

ToxCast, SeqAPASS, and EcoTox: A multi-tool case study

Introduction: Claire Holesovsky

ToxCast: Madison Feshuk, MPHTM

SeqAPASS: Marissa Brickley & Dr. Carlie LaLone

EcoTox Knowledgebase: Dr. Jennifer Olker

Outline & Disclaimer

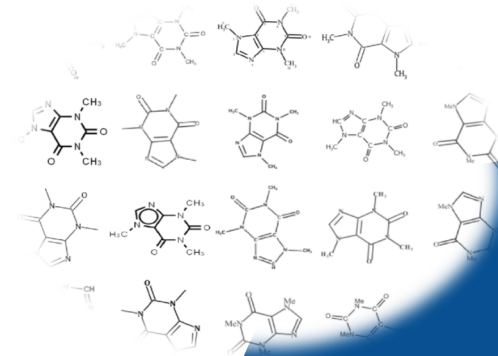
- Introduction
- ToxCast
- SeqAPASS
- ECOTOX
- Questions

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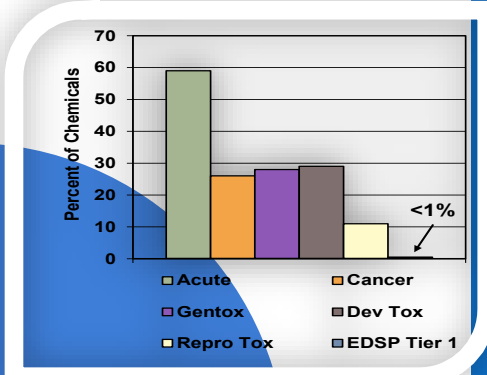
Company or product names do not constitute endorsement by US EPA.

Need for Alternative Approaches for Next-Gen Risk Assessment

- Several limitations to traditional *in vivo* toxicology testing
- EPA needs rapid and efficient methods to prioritize, evaluate, and regulate thousands of chemicals in commerce
- New Approach Methods (NAMs) can provide information on hazard + exposure to inform research and decisions



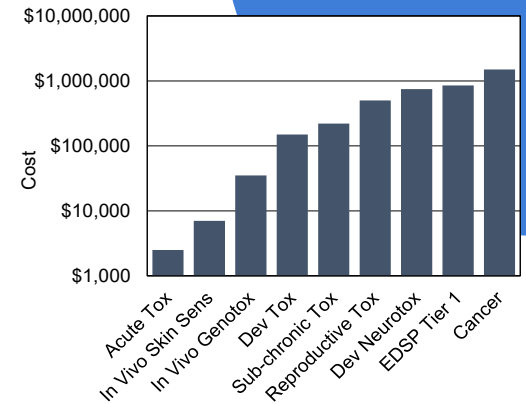
Too Many Chemicals



Time

Modified from Judson et al., EHP 2010

Cost



Ethics



Introduction

- ToxCast data are predominantly based on mammalian models, but still may have value in ecological risk assessments.
- This case study will explore how one may review ToxCast derived values in combination with curated values from Ecotoxicology Knowledgebase (ECOTOX) as well as cross-species applicability through Sequence Alignment to Predict Across Species Susceptibility (SeqAPASS) tool.
- The process can be adapted for any given chemical and target depending on available data in either database.
 - Today's chemical of interest will be 17alpha-Ethinylestradiol (EE2, DTXSID5020576).

Tools Overview



Toxicity Forecasting (ToxCast)
Accessible Bioactivity Data for Toxicology

Consider activity and potency estimates for diverse biological and chemical targets (mammalian focus)

<https://www.epa.gov/comptox-tools/toxicity-forecasting-toxcast>



Sequence Alignment to Predict Across Species Susceptibility (SeqAPASS)

Consider protein target similarities for cross species extrapolation of chemical toxicity results

