

New Computational Tools from EPA: The CompTox Chemicals Dashboard and Generalized Read Across

Grace Patlewicz and Antony Williams

National Center for Computational Toxicology U.S. Environmental Protection Agency, RTP, NC

This work was reviewed by the U.S. EPA and approved for presentation but does not necessarily reflect official Agency policy.

May 9th 2019

Earlier Dashboard Applications: Single architecture in development







EPA United States Environmental Prot				
Cat: Chemical and Product Cat	egories			Contact Us
are here: EPA Home . Computational To	cicology Research » Chemica	d Use		
PHome PSearch *Results	Dictionary & Downlo	ad #Help		
hemical: BISPHENOL A				
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se Information:				
CPCat Description o	Source Description ¢	ACTOR Data Set/List o	Source o	Class of Chemical Category
consumer_use_ACToRUseDB	Consumer Use		ACToR UseDB	Use Categories
personal_care_ACToRUseDB	Personal Care Product		ACToR UseDB	Use Categories
industrial_manufacturing_ACToRUseDB	Chemical Industrial		ACToR UseDB	Use Categories
child_use detected	Consumer Products	The Danish EPA:Exposure of 2-year-olds to chemical substances in Consumer Products. This project included a survey of the products as well as chemical analyses and risk assessments of a number of period and the test of the period behavior areas in the constant with the period behavior.	ACToR Data Sets and Lists	Use Categories

	€FP∆	ED	SP21 D	ashboard		
	United State Environmer Agency	es Endo ntal Protection	crine Disrupt	ion Screening Program for	he 21st Century	
Chemical Summary	Public Information	Bioactivity Summary	Bioactivity	High-Throughput Exposure	Assay Definitions	Dosimetry
EDSP Dashboard O	verview					
EDSP Dashboar	d Overview					
Congress requires El Screening Program f	PA's Endocrine Disruptor : or the 21st Century Dasht	Screening Program to evaluate	ate chemicals fo to provide acces	r potential endocrine disruption, and is to new chemical data on over 1,8	there are thousands of 00 chemicals of interest	chemicals of interest to the program. EPA researchers developed the Endocrine Disruption t.
The purpose of the E	DSP21 Dashboard is to h	elp the Endocrine Disruptor	Screening Prog	am evaluate chemicals for endocrin	e-related activity.	
The data for this very	sion of the Dashboard con	nes from various sources -				
 Rapid, autom Chemical exp High quality o Physchem Pr 	ated (or in vitro high-throu; osure data and prediction hemical structures and an operties Database (PhysC	ghput) chemical screening da models (ExpoCastDB). notations (DSSTox). ChemDB).	ata generated by	the EPA's Toxicity Forecaster (Tox	Cast) project and the fe	Ideral Toxicity Testing in the 21st century (Tox21) collaboration.
ToxCast Data Us	e Considerations					
The activity o Careful review Interpretation	f a chemical in a specific : is required to determine t of ToxCast data is expect	assay does not necessarily i the use of the data in a parti ted to change over time as b	mean that it will cular decision oc oth the science	cause toxicity or an adverse health ntext. and analytical methods improve.	outcome. There are man	ny factors that determine whether a chemical will cause a specific adverse health outcome.
EPA will continuous?	y add functionality and imp	prove overall usability and pe	rformance.			
To get the best possi	ble experience using the B	EDSP Dashboard application	we recommend	l using Mozilla Firefox or Google Cl	rome.	
90						

The CompTox Portal https://comptox.epa.gov/





CompTox Chemicals Dashboard



• A publicly accessible website delivering access:

- ~875,000 chemicals with related property data
- Experimental and predicted physicochemical property data
- Integration to "biological assay data" for 1000s of chemicals
- Information regarding consumer products containing chemicals
- Links to other agency websites and public data resources
- "Literature" searches for chemicals using public resources
- "Batch searching" for thousands of chemicals
- DOWNLOADABLE Open Data for reuse and repurposing

CompTox Chemicals Dashboard





CompTox Chemicals Dashboard Chemicals



Separation United States Environmental Protection Agency	Home Advanced Search Batch Search Lists 🛩 Predictions Downloads	Share 🔻
WITED STATES	875 Thousand Chemicals	
	Chemicals Product/Use Categories Assay/Gene	- 1
O THE REAL PROPERTY OF	Q Bisphenol A	- 1
AL PROTECT	Bisphenol A DTXSID7020182	
	Bisphenol A bis(2-hydroxyethyl ether) diacrylate DTXSID6066991	
	Bisphenol A bis(2-hydroxyethyl ether) dimethacrylate DTXSID 1066992	
	Bisphenol A bis(2-hydroxypropyl) ether DTXSID8051592	
	Bisphenol A carbonate polymer DTXSID6027840	
4	Bisphenol A diglycidyl ether DTXSID6024624	- 1
	Bisphenol A glycidyl methacrylate DTXSID7044841	
	Bisphenol A propoxylate diglycidyl ether DTXSID10399098	•

