Supporting Chemical Evaluations Using Transparent and Accessible Data

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The views expressed in this presentation are those of the authors and do not necessarily reflect the views or policies of the US EPA

Conflict of Interest Statement

The author declares no conflict of interest.

Abbreviations

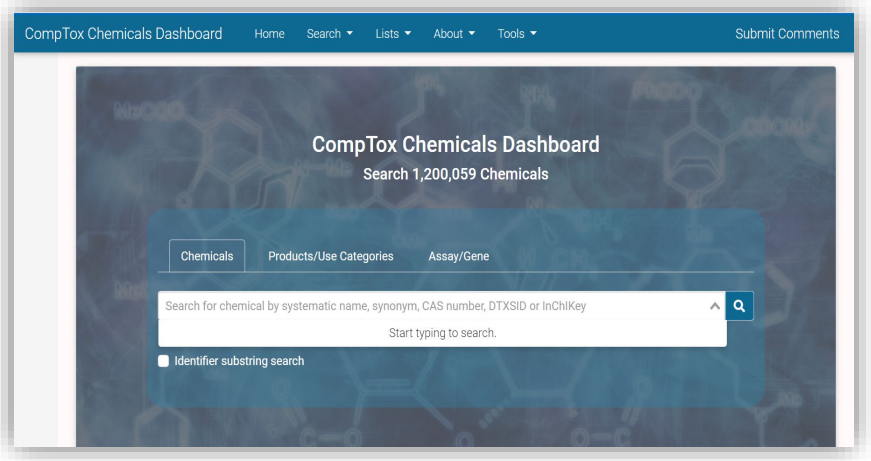
- **AED**: Administered Equivalent Dose
- **BPA**: bisphenol A
- **CCD**: CompTox Chemicals Dashboard
- **CHR**: chronic study type
- **EPA**: US Environmental Protection Agency
- **ER**: estrogen receptor
- **GenRA**: Generalized Read Across (web application)
- **GHS**: Globally Harmonized System of Classification and Labeling of Chemicals
- **HTTK:** High throughput toxicokinetics
- **IRIS**: EPA's Integrated Risk Information System
- **IVIVE:** in vitro to in vivo extrapolation
- **LOAEL**: Lowest Observed Adverse Effect Level
- **MGR**: multigeneration reproduction study type
- **POD**: Point of departure
- **QMRF:** QSAR Model Reporting Format
- **RfD**: Reference Dose
- **SUB:** Subchronic study type
- **ToxCast:** US EPA's Toxicity Forecaster program
- **webTEST**: Toxicity Estimation Software (web application)

Agenda

- CompTox Chemicals Dashboard
  - Vision
  - Case Study
    - Bisphenol A & B
    - Navigation and Orientation
    - webTEST & GenRA
- Wrap up

Easy access to data improves efficiency and ultimately accelerates chemical risk assessment

CompTox Chemicals Dashboard

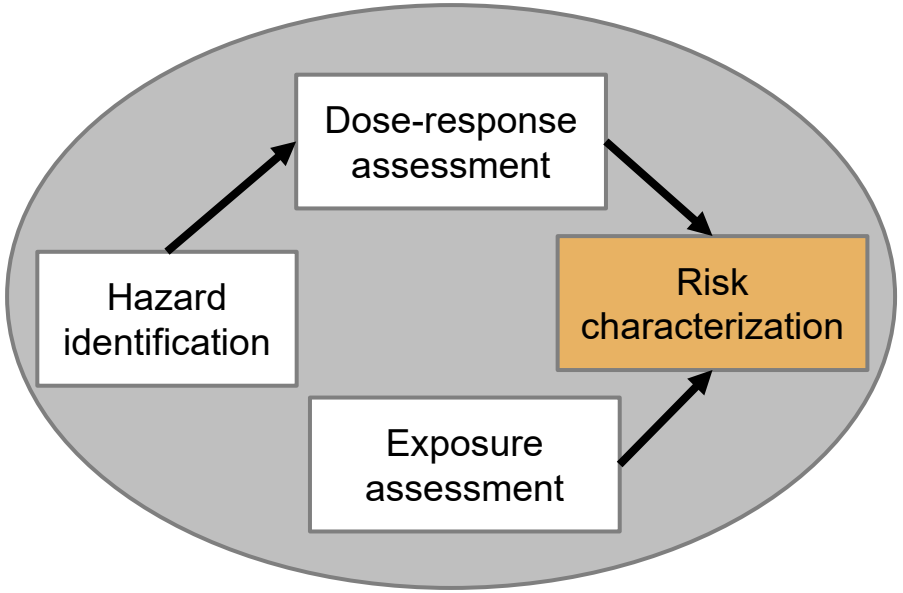


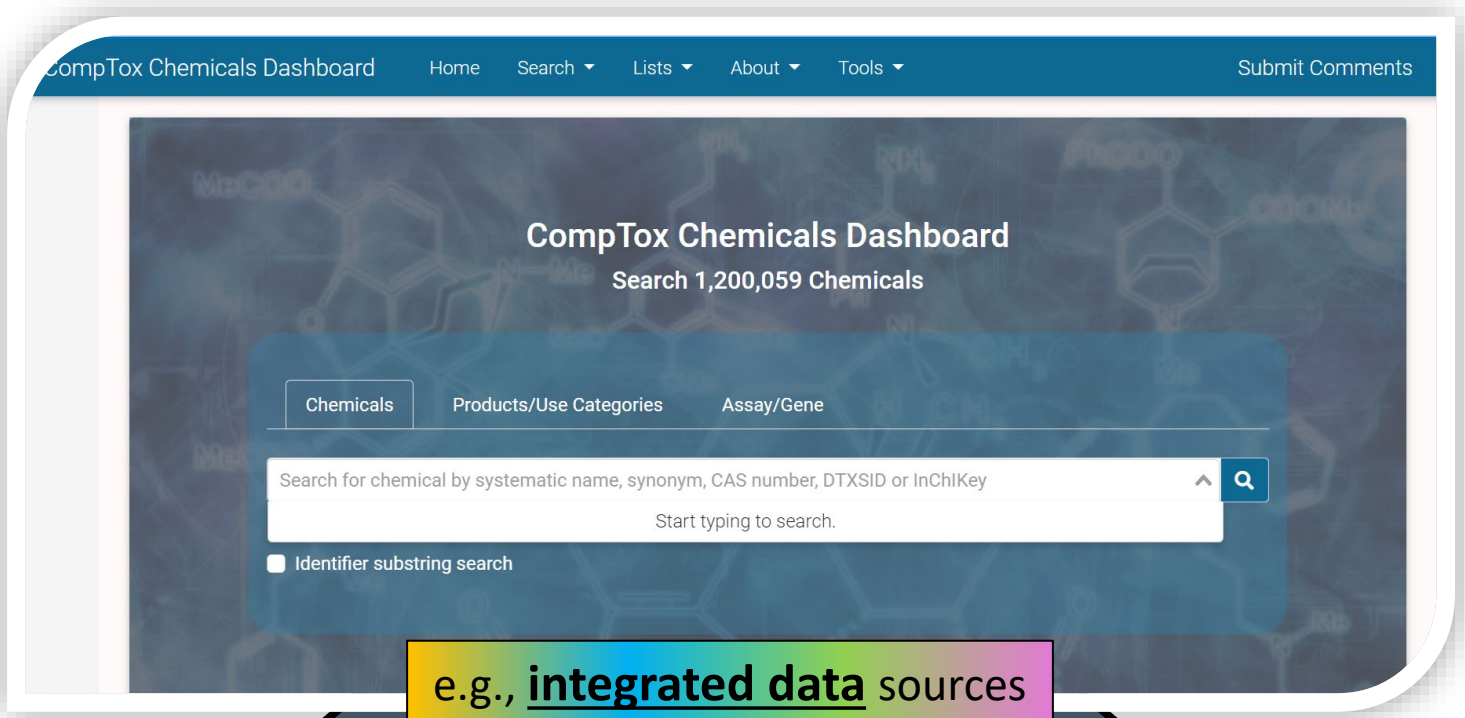
https://comptox.epa.gov/dashboard/

- **Centralized location** for publicly available chemical toxicity data
- Combination of existing legacy, and high throughput and predictive model data
- Publicly accessible, periodically updated, curated
- Supports EPA and partner decision making
  - e.g., Well-studied chemicals: data can be found in most areas
  - e.g., Data-poor substances: limited data, but may find in vitro and/or modeled data, similar compounds, and literature search information

Dashboard Data Contents

- **Chemistry**: Chemical characterization
- **Hazard/Bioactivity**: safety classifications, human health & ecological data, *in vivo* animal data, biological targets (effect), dose-response characterization (dose)
- **Exposure/Toxicokinetics**: measured and predicted





e.g., **integrated data** sources

Chemistry

DSSTox

Toxicity Estimation Software Tool (TEST)

EPISuite

ECOTOX Knowledgebase

ToxValDB

30+ worldwide sources: e.g., ATSDR, IRIS, HESS, ECHA, EFSA, DOD, Health Canada

OPERA

Percepta/ACD Labs

Exposure

NHANES

Chemical and Products Database (CPDat)

Chemical and Products Categories (CPCat)

Chemical Data Reporting (CDR)

High Throughput Toxicokinetics (HTTK)

Hazard

ToxRefDB

Bioactivity

invitroDB

SeqAPASS

AOP wiki

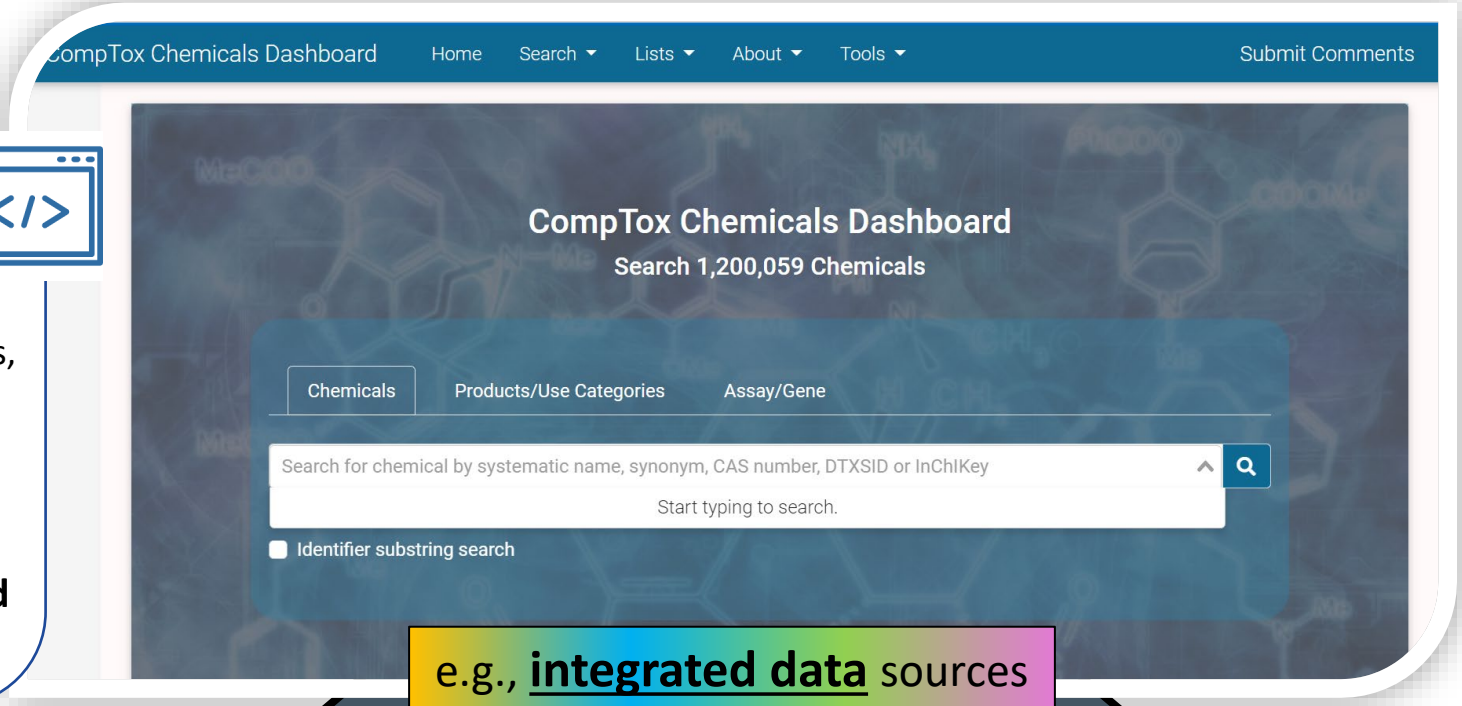
ToxCast

High Throughput Transcriptomics (HTTr)

High Throughput Phenotypic Profiling (HTPP)

e.g., **embedded iframes**

- **EPA's Toxics Release Inventory**
- **Google Scholar**
- **PubChem links** (e.g., Articles, Patents, Bioassays, GHS Classification)
- **Integrated Risk Information System (IRIS)**
- **Provisional Peer-Reviewed Toxicity Value (PPRTV)**



