

	QMRF identifier (JRC Inventory): Q13-412-0071
	QMRF Title: Toxtree: Benigni-Bossa rulebase for genotoxic and non-genotoxic carcinogenicity
	Printing Date: Dec 11, 2019

1. QSAR identifier

1.1. QSAR identifier (title):

Toxtree: Benigni-Bossa rulebase for genotoxic and non-genotoxic carcinogenicity

1.2. Other related models:

1.3. Software coding the model:

Toxtree

Standalone software application downloadable from the Joint Research Centre (JRC) website
<http://ecb.jrc.ec.europa.eu/qsar/qsar-tools/index.php?c=TOXTREE>

2. General information

2.1. Date of QMRF:

June 2010.

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:

[1] Romualdo Benigni Romualdo Benigni rbenigni@iss.it

[2] Cecilia Bossa cecilia.bossa@iss.it

2.6. Date of model development and/or publication:

2008

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

Benigni R, Bossa C, Jeliaskova N, Netzeva TI and Worth AP (2008) The Benigni / Bossa rulebase for mutagenicity and carcinogenicity – a module of ToxTree. Rapporto tecnico EUR 23241 EN, JRC 43517. Luxembourg: Office for Official Publications of the European Communities. - Scientific and Technical Research Series; ISSN 1018-5593.

http://ecb.jrc.ec.europa.eu/documents/QSAR/EUR_23241_EN.pdf

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:

Rodents (rats and mice)

3.2.Endpoint:

4.Human Health Effects 4.12.Carcinogenicity

3.3.Comment on endpoint:

The "Benigni-Bossa rulebase" includes structural alerts (SAs) for both genotoxic and non-genotoxic carcinogenicity.

3.4.Endpoint units:

Noncarcinogen/ Carcinogen (overall negative/positive score from four experimental groups: rat, mice, male, female). A chemical was considered to be a carcinogen if at least one experimental group gave a positive result.

3.5.Dependent variable:

3.6.Experimental protocol:

3.7.Endpoint data quality and variability:

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:

4.4.Descriptor selection:

4.5.Algorithm and descriptor generation:

4.6.Software name and version for descriptor generation:

4.7.Chemicals/Descriptors ratio:

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:

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, and not through data mining algorithms.

6.6.Pre-processing of data before modelling:

6.7.Statistics for goodness-of-fit:

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

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:

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:

External validation set: ISSCANv3a database, freely available, ref 3, section 9.2

7.6.Experimental design of test set:

Not Applicable

7.7.Predictivity - Statistics obtained by external validation:

Carcinogenicity: overall accuracy = 0.70. Ames Mutagenicity: overall accuracy = 0.79.

7.8.Predictivity - Assessment of the external validation set:

ISSCANv3a database contains carcinogenicity and Ames mutagenicity data available in the public domain, critically reviewed.

7.9.Comments on the external validation of the model:

ISSCANv3a substances were checked for the presence/absence of any of the SAs for carcinogenicity. One chemical is to be classified positive if at least one alert is found. The validation study is reported in Benigni et al (2010), ref 2 section 9.2.

8.Providing a mechanistic interpretation - OECD Principle 5

8.1.Mechanistic basis of the model:

The alerts were derived from existing mechanistic knowledge, and not through data mining algorithms. A wide range of reference sources was considered.

8.2.A priori or a posteriori mechanistic interpretation:

A priori (see Point 6.1).

8.3.Other information about the mechanistic interpretation:

9.Miscellaneous information

9.1.Comments:

9.2.Bibliography:

[1]Benigni R, Bossa C, Jeliaskova 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://ecb.jrc.ec.europa.eu/documents/QSAR/EUR_23241_EN.pdf

[2]Benigni R, Bossa C, Tcheremenskaia O & Giuliani A (2010). Alternatives to the carcinogenicity bioassay: in silico methods, and the in vitro and in vivo mutagenicity assays. Expert Opinion on Drug Metabolism & Toxicology 6, 809-819.

[3]ISSCANv3a database <http://www.iss.it/ampp/dati/cont.php?id=233&lang=1&tipo=7>

9.3.Supporting information:

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

10.Summary (JRC QSAR Model Database)

10.1.QMRF number:

Q13-412-0071

10.2.Publication date:

2013-07-02

10.3.Keywords:

Toxtree;Benigni-Bossa rulebase;genotoxic carcinogenicity;nongenotoxic carcinogenicity;rodent;rat;mouse;

10.4.Comments:

former Q26-35-35-295