

## OECD QSAR Toolbox v.3.4

Example for predicting Repeated dose  
toxicity of 2,3-dimethylaniline

# Outlook

- **Background**
- Objectives
- The exercise
- Workflow
- Save prediction

## Background

- This is a step-by-step presentation designed to take the user through the workflow for filling data gap for Repeated dose toxicity by read-across based on an analogue approach.

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# Objectives

**This presentation demonstrates a number of functionalities of the Toolbox:**

- Identify analogues for a target chemical.
- Retrieve experimental results available for those analogues.
- Fill data gaps by read across.

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## The exercise

- In this exercise we will predict the repeated dose toxicity of **2,3-dimethylaniline CAS 87-59-2**
- Define initial category of similar analogues based on US-EPA New chemical categories.
- Gather available experimental data for the target chemical and identified analogues
- Apply read across prediction based on analogue approach

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# Workflow

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

# Outlook

- Background
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- **Workflow**
  - **Input**

# Chemical Input Overview

- 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

### User Alternatives for Chemical ID:

#### A. Single target chemical

- 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
- Chemical IDs such as EC number, EINECS number
- Query Tool

#### B. Group of chemicals

- User List/Inventory
- Specialized Databases

## Getting Started

- Open the Toolbox.
- The six modules in the workflow are seen listed next to "QSAR TOOLBOX".
- **Click** on "Input" (see next screen shot)

# Chemical Input Screen

## Input target chemical by CAS#

The screenshot displays the QSAR Toolbox interface. At the top, the 'Document' menu is open, showing options like 'New', 'Open', 'Close', and 'Save'. A red box highlights the 'CAS#' button in the 'Single Chemical' section, with a callout bubble containing the number '1'. Below the main interface, a blue box contains the instruction '1. Click on CAS#'. The main area displays a 'Structure' field and a tree view of chemical properties including Substance Identity, Physical Chemical Properties, Environmental Fate and Transport, Ecotoxicological Information, and Human Health Hazards.

1. Click on CAS#

# Chemical Input Screen

## Enter CAS# 87-59-2

Selected	CAS	Smiles	Depiction	Names	CAS/Name	2D/Name	CAS/2D
1. Yes	87-59-2	Cc1cccc(C)c1			1:: High 1:: Av 2:: Bi 3:: Ec 4:: El 5: 2:: Low (A) 6: 1:: Av (A) 7: 2:: Bi 8: 3:: High (A)	1:: High 1:: Av 2:: To 3:: Pl 4:: El 5: 5: Bi 6: 6: Ec 7: 7: R 2:: Low (A) 1: 1: Av (A) 2: 2: Bi 3: 3: High 1: 1: Ec 2: 2: Pl	

1. **Enter** the CAS# In the blank field; 2. **Click** Search button; 3. **Press** OK

# Chemical Input

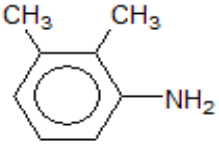
## Target chemical identity

The Toolbox now searches the databases to find out if the CAS# you entered is linked to a molecular structure stored in the Toolbox. It is displayed as a 2-dimensional depiction.

Search by CAS #

87592  Tautomeric sets

Select All Clear All Invert Selection Selected 1 of 1

Selected	CAS	Smiles	Depiction	Names	CAS/Name	2D/Name	CAS/2D
1. Yes	87-59-2	Cc1cccc(			1:: High 1:: Ar 2:: Bi 3:: Ec 4:: El 5:: Ph 6:: R 7:: T 8:: 3:: High 1:: B	1:: High 1:: Ar 2:: T 3:: Ph 4:: El 5:: Bi 6:: Ec 7:: R 2:: Low 1:: Ar 2:: Bi 3:: High 1:: Ec	: High A A A A A A A A



# Chemical Input

## Target chemical identity

- **Double click** "Substance Identity" displays the chemical identification information.
- The user should note that existing names of the target chemical are presented in different colours. This indicates the reliability of relation CAS-Name for the target chemical(see next screen shots).
- The workflow on the first module is now complete, and the user can proceed to the next module.

# Chemical Input

## Target chemical identity

The screenshot displays the QSAR Toolbox software interface. The top navigation bar includes tabs for Document, Single Chemical, and Chemical List. Below this is a toolbar with icons for New, Open, Close, Save, CAS#, Name, Structure, Select, Delete, Query, ChemIDs, DB, Inventory, and List. The main workspace is divided into several panels:

- Documents:** Shows a document titled "CAS: 87-59-2".
- Filter endpoint tree...:** A search filter is set to "[target]".
- Structure:** Displays the chemical structure of 2,3-dimethylaniline, which is circled in red.
- Substance Identity:** A list of identifiers is shown, also circled in red:
  - 87-59-2
  - EINECS:2017550
  - 2,3-dimethylaniline
  - dimethylaniline, 2,3-
  - 2,3-xylidine
  - 2,3-dimethylbenze...
  - 2,3-dimethyl-aniline
  - benzenamine, 2,3-...
  - 118
  - 2,3-dimethyl-pheny...
  - C8H11N
  - Cc1cccc(N)c1C
- Physical Chemical Properties:** Includes checkboxes for Environmental Fate and Transport, Ecotoxicological Information, and Human Health Hazards.
- Chemical Name:** Shows the SMILES string Cc1cccc(N)c1C.
- Structure:** Shows the chemical structure of 2,3-dimethylaniline with methyl groups labeled CH<sub>3</sub> and an amino group labeled NH<sub>2</sub>.

# Outlook

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  - 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.
- Available information includes likely mechanism(s) of action, as well as observed or simulated metabolites.

# Profiling

## Side-Bar to Profiling

- For most of the profilers, background information can be retrieved by highlighting one of the profilers (for example, Repeated dose toxicity (HESS) and clicking on “View” (see next screen shot).

# Profiling Side-Bar to Profiling

**1** Highlight the profiler

**2** Click View

Repeated dose (HESS) - Profiling Scheme Browser

List with categories

Textual description

**Anilines (Hemolytic anemia with methemoglobinemia) Rank A**

**1. Toxicity Information**

The toxicant of methemoglobinemia induced by anilines is considered to be N-hydroxyl anilines that are metabolites of anilines in the liver<sup>1,2</sup>. The hemolytic anemia induced by anilines is considered to be related to the oxidation of erythrocytes by N-hydroxyl anilines<sup>3, 4</sup>.

- 1) Anilines are metabolized in hepatocytes by oxidases such as P450 to N-hydroxyl anilines.
- 2) N-hydroxyl anilines react with hemoglobin (Hgb) in erythrocytes to produce nitrosoaniline and methemoglobin (Met-Hgb). The resulting increase in the concentration of Met-Hgb is observed in hematological examination.
- 3) Erythrocytes are degenerated (peroxidation of lipid membrane etc.) by reactive oxygen species (ROS) produced in the above reaction<sup>3</sup>.
- 4) Phagocytosis of degenerate erythrocytes, mainly in the spleen, results in hemolysis<sup>4</sup>.
- 5) The result is: decrease in red blood cells (RBC), decrease in Hgb, decreased hematocrit (Hct) and increase in reticulocytes (Ret) observed upon hematological examination in RDT test. In addition, pigmentation of hemosiderin and congestion are observed in the spleen on histopathological examination<sup>5</sup>.
- 6) As a compensatory response to anemia, extramedullary hematopoiesis (mainly in the spleen) is observed on histopathological examination<sup>4</sup>.