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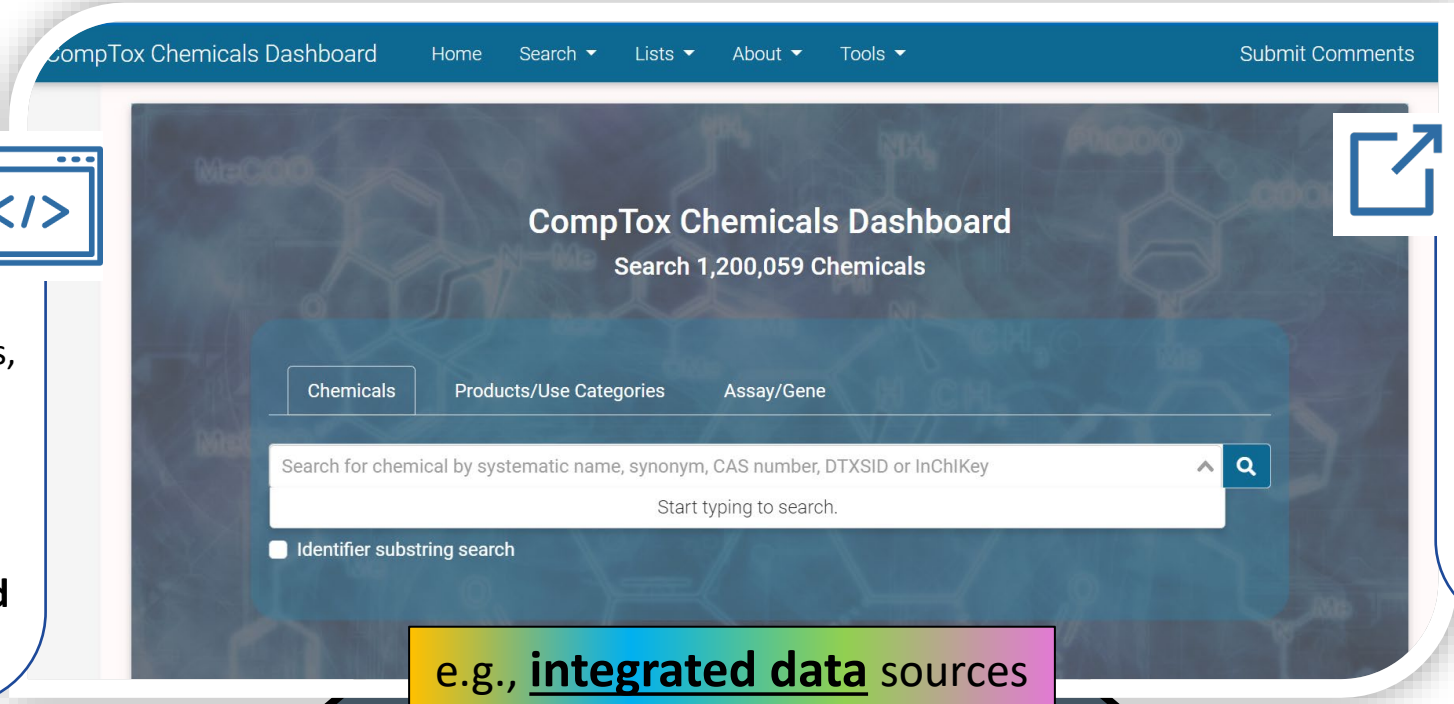

e.g., **linked** sources

- **General**
  - ECHA, MSDS, NIOSH, NIST, Wiki
- **Toxicology**
  - CalEPA, CTD, ECOTOX, AOP Wiki
- **Publications**
  - Google, IRIS, PubMed, Regulations.gov
- **Analytical**
  - MONA, NIST, PDB, Tox21 QC
- **Prediction**
  - NMDB, NMRShiftDB, LSERD

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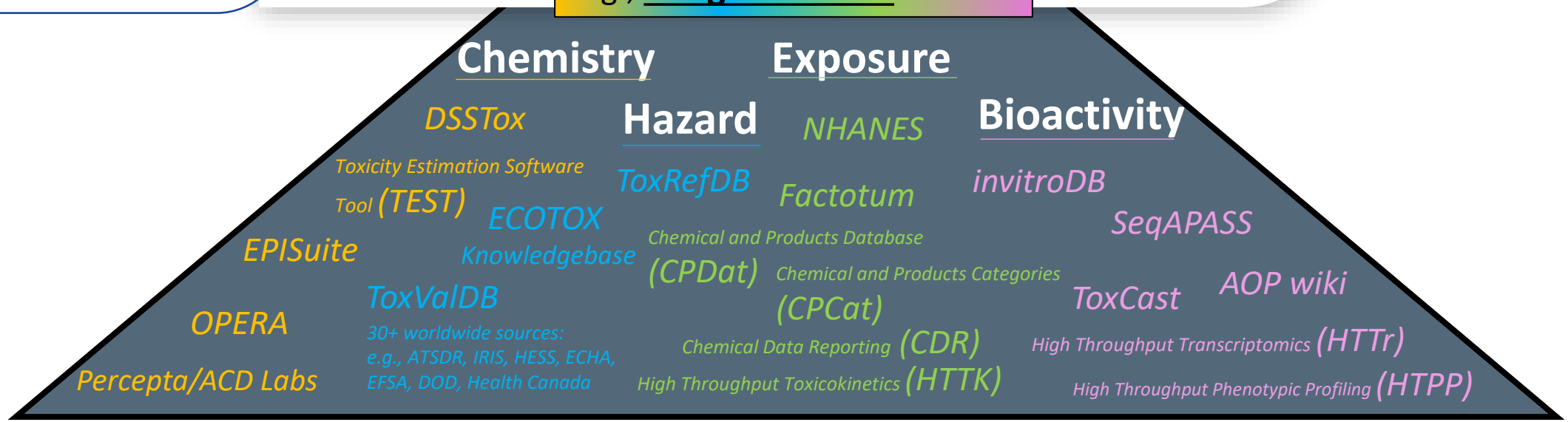

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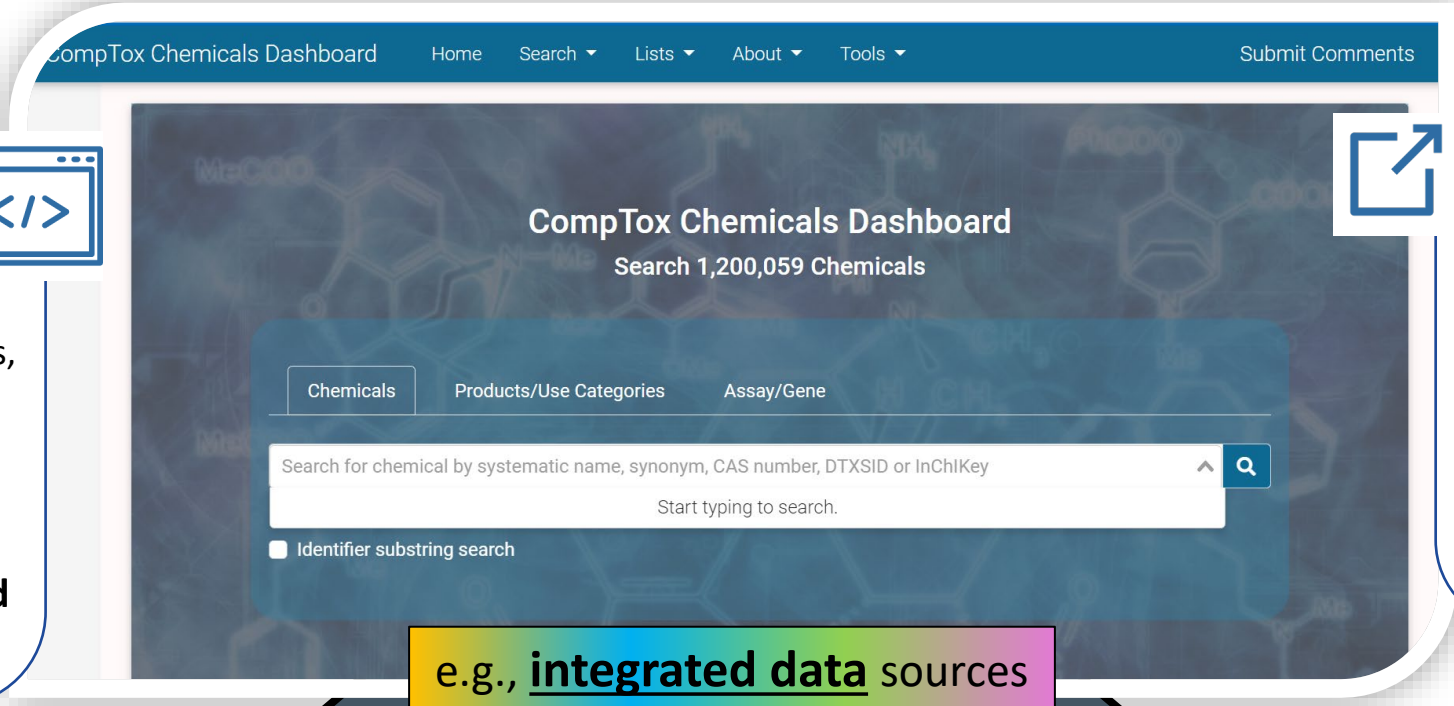

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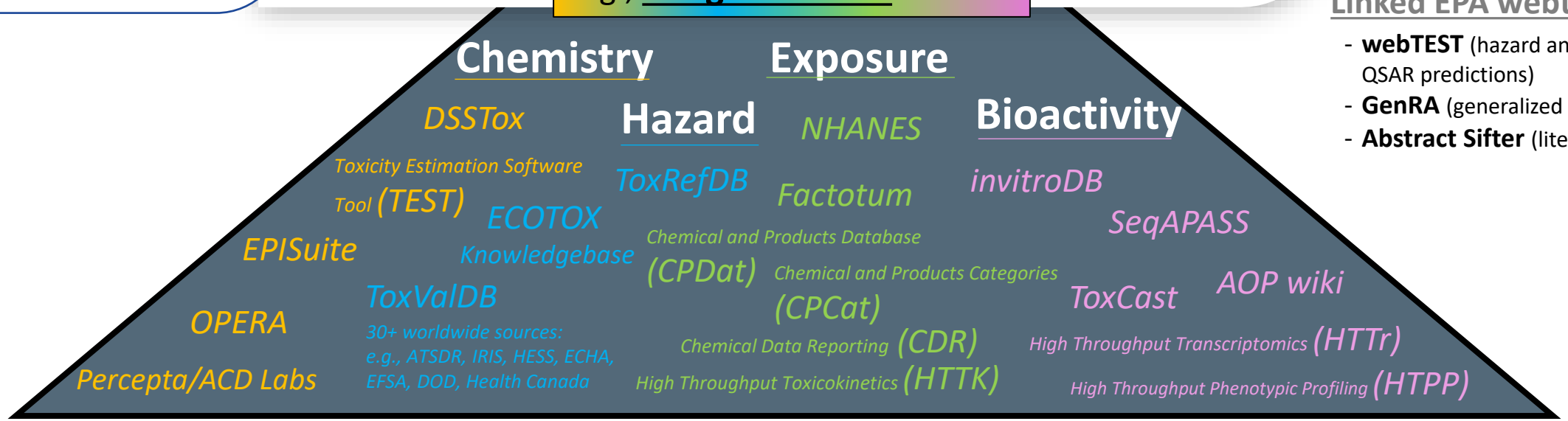


Linked EPA webtools

- **webTEST** (hazard and physchem QSAR predictions)
- **GenRA** (generalized read-across)
- **Abstract Sifter** (literature search)

Team Approach

EPA/ORD/Center for Computational Toxicology and Exposure

Efforts include many more than who are shown here

Many external collaborators provided data & links

Exploration Case Study

- Bisphenol A: A well-studied chemical
  - Chemistry: physchem properties
  - Hazard: quantitative risk assessment values, IRIS, in vivo data
  - Bioactivity: high throughput screening data
  - Exposure: Biomonitoring data

- Bisphenol B: A limited-studied chemical
  - Chemistry: physchem properties
  - Hazard: webTEST (predictions) & GenRA (data gap-filling using)
  - Bioactivity: high throughput screening data
  - Exposure: predictions

