QSAR Prediction Reporting Format (QPRF)

The QPRF is a harmonised template for summarising and reporting substance-specific predictions generated by (Q)SAR models. The present QPRF is generated by LMC software, University "Prof. As. Zlatarov", Bourgas, Bulgaria

QSAR prediction for O=C1N(CC(Br)CBr)C(=O)N(CC(Br)CBr)C(=O)N1CC(Br)CBr

1. SUBSTANCE

1.1 CAS number (found in LMC SMILES/CAS database):

52434-90-9

1.2 EC number:

not reported

1.3 Chemical name:

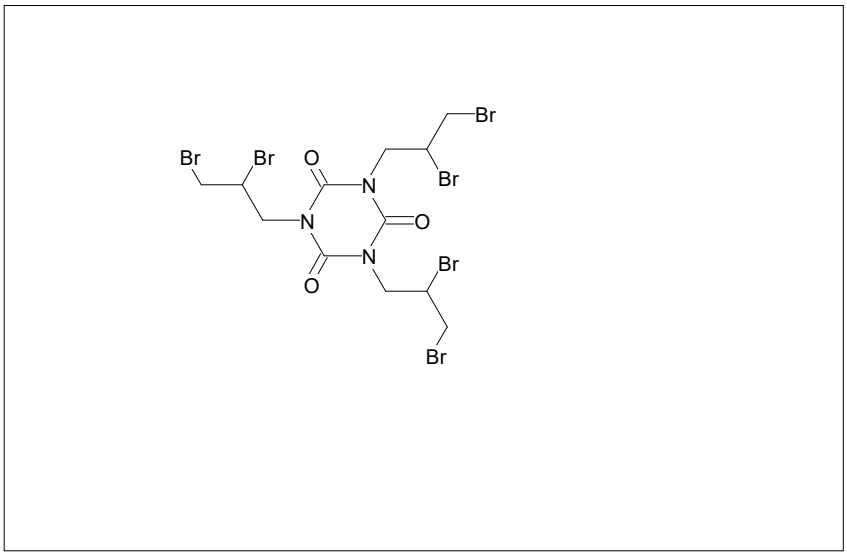
1,3,5-tris(2,3-dibromopropyl)-1,3,5-triazinane-2,4,6-trione
1,3,5-Triazine-2,4,6(1H,3H,5H)-trione, 1,3,5-tris(2,3-dibromopropyl)-
1,3,5-Tris(2,3-dibromopropyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione

1.4 Structural formula:

a. Molecular formula:

C12H15Br6N3O3

b. 2D structure:



1.5 Structure codes:

a. SMILES (used for prediction):

O=C1N(CC(Br)CBr)C(=O)N(CC(Br)CBr)C(=O)N1CC(Br)CBr

b. Other structural representation:

No other structural representations are used to generate the prediction

c. Stereochemical features:

Stereochemical features are not used to generate the prediction

2. GENERAL INFORMATION

2.1 Report date:

16.06.2022

2.2 Report authors:

Contact details are not provided by the author of prediction

2.3 Data sponsors:

Data sponsors are not provided by the author of prediction

3. PREDICTION

3.1 Endpoint (OECD Principle 1):

a. Endpoint:

Bacterial Reverse Mutation Test

b. Dependent variable:

in vitro Ames positive, in vitro Ames negative

3.2 Algorithm (OECD Principle 2):

a. Model or submodel name:

Ames mutagenicity S9 activated

b. Model version:

v.18.18

c. Reference to QMRF:

available in OASIS TIMES v.2.31.2.82

d. Predicted value (model result):

in vitro Ames positive

Concomitant predictions :

Alert info:

- Haloalkane Derivatives Containing Chain Heteroatom
  Alert Reliability: High, AP>0.60 (Num of tr.set chem>=10)
  Estimation Alert Performance = 0.962
  Confidance Estimation = 0.924 - 0.993
  p-value = < 1.0E-10

Active: Parent

e. Predicted value (comments):

No additional comments are provided by the author of prediction

f. Input for prediction:

SMILES

g. Descriptor values:

not reported

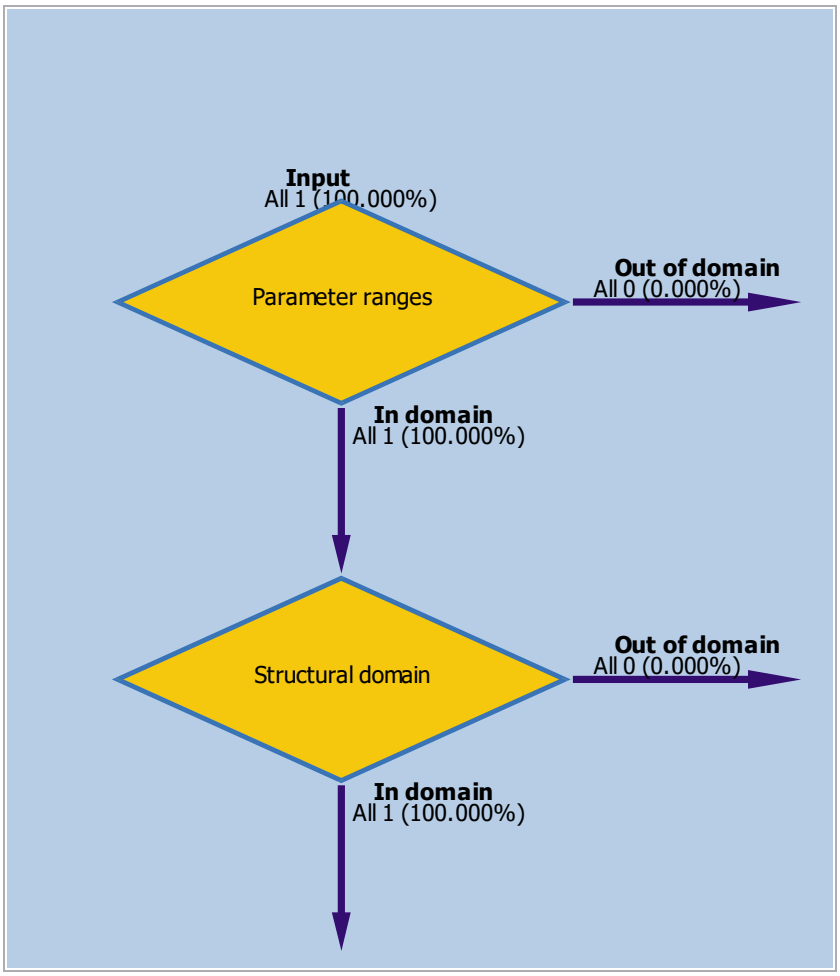
h. Observed Meta Data:

not reported

3.3 Applicability domain (OECD Principle 3):

a. Domain:

The LMC stepwise approach was used to define the applicability domain. It contains two layers:
・General properties requirements (log KOW, MW)
・Structural domain (Atom Centered Fragments (ACFs))
Details could be found in:
・Dimitrov S, Dimitrova G., Pavlov T., Dimitrova N., Patlewicz G., Niemela J., Mekenyan O., A stepwise approach for defining the applicability domain of SAR and QSAR models, J. Chem. Inf. Model., 45, 839-849 (2005)



i. Parameter domain:

Log(Kow)::
range = [-18.9 .. 35.2]
calculated: 7.37 (In domain)

MOL._WEIGHT
range = [18 .. 2370]Da
calculated: 729Da (In domain)

CONCLUSION:
The chemical fulfils the general properties requirements

ii. Structural fragment domain:

The following ACF are identified:
Fragments in correctly predicted training chemicals ? 100.00%
Fragments in non-correctly predicted training chemicals ? 0.00%
Fragments not present in the training chemicals ? 0.00%

CONCLUSION:
The chemical is in the interpolation structural space

b. Structural analogues in the training set:

List of chemicals from local training sets are available in Appendix 4

c. Considerations on structural analogues:

No additional comments on structural analogues are provided by the author of prediction

3.4 Appropriate measures of goodness-of貿it, robustness and predictivity (OECD principle 4):

External Validation:

A large number of chemicals (12,134) with highly reliable Ames data have been used in a screening exercise of NIHS Japan to help increasing the predictive power of the major QSAR models for predicting Ames mutagenicity (http://www.nihs.go.jp/dgm/amesqsar.html). This exercise is scheduled for accomplishing in three Phases by distributing approximately 4,000 chemicals for screening in each Phase.
The Ames assays were conducted according to the OECD TG471 and Industrial Safety and Health Act in Japan under GLP-compliant conditions. Based on their Ames data, investigated chemicals are classified into three categories:

・Strongly positive mutagens (Class A) - generally induce more than 1,000 revertants/mg in at least one Ames strains in the presence or absence of rat S9,

・Positive mutagens (Class B) ・reproducibly induce revertant colonies with dose-dependent manner, different from Class A mutagens,

・Negative Ames substances (Class C).

As a result of the screening, when accounting for the model domain, the TIMES_Ames model (+S9) shows balanced predictions in terms of sensitivity of 80% (for Class A chemicals) and specificity of 91%. This result is acceptable given the interlaboratory reproducibility of Ames data which is 85% [Piegorsch, W.W., Zeiger, E. 1991. Measuring intra-assay agreement for the Ames Salmonella assay. Lecture notes in Medical Informatics; Springer-Verlag: Heidelberg: 35-41]. The Ames model (-S9) has not been evaluated in this screening exercise, because the experimental Ames data are provided without information whether they are obtained with or without S9 metabolic activation. Due to the lack of information for the presence or absence of S9 metabolic activation (critically important for TIMES models), the screened chemicals cannot be used for modifying the TIMES Ames models.

Statistics for goodness-of-fit:

・Sensitivity = (predicted positive/observed positive) = 89%
・Specificity = (predicted negative/observed negative) = 91%
・Concordance = (correct predicted positive and negative chemicals in respect to all training set chemicals) = 90%

3.5 The chemical and biological mechanisms according to the model underpinning the predicted result (OECD principle 5):

Detailed information about mechanistic basis of the model underpinning the prediction is available in model QMRF, section 8.