Synthesis and mutagenic risk of Avanafil's potential genotoxic impurities

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I. High resolution mass spectra

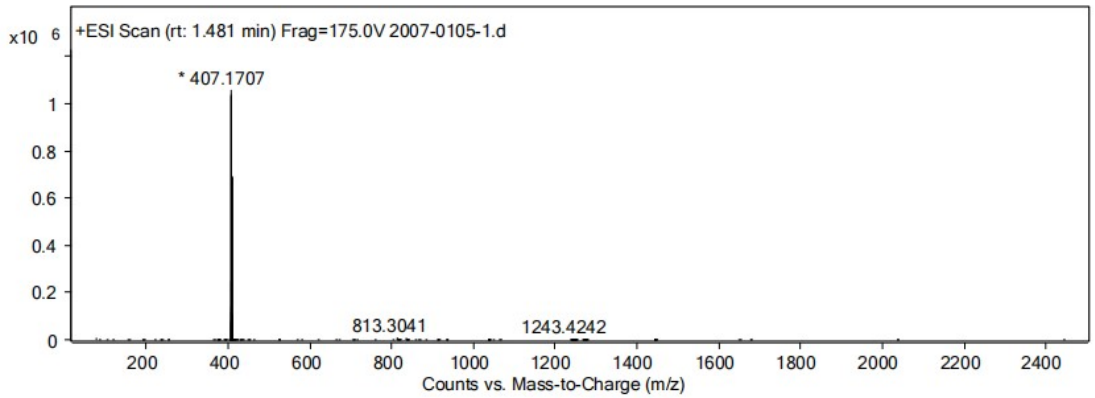


Figure S1 High resolution mass spectrum of Imp-E

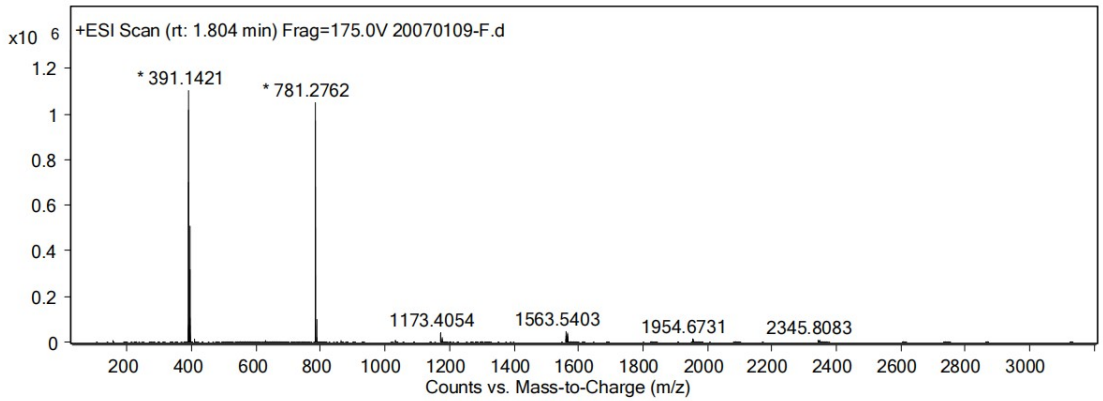


Figure S2 High resolution mass spectrum of Imp-F

II. NMR spectra

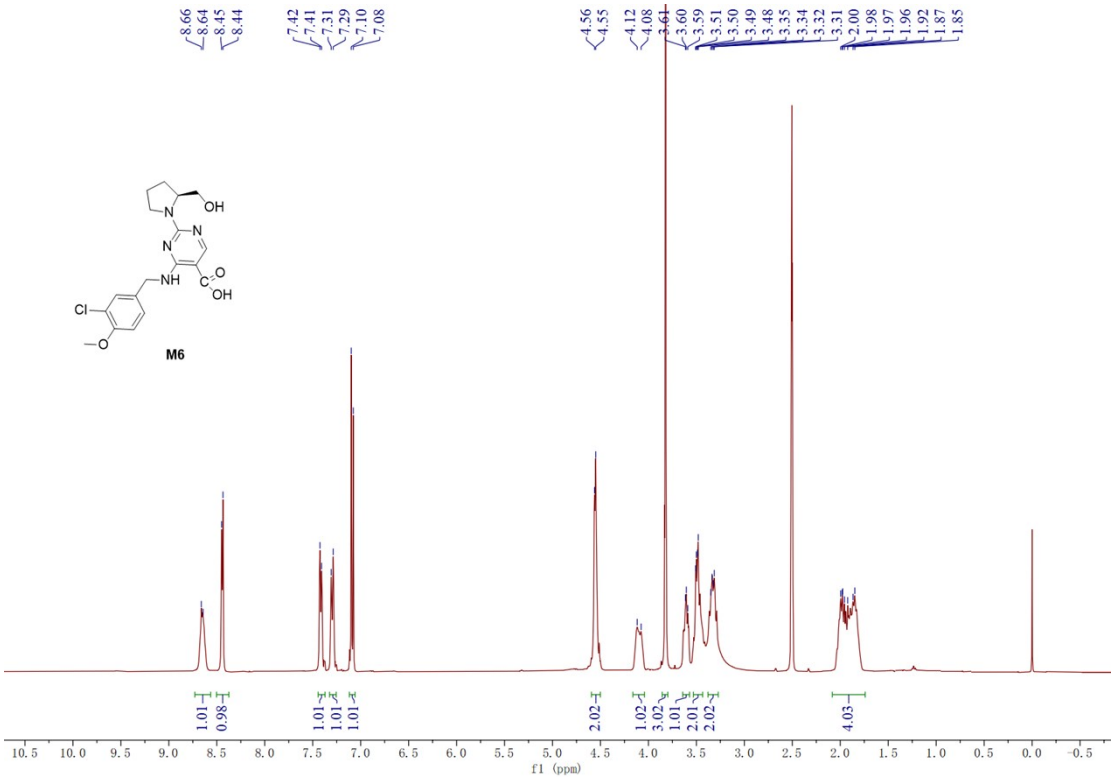


Figure S3 ^{1}H NMR spectra of M6 (DMSO-d_6)

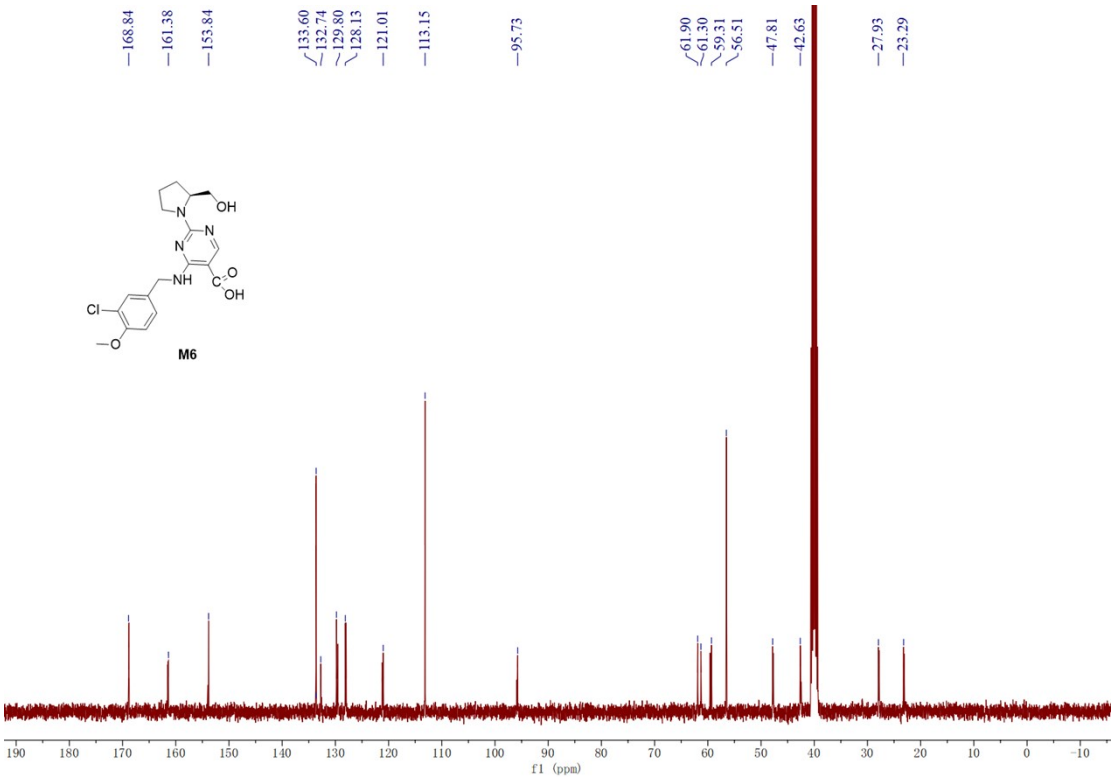


Figure S4 ^{13}C NMR spectra of M6 (DMSO-d_6)

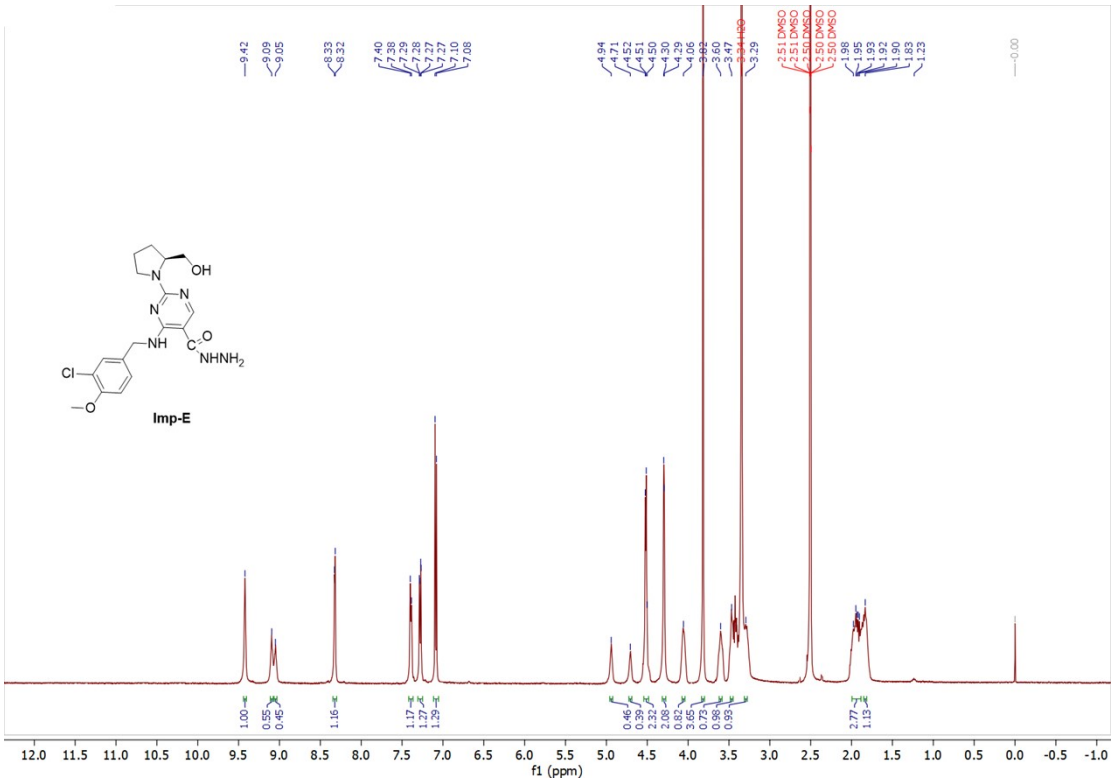


Figure S5 ^{1}H NMR spectra of Imp-E (DMSO-d_6)