Live Demo

Navigation and Capabilities

Backup

Navigation & Capabilities

Basic Search

- Chemical
- Product/Use Category
- Assay/Gene

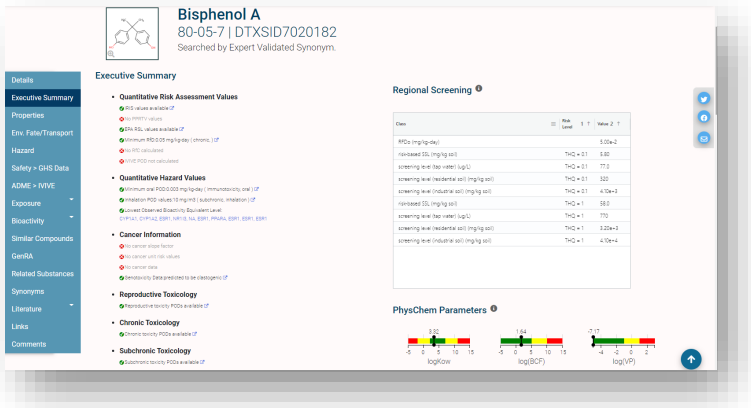
Advanced Search

- Mass
- Molecular Formula
- Both

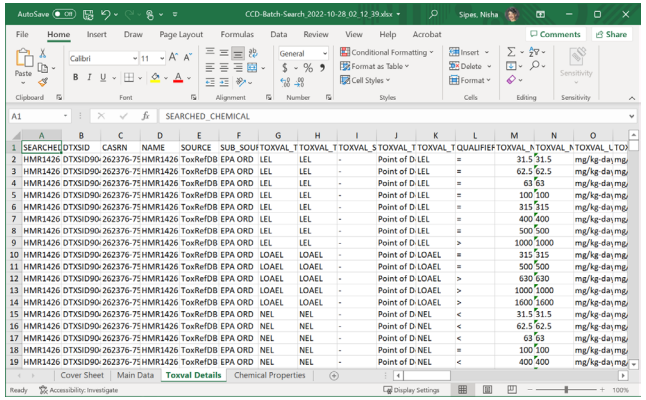
Batch Search

- Several incl. chemical lists
- User defined

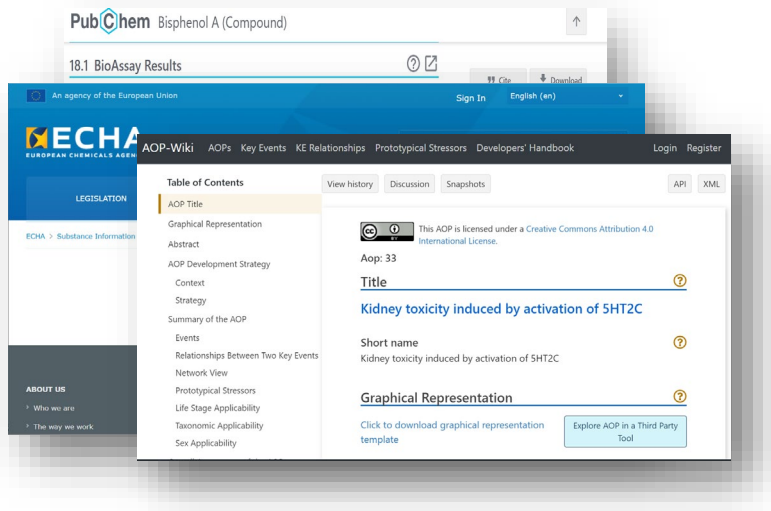
In Application Viewing



Data Download

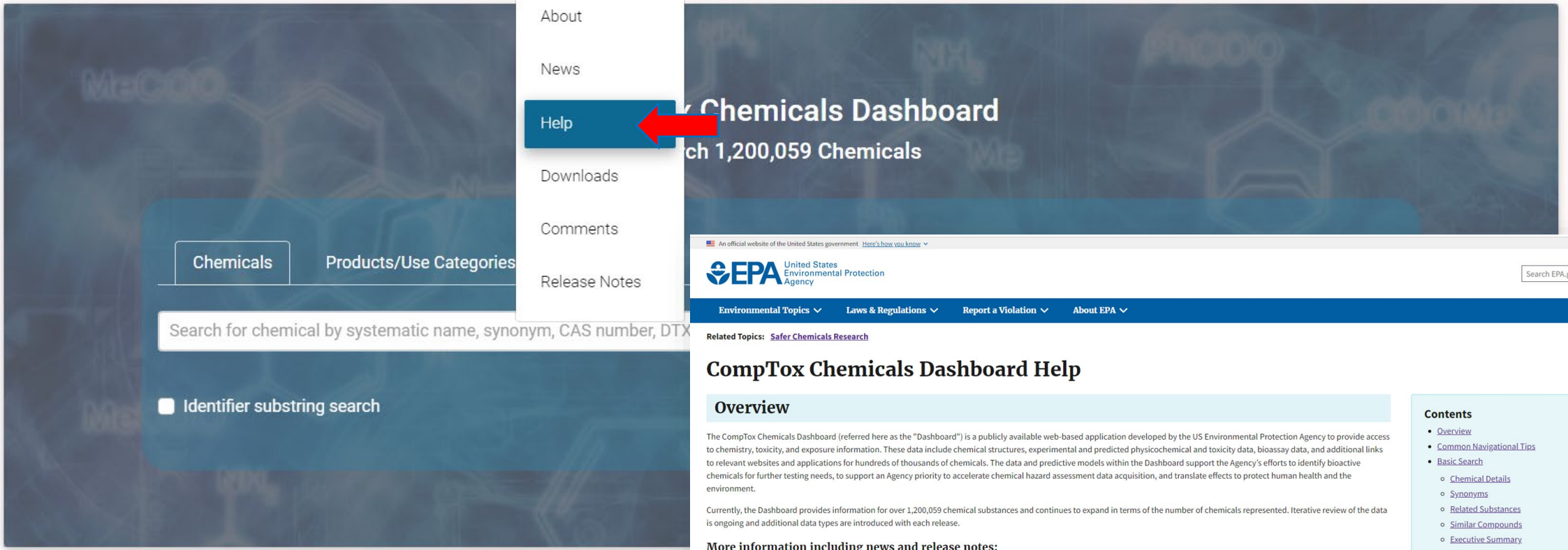


Links (embedded & links out)



Backup

CCD Help Page

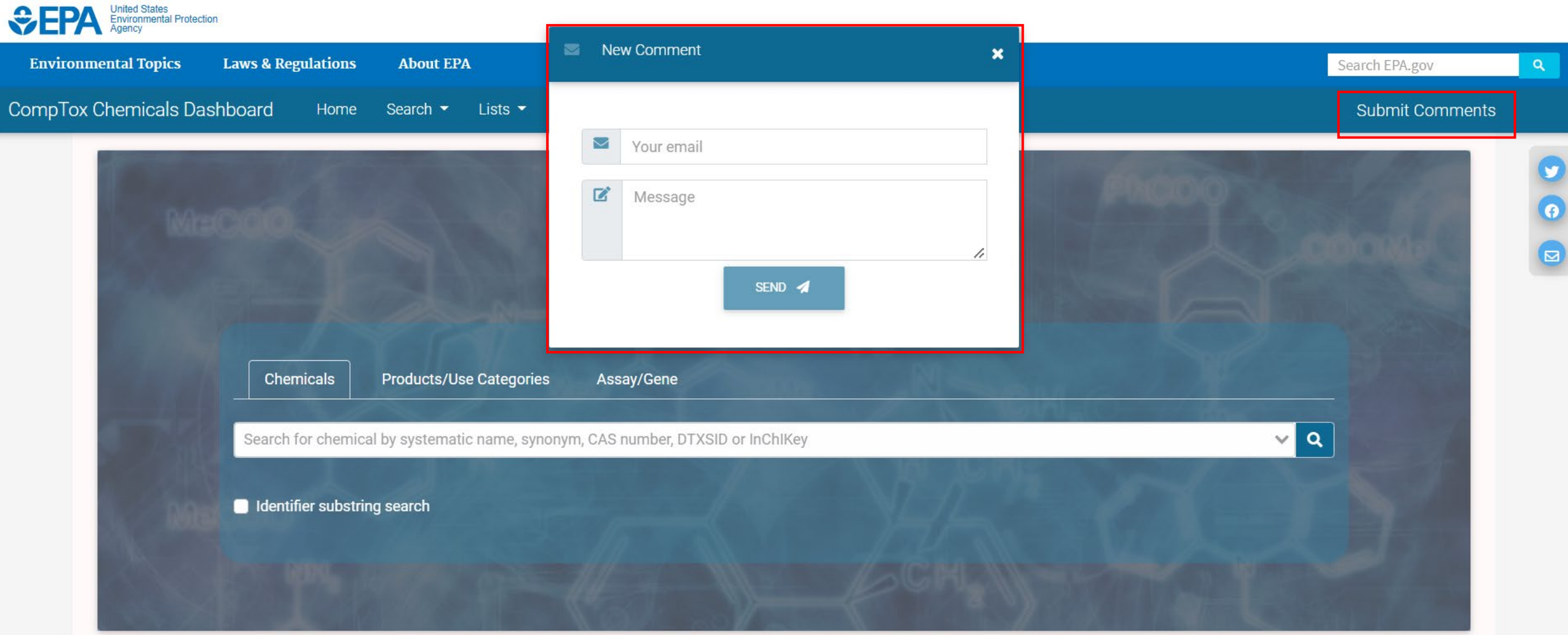


https://www.epa.gov/chemical-research/comptox-chemicals-dashboard-help

Backup

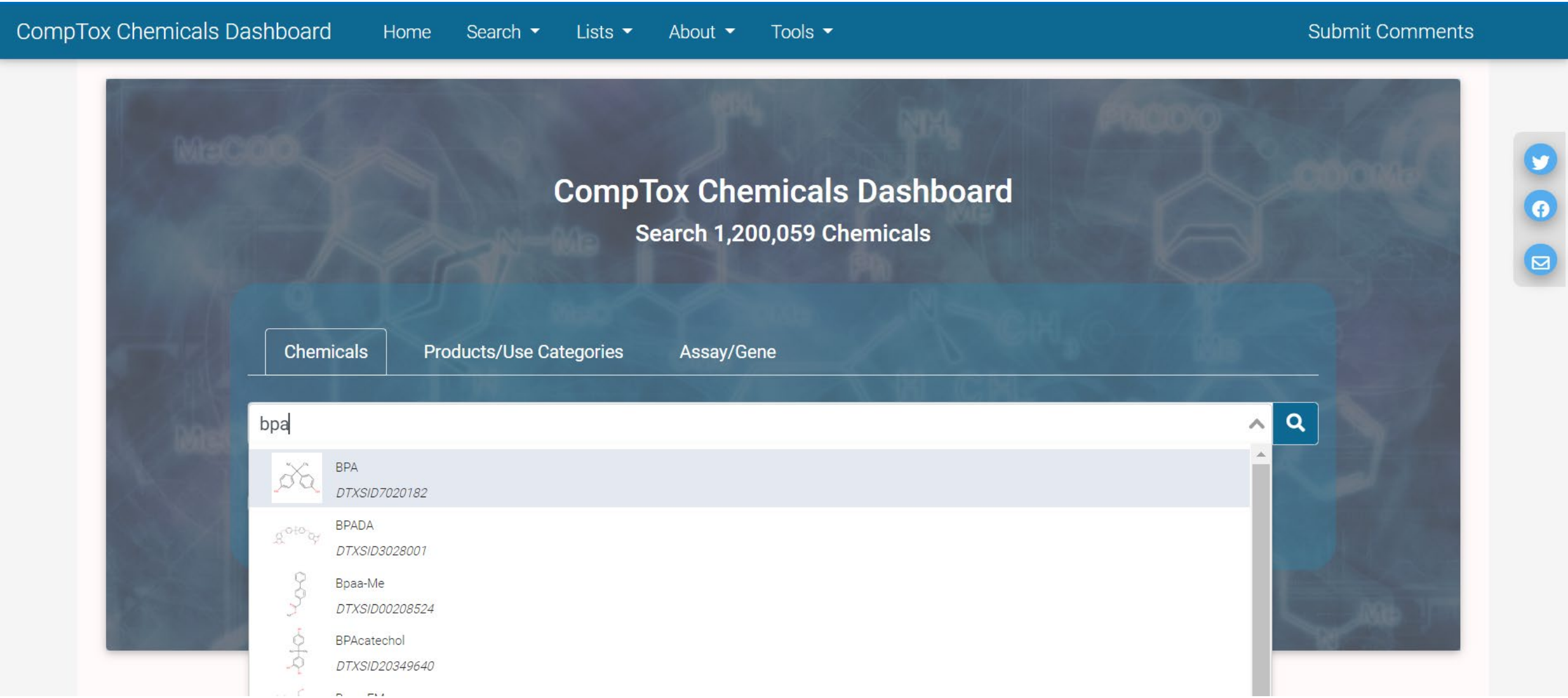
Submit Comments

-to ask a question, report bugs, or submit feedback



Basic Chemical Search on BPA

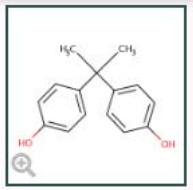
Backup



Backup

Navigation Tabs

CompTox Chemicals Dashboard | Home | Search | Lists | About | Tools | Submit Comments | Search all data



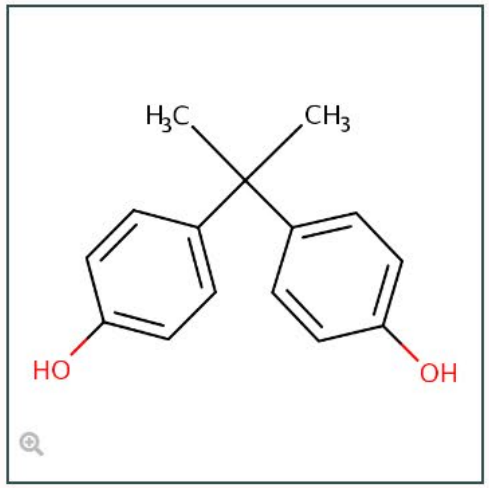
Bisphenol A

80-05-7 | DTXSID7020182

Searched by Expert Validated Synonym.

- Chemical Details
- Executive Summary
- Physchem Prop.
- Env. Fate/Transport
- Hazard
- Safety > GHS Data
- ADME > IVIVE
- Exposure
- Bioactivity
- GenRA
- Literature
- Links
- Comments

Chemical Details



Wikipedia

Bisphenol A (**BPA**) is a chemical compound primarily used in the manufacturing of various plastics. It is a colourless solid which is soluble in most common organic solvents, but has very poor solubility in water. BPA is produced on an industrial scale by the condensation of phenol and acetone, and has a global production scale which is expected to reach 10 million tonnes in 2022.

BPA's largest single application is as a co-monomer in the

Read more

Quality Control Notes

Intrinsic Properties

Molecular Formula: $C_{15}H_{16}O_2$ | MOL FILE | FIND ALL CHEMICALS

Average Mass: 228.291 g/mol | ISOTOPE MASS DISTRIBUTION

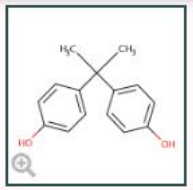
Monoisotopic Mass: 228.11503 g/mol

Structural Identifiers

Backup

Chemical Landing Page

CompTox Chemicals Dashboard | Home | Search | Lists | About | Tools | Submit Comments | Search all data



Bisphenol A

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Searched by Expert Validated Synonym.

- Chemical Details
  - Details
  - Synonyms
  - Related Substances
  - Similar Compounds
- Hazard
- Safety > GHS Data
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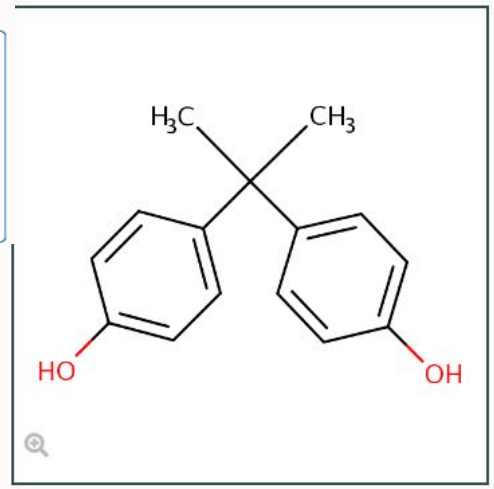
Chemical Details



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Structural Identifiers

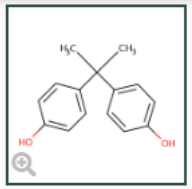
Backup

Executive Summary Tab

Overview of data

- Quantitative toxicity values
- ADME
- Exposure
- Adverse Outcome Pathway (AOP) links
- Physchem & fate & transport
- Plots: hazard Point-of-Departure (POD) oral/inhalation and in vitro bioactivity summary

CompTox Chemicals Dashboard | Home | Search | Lists | About | Tools | Submit



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Executive Summary

- **Quantitative Risk Assessment Values**
  - IRIS values available
  - No PPRTV values
  - EPA RSL values available
  - Minimum RfD:0.05 mg/kg-day (chronic,)
  - No RfC calculated
  - IVIVE POD not calculated
- **Quantitative Hazard Values**
  - Minimum oral POD:0.003 mg/kg-day (immunotoxicity, oral)
  - Inhalation POD values:10 mg/m3 (repeat dose, inhalation)
  - Lowest Observed Bioactivity Equivalent Level: CYP1A1, CYP1A2, ESR1, NR1I3, NA, ESR1, PPARA, ESR1, ESR1, ESR1
- **Cancer Information**
  - No cancer slope factor
  - No cancer unit risk values
  - No cancer data
  - Genotoxicity Data:predicted to be clastogenic
- **Reproductive Toxicology**
  - Reproductive toxicity PODs available

