

Society of Toxicology 2019 Undergraduate Education Program
Going for Your First Drive in Toxicology: Using the CompTox Chemicals
Dashboard
STUDENT VERSION

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There are many roles for a toxicologist. Some work in laboratories doing original research, but others play a key role in chemical risk assessment. An important aspect of this work is analyzing and synthesizing existing data on the chemical of interest. The United States Environmental Protection Agency's Comptox Chemicals Dashboard (<https://comptox.epa.gov/dashboard>) was created as a tool for toxicologists to access key information on chemicals, including traditional and new approaches to consider chemical hazard and potential for exposure.

HANDOUT:

You are Dr. Assessor and you have been asked to come to Fake City, USA, to address what seems to be a chemical contamination in the groundwater and you are asked to determine if there is a concern for public health. Based on the analysis of the chemicals in the groundwater, you know there are three main chemicals (Chemical A, B and C). You are tasked with prioritizing these chemicals to focus resources on what is the best path forward to protect public health.

To start, you want to review as much information as you can on these three chemicals. Using the CompTox Chemicals Dashboard, look for information on these three chemicals that can help you to determine which of these three chemicals is of more potential concern for hazard.

Chemical A Executive Summary

Quantitative Risk Assessment Values

- ✔ IRIS values available [↗](#)
- ✘ No PPRTV values
- ✔ EPA RSL values available [↗](#)
- ✔ Minimum RID: 0.000045 mg/kg-day (chronic, ACToR, dermal, 4) [↗](#)
- ✔ Minimum RIC: 0.0020 mg/m3 (chronic, IRIS, inhalation, 8) [↗](#)
- ✘ IVIVE POD not calculated

Quantitative Hazard Values

- ✔ Minimum oral POD: 0.0051 mg/kg-day (chronic, IRIS, oral, 8) [↗](#)
- ✔ Minimum inhalation POD: 0.021 mg/m3 (chronic, IRIS, inhalation, 8) [↗](#)
- ✔ Lowest Observed Bioactivity Equivalent Level: TP53

Cancer Information

- ✔ Cancer slope factor: 2.67 (mg/kg-day)⁻¹ (ACToR, dermal, 4) [↗](#)
- ✔ Inhalation unit risk: 0.11 (mg/m3)⁻¹ (ACToR, inhalation, 4) [↗](#)
- ✔ Carcinogenicity data available: IARC: Group 1, Carcinogenic to humans NIOSH potential occupational carcinogen NTP Report on Carcinogens (ROC 12): Reasonably Anticipated to be Human Carcinogen NLM ToxNet HSDB carcinogenicity warning University of Maryland carcinogenicity warning: [↗](#)
- ✘ No genotoxicity findings reported

Reproductive Toxicology

- ✔ 21 Reproductive toxicity PODs available [↗](#)

Chronic Toxicology

- ✔ 290 Chronic toxicity PODs available [↗](#)

Subchronic Toxicology

- ✔ 12 Subchronic toxicity PODs available [↗](#)

Developmental Toxicology

- ✘ No developmental toxicity data available.

Acute Toxicology

- ✔ 179 Acute toxicity PODs available [↗](#)

Subacute Toxicology

- ✘ No subacute toxicity data available.

Neurotoxicology

- ✘ No neurotoxicology data available.

Endocrine System

- ✘ No endocrine disruption relevant data

ADME

- ✘ No HTTK data

Fate and Transport

- ✘ No bioaccumulation concern.
- ✔ Volatility concern: VP= 94.3 mm
- ✔ Biodegradation predictions are available [↗](#)
- ✔ BCF predictions are available [↗](#)
- ✔ Vapor Pressure predictions are available [↗](#)

Exposure

- ✔ Exposure Estimates have been predicted using the SEEM modeling methodology [↗](#)

AOP Information

- ✔ No AOPs available

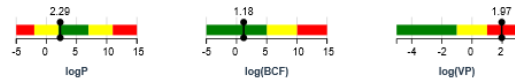
Other Notes

- ✘ No water quality values available.
- ✔ 33 Air quality values available. [↗](#)
- ✔ 29 Occupational exposure values available. [↗](#)

