### QSAR TOOLEOX

The OECD QSAR Toolbox for Grouping Chemicals into Categories

### OECD QSAR Toolbox v.4.4.1

Example for predicting acute aquatic toxicity to fish of a mixture with known components

### **Outlook**

- Background
- Keywords
- Objectives
- The exercise
- Workflow
- Save/Load

### Background

 This is a step-by-step presentation designed to take the user of the Toolbox through the workflow of predicting acute aquatic toxicity to fish of a mixture with known components.

### **Outlook**

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### **Keywords**

**TARGET CHEMICAL -** chemical of interest, in this case this is mixture with define components

**MODULE –** a Toolbox module is a section dedicated to specific actions and options

WORKFLOW - the use, in combination, of the different modules (e.g. prediction workflow: from input to report)

**PROFILER** - algorithm (rule set) for the identification of specific features of the chemicals. Several types of profilers are available, such as structural (e.g. Organic functional groups), mechanistic (e.g. Protein binding by OECD) and endpoint-specific (e.g. in vitro in vitro mutagenicity (Ames test) alerts by ISS) profilers.

**ALERT** - the profilers consist of sets of rules or alerts. Each of the rules consists of a set of queries. The queries could be related to the chemical structure, physicochemical properties, experimental data, comparison with the target or list with substances and external queries from other predefined profilers (reference queries).

**CATEGORY** – "group" of substances sharing same characteristics (e.g. the same functional groups or mode of action). In a typical Toolbox workflow, it consists of the target chemical and its analogues gathered according to the selected profilers

**ENDPOINT TREE** – Endpoints are structured in a branched scheme, from a broader level (Phys-Chem properties, Environmental Fate and transport, Ecotoxicology, Human health hazard) to a more detailed one (e.g. EC3 in LLNA test under Human health hazard-Skin sensitization)

**DATA MATRIX** – Table reporting the chemical(s) and data (experimental results, profilers outcomes, predictions). Each chemical is in a different column and each data in a different row

**MOAD of ACTION(MOA)** – profiling pattern of the chemicals available on data matrix with respect to the applied profilers

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### **Objectives**

- This presentation reviews a number of functionalities of the Toolbox:
  - The 2D editor for defining Mixture components
  - Filling data gaps by Similar mode approach

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### **Exercise**

#### $\succ$ In this exercise we will:

- predict the aquatic toxicity to fish (LC50, mortality, 96h, *Pimephales promelas*) of a target substance which represents a mixture with defined constituents;
- investigate the mode of action of constituents of the mixture;
- gather available experimental data for target and its constituents;
- Predict acute aquatic toxicity using Similar mode approach.

The target substance will consists of three constituents with quantities as follows:



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### Workflow

- The Toolbox has six modules which are used in a sequential workflow:
  - Input
  - Profiling
  - Data
  - Category Definition
  - Data Gap Filling
  - Report

### **Outlook**

- Background
- Keywords
- Objectives
- The exercise
- Workflow
  - Input

### **Input** Overview

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

### **Input** Input chemical(s)

#### Alternative ways to input chemical(s):

A.Single target substance

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

**B**.Group of chemicals

- User List/Inventory
- Specialized Databases

### Input Input Screen



The OECD QSAR Toolbox for Grouping Chemicals into Categories

### **Input** Input a mixture

- In the current example our target substance will be a mixture.
- We will draw its components within the "Composition" tool.
- Consecutively, the quantities of the mixture components will be defined.

### **Input** Input target substance by drawing

QSAR TOOLBOX			
	▶ Input ▶ Profiling ▶	Composition editor	– 🗆 🗙 🔜 🛶
Document New Open Close Save Documents ♥ Document 1	Input Profiling Single Chemical CAS# Name Structure Composition Select	Constituents (0) Impurities (0) Additives (0)	- C X 2 3 Remove
			OK Cancel
1. Click on the	<b>Composition</b> button;		

- 2. Select "Multiconstituent" from the drop-down menu for the type of the substance;
- 3. Click **Add** in order to add constituent. Our target substance consists of three constituents, so <u>click</u> <u>three times</u> on the Add button.