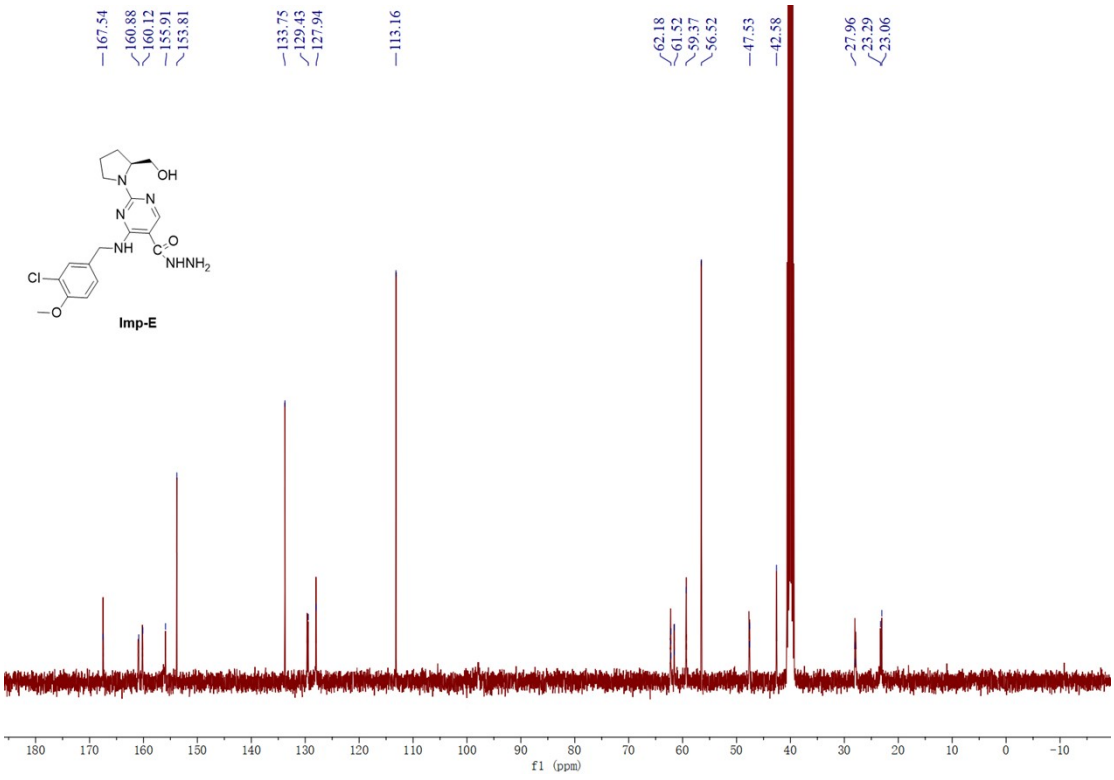


Figure S6 ^{13}C NMR spectra of Imp-E (DMSO-d_6)

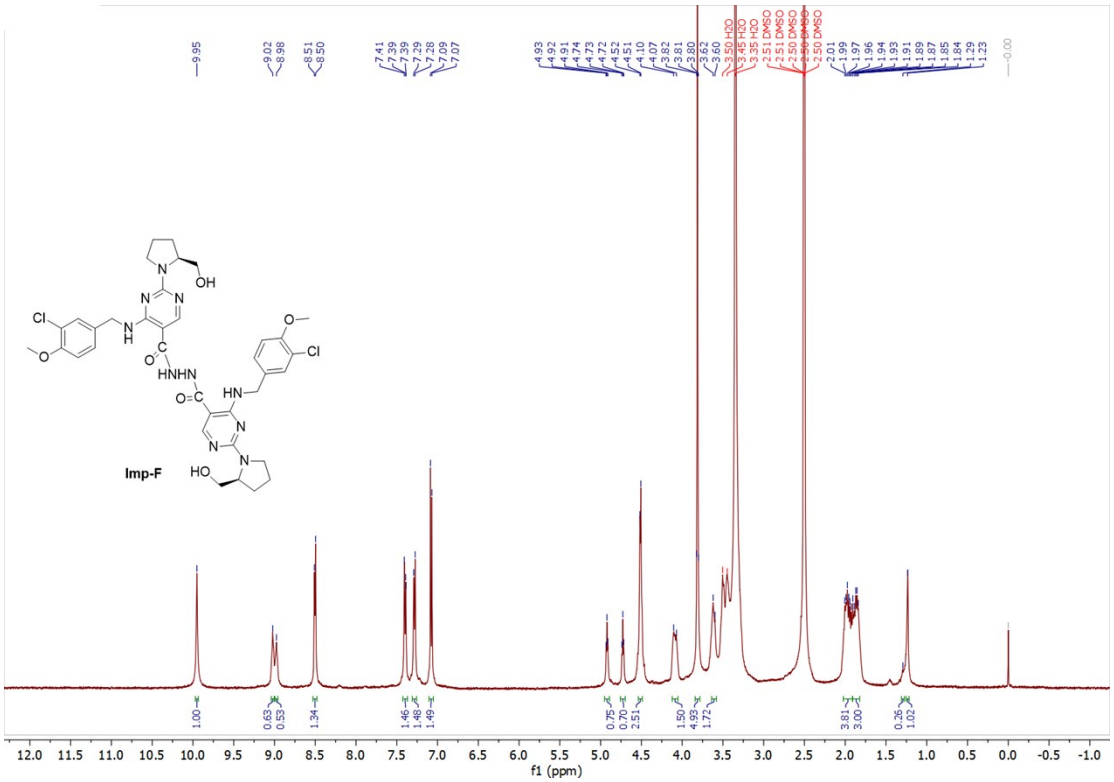


Figure S7 ^{1}H NMR spectra of Imp-F (DMSO-d_6)

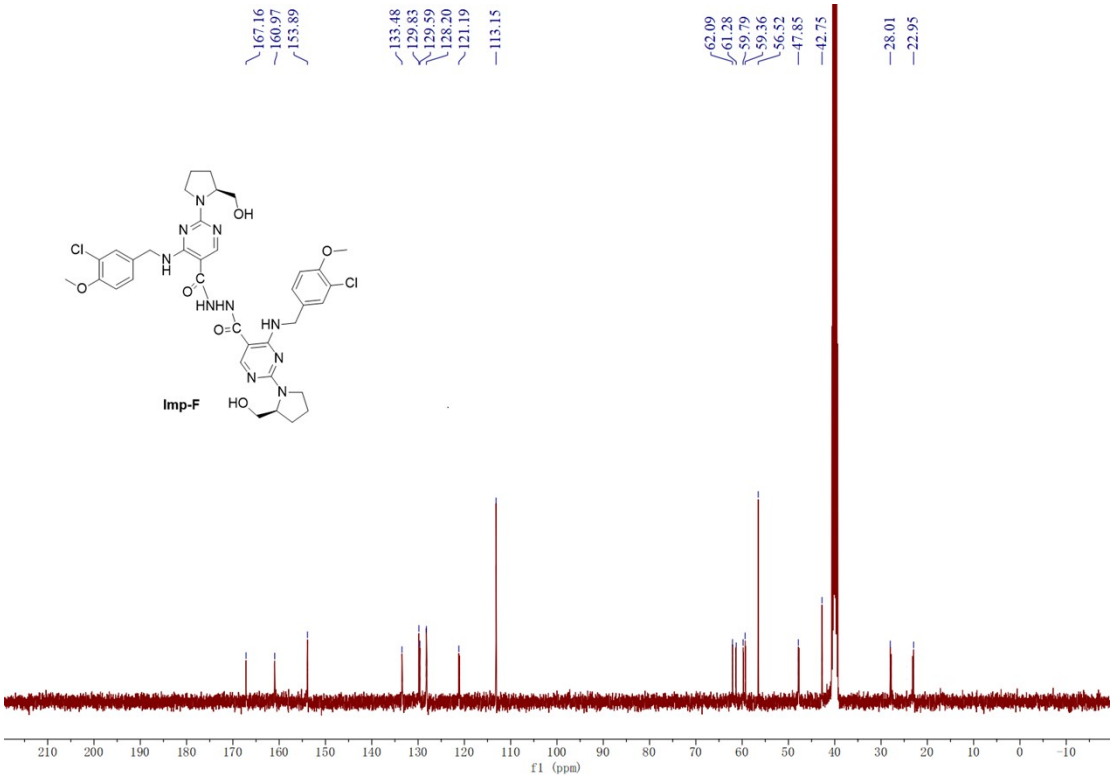


Figure S8 ^{13}C NMR spectra of Imp-F (DMSO-d_6)

III. Liquid chromatogram

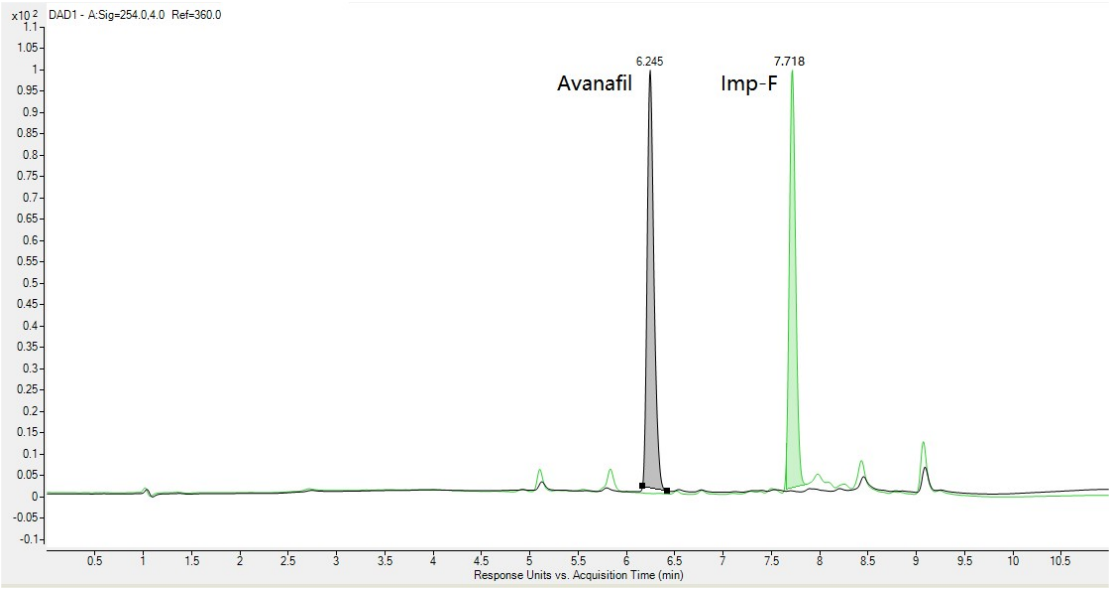


Figure S9. Liquid chromatogram of Avanafil and Imp-F.

