What is new in OASIS CATALOGIC

5.17.1

I. Modifications in the platform

- Documented Metabolism database version is updated from 3.4.1 to 3.4.2 (compatible with MetaPath version 5.4.2).
- The speed of calculation of EPI Win logKow and Water solubility parameters has been significantly accelerated.
- The ***Load toxicity models functionality*** has been moved to the *INPUT* tab.
- Ability to ***load multiple toxicity models at once***.
- The ***Report functionalities*** have been moved to the *FATE* tab.
- The new option ***"Adaptive Probability to Obtain" threshold*** enables dynamic change of the probability threshold, confining the propagation of the metabolic map. This allows metabolization to be simulated adequately for large symmetric molecules.
- The new option ***"Merge equal branches"*** removes the duplicated equal branches. Instead of all, only one branch remains, representing the duplicated branches. The count of merged branches is the property of the representative branch. The number is also used in the metabolism formalism to correctly calculate the properties (e.g., quantities) of resulting metabolites in the same way as when all the branches are presented separately. So, this new option does not affect the calculations of metabolic properties but improves the 2D visualization of the simulated metabolic map and uses less memory.
- New applicability domains have been extracted for all models because of the new version of Domain Manager.
- Docking with ***OECD QSAR Toolbox v.4.7***.

II. Modifications in the models, existing and new functionalities

- Modifications in biodegradation models:

    - The performance of the CATALOGIC Kinetic 301F model was improved with respect to simulated metabolism and predicted BODs of monomers and iso-olefins.
    - The training set of the CATALOGIC Kinetic 301F model was expanded with 11 monomers and 5 iso-olefins.
- Modifications in hydrolysis models:
    - The training set of the Neutral hydrolysis rate constant model was expanded with 2 chemicals.
    - The training set of the Hydrolysis pH5 model was expanded with 12 chemicals.
- ***Improvements in the QPRF associated with QAF documentation*** – the updates are in accordance with the new QPRF template, taking into account all new and modified sections of the QAF documentation.
- ***Improvements in the QMRF associated with QAF documentation*** – the updates are in accordance with the new QMRF template, taking into account all new and modified sections of the QAF documentation.
- ***New functionality in the BCF models*** allows to change and save the bioaccumulation assessment threshold that appears in the BCF chart (*FATE* tab > Options > View options).
- Generation of customized ***QPRF*** is also allowed for the ***metabolic simulators*** where the tissue specific metabolism is considered only, with no relation to the endpoints.
- The ***visualization of transformations names*** is improved, i.e., the full transformation names are already visible on the simulated 2D map and reported in the QPRFs.
- ***Color legend*** is implemented in the 2D map with simulated metabolism to support the explanation of different highlighting.
- The ***Clustering*** functionality is expanded with new criteria for grouping of chemicals, based on 2D/3D parameters and custom structural fragment.
- The complex ***Flexible search*** combined with metabolism is already allowed to be explained (so far, flexible search without metabolism was allowed for explain only).

- The simulated ***metabolic maps*** could be already filtered based on different criteria and applying the ***Flexible search functionality*** (e.g., using the knowledge from Toolbox, 2D/3D parameters, structure similarity, etc.).
- ***New functionality*** showing the quantity distribution of parent/metabolites over the time is implemented in the *Metabolite distribution* window.

5.16.1

I. Modifications in the platform

- Documented Metabolism database version is updated from 3.4.0 to 3.4.1 (compatible with MetaPath version 5.4.1).
- EPIWin v.4.11 module is used for the calculations of logKow and Water solubility parameters accounted in the parametric layer of the applicability domain. Interface with the package is improved to work in a hidden Windows desktop to avoid unpleasant flashing when starting individual programs.
- Docking with ***OECD QSAR Toolbox v.4.6***.

II. Modifications in the models, existing and new functionalities

- Modifications in biodegradation models:
  - The performance of the CATALOGIC 301C model was improved with respect to simulated metabolism and predicted BODs of PFAS.
- Modifications in bioaccumulation models:
  - The training set of the BCF base-line model was expanded with 16 proprietary chemicals.
  - For five chemicals already present in the training set of the model the observed BCF values have been updated with new ones (re-tested NITE data).
- Modifications in hydrolysis models:
  - The training set of the Neutral hydrolysis rate constant model was expanded with 9 chemicals.
- ***A new functionality*** for searching in databases with documented metabolism data has been introduced in the software. It:
  - provides experimental data support for each molecular transformation.
  - allows the metabolic transformations to be associated with the treatment groups and to check their validity.
  - is organized as a ***local training set*** of the respective transformation.

- ***Improvements in the QPRF*** – more than one graph with the distribution of metabolites based on different parameters (e.g., quantity, logKow, etc.) could be reported as an Appendix; comments could be provided for each of the Appendices independently; update of the save/load functionalities.

- ***Metabolism similarity report and export*** – the new types of report and export are introduced allowing to report/export the results after comparison between chemicals and their metabolites based on selected criteria (e.g., similarity in metabolic transformations, mechanistic or structural similarity, etc.).

- ***Batch mode report*** – this type of report is very useful when there is a need to run a huge list of chemicals. It automatically saves the results for each chemical to a predefined file on the computer. In the event of an error or crash, the results for all the chemicals that have already gone through the model will be saved and will not be lost.

- ***Tree report*** – providing IDs of parent and all generated metabolites; the level of generation and predecessor of each metabolite; indication for observed metabolite; quantities and prediction results of metabolites; the transformations responsible for generating the metabolites and their probabilities.

III. New models

- ***A new model*** has been developed to predict bioconcentration factor (BCF) of PFAS.
- ***A new model*** has been developed to predict the acute aquatic toxicity of Cyprinidae (LC50 96h).