Constituent 1



### Drawing Constituent 1 of the target mixture

Weight = 90%

			<ul><li>2D</li></ul>	) Editor	3	– o x
Composition editor		2	SMILE	ES/inchi v 0		x _
	ldentity —					$, \mathbf{O} \equiv \mathbf{N},$
	CAS:			Rectangle Y		
	lype: Name:	Multiconstituent				
	IUPAC:					
	Synonyms:				🦲 Clear A	All X
	SMILES:			OH2		
Constituents (1) Impur	ities (0) Additi	ives (0)	С			Want to clear eventhing?
	dentity		Ν			Han to clear creifannig.
OH <sub>2</sub>	CAS:		0			
	ype: N	Aonoconstituent *	S		$\neg /$	Yes No
	UPAC:		F		4	
e e e e e e e e e e e e e e e e e e e	ynonyms:	Edit	Р			
	MILES: O	Edit	CI			
l ' ſ	oncentration -		Br			
	Typical conce	entration				OK Cancel
	×	Family: Mass V Unit: V				
	Concentratio	n range				
	¥	v Family: Mass v Unit: v				
	L		J			

- 1. Click Edit on the SMILES row to define the structure of the first constituent;
- 2. The 2D editor appears;
- 3. Click the Clean button to clean everything;
- 4. Confirm with **Yes**.

Drawing Constituent 1 of the target mixture

2D Editor		– 🗆 X
$\odot$		
Smiles v CCCCO		X
<b>F</b>		
Snap Line	Object ex	xplorer X
	Atom: O	
	1	
	Element:	0 ~
H <sub>3</sub> C V OH	Charge:	0 ~
	Hybridization:	undefined $\vee$
	Valent state:	v4 ~
s <b>3</b>	Isotope:	0
F	Implicit hydrogens:	3
P	Atom number:	6
	Aromatic:	False
Select the Drawing tool;	Parity:	None
Draw carbon chain with five carbon atoms; Click on the oxygen symbol (i.e. <b>O</b> );	Radical:	undefined 5
Click over the last carbon atom to change it to oxygen; Confirm with <b>OK</b> .		OK Cancel

Constituent 1



Weight = 90%

1. 2.

3.

4.

5.

### Define quantities of mixture`s constituents

- Quantities of the constituents should be added manually.
- There are several ways to add mixture quantity:
  - Mass fraction
  - Mass
  - Amount of substance
  - Molality
  - Mole fraction
  - Mass concentration
  - Molar concentration
- In the current example we will select "Mass fraction %" in "Weight %"

Mass fractionMassAmount of substanceMass fractionMolalityMole fractionMass concentrationMolar concentration

### **Input** Define the quantity of Constituent 1



Weight = 90%

H<sub>2</sub>C<sub>2</sub>

Constituent 1

### **Input** Drawing Constituent 2 of the target mixture



Weiaht = 1%

Composition editor	lelentite.	2	2	SMILES/Inchi × 0
	CAS:			
	Type:	Multiconstituent		Partanda X
	Name:			
	IUPAC:		=1	
	Synonyms:		= [	
	SMILES:		니는	
Constituents (3) Impurit	ties (0) Additiv	ac (0)	귀불	Clear All X
			<b>-</b> (	0H2
OH2 CH2 CH2 CH2 CH2 CH2 CH2 CH2 C	entityAS: AS:MI IPAC: MILES: O oncentration Typical concen	tration		C Want to clear everything? W Ves No F P Cl Br
				OK Cancel
	-Concentration	range Family: Mass fraction × Unit:	~	

Now we move down to the second constituent and repeat the same steps:

- 1. Click Edit on the SMILES row to define the structure of the second constituent;
- 2. The 2D editor appears;
- 3. Click the **Clean button** to clean everything;
- 4. Confirm with **Yes**.

Constituent 2



Weight = 1%

### Drawing Constituent 2 of the target mixture

2D Editor Х  $\bigcirc$ C1=CC(=C(C(=C1C(C)=O)CI)CI)CI Smiles x .... Select the Benzene scaffold (1a) and paste it into Make first C ~ the drawing pane (1b). 2а Select the Drawing tool (2a) and draw the **2b** connections to the benzene (2b). Second click over a bonds converts it to double bond. CI Click on the oxygen symbol (i.e. **O**) (3a) and click **1a** over the carbon atom connected with double bond **4b** (3b). **1b** Click on the chlorine symbol (i.e. **CI**) (4a) and click <u>`</u>CI over the carbon atoms that should be changed (3b). 3a Confirm with **OK** (5). H<sub>3</sub>C 0 Isotope: 3 Implicit hydrogens: **3b** 6 Atom number: False Aromatic: **4a** Parity: None Radical: undefi 5 OK Cancel