Regional Screening

Class		
RFDo (mg/kg-day)		
risk-based SSL (mg/kg soil)	THQ = 0.1	5.80
screening level (tap water) (ug/L)	THQ = 0.1	77.0
screening level (residential soil) (mg/kg soil)	THQ = 0.1	320
screening level (industrial soil) (mg/kg soil)	THQ = 0.1	4.10e+3
risk-based SSL (mg/kg soil)	THQ = 1	58.0
screening level (tap water) (ug/L)	THQ = 1	770
screening level (residential soil) (mg/kg soil)	THQ = 1	3.20e+3
screening level (industrial soil) (mg/kg soil)	THQ = 1	4.10e+4

PhysChem Parameters

Backup

PhysChem Properties Tab

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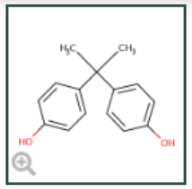

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Searc

Can click to see more information. E.g., OPERA predictions have metadata including QMRF

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Properties: Summary

Summary | Search Chemical Properties

EXPORT

Summary

Property	Experimental average	Predicted average	Experimental median	Predicted median	Experimental range	Predicted range
Polarizability	-	27.0 (1)	-	27.0	-	27.0
Henry's Law	-	1.25e-7 (1)	-	1.25e-7	-	1.25e-7
Boiling Point	200 (1)	367 (4)	200	362	200	343 to 401
Flash Point	-	190 (2)	-	190	-	188 to 192
Melting Point	155 (7)	136 (3)	156	132	153 to 156	125 to 153
Molar Refractivity	-	68.2 (1)	-	68.2	-	68.2
Molar Volume	-	200 (1)	-	200	-	200
Viscosity	-	9.66 (1)	-	9.66	-	9.66
Surface Tension	-	46.0 (1)	-	46.0	-	46.0
Density	-	1.17 (2)	-	1.17	-	1.14 to 1.20
Vapor Pressure	-	1.07e-6 (3)	-	5.34e-7	-	6.78e-8 to 2.59e-6
Water Solubility	8.55e-4 (3)	1.69 (4)	5.26e-4	1.00e-3	5.25e-4 to 1.51e-3	7.45e-4 to 6.76
Thermal Conductivity	-	150 (1)	-	150	-	150

- Polarizability
- Henry's Law
- Boiling Point
- Flash Point
- Melting Point
- Molar Refractivity
- Molar Volume
- Viscosity
- Surface Tension
- Density
- Vapor Pressure
- Water Solubility
- Thermal Conductivity
- Index of Refraction
- LogKoa: Octanol-Air
- LogKow:Octanol-Water

Ability to look at parameter-specific tables

Backup

Environmental Fate/Transport Tab

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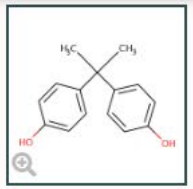

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Env. Fate/Transport: Summary

Summary | Search Fate/Transport

EXPORT

Summary

Property	Experimental average	Predicted average	Experimental median	Predicted median	Experimental range	Predicted r	
Atmos. Hydroxylation Rate		1.64e-11 (1)		1.64e-11	-	1.64e-11	
Biodeg. Half-Life		15.1 (1)		15.1	-	15.1	
Fish Biotrans. Half-Life (Km)	1.86 (1)	1.86 (1)	1.86	1.86	1.86	1.86	
Soil Adsorp. Coeff (Koc)		1.34e+3 (2)		1.34e+3	-	1.24e+3 to 1.44e+3	L/kg
Bioaccumulation Factor		173 (1)		173	-	173	
Bioconcentration Factor	54.7 (13)	101 (4)	23.5	94.6	1.70 to 250	43.7 to 173	

- Atoms. Hydroxylation Rate
- Biodeg. Half-Life (Km)
- Soil Adsorp. Coeff (Koc)
- Bioaccumulation Factor
- Bioconcentration Factor

Ability to look at parameter-specific tables

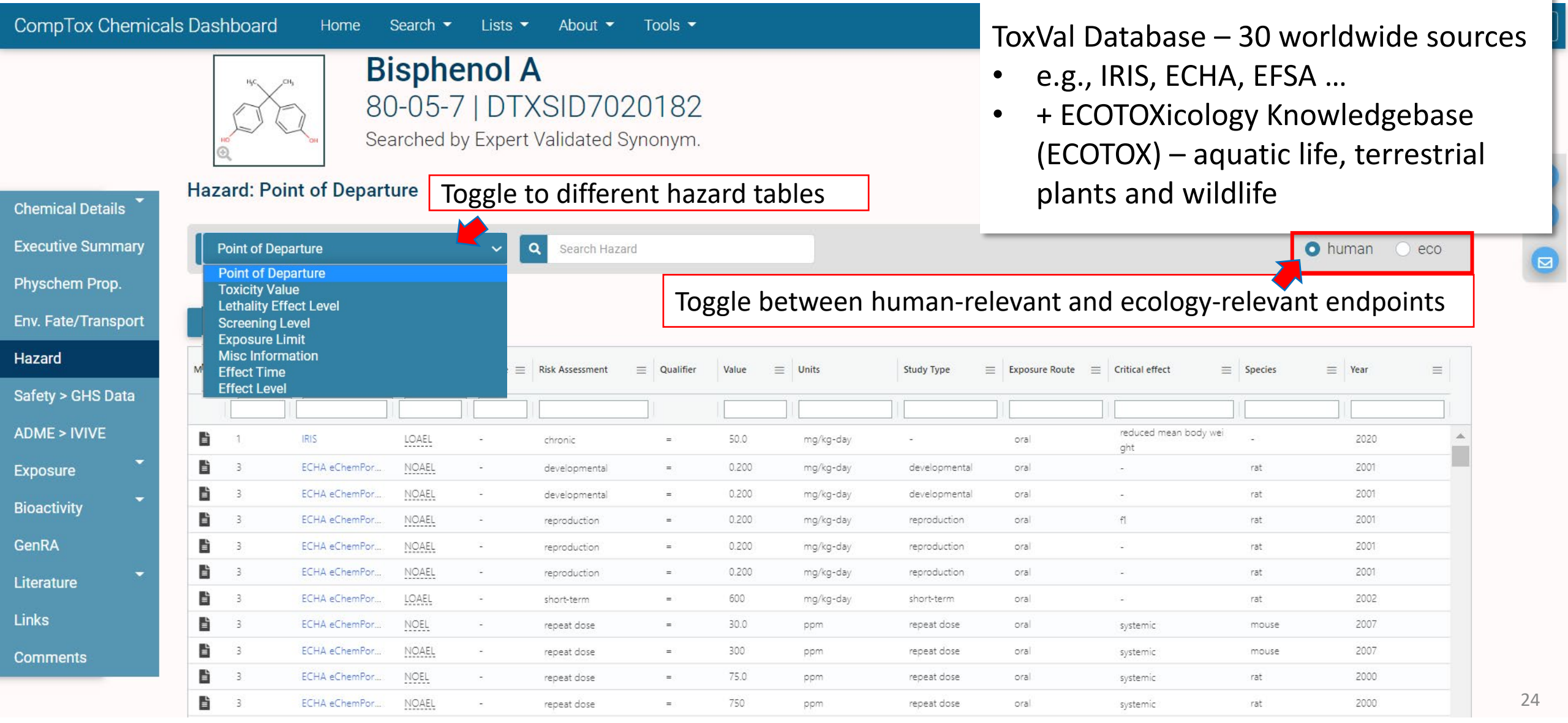
Backup

Hazard Tab

Traditional animal studies toward human toxicity & ecotoxicology

ToxVal Database – 30 worldwide sources

- e.g., IRIS, ECHA, EFSA …
- + ECOTOXicology Knowledgebase (ECOTOX) – aquatic life, terrestrial plants and wildlife



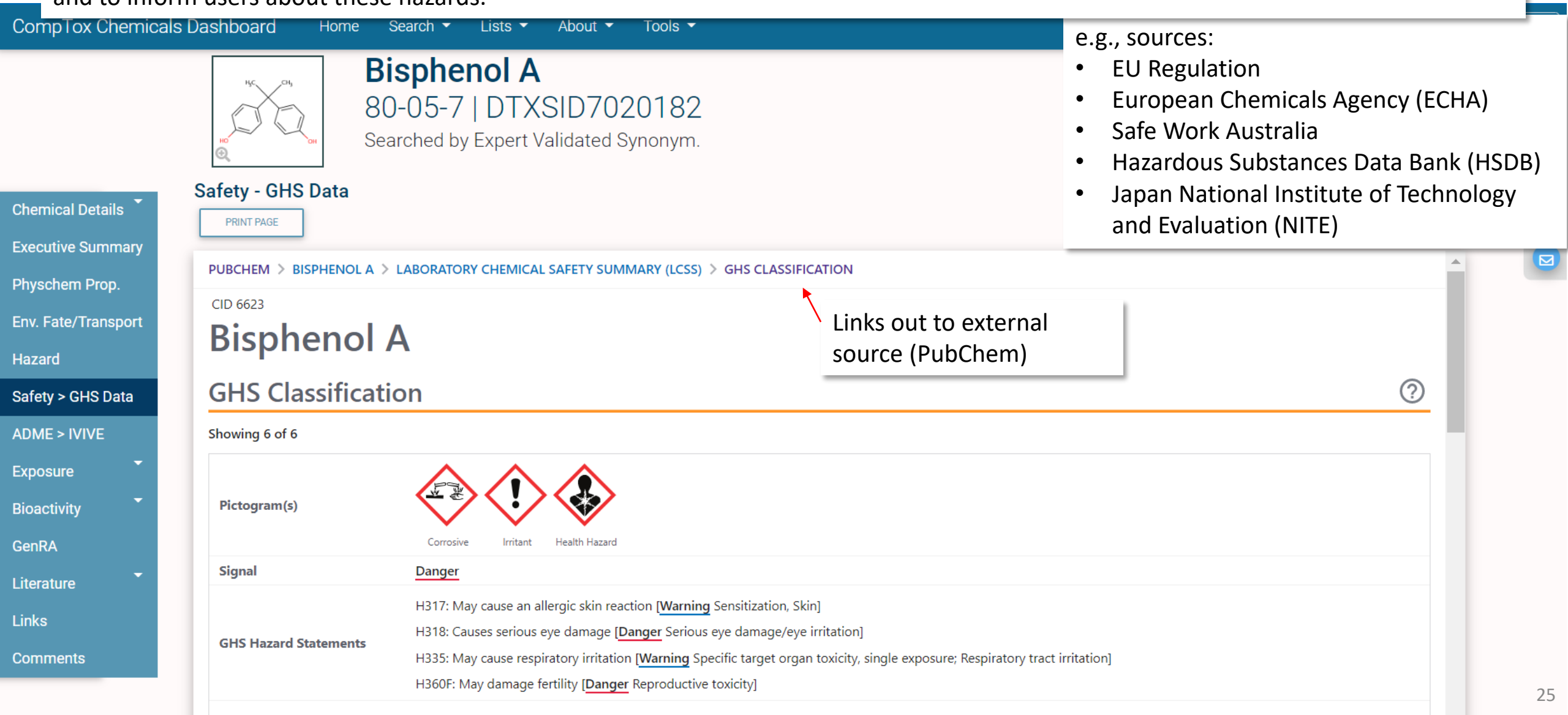
Backup

Safety > GHS tab

GHS (Globally Harmonized System of Classification and Labelling of Chemicals) is a United Nations system to identify hazardous chemicals and to inform users about these hazards.

e.g., sources:

- EU Regulation
- European Chemicals Agency (ECHA)
- Safe Work Australia
- Hazardous Substances Data Bank (HSDB)
- Japan National Institute of Technology and Evaluation (NITE)



Links out to external source (PubChem)

Backup

ADME > IVIVE Tab

ADME – Absorption, Distribution, Metabolism, Excretion
IVIVE – in vitro to in vivo extrapolation

Relevant data related to high throughput toxicokinetics

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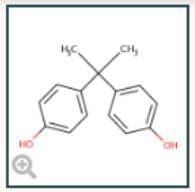

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ADME - IVIVE

Search ADME IVIVE

EXPORT

IVIVE

Label	Species	Measured	Predicted	Units	Model	Percentile	Reference	Data Source Species
	(1) Human				(3) 1compartment,3cor	(2) NA,95%		
Intrinsic Hepatic Clearance	Human	19.90	NA	uL/min/million hepatocytes	NA	NA	Wambaugh 2019	Human
Fraction Unbound in Plasma	Human	0.04	NA		NA	NA	Wambaugh 2019	Human
Volume of Distribution	Human	NA	6.34	L/kg	1compartment	NA	NA	Human
PK Half Life	Human	NA	28.28	hours	1compartment	NA	NA	Human
Steady-State Plasma Concentra	Human	NA	2.35	mg/L	3compartmentss	95%	NA	Human

Backup

Exposure Tabs

Reported and measured data - come from public sources (e.g., MSDS sheets, EPA's Toxics Release Inventory, National Health, Nutrition Examination Survey (NHANES) biomonitoring data, EPA's Chemical Data Reporting (CDR) Rule - issued under the Toxic Substances Control Act (TSCA))

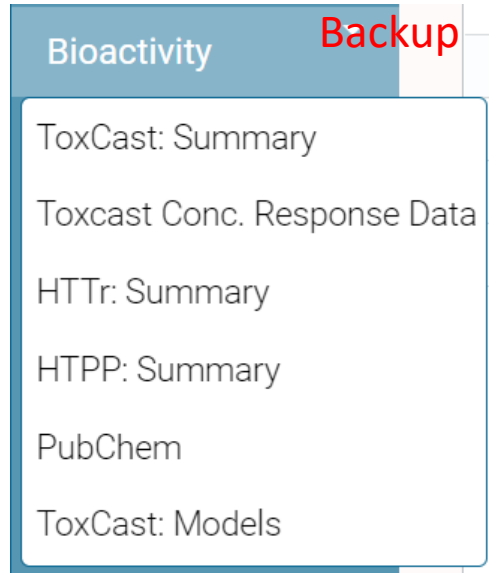
Predicted data – for predicted probability of functional use and exposure predictions - use various inputs, including physchem and env./fate transport data

