	QMRF identifier (JRC Inventory): **Q13-33-0049**
	QMRF Title: **QSAR for narcosis to fathead minnow, including non-polar and polar narcosis**
	Printing Date: **Dec 11, 2019**

1.QSAR identifier

1.1.QSAR identifier (title):

QSAR for narcosis to fathead minnow, including non-polar and polar narcosis

1.2.Other related models:

1.3.Software coding the model:

2.General information

2.1.Date of QMRF:

30 December 2009

2.2.QMRF author(s) and contact details:

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2.3.Date of QMRF update(s):

2.4.QMRF update(s):

2.5.Model developer(s) and contact details:

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2.6.Date of model development and/or publication:

The model was published for the first time in 2005 (Pavan et al., 2005), although the data set was known earlier.

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

Pavan M, Worth AP & Netzeva TI (2005). Preliminary analysis of an aquatic toxicity dataset and assessment of QSAR models for narcosis. JRC Report No. 21749 EN. http://ecb.jrc.ec.europa.eu/qsar/

2.8.Availability of information about the model:

Non-proprietary. Defined algorithm. Training and test sets available.

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

3.Defining the endpoint - OECD Principle 1

3.1.Species:

Pimephales promelas (fathead minnow).

3.2.Endpoint:

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

3.3.Comment on endpoint:

LC50 - the concentration causing 50% lethality in Pimephales promelas, after an exposure of 96 hours.

3.4.Endpoint units:

Moles per litre

3.5.Dependent variable:

log LC50

3.6.Experimental protocol:

See: Veith et al. (1983) and Verhaar et al. (1995).

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 QSAR

Log LC50 = -0.810 LogKow - 1.74

4.3.Descriptors in the model:

Log Kow The descriptor (log Kow) data are both experimental and calculated values. Even if Kow is usually considered a good physicochemical descriptor, there is no evidence that the measurements were made by the same protocol, in the same laboratory. Thus a certain amount of variability could be present.

4.4.Descriptor selection:

The descriptor (log Kow) was selected a priori.

4.5.Algorithm and descriptor generation:

The descriptor data are both experimental and calculated values.

4.6.Software name and version for descriptor generation:

4.7.Chemicals/Descriptors ratio:

144/1= 144 chemicals / descriptor

5.Defining the applicability domain - OECD Principle 3

5.1.Description of the applicability domain of the model:

The QSAR model was defined by the developer to be applicable to chemicals with logKow values in range from -1.31 to 6.20. However, the model is not reccomended for chemicals with logKow < 1 due to large error for both non-polar and polar narcotics. It works best in the range 3 < logKow < 6. The model is applicable to chemicals acting by the narcosis mode of action, and it is recommended only when the precise mechanism (i.e. non-polar or polar narcosis) is difficult to determine. The structural domain includes aliphatic and aromatic hydrocarbons, halogenated aliphatic and aromatic hydrocarbons, ethers, alcohols, aromatic nitrocompounds, anilines and phenols (in case of phenols and anilines, only when the presence of an additional substituent on the benzene ring does not change the mechanism of action).

5.2.Method used to assess the applicability domain:

Expert judgement

5.3.Software name and version for applicability domain assessment:

5.4.Limits of applicability:

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:

6.6.Pre-processing of data before modelling:

6.7.Statistics for goodness-of-fit:

The model was trained with data for 144 chemicals.

Predictor=Constant Coeff.= -1.74 SE=0.070;

Predictor=LogKow Coeff.=-0.810 SE=0.026;

The following fitness regression parameters were calculated for this QSAR:

R^2= 87.55 (Coefficient of determination);

R^2adj = 87.46 (Coefficient of determination adjusted for the degrees of freedom);

s = 0.455 (Standard error of the estimate);

F = 998.3 (Fisher function);

LOF = 0.21 (Friedman modified);

SDEC = 0.452 (Standard Deviation Error in Calculation);AIC = 0.213 (Akaike Information Criterion);

FIT = 6.83 (Kubinyi function).

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

The model was evaluated by leave-one-out internal cross-validation (Q2LOO).

Q2LOO = 87.06 (explained variance in prediction);

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:

The model was evaluated bootstrap with 5000 iterations.

Q2bootstrap = 87.11 (explained variance in prediction by bootstrapping);

6.12.Robustness - Statistics obtained by other methods:

SDEP = 0.461 (Standard Deviation Error in Prediction).

7.External validation - OECD Principle 4

7.1.Availability of the external validation set:

Yes

7.2.Available information for the external validation set:

CAS RN: Yes

Chemical Name: Yes

Smiles: Yes

Formula: No

INChI: No

MOL file: No

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

All

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

All

7.5.Other information about the external validation set:

7.6.Experimental design of test set:

For external validation, a subset of a list containing 177 OECD SIDS chemicals (ENV/JM/TG(2004)26) with measured LC50 values to fathead minnow was used. The chemicals in the test set are within the range of log Kow of the training set and classified as narcotics (either non-polar or polar) in a consensus mechanism of action classification.

7.7.Predictivity - Statistics obtained by external validation:

N. ext = 17

Q^2ext = 84.31

SDEPext = 0.637

The two nonyl phenols were excluded from these statistics due to high leverage.

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:

The mechanistic interpretation for logKow is related to the partitioning of the substance from water into the organism's lipid phase. It reflects bioavailbility of the chemical in fish..

8.2.A priori or a posteriori mechanistic interpretation:

A priori.

8.3.Other information about the mechanistic interpretation:

9.Miscellaneous information

9.1.Comments:

Comment on the algorithm: n = 144 (combination of the training sets of the models for non-polar narcosis and polar narcosis in EU TGD on risk assessment)

9.2.Bibliography:

[1]Veith GD, Call DJ & Brooke LT. (1983). Structure-toxicity relationships for the fathead minnow, Pimephales promelas: Narcotic industrial chemicals. Canadian Journal of Fisheries and Aquatic Sciences 40, 743-748

[2]Verhaar HJM, Mulder W & Hermens JLM (1995). QSARs for ecotoxicity. In: Overview of structure-activity relationships for environmental endpoints, Part 1: General outline and procedure. Hermens

JLM. (Ed), Report prepared within the framework of the project “QSAR for Prediction of Fate and Effects of Chemicals in the Environment”, an international project of the Environmental Technologies RTD Programme (DGXII/D-1) of the European Commission under contract number EV5V-CT92-0211 http://ecb.jrc.ec.europa.eu/qsar/information-sources/

9.3.Supporting information:

Narcosis to fathead minnow Training_144.sdf	http://qsardb.jrc.ec.europa.eu/qmrf/protocol/Q13-33-0049/attachment/A715
Narcosis to fathead minnow Test_17.sdf	http://qsardb.jrc.ec.europa.eu/qmrf/protocol/Q13-33-0049/attachment/A716

Test set(s)

10.Summary (JRC QSAR Model Database)

Supporting information

10.1.QMRF number:

Q13-33-0049

10.2.Publication date:

2013-06-28

10.3.Keywords:

acute fish toxicity;narcosis;fathead minnow;

10.4.Comments:

former Q15-28-8-162