### **Input** Define the quantity of Constituent 2



Constituent 2



**Constituent 3** 



### Drawing Constituent 3 of the target mixture

Weight = 9%

Composition edit	tor	[
	CAS: 2	
Constituents (3) Im	IUPAC:	Rectangle ·
OH2 2 3	Identity       CAS:       Type:       Monoconstituent       Name:       IUPAC:       Synonyms:       SMILES:       O       Edit       SMILES:       Concentration       Typical concentration       V       Family:       Mass fraction       V	C C Want to clear everything? V Ves No F 4
	Concentration range	OK Cancel
	Family: Mass fraction v Unit: v	

Now we move down to the last (third) constituent and repeat the same steps:

- 1. Click **Edit** on the SMILES row to define the structure of the second constituent;
- 2. The 2D editor appears;
- 3. Click the Clean button to clean everything;
- 4. Confirm with **Yes**.

### Drawing Constituent 3 of the target mixture

2D Editor  $\times$ **2a**  $\bigcirc$ SMILES/Inchl =C(C=C1)C(C1=CC=CC=C1)=O x .... Select the Benzene scaffold (1a) and paste it two **3b** times in the drawing pane (apply two left clicks) **2b** (1b). **1a** Select the Drawing tool (2a) and draw connection between both rings (2b). Double click over a bond converts it to double bond. Click on the oxygen symbol (i.e. O) (3a) and click over the carbon atom connected with double bond (3b). **3a** Confirm with **OK** (4). 1b 4 OK Cancel

#### **Constituent 3**



Weight = 9%

### **Input** Define the quantity of Constituent 3

Composition editor  $\times$ Identity CAS: Multiconstituent Type: Name: IUPAC: Synonyms: Edit SMILES: Edit Constituents (3) Impurities (0) Additives (0) Add Identity Remove CAS: For Constituent 3 of the target 0,0 Type: Monoconstituent mixture define: Name: 1) Family: Mass fraction IUPAC: Edit 2) Unit: weight % Synonyms: SMILES: O=C(c1ccccc1)c1ccccc1 3) qualifier: Equal to (i.e. =) 2 3 Concentration 4) quantity: 9 Typical concentration Family: Mass fraction Unit: weight % 9 3 entration ra Δ Family: Mass fraction ~ Unit: v 5 OK Cancel

Now all three constituents of the target mixture are defined. Click **OK** (5).

Constituent 3

Weight = 9%

### **Input** Target substance identity



## Define target endpoint - overview

- The Define target endpoint functionality allows entering the endpoint of interest e.g., EC3, LC50, gene mutation etc.
- The relevant profiles and databases become highlighted in color once the targeted endpoint is preliminary defined by this functionality;
- Calculation of alert performance (AP) is only possible if the target endpoint is preliminary defined;
- There are different ways for defining the target endpoint (via the button from the Input module or by right click from the endpoint tree). For more details press F1 button in order to see the online help.

### **Input** Define target endpoint



### **Input** Define target endpoint



### **Input** Mixture decomposition

- In the current example we will predict the aquatic toxicity of a mixture based on its constituents.
- A specific option "Decomposition" allows all constituents of a mixture as well as available additives/impurities to be shown in the data matrix.
- Once the constituents are on the data matrix, the user can handle them as individual substances and further, to use them for predicting the whole mixture.

### **Input** Mixture decomposition



### **Input** Mixture decomposition



### **Outlook**

- Background
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#### • Workflow

- Input
- Profiling

### **Profiling** Overview

- "Profiling" refers to the electronic process of retrieving relevant information on the target compound, other than environmental fate, ecotoxicity and toxicity data, which are stored in the Toolbox database.
- The available information includes likely mechanism(s) of action, as well as observed or simulated metabolites.
- For most of the profilers, background information can be retrieved by selection of a profilers (for example, Acute aquatic toxicity MOA y OASIS) and then click on "About" or "View" (see the next slide).

### **Profiling** Side-Bar to Profiling



### **Profiling** Side-Bar to Profiling



### **Profiling** Profiling the target substance



### **Profiling** Profiling the target substance

- The actual profiling will take several seconds depending on the number and type of selected profilers.
- The results of profiling automatically appear as a dropdown box under the target substance.
- In this example the target mixture and its constituents are profiled by all profilers defined as suitable (highlighted in green) for aquatic toxicity:
  - Acute aquatic toxicity classification by Verhaar (Modified);
  - Aquatic toxicity classification by ECOSAR;
  - US-EPA New Chemical Categories;
  - Acute aquatic toxicity classification MOA by OASIS.

