QSAR APPLICATION TOOLBOX, v 4.2
BASIC PRACTICAL TRAINING WORKSHOP

BARCELONA, SPAIN
11-12 June 2018
AGENDA

Monday, 11 June 2018 (09:00 – 17:00)

09:00 -09:30 Registration and Toolbox loading onto computers. Welcome and Introductions/Announcements.

09:30-10:30 QSAR Principles. Toolbox description. Workflow. Categorization. Demonstration.

10:30-11:00 **Introduction of basic functionalities**

- **Input** – single chemical or list of chemicals
  - ✓ Structure information (Chem ID – CAS, Name, SMILES, EC Number, InChi, Composition)
  - ✓ Mixtures
  - ✓ Structure drawing
  - ✓ SMARTS search
  - ✓ Query tool
- **Profiling**
  - ✓ Profiling schemes - documentation
  - ✓ Metabolisms – observed and simulated
- **Data**
  - ✓ Databases and inventories
  - ✓ Database statistic
  - ✓ Import/export
  - ✓ Interface with IUCLID6
  - ✓ Scale conversions
- **Category definition**
  - ✓ Alert performance
  - ✓ Clustering
  - ✓ Consistency check (Category elements)
- **Data Gap Filling**
  - ✓ Read across
  - ✓ Trend analysis

- ✓ QSAR
- ✓ Automated and standardized workflows – batch mode
- ✓ Docking external models
- ✓ External QSAR models
- ✓ Endpoint vs. endpoint correlation

- **Reporting**
  - ✓ Prediction report
  - ✓ Category report
  - ✓ Data matrix
  - ✓ Read Across Assessment Framework (RAAF)
- **User interface – document tree, data matrix, etc.**
- **Structural similarity**
- **AOP**

<u>Example 1.</u> Predicting Acute aquatic toxicity to *Tetrahymena pyriformis*, IGC50 (CAS 66251)

- Selecting target endpoint
- Profiling: profilers boundaries (SMARTS) and relevancy of profilers
- Data: availability and database reliability
- Forming categories (relevant profilers) – use of empirical and mechanistic categorizations
- Data gap filling (relevant subcategorization)
- Consistency check (Applying category elements)
- Building reports – Prediction report, Category report and Data matrix
- Document tree

11:00-11:30 Coffee Break

11:30-13:00 **Parallel running** (CAS 66-25-1)

13:00-14:15 Lunch

14:15-15:00 **<u>Example 2.</u> Predicting Skin sensitization** (CAS 366448-53-5)

(reactive parent; multifunctional chemical)

- Selecting target endpoint (Skin sensitization) – complete and limited selection
- Analyzing profilers by endpoint relevancy
- Data availability
- Category building

- Alert Performance (AP) – selection of alerts for primary categorization
- Applying read across for EC3
- Accepting prediction
- Consistency check (Applying category elements)
- Building reports - Prediction report, Category report and Data matrix
  - Adding observed SS data for analogues
  - Adding molecular parameters

Example 3. Predicting Skin sensitization (CAS 122-04-3)

- Scale conversion – application for combined use of data obtained by different assays
- Model domain
- Saving SAR as a categorical model
- Screening inventories

15:00-15:30 **Parallel running** (CAS 366448-53-5 and CAS 122-04-3)

15:30-16:00 Coffee Break

Automated and Standardized workflows

Example 4. Predicting Skin sensitization (CAS 366448-53-5)

- Execution of SW
  - Activation of workflow. Selecting endpoint.
  - Calculating AP - selection of alerts for primary categorization
  - Accepting prediction
  - Report
- Execution of AW
  - Activation of workflows
  - Selecting endpoint (EC3)
  - Report
    - Adding molecular parameters
    - Adding EC3 keratinosens

16:00-17:00 **Example 5. Predicting acute aquatic toxicity (120-83-2)**

- Execution of SW
  - Activation of workflow
  - Selecting associated databases
  - Selecting a category for primary grouping
  - Subcategorization by relevant profilers
  - Accepting prediction
  - Report
- Execution of AW
  - Activation of workflow
  - Executing for *P.promelas* LC50 96h
  - Accepting prediction
  - Report
    - Adding experimental data for analogues
    - Adding molecular parameters

Example 6. Predicting Fate and Ecotoxicity effects (CAS 120-82-1)

- Bioconcentration factor - BCF
- Biodegradation (BOD)
- Acute aquatic toxicity
- Saving QSAR as a regression model.
- Dynamic conversion of parameter units
- "Sufficiency" of the QSAR accuracy and variation of experimental error
- Saving models and model applicability domain – building (QMRF)
- Reporting prediction results.
- Using derived models for predictions within the model applicability domain
- Screening external inventory with the obtained model
- Demo of PBT example prioritization scheme

Batch mode implementation of AW and SW

Example 7. Run example lists of chemicals

<u>Example 8.</u> Predicting Skin sensitization and Mutagenicity (-/+ S9) (CAS 13197-76-7 Lauryl hydroxysultaine).

17:00 Adjourn

Tuesday, 12 June 2018 (09:00 – 17:00)

09:00-11:00 **<u>Example 9.</u> Predicting Fate, Ecotoxicity and Toxicity effects** (CAS 98-01-1 Furfural).

- Biodegradation
- Acute toxicity fish
  - The complementarily of OECD and OASIS protein binding profiles
  - Filter by test conditions (holds for data point – not for chemicals)
- Acute toxicity Daphnia – reproduction
- Acute toxicity Algae
- Ames (-S9, +S9). Alert performance – profilers with low AP. OECD Guidance 471
- Skin sensitization (GPMT)

Parallel running CAS 98-01-1

11:00-11:30 Coffee Break

11:30-13:00 **<u>Example 10.</u> Predicting Carcinogenicity** (CAS 60784-46-5). **Collecting weight of evidences** (WoE).

- Presentation of basic principles
- AMES (-S9;+S9) – OFG
- Alert performance
- Chromosomal aberration
- Carcinogenicity
- Demonstrating the Model domain
- Saving SAR as a categorical models
- Apply SAR on inventory

13:00-14:15 Lunch

14:15-14:45 **Demo of MetaPath platform**

- Profiling and metabolism of CAS 13013-17-7
- Demo of metabolic maps with quantitative information and how to use this information in DGF

14:45-15:30 **<u>Example 11.</u> Predicting Fate, Ecotoxicity and Toxicity effects** (CAS 9002-92-0)

- Biodegradation
- Acute fish
- Genotoxicity – Ames mutagenicity
- Skin sensitization

15:30-16:00 Coffee break

16:00-16:30 **Parallel running 9002-92-0**

16:30-17:00 **<u>Example 12.</u> Predicting genotoxicity and carcinogenicity** (CAS 80-62-6)

- AMES mutagenicity – +S9 and -S9
- Chromosomal aberration (CA)
- Carcinogenicity

17:00 Presentation of Certificates and Adjourn