CompTox Chemicals Dashboard Products and Use Categories



NITED STATE	875 Thousand Chemicals	
NVN SV	Chemicals Product/Use Categories Assay/Gene	
40E	Q hair color	
AL PROTECT	CPDat PRODUCT category: personal care hair color hair colors and dyes characterized as permanent	
	CPDat PRODUCT category: personal care hair color hair colors and dyes characterized as for professional use	
	CPDat PRODUCT category: personal care hair color hair colors and dyes characterized as temporary	
	CPDat PRODUCT category: personal care hair color hair coloring products not otherwise categorized	
	CPDat PRODUCT category: personal care hair color activator chemical activators for hair coloring products	
	CPDat PRODUCT category: personal care hair color developer chemical developers for hair coloring products	
	CPDat PRODUCT category: personal care hair color toner chemical toners for hair coloring products	
4	00 new chemical substances being added, improved support for Toxcast bioassay available. This short video summarizes the advantages of the dasl of multiple chemical lists and new user interface enhancements across the look forward to your feedback	

-

CompTox Chemicals Dashboard Assays and Genes



Separate United States Environmental Protection Agency	Home Advanced Search Batch Search Lists 🛩 Predictions Downloads	Share 🔻						
NITED STATE	875 Thousand Chemicals							
FINITION STATE	Chemicals Product/Use Categories Assay/Gene	- 1						
DATE AND A DATE OF A DATE	Q ESR	- 1						
AL PROTECT	ASSAY: TOX21_ESRE_BLA_ch1 Data from the assay component TOX21_ESRE_BLA_ch1 was analyzed into 1 a	- 1						
	ASSAY: TOX21_ESRE_BLA_ch2 Data from the assay component TOX21_ESRE_BLA_ch2 was analyzed into 1 a	- 1						
	ASSAY: TOX21_ESRE_BLA_ratio Data from the assay component TOX21_ESRE_BLA_ratio was analyzed into 1	- 1						
	ASSAY: TOX21_ESRE_BLA_viability TOX21_ESRE_BLA_viability used a type of growth reporter where loss-of							
	GENE: ESR1 estrogen receptor 1	- 1						
	GENE: esr1.L estrogen receptor 1 L homeolog	- 1						
	GENE: ESR2 estrogen receptor 2 (ER beta)							
•	GENE: esr2.L estrogen receptor 2 L homeolog							
	GENE: esr2a EENE: esr2b							
	estrogen receptor 2b	•						

Detailed Chemical Pages



	Bisphenol A 80-05-7 DTXSID7020182 Searched by DSSTox Substance Id.	
DETAILS EXECUTIVE SUMMARY PROPERTIES ENV. FATE/TRANSPORT HAZARD ADME EXPOSURE BIOACTIVITY SIMILAR COMPOUNDS GENRA (BETA) RELATED SUBSTANCES	H ₃ C CH ₃ HO OH	Wikipedia Bisphenol A (BPA) is an organic synthetic compound with the chemical formula (CH ₂) ₂ C(C ₂ H ₄ OH) ₂ belonging to the group of diphenylmethane derivatives and bisphenols, with two hydroxyphenyl groups. It is a coloriess solid that is soluble in organic solvents, but poorly soluble in water. It has been in commercial use since 1957. BPA is a starting material for the synthesis of plastics, primarily Read more Intrinsic Properties Structural Identifiers Linked Substances Presence in Lists
SYNONYMS		Quality Control Notes
LINKS		

An "Executive Summary"





Physicochemical properties



EFA Environmental Prote Agency	ction Home Advanced Search	Batch Search Lists V Predie	tions Downloads		Copy 🔻 Share	 Submit Comment 	Q Search all data	
	Bisp Bisp 80-C	ohenol A)5-7 DTXSID7 d by Expert Validated Sync	7020182					
DETAILS	Property							
EXECUTIVE SUMMARY	Summary			6				
PROPERTIES				Summary	1			
ENV. FATE/TRANSPORT	🛓 Download 🔻 🛛 Colum	ns 🗸					Sea	rch query
HAZARD	Property 🗘	Experimental average 🗘	Predicted average 🗘	Experimental median 🗘	Predicted median 🗘	Experimental range 🗘	Predicted range	≎ Unit ¢
ADME	LogP: Octanol-Water	3.32 (1)	3.29		3.43	3.32	2.40 to 3.64	
EXPOSURE	Melting Point	155 (7)	139	156	138	153 to 156	125 to 157	°C
	Boiling Point	200 (1)	363		360	200	343 to 401	°C
BIOACTIVITY	Water Solubility	5.26e-4 (1)	9.62e-4		1.00e-3	5.26e-4	5.35e-4 to 1.31e-3	mol/L
TOXCAST: SUMMARY	Vapor Pressure	-	8.37e-7		3.43e-7	-	6.83e-8 to 2.59e-6	mmHg
EDSP21	Flash Point	-	190		190	-	188 to 192	°C
	Surface Tension	-	46.0			-	46.0	dyn/cm
TOXCAST/TOX21	Index of Refraction	-	1.60			-	1.60	
PUBCHEM	Molar Refractivity	-	68.2			-	68.2	cm^3
TOXCAST: MODELS	Polarizability	-	27.0			-	27.0	Å^3
	Density	-	1.17		1.17	-	1.14 to 1.20	g/cm^3
SIMILAR COMPOUNDS	Molar Volume	-	200			_	200	cm^3

