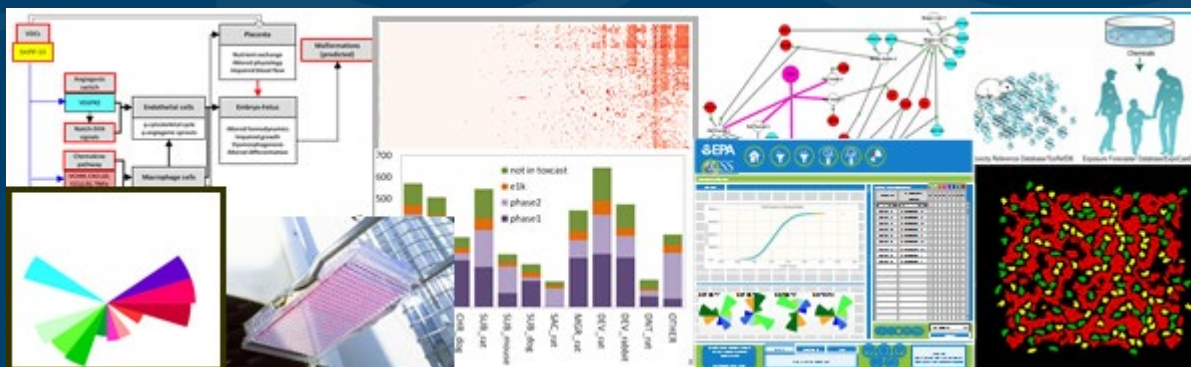


Going for Your First Drive in Toxicology: Using the Comptox Chemicals Dashboard



CDI
Baltimore MD
March 10, 2019

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US Environmental Protection Agency

The views expressed in this presentation are those of the author and do not necessarily reflect the views or policies of the U.S. EPA

Regulatory Agencies Make a Broad Range of Decisions on Chemicals...



Harmful algal bloom initiative funds additional research

Written by J. Patrick Taten
February 16, 2018
Hits: 472

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The Ohio Department of Higher Education (ODHE) has awarded \$3.5 million in funding for 21 additional projects in its ongoing Harmful Algal Bloom Research Initiative.

HABRI is a statewide response to the threat of harmful algal blooms that arose out of the 2014 Toledo drinking water crisis, where elevated levels of the algal toxin microcystin in Lake Erie threatened water supplies for more than 500,000 people in Northwest Ohio.

"I am proud of the work that is being done, and that researchers from our public and private higher education institutions continue to work together to address this issue," said Ohio Department of Higher Education Chancellor John Carey. "Using the talent of Ohio's researchers and students to solve pressing problems makes sense."

Montana preparing to take over after \$600M EPA asbestos cleanup near Libby

Associated Press Sep 21, 2017

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Widespread asbestos contamination has killed an estimated 400 people in

TheIntelligencer

Congress budget deal sets table for \$7M PFAS study

By Kyle Bagenstose

Posted Feb 9, 2018 at 3:18 PM

Updated Feb 9, 2018 at 3:18 PM

But the nationwide health study, which could well include Bucks and Montgomery County residents exposed to toxic chemicals in drinking water, isn't a done deal.

ChemicalWatch

GLOBAL RISK & REGULATION NEWS

ToxCast and Tox21 high-throughput data identify potential EDCs

Fifra SAP set to discuss androgen receptor model

23 November 2017 / Alternative approaches to testing, EDCs, United States

ToxCast¹ and Tox21² high-throughput screening data provide a "rapid and effective resource" for identifying substances with the potential to activate human oestrogen (estrogen) receptors (ERs), according to a top US Environmental Protection Agency (EPA) official.

Stan Barone, acting director of the EPA's Office of Chemical Safety and Pollution Prevention, was describing progress in using ER high-throughput assays for tier 1 of the Endocrine Disruptor Screening Program (EDSP) at a workshop on toxicity



The New York Times

https://nyti.ms/KIDgRu

U.S.