### **Profiling** Profiling the target substance



### **Outlook**

- Background
- Keywords
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- The exercise
- Workflow
  - Input
  - Profiling
  - Data

### Data

- "Data" refer to the electronic process of retrieving the environmental fate, ecotoxicity and toxicity data that are stored in the Toolbox database.
- Data gathering can be executed in a global fashion (i.e., collecting all data of all endpoints) or on a more narrowly defined basis (e.g., collecting data for a single or limited number of endpoints).
- In case of defined endpoint, the databases containing data for this endpoint, will be highlighted in green. The user could select all or just some of them.
- In this example, we will use all highlighted databases.

### **Data** Gather data



### **Data** Available experimental data

QSAR TOOLEOX	P C I J C C C C C C C C C C C C C C C C C	Category definition ▶ Category definition ▶ Data Gap Filling ▶ Report	× • • ∧ • ₽ ₽ ₽
Data Import Export	Delete		The OECD QSAR Toolbox for Grouping Chemicals into Categories
	Filter endpoint tree		Developed by LMC, Bulgaria
Documents      Databases     Databases     Selected      Select All     Unselect All     Invert      Select All     Unselect All     Invert      Select	Structure		
Aquatic Japan MBE V Aquatic QASIS V EQHA REACH V ECOTOX Food TOX Hazard EFSA TOX Human Health Hazards	Inhibition of Total R     Boblity     Mobility     Hortality     The Interview of the	242 points added across 3 chemicals. MS: 300 mg/L MS: >100 mg/L MS: 194E+03 mg/L	
		OK         Ms: 9.38-c03 mg/L           MS: 0.45 % v/v         MS: 0.45 % v/v           2/18         MS: 5 mg/L         MS: 500 mg/L           1/1         MS: 88+122 mg/kg         MS: 1.94E+03 mg/L           2/3         MS: 5 mg/L         MS: 1.94E+03 mg/L	
	Animalia (animals)	Image: spin regel fishes       1/1       242 experimental results for aquatic toxicity available for the three mixture`s constituents.         Image: spin regel fishes       1/2       MS: 1E-03 mg/L	are
<ul> <li>Inventories</li> </ul>	Oryzias latines     Pimephales promelas     Undefined Enapole     Orgenia reticulata	1/2         MSi >10 mg/L         MSi 10.9 (9,64+12.3) mg/L         MSi 1.99 mg/L         MSi 1.38E+03 mg/L           3/19         MSi 10.9 mg/L         MSi 1.99 mg/L         MSi 1.4E+03 mg/L         MSi 1.4E+03 mg/L           1/2         MSi 0.991+62.4 mg/L         MSi 1.74E+03 mg/L         MSi 1.74E+03 mg/L           2/2         MSi 155 mg/L         MSi 1.74E+03 mg/L	
	Undefined Kingdom - t 4+5 d - t 31 d	1/1         MS: 5 mg/L           1/2         MS: 2.1E+03 mg/L           1/1         MS: 8.66 mg/L           1/2         MS: 5.56 mg/L           1/8         MS: 33.1 mg/L	1
4	C 31-33 d	19 out of 242 data points are experimental data for the investigated endpoint: LC 50;96h; <i>Pimephales promelas</i>	×

### Recap

- We have entered a mixture with three constituents. The quantity of each constituent has been defined.
- The profiling results showed the same mode of action for the three constituents of the mixture.
- We have collected the available aquatic toxicity experimental data for the constituents of the target mixture. 19 experimental results for the defined target endpoint have been found.
- Now we are ready to continue with next step of the workflow Data Gap Filling.

