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:

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 available Ames 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.
6.1. 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.

7.1. 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:
7.5. Other information about the external validation set:

ISSSTY database, part of the cluster ISSTOX:

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:


9.3. Supporting information:

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<th>Training set(s)</th>
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Test set(s) 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:
   old # Q26-47-50-434