Thousands Without Water After Spill in West Virginia

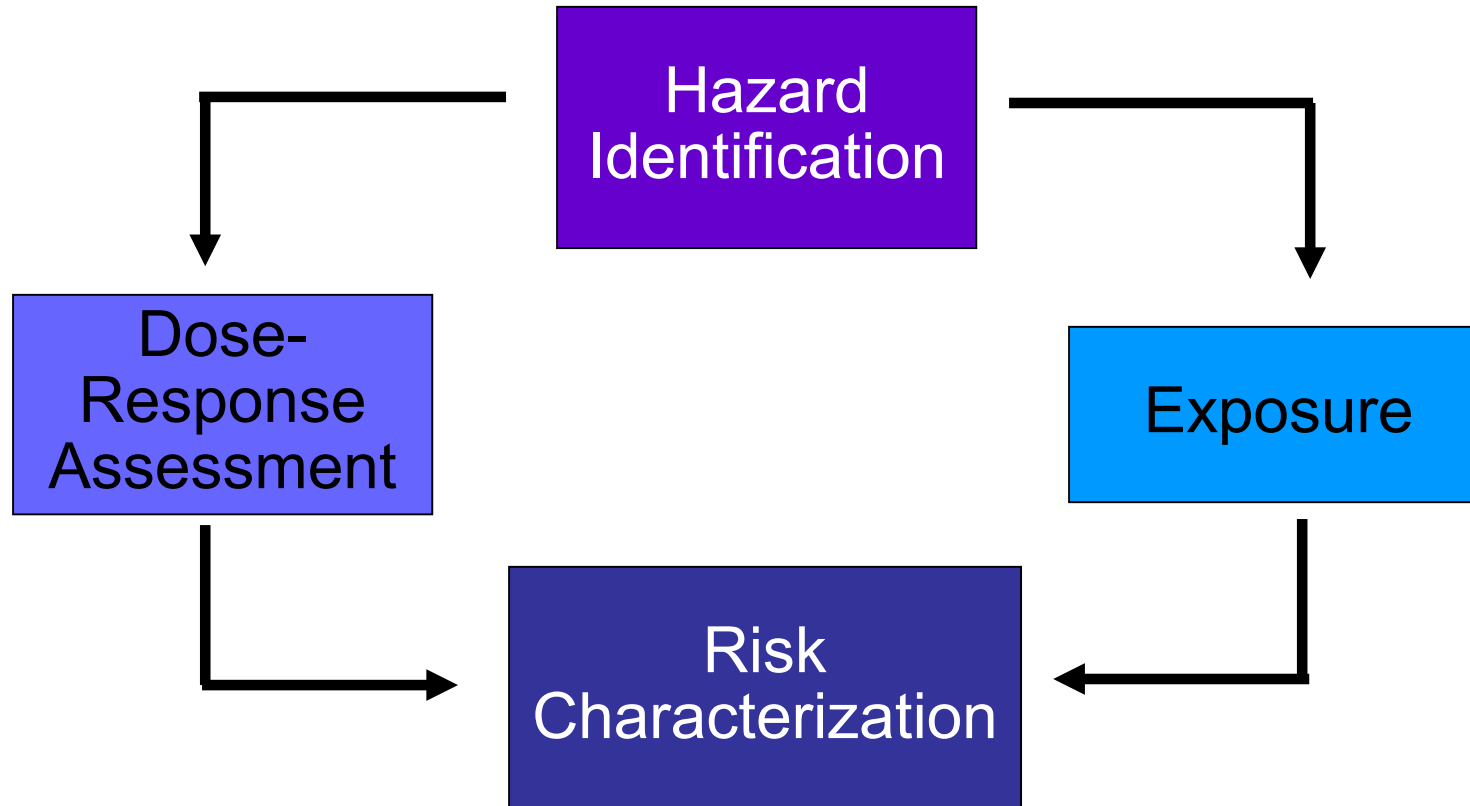
By TRIP GABRIEL JAN. 10, 2014

CHARLESTON, W.Va. — As 300,000 people awoke on Friday to learn that their tap water was unsafe for brushing teeth, brewing coffee or showering, residents and businesses expressed a mix of anger and anxiety in coping with an industrial accident with no clear end in sight.