IV. Identification of TA98, TA97, TA100, TA1535, TA102

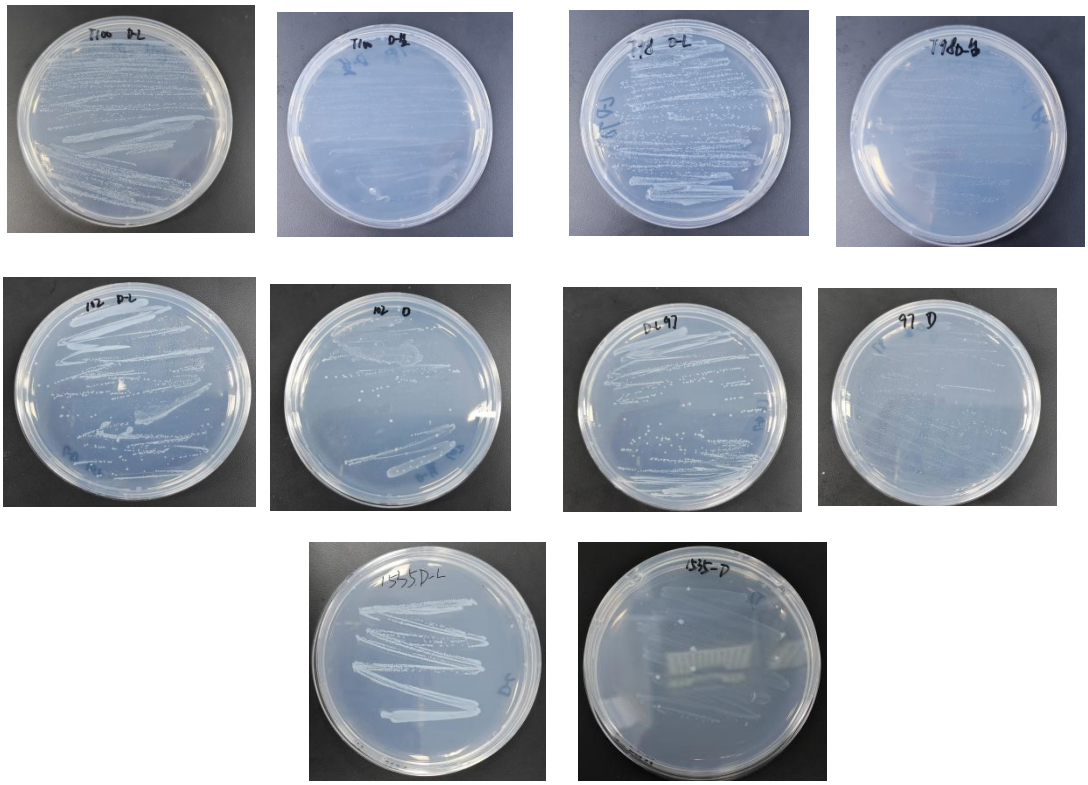


Figure S10 Identification of TA98, TA97, TA100, TA1535, TA102 histidine defects

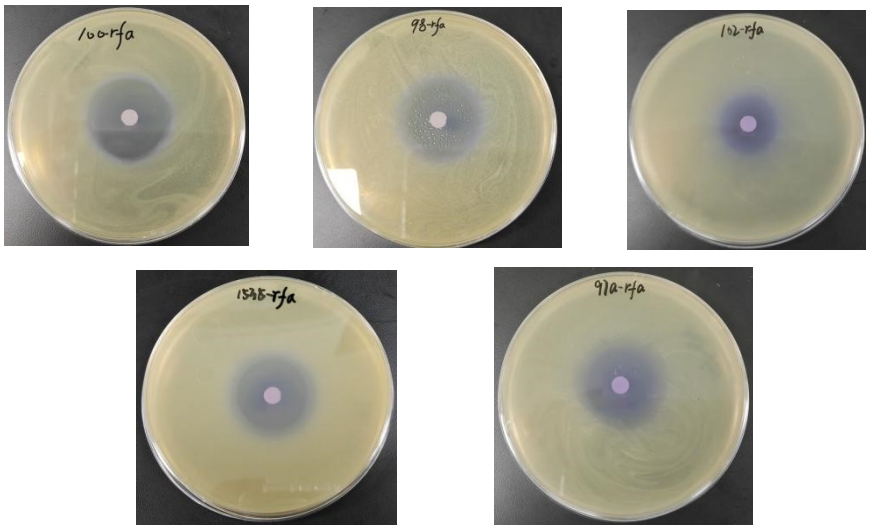


Figure S11 Identification of lipopolysaccharide barrier defects of TA98, TA97a, TA100, TA1535, TA102

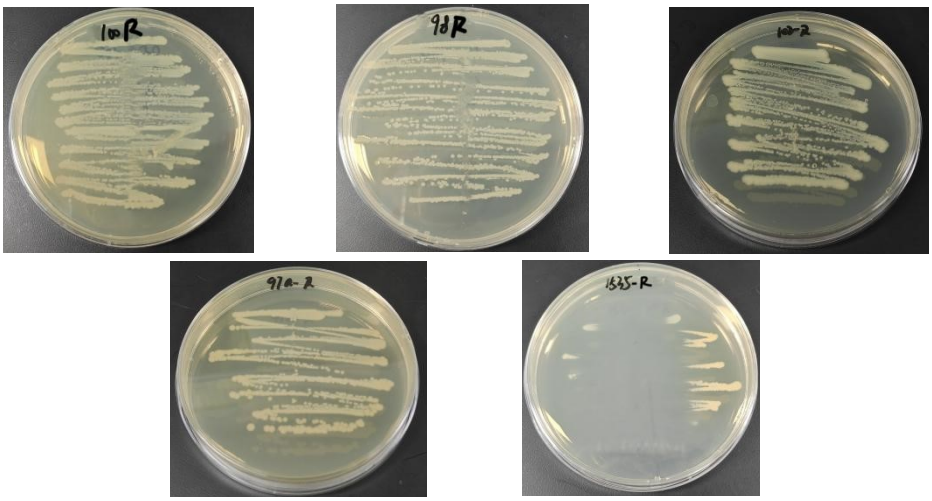


Figure S12 Identification of TA98, TA97, TA100, TA1535, TA102 resistance to ampicillin

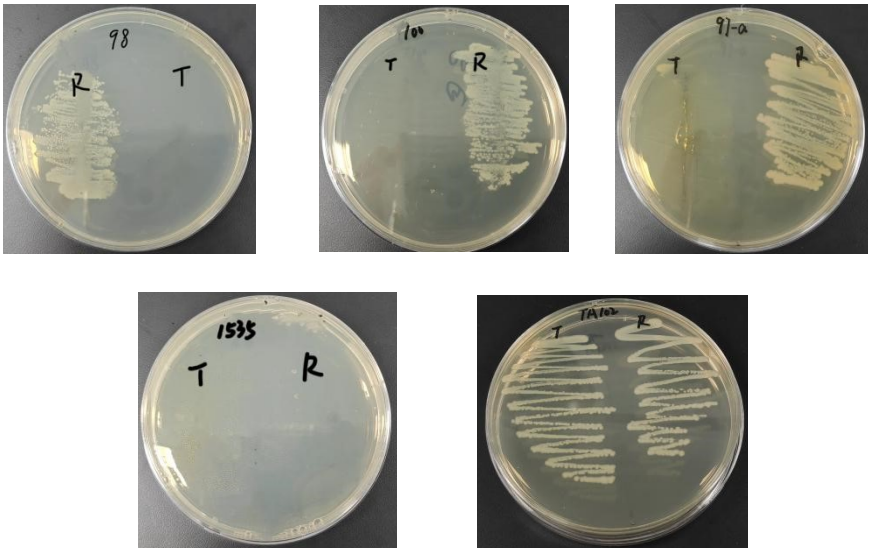


Figure S13 Identification of tetracycline resistance of TA98, TA97, TA100, TA1535 and TA102

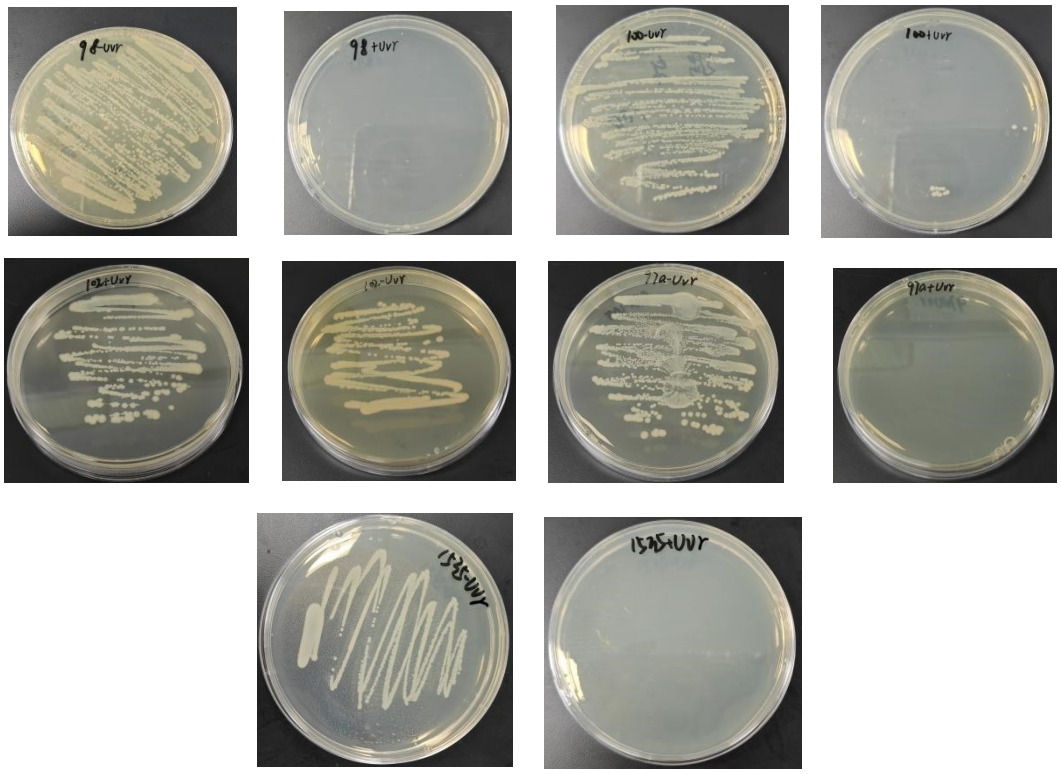


Figure S14 uvrB repair defect identification of TA98, TA97, TA100, TA1535, TA102

V. Prediction reports

ICH M7 Report

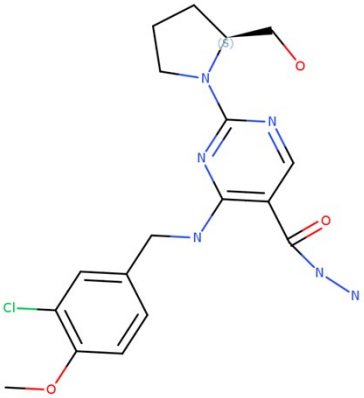
Report Information

Author	Report date	Prediction date
admin	30 October 2023 12:41:35	30 October 2023 12:40:53

