QSAR TOOLBOX

The OECD QSAR Toolbox for Grouping Chemicals into Categories

User manual

Toolbox 3.4 Release Notes

Document history

Version	Comment
Version 1.0	July 2016: Toolbox 3.4 Release Notes

Issue date: July 2016

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 3.4 installation is a major update of Toolbox. It can be installed as a separate product alongside previous major releases of Toolbox (3.3, 3.2, etc.)

2 System Requirements

Minimum system requirements

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OS: Windows XP

CPU: Core 2 duo at 1.8 GHz or equivalent AMD CPU

RAM: At least 3GB of RAM

HDD: 14 GB free hard drive space

File system: NTFS

Recommended system requirements

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OS: Windows 7 64 bit 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

3 Change log

1. **New features**
   - New metadata fields associated with ECHA CHEM chemical ID like number of compositions, additives, impurities have been added. This functionality concerns metadata table under double click on the measured data and filter by test condition functionality
   - Possibility to export calculated ionization values along with the profiling result for pka and pkb (Acidic [20,30)|Basic [0,10)) for the chemicals on datamatrix
   - Possibility to find the location in the endpoint tree of the QSAR methods when click on the model (once clicking on the model to show/highlight where it is located in the endpoint tree)
   - Endpoint vs. endpoint feature: possibility to change units
   - Endpoint vs. endpoint feature: on the graph with the correlation table on x axis to be written the second endpoint ERBA, etc.; on y axis to be written Count, or number of chemicals – no AC50
   - Similarity options: aromatic ring are unchecked by default
   - New metadata field for qualifiers of data values has been implemented
   - ToxCast database has been added to the list of existing Toolbox databases under Human health hazard sections
   - Description for "Data usage" calculations has been added to the content of F1 help
   - Changed color of pass/not pass status of AOP nodes
   - Notifying messages for different TB operation have been implemented for better usage

2. **Databases**

   A. Updated database

   - Genotoxicity OASIS - 74 new chemicals with 1523 new experimental data
   - Hydrolysis rate constant OASIS – 4 new chemicals with 4 experimental data
   - ECOTOX – 416 new chemicals with 90 932 experimental data
   - Repeated dose toxicity HESS database – 79 new chemicals with 62 179 data
   - ECHA CHEM – 695 chemicals with 25 426 experimental data
   - Skin sensitization database – Added are new 519 EC3 data for 206 chemicals within the database
   - GSH Experimental RC50 – 1045 new chemicals with 1819 data points
   - Chemical reactivity COLIPA – Added are 248 new chemicals with 607 data points
   - Dendritic cell COLIPA is following distribution of data based on assay type:
     - MUSST – data for 113 chemicals with 142 data are newly added
     - mMUSST – 64 chemicals with 64 data points are added

- h-CLAT – 123 new chemicals with 473 experimental data
- Keratinocyte gene expression Givaudan – 223 new chemicals with 791 experimental data

B. New database

- Acute oral toxicity (ChemIDPlus) – 10154 chemicals with 10154 data concerning *in vivo* acute toxicity data (LD50)
- ZEBET database - 362 chemicals with 3867 *in vitro* cytotoxicity data (IC50) and 348 chemicals with 2734 *in vitro* LD50 experimental data
- Keratinocyte gene expression LuSens – associated with AOP workflow. DB includes 79 chemicals with 148 data points

3. Profilers

A. Updated profilers

- ***General mechanistic:***
  - **DNA binding by OASIS v1.4 –** 33 out of 78 structural alerts have been updated and 5 new alerts have been added
  - **Protein binding by OSASIS v1.4** – 4 out 101 structural alerts have been updated and 29 new structural alerts have been added
  - **DPRA Cysteine peptide depletion** – correction of one structural boundary for a single category
  - **DPRA Lysine peptide depletion** – correction of one structural boundary for a single category
  - **Hydrolysis half-life (pH 6.5-7.4)** – improvement of profiler due to the additional transformation reactions implemented into the hydrolysis simulator.
- ***Endpoint specific:***
  - **DNA alerts for AMES by OASIS v.1.4** – 33 out of 78 structural alerts have been updated and 5 new alerts have been added
  - **Protein binding alerts for skin sensitization by OASIS v1.4** – 14 out of 100 structural alerts have been updated. Name for the two of the categories undergo some change.
  - **Protein binding alerts for Chromosomal aberration by OASIS v.1.2** – 5 new structural alert have been added
  - **Oncologic Primary Classification** – alteration of 5 category names. Specific "major highlights of SAR features and mechanistic understanding" has been added to each 48 profiler categories
  - **In vivo Micronucleus alerts by ISSTY** – correction of H-acceptor-bond category

- ***Empiric:***
  - **Organic Functional groups –** 13 out of 502 categories are updated and 8 are new for the profiler
  - **Organic Functional groups (nested) -** 13 out of 502 categories are updated and 8 are new for the profiler
  - **Organic functional groups, Norbert Haider (checkmol) –** correction of one structural boundary for a single category
- ***Toxicological***
  - **Repeated dose (HESS)** – addition of 9 new toxicological categories

B. New profilers:

- **DNA alerts for CA and MNT by OASIS v.1.1** – This is endpoint-specific profiler based on 83 structural alerts responsible for interaction of chemicals with DNA especially related to Chromosomal aberration and Micronucleus tests.

C. Modifications:

- Concerns existing "About" forms associated with 6 Toolbox profilers. Improvements have been done with regards to the modifications implemented in the profilers
- Mechanistic justification for better distinguishing between general and endpoints specific DNA profilers has been provided within help files associated with the respective category

4. Metabolic simulators

A. Updated simulators

- **Autoxidation simulator** – 70 new metabolic transformations has been added. New options have been set associated with reducing number of generated autoxidation products.
- **Hydrolysis simulator (neutral)** – modifications and new metabolic transformations have been added due to improvement of the model
- **Microbial metabolism simulator** – 57 new and 127 modified metabolic transformations have been added
- **Rat liver S9 metabolism simulator** – update of 8 metabolic transformations
- **Skin metabolism simulator** – 10 new and modifications in few numbers of metabolic transformations have been developed. New options have been set associated with reducing number of generated metabolites.

B. New simulators

- ***in vivo* Rat metabolism simulator** – the in vivo metabolic simulator consists of 609 abiotic and enzymatic transformations which are characteristic for the metabolism of *in vivo* experimental systems such as rodent (mostly rat)

5. **Bug fixes**
   - Scroll bar is added within 2D picture in order to see full list with chemical names of the structure
   - Software feedback presented as “notifying messages” is implemented for different TB functions, such as loading database, files, executing query, predicting list with chemicals etc.
   - Fixed bug related to missing default scales selected on some
   - Fixed bug related to structural query in linear profiling schemes to work with "Any bond" mode
   - Fixed bug related to searching queries including ratio data type. This holds for Query tool functionality
   - Fixed bug associated with wrong profiling results (N/A) for two of the endpoint specific profilers
   - Fixed bug related to endpoint vs. endpoint correlation and the way chemicals are subcategorized
   - Fixed bugs related to AOP assessment of nodes when measured and experimental data are combined

OECD

2, rue André Pascal

75775 Paris Cedex 16

France

Tel.: +33 1 45 24 82 00