### **Outlook**

- Background
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  - Input
  - Profiling
  - Data
  - Data Gap filling

### **Data Gap Filling** Overview

- "Data Gap Filling" module give access to two different data gap filling tools:
  - Independent MOA- all components are with different mode of action
  - Similar MOA- all components are with similar mode of action
- More details about different MOAs could be found in F1 (also more details are given on next six slides)
- In this particular case all components of the current mixture are with similar mode of action. In this respect Similar MOA is applied

### **Data Gap Filling** Independent MOA

**Assumption** – combined effect can be calculated from the effects caused by the individual mixture components by following the statistical concept of independent random events

Mixture response:  $E(\mathbf{e})$ 

$$C_{Mix}$$
) = 1 -  $\prod_{i=1}^{N} [1 - E(C_i)]$ 

3.7

 $E(C_{Mix})$  - the effect provoked by the total mixture

 $E(C_i)$  - the effects that the individual components would cause if applied singly at that concentration at which they are present in the mixture

**Problem -** dose-response relationships are practically unknown

### Data Gap Filling Similar MOA

**Assumption** – components in a mixture contribute to the joint effect, in proportion to their prevalence and individual potency

- Components act at the same target site
- Components act by the same mechanism
- Components have similar effect (rather than mechanism)

Method for calculation of toxic effects of a mixture with components acting by same mechanisms is given on next slide

### Data Gap Filling Similar MOA

### **Toxicity Equivalence Factor**



*i* – index (reference) chemical

 $ED_{resp}$  – dose (concentration) of a chemical that cause a specified response (fraction of animals that respond, fractional change in a measured physiological value, etc.)

#### **Toxicity Equivalent Concentration**

 $TEC_j^{(i)} = TEF_j^{(i)}d_j$ 

Dose (concentration) of the reference chemical *i* that will cause the same effect as chemical *j* at dose (concentration)  $d_i$ 

#### Index Toxicity Equivalent Concentration

$$ITEC = \sum_{j=1}^{J} TEC_{j}^{(i)} = \sum_{j=1}^{J} TEF_{j}^{(i)}d_{j}$$

Equivalent dose (concentration) of the reference chemical *i* that will cause the same effect as the mixture

### Data Gap Filling Similar MOA

**Toxic effect of mixture -** response (fraction of animals that respond, fractional change in a measured physiological value, etc.) as a result of exposure to mixture



$$Effect^{Mixture} = f_i(ITEC)$$

 $f_i$  - dose-response function of the index chemical

Illustration of calculating effect of mixture is given on next two slides

### **Data Gap Filling** Similar MOA (Illustration)

Reference chemical: Component 1 (i = 1)



### **Data Gap Filling** Similar MOA (Illustration)

Reference chemical: Component 1 (i = 1)



The OECD QSAR Toolbox for Grouping Chemicals into Categorie

### Data Gap Filling Case study

- In this particular case all components of the current mixture are with similar mode of action. In this respect Similar MOA is applied
- Application of Similar MOA for our case study is illustrated on next slides

### **Data Gap Filling** Apply Similar MOA



- 1. Highlight the data box corresponding to *Pimephales promelas/LC50/96h* under the target substance;
- 2. Click on **Similar MOA** button.

### **Data Gap Filling** Apply Similar MOA

QSAR TOOLBOX	put	Prince or 6 Note Gap Filling > Report		
Gap Filling Discrete Control of			Possible data inconsistency      Metadata     Duration	<ul> <li>The OECD QSAR Toolbox for Grouping Chemicals into Categories</li> <li>Developed by LMC, Bulgaria</li> </ul>
Documents	Filter endpoint tree	Parent chemical [target] Constituent #1	▷ Effect	^
Data Gap Filling Settings     Only endpoint relevant     At this position:	Structure	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	<ul> <li>▶ Endpoint</li> <li>▶ Kingdom</li> <li>■ Native scale/unit</li> <li>■ Mg/L (2 chemicals; 10 data)</li> <li>■ Mg/L (3 chemicals: 3 data)</li> </ul>	
Automated workflows 0 Standardized workflows 0	Inhibition of Total Respiration     Introxication     Mobility	1/2         MS: 31.6 mg/L           2/12         MS: 0.28 (0.21÷0.37) mg/L           2/12         MS: 4.47 mg/L	Lyg/L (3 chemicals; 6 data)     Phylum     Superclass     Test organisms (species)	
		1/2 1/1 1/1 1/1 2/8 MS-76 mm/l	Pimephales promelas (3 chemicals; 19 data)  Select scale/unit to use	
		2/18         MS: 5 mg/L           1/1         MS: 88+122 mg/L           2/3         MS: 5 mg/L	ofer 10 mative data and 15 converted     log(1/mol/L) [0 native data and 19 converted]     mg/L [10 native data and 5 converted]	^
	Animalia (animals)     Animalia (animals)     Animalia (animals)     Ghordata (chordates)     Ghordata (chordates)     Ghordata (chordates)	1/1	<ul> <li>mol/L [3 native data and 16 converted]</li> <li>mol/m<sup>3</sup> [0 native data and 19 converted]</li> <li>µg/L [6 native data and 13 converted]</li> </ul>	v
	Alburnus alburnus     Clepomis macrochirus     Cleuciscus idus     Cleuciscus idus     Cleuciscus idus	1/2 1/1 1/1 1/2 MS: >10 mg/L	Converted data 10 from scale/unit mg/L 3 from scale/unit mol/L	^
	Pimephales promelas	3/19 MS: 10.9 (9.64+12.3) mg/L MS: 10.9 mg/L	6 from scale/unit μg/L	~
	Undefined Endpoint     Decilia reticulata     Undefined Kingdom     Undefined Kingdom     4+5 d	1/3         MS: 0.03 mg2           1/3         MS: 0.091+62.4 mg/L           2/2         MS: 15.5 mg/L           1/1         MS: 56 mg/L           1/2         MS: 15.5 mg/L	Chemicals 3/3; Data 19/19 OK Cance M5: 2.1E+03 mg/L	el