Derek version	Sarah version	Nexus Version
Derek Nexus: 6.2.1	Sarah Nexus: 3.2.1	Nexus: 2.5.2

Species	Endpoint
bacterium	Mutagenicity in vitro

Prediction Summary - Impurity-E.cdx



Derek: Plausible

Sarah: Negative

Smiles:

C1(=C(C=CC(=C1)CNC2=C(C=NC(=N2)N3[C@@H](CCC3)CO)C(=O)NN)OC)Cl

Average Mol Mass:	406.87
Exact Mol Mass:	406.152
Log Kp:	-3.78
Log P:	2.0

Expert Review Summary

In Silico Overall Conclusion: Positive (Calculated Call)

ICH M7 Cohort of Concern: No

Review status: Review not started

Prediction Detail – Derek Nexus

Derek Knowledge Base	Version	Last Modified Date	Certified by
Derek KB 2022 2.0	2.0	13/07/2022 18:02:45	Lhasa Limited, Leeds, Yorkshire, UK

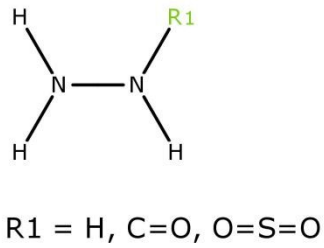
Perceive Mixtures	Perceive Tautomers
No	No

Alert(s) matched:

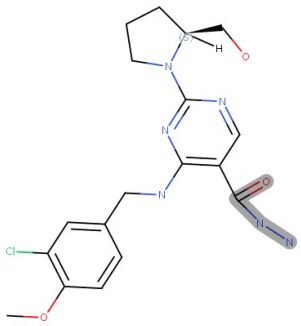
Hydrazine or monoacyl- or monosulphonyl-hydrazine

Alert: 033 Hydrazine or monoacyl- or monosulphonyl-hydrazine (from KB: Derek KB 2022 2.0)

Alert Description Image



Match with query compound



Comments

Chromosome damage (clastogenicity): in vitro chromosome aberration test
Mutagenicity: Ames test

Able to release hydrazine or monoacyl- or monosulphonyl-hydrazine, but not from hydrazones.

Compounds that have tested positive in the Ames test include hydrazine sulphate [NTP], hydrazine hydrate [Parodi et al, Poso et al], carbamylhydrazine [Parodi et al] and isoniazid [Braun et al, Parodi et al], typically in Salmonella typhimurium strain TA1535. In general, activity is reported to be greater in the absence of S9 mix, and in the case of carbamylhydrazine, the addition of S9 mix removed activity.

Positive results in the in vitro chromosome aberration test have been reported for hydrazine sulphate [Natarajan and van Kesteren-van Leeuwen] and isoniazid [Sofuni].

References

- Poso A, von Wright A and Gynther J. (1995)
  An empirical and theoretical study on mechanisms of mutagenic activity of hydrazine compounds., *Mutation Research*, 332 , 63-71
  DOI: 10.1016/0027-5107(95)00155-2
- Sofuni T (editor). (1999)
  Revised Edition 1998 Data Book of Chromosomal Aberration Test in Vitro., *Data Book* of Chromosomal Aberration Test in Vitro, , All pages

- Natarajan AT and van Kesteren-van Leeuwen AC. (1981)
  Mutagenic activity of 20 coded compounds in chromosome aberrations/sister chromatid exchanges assay using Chinese hamster ovary (CHO) cells., *Evaluation of* Short-Term Tests for Carcinogens: Report of the International Collaborative Program (Progress in Mutation Research, volume 1), , 551-559

- National Toxicology Program (NTP). (1981)
  Salmonella study summary of hydrazine sulfate (CAS RN 10034-93-2)., *National Toxicology* Program Web Server, ,

- Braun R, Jakel HP and Schoneich J. (1984)
  Genetic effects of isoniazid and the relationship to in vivo and in vitro biotransformation., *Mutation Research*, 137 , 61-69

- Parodi S, de Flora S, Cavanna M, Pino A, Robbiano L, Bennicelli C and Brambilla G. (1981)
  DNA-damaging activity in vivo and bacterial mutagenicity of sixteen hydrazine derivatives as related quantitatively to their carcinogenicity., *Cancer Research*, 41 , 1469-1482

Validation comments

Chromosome damage: in vitro chromosome aberration test

The alert has demonstrated the following predictive performance:

1) Sofuni data set: 0 compounds activate this alert
2) FDA CFSAN data set: 1 compound activates this alert of which 1 is reported positive (positive predictivity = 100%)
3) CGX data set: 2 compounds activate this alert of which 2 are reported positive (positive predictivity = 100%)

1) A collection of in vitro chromosome aberration test data for 712 compounds from the following source: Revised Edition 1998 Data Book of Chromosomal Aberration Test in Vitro, Sofuni T (editor), Life-Science Information Center, Tokyo, 1999.

2) A collection of in vitro chromosome aberration test data for 2172 compounds derived from the FDA/CFSAN/OFAS knowledge base.

3) A collection of in vitro chromosome aberration test data for 488 compounds from the following reference: Kirkland D, Aardema M, Henderson L and Muller L. Evaluation of the ability of a battery of three in vitro genotoxicity tests to discriminate rodent carcinogens and non-carcinogens. I. Sensitivity, specificity and relative predictivity. Mutation Research, 2005, 584, 1-256, available at "http://dx.doi.org/10.1016/j.mrgentox.2005.02.004".

In assessing predictive performance, it should be noted that:

- Mammalian in vitro chromosome damage predictions in Derek associated with a reasoning level of equivocal or above have been considered positive;
- Predictions do not take into account (i) the tautomeric forms of compounds or (ii) the individual components of mixtures;
- The classification of compounds from the Sofuni data set as positive or negative is based upon an overall result which includes both polyploidy and structural chromosome aberration results;
- The classification of compounds from the FDA CFSAN data set as positive or negative is based upon a composite activity score for aberrations in vitro;
- Compounds in the data sets assigned responses other than positive or negative have been excluded from the analysis;
- No account has been taken of other chromosome damage alerts which may also be present in some compounds;
- No comparison has been made between the protocol used to obtain positive experimental results, including exposure time and metabolic activation, and the expected profile which may be included in the comments for an alert;
- Information from the data sets may have been used previously as supporting evidence for the derivation of some alerts;
- Some compounds may be present in more than one of the data sets analysed.

Mutagenicity: Ames test

The alert has demonstrated the following predictive performance:

1) Proprietary data set 1: 9 compounds activate this alert of which 6 are reported positive (positive predictivity: 67%)
2) Proprietary data set 2: 0 compounds activate this alert
3) FDA CFSAN data set: 10 compounds activate this alert of which 6 are reported positive (positive predictivity: 60%)
1) A proprietary collection of Ames test data for 1812 chemicals.
2) A proprietary collection of Ames test data for 475 chemicals contributed by Bayer Schering Pharma AG.

3) A collection of Ames test data for 8421 compounds derived from the FDA/CFSAN/OFAS knowledge base.

In assessing predictive performance, it should be noted that:

- Bacterial mutagenicity predictions in Derek associated with a reasoning level of equivocal or above have been considered positive;
- Predictions do not take into account (i) the tautomeric forms of compounds or (ii) the individual components of mixtures;
- The classification of compounds from the FDA CFSAN data set as positive or negative is based upon composite activity scores for Salmonella and E.coli. Positive results in either Salmonella or E.coli leads to an overall active call;
- Compounds in the data sets assigned responses other than positive or negative have been excluded from the analysis;
- No account has been taken of other mutagenicity alerts which may also be present in some compounds;
- No comparison has been made between the strain and S9 dependency of positive experimental results and the expected profile which may be included in the comments for an alert;
- Information from the data sets may have been used previously as supporting evidence for the derivation of some alerts;
- Some compounds may be present in more than one of the data sets analysed.

eg Examples for Alert 033 Hydrazine or monoacyl- or monosulphonyl-hydrazine

Example 1: hydrazine sulphate

CAS Registry Number®: 10034-93-2

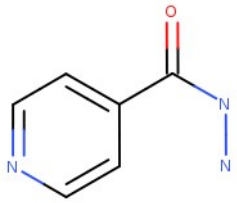
Test Data (hydrazine sulphate)

	Species	Assay	Endpoint(s)	Result
1)	Salmonella typhimurium	Ames test	Mutagenicity in vitro	positive

References

• National Toxicology Program (NTP). (1981)
Salmonella study summary of hydrazine sulfate (CAS RN 10034-93-2)., *National Toxicology Program Web Server*, ,

Example 2: isoniazid



CAS Registry Number®: 54-85-3

Test Data (isoniazid)

1)	Species	Assay	Endpoint(s)	Result
	Salmonella typhimurium	Ames test	Mutagenicity in vitro	positive

References

• Braun R, Jakel HP and Schoneich J. (1984)
Genetic effects of isoniazid and the relationship to in vivo and in vitro biotransformation., *Mutation Research*, 137 , 61-69
• Parodi S, de Flora S, Cavanna M, Pino A, Robbiano L, Bennicelli C and Brambilla G. (1981)
DNA-damaging activity in vivo and bacterial mutagenicity of sixteen hydrazine derivatives as related quantitatively to their carcinogenicity., *Cancer Research*, 41 , 1469-1482

Example 3: hydrazine hydrate

CAS Registry Number®: 7803-57-8

Test Data (hydrazine hydrate)

1)	Species	Assay	Endpoint(s)	Result
	Salmonella typhimurium	Ames test	Mutagenicity in vitro	positive

References

• Poso A, von Wright A and Gynther J. (1995)

An empirical and theoretical study on mechanisms of mutagenic activity of hydrazine compounds., *Mutation Research*, 332 , 63-71
DOI: 10.1016/0027-5107(95)00155-2

***Mutagenicity in vitro* in bacterium is PLAUSIBLE (from KB: Derek KB 2022 2.0)**

The parameters that have influenced your prediction are: substructures in the input structure, which have the potential to cause mutagenicity; your selected species, which is bacterium.

Rule 610: If [species bacterium] is [certain] then [Species dependent variable 27] is [plausible]

- species bacterium **is** CERTAIN

In bacteria the variable "Species dependent variable 27" is plausible.

Rule 83: If [alert 033] is [certain] then [Mutagenicity in vitro] is [Species dependent variable 27]

- alert 033 **is** CERTAIN
- Species dependent variable 27 **is** PLAUSIBLE

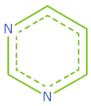
If a chemical contains alert 33 then it is considered plausible that the chemical will cause mutagenicity in vitro in bacteria. The variation in rule outcome with species is achieved via use of the variable "Species dependent variable 27".