Databases are developed for public consumption. E.g.,

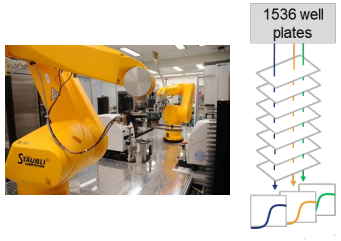
- EPA's Chemical and Products Database (CPDat)
- EPA's Chemical/Product Categories Database (CPCat)

Bioactivity Tabs (in vitro)

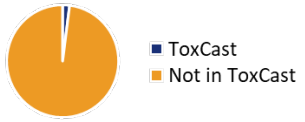
Backup



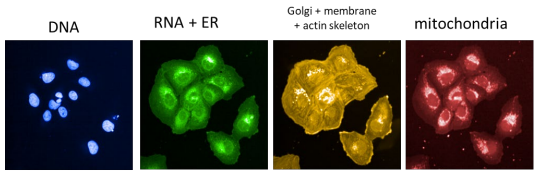
- High-throughput chemical screens to generate biological data on hundreds to thousands of chemicals
  - US EPA's Toxicity Forecasting (ToxCast) Program www.epa.gov/chemical-research/toxicity-forecasting
  - e.g., chemical-biological receptor interaction, metabolomics changes, functional cellular changes (neural network function), zebrafish development
  - Tox21 – intergovernmental US collaboration
  - invitroDB database (v3.5) www.epa.gov/chemical-research/exploring-toxcast-data-downloadable-data



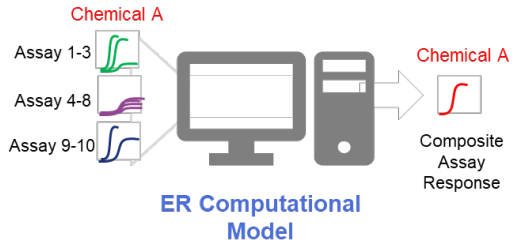
- High-throughput transcriptomics (HTTr)



- High-throughput phenotypic profiling (HTPP)



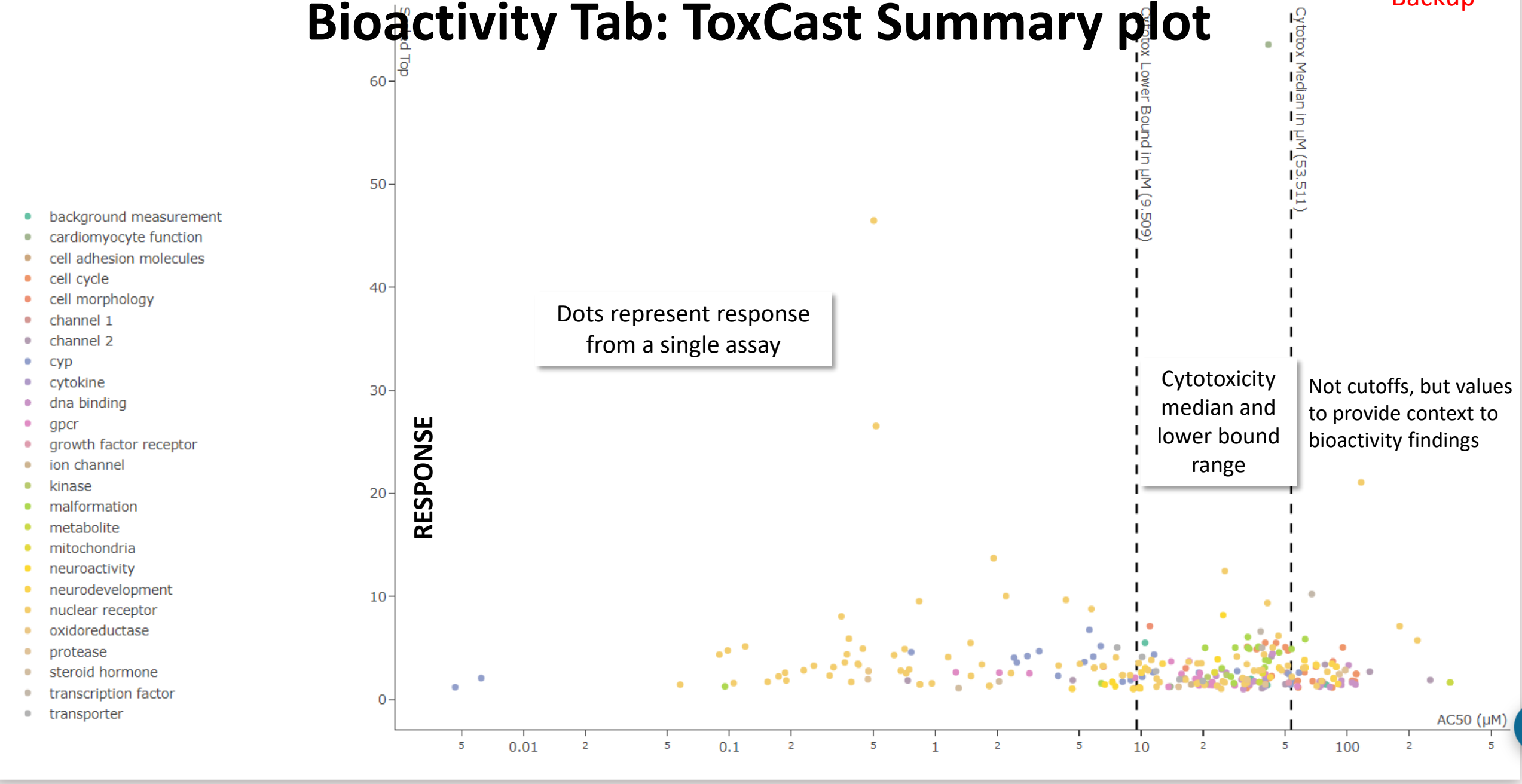
- Development of predictive models utilizing individual assay data (e.g., estrogen receptor [ER] model)



- PubChem Bioassay iframe

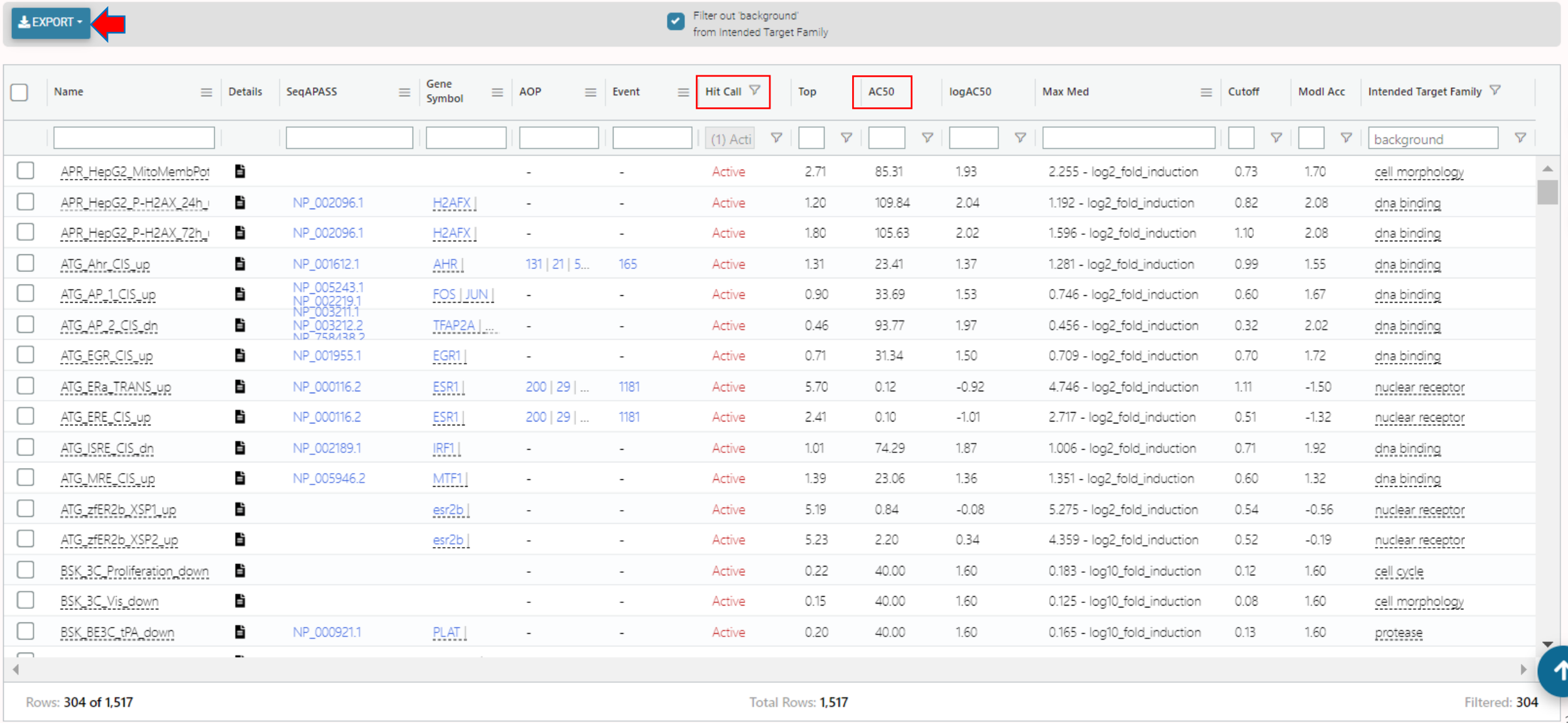
Backup

Bioactivity Tab: ToxCast Summary plot



Bioactivity Tab: ToxCast Summary Data Table

Backup

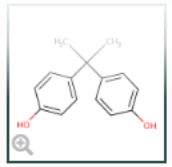


Name	Details	SeqAPASS	Gene Symbol	AOP	Event	Hit Call	Top	AC50	logAC50	Max Med	Cutoff	Modl Acc	Intended Target Family
						(1) Acti							background
APR_HepG2_MitoMembPot				-	-	Active	2.71	85.31	1.93	2.255 - log2_fold_induction	0.73	1.70	cell morphology
APR_HepG2_P-H2AX_24h		NP_002096.1	H2AFX |	-	-	Active	1.20	109.84	2.04	1.192 - log2_fold_induction	0.82	2.08	dna binding
APR_HepG2_P-H2AX_72h		NP_002096.1	H2AFX |	-	-	Active	1.80	105.63	2.02	1.596 - log2_fold_induction	1.10	2.08	dna binding
ATG_Ahr_CIS_up		NP_001612.1	AHR |	131 | 21 | 5...	165	Active	1.31	23.41	1.37	1.281 - log2_fold_induction	0.99	1.55	dna binding
ATG_AP_1_CIS_up		NP_005243.1 NP_002219.1	FOS | JUN |	-	-	Active	0.90	33.69	1.53	0.746 - log2_fold_induction	0.60	1.67	dna binding
ATG_AP_2_CIS_dn		NP_003211.1 NP_003212.2	TFAP2A | ...	-	-	Active	0.46	93.77	1.97	0.456 - log2_fold_induction	0.32	2.02	dna binding
ATG_EGR_CIS_up		NP_001955.1	EGR1 |	-	-	Active	0.71	31.34	1.50	0.709 - log2_fold_induction	0.70	1.72	dna binding
ATG_ERa_TRANS_up		NP_000116.2	ESR1 |	200 | 29 | ...	1181	Active	5.70	0.12	-0.92	4.746 - log2_fold_induction	1.11	-1.50	nuclear receptor
ATG_ERE_CIS_up		NP_000116.2	ESR1 |	200 | 29 | ...	1181	Active	2.41	0.10	-1.01	2.717 - log2_fold_induction	0.51	-1.32	nuclear receptor
ATG_ISRE_CIS_dn		NP_002189.1	IRF1 |	-	-	Active	1.01	74.29	1.87	1.006 - log2_fold_induction	0.71	1.92	dna binding
ATG_MRE_CIS_up		NP_005946.2	MTF1 |	-	-	Active	1.39	23.06	1.36	1.351 - log2_fold_induction	0.60	1.32	dna binding
ATG_zfER2b_XSP1_up			esr2b |	-	-	Active	5.19	0.84	-0.08	5.275 - log2_fold_induction	0.54	-0.56	nuclear receptor
ATG_zfER2b_XSP2_up			esr2b |	-	-	Active	5.23	2.20	0.34	4.359 - log2_fold_induction	0.52	-0.19	nuclear receptor
BSK_3C_Proliferation_down				-	-	Active	0.22	40.00	1.60	0.183 - log10_fold_induction	0.12	1.60	cell cycle
BSK_3C_Vis_down				-	-	Active	0.15	40.00	1.60	0.125 - log10_fold_induction	0.08	1.60	cell morphology
BSK_BE3C_tPA_down		NP_000921.1	PLAT |	-	-	Active	0.20	40.00	1.60	0.165 - log10_fold_induction	0.13	1.60	protease

Rows: **304 of 1,517** Total Rows: **1,517** Filtered: **304**

Bioactivity Tab: Conc. Response Data

Backup



Bisphenol A

80-05-7 | DTXSID7020182

Searched by Approved Name.