Schools were closed, restaurants locked their doors and hotels refused reservations. Store shelves were quickly stripped of bottled water, and traffic snarled as drivers waited to fill jugs from tankers delivered by the National Guard.

The Risk Assessment Paradigm: The “Red Book”

Follow the National Academy of Sciences (NAS) four-step risk assessment paradigm



National Research Council's *Risk Assessment in the Federal Government: Managing the Process*, 1983.

<http://books.nap.edu/books/030904894X/html/1.html>

Covering All the Components of a 21st Century Risk Assessment

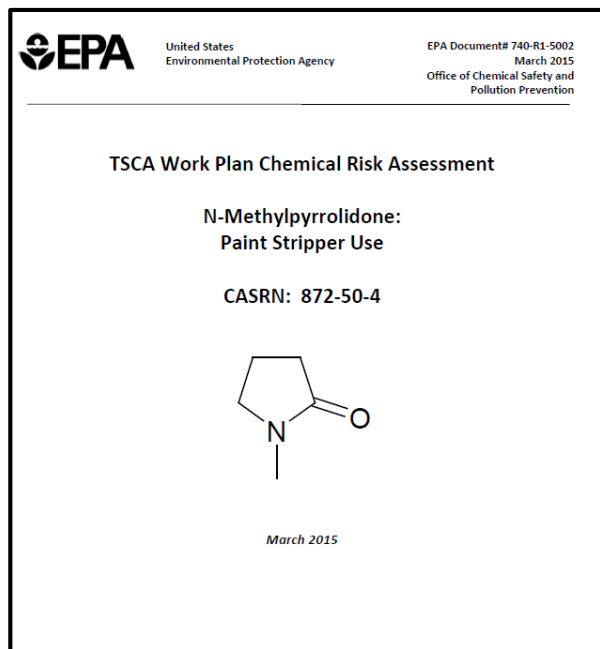


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Variability ✓

Risk Summary ✓

Uncertainty ✓

Phys Chem ✓

Exposure ✓

Hazard ✓

Dose Response ✓

PK, and PODs ✓

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

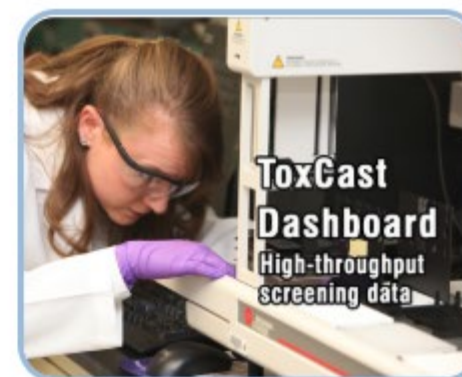
Provide Data Through Support Dashboards The CompTox Portal (<http://comptox.epa.gov>)

Environmental Topics

Laws & Regulations

About EPA

Search EPA.gov



Chemistry Data

Bioactivity Data

**National Center for
Computational Toxicology**

Literature Data

10 records

Example Exec Summary

Quantitative Risk Assessment Values

- ✓ IRIS values available [↗](#)
- ✗ No PPRTV values
- ✓ EPA RSL values available [↗](#)
- ✓ Minimum RfD: 0.050 mg/kg-day (chronic, IRIS, oral, 8) [↗](#)
- ✗ No RfC calculated
- ✗ IVIVE POD not calculated

Quantitative Hazard Values

- ✓ Minimum oral POD: 3.8 mg/kg-day (reproductive, HPVIS, oral, 6) [↗](#)
- ✗ No inhalation POD values
- ✓ Lowest Observed Bioactivity Equivalent Level: CYP1A1, CYP1A2, Tpo, ESR2, ESR1, ESR1, NR1I3, PPARA, NR1I2, Cyp2c11, MMP3, Esr1

Cancer Information

- ✗ No cancer slope factor
- ✗ No inhalation unit risk value
- ✓ Carcinogenicity data available: University of Maryland carcinogenicity warning; [↗](#)
- ✗ No genotoxicity findings reported

Reproductive Toxicology

- ✓ 200 Reproductive toxicity PODs available [↗](#)

