	QMRF identifier (JRC Inventory): **Q13-33-0075**
	QMRF Title: **Non-polar narcosis QSAR for Tetrahymena pyriformis acute toxicity**
	Printing Date: **Dec 11, 2019**

1.QSAR identifier

1.1.QSAR identifier (title):

Non-polar narcosis QSAR for Tetrahymena pyriformis acute toxicity

1.2.Other related models:

None

1.3.Software coding the model:

2.General information

2.1.Date of QMRF:

7 September 2009

2.2.QMRF author(s) and contact details:

[1]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]Liverpool John Moores University

2.3.Date of QMRF update(s):

2.4.QMRF update(s):

2.5.Model developer(s) and contact details:

[1]Ellison CM 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:

7 September 2009

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

Ellison CM, Cronin MTD, Madden JC and Schultz TW (2008) Definition of the structural domain of the baseline non-polar narcosis model for Tetrahymena pyriformis. SAR and QSAR in Environmental Research 19, 751–783

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 measured according to: I. Kahn and al. Altern. Lab. Anim. 35 (2007), pp. 15–24.

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)= 0.825 log P - 2.07

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 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:

87 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 -0.78 to 5.75. The acute toxicity values (negative logarithm of molar value) ranged from -2.51 to 1.67.

The compounds selected have been identified as non-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 alkyl, halogen and ketone substituted mono-aromatic and (fully saturated) alkyl compound.

5.2.Method used to assess the applicability domain:

None

5.3.Software name and version for applicability domain assessment:

5.4.Limits of applicability:

Non-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:

87 simple organic compounds including alkyl, halogen and keto

6.6.Pre-processing of data before modelling:

None

6.7.Statistics for goodness-of-fit:

r^2adjusted for degrees of freedom = 0.957

standard error = 0.270

Fishers statistic = 1895

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

leave-one-out cross validated r^2 =0.954

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 non-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 non-polar narcotic compounds. Compounds in this data set were selected a priori on the basis that they acted as non-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 non-polar narcosis (also termed baseline or minimum toxicity) for acute fish toxicity.

9.2.Bibliography:

Kahn I et al. (2007) Alternatives to Laboratory Animals 35, 15–24

9.3.Supporting information:

Tetrahymena - Non Polar narcosis training_87.sdf	http://qsardb.jrc.ec.europa.eu/qmrf/protocol/Q13-33-0075/attachment/A773

Test set(s)Supporting information

10.Summary (JRC QSAR Model Database)

10.1.QMRF number:

Q13-33-0075

10.2.Publication date:

2013-07-03

10.3.Keywords:

Tetrahymena pyriformis;acute fish toxicity;non-polar narcosis;

10.4.Comments:

former Q27-40-8-320