The mechanism of this toxicity is common to experimental animals and humans.

1/0/0

# Profiling Side-Bar to Profiling

1. Switch Basic to Advanced

# Profiling

## Side-Bar to Profiling results

The screenshot displays the QSAR Toolbox Profiling interface. The top navigation bar includes 'Input', 'Profiling', 'Endpoint', 'Category Definition', 'Data Gap Filling', and 'Report'. The 'Profiling' section is active, showing 'Profiling methods' and 'Metabolism/Transformations' panels on the left. The main area shows a 'Filter endpoint tree...' with a search box containing '1 [target]'. The tree is expanded to show 'Profile' > 'General Mechanistic' > 'DNA binding by OASIS v.1.4'. The results list on the right includes:

- Radical
- Radical >> Radical...
- Radical >> Radical...
- SN1
- SN1 >> Nucleophil...
- SN1 >> Nucleophil...
- SN1
- SN1 >> Nitrenium ...
- SN1 >> Nitrenium ...
- Alkyl arenes
- Aniline
- Aryl
- Alkyl arenes
- Aniline
- Overlapping groups
- Anilines (Hemolyti...
- Anilines (Hepatoto...

Two red callout boxes provide context:

- The first callout points to the 'Radical' and 'SN1' entries, stating: "The target has a potential to interact with DNA according to DNA binding profilers".
- The second callout points to the 'Anilines (Hemolyti...)' and 'Anilines (Hepatoto...)' entries, stating: "The target chemical could cause RDT toxicity through two different effects according to RDT profiler".



# Profiling Side-Bar to Profiling

**Repeated dose (HESS)**

**Anilines (Hemolytic anemia with methemoglobinemia) Rank A**

Target

Structural boundary of the category

Boundary Options: Metabolism

Fragment: c1(N(\*\*Exh13\*\*)c(\*\*Exh14)c(\*\*Exh14)c(\*\*Exh14)c(\*\*Exh14)c1\*\*Exh14

Common Fragments

Definition	1	2	3	4	5	6	7	8	9
1	[Exh13]	H	H-C-H	H-C-H					

Mechanistic justification of the category

Profile Description

**Anilines (Hemolytic anemia with methemoglobinemia) Rank A**

**1. Toxicity Information**

Repeated dose (HESS)

Anilines (Hemolytic anemia with methemoglobinemia) Rank A

1

**1. Double click on the cell with profiling result to see why this chemical is classified as Anilines**

# Outlook

- Background
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  - Input
  - Profiling
  - **Endpoint**

# Endpoint Overview

- “Endpoint” refers to the electronic process of retrieving the environmental fate, ecotoxicity and toxicity data that are stored in the Toolbox.
- Data gathering can be executed in a global fashion (i.e., collecting all data for all endpoints) or on a more narrowly defined basis (e.g., collecting data for a single or limited number of endpoints).

# Endpoint

## Case study

- In this example, we limit our data gathering to a single toxicity endpoint: repeated dose toxicity
- In this example, we collect data from the databases containing experimental results for Repeat dose toxicity (Repeated Dose Toxicity (HESS)).
- **Click** on “Endpoint” in the Toolbox workflow.
- **Expand the** “Human Health Hazards” section
- **Click** on the box to select that database.
- **Click** on “Gather data” (see next screen shot).

# Endpoint Gather data

The screenshot displays the QSAR Toolbox software interface. The top toolbar includes buttons for 'Gather', 'Import', 'Export', 'Delete', and 'Tautomerize'. The 'Databases' list on the left is expanded to show 'Human Health Hazards' (1), with 'Repeated Dose Toxicity HESS' selected (2). The 'Gather' button is circled (3). The right panel shows a filter endpoint tree with 'Repeated dose (HESS)' selected, and a chemical structure of 2,4-dimethylaniline is displayed.

1. **Expand** the Human Health Hazards section
2. **Select** database related to the target endpoint: Repeated dose toxicity HESS
3. **Click** Gather

# Endpoint Gather data

Repeated values for: 118 data-points, 24 groups, 1 chemicals

	Endpoint	CAS	Structure	Value	Dose	Duration	Effect	Examination items
<input checked="" type="checkbox"/>	NOEL	87-59-2	<chem>Cc1ccc(N)cc1C</chem>	300 mg/kg/day	12;300 mg/kg/day	28 Days	Basophilic change/Regen	Histopathological findings
<input checked="" type="checkbox"/>	NOEL	87-59-2		300 mg/kg/day	12;300 mg/kg/day	28 Days	Basophilic change/Regen	Histopathological findings
<input checked="" type="checkbox"/>	NOEL	87-59-2		300 mg/kg/day	12;300 mg/kg/day	28 Days	Basophilic change/Regen	Histopathological findings
<input checked="" type="checkbox"/>	NOEL	87-59-2		300 mg/kg/day	12;300 mg/kg/day	28 Days	Basophilic change/Regen	Histopathological findings
<input checked="" type="checkbox"/>	NOEL	87-59-2		300 mg/kg/day	12;300 mg/kg/day	28 Days	Basophilic change/Regen	Histopathological findings
<input checked="" type="checkbox"/>	NOEL	87-59-2		300 mg/kg/day	12;300 mg/kg/day	28 Days	Dilatation	Histopathological findings
<input checked="" type="checkbox"/>	NOEL	87-59-2	300 mg/kg/day	12;300 mg/kg/day	28 Days	Dilatation	Histopathological findings	

Buttons: Select one, Invert, Check All, Uncheck All, **OK**, Cancel

Message box: QSAR Toolbox 3.4.0.17  
862 data points gathered across 1 chemicals. **OK**

1. **Select OK.**
2. The message informs you for number of retrieved data points. **Click OK**

# Endpoint Gather data

The screenshot displays the QSAR Toolbox interface. On the left, the 'Databases' panel shows 'Human Health Hazards' selected, with 'Repeated Dose Toxicity HESS' checked. The 'Filter endpoint tree...' window shows a tree structure where 'Repeated Dose Toxicity' is expanded to show 'LOEL' and 'NOEL' entries. A red box highlights these entries, and a red arrow points from a text box to them. The text box says: 'Measured data for the target appeared on data matrix. We will try to reproduce measured data by read-across'. The chemical structure of the target is shown as a benzene ring with two methyl groups and one amino group.

## Recap

- In the first module, you have entered the target chemical being sure of the correctness of the structure.
- In the second module, you have profiled the target chemical and found that the target could cause RDT toxicity through two different effects
- In the third module, you have found that there is an experimental RDT data for the target structure. We will try to reproduce it using read across analysis
- But before the user can proceed with the “Filling Data Gap” module, he/she should define a category with similar analogues
- **Click** on “Category Definition” to move to the next module.



