	QMRF identifier (JRC Inventory): **Q13-33-0073**
	QMRF Title: **Polar narcosis QSAR for Tetrahymena pyriformis acute toxicity**
	Printing Date: **Dec 11, 2019**

1.QSAR identifier

1.1.QSAR identifier (title):

Polar narcosis QSAR for Tetrahymena pyriformis acute toxicity

1.2.Other related models:

None

1.3.Software coding the model:

N/A

2.General information

2.1.Date of QMRF:

7 September 2009

2.2.QMRF author(s) and contact details:

[1]Fania Bajot Liverpool John Moores University

[2]Mark Cronin Liverpool John Moores University + 44 151 231 2402 m.t.cronin@ljmu.ac.uk

http://www.staff.livjm.ac.uk/phamcron/qsar/qsar1.htm

2.3.Date of QMRF update(s):

2.4.QMRF update(s):

2.5.Model developer(s) and contact details:

[1]Fania Bajot Liverpool John Moores University

[2]Mark Cronin Liverpool John Moores University + 44 151 231 2402 m.t.cronin@ljmu.ac.uk

http://www.staff.livjm.ac.uk/phamcron/qsar/qsar1.htm

2.6.Date of model development and/or publication:

11 September 2009

2.7.Reference(s) to main scientific papers and/or software package:

2.8.Availability of information about the model:

The model is non-proprietary. Information on the algorithm and training set is publicly available.

2.9.Availability of another QMRF for exactly the same model:

None

3.Defining the endpoint - OECD Principle 1

3.1.Species:

Tetrahymena pyriformis

3.2.Endpoint:

3.Ecotoxic effects 3.3.Acute toxicity to fish (lethality)

3.3.Comment on endpoint:

40-h assay

3.4.Endpoint units:

Moles per litre

3.5.Dependent variable:

Tetrahymena pyriformis 50% growth inhibition concentration (IGC50) (moles per litre) were logarithmically transformed (to base 10) and multipled by minus 1

3.6.Experimental protocol:

Toxicity data were extracted from Enoch, S. J.(2008) Chemosphere 71: 1225-1232.

3.7.Endpoint data quality and variability:

4.Defining the algorithm - OECD Principle 2

4.1.Type of model:

QSAR

4.2.Explicit algorithm:

Linear regression analysis

log (1/IGC50) = 0.619 log P - 0.997

4.3.Descriptors in the model:

log P dimensionless logarithm of octanol-water partition coefficient

4.4.Descriptor selection:

One descriptor (log P) chosen empirically from a knowledge of mechanism of action

4.5.Algorithm and descriptor generation:

log P was calculated from SMILES string

4.6.Software name and version for descriptor generation:

KOWWIN v1.67

KOWWIN is part of the EPISuite software

Available for download from http://www.epa.gov/oppt/exposure/pubs/episuite.htm

http://www.epa.gov/oppt/exposure/pubs/episuite.htm

4.7.Chemicals/Descriptors ratio:

138 = 138 chemicals / 1 descriptor

5.Defining the applicability domain - OECD Principle 3

5.1.Description of the applicability domain of the model:

Applicability domain covers a log P range from 0.26 to 5.99. The acute toxicity values (negative logarithm of molar value) ranged from -1.5 to 2.63.

The compounds selected have been identified as polar narcotics to fish. i.e. they are non-reactive and cause lethality by accumulation at cellular membranes. They are characterised by being simple organic compounds including phenol derivatives and aniline derivatives compounds.

5.2.Method used to assess the applicability domain:

None

5.3.Software name and version for applicability domain assessment:

N/A

5.4.Limits of applicability:

Polar narcosis mechanism of acute fish toxicity.

6.Internal validation - OECD Principle 4

6.1.Availability of the training set:

Yes

6.2.Available information for the training set:

CAS RN: Yes

Chemical Name: Yes

Smiles: Yes

Formula: No

INChI: No

MOL file: No

6.3.Data for each descriptor variable for the training set:

All

6.4.Data for the dependent variable for the training set:

All

6.5.Other information about the training set:

138 simple organic compounds including phenol derivatives and aniline derivatives compounds.

6.6.Pre-processing of data before modelling:

None

6.7.Statistics for goodness-of-fit:

r^2adjusted for degrees of freedom = 0.763

standard error = 0.397

Fishers statistic = 443

6.8.Robustness - Statistics obtained by leave-one-out cross-validation:

leave-one-out cross validated r^2= 0.758

6.9.Robustness - Statistics obtained by leave-many-out cross-validation:

6.10.Robustness - Statistics obtained by Y-scrambling:

6.11.Robustness - Statistics obtained by bootstrap:

6.12.Robustness - Statistics obtained by other methods:

7.External validation - OECD Principle 4

7.1.Availability of the external validation set:

No

7.2.Available information for the external validation set:

CAS RN: No

Chemical Name: No

Smiles: No

Formula: No

INChI: No

MOL file: No

7.3.Data for each descriptor variable for the external validation set:

No

7.4.Data for the dependent variable for the external validation set:

No

7.5.Other information about the external validation set:

7.6.Experimental design of test set:

7.7.Predictivity - Statistics obtained by external validation:

7.8.Predictivity - Assessment of the external validation set:

7.9.Comments on the external validation of the model:

8.Providing a mechanistic interpretation - OECD Principle 5

8.1.Mechanistic basis of the model:

All compounds are considered to act by polar narcosis. This is well established for non-reactive compounds. Acute lethality is brought about by accumulation in cellular membranes causing their disurption and ultimately death of the organism. The ability of the compound to accumulate in a cellular membrane is thought to be related to its intrinsic hydrophobicity. Hydrophobicity of these compounds is modelled by log P.

8.2.A priori or a posteriori mechanistic interpretation:

As stated in Section 8.1, hydrophobicity is related to log P and is known to the controlling factor in the acute lethal toxicity of polar narcotic compounds. Compounds in this data set were selected a priori on the basis that they acted as polar narcotics.

8.3.Other information about the mechanistic interpretation:

9.Miscellaneous information

9.1.Comments:

This model is related to a large number of models for polar narcosis for acute fish toxicity.

9.2.Bibliography:

Enoch SJ (2008) Chemosphere 71, 1225-1232.

9.3.Supporting information:

Training set(s)Test set(s)Supporting information

10.Summary (JRC QSAR Model Database)

10.1.QMRF number:

Q13-33-0073

10.2.Publication date:

2013-07-03

10.3.Keywords:

Tetrahymena pyriformis;acute fish toxicity;polar narcosis;

10.4.Comments:

former Q27-39-8-319