- Details
- Executive Summary
- Properties
- Env. Fate/Transport
- Hazard
- Safety > GHS Data
- ADME > IVIVE
- Exposure
- Bioactivity
  - ToxCast: Summary
  - Toxcast Conc. Response Data
  - HTTr: Summary
  - HTPP: Summary
  - PubChem
  - ToxCast: Models
- Links
- Comments

Concentration Response Data

Analytical Data on Tox21 Browser

EXPORT

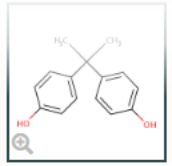
Links out to concentration-response plots

Name	Description	Endpoint Name	Active	Details	Rep. Plot	All Plots	Gene	Intended Target	Cell Line	Cell Format
ASSAY SOURCE: ACEA	ACEA Biosciences	ACEA_AR_agonist_80hr	Inactive				AR	steroidal	prostate	cell line
ASSAY SOURCE: ACEA	ACEA Biosciences	ACEA_AR_agonist_AUC_viability	Active				-	cytotoxicity	prostate	cell line
ASSAY SOURCE: ACEA	ACEA Biosciences	ACEA_AR_antagonist_80hr	Active				AR	steroidal	prostate	cell line
ASSAY SOURCE: ACEA	ACEA Biosciences	ACEA_AR_antagonist_AUC_viability	Active				-	cytotoxicity	prostate	cell line
ASSAY SOURCE: ACEA	ACEA Biosciences	ACEA_ER_80hr	Active				ESR1	steroidal	breast	cell line
ASSAY SOURCE: ACEA	ACEA Biosciences	ACEA_ER_AUC_viability	Inactive				-	cytotoxicity	breast	cell line
ASSAY SOURCE: APR	Apredica	APR_HepG2_CellCycleArrest_1h_dn	Inactive				-	proliferation	liver	cell line
ASSAY SOURCE: APR	Apredica	APR_HepG2_CellCycleArrest_1h_up	Inactive				-	arrest	liver	cell line
ASSAY SOURCE: APR	Apredica	APR_HepG2_CellCycleArrest_24h_dn	Inactive				-	proliferation	liver	cell line
ASSAY SOURCE: APR	Apredica	APR_HepG2_CellCycleArrest_24h_up	Inactive				-	arrest	liver	cell line
ASSAY SOURCE: APR	Apredica	APR_HepG2_CellCycleArrest_72h_dn	Inactive				-	proliferation	liver	cell line
ASSAY SOURCE: APR	Apredica	APR_HepG2_CellCycleArrest_72h_up	Inactive				-	arrest	liver	cell line
ASSAY SOURCE: APR	Apredica	APR_HepG2_CellLoss_1h_dn	Inactive				-	cytotoxicity	liver	cell line
ASSAY SOURCE: APR	Apredica	APR_HepG2_CellLoss_1h_up	Inactive				-	proliferation	liver	cell line

Rows: 1,398 Total Rows: 1,398

Bioactivity Tab: Conc. Response Data

Backup



Bisphenol A

80-05-7 | DTXSID7020182

Searched by Approved Name.

- Details
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- ADME > IVIVE
- Exposure
- Bioactivity
  - ToxCast: Summary
  - Toxcast Conc. Response D
  - HTTr: Summary
  - HTPP: Summary
  - PubChem
  - ToxCast: Models
- Links
- Comments

Concentration Response Data

Analytical Data on Tox21 Browser

Can filter by EDSP associated data

EXPORT

Name	Description	Endpoint Name	Active	Details	Rep. Plot	All Plots	Gene	Intended Target	Cell Line	Cell Format
(4) EDSP AR,EDSP ER,EDSP steroi										
EDSP AR		ATG_AR_TRANS_up	Inactive				AR	steroidal	liver	cell line
EDSP AR		NVS_NR_cAR	Active				AR	steroidal	NA	cell-free
EDSP AR		NVS_NR_hAR	Active				AR	steroidal	NA	cell-free
EDSP AR		NVS_NR_rAR	Active				Ar	steroidal	prostate	tissue-based ce...
EDSP AR		OT_AR_ARELUC_AG_1440	Inactive				AR	steroidal	ovary	cell line
EDSP AR		OT_AR_ARSRC1_0480	Inactive				SRC	steroidal	kidney	cell line
EDSP AR		OT_AR_ARSRC1_0960	Active				SRC	steroidal	kidney	cell line
EDSP AR	Androgen receptor assays used ...	TOX21_AR_BLA_Agonist_ratio	Inactive				AR	steroidal	kidney	cell line
EDSP AR	Androgen receptor assays used ...	TOX21_AR_BLA_Antagonist_ratio	Active				AR	steroidal	kidney	cell line
EDSP AR	Androgen receptor assays used ...	TOX21_AR_BLA_Antagonist_viability	Inactive				-	cytotoxicity	kidney	cell line
EDSP AR	Androgen receptor assays used ...	TOX21_AR_LUC_MDAKB2_Agonist	Inactive				AR	steroidal	breast	cell line
EDSP AR	Androgen receptor assays used ...	TOX21_AR_LUC_MDAKB2_Antagonist_0.5nM_R18...	Active				AR	steroidal	breast	cell line
EDSP AR	Androgen receptor assays used ...	TOX21_AR_LUC_MDAKB2_Antagonist_0.5nM_R18...	Inactive				-	cytotoxicity	breast	cell line
EDSP AR	Androgen receptor assays used ...	TOX21_AR_LUC_MDAKB2_Antagonist_10nM_R1881	Active				AR	steroidal	breast	cell line

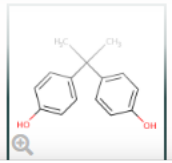
Search...

- ASSAY SOURCE: UPITT
- ASSAY SOURCE: VALA
- EDSP AR
- EDSP ER
- EDSP steroidogenesis
- EDSP thyroid

Rows: 84 of 1,498 Total Rows: 1,498 Filtered: 84

Backup

Bioactivity Tab: Conc. Response Data



Bisphenol A

80-05-7 | DTXSID7020182

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- Details
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  - ToxCast: Summary
  - Toxcast Conc. Resp
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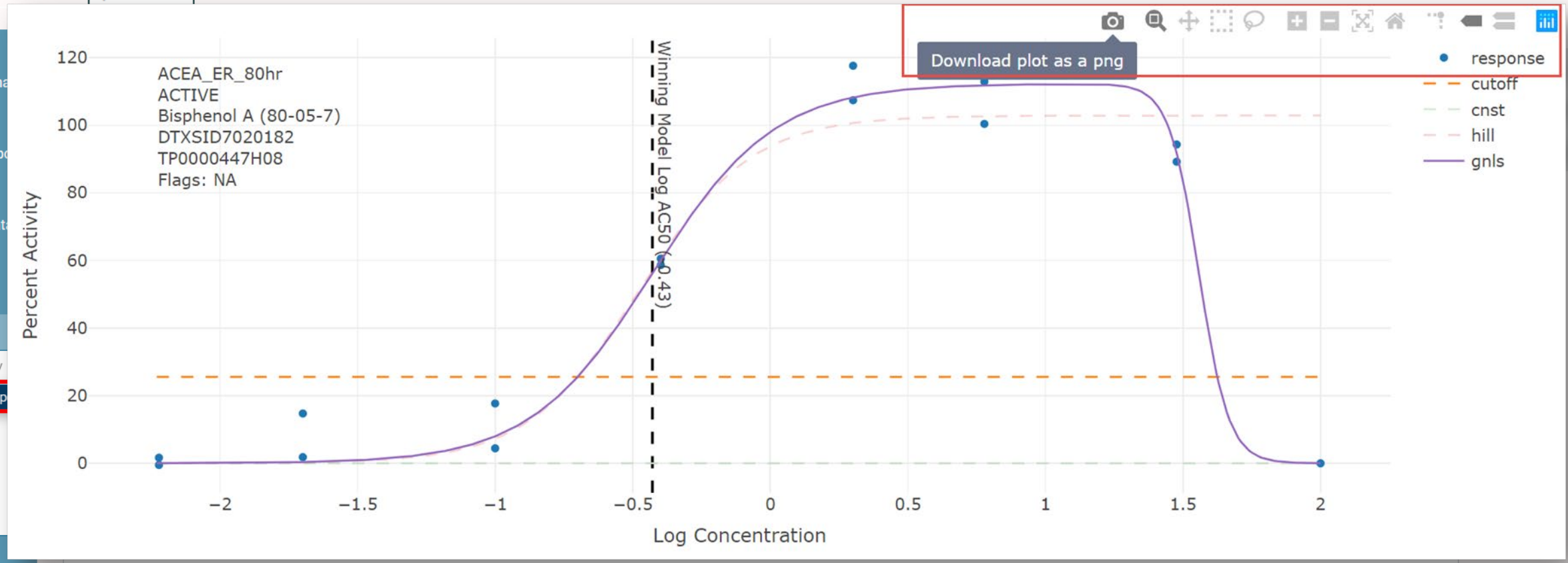
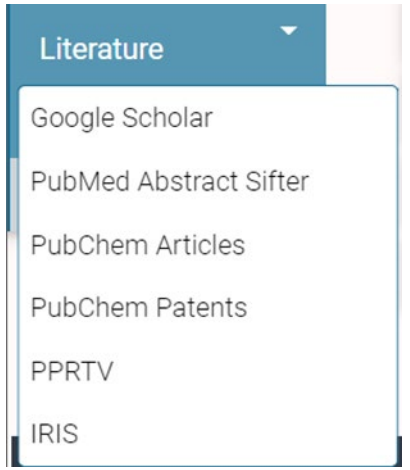
  - PubChem
  - ToxCast: Models
- Links
- Comments



Rows: 1,398 Total Rows: 1,398

Backup

Literature Tabs



- Perform searches of publications containing the chemical, as well as user-defined terms
  - Google Scholar
  - PubMed Abstract Sifter

- Direct visualization of curated chemical database information
  - PubChem Articles
  - PubChem Patents
  - PPRTV (EPA's Provisional Peer-Reviewed Toxicity Value)
  - IRIS (EPA's Integrated Risk Information System)

BPA
Measured hazard and exposure data

Backup

Measured hazard and exposure values for BPA

Executive Summary

- **Quantitative Risk Assessment Values**
  - IRIS values available
  - No PPRTV values
  - EPA RSL values available
  - Minimum RfD:0.05 mg/kg-day (chronic,)
  - No RfC calculated
  - IVIVE POD not calculated

Literature > IRIS

Noncancer Assessment

Reference Dose for Oral Exposure (RfD) (PDF) (8 pp, 93 K)

Last Updated: 09/26/1988

System	RfD (mg/kg-day)	Basis	PoD	Composite UF
Other	5×10^{-2}	Reduced mean body weight	LOAEL : 5.0×10^{1} mg/kg-day	1000

Exposure > Biomonitoring

National Health and Nutrition Examination Survey (NHANES) Inferences (mg/kg-bw/day)

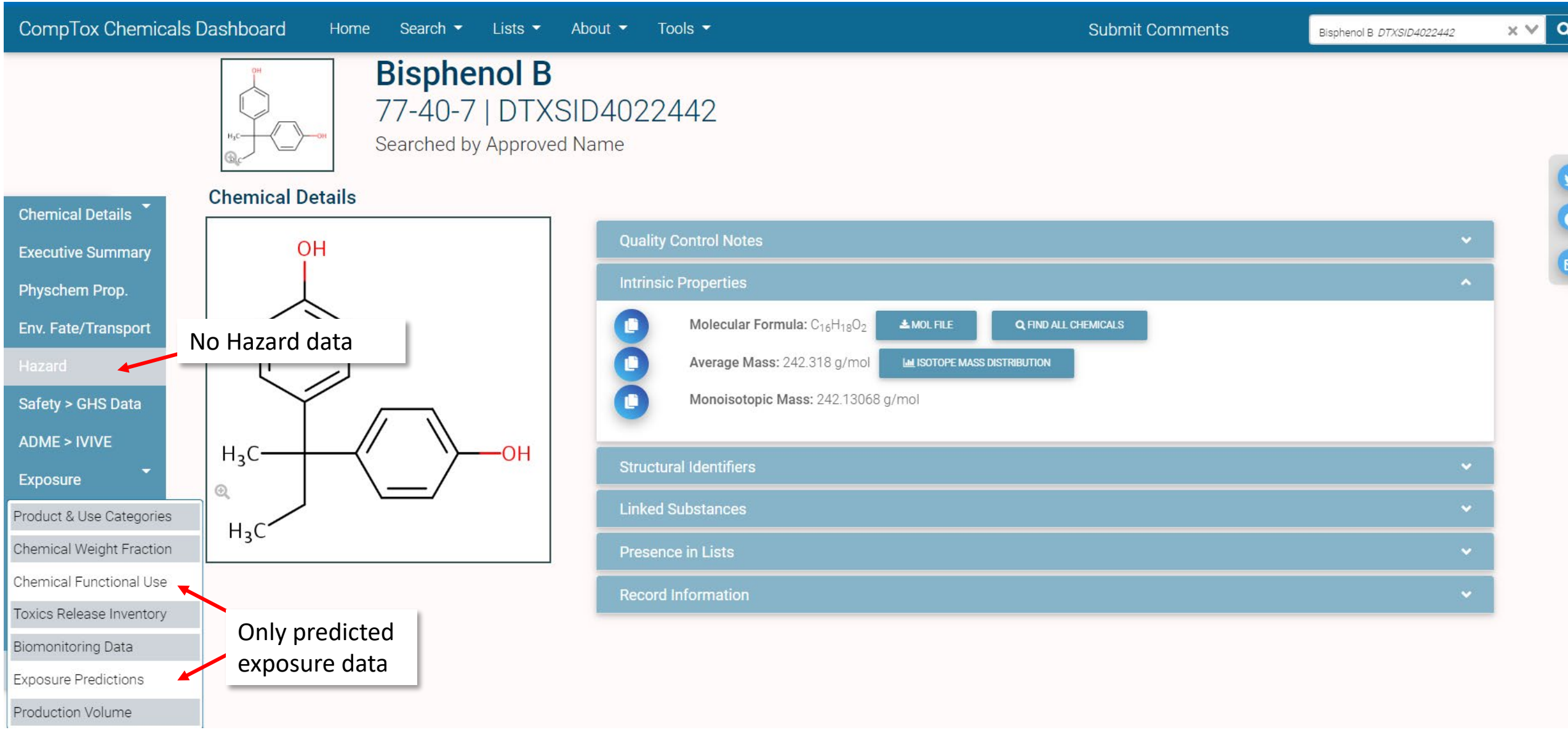
Demographic	Lower Bound (Median)	Upper Bound (Median)
Age 6-11	3.80e-5	4.92e-5
Age 12-19	2.55e-5	3.38e-5
Age 20-65	2.79e-5	3.27e-5
Age 65+	1.91e-5	2.31e-5
BMI < 30	3.02e-5	3.30e-5
BMI > 30	2.38e-5	2.74e-5
Females	2.58e-5	3.03e-5
Males	2.94e-5	3.37e-5
Repro. Age Females	2.83e-5	3.31e-5
Total	2.86e-5	3.08e-5

Hazard: 5 x 10^-2mg/kg/day (RfD)
Exposures: ~ 5 x 10^-5 mg/kg/day (max)

Bisphenol B

Backup

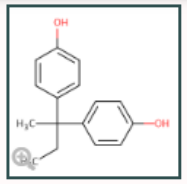
Landing page



Backup

Physchem Properties

CompTox Chemicals Dashboard | Home | Search | Lists | About | Tools | Submit Comments | Bisphenol B DTXSID4022442