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  - Endpoint
  - **Category definition**

# Category Definition

## Grouping methods

- The different grouping methods allow the user to group chemicals into chemical categories according to different measures of “similarity” so that within a category data gaps can be filled by read-across.
- Detailed information about grouping chemical (Chapter 4) could be found in document “Manual for Getting started” published on OECD website:

<http://www.oecd.org/chemicalsafety/risk-assessment/theoecdqsartoolbox.htm>

## Basic guidance for category formation and assessment

### Suitable categorization phases:

1. Structure-related profilers
2. Endpoint specific profilers (for sub-cat)
3. Additional structure-related profilers, if needed to eliminate dissimilar chemicals (to increase the consistency of category) (e.g. chemical elements)

### Performing categorization:

1. The categorization phases should be applied successively
2. The application order of the phases depend on the specificity of the data gap filling
3. More categories of same Phase could be used in forming categories
4. Some of the phases could be skipped if consistency of category members is reached

**Graphical illustration of suitable categorization phases is shown on next slide**

## Suitable Categorization/Assessment Phases

### Phase I. Structure based

- US EPA Categorization
- OECD Categorization
- Organic functional group
- Structural similarity
- ECOSAR

**Broad grouping  
Endpoint Non-specific**

**Repeating Phase I due to Multifunctionality of chemicals**

### Phase II. Mechanism based

- DNA binding mechanism
- Protein binding mechanism
- Genotoxicity/carcinogenicity
- Cramer rules
- Verhaar rule
- Skin/eye irritation corrosion rules
- Repeated dose profiler (NITE)

**Subcategorization  
Endpoint Specific**

**Metabolism accounted for**

### Phase III. Eliminating dissimilar chemicals

**Apply Phase I – for structural dissimilarity  
Filter by test conditions – for Biological dissimilarity**

**Subcategorization  
Endpoint Specific**

# Category Definition

## Grouping methods –phase I

### Suitable Categorization/Assessment Phases

#### Phase I. Structure based

- US EPA Categorization
- OECD Categorization
- Organic functional group
- Structural similarity
- ECOSAR

**Broad grouping**  
**Endpoint Non-specific**

### Phase I categorization in Toolbox

Filter endpoint tree... [1 [target]]

Structure

Substance Identity

Physical Chemical Properties

Environmental Fate and Transport

Ecotoxicological Information

Human Health Hazards

Profile

- Predefined
  - OECD HPV Chemical Categories
  - US-EPA New Chemical Categories
- Endpoint Specific
  - Aquatic toxicity classification by ECOSAR
- Empiric
  - Organic Functional groups
  - Organic Functional groups (nested)

Not categorized

Anilines (Acute tox...)

Anilines (Hindered)

Alkyl arenes

Aniline

Aryl

Alkyl arenes

Aniline

Overlapping groups

43 analogues are identified

12 analogues are identified

11 analogues are identified

7 analogues are identified

15 analogue is identified

Structural similarity, Dice ACF, 50%

# Category Definition

## Grouping methods

- Based on these classifications and basic guidance for grouping chemicals explained on the previous slides the US-EPA (as broader group: 43 analogues) is used for defining initial group of analogues (phase I)
- For refinement of category and eliminating dissimilar chemicals a sequence of endpoint specific and structural profilers are applied (phase II):
  - US-EPA New chemical categories
  - Repeated dose (HESS)
  - Chemical elements
  - Structural similarity

# Category Definition

## Defining US-EPA New Chemical categories

The screenshot illustrates the 'Category Definition' process in the QSAR Toolbox. The main window shows the 'Category Definition' tab selected in the top menu. The left sidebar lists various grouping methods, with 'US-EPA New Chemical Categories' highlighted (1). The 'Define' button in the toolbar is circled (2). The 'US-EPA New Chemical Categories' dialog box is open, showing a list of target profiles, with the 'OK' button circled (3). The 'Define category name' dialog box is also open, showing the category name 'Acute toxicity (US-EPA New Chemical Categories)' and the 'OK' button circled (4).

1. **Highlight** the "US-EPA New Chemical Categories"
2. **Click** Define
3. **Click** OK to confirm the defined category for the target chemical
4. **Click** OK

# Category Definition

## Defining US-EPA New Chemical categories

Repeated values for: 3834 data-points, 908 groups, 857 chemicals

Data points...

	Endpoint	CAS	Structure	Value	Dose
<input checked="" type="checkbox"/>	NOEL	95-78-3	<chem>O=C1C=CC(=O)N1</chem>	12 mg/kg/day	12;300 mg/kg/day
<input checked="" type="checkbox"/>	NOEL	95-78-3	<chem>O=C1C=CC(=O)N1</chem>	12 mg/kg/day	12;300 mg/kg/day
<input checked="" type="checkbox"/>	NOEL	95-51-2	<chem>Nc1ccccc1Cl</chem>	160 mg/kg/day	10;160 mg/kg/day
<input checked="" type="checkbox"/>	NOEL	95-51-2	<chem>Nc1ccccc1Cl</chem>	160 mg/kg/day	10;160 mg/kg/day
<input checked="" type="checkbox"/>	NOEL	95-51-2	<chem>Nc1ccccc1Cl</chem>	160 mg/kg/day	10;160 mg/kg/day
<input checked="" type="checkbox"/>	NOEL	95-51-2	<chem>Nc1ccccc1Cl</chem>	160 mg/kg/day	10;160 mg/kg/day
<input checked="" type="checkbox"/>	NOEL	131-87-0	<chem>Nc1ccccc1Cl</chem>	100 mg/kg/day	10;100 mg/kg/day
<input checked="" type="checkbox"/>	NOEL	131-87-0	<chem>Nc1ccccc1Cl</chem>	100 mg/kg/day	10;100 mg/kg/day

Buttons: Select one, Invert, Check All, Uncheck All, **OK** (circled), Cancel

Message box: QSAR Toolbox 3.4.0.17  
25873 data points gathered across 43 chemicals.  
OK

Callout 1: Points to the OK button in the main window.

Callout 2: Points to the OK button in the message box.

1. **Click** OK to retrieve all available experimental data
2. The message informs you for number of retrieved data points. **Click** OK



## Defining US-EPA New Chemical categories

The experimental results for the analogues appeared on datamatrix

The screenshot shows the QSAR Toolbox 3.4.0.17 interface. The main window displays a datamatrix table with 8 columns representing different chemical structures. The left sidebar shows a tree view of endpoints, with 'Repeated Dose Toxicity' and 'Sensitisation' highlighted in red. A blue callout box with the number '1' points to the first two rows of the datamatrix table.

Endpoint	1 [target]	2	3	4	5	6	7	8
Structure	<chem>Cc1ccc(N)cc1</chem>	<chem>Nc1ccc(Cl)cc1</chem>	<chem>O=[N+]([O-])c1ccc(N)cc1</chem>	<chem>Nc1ccc(Cl)cc1</chem>	<chem>Nc1ccc(Cl)cc1</chem>	<chem>Nc1ccc(Cl)cc1</chem>	<chem>Nc1ccc(Cl)cc1</chem>	<chem>Nc1ccc(Cl)cc1</chem>
Repeated Dose Toxicity	(39/1172)	M: 12 mg/kg/day, ...	M: 160 mg/kg/day, ...		M: 192 mg/kg/day, ...	M: 250 mg/kg/day, ...	M: 100 mg/kg/day, ...	M: 192 mg/kg/day, ...
NOEL	(43/24701)	M: 12 mg/kg/day, ...	M: 160 mg/kg/day, ...	M: 100 mg/kg/day, ...	M: 192 mg/kg/day, ...	M: 125 mg/kg/day, ...	M: 100 mg/kg/day, ...	M: 92.3 mg/kg/day, ...
Sensitisation								

1. Chemical statistics presenting the number of chemicals and the available experimental data for the two endpoints.

## Recap

- In this module, you have defined the category of similar analogues.
- In the next module, you should apply read across in order to fill in data gap
- But before the user can proceed with the “Filling Data Gap” module, he/she should navigate to the target endpoint: In our case we will predict RDT of target for two endpoints: Total NOEL and Total LOEL; Route: Oral (gavage)
- Total NOEL and Total LOEL values coincide with minimal values for all LOELs (NOELs) of the current chemical (more info could be found on next snapshot)
- **Click** on “Data Gap Filling” to move to the next module.