Chronic Toxicology

- ✓ 340 Chronic toxicity PODs available [↗](#)

Subchronic Toxicology

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

Developmental Toxicology

- ✓ 6 Developmental toxicity PODs available [↗](#)

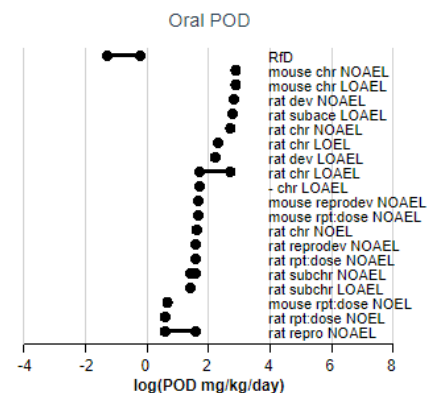
Acute Toxicology

- ✓ 391 Acute toxicity PODs available [↗](#)

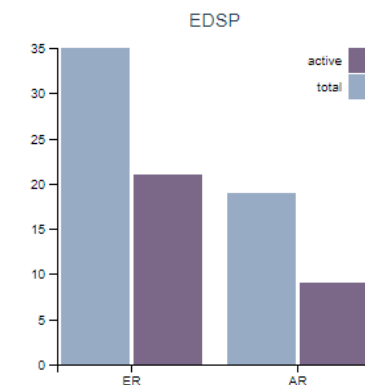
Subacute Toxicology

- ✓ 1 subacute toxicity PODs available [↗](#)

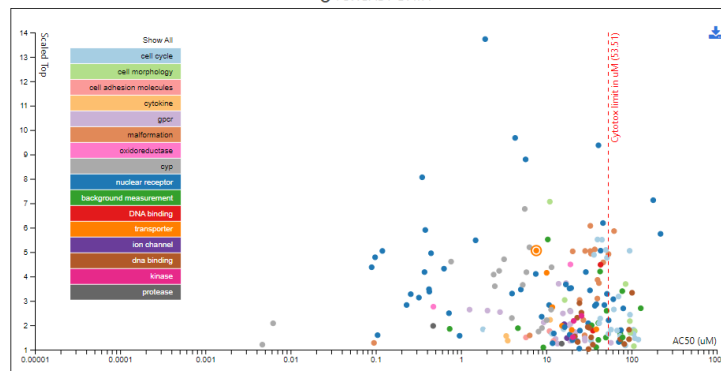
POINT-OF-DEPARTURE PLOTS



ASSAY PLOTS



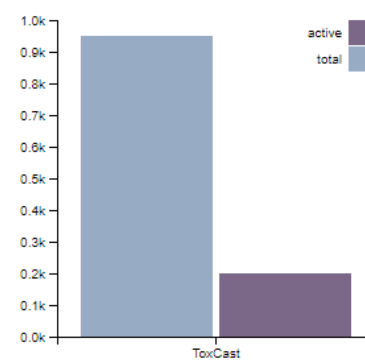
TOXCAST DATA



ASSAY DETAILS

ACS0 (uM): 7.64
Scaled top: 5.06
Assay Endpoint Name: NVS_TR_hDAT
Gene Symbol: SLC6A3
Organism: human
Tissue: NA
Assay Format Type: biochemical
Biological Process Target: receptor binding
Detection Technology: Filter-based radiodetection
Analysis Direction: positive
Intended Target Family: transporter
Description: Data from the assay component NVS_TR_hDAT was analyzed into 1 assay endpoint. This assay endpoint, NVS_TR_hDAT, was analyzed in the positive fitting direction relative to DMSO as the negative control and baseline of activity, _x0000_x0000. Using a type of binding reporter, loss-of-signal activity can be used to understand changes in the binding as they relate to the gene SLC6A3_x0000_x0000. Furthermore, this assay endpoint can be referred to as a primary readout, because the performed assay has only produced 1 assay endpoint, _x0000_x0000. To generalize the intended target to other related targets, this assay endpoint is annotated to the "transporter" intended target family, where the subfamily is "neurotransmitter transporter".

ToxCast



Thank You for Your Attention!



EPA's National Center for Computational Toxicology