Detailed OPERA Prediction Reports





Other Data: Human and Ecological Chemical Hazard Data



DETAILS		t of Denarture	<u> </u>									
EXECUTIVE SUMMARY	L Dowr	nload 💌				_						
PROPERTIES							🛉 Huma	n 💋 Eco				
ENV. FATE/TRANSPORT	Column	s ~ 10	~			L						
HAZARD	More +	Priority \$	Toxval type 🗘	Subtype 🗘	Risk assessment class 🗘	Value 🔨	Units 🗘	Study type 🗘	Exposure route 🗘	Species 🕈	Subsource 🗘	Sou
▶ ADME		5	BMDL-10	-	chronic	0.609	mg/kg-day	human	-	mouse	EFSA CEF	EFS
▶ EXPOSURE		5	NOEL	Systemic	repeat dose	3.75	mg/kg-day	repeat dose toxicity : oral	oral	rat	-	ECH
BIOACTIVITY						0.75						
SIMILAR COMPOUNDS		6	NOAEL	-	reproductive	3.75	mg/kg-day	reproductive	orai	rat	-	HPV
GENRA (BETA)		5	NOEL	Systemic	repeat dose	3.75	mg/kg-day	repeat dose toxicity : oral	oral	rat	-	ECH
RELATED SUBSTANCES		5	NOEL	Systemic	repeat dose	4.5	mg/kg-day	repeat dose toxicity : oral	oral	mouse	-	ECH
SYNONYMS		5	NOEL	Systemic	repeat dose	4.5	mg/kg-day	repeat dose toxicity : oral	oral	mouse	-	ECH
▶ LITERATURE		7	LEL	-	subchronic	5	mg/kg-day	subchronic	oral	rat	unpublished_submission	ToxR
LINKS		7	nel	-	chronic	5	mg/kg-day	reproductive multigeneration	oral	rat	open_lit	ToxR
COMMENTS		5	NOAEL	-	chronic	5	mg/kg-day	human	-	mouse	EFSAAFC	EFSA
		7	nel	-	subchronic	5	mg/kg-day	subchronic	oral	rat	unpublished_submission	ToxR

Hazard Data from "ToxVal_DB"

- tobago containa fallowing data:
- ToxVal Database contains following data:
 - -30,050 chemicals
 - -772,721 toxicity values
 - -29 sources of data
 - -21,507 sub-sources
 - -4585 journals cited
 - -69,833 literature citations

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Sources of Exposure to Chemicals



	Bisphenol A 80-05-7 DTXSID70201 Searched by DSSTox Substance Id.	82			
DETAILS		Product ar	nd Use Categories (PUC	s) ()	
EXECUTIVE SUMMARY	📩 Download 👻				
PROPERTIES	Columns v 10 v				Search query
ENV. FATE/TRANSPORT	Product or Use Categorization		ization type	Number of Unique Products	
HAZARD	manufacturing, metals	CPCat C	assette	17	
ADME	adhesive	CPCat C	assette	17	
	EXPOSURE		assette	16	
• EXPOSORE		CPCat C	assette	12	
PPODUCT &			assette	11	
FRODUCT	USE CATEGORIES	CPCat C	assette	8	
		CPCat C	assette	8	
CHEMICAL W	EIGHT FRACTION	CPCat C	assette	8	
		CPCat C	assette	7	
CHEMICAL F	UNCTIONAL USE	CPCat C	assette	6	
TOXICS RELE	EASE INVENTORY	First << 1 2	3 4 5 6 7 8 9 10	> >> Last	
MONITORING	B DATA				

Sources of Exposure to Chemicals





In Vitro Bioassay Screening ToxCast and Tox21





In Vitro Bioassay Screening ToxCast and Tox21





Bioactivity: Downloadable Data

https://www.epa.gov/chemical-research/exploring-toxcast-datadownloadable-data



Exploring ToxCast Data: Downloadable Data

The results after processing through the Pipeline are available on the <u>ToxCast Dashboard</u>, and for most users EPA recommends accessing the data there.

- <u>ToxCast Chemicals</u>
- <u>ToxCast Assays</u>

ToxCast Data and Information

- ToxCast & Tox21 Summary Files. Data for a single chemical endpoint pair for thousands of chemicals and assay endpoints for 20 variables such as the activity or hit call, activity concentrations, whether the chemical was tested in a specific assay, etc.
 - Download ToxCast Summary Information
 - <u>Download ReadMe</u>
- ToxCast & Tox21 Data Spreadsheet. A spreadsheet of EPA's analysis of the chemicals screened through ToxCast and the Tox21 collaboration which includes EPA's activity calls from the screening of over 1,800 chemicals.
 - <u>Download Data</u>
 - <u>Download ReadMe</u>
- ToxCast Data Pipeline R Package. The R computer programming package used to process and model all EPA ToxCast and Tox21 chemical screening data. The files include the R programming package as well as documents that provide overviews of the data analysis pipeline used and the R package. Users will need experience with R to use these files.
 - <u>Download Package</u>
 - <u>TCPL Overview</u>

