QSAR APPLICATION TOOLBOX (Version 3.0)
ADVANCED TRAINING WORKSHOP

BARCELONA, SPAIN
7-8 November 2012

AGENDA

Wednesday, 7 November 2012

0900-0915 Registration
Welcome and Introductions/Announcements – Russo

0915-1000 QSAR Toolbox: Description; workflows, grouping methods databases, estimation methods and plans for future development – Mekenyan

1000-1100 Categorization of chemicals. Recommendations.

1100-1130 Coffee Break

1130-1200 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.
    - ✓ Within the Toolbox environment
    - ✓ As QMRF (xml format).

1200-1300 Enhanced functionalities of QSAR Toolbox

- Predicting genotoxicity and carcinogenicity of 3,4-Xylidene (CAS 95647)
  - ✓ AMES Mutagenicity (-S9, +S9) – use maximum values
  - ✓ Role of metabolism (liver S9) for categorization of 3,4-Xylidene for AMES (with S9) – use maximum values
  - ✓ Chromosomal aberration (S9 and +S9; combine all data: for +S9) – use maximum values; DNA + liver metabolism
  - ✓ Carcinogenicity – profiling with accounting for metabolism (DNA + Liver) – maximum values used; atom type (halogenated derivatives)
- Save categorical models as:
  - ✓ SAR
  - ✓ Category (domain) in existing profile
- Use of the new category for screening purposes

- Predictions acute toxicity of (CAS 13013177).
  - Filtering by test conditions
  - Collecting weights of evidence by using:
    - ✓ Toolbox derived model (trend analysis)
    - ✓ External QSAR models (ECOSAR, M4)
- Refining external models using data for analogues
- Import/export of QSAR (regression) models.
- Deriving multiparametric QSARs
- 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
- Reporting prediction results. Customized reports
    - ✓ Changing report design
- Import/export of data by Vertical and horizontal layouts. Building proprietary databases
- 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
- Import/Export of QSARs
- Docking external (Q)SAR models to Toolbox:
    - ✓ Docking of CATALOGIC and TIMES to Toolbox
    - ✓ Examples of joint use of external models and Toolbox
- Using EChA-Chem database: CAS 25155-25-3 (use of EChA-Chem database)
- General mechanistic vs. endpoint specific alerts:
    - ✓ Skin sensitization - CAS 5406122

- ✓ Mutagenicity (AMES) - CAS 25155-25-3 (with and without S9 activation)
- Repeated dose toxicity:
  - ✓ CAS 108-690 – anemia, total (whole boddy) value
  - ✓ CAS 123-308
- Implementation of AOP for skin sensitization in Toolbox
  - ✓ CAS 553 979
  - ✓ CAS 97530
  - ✓ CAS 106 503

1300-1415 Lunch

1400-1530 Enhanced functionalities of QSAR Toolbox (Contd)

1530-1600 Coffee Break

1600-1700 Enhanced functionalities of QSAR Toolbox (Contd)

1700 Adjourn

Thursday, 8 November 2012

0900-1000 Regulatory use of QSAR. The role of QSAR Toolbox (oral)

1000-1030 Workflow for category evaluation associated with chemical submissions in Europe (oral). Examples for analogue evaluation based on aldehydes for acute toxicity to fish

1030-1100 Toolbox 3.0. Detailed overview of new functionalities in 3.0

- Biodegradation – CAS 79925
- Hydrolysis rate – CAS 4346-18-3; CAS 55389, CAS 106-88-7
- Hydrolysis simulator – CAS 142-22-3
- Ionization – CAS 121-47-1; CAS 632-46-2; CAS 100-02-7
- Autoxidation – CAS 13466-78-9
- Query Tool for data mining in Toolbox databases

1100-1130 Coffee Break

1130-1230 Handling of metabolism

- Predicting Skin sensitization of CAS 28069-72-9
- Predicting AMES + S9 of Safrole (CAS 94-59-7)

1230-1300 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

1300-1415 Lunch

1415-1530 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

1430-1530 Running of examples proposed by attendees (I)

NOTE: Participants are invited to bring an example of their own choosing for this session

1530-1600 Coffee Break

1600-1700 Running of examples proposed by attendees (II)

1700 Presentation of Certificates and Adjourn – Russo