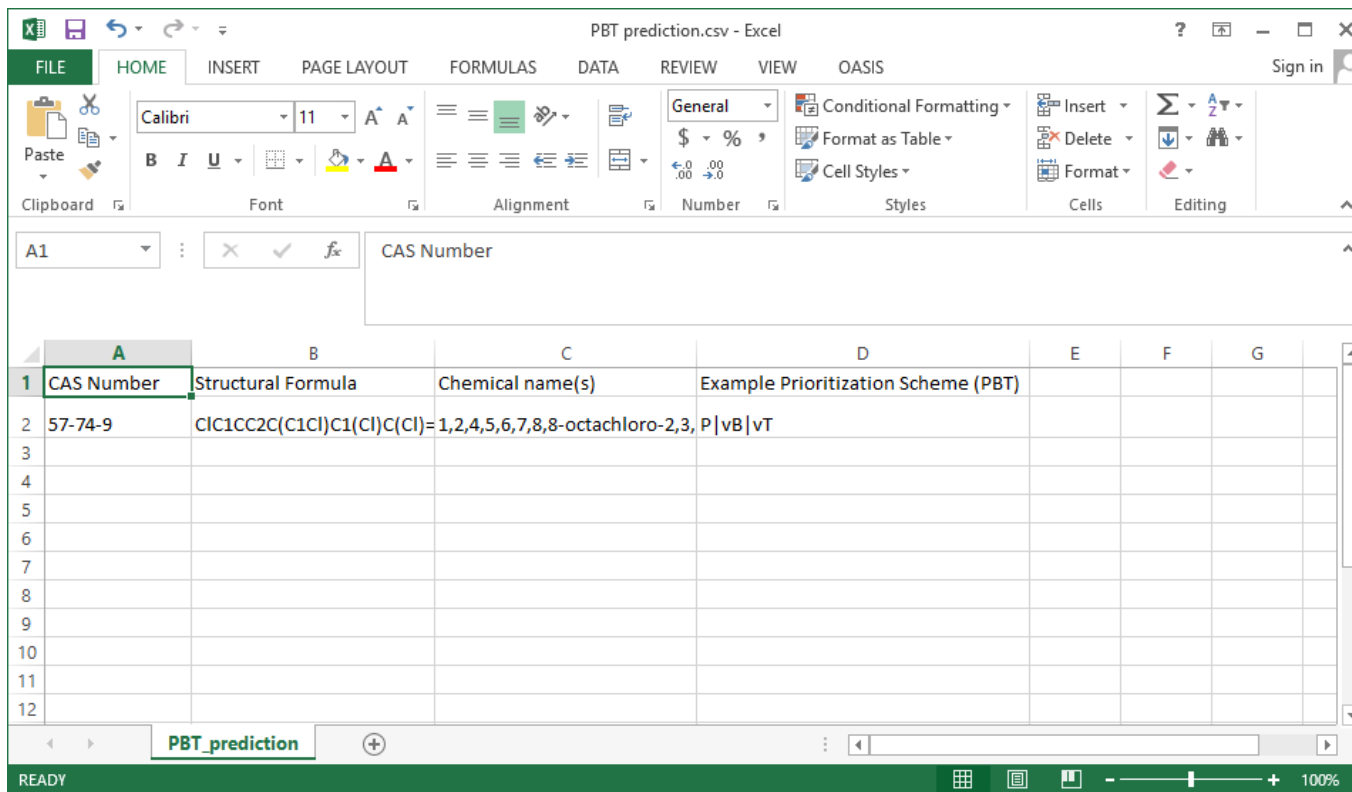


# Export of the results



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.