The user will be informed if there is different experimental data in the appeared window. In our case there are 3 chemicals with 19 data belonging to 3 different units: mg/l; mol/l and  $\mu$ g/l. The data could be converted each other. By default for the gap filling is used log (1/mol/L) unit, which is a expected mathematical expression for linear relationships. Click **OK** 

### **Data Gap Filling** Results of Similar MOA

QSAR TOOLBOX	ut Profiling	► Data	Category definition	01010 01 0 10100 Data Gap Filling	Report					
Gap Filling Workfle	ow D									The OECD QSAR Toolbox for Grouping Chemicals into Categories
Trend analysis Read across (Q)SAR Standardized A	Automated									Developed by LMC, Bulgaria
<ul> <li>Documents</li> </ul>	Filter endpoint tree	<b>Y</b>	Parent chemical Constit	uent #1 Constituent #2	Constituent #3					
<ul> <li>Data Gap Filling Settings</li> </ul>			~~~~~~ <u>~</u> ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~							
✓ Only endpoint relevant	Structure		C		нус					
At this position:			စံုစ							
QSARs 0		nordata (chordates)								
Automated workflows 0 Standardized workflows 0		Actinopterygli (ray-finned     E Alburnus alburnus 1/2			MS: 2.3E+03 mg/L					
In nodes below:		Lepomis macrochirus 1/1			MS: 100 (100÷50					
QSARs 0		teuciscus idus 1/1     Tryzias latipes 1/2	MS: >1	0 mg/L	MS: TE+03 mg/L					
Automated workflows 0 Standardized workflows 0		- Pimephales promelas								
		LC50 3/19 Undefined End.,, 1/3	MS: 10 MS: 0.9	.9 mg/L _MS: 1.99 mg/L 191÷62.4	MS: 1.38E+03 m					
		Poecilia reticulata 2/2	MS: 15	.5 mg/L	MS: 1.74E+03 m					
		atyhelminthes (flatworms) 1/1 fined Kingdom 1/2	MS: 5 r	ng/L	MS: 2.1E+03 (1.9					
		1/1	MS: 8.6	i6 mg/L						
	- ⊕ 7 d	1/8	MS: 5.8	1 mg/L						
	-+ 31+33 d	1/2	MS: 3.3	11 mg/L			J <b>1</b>			
	L== 32 d <	1/2	MS-33	12 ma/l			4			>
	<b>D</b> 11				Decelses	contration addition for LC50, bared o	n 2 valuer			Colort / Else data
	Descriptors				Predicte	d: 82.9 mg/L	il 5 values			Select / filter data
	Prediction								•	Descriptors / data
		-								Calculation options
		₩ 2 2								Visual options
		/[)60								Information
		CO 10								Miscellaneous 🤈
		~ •								
		0.8 1	1.2	1.4 1.6	1.8	2 2.2 2.4	2.6 2.8	3 3.2	3.4 3.6	
		Active descriptor X log Kow	~			log Kow			(	Accept prediction
										×

#### 1. Predicted result is 82.9 mg/l; 2. Click Accept prediction

### Data Gap Filling Results

- The components of the mixture have the same mode of action.
- By accepting the prediction the data gap is filled (see next screen shot).