Resources

- <u>Toxicity Forecaster (ToxCast)</u> Fact Sheet
- <u>ToxCast Publications</u>
- <u>ToxCast Citation</u>
- <u>About ToxCast</u>

ToxCast/Tox21 Data Analytical QC of the chemicals





Access to Analytical QC Data



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GenRA (Generalised Read-Across)



- <u>Read-across:</u> the method of filling a data gap whereby a chemical with existing data values is used to make a prediction for a 'similar' chemical.
- <u>Target chemical:</u> a chemical which has a data gap that needs to be filled i.e. the subject of the read-across.
- <u>Source analogue:</u> a chemical identified as an appropriate chemical for use in a read-across based on similarity to the target chemical and existence of relevant data.





- Predicting toxicity as a similarity-weighted activity of nearest neighbors based on chemistry and/or bioactivity descriptors
- Systematically evaluates read-across performance and uncertainty using available data

Jaccard similarity:

Implementing GenRA within the workflow



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GenRA Step Two: Data Gap Analysis & Generate Data Matrix 3 Summary Data Gap Analysis Generate Data Matrix 0 0 Group: ToxRef • By: Tox Fingerprint v Neighbors by: Chem: Morgan Fgrprts V Filter by: invivo data 🔻 bio 427 bio decr Chin Ct tot the Pyrasulfolole n Cloroconazole enbucone20 Melconezole Het acount TettaConaço Flusile2016 onazole Myclobular Ethylene glycol Ethion luconazole 3 15 0 CHR:Abdominal Cavity 819 Hexaconazole 43 18 345 R.A. CHR:Adrenal Gland Flusilazole 28 <mark>819</mark> 9 345 Butanal oxime Myrcene CHR:Artery (General) Cyproconazole 819 16 408 14 H,C DI CHR:Auditory Startle Re. Pyrasulfotole metabolite 0 0 18 CHR:Bile duct Acrolein diethyl ... Myclobutanil 15 818 15 Ethoprop CHR:Blood Chlorethoxyfos Fenbuconazole 34 819 17 CHR:Blood vessel 35 819 20 Tetraconazole CHR:Body Weight 35 215 15 82 Metconazole Fosamine amm. CHR:Bone 2-Ethoxyethyl a ... 46 180 Ipconazole 16 11. CHR:Bone Marrow Bromuconazole 24 13 345 Methyleugenol CHR:Brain bis(2-Chloro-1-... # of Analogs 10 Next nchus Data gap analysis





GenRA in practice – step by step



- Analogue identification:
- Similarity based on Morgan chemical fingerprints and selecting a default of 10 source analogues



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Data matrix view of source analogues relative to target chemical

Run Read-Across GenRA 💙	Min+: 0	•	Min-: 0	•	Filter:			s	imilarity Weig	ht:	Downloa	ad: Filetype 💙
	1.00 💿	0.39 🗸	0.31 🗸	0.29 🗸	0.29 🗸	0.26 🗸	0.24 🗸	0.22 🗸	0.21 🗸	0.21 🗸	0.20 🗸	
	÷,					0}0	×2	×p-				
	Fluconazole	Hexaconazole	Flusilazole	Cyproconazole	Pyrasulfotole m	Myclobutanil	Fenbuconazole	Tetraconazole	Metconazole	Ipconazole	Bromuconazole	
CHR:Abdominal Cavity									-			
CHR:Adrenal Gland												
CHR:Artery (General)												
CHR:Auditory Startle Re												
CHR:Bile duct												
CHR:Blood												
CHR:Blood vessel												
CHR:Body Weight												
CHR:Bone												

Data matrix for source substances





Look for commonality in profile across target effects

What are the most common effects across analogues



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- Predictions are binary (yes/no) for toxicity effects within ToxRefDB v1 studies.
- Predictions summarized on a study level basis. Red: "positive" and Blue: "negative".

GenRA in practice: Approach



Rank predictions based on the p-val and AUC values (where we have more confidence in the predictions)

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Rank based on the target organ effects observed for the source analogues

GenRA – Ongoing research



- Summarizing and aggregating the toxicity effect predictions to guide end users – what are the effects to be concerned about and which effect predictions are we most confident about
- Consideration of other information to define and refine the analogue selection – e.g. physicochemical similarity, metabolic similarity, reactivity similarity...
- EPA New Chemical Categories
- Quantifying the impact of physicochemical similarity on read-across performance
- Quantifying the impact of reactivity similarity on readacross performance



- Dose response information to refine scope of prediction beyond binary outcomes
- Transitioning from qualitative to quantitative predictions – how to apply and interpret GenRA in screening level hazard assessment
- Using quantitative data from acute rat oral toxicity, ToxRefDB v2

