QSAR APPLICATION TOOLBOX, v 4.1
BASIC PRACTICAL TRAINING WORKSHOP

BARCELONA, SPAIN
20-21 November, 2017
AGENDA

Monday, 20 November 2017 (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 (CAS 50-00-0; CAS 108-68-9)
  - ✓ Structure information (Chem ID, Composition)
  - ✓ Mixtures
  - ✓ SMARTS search
  - ✓ Query tool
- **Profiling**
  - ✓ Profiling schemes
  - ✓ Metabolisms – observed and simulated
- **Data**
  - ✓ Databases and inventories
  - ✓ Import/export
  - ✓ Scale conversions
- **Category definition**
  - ✓ Alert performance
- **Data Gap Filling**
  - ✓ Read across
  - ✓ Trend analysis
  - ✓ QSAR
  - ✓ Automated and standardized workflows – batch mode
  - ✓ Docking external models
  - ✓ External QSAR models
  - ✓ Endpoint vs. endpoint
- **Reporting**

- **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 (Acute aquatic toxicity)
- 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)
- Reporting (new reporting template; possibility to export experimental data and parameters)
- Document tree
- Database statistic

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 – complete and limited selection
- Analyzing profilers by endpoint relevancy
- Data availability (the databases where EC3 data are stored are green highlighted)
- Category building
- Alert Performance (AP) – selection of alerts for primary categorization
- Applying read across for EC3
- Accepting prediction
- Report
  - 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 (EC3 scale; Positive/Negative scale)
- 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
  - Subcategorization by using profile relevancy
  - 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 ("Aquatic OASIS" and "ECOTOX")
  - Selecting the second populated category: USEPA
  - Subcategorization by relevant profilers
  - Fish sensitivity

- 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; Cyprinus carpio, 56 days;
- Biodegradation (BOD)
- Acute aquatic toxicity (Pimephales promelas, LC50, 96 h) (120-82-1)
- 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 (DSL) with obtained model
- Demo of PBT example prioritization scheme

Batch mode implementation of AW and SW

Example 7. Run example lists of chemicals

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

17:00 Adjourn

Tuesday, 21 November 2017 (09:00 – 17:00)

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

- Biodeg – with biodegradation fragments (not strict) + similarity
- Acute toxicity fish (*Poecilia reticulate* – ECOSAR (Aldehydes)
  - The complementarily of OECD and OASIS protein binding profiles
  - Filter by test conditions (holds for data point – not for chemicals) – select a single fish (*Poecilia recticulata*)
- Acute toxicity Daphnia – reproduction
- Acute toxicity Algae
- Ames (-S9, +S9). Alert performance. 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
- Chrom. 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 (load file from Examples folder)

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

- Biodegradation

- Acute fish - with OFG nested; ECOSAR (Nonionic surfactant)
- Genotoxicity – AMES (using Filter by strain in DGF and remove (97A; according to OECD Guideline 471 four strains are necessary)
- 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 – use ECOSAR as a primary classification
- Chromosomal aberration (CA) – indication for positive effect
- Carcinogenicity

17:00 Presentation of Certificates and Adjourn