Bisphenol B

77-40-7 | DTXSID402

Searched by Approved Name

GenRA

Predictions

Abstract Sifter

Predicted properties available below, but can also predict some hazard endpoints using webTEST (Toxicity Estimation Software Tool)

Chemical Details
Executive Summary
Physchem Prop.
Env. Fate/Transport
Hazard
Safety > GHS Data
ADME > IVIVE
Exposure
Bioactivity
GenRA
Literature
Links
Comments

Properties: Summary

Summary | Search Chemical Properties

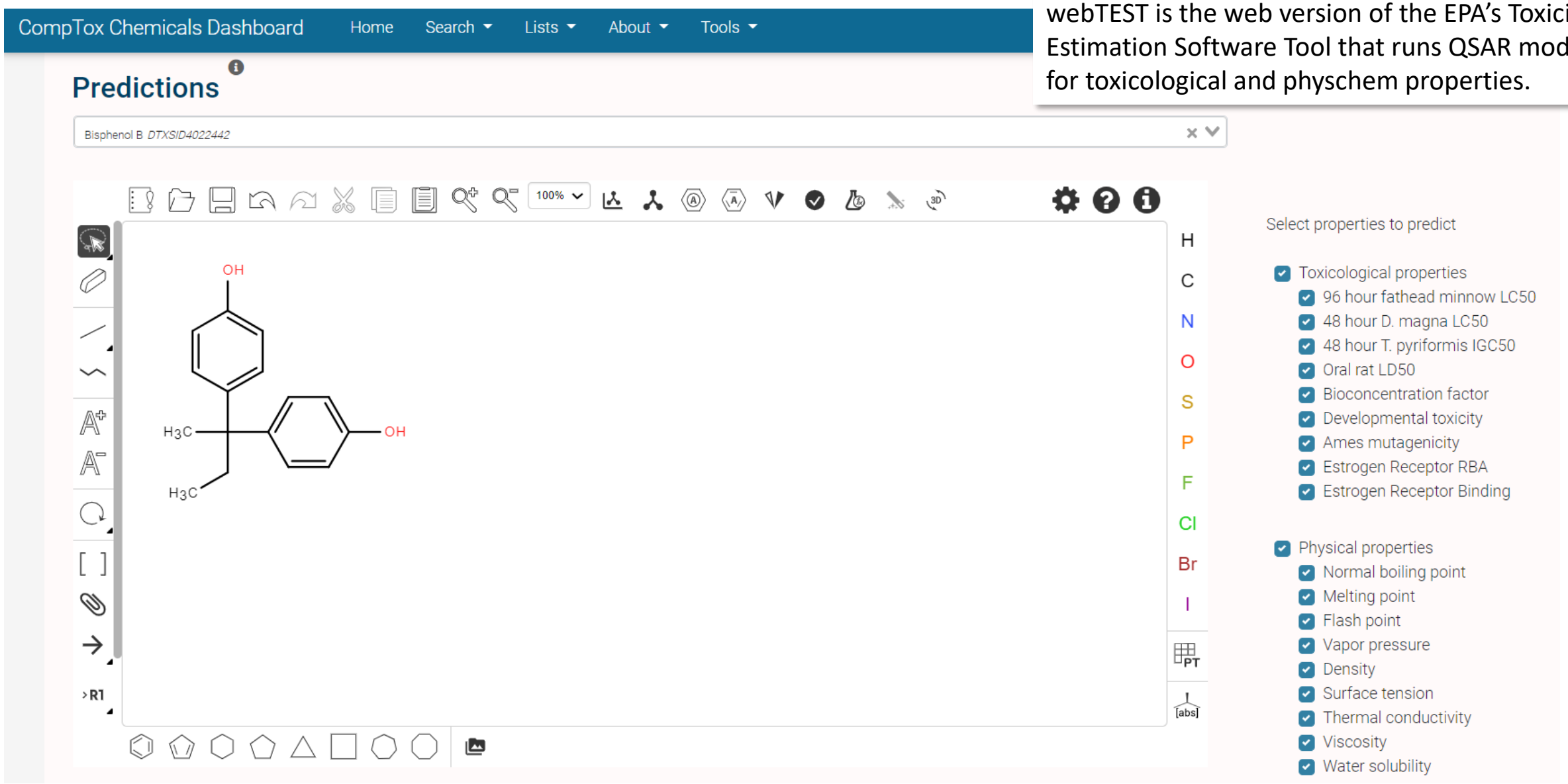
EXPORT

Summary

Property	Experimental average	Predicted average	Experimental median	Predicted median	Experimental range	Predicted range	Unit
Polarizability	-	28.9 (1)	-	28.9	-	28.9	Å^3
Henry's Law	-	1.26e-7 (1)	-	1.26e-7	-	1.26e-7	atm-m3/mole
Boiling Point	-	376 (4)	-	370	-	351 to 412	°C
Flash Point	-	194 (2)	-	194	-	192 to 196	°C
Melting Point	122 (3)	131 (3)	121	131	121 to 126	121 to 139	°C
Molar Refractivity	-	72.8 (1)	-	72.8	-	72.8	cm^3
Molar Volume	-	216 (1)	-	216	-	216	cm^3
Viscosity	-	10.4 (1)	-	10.4	-	10.4	cP
Surface Tension	-	45.0 (1)	-	45.0	-	45.0	dyn/cm
Density	-	1.15 (2)	-	1.15	-	1.12 to 1.18	g/cm^3
Vapor Pressure	-	6.26e-7 (3)	-	2.20e-7	-	3.87e-8 to 1.62e-6	mmHg
Water Solubility	-	4.76e-4 (3)	-	2.59e-4	-	1.21e-4 to 1.05e-3	mol/L
Thermal Conductivity	-	143 (1)	-	143	-	143	mW/(m*K)
Index of Refraction	-	1.59 (1)	-	1.59	-	1.59	-
LogKoa: Octanol-Air	-	8.99 (1)	-	8.99	-	8.99	-
LogKow: Octanol-Water	-	3.95 (4)	-	3.94	-	3.77 to 4.13	-

Predictions Tool

webTEST is the web version of the EPA's Toxicity Estimation Software Tool that runs QSAR models for toxicological and physchem properties.



Backup

webTEST predictions

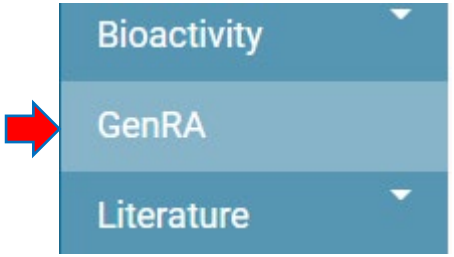
EXPORT

Property	Experimental Value	Consensus	Hierarchical clustering	Single model	Group contribution	Nearest neighbor
96 hour fathead minnow LC50		5.148 -Log10(mol/L) 1.725 mg/L	5.317 -Log10(mol/L) 1.169 mg/L	4.766 -Log10(mol/L) 4.158 mg/L	5.383 -Log10(mol/L) 1.002 mg/L	5.125 -Log10(mol/L) 1.816 mg/L
48 hour D. magna LC50		5.286 -Log10(mol/L) 1.253 mg/L	5.601 -Log10(mol/L) 0.608 mg/L	5.236 -Log10(mol/L) 1.407 mg/L	4.965 -Log10(mol/L) 2.625 mg/L	5.344 -Log10(mol/L) 1.098 mg/L
48 hour T. pyriformis IGC50		4.858 -Log10(mol/L) 3.358 mg/L	4.913 -Log10(mol/L) 2.958 mg/L		5.565 -Log10(mol/L) 0.660 mg/L	4.097 -Log10(mol/L) 19.398 mg/L
Oral rat LD50		2.014 -Log10(mol/kg) 2344.727 mg/kg	2.374 -Log10(mol/kg) 1025.084 mg/kg			1.655 -Log10(mol/kg) 5363.214 mg/kg
Bioconcentration factor		2.155 Log10 142.768	2.258 Log10 181.049	2.162 Log10 145.152	1.618 Log10 41.479	2.581 Log10 381.132
Developmental toxicity		true	true	true		
Ames mutagenicity		false	false			false
Estrogen Receptor RBA	-1.070 Log10 0.085	-1.668 Log10 0.021	-1.561 Log10 0.027	-1.394 Log10 0.040	-1.889 Log10 0.013	-1.827 Log10 0.015
Estrogen Receptor Binding	true	true	true	true	true	true
Normal boiling point		365.6 °C	370.6 °C		395.7 °C	330.3 °C
Melting point	120.5 °C	125.7 °C	138.3 °C		122.7 °C	116.2 °C
Flash point		191.7 °C	200.1 °C		176.9 °C	198.1 °C
		-5.791 Log10(mmHg)	-6.595 Log10(mmHg)		-6.313 Log10(mmHg)	-4.467 Log10(mmHg)

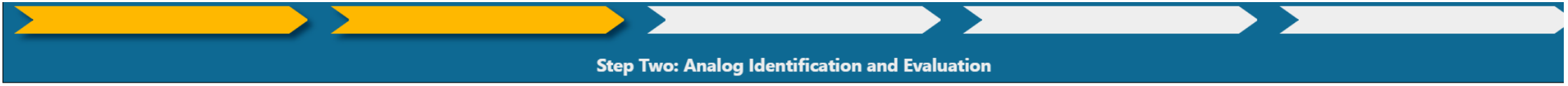
Rows: **18** Total Rows: **18**

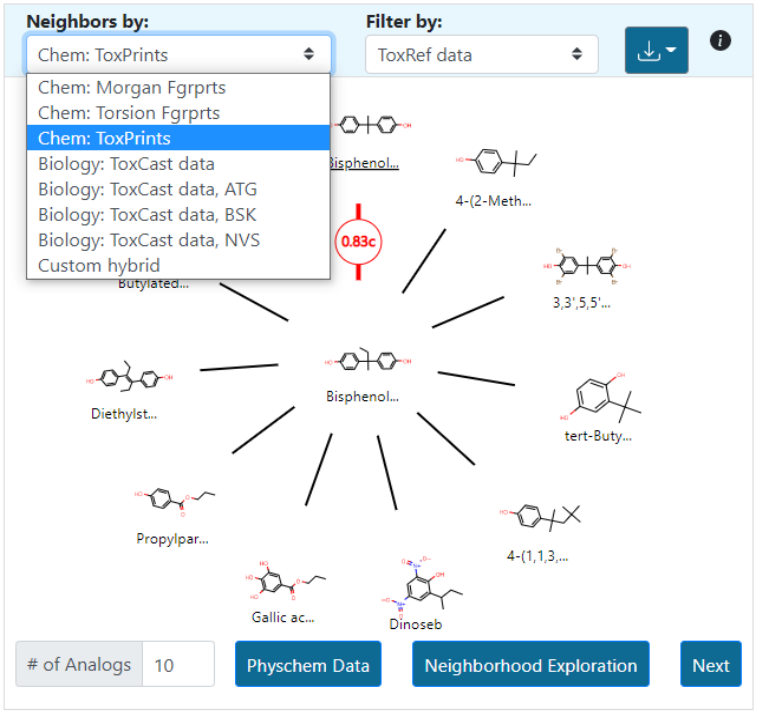
Backup

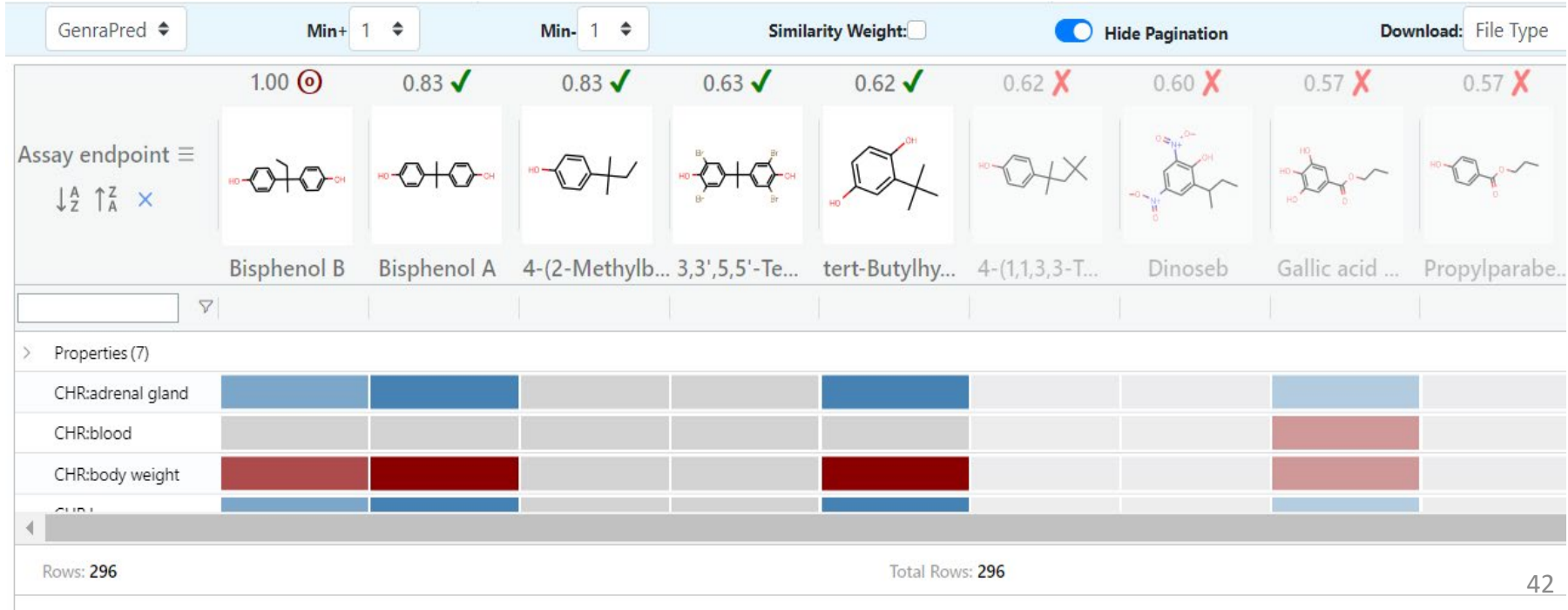
Generalized Read-Across (GenRA)



- Interactive workflow to:
  - search for target or draw it;
  - define fingerprints for similarity and number of analogs;
  - Examine what data exist for source analogs;
  - Inspect the consistency, concordance, and range of effects for analogs
  - Understand confidence in the prediction(s)