Names and CASRNs to Support Searches



Separation United States Environmental Protection Agency	Home Advanced Search Batch Search Lists • Predictions Downloads	Copy - Share - Submit Comment	Q Search all data
	Bisphenol A 80-05-7 DTXSID7020182 Searched by DSSTox Substance Id.		
DETAILS	25 🗸		Search query
EXECUTIVE SUMMARY	Synonym	\$	Quality \$
PROPERTIES	Bisphenol A		Valid
ENV. FATE/TRANSPORT	4,4'-(Propane-2,2-diyl)diphenol		Valid
HAZARD	Phenol, 4,4'-(1-methylethylidene)bis-		Valid
▶ ADME	80-05-7 Active CAS-RN		Valid
	BPA		Valid
F EAFOSORE	4,4'-Propane-2,2-diyldiphenol		Valid
► BIOACTIVITY	Phenol, 4,4'-(1-methylethylidene)bis-		Valid
SIMILAR COMPOUNDS	4-06-00-06717 Beilstein Registry Number		Beilstein
GENRA (BETA)	(4,4*-Dihydroxydiphenyl)dimethylmethane		Good
RELATED SUBSTANCES	2,2-Bis(4'-hydroxyphenyl) propane		Good
SYNONYMS	2,2'-Bis(4-hydroxyphenyl)propane		Good
	2,2-BIS-(4-HYDROXY-PHENYL)-PROPANE		Good
F LILINIONE	2,2-Bis(4-hydroxyphenyl)propane		Good
LINKS	2,2-Bis(p-hydroxyphenyl)propane		Good
COMMENTS	2,2-Di(4-Hydroxyphenyl) Propane		Good

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Literature Searches - Querying 29 Million PubMed abstracts



Ŷ	EPA United States Environmental Protection Agency	Home Advanced Search Batch Search Lists 🗸	Predictions Downloads	Copy 🔻	Share 🔻	Submit Comment	Q Search all data	
		Bisphenol A 80-05-7 DTXSID7020 Searched by DSSTox Substance Id.	0182					•
	DETAILS	1) Select PubMed starting point query then	2) click on Retrieve	Q	ptionally, edi	t the query before ret	rieving.	
	EXECUTIVE SUMMARY	Select a Query Term	Retrieve Articles		"80-05-7" OR	"Bisphenol A"		
	PROPERTIES	Hazard Fate and Transport					<i>n</i>)	
	ENV. FATE/TRANSPORT	Metabolism/PK/PD Chemical Properties Exposure Mixtures						
	ERATURE	Male Reproduction Androgen Disruption Female Reproduction GeneTox						ł
	GOOGLE SCHOLAR	Cancer Clinical Trials Embryo and embryonic development Child (infant through adolescent)						
	PUBMED ABSTRACT SIFTER	Dust and Exposure Food and Exposure Water and Exposure						
	PUBCHEM ARTICLES	Aigae						
	PUBCHEM PATENTS							
	PPRTV							
	IRIS							•

Abstract Sifter - Querying 28 Million PubMed abstracts

Bisphenol A

Hazard



2

DETAILS

EXECUTIVE SUMMARY

PROPERTIES

ENV. FATE/TRANSPORT

HAZARD ADME

EXPOSURE

BIOACTIVITY

GENRA (BETA)

SIMILAR COMPO

RELATED SUBS

SYNONYMS

LITERATURE

GOOGLE S

PUBMED ABSTRACT

PUBCHEM ARTICLES

PUBCHEM PATENTS

Searched by DSSTox Substance Id. 1) Select PubMed starting point query then 2) click on Retrieve.

80-05-7 | DTXSID7020182

To find articles quickly, enter terms to sift abstracts.

Retrieve Articles

118 of 118 articles loaded...

Optionally, edit the query before retrieving.

("80-05-7" OR "Bisphenol A") AND (NOAEL or NOEL OR LOEL or Rfd OR "reference dose" OR "reference concentration" OR "adverse effect level"[tiab] OR "cancer slope factor'[tiab])

