INTRODUCTION

x QSAR models for regulatory purpose should account for the specific intended use of a model.

x There are many QSAR models to predict aquatic toxicity giving acceptable results for baseline toxicity, but problems may arise for chemicals which exhibit excess toxicity through processes more complex than the narcotics.

AIM: to evaluate the performances of three QSAR models for fish acute toxicity (DEMETRA, ECOSAR and TOPKAT) on a pool of industries chemicals

MATERIALS & METHODS

QSAR MODELS TESTED

x DEMETRA\(^1\) (LC50 96h for Oncorhynchus mykiss), developed specifically for pesticides

x ECOSAR\(^2\) v. 0.99 (LC50 96h for fish), based on 40 submodels for specific chemical classes

x TOPKAT\(^3\) (LC50 96h for Pimephales promelas), based on 4 submodels for specific chemical classes

DATASET FOR TESTING MODELS

x MED-Duluth: 568 chemicals with data for LC50 96h for Pimephales promelas

x OECD-HPV\(^4\): data extracted with the OECD-Toolbox from the HPVC inventory. 186 compounds with experimental data with LC50 for fish have been selected, once pruned from inorganics, mixtures, and too variable data (see figure 1)


distribution of the most variable substances for Oncorhynchus mykiss

Fig. 1 – Variability of experimental data on LC50 96h for the OECD-HPV dataset for the most variable substances. P = pesticides; D = organics; I = inorganics

Comparison between Pimephales promelas & Oncorhynchus mykiss

Fig. 2 – Comparison of intraspecies variability of toxicity in fish. Good correlation of experimental toxicity justifies the use of any QSAR model besides the specific species addressed by the model

The results showed that DEMETRA model gave much less false negatives than the other models being able to predict less inert compounds and maintaining better performances on organic compounds that the other tested models.

These findings show interesting possibilities for further improvements, extending the DEMETRA model towards industrial chemicals.

REFERENCES:

1 http://www.demetra-project.eu/new.php
2 http://www.epa.gov/oppt/newchems/tools/21ecosar.htm
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4 http://www.epa.gov/NECT/dstox/sdf_epafhm.html
5 http://www.oecd.org/document/21/0,3343,en_2649_34379_33957015_1_1_1_1,00.html