Prediction Detail – Sarah Nexus

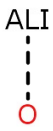
Sarah Model Name	Version	Certified
Sarah Model - 2022.2	1.10	Yes

The compound is predicted to be negative with 23% confidence for the 'Mutagenicity in vitro' endpoint in the model: 'Sarah Model - 2022.2'. Supporting hypotheses containing similar examples from the training set have been found.

Hypotheses

Structure	ID	Description	Result	Confidence	Examples
	**H-309**	Hypothesis	Negative	24%	1672
	**H-294**	Hypothesis	Negative	23%	5948
	**H-190**	Hypothesis	Negative	23%	403

Hypothesis: H-309



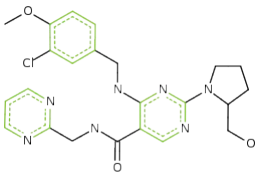
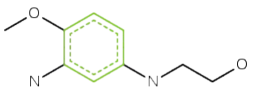
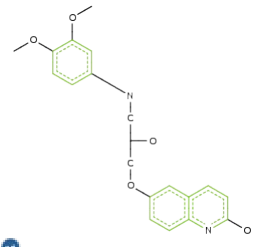
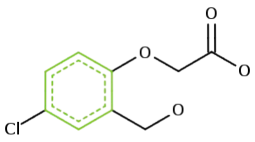
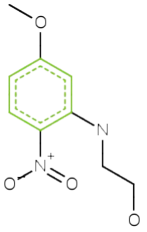
Sarah Result: Negative

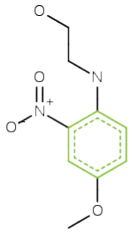
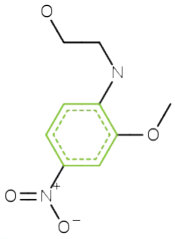
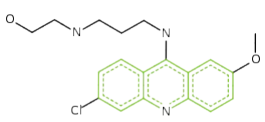
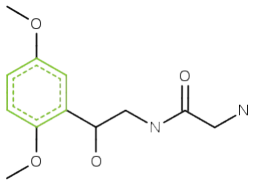
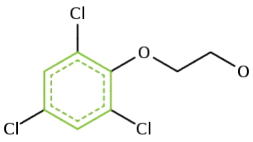
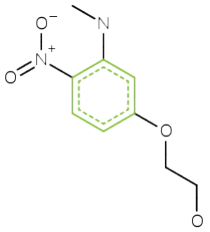
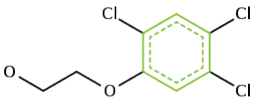
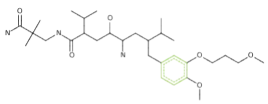
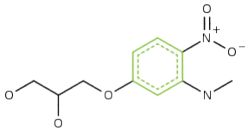
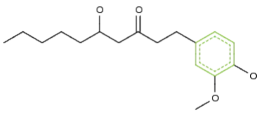
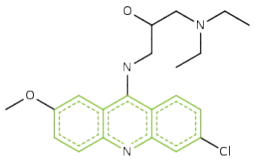
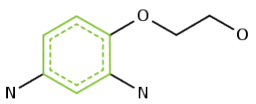
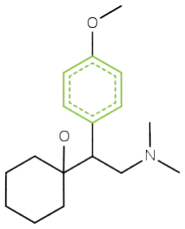
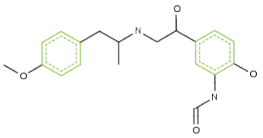
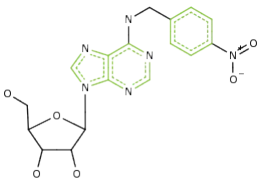
Confidence: 24%

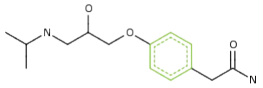
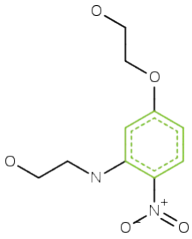
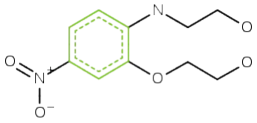
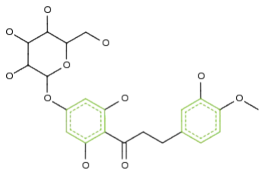
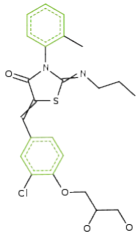
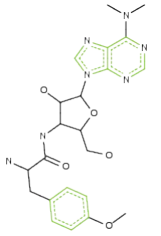
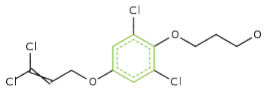
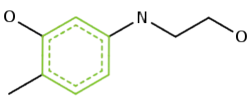
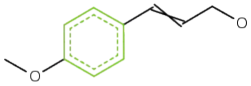
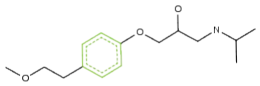
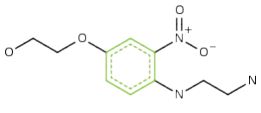
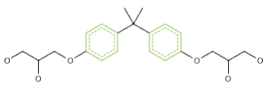
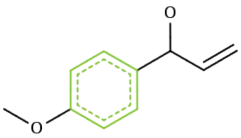
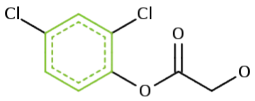
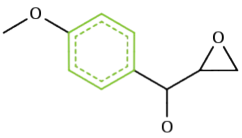
Examples: 1672

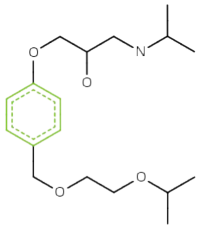
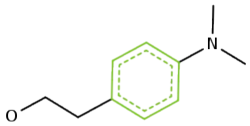
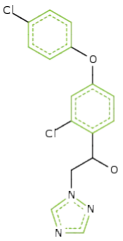
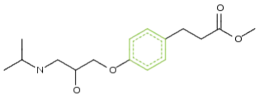
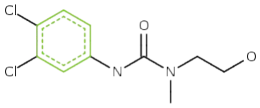
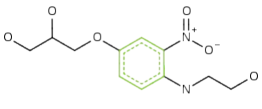
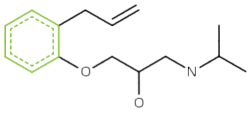
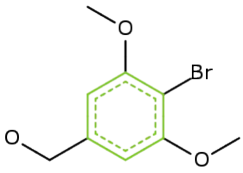
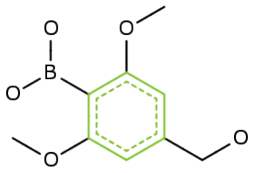
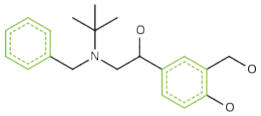
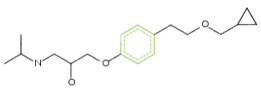
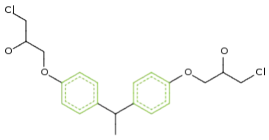
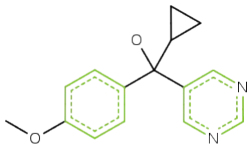
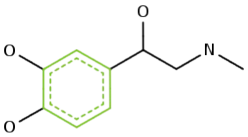
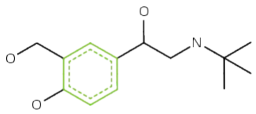
Hypothesis

Examples:

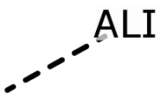
1 of 1672 Similarity: 68% Overall Call: (-Ve)	2 of 1672 Similarity: 23% Overall Call: (-Ve)	3 of 1672 Similarity: 22% Overall Call: (-Ve)	4 of 1672 Similarity: 22% Overall Call: (-Ve)	5 of 1672 Similarity: 19% Overall Call: (-Ve)
				
The training set compound has fired 0 Derek alert(s).	The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide	The training set compound has fired 0 Derek alert(s).	The training set compound has fired 0 Derek alert(s).	The training set compound has fired 0 Derek alert(s).

6 of 1672 Similarity: 19% Overall Call: (+Ve)  The training set compound has fired 0 Derek alert(s).	7 of 1672 Similarity: 19% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound	8 of 1672 Similarity: 19% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 365: Acridine or analogue	9 of 1672 Similarity: 18% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	10 of 1672 Similarity: 18% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).
11 of 1672 Similarity: 18% Overall Call: (-Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide	12 of 1672 Similarity: 17% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	13 of 1672 Similarity: 17% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	14 of 1672 Similarity: 17% Overall Call: (-Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide	15 of 1672 Similarity: 17% Overall Call: (+Ve)  The training set compound has fired 0 Derek alert(s).
16 of 1672 Similarity: 17% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 365: Acridine or analogue	17 of 1672 Similarity: 17% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide	18 of 1672 Similarity: 17% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	19 of 1672 Similarity: 17% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	20 of 1672 Similarity: 17% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound

21 of 1672 Similarity: 16% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	22 of 1672 Similarity: 16% Overall Call: (+Ve)  The training set compound has fired 0 Derek alert(s).	23 of 1672 Similarity: 16% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound	24 of 1672 Similarity: 16% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	25 of 1672 Similarity: 16% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).
26 of 1672 Similarity: 16% Overall Call: (+Ve)  The training set compound has fired 0 Derek alert(s).	27 of 1672 Similarity: 16% Overall Call: (+Ve)  The training set compound has fired 0 Derek alert(s).	28 of 1672 Similarity: 16% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	29 of 1672 Similarity: 16% Overall Call: (+Ve)  The training set compound has fired 0 Derek alert(s).	30 of 1672 Similarity: 16% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).
31 of 1672 Similarity: 16% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	32 of 1672 Similarity: 16% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	33 of 1672 Similarity: 16% Overall Call: (+Ve)  The training set compound has fired 0 Derek alert(s).	34 of 1672 Similarity: 16% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	35 of 1672 Similarity: 16% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 019: Epoxide

36 of 1672 Similarity: 15% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	37 of 1672 Similarity: 15% Overall Call: (+Ve)  The training set compound has fired 0 Derek alert(s).	38 of 1672 Similarity: 15% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	39 of 1672 Similarity: 15% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	40 of 1672 Similarity: 15% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).
41 of 1672 Similarity: 15% Overall Call: (+Ve)  The training set compound has fired 0 Derek alert(s).	42 of 1672 Similarity: 15% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	43 of 1672 Similarity: 15% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	44 of 1672 Similarity: 15% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	45 of 1672 Similarity: 15% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).
46 of 1672 Similarity: 15% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	47 of 1672 Similarity: 15% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 027: Alkylating agent	48 of 1672 Similarity: 15% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	49 of 1672 Similarity: 15% Overall Call: (+Ve)  The training set compound has fired 0 Derek alert(s).	50 of 1672 Similarity: 15% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).