Downlo

ad / Send to 🔻	Download Sifts

		PMID	Year	Title	Authors	Journal	Rev
		29573712	2018	Urinary bisphenol analogues and triclosan in children from south China and implications f	Chen; Fang; Ren; Fan; Zhang; Liu; Zhou; Chen; Yu;	Environmental pollution (Barking, Essex : 1987)	
		29306804	2018	Phosphorus flame retardants and Bisphenol A in indoor dust and PM2.5 in kindergartens	Deng; Li; Wu; Richard; Wang; Ho	Environmental pollution (Barking, Essex : 1987)	
		29268159	2017	Presence of diphenyl phosphate and aryl-phosphate flame retardants in indoor dust from	Björnsdotter; Romera-García; Borrull; de Boer; Rubi	Environment international	
		29172986	2017	Bisphenol A and Bisphenol S release in milk under household conditions from baby bottle	Russo; Barbato; Cardone; Fattore; Albrizio; Grumetto	Journal of environmental science and health. Part	
		29097150	2017	Prenatal bisphenol A (BPA) exposure alters the transcriptome of the neonate rat amygdal	Arambula; Jima; Patisaul	Neurotoxicology	
		28982642	2017	Systematic Review and Meta-Analysis of Early-Life Exposure to Bisphenol A and Obesity	Wassenaar; Trasande; Legler	Environmental health perspectives	1
50105		28890130	2017	Effects of perinatal bisphenol A exposure on the volume of sexually-dimorphic nuclei of ju	Arambula; Fuchs; Cao; Patisaul	Neurotoxicology	
TANCES		28641706	2017	Delayed onset of puberty in male offspring from bisphenol A-treated dams is followed by t	Oliveira; Romano; de Campos; Cavallin; Oliveira; R	Reproduction, fertility, and development	
		28608465	2017	Effect of bisphenol A on reproductive processes: A review of in vitro, in vivo and epidemiol	Tomza-Marciniak; Stępkowska; Kuba; Pilarczyk	Journal of applied toxicology : JAT	✓
		28503266	2017	Inhalation Toxicity of Bisphenol A and Its Effect on Estrous Cycle, Spatial Learning, and M	Chung; Han; Lee; Lee	Toxicological research	
		28377091	2017	Derivation of an oral Maximum Allowable Dose Level for Bisphenol A.	Goodman; Peterson; Hixon; Pacheco Shubin	Regulatory toxicology and pharmacology : RTP	✓
CHOLAR		28257732	2017	Bisphenol A release from orthodontic adhesives measured in vitro and in vivo with gas ch	Moreira; Matos; de Souza; Brigante; Queiroz; Roma	American journal of orthodontics and dentofacial ort	
	_	20240020	2017	Verentile transduction scheme based on electrolyte ented erannic field effect transister up	Piro: Mana: Reasoudia: Tibaldi: Acquetia: Neël: Pei	Piecescore & biselectronies	

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Abstract Sifter for Excel



F1CC	Open fo	earch r Science			Search	
BROWSE	GATEWAYS	HOW TO PUBLISH 🗸	ABOUT ~	BLOG		
SOFTWARE Abstra PubMe Nancy	TOOL ARTICLE ICT Sifter: a ed [versior Baker (10 ¹ , Thom etails	a comprehensive 1; referees: 2 a has Knudsen ² , Antony Williar	e front-er pproved]	Che	eck for updates	METRICS 629 VIEWS
	This article is	included in the Chemical In				
A second			formation Scier	nce gateway.		Get PDF

External Links to ~80 websites





Batch Searching

MS-Ready Formula(e)

Exact Formula(e)

Monoisotopic Mass



Batch Search



Step Three: Select Download Data or Display Chemicals

Please enter one identifier per line Enter Identifiers to Search (searches should be limited to <5000 identifiers) Select Input Type(s) Fuel oil, no. 1 Ethylene oxide **Identifiers** Chloromethane 1-Chloropropan-2-one Chemical Name 📢 n-Hexane Ammonia CASRN 6 Nickel carbonyl Phosgene Potassium cyanide InChlKey 🚺 Chlorodimethylsilane DSSTox Substance ID 🚯 InChIKey Skeleton 🚯

mical Data

Batch Searching



)	Select Output Format:	
	Excel 🗸	🚣 Download
	Customize Results Select All Select All in Lists	Presence in Lists: ICCVAM test method evaluation report: in vitro ocular toxicity test methods 40CFR355 A list of all PBDEs (Polybrominated diphenyl ethers)
	Chemical Identifiers DTXSID Chemical Name CAS-RN InChlKey IUPAC Name	 A list of all PCBs (Polychlorinated diphenyls) A list of polycyclic aromatic hydrocarbons Acute exposure guideline levels Algal Toxins Androgen Receptor Chemicals APCRA Chemicals for Prospective Analysis
	Structures Mol File () SMILES () InChl String () MS-Ready SMILES ()	 APCRA Chemicals for Retrospective Analysis APCRA Chemicals for Retrospective Analysis_App_List_448_Chemicals ATSDR Minimal Risk Levels (MRLs) for Hazardous Substances ATSDR Toxic Substances Portal Chemical List Bisphenol Compounds
	QSAR-Ready SMILES C Intrinsic And Predicted Propert Molecular Formula Average Mass Monoisotopic Mass	ies California Office of Environmental Health Hazard Assessment Chemicals with interesting names CMAP DNT Screening Library Drinking Water Suspects, KWR Water, Netherlands
	TEST Model Predictions OPERA Model Predictions	 EDSP Universe EPA Chemicals associated with hydraulic fracturing

