User manual

Document history

Version	Comment
Version 1.0	May 2024: Toolbox 4.7 Release Notes
Version 1.1	October 2024: Updated to reflect version 4.7.1
Version 1.2	July 2025: Updated to reflect version 4.8
Version 1.2.1	November 2025: Updated to reflect version 4.8.2

Issue date: November 2025

Language: English

If you have questions or comments that relate to this document, please send them to ehscont@oecd.org or visit the QSAR Toolbox discussion forum at https://community.oecd.org/community/toolbox_forum

Table of Contents

1 Overview

The Toolbox 4.8.2 installation is a major update of Toolbox 4.7.(1). It can be installed as a separate product alongside previous major releases of Toolbox (4.x, 3.4, 3.3, etc.). It is also a minor update for version 4.8 (from July 2025). Running the installer will patch the existing 4.8, both will not run concurrently with one another.

2 System Requirements

Minimum system requirements

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OS: 64 bit, Windows 7 or newer

CPU: Core 2 duo at 2 GHz or equivalent AMD CPU

RAM: At least 4GB of RAM

HDD: 18 GB free hard drive space

File system: NTFS

Microsoft .NET 6.0

Recommended system requirements

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OS: 64 bit, Windows 7 or newer

CPU: I5 at 2.4GHz or faster processor or equivalent AMD CPU

RAM: 6 GB of RAM

HDD: 20 GB free hard drive space

File system: NTFS

Microsoft .NET 6.0

3 Change log (4.8.2)

- Fixed memory leaks
- Custom IDs of substances from a custom database are transportable to other Toolbox versions
- Set default hierarchy for observed metabolism
- Fixed an issue when importing absorption rate data from IUCLID v.9
- Fixed an issue with importing test materials
- Fixed problem in saving document with deleted predictions
- Improved picture visualizations in the report
- Fixed database statistics for distribution by endpoints
- Eliminated potential deadlock while calculation basic parameters
- Sped up Data Query
- Fixed a false reading in enough memory check
- Fixed Addin packager when creating a database addin
- Fixed a false error message when importing a IUCLID6 Category
- Fixed a sequence contains no matching element when defining TE in workflow that has not been saved
- Fixed QSAR list showing duplicates when all the children leaf paths have the same QSAR
- Fixed filtering by metabolism options
- Fixed missing metabolite affiliation categories in Query Tool
- Fixed cis/trans bonds getting messed up

4 Change log (4.8)

I. Install

The QSAR Toolbox requires the installation of .NET 8.0. Two options are provided with the installation package.

- One is an online installer that requires the computer to be connected to the Internet but has the benefits of querying for the latest version.

- The other, offline installer, may be a bit outdated but has the benefit of not having to wait for a download and does not require Internet connectivity.

II. General modifications in the software

1. Import and visualization of structural and metadata information for substances belonging to metabolism databases
    - From Input/Metabolite Database, a metabolism database can be loaded and the structural information of the substances can be visualized on the data matrix.
    - From the new subsection implemented in the Data section – Data/Metabolite Databases - data from metabolism databases can be collected and visualized on the data matrix. This includes quantitative information for parents and metabolites, test organisms, matrix, etc.
    - The experimental data for parent and metabolites collected from metabolism databases appear on a new level of the Endpoint tree – Observed metabolism
    - Specific labels indicate whether the experimental data is for a parent chemical (PC) or a transformation product (TP).
    - A new meta data field of the experimental data has been added, allowing direct visualization of the metabolic map to which a parent or metabolite belongs to.
    - A new profiler has been developed in the Profiling section, part of the Predefined list - Metabolic Database Affiliation. It provides information for the name of the metabolism database the substance(s) loaded on the data matrix belongs to and whether the substance is presented in the database as a parent chemical or as a metabolite.
2. Profilers and simulators
    - Modifications in the alerts/functional groups
    - Updated transformation tables
3. Databases and inventories
    - Updated are two databases and one inventory
    - Two new databases are available as plugins
4. IUCLID export prediction wizard

- Export prediction results to specific QAF fields in IUCLID – the new fields associated with QAF are indicated with specific flag (QSAR Assessment Framework (QAF) field).
- The export wizard has been modified to better represent individual sections.

5. Cache updates
    - Profiling and metabolism caches
    - 2D and 3D parametric caches
6. Documentation
    - Update of F1 help
    - Update of documentation of profilers, simulators and databases
7. Updates to the Repository
    - Two new databases as plugins are available - “Ecotox pharmaceuticals database” and “EFSA Public MetaPath database”
8. Updates to the Web client
9. Other modifications and updates
    - Expansion of the Query tool allowing searching by taxonomy information
    - Expansion of the Workflow editor to work with specific information from metabolism databases.