# Total LOEL/NOEL

Filter endpoint tree... 1 [target]

CAS 108-69-0 Cc1ccc(N)cc1

Endpoint	LOEL (mg/kg/day)	NOEL (mg/kg/day)
<b>LOEL</b>	<b>Min M: 60 mg/kg/day</b>	
Rat		
Oral (Gavage)		
Adrenal	(1/1)M: 360 mg/kg/day	
Blood Serum (Sugar)	(1/1)M: 360 mg/kg/day	
Urinary Bladder	(1/2)M: 360 mg/kg/day, 360 mg/kg/day	
Urine	(1/11)M: 360 mg/kg/day, 360 mg/kg/day, 360 mg/kg/day	
Whole Body		
Lacrimation	(1/2)M: 360 mg/kg/day, 360 mg/kg/day	
Ptosis/Palpebral Closure	(1/2)M: 360 mg/kg/day, 360 mg/kg/day	
Salivation	(1/2)M: 360 mg/kg/day, 360 mg/kg/day	
<b>Total</b>	(1/2)M: 60 mg/kg/day, 60 mg/kg/day	
<b>NOEL</b>	<b>Min M: 10 mg/kg/day</b>	
Rat		
Oral (Gavage)		
Adrenal	(1/32)M: 60 mg/kg/day, 360 mg/kg/day, 360 mg/kg/day	
Blood Cell (Coagulation)	(1/8)M: 360 mg/kg/day, 360 mg/kg/day, 360 mg/kg/day, 360 mg/kg/day	
Blood Cell (Erythrocyte)	(1/30)M: 10 mg/kg/day, 10 mg/kg/day, 10 mg/kg/day, 10 mg/kg/day, 10 mg/kg/day	
Urinary Bladder	(1/10)M: 60 mg/kg/day, 60 mg/kg/day, 360 mg/kg/day, 360 mg/kg/day, ...	
Uterus	(1/3)M: 360 mg/kg/day, 360 mg/kg/day, 360 mg/kg/day	
Whole Body		
Abnormal Appearance	(1/2)M: 360 mg/kg/day, 360 mg/kg/day	
Abnormal Gait	(1/2)M: 360 mg/kg/day, 360 mg/kg/day	
Body Weight ↓	(1/2)M: 60 mg/kg/day, 60 mg/kg/day	
Ptosis/Palpebral Closure	(1/2)M: 60 mg/kg/day, 60 mg/kg/day	
<b>Total</b>	(1/2)M: 10 mg/kg/day, 10 mg/kg/day	

**Annotations:**

- Minimal value across all LOEL values (60 mg/kg/day)
- Total value coincide with minimal values for all LOELs (10; 60 mg/kg/day)
- Minimal value across all NOEL values (10 mg/kg/day)
- Total value coincide with minimal values for all LOELs (10; 60 mg/kg/day)

Now you are ready to continue with next module data gap filling

# Outlook

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- **Workflow**
  - Input
  - Profiling
  - Endpoint
  - Category definition
  - **Data gap filling**

# Data Gap Filling Overview

- “Data Gap Filling” module give access to three different data gap filling tools:
  - Read-across
  - Trend analysis
  - (Q)SAR models
- Depending on the situation, the most relevant data gap mechanism should be chosen, taking into account the following considerations:
  - Read-across is the appropriate data-gap filling method for “qualitative” endpoints like skin sensitisation or mutagenicity for which a limited number of results are possible (e.g. positive, negative, equivocal). Furthermore read-across is recommended for “quantitative endpoints” (e.g., 96h-LC50 for fish) in case a low number of analogues with experimental results are identified.
  - Trend analysis is the appropriate data-gap filling method for “quantitative endpoints” (e.g., 96h-LC50 for fish) if a high number of analogues with experimental results are identified.
  - “(Q)SAR models” can be used to fill a data gap if no adequate analogues are found for a target chemical.
- In this example, we use read-across.

# Data Gap Filling

## Interpreting Read-across

- In this example, all the analogues have repeated dose toxicity data (LOEL and NOEL values)
- Predicted values for the target compound is based on initial group of **Anilines** defined by US-EPA New Chemical categories
- The following subcategorizations are used for filtering the initial group of analogues:
  - US-EPA New chemical categories
  - Repeated dose (HESS)
  - Chemical elements
  - Structural similarity
- Before applying the read across, we should navigate to the target endpoint Total NOEL

See next screen shots

# Data Gap Filling

Navigation of endpoint tree: Repeated dose toxicity/**NOEL**/oral gavage/Total

The screenshot shows the QSAR Toolbox interface with the 'Data Gap Filling' tab selected. The endpoint tree on the left is expanded to the 'Total' node under 'Repeated Dose Toxicity'. The table below shows data for various chemical structures across different endpoints. A red callout '1' points to the 'total' filter field in the table header. A second red callout '2' points to the '+' sign next to the 'Total' node in the endpoint tree.

total	1 [target]	2	3	4	5	6	7	8
Structure								
Substance Identity								
Environmental Fate and Transport								
Human Health Hazards								
Repeated Dose Toxicity								
LOEL	(39/68)	M: 12 mg/kg/day, ...	M: 10 mg/kg/day, ...		M: 192 mg/kg/day,...	M: 250 mg/kg/day,...	M: 100 mg/kg/day,...	M: 192 mg/kg/day,...
NOEL								
Rat								
Oral (Feed)	(3/6)			M: <192 mg/kg/day...				M: 92.3 mg/kg/day...
Oral (Gavage)								
Whole Body								
Total	(39/70)	M: 12 mg/kg/day, ...	M: <10 mg/kg/day,...	M: 100 mg/kg/day		M: 125 mg/kg/day,...	M: 100 mg/kg/day,...	
Oral (water Co...)	(1/2)							
Profile								

1. **Type** "Total" in the filter field
2. **Expand** the tree to "Total" node by single left click on the "+" sign

# Data Gap Filling

## Apply read across for Total NOEL

The screenshot shows the QSAR Toolbox interface. The top navigation bar has 'Data Gap Filling' selected. The left sidebar has 'Read-across' selected. The main data table shows a 'total' column with a 'NOEL' row. A 'Possible data inconsistency' dialog box is open, showing a list of test guidelines with checkboxes. Red callouts and arrows highlight the steps: 1. Clicking the 'NOEL' cell in the table, 2. Selecting 'Read-across' in the sidebar, 3. Clicking the 'Apply' button, and 4. Clicking 'OK' in the dialog box.

1. **Click** on the cell corresponding to "NOEL" total value for the target chemical.
2. **Select** Read-across
3. **Click** Apply
4. **OK**



# Data Gap Filling

## Read-across

- The resulting plot is experimental results of all analogues (Y axis) according to a descriptor (X axis) with the default descriptor of log Kow (see next screen shot).
- The **RED** dot represents predicted results for the target chemical .
- The **BROWN** dots represent the experimental results available for the analogues that are used for the read-across.
- The **BLUE** dot represent the experimental results available for the analogues but not used for read-across.

