User manual

Toolbox 4.7 Release Notes

Document history

Version	Comment
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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

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1 Overview

The Toolbox 4.7 installation is a major update of Toolbox 4.6. It can be installed as a separate product alongside previous major releases of Toolbox (4.6, 4.5, 4.4, 4.3, 4.2, 4.1, 4.0, 3.4, 3.3, etc.)

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

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)

OECD

2, rue André Pascal

75775 Paris Cedex 16

France

Tel.: +33 1 45 24 82 00

Fax: +33 1 45 24 85 00

ECHA

Annankatu 18

00120 Helsinki

Finland

Tel.: +358-9-686180

Fax: +33 1 45 24 85 00

LMC

Yakimov St. #1 Prof. Assen Zlatarov" University

8010 Bourgas

Bulgaria

Tel.: +359 56 880230