5.15.2

I. Modifications in the platform

- The CATALOGIC software requires activation of a License key with an expiration period (depending on the contractual issues) to allow working with the system.
- Documented Metabolism database version is updated from 3.1.1 to 3.4.0 (Application (MetaPath) version 5.4.0).
- The list with cache files used for storing pre-calculated results has been extended to accelerate the work with the system.
- EPIWin v.4.11 module is used as default calculations of logKow, Molecular weight and Water solubility parameters accounted in the parametric layer of the applicability domain.
- In case the calculation from EPIWin v.4.11 cannot be done, the old dll module (Syracuse University) is applied.
- The panel displaying the current chemical detailed information is significantly redesigned and extended with context specific actions.
- Docking with ***OECD QSAR Toolbox version 4.5***

II. Modifications in the models, existing and new functionalities

- The prediction workflow has been improved organizing all the functionalities associated with explaining the predictions, searching for analogues supporting prediction, analogues supporting simulated metabolism, domain information and reporting.
- New functionalities have been introduced in the software for:
    - ***Evaluating adequacy of simulated metabolism*** by providing:
        - ***Experimental support*** – finding analogues with documented metabolism data based on selected criteria supporting selected sequence of simulated transformations
        - ***Theoretical support*** – mechanistic justification of the transformations simulating metabolism (help files have been developed for biodegradation and bioaccumulation models)

- ***Clustering*** – grouping of chemicals based on selected criteria
- ***Similarity matrix*** – contingency table for the similarity between chemicals based on selected criteria
- ***Selection of representatives*** – prioritization of the chemicals based on their metabolic/structural similarity compared to the other chemicals in the list
- Entropy – removing less informative chemicals based on selected criteria
- ***Metabolism similarity*** – calculate similarity between chemicals accounting different metabolic features
- ***Option to predict metabolites***, which pass dedicated filter.

- ***Help files*** with more detailed information are provided within the software platform.
- Flexible search functionality has been extended with:
  - Search by list (SMILES, Chemical name)
  - Search by Distance for Parameters
  - Masks could be added if fragment search is used
  - ***Transformation search***
- ***Improvements in the QPRF*** of the models – new organization of generation window, new appendix for analogues supporting metabolism, spell-check included for user-defined sections, save/load functionalities implemented.
- The categorization of transformations` names has been improved for BCF base-line models.
- Domain is not applied on hydrolysis products in models accounting for metabolism.

III. New models

- ***Acidic hydrolysis model at pH 5***

5.14.1

- The existing rules used for MOA classification were replaced by profiling schemes
- The rule system for defining ionizing chemicals was replaced with ionizing structural fragments defined by their SMILES
- New functionality for evaluating metabolism similarity accounting for different criteria is implemented by comparing:
    - generated metabolic maps of selected chemicals based on the same metabolic simulator
    - generated metabolic maps of a single chemical based on two different metabolic simulators
- Documented Metabolism database version is updated from 3.1.0 to 3.1.1
- Cache files with pre-caching results of generated metabolites, prediction results, etc. for the training sets of the models
- Improved visualization of the 2D depictions in the metabolic map for QPRF
- Flexible search improvements
- Improvements in the QMRF and QPRF files
- Additional supporting information – new help buttons
- Docking to QSAR Toolbox v.4.4

5.13.1

- Compiled with Delphi 10.2 Version 25.0 (previous was Delphi® XE3 Version 17.0)
- Database (ODB) version is changed from 4.6.6 to 4.6.7 associated with verification of existing unhandled 5AAR
- Toxic models are refactored to work on in memory structures instead of representation in on disc database
- Multi-threaded metabolization
- Ability to add custom analogues in QPRF
- Implementation of distributed cache
- Workflow acceleration

5.12.1

- Added search by observed data to the Flexible search functionalities.
- Added Flexible search functionality to the training sets of Acute aquatic toxicity models.
- Added *Default* button which allows returning to default options of metabolic models.

5.11.19

- Database (ODB) version is changed from 4.6.5 to 4.6.6. This will perform one time update of the existing ODB files. Some structures containing cis-trans stereo information may need to be recalculated.
- Model parameters in ODB files were transformed to multi parameters. These are parameters having more than one value described with metadata. The metadata contains information for source, author name, experimental conditions etc.
- Added new feature to Report that allow to be reported observed data or calculated MOPAC parameters.
- Added new functionalities and improvements in QPRF generation:
    - Added new functionality allowing automatic report creation for more than one prediction,
    - Added new QPRF report options allowing customization of system behavior during reports generation,
    - Content of report item related to model goodness-of-fit and external validation are populated automatically.

5.11.17

- New domain extraction mechanics. The domain is now extracted using the whole aromatic ring as a center atom.
- Added search by a predicted by metabolic model value to the Flexible search functionality.

5.11.16

- QPRF report is now available for all models. Added features for flexible searching for analogues in QPRF.
- Added feature to 2D map filter that allow filtering by individual (node) and aggregate quantity for a metabolite.

5.11.15

- User interface was redesigned using the Windows Ribbon Framework.
- 3D calculations were made multi-threaded to speed up local calculations on multi-core CPUs.
- New ODB file version combining functionalities of previous ODB, A01, SDB and FDB files.
- Sub-fragment search has been extended to use stereo information (in previous version tetrahedral and stereo configuration has been ignored). Now if query molecule has defined

stereo information the target should also contains same stereo configuration. To implement this feature also there is a change in SMILES notation.

5.11.14

- The module for SMILES canonization is updated to correct known cases of non-unique canonization. The existing ODB files will be updated automatically upon first opening.