# Data Gap Filling Read-across for NOEL

QSAR TOOLBOX

Input Profiling Endpoint Category Definition Data Gap Filling Report

The OECD QSAR Toolbox for Grouping Chemicals into Categories  
Developed by LMC, Bulgaria

Apply

Data Gap Filling Method

- Read-across
- Trend analysis
- (Q)SAR models

Target Endpoint

Human Health Hazards Repeated Dose Toxicity NOEL  
Rat Oral (Gavage) Whole Body Total

total	1 [target]	2	3	5	6	8	9	10
Structure	<chem>Nc1ccc(C)cc1</chem>	<chem>Nc1ccc(Cl)cc1</chem>	<chem>Nc1ccc(Cl)cc1</chem>	<chem>Nc1ccc(O)cc1</chem>	<chem>Nc1ccc(O)cc1</chem>	<chem>Nc1ccc(O)cc1</chem>	<chem>Nc1ccc(O)cc1</chem>	<chem>Nc1ccc(O)cc1</chem>
Total (38/68)	M. 12 mg/kg/day, ...	M. <10 mg/kg/day, ...	M. 100 mg/kg/day	M. 125 mg/kg/day, ...	M. 100 mg/kg/day, ...	M. 200 mg/kg/day	M. 3 mg/kg/day, 3 ...	M. 2

Descriptors Prediction

Read across prediction of NOEL,  
taking the average from the nearest 5 neighbours, based on 5 values from 5 neighbour chemicals,  
Observed target value: 12.0 mg/kg/day, Predicted target value: 7.52 mg/kg/day

Accept prediction

Return to matrix

- Select/filter data
- Selection navigation
- Gap filling approach
- Descriptors/data
- Model/(Q)SAR
- Calculation options
- Data usage
- Prediction approach options
- Use target data for prediction
- Set level of significance
- Visual options

Set usage of data per chemical:

- All
- Minimal
- Maximal
- Average
- Median
- Lower median
- Higher median

OK

Worst case scenario is applied. Follow the steps: 1. Select Calculation options 2. Click on the "Data usage". 3. Select "Maximal"\* 4. OK  
\*Maximal values are selected because (i.e log/1 of endpoint (LOEL)) correspond to maximal hazard

The OECD QSAR Toolbox for Grouping Chemicals into Categories

15.07.2016

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# Data Gap Filling

## Subcategorization by US-EPA New Chemical Categories

**1. Click Subcategorize**    **2. Select US-EPA New Chemical Categories**

**3. Click Remove to eliminate dissimilar chemicals.**

# Data Gap Filling

## Subcategorization by Repeated dose (HESS)

The screenshot displays the 'Data Gap Filling' workflow in the OECD QSAR Toolbox. The interface is divided into several sections:

- Left Panel (Grouping methods):** Lists various methods such as Carcinogenicity, DNA alerts, Eye irritation, etc. The 'Repeated dose (HESS)' method is highlighted with a red box and a callout '2'.
- Target Selection:** A dropdown menu shows 'Anilines (Hemolytic anemia with methemoglobinemia) Rank C' as the selected target.
- Chemical List:** A table of chemicals with their predicted values. The first row shows a chemical with a predicted value of 'M: 12 mg/kg/day'. A callout '1' points to the 'Subcategorize' button in the right panel.
- Read across prediction plot:** A scatter plot showing 'Read across prediction of NOEL, taking the average from the nearest 5 neighbours, based on 5 values from 5 neighbour chemicals, Observed target value: 12.0 mg/kg/day, Predicted target value: 7.52 mg/kg/day'. A callout '3' points to the 'Remove' button at the bottom.
- Right Panel (Accept prediction):** Contains a 'Return to matrix' section with a 'Subcategorize' button (callout '1') and other options like 'Mark chemicals by descriptor value', 'Filter points by test conditions', etc.

**3. Click Remove to eliminate dissimilar chemicals.**

# Data Gap Filling

## Subcategorization by Chemical elements

The screenshot displays the OECD QSAR Toolbox software interface during a 'Data Gap Filling' session. The main workspace shows a table of chemical structures and their predicted values. The 'Read across prediction of NOEL' plot shows the average from the nearest 5 neighbours, based on 5 values from 5 neighbour chemicals, with an observed target value of 12.0 mg/kg/day and a predicted target value of 7.52 mg/kg/day.

Three callout boxes highlight the steps:

1. Click Subcategorize.
2. Select Chemical elements.
3. Click Remove to eliminate two dissimilar chemicals.

# Data Gap Filling

## Subcategorization by Structural similarity

The screenshot displays the QSAR Toolbox software interface during a 'Data Gap Filling' operation. The main window has tabs for 'Endpoint', 'Category Definition', 'Data Gap Filling', and 'Report'. A 'Similarity options' dialog box is open, showing 'Molecular features' with 'Atom pairs' selected, and 'Calculation' options with 'Dice' and 'Atom type' selected. A 'Structural similarity' option is highlighted in the sidebar. A 'Select/filter data' menu is open, showing 'Subcategorize' selected. A Venn diagram and chemical structures are also visible.

Structural similarity is applied in order to refine the category to the most similar analogues

- 1. Click** Subcategorize.
- 2. Select** Structural similarity and modify default options (3) to the following: Dice, Atom pairs, Atom type; Count H attached.

# Data Gap Filling

## Subcategorization by Structural similarity

The screenshot shows the 'Subcategorization' window in the OECD QSAR Toolbox. The left sidebar lists various grouping methods, with 'Structural similarity' highlighted in a red box. The central workspace displays a scatter plot of log Kow values and a table of chemical structures with their corresponding predicted values. A blue callout box with the number '1' points to the first two bins in the top row of the workspace. Another blue callout box with the number '2' points to the 'Remove' button at the bottom. The right sidebar contains control options for the subcategorization process.

1. Hold Control button and select first two bins in order to eliminate them.
2. **Click** Remove to eliminate chemicals with similarity less than 60%

# Data Gap Filling

## Read across result for Total NOEL

The screenshot displays the QSAR Toolbox interface for Data Gap Filling. The main workspace shows a matrix of chemical structures and their corresponding NOEL values. The 'Total' row shows a predicted value of 9.60 mg/kg/day, which is circled in red. The 'Oral (water Containing)' row shows a predicted value of 12.0 mg/kg/day. A graph below the matrix plots NOEL (obs.) against log Kow, showing a cluster of points. A text box above the graph provides details about the read-across prediction: 'Read across prediction of NOEL, taking the average from the nearest 5 neighbours, based on 5 values from 5 neighbour chemicals, Observed target value: 12.0 mg/kg/day, Predicted target value: 9.60 mg/kg/day'. The predicted value is circled in red. On the right side of the interface, a panel contains several buttons, including 'Accept prediction' and 'Return to matrix', which are highlighted with red boxes and numbered '1' and '2' respectively.