### **Data Gap Filling** Predicted value for LC50

QSAR TOOLBOX	+		Ê	<b>H</b>	01010 01 0 10100	E					X e h e e E
Gap Filling	► Input	Protiling	P Data	Category definition	Data Gap Filling	► Report					The OECD QSAR Toolbox for Grouping Chemicals into Categories Developed by LMC, Bulgaria
Documents		Filter endpoint tree			Parent chemic	al [target]		Constituent #1	Constituent #2	Constituent #3	^
	MOA)	Structure			HgC	~ <u>~</u> ~	مړه	ÔŢÔ		Н <sub>3</sub> СОН	
		+ Inhibition of Tota	al Respiration		1/2		1	MS: 31.6 mg/L			
		+ Intoxication	arrespiration		2/12			MS: 0.28 (0.21+0.37) mg/L	•	MS: 300 mg/L	
		+ Mobility			2/12			MS: 4.47 mg/L		MS: >100 mg/L	
		- Mortality									
		- 🛨 1 h			1/2					MS: 1.94E+03 mg/L	
		+ 3 h			1/1					MS: 9.33E+03 mg/L	
		+ ± 4 h			1/1					MS: 0.45 % v/v	
		± 24 h			2/19			MS: 7.6 mg/L	•	MS: >500 mg/L	
		48 h			2/18			MS: 5 mg/L	•	MS: 500 mg/L	
<u></u>		1 00 h			1/1			MS: 88÷122 mg/kg		MS: 1945: 02 mg/l	
<ul> <li>Data Gap Filling Settings</li> </ul>					2/3			Mis: 5 mg/L		MS: 1.94E+05 mg/L	
			(animals)								
Only endpoint relevant			opoda (arthropods)		1/1					MS: 661 mg/L	
At this position:		- Chor	data (chordates)								
Select a cell with a rigid (bold) path			ctinopterygii (ray-finn	ed fishes,spiny rayed fish	es)						
Automated workflows 0			Alburnus alburnus		1/2					MS: 2.3E+03 mg/L	
Standardized workflows 0			± Lepomis macrochiru	15	1/1					MS: 100 (100+500) mg/L	
			Euciscus idus		1/1					MS: 1E+03 mg/L	
			① Oryzias latipes		1/2			MS: >10 mg/L			
			Pimephales promela	as							
			LC50	(	1/20 SMOA: 82.9 m	ıg/L		MS: 10.9 (9.64+12.3) mg/L MS: 10.9 mg/l	MS: 1.99 mg/L MS: 2 mg/l	MS: 1.38E+03 mg/L MS: 1.4E+03 mg/L	
			Undefined Endp	oint	1/3			MS: 0.991+62.4 mg/L	- Mo. 2 Mg/ 2	instruction ingre	
		4	<ul> <li>Poecilia reticulata</li> </ul>		2/2			MS: 15.5 mg/L	•	MS: 1.74E+03 mg/L	
		Platy	helminthes (flatworms	)	1/1			MS: 5 mg/L			
		Undefine	ed Kingdom		1/2					MS: 2.1E+03 mg/L	
		+ 4+5 d			1/1			MS: 8.66 mg/L			
		- + 7 d			1/8			MS: 5.86 mg/L			
		- + 31 d			1/2			MS: 33.1 mg/L			
		+ 31+33 d			1/2			MS: 3.31 mg/L			~
		<									>
1. Predicted 82.9 m	d va 1g/	alue for	LC50	of the	mixtu	re bas	sed c	on the exp	erimental d	ata of its comp	oonents is <sup>×</sup>

### **Outlook**

- Background
- Keywords
- Objectives
- The exercise
- Workflow
  - Input
  - Profiling
  - Data
  - Data Gap filling
  - Report

### Report

- Remember the report module allows the user to generate a report on the predictions performed with the Toolbox.
- The report can be printed or saved in different formats.
- Generating the report is shown on next screenshots.

### Report



- 2. Click on the cell corresponding to SMOA prediction;
- 3. Click on **Prediction** button. A wizard appears where the user could customize the sections;
- 4. Click Create report.
- 5. Click **OK** on the appeared message; Three report files for the mixture prediction could be generated;
- 6. Select **one of the reports** and click **Open** button.

×

### Report



### **Outlook**

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### Save the prediction result

### **Saving the prediction result**

- Saving functionality allows storing/restoring the current state of Toolbox documents including loaded chemicals, experimental data, profiles, predictions, etc.
- This 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 the file with TB prediction is illustrated on the next screenshots.

### Saving the prediction result



### **Open saved file**

