	QMRF identifier (JRC Inventory): **Q17-471-0031**
	QMRF Title: **Toxtree: ISS rulebase for in vitro mutagenicity (Ames test)**
	Printing Date: **Apr 16, 2018**

1.QSAR identifier

1.1.QSAR identifier (title):

Toxtree: ISS rulebase for in vitro mutagenicity (Ames test)

1.2.Other related models:

1.3.Software coding the model:

Toxtree (Estimation of Toxic Hazard - a Decision Tree Approach) v. 2.6.6
Software for estimation of toxic hazard by applying a decision tree approach
Ideaconsult Ltd
http://toxtree.sourceforge.net

2.General information

2.1.Date of QMRF:

15 January 2015

2.2.QMRF author(s) and contact details:

Simona Kovarich S-IN Soluzioni Informatiche Srl Via Ferrari 14, I-36100 Vicenza, Italy
simona.kovarich@s-in.it http://www.s-in.it/

2.3.Date of QMRF update(s):

2.4.QMRF update(s):

2.5.Model developer(s) and contact details:

[1]Romualdo Benigni rbenigni@iss.it
[2]Cecilia Bossa cecilia.bossa@iss.it
[3]Olga Tcheremenskaia olga.tcheremenskaia@iss.it

2.6.Date of model development and/or publication:

2011

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

[1]Benigni R & Bossa C (2011). Mechanisms of chemical carcinogenicity and mutagenicity: a review with implications for predictive toxicology. Chemical Reviews 111(4), 2507-2536. DOI: 10.1021/cr100222q
[2]Benigni R, Bossa C, Jeliazkova N, Netzeva TI & Worth AP (2008). The Benigni / Bossa rulebase for mutagenicity and carcinogenicity – a module of ToxTree. JRC report EUR 23241 EN. Luxembourg: Office for Official Publications of the European Communities. http://publications.jrc.ec.europa.eu/repository/

2.8.Availability of information about the model:

The model is non-proprietary.

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

None to date.

3.Defining the endpoint - OECD Principle 1

3.1.Species:

Salmonella typhimurium

3.2.Endpoint:

4.10.Mutagenicity 471Bacterial Reverse Mutation Test

3.3.Comment on endpoint:

Mutagenicity assessment based on bacterial reverse mutation test in Salmonella typhimurium.

3.4.Endpoint units:

Not applicable.

3.5.Dependent variable:

Mutagen/ Non Mutagen (overall negative/positive score from availableAmes test). A chemical was considered to be a mutagen if at least one strain (with or without metabolic activation) gave a positive result [ref 2; sect 9.2].

3.6.Experimental protocol:

Not applicable.

3.7.Endpoint data quality and variability:

No information available

4.Defining the algorithm - OECD Principle 2

4.1.Type of model:

Expert System

4.2.Explicit algorithm:

Expert System

Decision tree based on structural alerts. The structural alerts are available for inspection within the software

4.3.Descriptors in the model:

Not applicable

4.4.Descriptor selection:

Not applicable

4.5.Algorithm and descriptor generation:

Not applicable

4.6.Software name and version for descriptor generation:

N/A

4.7.Chemicals/Descriptors ratio:

Not applicable

5.Defining the applicability domain - OECD Principle 3

5.1.Description of the applicability domain of the model:

The applicability domain of each alert is defined by its modulating factors.

5.2.Method used to assess the applicability domain:

Not applicable

5.3.Software name and version for applicability domain assessment:

N/A

5.4.Limits of applicability:

See Point 5.1.

6.Internal validation - OECD Principle 4

6.1.Availability of the training set:

No

6.2.Available information for the training set:

CAS RN: No

Chemical Name: No

Smiles: No

Formula: No

INChI: No

MOL file: No

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

No

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

No

6.5.Other information about the training set:

The alerts were derived from existing mechanistic knowledge.

6.6.Pre-processing of data before modelling:

Not applicable.

6.7.Statistics for goodness-of-fit:

Not applicable.

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

Not applicable.

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

Not applicable.

6.10.Robustness - Statistics obtained by Y-scrambling:

Not applicable.

6.11.Robustness - Statistics obtained by bootstrap:

Not applicable.

6.12.Robustness - Statistics obtained by other methods:

Not applicable.

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: Yes

INChI: No

MOL file: Yes

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:

ISSSTY database, part of the cluster ISSTOX:
http://www.iss.it/meca/index.php?lang=1&id=199&tipo=25

7.6.Experimental design of test set:

Not applicable

7.7.Predictivity - Statistics obtained by external validation:

Sensitivity: 84%; Specificity: 70%

7.8.Predictivity - Assessment of the external validation set:

The overall mutagenicity value (Positive/Negative) was predicted by presence/absence of at least one structural alert

7.9.Comments on the external validation of the model:

ISSSTY database contains data on over 7000 chemicals. The data were downloaded automatically from the CCRIS database in the Toxnet website. [ref 2; sect 9.2]

8.Providing a mechanistic interpretation - OECD Principle 5

8.1.Mechanistic basis of the model:

The structural alerts (SAs) for mutagenicity are molecular functional groups or substructures that were mainly derived from existing mechanistic knowledge of their link to the mutagenic activity of chemicals. A wide range of reference sources was considered. As one or more SAs embedded in a molecular structure are recognised, the system flags the potential mutagenicity of the chemical.

8.2.A priori or a posteriori mechanistic interpretation:

A priori (see Point 6.1).

8.3.Other information about the mechanistic interpretation:

No information available.

9.Miscellaneous information

9.1.Comments:

No additional information available.

9.2.Bibliography:

[1]Benigni R & Bossa C (2011). Mechanisms of chemical carcinogenicity and mutagenicity: a review with implications for predictive toxicology. Chemical Reviews 111(4), 2507-2536.

[2]Benigni R, Battistelli CL, Bossa C, Tcheremenskaia O & Crettaz P (2013). New perspectives in toxicological information management, and the role of ISSTOX databases in assessing chemical mutagenicity and carcinogenicity. Mutagenesis 28, 401-409.

[3]Benigni R & Bossa C (2008). Structure alerts for carcinogenicity, and the Salmonella assay system: A novel insight through the chemical relational databases technology. Mutation Research. 659, 248-261.

9.3.Supporting information:

10.Summary (JRC QSAR Model Database)

10.1.QMRF number:

Q17-471-0031

10.2.Publication date:

2017-09-27

10.3.Keywords:

Toxtree;in vitro mutagenicity;Ames;ISS;

10.4.Comments:

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