Hypothesis: H-294



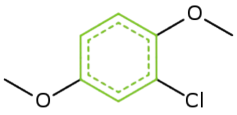
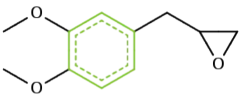
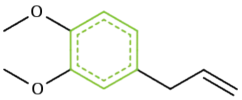
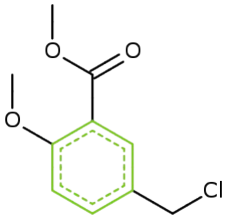
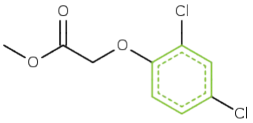
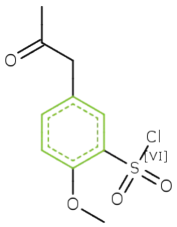
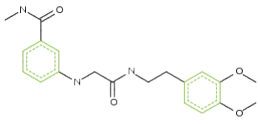
Sarah Result: Negative

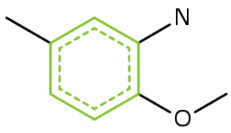
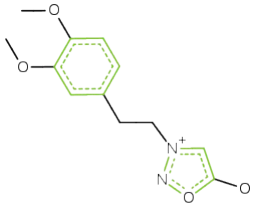
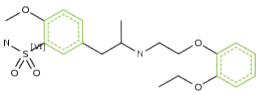
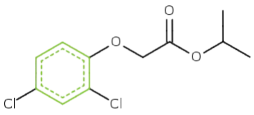
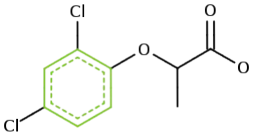
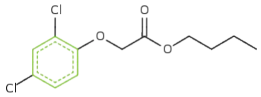
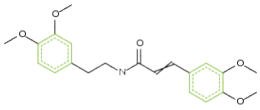
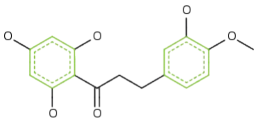
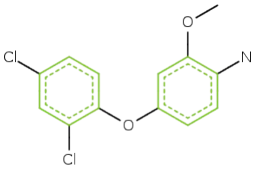
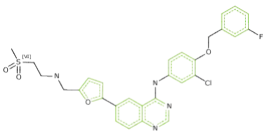
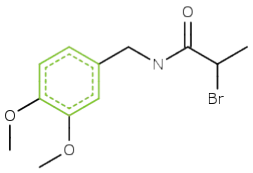
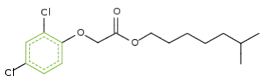
Confidence: 23%

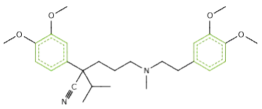
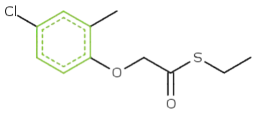
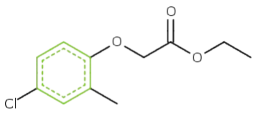
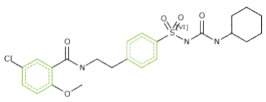
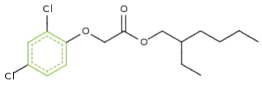
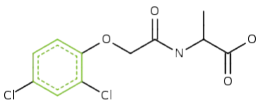
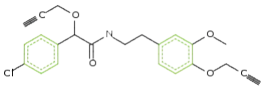
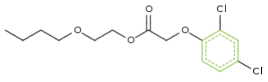
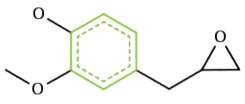
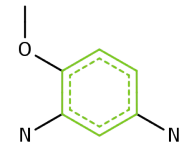
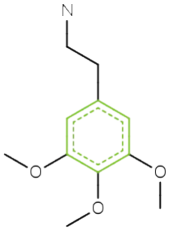
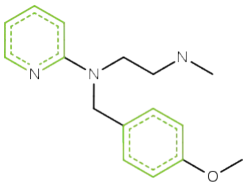
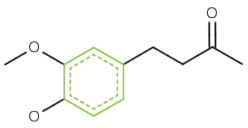
Examples: 5948

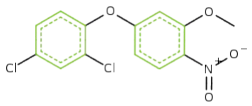
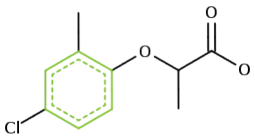
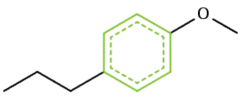
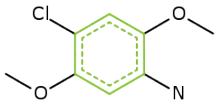
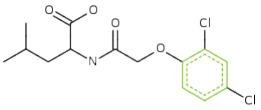
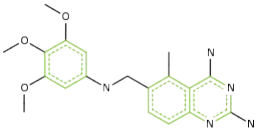
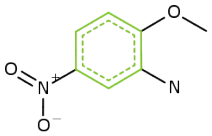
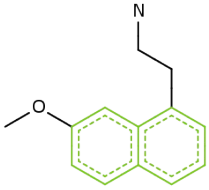
Hypothesis

Examples:

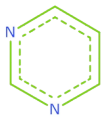
1 of 5948 Similarity: 68% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	2 of 5948 Similarity: 27% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	3 of 5948 Similarity: 24% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 019: Epoxide	4 of 5948 Similarity: 24% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	5 of 5948 Similarity: 23% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 027: Alkylating agent
6 of 5948 Similarity: 23% Overall Call: (-Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide	7 of 5948 Similarity: 22% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	8 of 5948 Similarity: 22% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	9 of 5948 Similarity: 22% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 315: Acid halide	10 of 5948 Similarity: 22% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).

11 of 5948 Similarity: 21% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide	12 of 5948 Similarity: 21% Overall Call: (+Ve)  The training set compound has fired 0 Derek alert(s).	13 of 5948 Similarity: 21% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	14 of 5948 Similarity: 20% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	15 of 5948 Similarity: 20% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).
16 of 5948 Similarity: 20% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	17 of 5948 Similarity: 20% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	18 of 5948 Similarity: 20% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	19 of 5948 Similarity: 20% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide	20 of 5948 Similarity: 19% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).
21 of 5948 Similarity: 19% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	22 of 5948 Similarity: 19% Overall Call: (+Ve) The training set compound has fired 0 Derek alert(s).	23 of 5948 Similarity: 19% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound	24 of 5948 Similarity: 19% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 027: Alkylating agent	25 of 5948 Similarity: 19% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).

26 of 5948 Similarity: 19% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	27 of 5948 Similarity: 19% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	28 of 5948 Similarity: 19% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	29 of 5948 Similarity: 19% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	30 of 5948 Similarity: 19% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 027: Alkylating agent
31 of 5948 Similarity: 19% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	32 of 5948 Similarity: 19% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	33 of 5948 Similarity: 19% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	34 of 5948 Similarity: 19% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 365: Acridine or analogue	35 of 5948 Similarity: 19% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).
36 of 5948 Similarity: 19% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 019: Epoxide	37 of 5948 Similarity: 19% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide	38 of 5948 Similarity: 19% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	39 of 5948 Similarity: 18% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	40 of 5948 Similarity: 18% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).

41 of 5948 Similarity: 18% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	42 of 5948 Similarity: 18% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound	43 of 5948 Similarity: 18% Overall Call: (-Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide	44 of 5948 Similarity: 18% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	45 of 5948 Similarity: 18% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).
46 of 5948 Similarity: 18% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide	47 of 5948 Similarity: 18% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	48 of 5948 Similarity: 18% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	49 of 5948 Similarity: 18% Overall Call: (+Ve)  The training set compound has fired 2 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 2 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound 352: Aromatic amine or amide	50 of 5948 Similarity: 18% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).

Hypothesis: H-190



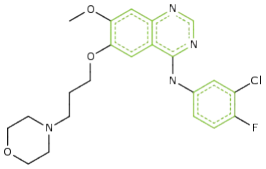
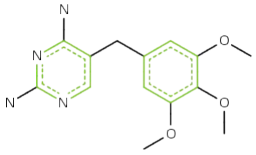
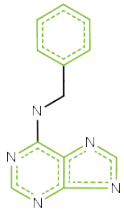
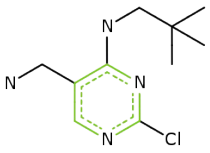
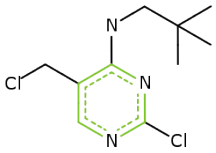
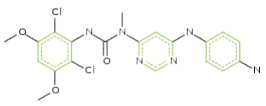
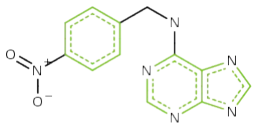
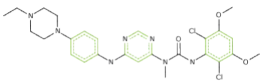
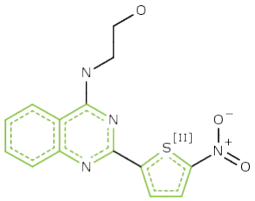
Sarah Result: Negative

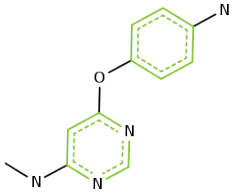
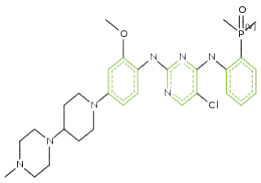
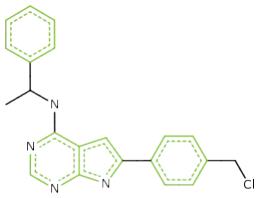
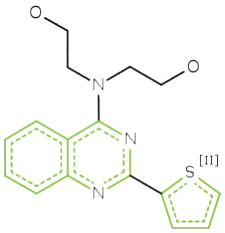
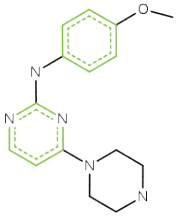
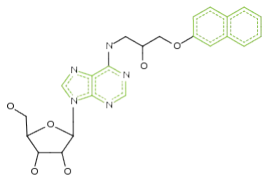
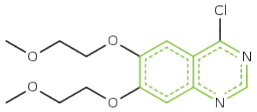
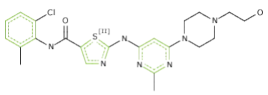
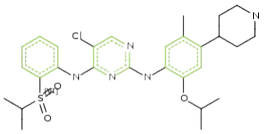
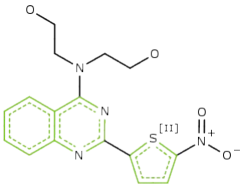
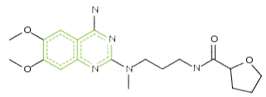
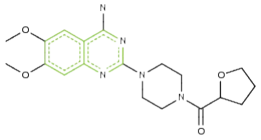
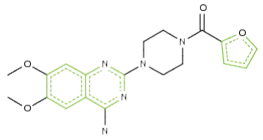
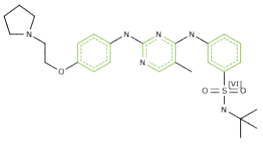
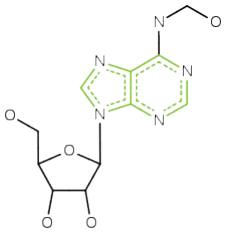
Confidence: 23%