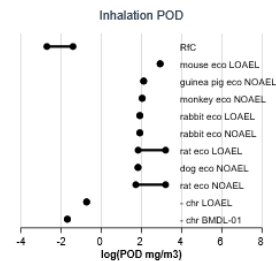
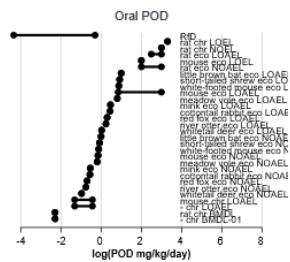
REGIONAL SCREENING

Class	THQ	Value
screening level (residential Soil) (mg/kg-day)	-	0.94
screening level (industrial soil) (mg/kg-day)	-	6
screening level (residential air) (ug/m3)	-	0.48
screening level (industrial air) (ug/m3)	-	3
screening level (tap water) (ug/L)	-	0.49
risk-based SSL (mg/m3)	-	0.00018
screening level (residential Soil) (mg/kg-day)	THQ=0.1	0.41
screening level (industrial soil) (mg/kg-day)	THQ=0.1	1.9
screening level (residential air) (ug/m3)	THQ=0.1	0.21
screening level (industrial air) (ug/m3)	THQ=0.1	0.88
screening level (tap water) (ug/L)	THQ=0.1	0.28
screening level (MCL) (ug/L)	-	5
GIABS (mg/kg-day)	-	1
Csat (mg/kg-day)	-	990
risk-based SSL (mg/m3)	THQ=0.1	0.0001
MCL-based SSL (mg/kg-day)	-	0.0018
cancer slope factor ((mg/kg-day) ⁻¹)	-	0.046
inhalation unit risk ((ug/m3) ⁻¹)	-	0.0000041
RfDo (mg/kg-day)	-	0.0005
RFCl (mg/m3)	-	0.002

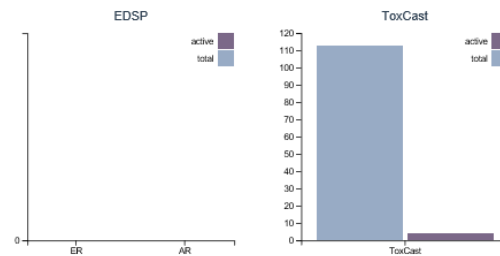
PHYSICHEM PARAMETERS



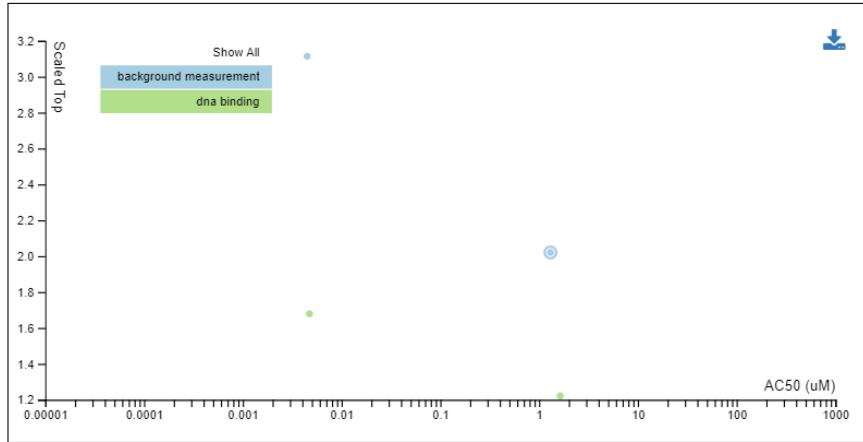
POINT-OF-DEPARTURE PLOTS



ASSAY PLOTS



TOXCAST DATA



ASSAY DETAILS

AC50 (uM): 1.30
Scaled top: 2.02
Assay Endpoint Name: TOX21_p53_BLA_p3_ch2
Gene Symbol:
Organism: human
Tissue: intestinal
Assay Format Type: cell-based
Biological Process Target: regulation of transcription factor activity
Detection Technology: GAL4 b-lactamase reporter gene
Analysis Direction: positive
Intended Target Family: background measurement
Description: NA

Chemical B Executive Summary

Quantitative Risk Assessment Values

- ✗ No IRIS values
- ✗ No PPRTV values
- ✗ No EPA RSL values
- ✗ No RID calculated
- ✗ No RRC calculated
- ✗ IVIVE POD not calculated

Quantitative Hazard Values

- ✗ No oral POD values
- ✗ No inhalation POD values
- ✗ No in vitro activity below 1 uM.