Excel Output



	A	В	С	D	E	F	G	H
1	INPUT	FOUND_BY	DTXSID	PREFERRED_NAME	EXPOCAS	EXPOCAS	NHANES	TOXVAL_D
2	1445-75-6	CAS-RN	DTXSID5024051	Diisopropyl methylpho:	2.09e-08	Y	-	Y
3	50-00-0	CAS-RN	DTXSID7020637	Formaldehyde	1.32e-06	Y	-	Y
4	107-06-2	CAS-RN	DTXSID6020438	1,2-Dichloroethane	4.9e-06	Y	-	Y
5	57-12-5	CAS-RN	DTXSID6023991	Cyanide	-	-	-	Y
6	7550-45-0	CAS-RN	DTXSID8042476	Titanium tetrachloride	-	-	-	Y
7	79-01-6	CAS-RN	DTXSID0021383	Trichloroethylene	7.27e-06	Y	-	Y
8	121-82-4	CAS-RN	DTXSID9024142	Cyclonite	6.72e-08	Y	-	Y
9	108-05-4	CAS-RN	DTXSID3021431	Vinyl acetate	8.3e-05	Y	-	Y
10	7803-51-2	CAS-RN	DTXSID2021157	Phosphine	-	-	-	Y
11	122-66-7	CAS-RN	DTXSID7020710	1,2-Diphenylhydrazine	1.49e-07	Y	-	Y
12	101-77-9	CAS-RN	DTXSID6022422	4,4'-Methylenedianiline	6.08e-06	Y	-	Y
13	14017-34-6	CAS-RN	DTXSID90161250	Selenium difluoride	-	-	-	-
14	75-44-5	CAS-RN	DTXSID0024260	Phosgene	-	-	-	Y
15	621-64-7	CAS-RN	DTXSID6021032	N-Nitrosodipropylamine	4.55e-07	Y	-	Y
16	75-09-2	CAS-RN	DTXSID0020868	Dichloromethane	2.02e-06	Y	-	Y
17	100-41-4	CAS-RN	DTXSID3020596	Ethylbenzene	8.32e-05	Y	-	Y
18	7440-28-0	CAS-RN	DTXSID2036035	Thallium	-	-	-	Y
19	108-88-3	CAS-RN	DTXSID7021360	Toluene	8.61e-05	Y	-	Y
20	111-44-4	CAS-RN	DTXSID9020168	Bis(2-chloroethyl) ethe	2.82e-07	Y	-	Y
21	7440-42-8	CAS-RN	DTXSID3023922	Boron	-	-	-	Y
22	7440-29-1	CAS-RN	DTXSID6049800	Thorium	-	-	-	Y

List of Chemicals



	nited States vironmental Protection jency	Home Advanced Search Batch S	Search Lists 🗸	Predictions	s Downloads	Share - Q. Search all data	
			Lists of C List of As	says	Select List		
	Show 10 Tentries	4				Download Search:	
	List Acronym	List Name	🔶 🛛 Last Up	dated 🔶	Number of Chemicals	List Description	
	40CFR355	40CFR355	2018-01-0	5	354	Extremely Hazardous Substance List and Threshold Planning Quantities; Emergency Planning and Release Notification Requirements; Final Rule. (52 FR 13378)	
	AEGLVALUES	Acute exposure guideline levels	2018-04-2	0	174	Acute exposure guideline levels (AEGLs) describe the human health effects from once-in-a- lifetime, or rare, exposure to airborne chemicals.	
	ALGALTOX	Algal Toxins	2017-11-2	1	54	A set of algal toxins of interest	
	APCRA_PRO	APCRA Chemicals for Prospective Analysi	is 2018-02-1	4	204	The APCRA prospective case study list of approximately 200 chemicals as of January 2018, developed by ECHA in consultation with EPA and other partners	
	APCRA_RETRO	APCRA Chemicals for Retrospective Analy	ysis 2018-02-1	4	380	The APCRA retrospective case study list of 380 chemicals that have ToxCast/Tox21 data, httk, and point-of-departure values that meet case study criteria in ToxVaIDB.	
	APCRAAPPLIST	APCRA Chemicals for Retrospective Analysis_App_List_448_Chemicals	2018-05-2	3	447	The APCRA retrospective case study list of 380 chemicals that have ToxCast/Tox21 data, httk, and point-of-departure values that meet case study criteria in ToxVaIDB. This is the EDITABLE app list	
	ARCHEMICALS	Androgen Receptor Chemicals	2018-05-0	1	110	The list of chemicals used to identify references with in vitro AR binding . From Kleinstreuer et al http://pubs.acs.org/doi/abs/10.1021/acs.chemrestox.6b00347	
	ATHENSSUS	University of Athens Surfactant and Suspe List	ect 2017-07-1	4	60	ATHENSSUS is a compilation of suspects, predicted transformation products and surfactants screened in wastewater by University of Athens, as described in Gago-Ferrero et al 2015, DOI: 10.1021/acs.est.5b03454	
comptox-prod.epa.gov/da	ashboard/chemical_lists	ical	2017-03-1	1	200	The Agency for Toxic Substances and Disease Registry (ATSDR)is a federal public health	•

Real-Time Predictions





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PEPA United States Environmental Protection Agency