1. **Click** Accept prediction

2. **Click** Return to matrix



# Data Gap Filling

## Result of read-across prediction

QSAR TOOLBOX

Input Profiling Endpoint Category Definition **Data Gap Filling** Report

The OECD QSAR Toolbox for Grouping Chemicals into Categories  
Developed by LMC, Bulgaria









Apply

Data Gap Filling Method

- Read-across
- Trend analysis
- (Q)SAR models

Target Endpoint

Human Health Hazards Repeated Dose Toxicity NOEL  
Rat Oral (Gavage) Whole Body Total

total	1 [target]	2	3	4	5	6	7	8
Structure								
Substance Identity								
Environmental Fate and Transport								
Human Health Hazards								
Repeated Dose Toxicity								
LOEL	(39/68) M: 12 mg/kg/day, ...	M: 10 mg/kg/day, ...		M: 192 mg/kg/day,...	M: 250 mg/kg/day,...	M: 100 mg/kg/day,...	M: 192 mg/kg/day,...	M: 1E3
NOEL								
Rat								
Oral (Feed)	(3/6)			M: <192 mg/kg/da...			M: 92.3 mg/kg/day...	
Oral (Gavage)								
Whole Body								
Total	(39/7) M: 12 mg/kg/day, ... R: 9.6(2.73;33.8)	M: <10 mg/kg/day,...	M: 100 mg/kg/day		M: 125 mg/kg/day,...	M: 100 mg/kg/day,...		M: 200
Oral (water Containing)	(1/2)							
Profile								

1. Read across prediction 9.6 mg/kg/day coincide with experimental data (12 mg/kg/day)

# Data Gap Filling

## Apply read-across for Total LOEL

The screenshot shows the QSAR Toolbox interface during a data gap filling operation. The 'Data Gap Filling' menu item is active. In the left sidebar, 'Read-across' is selected under 'Data Gap Filling Method'. The main table displays a chemical structure and its associated toxicity data, including a 'LOEL' value of 12 mg/kg/day. A dialog box titled 'Possible data inconsistency' is open, showing a list of test guidelines with checkboxes. The 'OK' button in the dialog box is highlighted.

1. **Click** on the cell corresponding to "LOEL" total value for the target chemical.
2. **Select** Read-across
3. **Click** Apply
4. **OK**

# Data Gap Filling Read-across for LOEL

QSAR TOOLBOX

Input Profiling Endpoint Category Definition Data Gap Filling Report

About Update

The OECD QSAR Toolbox for Grouping Chemicals into Categories  
Developed by LMC, Bulgaria

Filing

Apply

Data Gap Filling Method

- Read-across
- Trend analysis
- (Q)SAR models

Target Endpoint

Human Health Hazards Repeated Dose Toxicity LOEL  
Rat Oral (Gavage) Whole Body Total

total	1 [target]	2	5	6	8	9	10	11
Structure								
Total (34/58)	M: 12 mg/kg/day, ...	M: 10 mg/kg/day, ...	M: 250 mg/kg/day, ...	M: 100 mg/kg/day, ...	M: 1E3 mg/kg/day	M: 10 mg/kg/day, ...	M: 10 mg/kg/day	M: 6

Descriptors Prediction

Read across prediction of LOEL,  
taking the average from the nearest 5 neighbours, based on 5 values from 5 neighbour chemicals,  
Observed target value: 26.8 mg/kg/day, Predicted target value: 30.1 mg/kg/day

LOEL (obs.), log(1 mol/kg/day)

Accept prediction

Return to matrix

- Select/filter data
- Selection navigation
- Gap filling approach
- Descriptors/data
- Model/(Q)SAR
- Calculation options
  - Data usage
  - Prediction approach options
  - Use target data for prediction
  - Set level of significance
- Visual options

Set usage of data per chemical:

- All
- Minimal
- Maximal
- Average
- Median
- Lower median
- Higher median

OK

Worst case scenario is applied. In this respect

1. **Select** Calculation options
2. **Click** on the "Data usage."
3. **Select** "Maximal"\*
4. **OK.**

\*Maximal values are selected because (i.e log/1 of endpoint (LOEL)) correspond to maximal hazard

# Data Gap Filling

## Subcategorization by US-EPA New Chemical Categories

The screenshot displays the QSAR Toolbox software interface. On the left, the 'Subcategorization' panel shows a tree view of grouping methods. A red box highlights 'US-EPA New Chemical Categories' with a callout '2'. Below it, a list of chemical categories is shown, with 'Anilines (Acute toxicity)' selected. A 'Remove' button is highlighted with a callout '3'. The main workspace shows the 'Data Gap Filling' tab. A table lists chemical targets with their predicted target values. Below the table is a scatter plot of log Kow vs. predicted target values. A text box above the plot reads: 'Read across prediction of LOEL, taking the average from the nearest 5 neighbours, based on 5 values from 5 neighbour chemicals, Observed target value: 12.0 mg/kg/day, Predicted target value: 19.6 mg/kg/day'. On the right, the 'Accept prediction' panel has a 'Subcategorize' button highlighted with a callout '1'.

**1. Click Subcategorize**  
**3. Click Remove to eliminate dissimilar chemicals.**

**2. Select US-EPA New Chemical Categories**

# Data Gap Filling Subcategorization by Repeated dose (HESS)

The screenshot displays the QSAR Toolbox interface for subcategorization. On the left, the 'Grouping methods' sidebar is open, with 'Repeated dose (HESS)' highlighted in a red box (callout 2). The main workspace shows a table of chemical structures and their predicted values, with the 'log Kow' axis on the x-axis of the scatter plot below. A callout (1) points to the 'Subcategorize' button in the 'Accept prediction' panel on the right. A callout (3) points to the 'Remove' button at the bottom of the sidebar.

1. Click Subcategorize.
2. Select Repeated dose (HESS)
3. Click Remove to eliminate dissimilar chemicals.

# Data Gap Filling

## Subcategorization by Chemical elements

The screenshot displays the QSAR Toolbox software interface during a 'Data Gap Filling' session. The main workspace shows a table of chemical groups with their respective molecular structures and predicted values. Below this is a scatter plot of log Kow values. The left sidebar contains various grouping methods, with 'Chemical elements' highlighted. The right sidebar shows the 'Select/filter data' panel, where 'Subcategorize' is selected. Three numbered callouts indicate the steps: 1. Clicking 'Subcategorize' in the right panel; 2. Selecting 'Chemical elements' in the left sidebar; 3. Clicking 'Remove' at the bottom of the left sidebar.

1. Click Subcategorize

2. Select Chemical elements

3. Click Remove to eliminate dissimilar chemicals.

# Data Gap Filling

## Subcategorization by Structural similarity

The screenshot displays the QSAR Toolbox interface for subcategorization. The main window shows a list of grouping methods on the left, with 'Structural similarity' selected and highlighted in red (2). The 'Similarity options' dialog is open, showing 'Dice' as the measure and 'Atom pairs' as the molecular features. The 'Similarity' window shows a Venn diagram and a scatter plot of log Kow values. The 'Accept prediction' window is open, showing the 'Subcategorize' option selected (1). A red circle highlights the similarity percentage ranges (3), and a blue box highlights the 'Remove' button (4).

Structural similarity is applied in order to refine the category to the most similar analogues

1. **Click** Subcategorize.
2. **Select** Structural similarity and apply the similarity options as with Total NOEL: Dice, Atom pairs, Atom type; Count H attached
3. **Select** first two categories (hold Ctrl button)
4. **Click** Remove to eliminate chemicals with similarity less than 60%

# Data Gap Filling

## Read across result for Total LOEL

The screenshot shows the QSAR Toolbox interface during the Data Gap Filling process. The top navigation bar includes buttons for Input, Profiling, Endpoint, Category Definition, Data Gap Filling, and Report. The left sidebar shows the 'Data Gap Filling Method' section with options for Read-across, Trend analysis, and (Q)SAR models. The main area displays a 'Structure' panel with chemical structures and a 'Descriptors' panel with a scatter plot. The scatter plot shows LOEL (obs.) log10 (mg/kg/day) on the y-axis and log Kow on the x-axis. A callout box highlights the predicted LOEL value of 17.5 mg/kg/day. A right sidebar contains a list of actions, with 'Accept prediction' and 'Return to matrix' highlighted by callout boxes.