III. Input

New functionality is implemented - “Metabolite Database”, allowing loading of the structural information from metabolism databases.

IV. Profiling schemes

1. New profilers
    - Metabolic Database Affiliation – indicating whether a substance or a list of substances loaded on the data matrix belong to a metabolism database
2. Updated profilers – 13 profilers have been updated
    - Hydrolysis half-life (pH 6.5-7.4)
    - Toxic hazard classification by Cramer

Significant modifications in the Cramer profiling scheme have been done in terms of providing more transparent results, increasing the performance and improving the reporting capabilities.

- Acute Oral Toxicity
- DART scheme
- DNA alerts for AMES, CA and MNT by OASIS
- Oncologic Primary Classification
- rtER Expert System - USEPA
- Organic functional groups
- Organic functional groups (nested)
- Organic functional groups (US EPA)
- Organic functional groups, Norbert Haider (checkmol)
- Tautomers unstable
- Repeated dose (HESS)

Note: A summary of the updates and modifications to the profiling scheme can be found in the corresponding changelog sections (Select profiling scheme>View>Scheme sheet– find the changelog sheet in the middle of the screen; or go to the About> Documentation> find the changelog section in the document)

V. Documented/simulated metabolism

1. Documented metabolism databases – one new metabolism database "*EFSA residues public*" which will be available in this section once downloaded and installed from the Repository website.
2. Updated metabolic simulators – seven updated metabolic simulators
    - Autoxidation
    - Hydrolysis neutral
    - Hydrolysis acidic
    - Hydrolysis basic
    - Microbial metabolism
    - In vitro rat liver
    - In vivo rat liver

Note: A summary of the updates and modifications to the simulators can be found in the corresponding changelog sections described in: About> Documentation> find the changelog section in the document.

VI. Data and data matrix

1. New endpoint tree level is implemented "*Observed metabolism*", where data from metabolism database are visualized.
2. New subsection in the Data module is implemented "*Metabolite Databases*", allowing selection of metabolism databases for collecting experimental data for parents and metabolites.
3. Specific labels indicate whether the experimental data collected from metabolism databases is for a parent chemical (PC) or for a transformation product (TP).
4. A new meta data field of the experimental data has been added (accessed through double click on experimental data value on the data matrix), allowing direct visualization of the metabolic map to which a parent or metabolite belongs to.

VII. Databases and inventories

1. New and updated databases

#	Name of the database	Status	Number of updated/new chemicals with data
1	ECOTOX	updated	97/ 38,676
2	Hydrolysis DB	updated	18 / 18
3	Ecotox pharmaceuticals*	new	362 / 1,087
4	EFSA residues public*	new	211/ 11,000

*Available as downloadable plug-ins at the Repository

2. Updated inventories

#	Name of the inventory	Status	Number of new chemicals

1	AICS Inventory	updated	74

VIII. Category definition

No updates

IX. Data Gap Filling

1. Expansion of the Workflow editor associated with documented metabolism

X. Query tool

- Possibility to search by taxonomy information

XI. Repository

1. New plugins

Two new databases have been added which can be automatically downloaded and installed by using the Repository client:

- Ecotox pharmaceuticals – consisting of 362 pharmaceutical chemicals with toxicity values of EC50, IC50, LC50 and NOEC values for various aquatic species (algae, crustaceans or fishes)
- EFSA residues public – a Metapath database of 211 substances and 11,000 data including metabolic maps, quantities, matrices, species, etc. for parents and metabolites.

2. Updated plugins – two plugins
    - KATE plugin - for predicting toxicity to aquatic organisms
    - ECHA Unlocking plugin

XII. Web Client

The version number has been aligned to match the major.minor version of the desktop app. This aims to reduce confusion.

1. Data matrix section:
    - fixed issues related to Excel export
    - fixed issues related to loading a list with SMILES
    - fixed an issue related to loading a list with CAS numbers

- fixed an issue related to metabolites retrieval
- fixed an issue related to the application of QSAR models
- added index numbers in the load list component
- hid private CAS numbers (negative numbers)

2. IUCLID search section:
    - fixed an issue preventing IUCLID search results listing
    - enabled depiction of structures from IUCLID search results
    - enriched IUCLID search export with title details and SMILES