Cancer Information

- ✗ No cancer slope factor
- ✗ No inhalation unit risk value
- ✗ No cancer data
- ✗ No genotoxicity data

Reproductive Toxicology

- ✗ No reproductive toxicity data available.

Chronic Toxicology

- ✗ No chronic toxicity data available.

Subchronic Toxicology

- ✗ No subchronic toxicity data available.

Developmental Toxicology

- ✗ No developmental toxicity data available.

Acute Toxicology

- ✗ No acute toxicity data available.

Subacute Toxicology

- ✗ No subacute toxicity data available.

Neurotoxicology

- ✗ No neurotoxicology data available.

Endocrine System

- ✗ No endocrine disruption relevant data

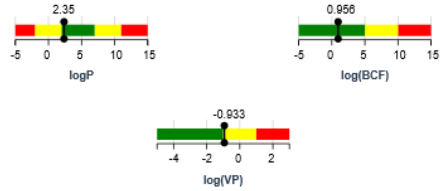
ADME

- ✗ No HTTK data

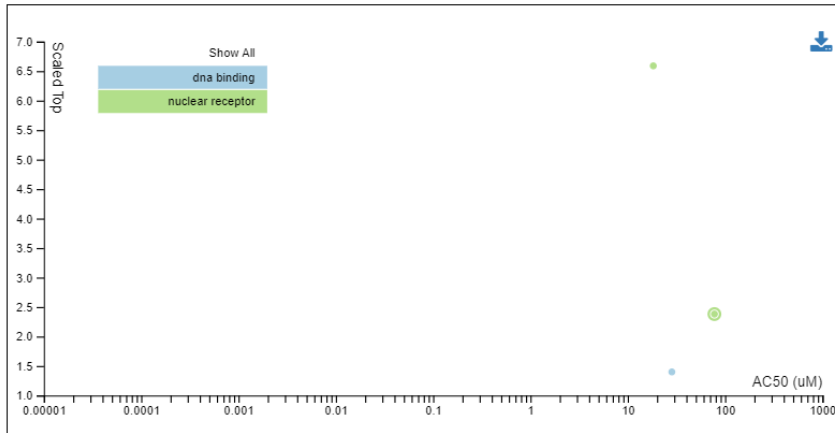
Fate and Transport

- ✗ No bioaccumulation concern.
- ✗ No volatility concern.
- ✔ Biodegradation predictions are available [↗](#)

PHYSICHEM PARAMETERS



TOXCAST DATA



ASSAY DETAILS

AC50 (uM): 77.69

Scaled top: 2.38

Assay Endpoint Name: ATG_Era_TRANS_up

Assay Description: 117

Gene Symbol: ESR1

Organism: human

Tissue: liver

Assay Format Type: cell-based

Biological Process Target: regulation of transcription factor activity

Detection Technology: RT-PCR and Capillary electrophoresis

Analysis Direction: positive

Intended Target Family: nuclear receptor

Description: Data from the assay component ATG_Era_TRANS was analyzed into 1 assay endpoint. This assay endpoint, ATG_Era_TRANS_up, was analyzed in the positive fitting direction relative to DMSO as the negative control and baseline of activity