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Property	Experimental Value	Consensus	Hierarchical clustering	Single model	Group contribution	Nearest neighbor
96 hour fathead minnow LC50		6.051 -Log10(mol/L) 0.278 mg/L	5.678 -Log10(mol/L) 0.656 mg/L	5.572 -Log10(mol/L) 0.836 mg/L	5.908 -Log10(mol/L) 0.386 mg/L	7.047 -Log10(mol/L) 0.028 mg/L
48 hour D. magna LC50		5.591 -Log10(mol/L) 0.802 mg/L	5.548 -Log10(mol/L) 0.884 mg/L	6.169 -Log10(mol/L) 0.212 mg/L	5.518 -Log10(mol/L) 0.948 mg/L	5.128 -Log10(mol/L) 2.329 mg/L
48 hour T. pyriformis IGC50		5.590 -Log10(mol/L) 0.804 mg/L	6.390 -Log10(mol/L) 0.127 mg/L		5.588 -Log10(mol/L) 0.806 mg/L	4.790 -Log10(mol/L) 5.068 mg/L
Oral rat LD50		2.400 -Log10(mol/kg) 1243.951 mg/kg	2.232 -Log10(mol/kg) 1829.942 mg/kg			2.568 -Log10(mol/kg) 845.609 mg/kg
Bioaccumulation factor		3.066 Log10 1164.438	3.090 Log10 1230.849	2.717 Log10 521.420	3.257 Log10 1806.262	3.200 Log10 1585.959
Developmental toxicity		true	true	true		true
Ames mutagenicity		false	false			false
Estrogen Receptor RBA		-0.710 Log10 0.195	-1.692 Log10 0.020	-1.515 Log10 0.031		1.077 Log10 11.931
Estrogen Receptor Binding		false	false	false		true
Normal boiling point		345.2 °C	306.6 °C		408.2 °C	320.7 °C
Melting point		74.3 °C	63.8 °C		41.0 °C	118.2 °C
Flash point		161.7 °C	143.5 °C		152.7 °C	188.9 °C
Vapor pressure		-5.955 Log10(mmHg) 1.109*10^-6 mmHg	-5.534 Log10(mmHg) 2.925*10^-6 mmHg		-5.903 Log10(mmHg) 1.249*10^-6 mmHg	-6.428 Log10(mmHg) 3.735*10^-7 mmHg
Density		0.959 g/cm³	0.977 g/cm ³		0.843 g/cm ³	1.057 g/cm ³

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Real-Time Predictions



Predicted Fathead minnow LC50 (96 hr) for O(C1=CC=C(C=C1C)C(C2=CC=C(OC)C(CC)C(CC)C)C)C)C from Consensus method

Prediction results					
Endpoint	Experimental value	Predicted value			
Fathead minnow LC ₅₀ (96 hr) -Log10(mol/L)	N/A	6.05			
Fathead minnow LC ₅₀ (96 hr) mg/L	N/A	0.28			



	CAS	Structure	Similarity Coefficient	Experimental value -Log10(mol/L)	Predicted value -Log10(mol/L)
Predictions for the test chemical and for the most similar chemicals in the external test set	O(C1=CC=C(C=C1C)C(C2=CC=C(OC)C(=C2)C(C)C)(C)C)C (test chemical)	AA.		N/A	6.05
If the predicted value matches the experimental values for similar chemicals in the test set (and the similar chemicals were predicted value prediction results (colors defined in table below)	<u>61096-84-2</u>	~	0.74	4.95	4.97
0 MAE = 0.50 0 0 7/3 0 0 0 7/3 0 0 0	<u>23184-66-9</u>		0.73	5.65	5.17
4 6.5 6.5 6.0 5.5 0 5.0 0 7 0 8 0.55 9 0 8 0.50 *Mean absolute error in -Log10(mol/L)	39515-41-8	X	0.72	8.17	7.32
9 4.3 0<	<u>55792-61-5</u>		0.71	5.77	4.92
	<u>1929-73-3</u>	al	0.71	5.05	5.19
	<u>52645-53-1</u>	aant	0.70	7.21	7.67
	<u>596-85-0</u>		0.70	6.38	5.47

Not just chemical "structures"



 Chemicals in commerce, of interest to the EPA, are not all easily represented by structures

- Different chemical substances supported
 - "UVCB chemicals" Unknown or Variable Composition, Complex Reaction Products and Biological Materials
 - Homologous series as Markush Structures

Markush Structures









- Our data are licensed as public domain data
 - available from downloads page
 - registered to Figshare
 - SQL data dumps
- Collection of web services for old dashboards are available – API is being fully revamped

In Progress: Structure, Substructure and Similarity Searching





In Progress : pKa Prediction Model

 pKa prediction models based on Open
 Data Set of 8000 chemicals – acidic, basic and amphoteric chemicals



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Agency



https://comptox.epa.gov/dashboard/web-test/WS?smiles=CCO&method=hc

JSON Raw Data Head	ers
Save Copy	
uuid:	"55547f4f-f966-48e8-b831-a0d217998064"
predictionTime:	1520539090089
software:	"T.E.S.T (Toxicity Estimation Software Tool)"
softwareVersion:	"5.01"
condition:	"25°C"
endpoint:	"Water solubility at 25°C"
method:	"Hierarchical clustering"
<pre>▼ predictions:</pre>	
▼0:	
id:	"C_1520539090089"
smiles:	"OCC"
expValMolarLog:	"-1.337"
expValMass:	"1001180.703"
predValMolarLog:	"-1.338"
predValMass:	"1002625.241"
molarLogUnits:	"-Log10(mol/L)"
massUnits:	"mg/L"

Conclusion



- Transparent access to data supporting computational toxicology
- CompTox Chemicals Dashboard provides access to data for ~875,000 chemicals
- Ongoing expansion of functionality to serve all data streams for NCCT
- Generalized Read-Across module is an intuitive, integrated dashboard module. Showing great promise and clear development path ahead

Acknowledgements





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