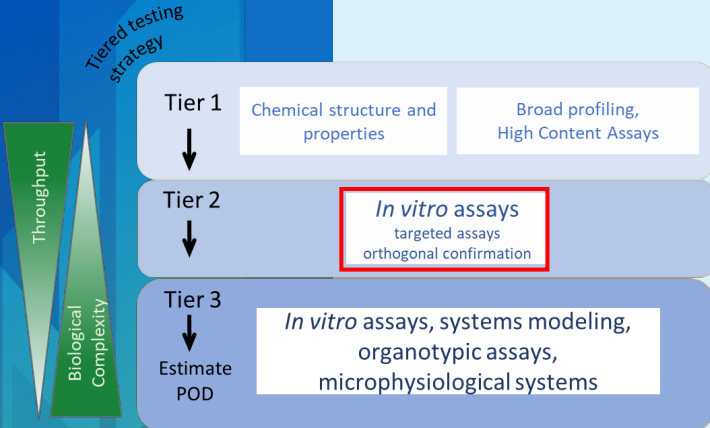
<https://seqapass.epa.gov/seqapass/>



Ecotoxicology Knowledgebase (ECOTOX)

Consider available chemical environmental toxicity data on aquatic and terrestrial species from literature

<https://cfpub.epa.gov/ecotox/>



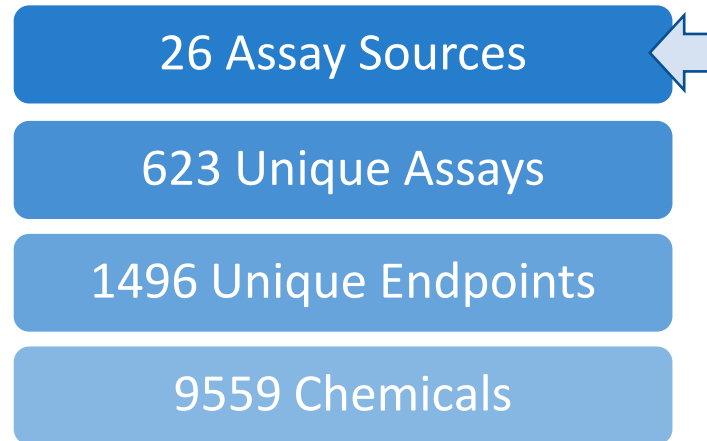
Toxicity Forecasting (ToxCast)

Madison Feshuk

(with contributions from Katie Paul Friedman)

ToxCast Database Coverage

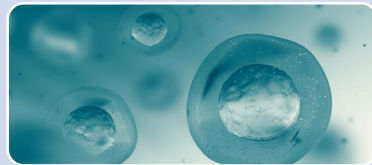
The Toxicity Forecaster (ToxCast) program curates and makes publicly available targeted bioactivity screening data. Latest database release (v4.1) includes:



← Including a TOX21 assay source for data generated by the TOX21 program



Diverse biology with **over 500 mapped gene targets**, including:



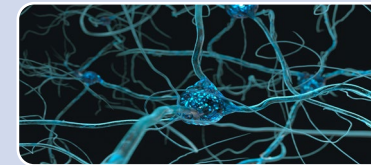
Endocrine-Related:
Estrogen Receptor,
Androgen Receptor,
Thyroid,
Steroidogenesis



Cellular Signaling Pathways:
Cytotoxicity,
Proliferation, Stress,
Mitochondrial Toxicity