5 Change log (4.7.1)

- Fixed an issue with reporting where a 10 chemical restriction would trigger
- Improved addin packager (added "help" button/manual)
- Added a skin sensitization scale transformation
- Added feature for specifying About information during database import
- Fixed the download link from the QSAR Toolbox About window
- Fixed an issue when Searching by fragment when there isnt target chemical on DM producing exceptions
- Show Only custom databases in the list with databases for packaging
- Fixed an issue when using exact match, profiler not selected, and category with metabolism
- Fixed an issue when minimizing workflow, added save dialog
- Fixed an issue when importing of a database twice produce
- Relaxed Client restrictions when deploying to Windows server
- Reworked DB Deployment to address installing from network location use cases
- Fixed an issue where a third party addin conflicts with EPI parameters
- Fixed an issue with "filter by metadata" feature of the data matrix export
- Fixed an issue where Toolbox Client would crash when calculating through the API

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7 Change log (4.7)

I. General modifications

- Interface extension allowing (un)registering of additional MetaPath databases.

It is installed automatically with the QSAR Toolbox installation and can be accessed through the Windows search with the name “QSAR Toolbox Addin Packager”.

- Better representation of observed metabolites on the data matrix

Additional data fields are transferred from MetaPath database to Toolbox, such as: the number of observed maps which are available per chemical; the test organism; various quantitative information for the observed metabolites, etc.

- Profilers and simulators
  - modifications in basic modules of the system (such as the equalizer)
  - modified rigid endpoint path for Environmental fate and transport
  - modifications in the alerts or other functional groups
  - updated transformation tables (used in OASIS software)
- Databases and inventories
  - Correction of the ID information
  - Addition of new chemicals and data
- Cache
  - Profiling and metabolism caches
  - 2D and 3D parametric caches
- Documentation
  - Update of F1 help
  - Updates of the documentation of some profilers and databases
- Mapping of additional OHTs

Mapping of seven additional OECD Harmonized templates (OHTs) related to phys-chem properties (such as pH, self-reactive substances, corrosive to metals etc) and endocrine disrupter tests (aquatic vertebrates and mammals in vivo screening tests). As a result, additional chemicals with data were imported in the ECHA REACH database.

- TEDRA plug-in modifications:
  - Transfer of Endpoint summary for toxicokinetics results

- related to the mapping of the new OHTs

II. Input

1. Possibility to enter a specific structure without automatic assignment of ID – this allow a UVCB representative structure to be entered and predicted in Toolbox
2. Improving the handling of chemical with stereo information and multi-constituents
3. Inclusion of a new row in the Structure info section allowing manual entering of user comments for a substance

III. Profiling

1. New features/functionalities

The new implementations in the Profiling concern the *Toxic hazard classification by Cramer* profiling scheme, as follows:

- Transparency of profiling results is increased providing on the data matrix additional summarized information for the sequence of the applied rules and indication if the chemical answers with yes or no (e.g., CAS 139-05-9: 1N,2N,3Y,4Y,7N,16N,17N,19N,23N,24Y,18N – Class I). The additional information could be further used for grouping of chemicals sharing a common pathway.
- Printable report of the profiling results is already implemented including the following type of information: list with all rules applied to the target chemical; information for the outcome of each rule (Yes/No); short description of the structural/parametric boundaries where the answer is "Yes"; links to download the mechanistic interpretation (i.e., help file) of each rule covered by the target

2. Profiling schemes

- Updated profilers - 21 profilers have been updated
  - Eye irritation/corrosion Inclusion rules by BfR
  - Example Prioritization Scheme (PBT)
  - Oncologic Primary Classification
  - Organic functional groups (US EPA)

- Organic functional groups, Norbert Haider (checkmol)
- Protein binding potency GSH
- Toxic hazard classification by Cramer
- rtER Expert System - USEPA
- Substance type
- Chemical elements
- DART scheme
- DNA binding by OASIS
- Groups of elements
- Hydrolysis half-life (pH 6.5-7.4)
- OECD HPV Chemical Categories
- Organic functional groups
- Organic functional groups (nested)
- Repeated dose (HESS)
- US-EPA New Chemical Categories
- DNA alerts for AMES, CA and MNT by OASIS
- Protein binding alerts for Chromosomal aberration by OASIS

Note: The *Toxic hazard classification by Cramer* profiling scheme has been significantly modified based on extensive discussions with the EFSA working group of flavourings. The experts revised the practical implementation of the 33 original Cramer rules, suggested modifications where it was needed and approve the version of the Cramer profiler that is available in Toolbox 4.7. In addition, the files associated with the mechanistic interpretation of each rule are also updated to cover the latest modifications.