1. Click Accept prediction

2. Click Return to matrix



# Data Gap Filling

## Result of read-across prediction

The screenshot displays the QSAR Toolbox interface during a data gap filling process. The 'Data Gap Filling Method' is set to 'Read-across'. The 'Target Endpoint' is 'Human Health Hazards Repeated Dose Toxicity LOEL Rat Oral (Gavage) Whole Body Total'. The main table shows results for various chemical structures across eight columns. A callout box labeled '1' highlights a specific cell in the 'Repeated Dose Toxicity' section, where the predicted LOEL (17.5 mg/kg/day) coincides with the experimental LOEL (12 mg/kg/day).

total	1 [target]	2	3	4	5	6	7	8
Structure	<chem>Cc1ccc(N)cc1</chem>	<chem>Nc1ccc(Cl)cc1</chem>	<chem>Nc1ccc(Cl)cc1</chem>	<chem>Nc1ccc(Cl)cc1</chem>	<chem>Nc1ccc(Cl)cc1</chem>	<chem>Nc1ccc(Cl)cc1</chem>	<chem>Nc1ccc(Cl)cc1</chem>	<chem>Nc1ccc(Cl)cc1</chem>
Substance Identity								
Environmental Fate and Transport								
Human Health Hazards								
Repeated Dose Toxicity								
LOEL								
Rat								
Oral (Feed)	(3/6)				M: 192 mg/kg/day,...			M: 192 mg/kg/day,...
Oral (Gavage)								
Whole Body								
Total	(35/6)	M: 12 mg/kg/day, ... R: 17.5(3.35,91.1)	M: 10 mg/kg/day, ...			M: 250 mg/kg/day,...	M: 100 mg/kg/day,...	M: 1E:
Oral (water Containing)	(1/2)							
NOEL	(43/79)	M: 12 mg/kg/day, ... R: 9.6(2.73,33.8) ...	M: <10 mg/kg/day,...	M: 100 mg/kg/day	M: <192 mg/kg/day,...	M: 125 mg/kg/day,...	M: 100 mg/kg/day,...	M: 92.3 mg/kg/day... M: 200
Profile								

1. Read across prediction for LOEL: 17.5 mg/kg/day coincide with experimental LOEL: 12 mg/kg/day

# Read across predictions for 2,3 dimethylaniline (CAS 87-59-2) Result

## Ultimate prediction:

Total NOEL – 9.6 mg/kg/day

Total LOEL – 17.5 mg/kg/day

**Based on obtained results (for total LOEL and total NOEL) the target chemical is classified as *Category 2* regarding GHS classification <sup>1</sup>**

Table 3.9.2: Guidance values to assist in Category 2 classification

Route of exposure	Units	Guidance value range (dose/concentration)
Oral (rat)	mg/kg bw/d	10 - 100
Dermal (rat or rabbit)	mg/kg bw/d	20 - 200
Inhalation (rat) gas	ppm/6h/d	50 - 250
Inhalation (rat) vapour	mg/litre/6h/d	0.2 - 1.0
Inhalation (rat) dust/mist/fume	mg/litre/6h/d	0.02 - 0.2

<sup>1</sup> Globally Harmonized System of Classification and Labeling of Chemicals (GHS):  
[http://www.unece.org/fileadmin/DAM/trans/danger/publi/ghs/ghs\\_rev04/English/ST-SG-AC10-30-Rev4e.pdf](http://www.unece.org/fileadmin/DAM/trans/danger/publi/ghs/ghs_rev04/English/ST-SG-AC10-30-Rev4e.pdf)

# Outlook

- Background
- Objectives
- The exercise
- **Workflow**
  - Input
  - Profiling
  - Endpoint
  - Category definition
  - Data gap filling
- **Report**

## Report

- Remember the report module allows you to generate a report on the predictions performed with the Toolbox. This module contains predefined report templates as well as a template editor with which users can define their own user defined templates. The report can then be printed or saved in different formats.
- Generating the report is shown on next screenshots

# Report

The screenshot illustrates the 'Report' workflow in the QSAR Toolbox. On the left, the 'Target Endpoint' tree is expanded to 'Repeated Dose Toxicity' > 'Oral (Gavage)' > 'Whole Body' > 'Total'. The main table shows two chemical structures with their respective predictions. A context menu is open over the first prediction, with 'Report' selected. A dialog box titled 'Select prediction to edit reporting info' is open, showing a list of predictions with a callout '3' pointing to a specific entry.

Structure	1 [target]	2	3
Structure	<chem>Cc1ccc(N)cc1</chem>	<chem>Nc1ccc(Cl)cc1</chem>	
Substance Identity			
Environmental Fate and Transport			
Human Health Hazards			
Repeated Dose Toxicity			
LOEL			
Rat	(3/6)		
Oral (Feed)	(35/61)	M: 12 mg/kg/day, ... R: 17.5(3.35-84.1)	M: 10 mg/kg/day, ...
Oral (Gavage)	(1/2)		
Whole Body	(43/79)	M: 12 mg/kg/day R: 9.6(2.7-33.8)	M: 100 mg/kg/day
Total			M: <192 mg/kg/day...
NOEL			M: 125 mg/kg/day, ...
Profile			M: 100 mg/kg/day, ...

1. **Select** prediction
2. **Right Click** and **Select** Report
3. **Select** the prediction for which you want to generate the report

# Report

The screenshot displays the QSAR Toolbox software interface. The top menu bar includes options like Input, Profiling, Endpoint, Category Definition, Data Gap Filling, and Report. Below the menu is a toolbar with icons for Reports (Create, Print, Close, Save as) and Repository (Register, Unregister, Update, Clone, Design). On the left, there are panels for 'Available data to report' and 'Available report templates'. The main window shows a report titled 'Prediction of LOEL for 2,3-dimethylaniline' (3 / 22). A callout box with the number '1' points to the text 'QSAR Toolbox prediction based on read-across' which is circled in red. The report content includes a title, a summary, and a table header for endpoint and descriptor values.

Prediction of LOEL for 2,3-dimethylaniline 3 / 22

**1** QSAR Toolbox prediction based on read-across

**Prediction of LOEL for 2,3-dimethylaniline**

**Summary**

Toxicity of the target chemical (17.5 mg/kg/day) is predicted from category members using read-across based on 5 values within the range 2.00 - 50.0 mg/kg/day from 5 nearest neighbours compared by prediction descriptors. Category members are single chemicals or mixtures and are selected based on the profile of the target chemical. Only chemicals having experimental data are listed in the category.

The target chemical FALLS within applicability domain of the prediction (see Section 4.3 for details).

The data used for calculating the current prediction is taken from 10 experimental values selected from the following database(s):

1. Repeated Dose Toxicity HESS

Below is a summary table for endpoint & descriptor values for the target chemical and the category members.

Experimental values from data matrix are presented in bold font. Recalculated endpoint values (if required by selected data usage option in Gap Filling) are presented in italic font. Recalculated endpoint values based on experimental data only are presented in bold and italic font.