Backup

Generalized Read-Across (GenRA)

Output file, filtered by pvalue

	A	B	C	D	E	F	G	H	I	J	K	L
1	**chem_id**	DTXCID002442	DTXCID002442_ur	DTXCID30182	DTXCID30182_uni	DTXCID001771	DTXCID001771_ur	DTXCID406081	DTXCID406081_ur	DTXCID60220	DTXCID60220_units	
2	**role**	target		analog		analog		analog		analog		
3	**preferred name**	Bisphenol B		Bisphenol A		4-(2-Methylbutan-2-yl)phenol		3,3',5,5'-Tetrabromobisphenol A		tert-Butylhydroquinone		
4	**dsstox_sid**	DTXSID4022442		DTXSID7020182		DTXSID8021771		DTXSID1026081		DTXSID6020220		
5	**dsstox_cid**	DTXCID002442		DTXCID30182		DTXCID001771		DTXCID406081		DTXCID60220		
6	**molecular weight**	242.318		228.291		164.248		543.875		166.22		
7	**similarity**	1		0.833		0.833		0.625		0.615		
8	**Melting °C**	121.02		152.696		94.4421		180.942		127.597		
9	**Boiling °C**	351.077		343.191		262.12		416.811		273.025		
10	**log Kow**	3.76543		3.32044		3.49129		6.66284		3.30226		
11	**Vap. press. mmHg**	3.87405E-08		6.77917E-08		0.00205254		5.30107E-09		0.000212376		
12	**Water sol. mol/L**	0.00025924		0.000745153		0.00102885		1.78323E-06		0.00944581		
13	**Henry's Law atm-m3/mole**	1.25516E-07		1.25155E-07		6.21129E-07		1.76603E-08		1.8034E-07		
14												
34	CHR:liver	**Pos; ACT=0.575; pval=0.47**		149.999	mg/kg/day	no_data		no_data		no_effect		
119	MGR:kidney	**Pos; ACT=0.571; pval=0.45**		500	mg/kg/day	no_data		no_effect		no_data		
138	MGR:preputial separation	**Pos; ACT=0.571; pval=0.41**		45	mg/kg/day	no_data		no_effect		no_data		
232	SUB:body weight	**Neg; ACT=0.425; pval=0.485**		no_data		no_effect		no_data		400	mg/kg/day	
271	SUB:nose	**Neg; ACT=0.425; pval=0.49**		no_data		no_effect		no_data		400	mg/kg/day	
291	SUB:spleen	**Neg; ACT=0.425; pval=0.44**		no_data		no_effect		no_data		200	mg/kg/day	
292	SUB:stomach	**Neg; ACT=0.425; pval=0.49**		no_data		no_effect		no_data		2200	mg/kg/day	
304												

Backup

Bioactivity ToxCast Summary data

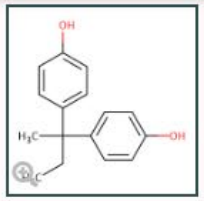
Name	Details	SeqAPASS	Gene Symbol	AOP	Event	Hit Call	Top	AC50	logAC50	Max Med	Cutoff	Modl Acc	Intended Target Family
						(1) Acti							background
ATG_HIF1a_CIS_up		NP_001521.1	HIF1A |	122 | 123 | ...	801	Active	0.91	0.07	-1.13	1.105 - log2_fold_induction	0.77	-1.04	dna binding
OT_ER_ERbERb_0480		NP_001428.1	ESR2 |	-	-	Active	121.72	0.10	-0.99	116.461 - percent_activity	20.00	-1.49	nuclear receptor
TOX21_ERa_LUC_VM7_Ago		NP_000116.2	ESR1 |	200 | 200 |...	1181	Active	94.54	0.11	-0.94	100.771 - percent_activity	20.00	-1.40	nuclear receptor
ATG_ERa_TRANS_up		NP_000116.2	ESR1 |	200 | 29 | ...	1181	Active	3.43	0.13	-0.88	2.982 - log2_fold_induction	1.11	-1.13	nuclear receptor
OT_ER_ERbERb_1440		NP_001428.1	ESR2 |	-	-	Active	168.24	0.14	-0.84	161.715 - percent_activity	20.00	-1.34	nuclear receptor
CCTE_Deisenroth_AIME_38			ESR1	-	-	Active	106.13	0.17	-0.78	115.597 - percent_activity	22.27	-1.04	nuclear receptor
ATG_ERE_CIS_up		NP_000116.2	ESR1 |	200 | 29 | ...	1181	Active	2.23	0.17	-0.78	2.426 - log2_fold_induction	0.51	-1.11	nuclear receptor
OT_ERa_EREGFP_0120		NP_000116.2	ESR1 |	200 | 29 | ...	1181	Active	92.21	0.18	-0.74	90.719 - percent_activity	20.00	-0.97	nuclear receptor
NVS_NR_bER		NP_001001443.1	ESR1 |	200 | 29 | ...	1181	Active	78.76	0.21	-0.69	82.054 - percent_activity	24.17	-0.84	nuclear receptor
NVS_NR_mERa			Esr1 |	200 | 29 | ...	1181	Active	89.86	0.22	-0.66	96.079 - percent_activity	25.96	-0.88	nuclear receptor
OT_ERa_EREGFP_0480		NP_000116.2	ESR1 |	200 | 29 | ...	1181	Active	86.94	0.22	-0.66	87.041 - percent_activity	20.00	-0.80	nuclear receptor
OT_ER_ERaERb_1440		NP_000116.2 NP_001428.1	ESR1 | ESR...	-	-	Active	160.70	0.23	-0.63	144.522 - percent_activity	20.00	-1.19	nuclear receptor
OT_ER_ERaERb_0480		NP_000116.2 NP_001428.1	ESR1 | ESR...	-	-	Active	146.40	0.25	-0.60	124.584 - percent_activity	23.30	-1.17	nuclear receptor
TOX21_ERb_BLA_Antagonis		NP_001428.1	ESR2 |	-	-	Active	69.15	0.25	-0.61	73.867 - percent_activity	24.25	-0.82	nuclear receptor
NVS_NR_hER		NP_000116.2	ESR1 |	200 | 29 | ...	1181	Active	94.62	0.27	-0.57	96.294 - percent_activity	24.39	-1.00	nuclear receptor
TOX21_CAR_Agonist_viabilli				-	-	Active	45.58	0.27	-0.57	36.170 - percent_activity	20.00	-0.92	cell cycle

Rows: **292 of 1,040** Total Rows: **1,040** Filtered: **292**

Backup

Exposure predictions

CompTox Chemicals Dashboard | Home | Search | Lists | About | Tools | Submit Comments | Search all data



Bisphenol B

77-40-7 | DTXSID4022442

Searched by Approved Name.

- Chemical Details
- Executive Summary
- Physchem Prop.
- Env. Fate/Transport
- Hazard
- Safety > GHS Data
- ADME > IVIVE
- Exposure
- Bioactivity
- GenRA
- Literature
- Links

Exposure - Exposure Predictions (mg/kg-bw/day)

Search Demographics Predictions Data | EXPORT

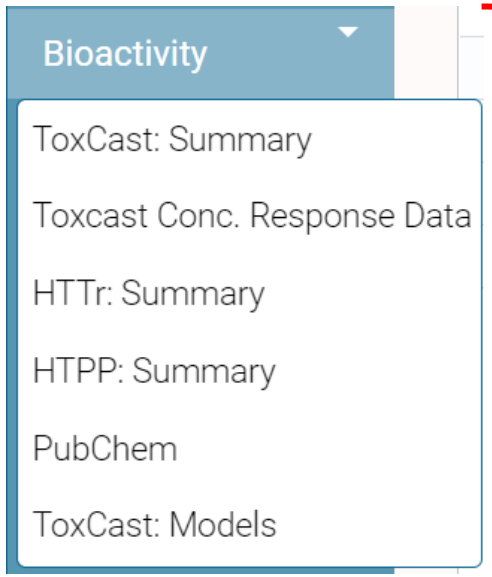
Demographics Predictions Data

Demographic	Predictor	Median	Upper 95%ile	Units
	(2) SEEM2 Heuristic,SEEM3 Consensus			
Age 6-11	SEEM2 Heuristic	2.39e-7	4.47e-5	mg/kg/day
Age 12-19	SEEM2 Heuristic	2.53e-7	6.67e-5	mg/kg/day
Age 20-65	SEEM2 Heuristic	2.14e-7	5.24e-5	mg/kg/day
Age 66+	SEEM2 Heuristic	2.31e-7	4.49e-5	mg/kg/day
BMI <= 30	SEEM2 Heuristic	2.79e-7	6.82e-5	mg/kg/day
BMI > 30	SEEM2 Heuristic	2.00e-7	5.15e-5	mg/kg/day
Females	SEEM2 Heuristic	1.48e-7	4.17e-5	mg/kg/day
Males	SEEM2 Heuristic	1.57e-7	2.34e-5	mg/kg/day
Repro. Age Females	SEEM2 Heuristic	1.22e-7	3.31e-5	mg/kg/day

Exposure estimate: ~ 7 x 10^-5 mg/kg/day (max)

Back to Slides

Reverse Toxicokinetics on Bioactivity data



Gather a bioactivity concentration

- Lowest X%
- Lowest AC50

Calculate Administered Equivalent Dose (AED)

1. HTTK r-package
2. A straightforward equation : *(Bioactivity conc. [micromolar]) x (1mg/kg/day) x (1/steady-state plasma concentration from ADME > IVIVE tab [micromolar])* . Make sure to check units
3. NIEHS WebICE tool

Exploration Case Study

- Bisphenol A: A well-studied chemical
  - Chemistry: physchem properties
  - Hazard: quantitative risk assessment values, IRIS, in vivo data
  - Bioactivity: high throughput screening data
  - Exposure: Biomonitoring data

- Bisphenol B: A limited-studied chemical
  - Chemistry: physchem properties
  - Hazard: GenRA (data gap-filling using)
  - Bioactivity: high throughput screening data
  - Exposure: predictions

Summary

- The CompTox Chemicals Dashboard allows public access of environmental chemical data to support EPA and partner decision making
- Currently >1.2 million chemicals providing chemistry, toxicity and exposure information
- Measured data (when available) are provided, along with predictions and the capability to make predictions, as well as search the literature for up-to-date information

Thank you!

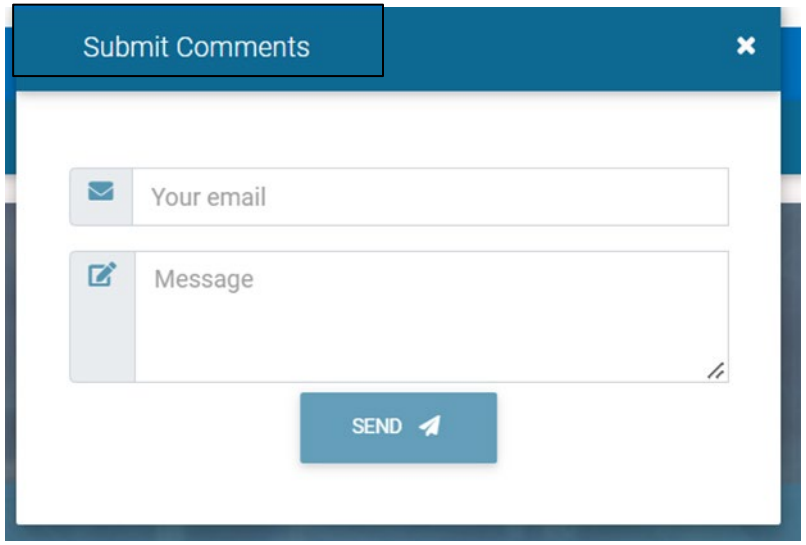
Nisha Sipes, PhD

Assistant Center Director

CompTox Chemicals Dashboard Product Owner

US EPA ORD Center for Computational Toxicology and Exposure

sipes.nisha@epa.gov



Resources

References

- https://www.epa.gov/chemical-research/new-approach-methods-nams-training
  - Link to past presentations, videos, and other references for EPA ORD's web applications, including the CompTox Chemicals Dashboard

- https://www.epa.gov/chemical-research/downloadable-computational-toxicology-data
  - Link to downloadable data, including ToxCast data (invitroDB), ToxRefDB, ToxValDB, and others.

- CompTox Chemicals Dashboard
  - Williams AJ, et al. The CompTox Chemistry Dashboard: a community data resource for environmental chemistry. J Cheminform. 2017 Nov 28;9(1):61.
  - Lowe CN and Williams AJ. Enabling High-Throughput Searches for Multiple Chemical Data Using the U.S.-EPA CompTox Chemicals Dashboard. J. Chem. Inf. Model. 2021, 61, 2, 565–570. Publication Date: January 22, 202
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Hazard

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- ToxValDB - https://epa.figshare.com/articles/presentation/ToxValDB_Compiling_Publicly_Available_In_Vivo_Toxicity_Data/7800653

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Predictions

- GenRA - Helman G, et al. Generalized Read-Across (GenRA): A workflow implemented into the EPA CompTox Chemicals Dashboard. ALTEX. 2019;36(3):462-465.
- WebTEST - U.S. EPA (2020). "User's Guide for T.E.S.T. (version 5.1) (Toxicity Estimation Software Tool): A Program to Estimate Toxicity from Molecular Structure." https://www.epa.gov/sites/default/files/2016-05/documents/600r16058.pdf

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Exposure

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High Throughput Toxicokinetics (HTTK)

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- Wambaugh, JF et al., 2015. Toxicokinetic Triage for Environmental Chemicals. Toxicol Sci., 147(1):55-67.
- Wetmore, BA, et al. 2015. Quantitative in vitro-in vivo extrapolation in a high-throughput environment. Toxicol. 332:94-101
- Rotroff, DM et al., 2010. Incorporating Human Dosimetry and Exposure into High-Throughput In Vitro Toxicity Screening. Toxicol. Sci., 117 (2):348-358.

References

In vitro to in vivo extrapolation (IVIVE)

- Utilizing HTTK R-package, slide 41: https://epa.figshare.com/articles/presentation/Computational_Toxicology/17407460
- Calculation, slide 28: https://epa.figshare.com/articles/presentation/Overview_of_the_CompTox_Chemicals_Dashboard_and_ToxCast_Tox21_Screening_Program_Tools_for_Users/17396306
- WebICE https://ice.ntp.niehs.nih.gov/Tools

Data download available