QSAR APPLICATION TOOLBOX (Version 3.0)
BASIC TRAINING WORKSHOP

BARCELONA, SPAIN
5-6 November 2012

AGENDA

Monday, 5 November 2012

09:00-09:30 Registration and Toolbox loading onto computers

09:30-09:45 Welcome and Introductions/Announcements – Russo

09:45-11:00 Toolbox functionalities. Forming of Categories – oral –Mekenyan

- Description of Toolbox. Workflow. Functionalities
- Skin sensitization and Mutagenicity (-/+ S9); CAS # 13197-76-7 (lauryl hydroxysultaine)
- Forming categories
- Bioconcentration; CAS # 120-82-1 (1,2,4-trichlorobenzene); *Cyprinus carpio*, 56 days;
- Acute aquatic toxicity; CAS # 120-82-1; *Pimephales promelas*, LC50, 96 h

11:00-11:30 Coffee Break

11:30-13:00 Introducing basic functionalities (parallel running CAS 66-25-1 for IGC50)

- Input – single chemical or list of chemicals. QA of chemical ID
- Profiling – explanation of identified categories
- Extracting data – data source, quality of data, building data matrix
- Forming categories – use of empirical and mechanistic categorizations
- Data gap filling
- Reporting

13:00-14:15 Lunch

14:15-15:30 Enhanced functionalities and analysis – Part I

- 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. Standard reports
  - ✓ Toolbox Prediction Reporting Format (TPRF)
  - ✓ Chemical Model Reporting Format (QMRF)
  - ✓ Chemical Category Reporting Format (CCRF)
- Using derived models for predictions within the model applicability domain
- Screening external inventory (DSL) with obtained model

15:30-16:00 Coffee Break
16:00-17:00 Enhanced functionalities and analysis – Part I, continuing
17:00 Adjourn

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09:00-10:00 Enhanced functionalities and analysis – Part II

- Skin allergy of 4-nitrobenzoyl chloride (CAS 122-04-3)
- Scale conversion – application for combined use of data obtained by different assays
- Predicting Skin sensitization of Lauryl hydroxysultaine CAS 13197-76-7
  - Model domain derived by Toolbox
  - Saving SAR as a categorical models
- Predicting acute toxicity of 3,4-Xylidene (CAS 95-64-7)
  - Filtering by QA and test conditions.
  - Demonstrating the Model domain
  - Saving QSAR (regression) models.
    - ✓ Within the Toolbox environment
    - ✓ As QMRF (xml format).
- Reporting prediction results. Standard reports
- Profiling and metabolism (CAS 13013-17-7) – use MetaPath platform
- Predicting for CAS 13013-17-7
  - Predicting acute toxicity for CAS 13013-17-7.
    - ✓ Filtering by test conditions
    - ✓ Saving the QSAR (regression) models. Model domain.
    - ✓ Predictions by external QSAR models
  - AMES (-S9, +S9). Data usage in data prediction making for categorical endpoints:
    - ✓ Minimum/Maximum/Average
    - ✓ Lowest/Highest median
    - ✓ Lowest/Highest mode

11:00-11:30 Coffee Break
11:30-13:00 Enhanced functionalities and analysis – Part II (Contd.)
13:00-14:15 Lunch
14:15-15:30 Parallel running of Toolbox on selected examples

- Fate, Ecotoxicity and Toxicity effects of furfural (CAS 98-01-1)
  - Biodeg – with biodegradation fragments (not strict) + similarity
  - Acute fish
    - ✓ Using a new category (not the endpoint specific Biodeg category)
    - ✓ The complementarily of OECD and OASIS protein binding profiles

        - ✓ Filter by test conditions (holds for tests – not for chemicals) – select a single fish (Poecilia recticulata)
    - Acute Daphnia
    - Acute Algae
    - Ames (-S9, +S9): - ultimate prediction – negative; try the categories of
        - aldehydes (above used) – does not work
        - DNA-OASIS (positive alert provides negative predictions)
            - Save model as a category
            - Save model as a SAR
            - Screen DSL with derived model/category
        - Are the alerts adequate?
            - Positive alerts are just categorization tools
            - Positive alerts do not necessarily mean positive effects
        - Adding new knowledge – aromatic aldehydes

- Fate, Ecotoxicity and Toxicity effects of furfural (Dodecyloxy)ethanol (CAS 9002920)
    - Biodegradation
        - with organic functional groups – nested;
        - biodegradation fragments (strict)
        - CATABOL – docked to Toolbox (just mentioning)
    - Acute fish - with organic functional groups – nested
    - Genotoxicity – AMES
    - Skin sensitization
- The capabilities of protein binding potency – predicting Ecotoxicity (IGC50) of CAS 557-48-2
- Predicting genotoxicity and carcinogenicity of 2-Propenoic acid, 2-methyl-, methyl ester, CAS 80-62-6 (validating experimental data for carcinogenicity)
    - AMES mutagenicity – +S9 and -S9 – use ECOSAR as a primary classification
    - Read-across for chromosomal aberration (CA)
    - Read-across for carcinogenicity

15:30-16:00 Coffee Break

16:00-17:00 Enhanced functionalities and analysis – Part III

- Vertical and horizontal import/export of data. Building a proprietary data base
- How to handle inconsistency between CAS and structure (CAS 50-28-2)

17:00 Presentation of Certificates and Adjourn