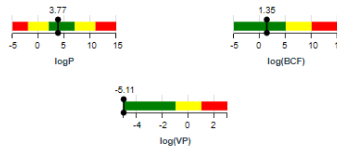
Chemical C Executive Summary

- Quantitative Risk Assessment Values**
- No IRIS values
 - No PPRTV values
 - EPA RSL values available
 - Minimum RID: 0.000030 mg/kg-day (chronic, ACT5R, oral, 7)
 - Minimum RIC: 0.000020 mg/m3 (subchronic, RAIS, inhalation, 7)
 - NIVE POD not calculated
- Quantitative Hazard Values**
- Minimum oral POD: 0.0024 mg/kg-day (subchronic, ToxRefDB, oral, 7)
 - No inhalation POD values
 - Lowest Observed Bioactivity Equivalent Level: Cyp2b1 , Cyp2b1 , CYP2J2 , CYP2C19 , CYP2B6
- Cancer Information**
- No cancer slope factor
 - No inhalation unit risk value
 - Carcinogenicity data available: IARC: Group 3. Not classifiable as to its carcinogenicity to humans EPA OPP cancer class: C NLM ToxNet HSDB carcinogenicity warning University of Maryland carcinogenicity warning;
 - No genotoxicity findings reported
- Reproductive Toxicology**
- 51 Reproductive toxicity PODs available
- Chronic Toxicology**
- 215 Chronic toxicity PODs available
- Subchronic Toxicology**
- 32 Subchronic toxicity PODs available
- Developmental Toxicology**
- No developmental toxicity data available.
- Acute Toxicology**
- 907 Acute toxicity PODs available
- Subacute Toxicology**
- No subacute toxicity data available.
- Neurotoxicology**
- No neurotoxicology data available.
- Endocrine System**
- No significant ER or AR activity.
- ADME**
- No HTTK data
- Fate and Transport**
- No bioaccumulation concern.
 - No volatility concern.
 - Biodegradation predictions are available
 - SCF predictions are available
 - Vapor Pressure predictions are available
- Exposure**
- Exposure estimates are available based on NHANES and SEEM
- AOP Information**
- AOP Links: 36, 58, 60, 61, 66, 124, 150, 163, 175, 187, 195, 200
- Other Notes**
- No water quality values available.
 - 20 Air quality values available
 - 51 Occupational exposure values available.

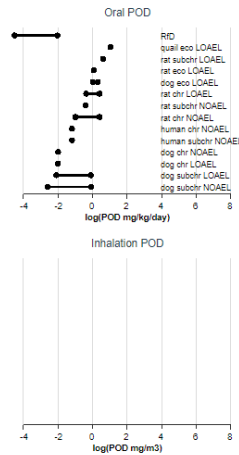
REGIONAL SCREENING

Class	THQ	Value
screening level (residential soil) (mg/kg-day)	THQ=1	380
screening level (residential soil) (mg/kg-day)	THQ=0.1	38
screening level (industrial soil) (mg/kg-day)	THQ=1	4600
screening level (industrial soil) (mg/kg-day)	THQ=0.1	460
screening level (tap water) (ug/L)	THQ=1	86
screening level (tap water) (ug/L)	THQ=0.1	8.6
GIABS (mg/kg-day)	-	1
ABS (mg/kg-day)	-	0.1
risk-based SSL (mg/m3)	THQ=1	0.43
risk-based SSL (mg/m3)	THQ=0.1	0.043
RfDs (mg/kg-day)	-	0.008