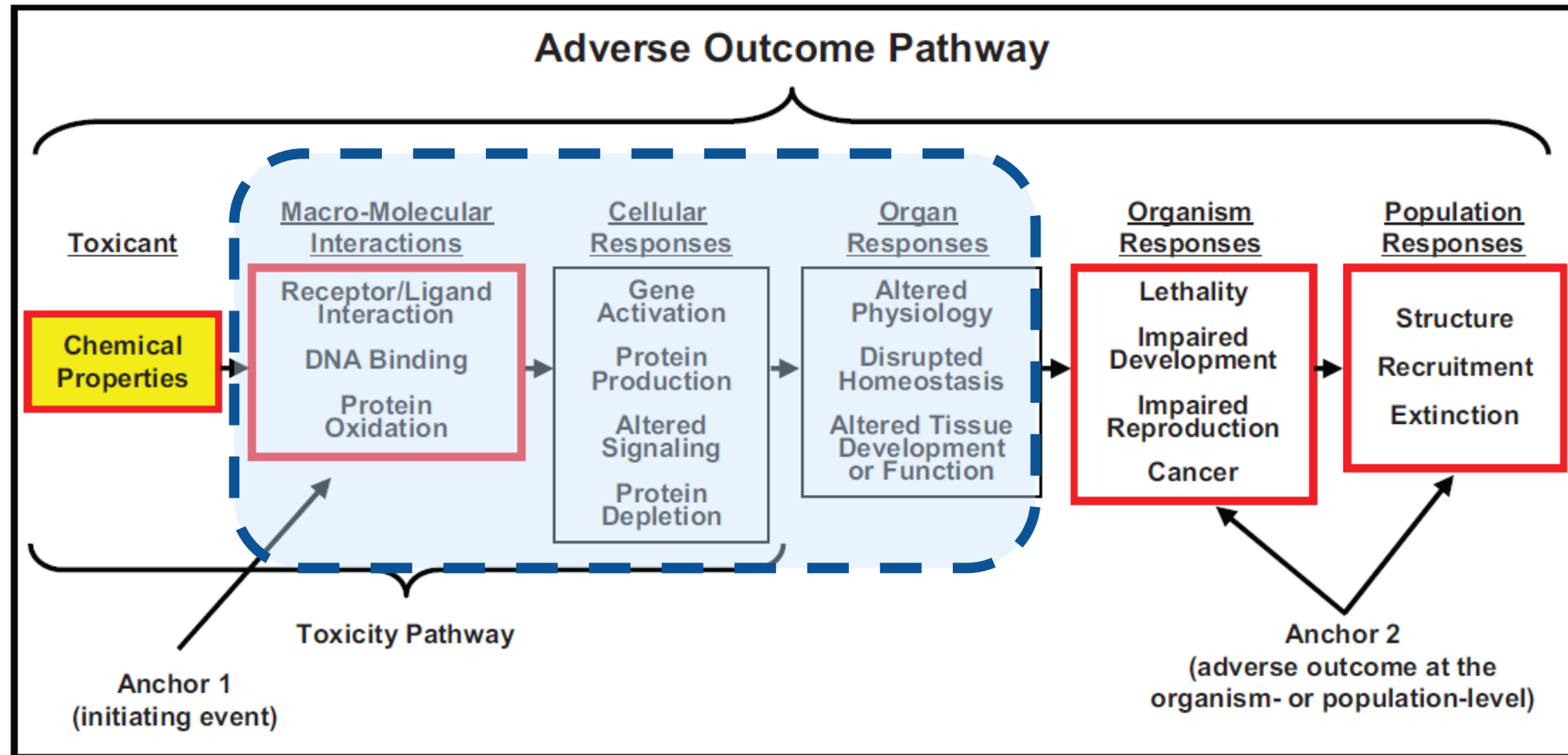


Protein Interactions:
Receptors,
Transporters, Ion Channels, Enzymes



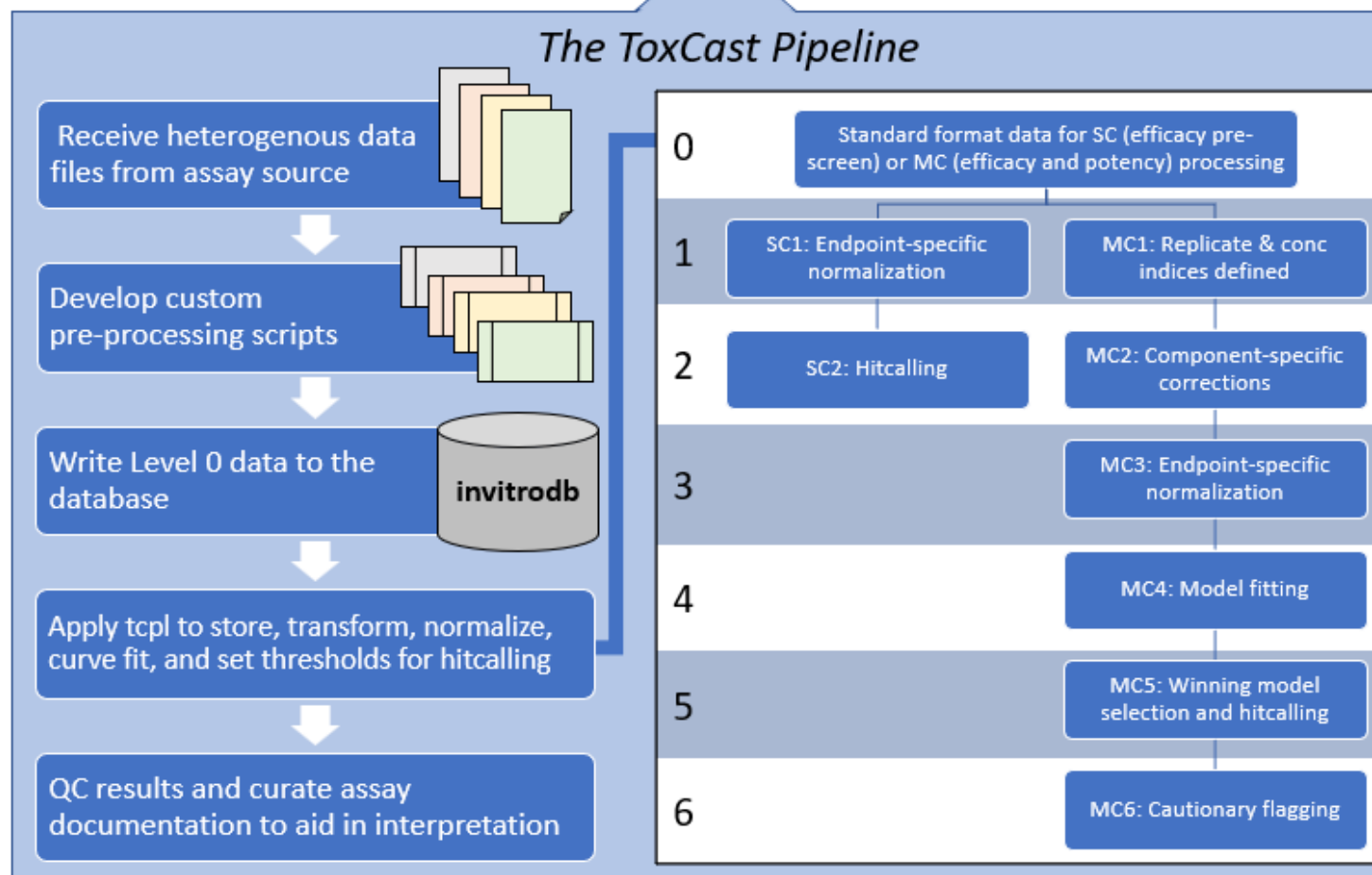
Complex Responses, e.g.
Immune Response,
Development,
Neurotoxicity, etc.

Heterogeneous targeted NAMs in ToxCast address a range of event types in the AOP framework