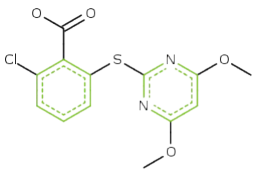
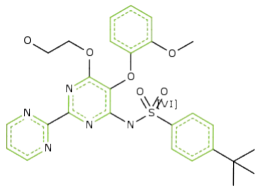
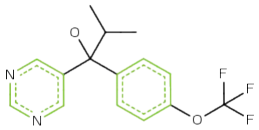
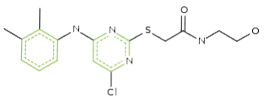
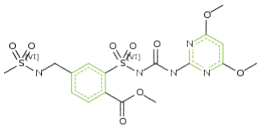
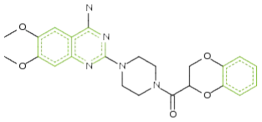
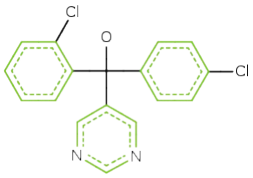
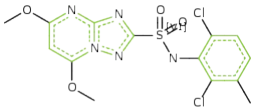
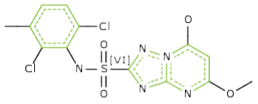
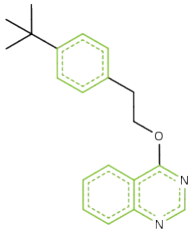
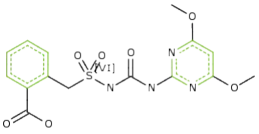
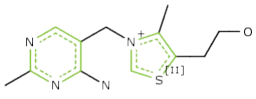
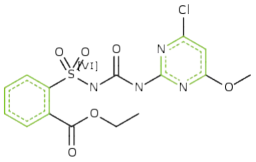
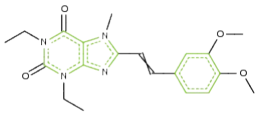
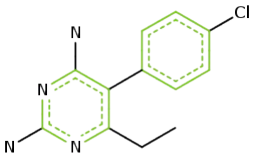
Examples: 403

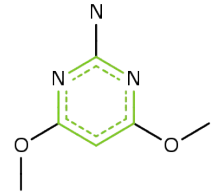
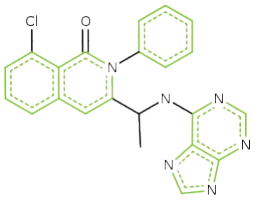
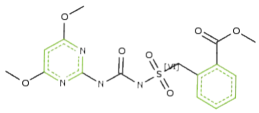
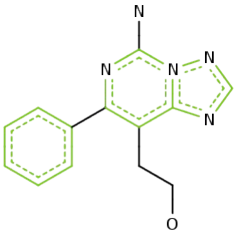
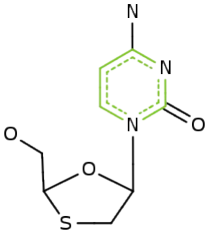
Hypothesis

Examples:

1 of 403 Similarity: 68% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	2 of 403 Similarity: 19% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	3 of 403 Similarity: 18% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	4 of 403 Similarity: 17% Overall Call: (-Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 870: Substituted 4-anilinoquinazoline	5 of 403 Similarity: 17% Overall Call: (+Ve)  The training set compound has fired 0 Derek alert(s).
6 of 403 Similarity: 17% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	7 of 403 Similarity: 17% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound	8 of 403 Similarity: 16% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	9 of 403 Similarity: 16% Overall Call: (-Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 027: Alkylating agent	10 of 403 Similarity: 16% Overall Call: (+Ve) The training set compound has fired 0 Derek alert(s).
11 of 403 Similarity: 16% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	12 of 403 Similarity: 15% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound	13 of 403 Similarity: 15% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	14 of 403 Similarity: 15% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	15 of 403 Similarity: 15% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound

16 of 403 Similarity: 14% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 351: Aromatic amine or amide	17 of 403 Similarity: 14% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	18 of 403 Similarity: 14% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 027: Alkylating agent	19 of 403 Similarity: 14% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	20 of 403 Similarity: 14% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 485: 2-Aminopyrimidine
21 of 403 Similarity: 14% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	22 of 403 Similarity: 14% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	23 of 403 Similarity: 14% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	24 of 403 Similarity: 13% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	25 of 403 Similarity: 13% Overall Call: (+Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound
26 of 403 Similarity: 13% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	27 of 403 Similarity: 13% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	28 of 403 Similarity: 13% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	29 of 403 Similarity: 13% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	30 of 403 Similarity: 12% Overall Call: (-Ve)  The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 307: N-Methylol compound or precursor

31 of 403 Similarity: 12% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	32 of 403 Similarity: 12% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	33 of 403 Similarity: 12% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	34 of 403 Similarity: 12% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	35 of 403 Similarity: 12% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).
36 of 403 Similarity: 12% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	37 of 403 Similarity: 12% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	38 of 403 Similarity: 12% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	39 of 403 Similarity: 12% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	40 of 403 Similarity: 11% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).
41 of 403 Similarity: 11% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	42 of 403 Similarity: 11% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	43 of 403 Similarity: 11% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	44 of 403 Similarity: 11% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).	45 of 403 Similarity: 11% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).

46 of 403 Similarity: 11% Overall Call: (-Ve)	47 of 403 Similarity: 11% Overall Call: (-Ve)	48 of 403 Similarity: 11% Overall Call: (-Ve)	49 of 403 Similarity: 11% Overall Call: (-Ve)	50 of 403 Similarity: 11% Overall Call: (-Ve)
 The training set compound has fired 0 Derek alert(s).	 The training set compound has fired 0 Derek alert(s).	 The training set compound has fired 0 Derek alert(s).	 The training set compound has fired 0 Derek alert(s).	 The training set compound has fired 0 Derek alert(s).

Glossary

Derek Prediction Outcomes

Certain

There is proof that the proposition is true.

Probable

There is at least one strong argument that the proposition is true and there are no arguments against it.

Plausible

The weight of evidence supports the proposition.

Equivocal

There is an equal weight of evidence for and against the proposition.

Doubted

The weight of evidence opposes the proposition.

Improbable

There is at least one strong argument that the proposition is false and there are no arguments that it is true.

Impossible

There is proof that the proposition is false.

Open

There is no evidence that supports or opposes the proposition.

Contradicted

There is proof that the proposition is both true and false.

Inactive, no misclassified or unclassified features

The query structure does not match any structural alerts or examples in Derek which show activity in a bacterial reverse mutation assay (Ames test). Additionally, the query structure does not contain any unclassified or misclassified features.

Inactive, contains misclassified features

Features in the molecule are found in non-alerting mutagens in the Lhasa reference set. The prediction remains negative and the misclassified features are highlighted to enable the negative prediction to be verified by expert assessment.

Inactive, contains unclassified features

Some features in the molecule have not been found in the Lhasa reference set. The prediction remains negative and the unclassified features are highlighted to enable the negative prediction to be verified by expert assessment.

Inactive, contains misclassified and unclassified features

The query structure contains features that are misclassified and features that are unclassified. These are highlighted on the structure.

CAS Registry Numbers® (CAS RN®)

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reference CAS Registry Numbers® against multiple sources to achieve a high level of accuracy.

Sarah Prediction Outcomes

Positive

The query structure is predicted to be positive in a bacterial reverse mutation assay (Ames test).

Negative

The query structure is predicted to be negative in a bacterial reverse mutation assay (Ames test).

Equivocal

A strong argument cannot be made based on the training set compounds and any hypotheses generated for the query compound for either activity or inactivity in a bacterial reverse mutation assay (Ames test). In the absence of a strong overall signal, an equivocal call has been made.

Out of Domain

At least one atom present in a fragment of the query compound is not represented by any of the fragments in the training set used to build the model. As a result, the compound is outside the training dataset domain and an overall prediction is not possible.

Confidence

The overall confidence for a prediction is determined from the confidence of the individual hypotheses activated by the structure. These are, in turn, based on the signal and the Tanimoto similarity of the nearest neighbours to the query structure used to build the hypothesis. In the absence of any hypotheses being activated by the query compound, the signal and Tanimoto similarity of the nearest neighbours from the entire training set are used to generate the overall confidence.

CAS Registry Numbers® (CAS RN®)

CAS Registry Numbers® are the intellectual property of the American Chemical Society; and are used by Lhasa Limited with the express permission of CAS. CAS Registry Numbers® have not been verified by CAS and may be inaccurate. Expert data scientists at Lhasa Limited cross reference CAS Registry Numbers® against multiple sources to achieve a high level of accuracy.

ICH M7 Sarah Example Icons

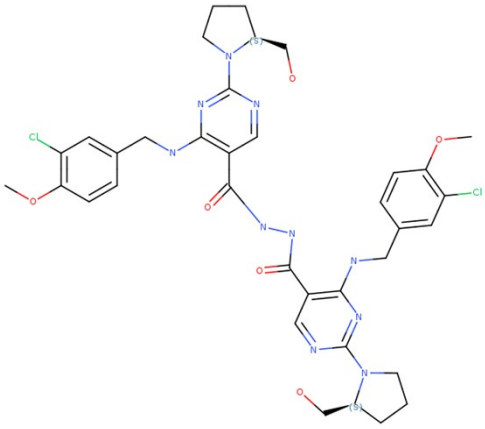
 **Example compound is Lhasa certified**

 **Derek alert has been fired for the example compound**

 **All Derek alerts fired for the example compound were for toxicophores not related to the hypothesis.**

Experimental data for the most sensitive strains relating to the hypothesis is missing for the example compound.

Prediction Summary - Impurity-F.cdx



Derek: Inactive
Sarah: Negative

Smiles:
C1(=C(C=CC(=C1)CNC2=C(C=NC(=N2)N3[C@@H](CCC3)CO)C(=O)NNC(C5=C(NCC=4C=CC(=C(C=4)Cl)OC)N=C(N=C5)N6[C@@H](CCC6)CO)=O)OC)Cl

Average Mol Mass:	781.69
Exact Mol Mass:	780.2666
Log Kp:	-3.68
Log P:	5.37

Expert Review Summary

In Silico Overall Conclusion: Negative (Calculated Call)

ICH M7 Cohort of Concern: No

Review status: Review not started

Prediction Detail – Derek Nexus

Derek Knowledge Base	Version	Last Modified Date	Certified by
Derek KB 2022 2.0	2.0	13/07/2022 18:02:45	Lhasa Limited, Leeds, Yorkshire, UK

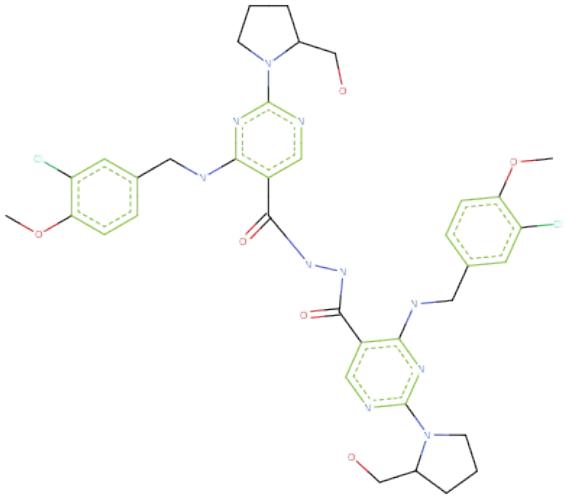
Perceive Mixtures	Perceive Tautomers
No	No

Mutagenicity in vitro in bacterium is INACTIVE (from KB: Derek KB 2022 2.0)

The parameters that have influenced your prediction are: substructures in the input structure, which have the potential to cause mutagenicity; your selected species, which is bacterium.