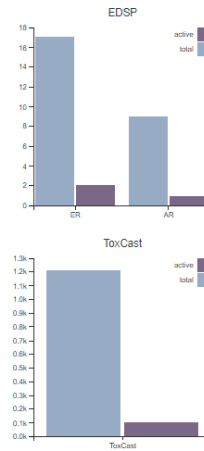
PHYSICHEM PARAMETERS



POINT-OF-DEPARTURE PLOTS

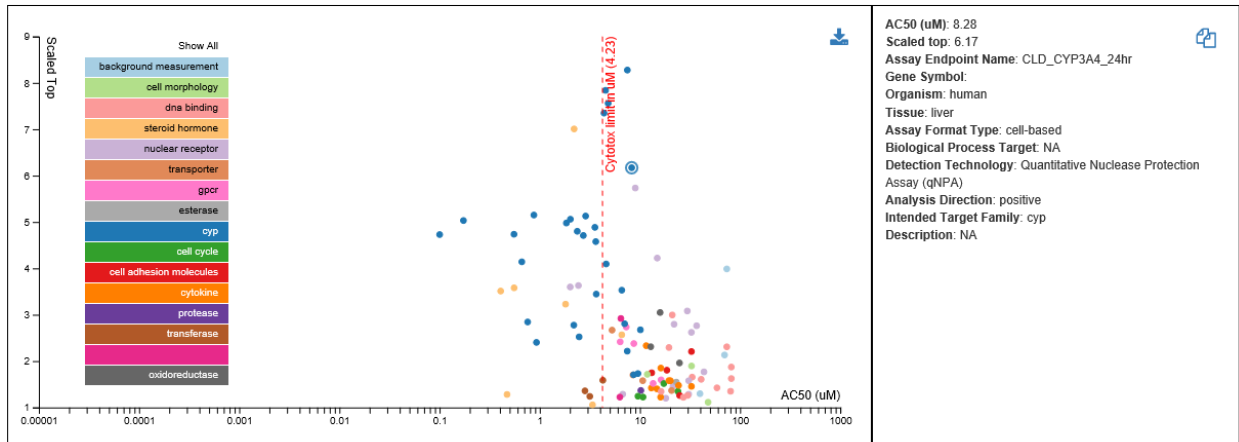


ASSAY PLOTS



TOXCAST DATA

ASSAY DETAILS



Acronyms and Definitions:

ADME – absorption, distribution, metabolism, and excretion: describes the disposition of a compound within an organism¹.

AOP – adverse outcome pathway: an analytical construct that describes a sequential chain of causally linked events at different levels of biological organisation that lead to an adverse health or ecotoxicological effect².

BCF – bioconcentration factor: a measure of the extent of chemical sharing between an organism and the surrounding environment³.

BMD – benchmark dose: A dose or concentration that produces a predetermined change in response rate of an adverse effect (called the benchmark response or BMR) compared to background³.

EDSP – endocrine disruptor screening program: US EPA program to screen pesticides, chemicals, and environmental contaminants for their potential effect on estrogen, androgen and thyroid hormone systems⁴.

LOAEL – lowest-observed-adverse-effect level: The lowest exposure level at which there are biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group³.

NOAEL – no-observed-adverse-effect level: The highest exposure level at which there are no biologically significant increases in the frequency or severity of adverse effect between the exposed population and its appropriate control; some effects may be produced at this level, but they are not considered adverse or precursors of adverse effects³.

POD – point of departure: The dose-response point that marks the beginning of a low-dose extrapolation. This point can be the lower bound on dose for an estimated incidence or a change in response level from a dose-response model (BMD), or a NOAEL or LOAEL for an observed incidence, or change in level of response³.

RfD – reference dose: An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used³.

RfC – reference concentration: An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark concentration, with uncertainty factors generally applied to reflect limitations of the data used³.

RSL – regional screening level: risk-based concentrations derived from standardized equations combining exposure information assumptions with EPA toxicity data⁵.

THQ – target hazard quotient: the ratio of the potential exposure to a substance and the level at which no adverse effects are expected. If the THQ is calculated to be less than 1, then no adverse health effects are expected as a result of exposure. If the THQ is greater than 1, then adverse health effects are possible⁵.

References:

¹Wikipedia (<https://en.wikipedia.org/wiki/ADME>)

²OECD (<http://www.oecd.org/chemicalsafety/testing/adverse-outcome-pathways-molecular-screening-and-toxicogenomics.htm>)

³US EPA Integrated Risk Information System (IRIS) Glossary

(https://iaspub.epa.gov/sor_internet/registry/termreg/searchandretrieve/glossariesandkeywordlists/search.do?details=&vocabName=IRIS%20Glossary#formTop)

⁴US EPA EDSP (<https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-edsp-overview>)

⁵US EPA Regional Screening Levels Frequent Questions (<https://www.epa.gov/risk/regional-screening-levels-frequent-questions#FQ1>)

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