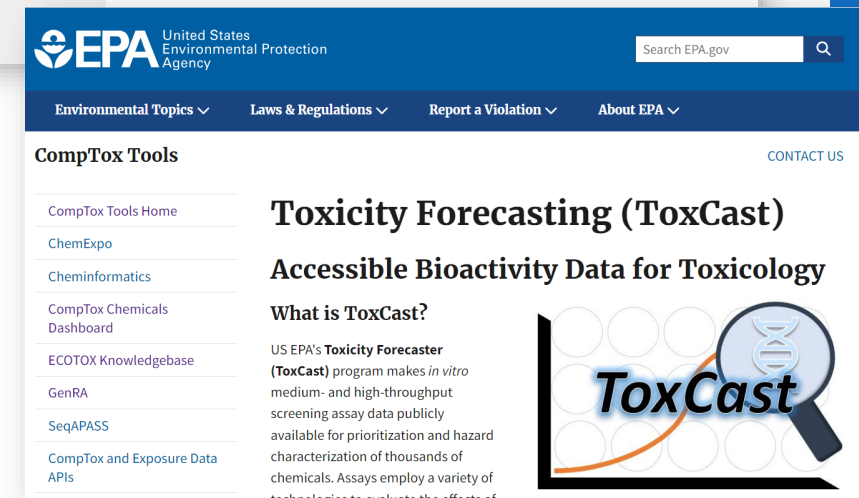
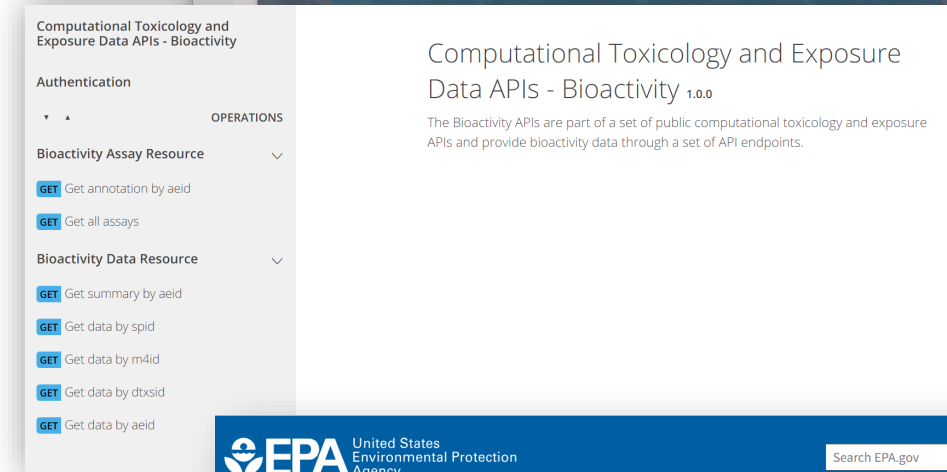
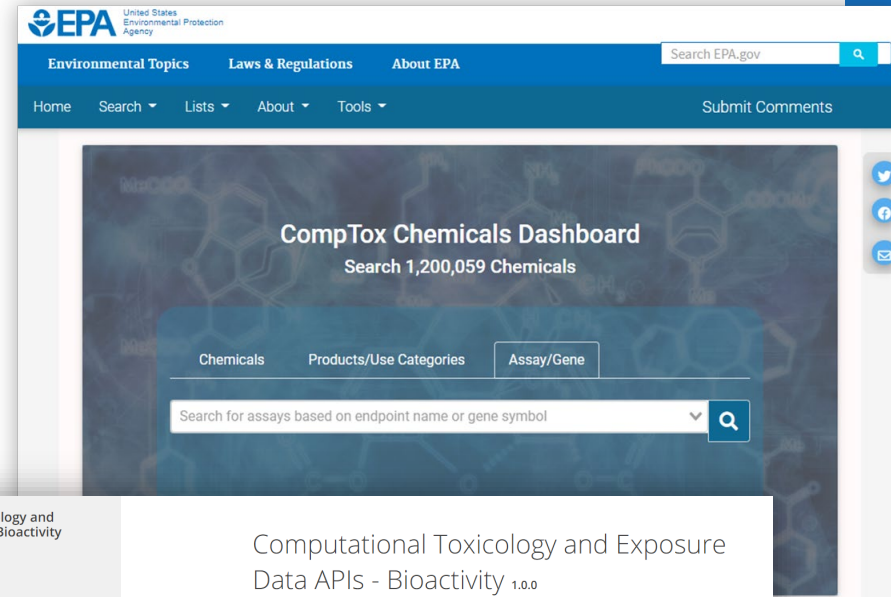
ToxCast Pipeline and Database