Overview

No misclassified or unclassified features



Details

The query structure does not match any structural alerts or examples for (bacterial in vitro) mutagenicity in Derek. Additionally, the query structure does not contain any unclassified or misclassified features and is consequently predicted to be inactive in the bacterial in vitro (Ames) mutagenicity test.

Prediction Detail – Sarah Nexus

Sarah Model Name	Version	Certified
Sarah Model - 2022.2	1.10	Yes

The compound is predicted to be negative with 21% confidence for the 'Mutagenicity in vitro' endpoint in the model: 'Sarah Model - 2022.2'. Supporting hypotheses containing similar examples from the training set have been found.

Hypotheses

Structure	ID	Description	Result	Confidence	Examples
	H-309	Hypothesis	Negative	24%	1672
	H-294	Hypothesis	Negative	16%	5948
	H-190	Hypothesis	Negative	21%	403

Hypothesis: H-309

Sarah Result: Negative

Confidence: 24%

Examples: 1672

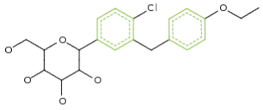
Hypothesis

Examples:

1 of 1672 Similarity: 66% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	2 of 1672 Similarity: 22% Overall Call: (-Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide	3 of 1672 Similarity: 22% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	4 of 1672 Similarity: 21% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	5 of 1672 Similarity: 19% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).
6 of 1672 Similarity: 19% Overall Call: (+Ve) The training set compound has fired 0 Derek alert(s).	7 of 1672 Similarity: 19% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound	8 of 1672 Similarity: 18% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 365: Acridine or analogue	9 of 1672 Similarity: 18% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	10 of 1672 Similarity: 18% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).
11 of 1672 Similarity: 18% Overall Call: (-Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide	12 of 1672 Similarity: 17% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	13 of 1672 Similarity: 17% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	14 of 1672 Similarity: 17% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 365: Acridine or analogue	15 of 1672 Similarity: 17% Overall Call: (-Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide

16 of 1672 Similarity: 17% Overall Call: (+Ve) The training set compound has fired 0 Derek alert(s).	17 of 1672 Similarity: 16% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide	18 of 1672 Similarity: 16% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	19 of 1672 Similarity: 16% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	20 of 1672 Similarity: 16% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound
21 of 1672 Similarity: 16% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	22 of 1672 Similarity: 16% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	23 of 1672 Similarity: 16% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	24 of 1672 Similarity: 16% Overall Call: (+Ve) The training set compound has fired 0 Derek alert(s).	25 of 1672 Similarity: 16% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound
26 of 1672 Similarity: 16% Overall Call: (+Ve) The training set compound has fired 0 Derek alert(s).	27 of 1672 Similarity: 16% Overall Call: (+Ve) The training set compound has fired 0 Derek alert(s).	28 of 1672 Similarity: 16% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	29 of 1672 Similarity: 16% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	30 of 1672 Similarity: 16% Overall Call: (+Ve) The training set compound has fired 0 Derek alert(s).

31 of 1672 Similarity: 16% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	32 of 1672 Similarity: 15% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	33 of 1672 Similarity: 15% Overall Call: (+Ve) The training set compound has fired 0 Derek alert(s).	34 of 1672 Similarity: 15% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	35 of 1672 Similarity: 15% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 019: Epoxide
36 of 1672 Similarity: 15% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	37 of 1672 Similarity: 15% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	38 of 1672 Similarity: 15% Overall Call: (+Ve) The training set compound has fired 0 Derek alert(s).	39 of 1672 Similarity: 15% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	40 of 1672 Similarity: 15% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).
41 of 1672 Similarity: 15% Overall Call: (+Ve) The training set compound has fired 0 Derek alert(s).	42 of 1672 Similarity: 15% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	43 of 1672 Similarity: 15% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	44 of 1672 Similarity: 15% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	45 of 1672 Similarity: 15% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).

46 of 1672 Similarity: 15% Overall Call: (-Ve)	47 of 1672 Similarity: 15% Overall Call: (-Ve)	48 of 1672 Similarity: 15% Overall Call: (+Ve)	49 of 1672 Similarity: 15% Overall Call: (-Ve)	50 of 1672 Similarity: 15% Overall Call: (+Ve)
				
The training set compound has fired 0 Derek alert(s).	The training set compound has fired 0 Derek alert(s).	The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 027: Alkylating agent	The training set compound has fired 0 Derek alert(s).	The training set compound has fired 0 Derek alert(s).

Hypothesis: H-294

Sarah Result: Negative

Confidence: 16%

Examples: 5948

Hypothesis

Examples:

1 of 5948 Similarity: 66% Overall Call: (-Ve)	2 of 5948 Similarity: 26% Overall Call: (-Ve)	3 of 5948 Similarity: 23% Overall Call: (+Ve)	4 of 5948 Similarity: 23% Overall Call: (-Ve)	5 of 5948 Similarity: 23% Overall Call: (+Ve)
The training set compound has fired 0 Derek alert(s).	The training set compound has fired 0 Derek alert(s).	The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 019: Epoxide	The training set compound has fired 0 Derek alert(s).	The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 027: Alkylating agent

6 of 5948 Similarity: 22% Overall Call: (-Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide	7 of 5948 Similarity: 22% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	8 of 5948 Similarity: 22% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	9 of 5948 Similarity: 22% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 315: Acid halide	10 of 5948 Similarity: 21% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).
11 of 5948 Similarity: 21% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide	12 of 5948 Similarity: 20% Overall Call: (+Ve) The training set compound has fired 0 Derek alert(s).	13 of 5948 Similarity: 20% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	14 of 5948 Similarity: 20% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	15 of 5948 Similarity: 20% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).
16 of 5948 Similarity: 20% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	17 of 5948 Similarity: 20% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	18 of 5948 Similarity: 20% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	19 of 5948 Similarity: 19% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	20 of 5948 Similarity: 19% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide

21 of 5948 Similarity: 19% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	22 of 5948 Similarity: 19% Overall Call: (+Ve) The training set compound has fired 0 Derek alert(s).	23 of 5948 Similarity: 19% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound	24 of 5948 Similarity: 19% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	25 of 5948 Similarity: 19% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 027: Alkylating agent
26 of 5948 Similarity: 19% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	27 of 5948 Similarity: 19% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	28 of 5948 Similarity: 19% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	29 of 5948 Similarity: 19% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	30 of 5948 Similarity: 19% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).
31 of 5948 Similarity: 18% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	32 of 5948 Similarity: 18% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	33 of 5948 Similarity: 18% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 027: Alkylating agent	34 of 5948 Similarity: 18% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 365: Acridine or analogue	35 of 5948 Similarity: 18% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).

36 of 5948 Similarity: 18% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 019: Epoxide	37 of 5948 Similarity: 18% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	38 of 5948 Similarity: 18% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide	39 of 5948 Similarity: 18% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	40 of 5948 Similarity: 18% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).
41 of 5948 Similarity: 18% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	42 of 5948 Similarity: 18% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound	43 of 5948 Similarity: 18% Overall Call: (-Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide	44 of 5948 Similarity: 18% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	45 of 5948 Similarity: 18% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).
46 of 5948 Similarity: 18% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	47 of 5948 Similarity: 18% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 352: Aromatic amine or amide	48 of 5948 Similarity: 17% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	49 of 5948 Similarity: 17% Overall Call: (+Ve) The training set compound has fired 2 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 2 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound 352: Aromatic amine or amide	50 of 5948 Similarity: 17% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).

Hypothesis: H-190

Sarah Result: Negative

Confidence: 21%

Examples: 403

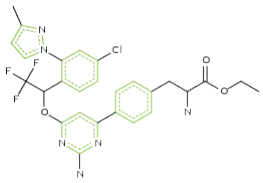
Hypothesis

Examples:

1 of 403 Similarity: 66% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	2 of 403 Similarity: 19% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	3 of 403 Similarity: 17% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	4 of 403 Similarity: 17% Overall Call: (-Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 870: Substituted 4-anilinoquinazoline	5 of 403 Similarity: 17% Overall Call: (+Ve) The training set compound has fired 0 Derek alert(s).
6 of 403 Similarity: 16% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	7 of 403 Similarity: 16% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound	8 of 403 Similarity: 16% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	9 of 403 Similarity: 16% Overall Call: (+Ve) The training set compound has fired 0 Derek alert(s).	10 of 403 Similarity: 16% Overall Call: (-Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 027: Alkylating agent

11 of 403 Similarity: 15% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	12 of 403 Similarity: 15% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound	13 of 403 Similarity: 15% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	14 of 403 Similarity: 15% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	15 of 403 Similarity: 14% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound
16 of 403 Similarity: 14% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	17 of 403 Similarity: 14% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 351: Aromatic amine or amide	18 of 403 Similarity: 14% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 027: Alkylating agent	19 of 403 Similarity: 14% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	20 of 403 Similarity: 14% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).
21 of 403 Similarity: 14% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 485: 2-Aminopyrimidine	22 of 403 Similarity: 13% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	23 of 403 Similarity: 13% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	24 of 403 Similarity: 13% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	25 of 403 Similarity: 13% Overall Call: (+Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 329: Aromatic nitro compound

26 of 403 Similarity: 13% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	27 of 403 Similarity: 12% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	28 of 403 Similarity: 12% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	29 of 403 Similarity: 12% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	30 of 403 Similarity: 12% Overall Call: (-Ve) The training set compound has fired 1 Derek alert(s). 0 alert(s) for toxicophores related to this hypothesis 1 alert(s) for toxicophores not related to this hypothesis 307: N-Methylol compound or precursor
31 of 403 Similarity: 12% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	32 of 403 Similarity: 12% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	33 of 403 Similarity: 12% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	34 of 403 Similarity: 12% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	35 of 403 Similarity: 12% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).
36 of 403 Similarity: 12% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	37 of 403 Similarity: 11% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	38 of 403 Similarity: 11% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	39 of 403 Similarity: 11% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	40 of 403 Similarity: 11% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).

41 of 403 Similarity: 11% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	42 of 403 Similarity: 11% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	43 of 403 Similarity: 11% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	44 of 403 Similarity: 11% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	45 of 403 Similarity: 11% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).
46 of 403 Similarity: 11% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	47 of 403 Similarity: 11% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	48 of 403 Similarity: 11% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	49 of 403 Similarity: 11% Overall Call: (-Ve) The training set compound has fired 0 Derek alert(s).	50 of 403 Similarity: 11% Overall Call: (-Ve)  The training set compound has fired 0 Derek alert(s).