	<i>Endpoint(s)</i>	<i>Descriptor(s)</i>
--	--------------------	----------------------

## 1. Report for LOEL

# Report

The screenshot displays the 'Report' window of the QSAR Toolbox. The interface includes a top menu bar with options like 'Input', 'Profiling', 'Endpoint', 'Category Definition', 'Data Gap Filling', and 'Report'. Below this is a toolbar with various actions such as 'Create', 'Print', 'Close', 'Save as', 'Register', 'Unregister', 'Update', 'Clone', and 'Design'. On the right side, there is a header for 'The OECD QSAR Toolbox for Grouping Chemicals into Categories' and 'Developed by LMC, Bulgaria'.

The main content area is titled 'Prediction [2]' and contains the following text:

- j. Predicted value (model result):** 17.5 mg/kg/day (circled in red with callout 1)
- k. Predicted value (comments):** Not provided by the user
- 4.3. Applicability domain (OECD Principle 3):** The target chemical FALLS within applicability domain (see Section 3.1. b for detailed description of the domain) (circled in red with callout 2)

Below the text is a logic tree diagram representing the applicability domain. It consists of 22 nodes, numbered 1 through 22. Nodes 1 through 10 are at the top level, with nodes 1, 2, 4, 6, 8, and 10 marked with green checkmarks, and nodes 3, 5, and 7 marked with red crosses. Nodes 11 through 22 are arranged in a hierarchical structure below, with nodes 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, and 22 marked with green checkmarks. The nodes are connected by lines, with 'AND' and 'NOT' operators indicating the logical relationships between them.

On the left side of the interface, there are two panels: 'Available data to report' (containing Predictions, QSARs, and Categories) and 'Available report templates' (divided into Standard and Custom templates).

1. Predicted value

2. Applicability domain

# Report

Prediction of LOEL for 2,3-dimethylaniline 12 / 22

*Appendix 1 - Category members*

**QSAR Toolbox prediction based on read-across**

**Prediction of LOEL for 2,3-dimethylaniline**

**APPENDIX 1 - Category members**

The 5 category members are reported in more detail

**1. Cat. member No.1:**

**1.1. CAS number:**  
95-64-7

**1.2. Other regulatory numbers:**  
Not reported

**1.3. Chemical name(s):**  
3,4-dimethylaniline (3,4-xylylidine)

*used for read-across*

## 1. Additional information for category members



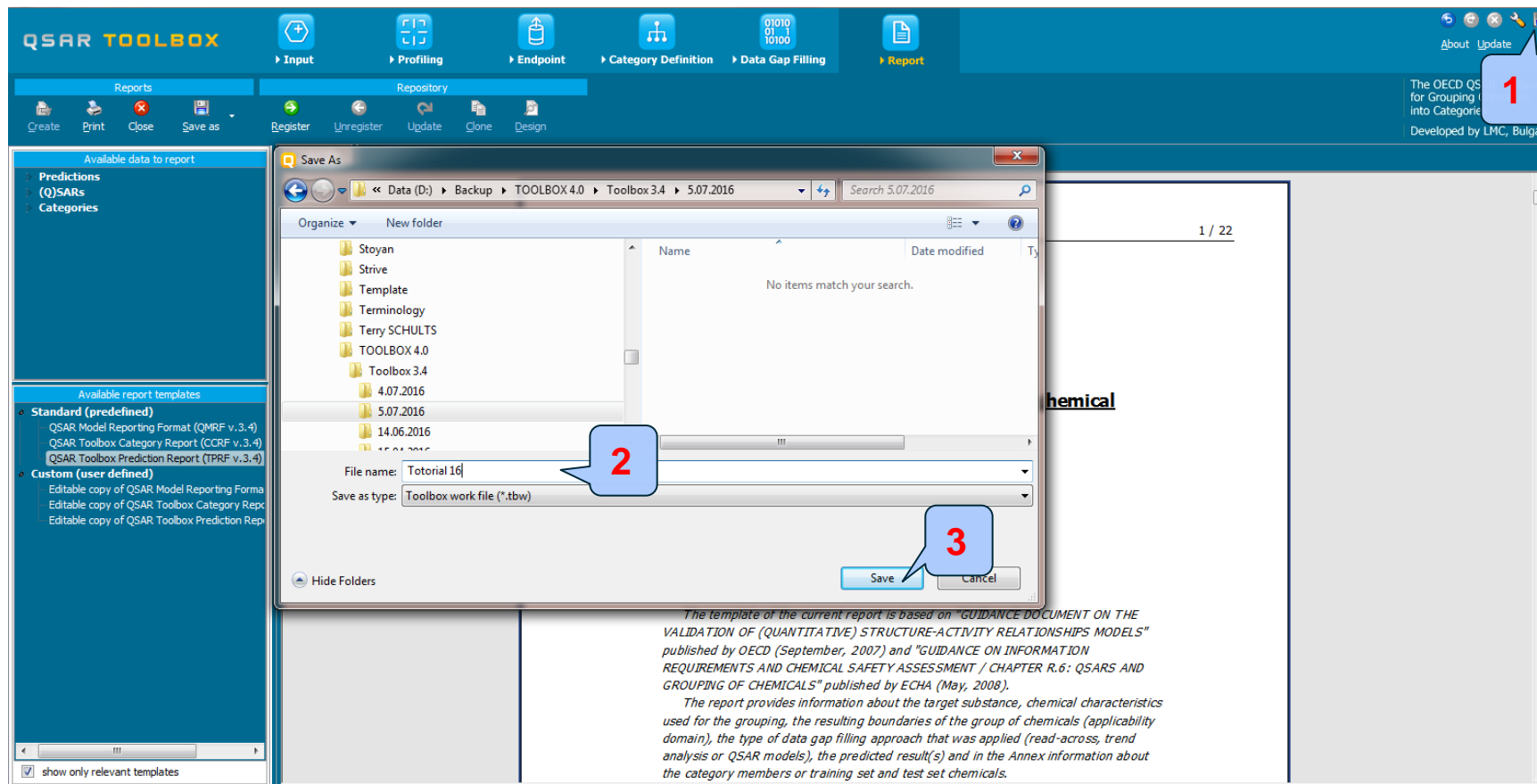
## Outlook

- Background
- Objectives
- The exercise
- Workflow
- **Save prediction**

## Saving the prediction result

- This functionality allow 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 next screenshots

# Saving the prediction result



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

# Open saved file

The screenshot illustrates the steps to open a saved file in the QSAR Toolbox. The interface includes a top menu bar with options like 'Input', 'Profiling', 'Endpoint', 'Category Definition', 'Data Gap Filling', and 'Report'. A 'Select file' dialog box is open, showing a file named 'Totorial 16.tbw' selected. The background shows a chemical structure and a table of data.

	5	6	7	8
	<chem>Nc1ccc(O)cc1</chem>	<chem>Nc1ccc(O)cc1</chem>	<chem>Nc1ccc(O)cc1</chem>	<chem>Nc1ccc(O)cc1</chem>
	mg/kg/day,...		M: 192 mg/kg/day,...	
		M: 250 mg/kg/day,...	M: 100 mg/kg/day,...	M: 1E3
	mg/kg/da...	M: 125 mg/kg/day,...	M: 100 mg/kg/day,...	M: 92.3 mg/kg/day,...
				M: 200

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