Process Overview



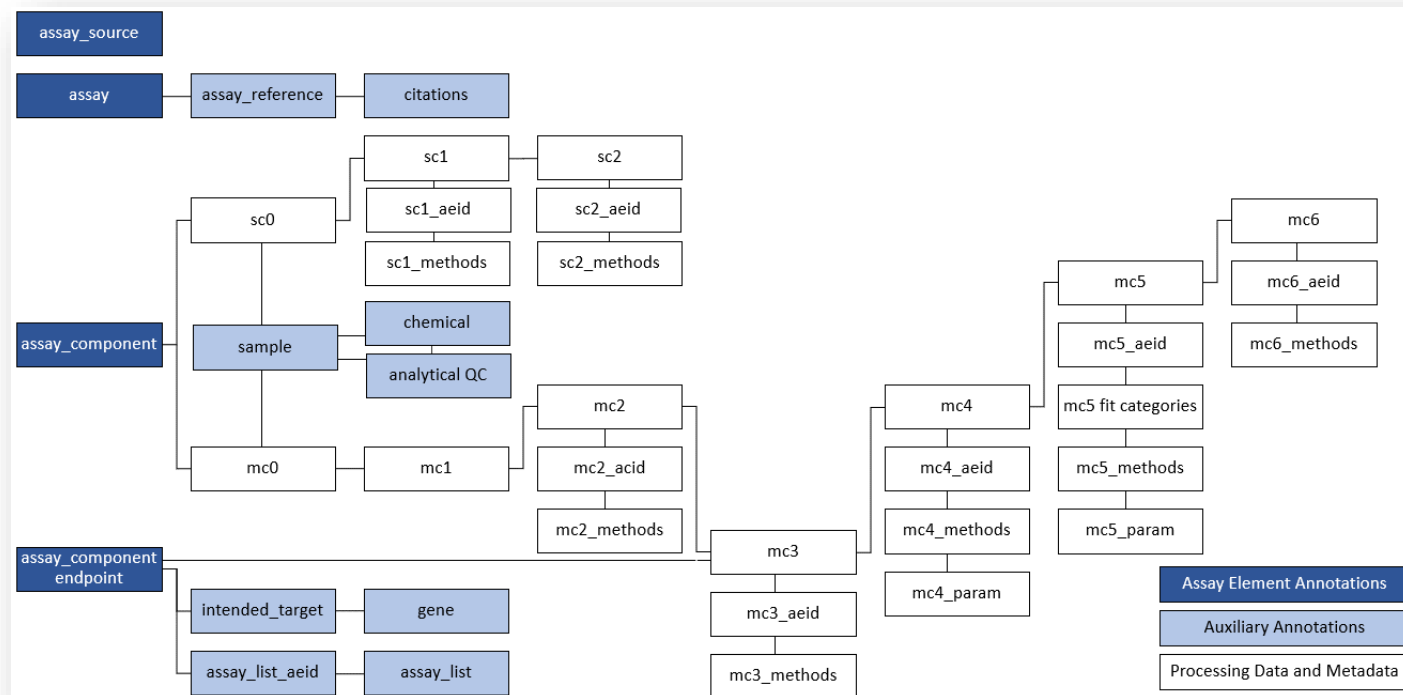
Exploring ToxCast

- Ongoing work has also focused on augmenting and diversifying how ToxCast data can be accessed for our users.
- ToxCast data is accessible via:
 - [CompTox Chemicals Dashboard](#)
 - [Computational Toxicology and Exposure - Bioactivity APIs](#)
 - [Downloadable Data Pages](#)



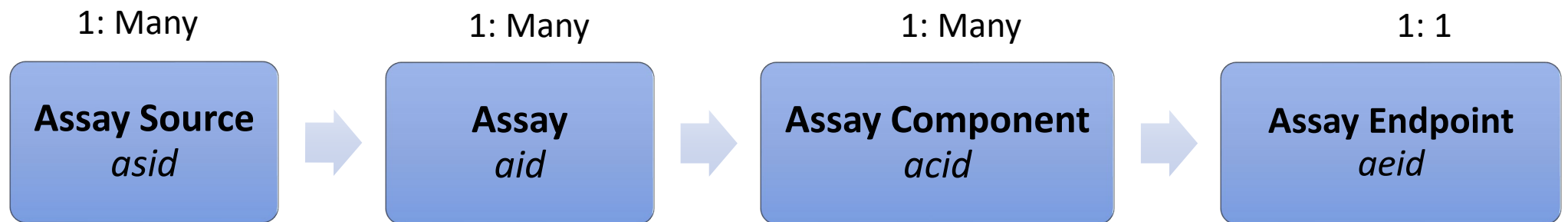
Database Structure

- ToxCast covers diverse biological space and annotations help us flexibly aggregate and differentiate processed ToxCast data for user needs
- The ToxCast database (invitrodb) captures the following types of information:
 - Assay Element Annotations
 - Auxiliary Annotations
 - Processing Data and Metadata



Assay Element Annotations

- Each annotation is assigned as a feature to an assay element level:
 - **Assay Source:** *Who* conducted the assay
 - **Assay:** *What* assay platform was used
 - **Assay Component:** “Raw” readout of *what* was measured
 - **Assay (component) Endpoint:** *How* the measurement is interpreted (i.e. normalized component data)

