QSAR Toolbox functionalities.
Category definition by accounting for metabolism.

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2019
Category definition

Grouping by accounting for metabolism

This is a procedure for finding analogues accounting for metabolic transformation of the chemicals.

Toolbox allows finding analogues that have:

• parent and its metabolites with defined profile
• metabolite with defined profile
• exact metabolite
• metabolite with defined parameter value
• metabolite similar to defined one
• logical combination of above searches
Category definition

Grouping by accounting for metabolism

Example: Analogues for **Skin sensitization** accounting for metabolism
Category definition

Grouping by accounting for metabolism

Example: Analogues for Skin sensitization accounting for metabolism
Category definition

Grouping by accounting for metabolism

Example: Analogues for *Skin sensitization* accounting for metabolism

- None – default options; no criteria is set
- Exact – provides opportunity to search for metabolites in the analogues having exact to the specified metabolite structure
- Parametric – to have specific value or range of variation of defined parameter (a list with all parameters currently available in the Toolbox is provided)
- Profile – to have specific category by selected profiler (a list with all profilers is provided)
- Structural – to have specific similarity based on the atom centered fragments
Criteria for parent and metabolites as a package

**Individual** criteria for parent and metabolites

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Category definition

**Grouping by accounting for metabolism**

Example: Analogues for *Skin sensitization* accounting for metabolism
Category definition

Grouping by accounting for metabolism

Example: Analogues for Skin sensitization accounting for metabolism

List with metabolism simulators highlighted by relevancy to selected target endpoint

Parametric query: log Kow in range 0-4

Profile query: to have “Quinone” alert by Protein binding (“Edit” for more details)

Similarity query: Similarity ≥ 70% (adjust options from “Options”)

Individual criteria for parent and metabolites
Category definition

Grouping by accounting for metabolism

Example: Analogues for Skin sensitization accounting for metabolism

Group with analogues found by accounting metabolism and setting different criteria for metabolites

Analogues found based on the criteria for parent and metabolites shown in the previous slide
Category definition

Grouping by accounting for metabolism

Example: Analogues for Skin sensitization accounting for metabolism

Profile query: To have same distribution of protein binding alerts in the package parent&metabolites as the target

“Edit” provides details for the protein binding alerts found in the package parent&metabolites for the target allowing their editing
Category definition

Grouping by accounting for metabolism

Example: Analogues for *Skin sensitization* accounting for metabolism

Group with analogues found by accounting for metabolism and setting profile criteria for the package parent&metabolites
Identification of activated metabolite representing target chemical

Example: Prediction of AMES Mutagenicity based on active metabolite
Category definition

Identification of activated metabolite representing target chemical

Example: Prediction of AMES Mutagenicity based on active metabolite

List with observed Rat Liver S9 metabolites

Active metabolite – DNA alert is identified
Example: Prediction of AMES Mutagenicity based on active metabolite

Category definition
Identification of activated metabolite representing target chemical

CAS 94-59-7
Category definition

Identification of activated metabolite representing target chemical

Example: Prediction of AMES Mutagenicity based on active metabolite

Prediction for selected metabolite based on read across

Predicted Gene Mutation: Positive

Prediction could be transferred to the parent
Identification of activated metabolite representing target chemical

Example: Prediction of AMES Mutagenicity based on active metabolite

When data (predicted or experimental) of a metabolite is used to predict the parent chemical, the data will be assigned to the “with S9” level.
Additional materials related to Category definition by accounting for metabolism are available at Toolbox website:

https://qsartoolbox.org

List with tutorials:
- Tutorial illustrating new options for grouping with metabolism
- Example for predicting skin sensitisation potential of (2E,6Z)-2,6-nonadien-1-ol accounting for skin metabolism
- Tutorial illustrating quantitative metabolic information and related functionalities