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|  | QMRF identifier (JRC Inventory):Q13-410-0072 |
| | QMRF Title:Toxtree: ToxMic rulebase for mutagenicity (in vivo micronucleus assay) |
| | Printing Date:Dec 11, 2019 |
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1.QSAR identifier

1.1.QSAR identifier (title):

Toxtree: ToxMic rulebase for mutagenicity (in vivo micronucleus assay)

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:

[1]Romualdo Benigni Experimental and Computational Carcinogenesis Unit, Environment and Health Department, Istituto Superiore di Sanita Viale Regina Elena 299, 00161 Rome, Italy
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[2]Cecilia Bossa Experimental and Computational Carcinogenesis Unit, Environment and Health Department, Istituto Superiore di Sanita Viale Regina Elena 299, 00161 Rome, Italy
 cecilia.bossa@iss.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

2.6.Date of model development and/or publication:

2009

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

[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 & Worth AP (2010). Structural analysis and predictive value of the rodent in vivo micronucleus assay results. Mutagenesis 25, 335-341.

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 4.10. Mutagenicity

3.3. Comment on endpoint:

The endpoint is the induction of in vivo micronuclei in rodents

3.4. Endpoint units:

Mutagen/ Non Mutagen (overall negative/positive score from available experiments in rodents). A chemical was considered to be a mutagen 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:

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 mainly from existing mechanistic knowledge.

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:

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:

Data for the validation set were retrieved from:

Chemical Carcinogenesis Research Information System (CCRIS) ref 3,
section 9.2 and 'FDA SAR Genetox Database'; Leadscope Inc., ref 4
section 9.2.

7.6.Experimental design of test set:

7.7.Predictivity - Statistics obtained by external validation:

In vivomicronucleus: overall accuracy = 0.57.

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 alerts were derived mainly from existing mechanistic knowledge. 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, Tcheremenskaia O & Worth AP (2009). Development of structural alerts for the in vivo micronucleus assay in rodents. JRC report EUR 23844 EN. Luxembourg: Office for Official Publications of the European Communities.

http://ecb.jrc.ec.europa.eu/DOCUMENTS/QSAR/EUR_23844_EN.pdf

[2] Benigni R, Bossa C & Worth AP (2010). Structural analysis and predictive value of the rodent in vivo micronucleus assay results. *Mutagenesis* 25, 335-341.

[3] Chemical Carcinogenesis Research Information System (CCRIS) <http://toxnet.nlm.nih.gov/cgi-bin/sis/search>

[4] FDA SAR Genetox Database'; Leadscope Inc.

http://www.leadscope.com/product_info.php?products_id577

9.3. Supporting information:

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

10. Summary (JRC QSAR Model Database)

10.1. QMRF number:

Q13-410-0072

10.2. Publication date:

2013-07-02

10.3. Keywords:

Toxtree; ToxMic rulebase; in vivo; mutagenicity; rodent; rat; mouse;

10.4. Comments:

former Q26-35-35-296