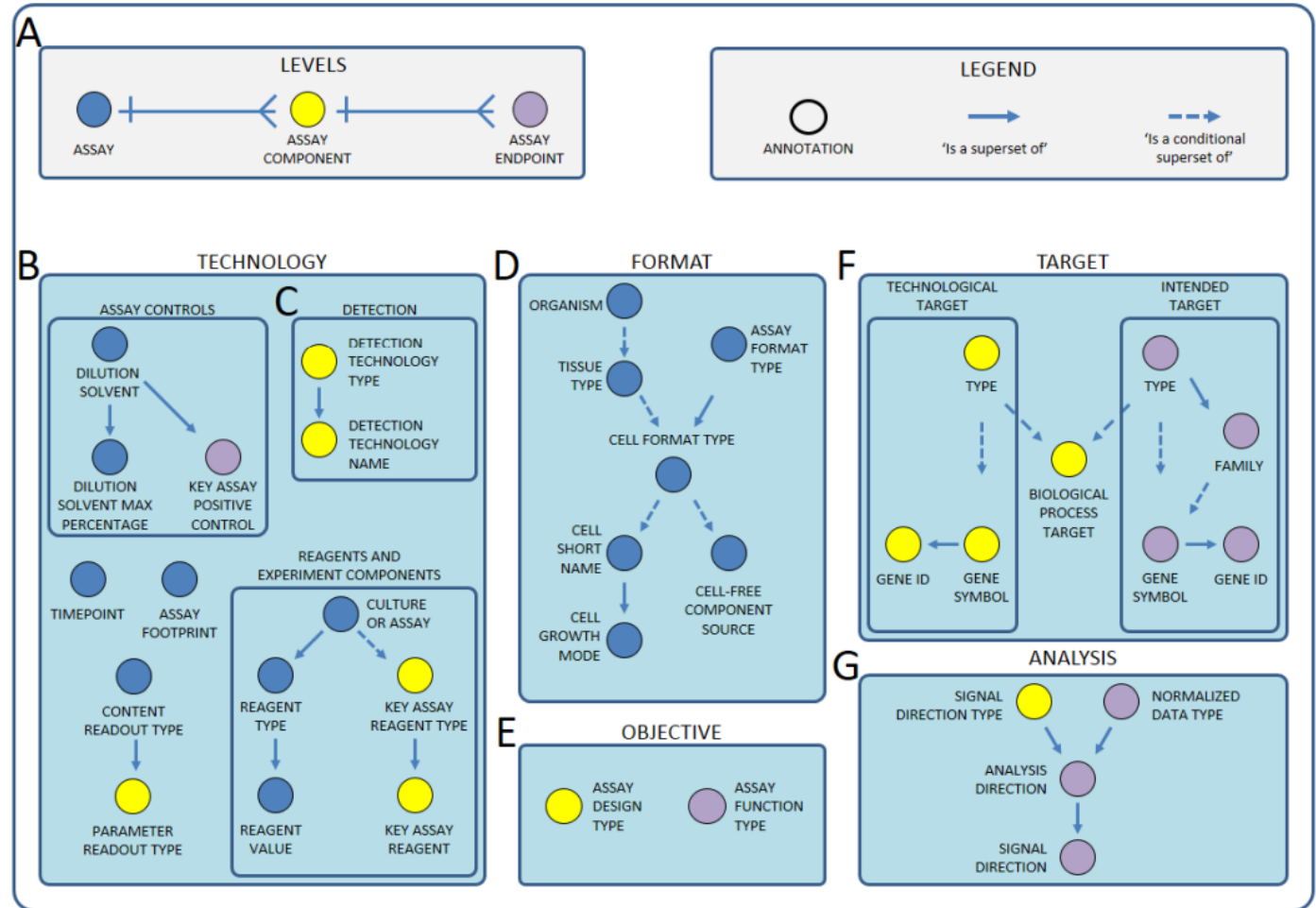


Note: All processing with tcpl occurs at the assay component or assay endpoint, depending on the processing type (single-concentration or multiple-concentration) and level. **No data is stored at the assay or assay source level.**

