QSAR APPLICATION TOOLBOX
ADVANCED TRAINING WORKSHOP

BARCELONA, SPAIN
3-4, June 2015

AGENDA

Wednesday, 3 June 2015 (09:00 – 17:30)

09:00-09:15 Registration

Welcome and Introductions/Announcements

09:15-10:00 OECD QSAR Toolbox: Description; workflows, grouping methods databases, estimation methods and plans for future development.

The new features and functionalities in Toolbox 3.3 as compared with 3.2 are described in the associated file.

10:00-11:00 Categorization of chemicals. Recommendations.

11:00-11:30 Coffee Break

11:30-12:00 Refreshing examples (parallel running):

- Predicting acute toxicity of 3,4-Xylidene (CAS 95-64-7)
  - ✓ Using external profile for (non)crowded anilines
  - ✓ Filtering by QA and test conditions (Poecilia reticulate, Pimephales promelas)
  - ✓ Demonstrating the Model domain
  - ✓ Using other(external) models for weights of evidence
  - ✓ Saving QSAR (regression) models.

12:00-13:00 Enhanced functionalities of QSAR Toolbox

- Predicting genotoxicity and carcinogenicity of 3,4-Xylidene (CAS 95647)
  - ✓ AMES Mutagenicity (-S9, +S9)
  - ✓ Chromosomal aberration - (Mammalian cell gene mutation assays; In vitro Chinese Hamster)

- ✓ Carcinogenicity – profiling with accounting for metabolism (DNA + Liver) – maximum values used; atom type (halogenated derivatives)
- ✓ Using external models (TIMES_AMES) for collecting weights of evidence

- Save categorical models as:
  - ✓ SAR
  - ✓ Category (domain) in existing profile
  - ✓ Use of the new category for screening purposes

13:00-14:015 Lunch

14:15-15:30 Enhanced functionalities of QSAR Toolbox

- Predicting Repeated Dose Toxicity of CAS 95-64-7 and 108-69-0
- Predicting developmental and reproductive toxicity (DART model of P&G) - 330-54-1
- Deriving multiparametric QSARs
- Import/export of QSAR (regression) models.
- Structural similarity - describing the options
- Scale conversion – application for combined use of data obtained by different assays
- Building a new categorization profile – Manually:
  - Profile for crowded anilines. Application for subcategorization (CAS 95-64-7)
  - Aldehydes. Application for screening purposes (use DSL)
    - ✓ Not aromatic, not alpha halogenated and
    - ✓ Possessing protein binding functionality (as parent and after metabolism)
    - ✓ Having logKow in range and size parameter in range
- Reporting prediction results. Standard reports. Detailed description of reporting settings
  - ✓ Toolbox Prediction Reporting Format (TPRF)
  - ✓ Chemical Model Reporting Format (QMRF)
  - ✓ Chemical Category Reporting Format (CCRF)
  - ✓ QMRF
  - ✓ Customized reports

15:30-16:00 Coffee Break

16:00-17:00 Enhanced functionalities of QSAR Toolbox

- Import/export of data by Vertical and horizontal layouts. Building proprietary databases (available in the Examples folder).
- Export of Toolbox predictions to IUCLID5 through:
  - ✓ XML files
  - ✓ WebServices
- Import of data for single chemical or multiple chemicals from IUCLID5 to Toolbox through:
  - ✓ XML files
  - ✓ WebServices
- Docking external (Q)SAR models to Toolbox:
  - ✓ Docking of CATALOGIC and TIMES to Toolbox
  - ✓ Examples of joint use of external models and Toolbox: Limonene CC(=C)C1CCC(C)=CC1
    - BOD – comparison of results obtained from TB and Catalogic
    - Skin sensitization - comparison of results obtained from TB and TIMES
- Using EChA_Chem Database in read-across: CAS 25584-83-2
  - ✓ Skin sensitization - Organic functional groups; max. values
  - ✓ AMES – Organic functional groups; (undefined test organism species (with and without metabolic activation)); max value; remove outlier by Filter by Test Guideline
  - ✓ Other endpoints
- Using External (Q)SAR models in Toolbox:
  - ✓ Explosive materials – input by smiles:

O=N(=O)C(CC=CCC(N(=O)=O)(N(=O)=O)N(=O)=O)(N(=O)=O)N(=O)=O

  - ✓ Photoinduced Toxicity (*D.magna*)– anthracene (120-12-7) and phenantrene (85-01-8)
  - ✓ 3T3 RNU (if apply need time to calculate 3D)
  - ✓ DART model of P&G - CAS 330-54-1
- New implementation of ECOSAR models in Toolbox
- Possibility to filter chemicals in data gap filling by making use of measured data -
  - ✓ CAS 95-64-7; Apply TA for LC50, 96h, species: *P. reticulate*
  - ✓ Filter less bioaccumulative chemicals using logKow

- ToxCast database in Toolbox
- Endpoint vs. endpoint correlations
  - ✓ Example 1: Correlation between ToxCast AC50 Estrogen receptor data and AC 50 Reporter Gene Assay ERα Agonist data
  - ✓ Filter by relative ERBA data

- Query Tool functionality
  - ✓ Example: Chemicals which are Ames positive, but with negative Carcinogenicity data

17:00 Adjourn

Thursday, 4 June 2015 (09:00 – 17:30)

09:00-10:00 Regulatory use of QSAR. The role of QSAR Toolbox (oral)

Workflow for category evaluation associated with chemical submissions in Europe (oral). Examples for analogue evaluation based on aldehydes for acute toxicity to fish

10:00-11:00 Evaluating category consistency of:

- ✓ aldehydes and
- ✓ acrylates/methacrylates (from the "Example" folder)

11:00-11:30 Coffee Break

11:30-13:00 Category evaluation associated with chemical submissions in Europe.

- Predicting CAS 15625-89-5:
  - ✓ Acute toxicity
  - ✓ AMES
  - ✓ Skin sensitization
- Predicting CAS 42978-66-5:
  - ✓ AMES Genotoxicity
  - ✓ Skin sensitization

13:00-14:15 Lunch

14:15-15:30 Parallel running.

- Handling of metabolism.

- ✓ Predicting Skin sensitization of CAS 28069-72-9
- ✓ Predicting AMES + S9 of Safrole (CAS 94-59-7)
- ✓ Predicting skin sensitization of CAS 97-53-0 - New categorization functionality applying metabolism (combining Protein binding alerts for SS with AU simulator)

- Handling of mixtures
  - ✓ Example mixture - {X=100}C(O)CCC_{X=1}C(C)(=O)c1c(Cl)c(Cl)c(Cl)cc1_{X=10}c1(C(=O)c2ccccc2)ccccc1
  - ✓ Predicting acute toxicity
  - ✓ Predicting skin sensitization

15:30-16:00 Coffee Break

16:00-17:00 Parallel running.

- Handling of tautomers for predicting toxicological endpoints:
  - ✓ Predicting Skin sensitization of CAS# 577-71-9 w and w/o accounting for tautomerism
  - ✓ Predicting Skin sensitization of CAS# 99-56-9 w and w/o accounting for tautomerism
  - ✓ Predicting Ames mutagenicity of CAS 621318 (CAS 120 376) w and w/o accounting for tautomerism. The role of metabolism applied on tautomeric sets.
- Handling of tautomers for predicting ecotoxicological endpoints
  - ✓ Predicting Acute toxicity of CAS# 65-45-2 accounting for tautomerism
  - ✓ Predicting Acute toxicity of CAS# 89-62-3 accounting for tautomerism
- AOPs and their implementation in Toolbox
  - ✓ CAS 553 979
  - ✓ CAS 97530
  - ✓ CAS 106 503

17:00 Presentation of Certificates and Adjourn