- New profilers: None

3. Documented/simulated metabolism

- Documented metabolism databases – No updates.
- Updated metabolic simulators
    - Dissociation simulator
    - Hydrolysis simulator (neutral)

- in vivo Rat metabolism simulator
- Microbial metabolism simulator
- Rat liver S9 metabolism simulator

IV. Data and data matrix

1. New features/functionalities

- Option to filter the information in the observed metabolisms
- Harmonization rules

a. The rigid endpoint tree for *Environmental Fate and Transport* and *ADME* properties have been modified

- The endpoint tree sublevels associated with the *Environmental Fate and Transport* level have been reorganized and simplified to resemble the IUCLID data tree structure
- The *ADME* sublevel which was part of the main *Human Health Hazards* level as an individual sublevel now is harmonized to the *Toxicokinetics, Metabolism and Distribution* sublevel

b. Aquatic toxicity to fish

The defined harmonization rules concern more than 104K data points that could be used for data gap filling purposes.

c. Acute oral toxicity

The defined harmonization rules concern more than 41K data points that could be used for data gap filling purposes.

2. Databases & inventories

- Updated Databases
  - Acute Oral toxicity DB – modified data for a few chemicals
  - Bioconcentration and logKow NITE - modification of chemical ID information for 61 chemicals. Addition of 40 new data points for logPow and 60 chemicals with around 60 data points for BCF
  - ECOTOX - addition of 220 chemicals and 32239 data points

- ECHA REACH – due to mappings of 7 additional OHTs the following new chemicals with data were imported (data referred to Dossiers subset):

✓ OHT 20: pH – 1160 chemicals with 1833 data

✓ OHT 23-2: Self Reactive Substances – 10 chemicals with 12 data

✓ OHT 23-4: Corrosive To Metals – 84 chemicals with 245 data

✓ OHT 23-5: Gases Under Pressure – 4 chemicals with 7 data

✓ OHT 48-2: Endocrine disrupter testing in aquatic vertebrates – in vivo – 26 chemicals with 279 data

✓ OHT 75-3: Endocrine disrupter mammalian screening – in vivo – 25 chemicals with 32 data

- Genotoxicity OASIS - addition of 71 chemicals with 669 data points
- GSH Experimental RC50 - chemical ID correction for a few chemicals
- Human skin sensitisation NICEATM/BfR - modification of chemical ID information and correction is some metadata information for few chemicals
- Hydrolysis rate constant OASIS - addition of a few new chemicals with data
- Toxicity data on pharmaceuticals (US FDA) - addition of 179 chemicals and ~33K data points

➢ Updated Inventories

- AIIC - 23 new chemicals are added

➢ New databases

- EASIS database

The database consists of 488 chemicals with 6012 data related to endocrine activity of chemicals donated by JRC for various endpoints associated with:

✓ Ecotoxicological toxicity - 197 chemicals with 1764 data

✓ Human health hazards - 324 chemicals with 3236 data

- ✓ Intermediate effects - mechanistic information for 101 chemicals with 1012 data

- New inventories – none

V. Category definition

1. (Sub)categorization by user-defined fragment and parametric criteria

New features have been implemented in the Category definition section allowing defining a category and further refine the collected analogues (subcategorization) by user-defined fragment and parametric criteria.

VI. Data Gap Filling

1. New features implemented in the workflow editor allowing:

- filtering of observed metabolite based on defined criteria
- manual input of a value related to QSAR prediction

VII. Report

1. QSAR prediction report has been modified according to the OECD QAF guidance document

2. QSAR justification document has been modified according to the OECD QAF guidance document

3. New option to include all analogues to the reports

4. QSAR prediction report: Option to remove the empty sections

VIII. Repository

1. Updated plug-ins

Three plug-ins have been updated, as follows:

- KATE – for predicting toxicity to aquatic organisms

- VEGA – for predicting various endpoints related to phys-chem, ENV and human endpoints
- PBT profiler – for providing PBT classification based on based on experimental and calculated data.

2. New plug-ins – none.

IX. Web Client

1. Features and improvements related to the data matrix

- Saving the matrix and restoring it from a file
- Exporting the matrix content in different file formats
- Generating reports for predictions (QPRF)
- Displaying metadata for predictions
- Buttons for executing actions from the matrix
- Automatic expansion of matrix rows with data

2. Features and improvements in the IUCLID search section

- Displaying multiple found documents within a single entity (dossier or dataset)
- Loading found IUCLID chemicals on the data matrix

3. Overall improvements and updates

- Improved module for loading lists of chemicals
- Improved task management (progress indication and stopping tasks)
- Improved handling of larger datasets
- Providing reports for QSAR models (QMRF)

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