Assay Element Annotations

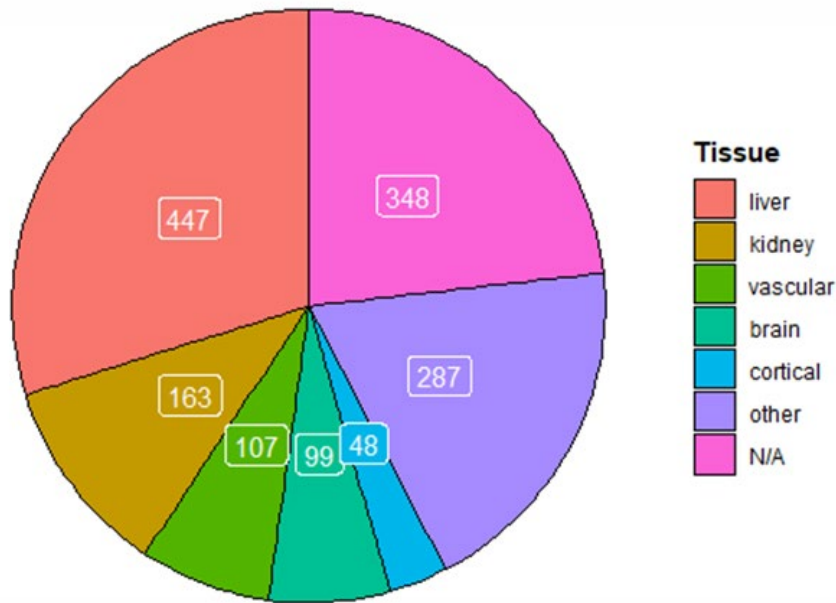
- Annotations follow Bioassay Ontology (BAO) framework capture four types of information:

- Identification (A)
 - Design (B-E)
 - Technology
 - Format
 - Objective
 - Target (F)
 - Technological target
 - Intended target
 - Biological process
 - Analysis (G)



Assay Element Annotations

- Most annotations employ controlled vocabulary within the database
- Some annotations are hierarchical
 - e.g., general 'intended_target_family' and more specific 'intended_target_family_sub'



Tissue of origin across all assays



Intended_target_family frequency across all endpoints

Auxiliary Annotations

- Capture additional information, including:
 - Assay list presence
 - Linkages to relevant Adverse Outcome Pathways (AOPs) and Key Events (KEs)
 - Relevant gene identifier(s) from National Center for Biotechnology Information (NCBI)
 - Reagents or experimental conditions
 - Publications describing assay design or results

The screenshot displays a database management interface. On the left, a 'SCHEMAS' panel shows a tree view of the 'invitrodb' database, listing various tables such as 'assay', 'assay_component', 'assay_component_descriptions', 'assay_component_endpoint', 'assay_component_endpoint_descriptions', 'assay_component_map', 'assay_descriptions', 'assay_list', 'assay_list_aeid', 'assay_reagent', 'assay_reagent_armitage', 'assay_reference', 'assay_source', 'chemical', 'chemical_assay_count', 'chemical_library', 'citations', 'class', 'cytotox', 'etl_metadata', 'flyway_schema_history', 'gene', and 'intended_target'. The main area shows a SQL query: `1 • select * from invitrodb.assay_component_endpoint;`. Below the query is a 'Result Grid' with the following data:

aeid	acid	assay_component_endpoint_name	export_ready	internal_ready	assay_component_endpoint_desc	assay_function_type	normalized_data_t
2	1	ACEA_ER_80hr	1	1	Data from the assay component ACEA_ER_80h...	signaling	percent_activity
4	2	APR_HepG2_CellCycleArrest_1hr	1	1	Data from the assay component APR_HepG2_C...	signaling	log2_fold_induction
6	3	APR_HepG2_CellLoss_1hr	1	1	Data from the assay component APR_HepG2_C...	viability	log2_fold_induction
8	4	APR_HepG2_MicrotubuleCSK_1hr	1	1	Data from the assay component APR_HepG2_M...	signaling	log2_fold_induction
10	5	APR_HepG2_MitoMass_1hr	1	1	Data from the assay component APR_HepG2_M...	signaling	log2_fold_induction
12	6	APR_HepG2_MitoMembPot_1hr	1	1	Data from the assay component APR_HepG2_M...	signaling	log2_fold_induction
14	7	APR_HepG2_MitoticArrest_1hr	1	1	Data from the assay component APR_HepG2_M...	signaling	log2_fold_induction
16	8	APR_HepG2_NuclearSize_1hr	1	1	Data from the assay component APR_HepG2_N...	signaling	log2_fold_induction
18	9	APR_HepG2_P-H2AX_1hr	1	1	Data from the assay component APR_HepG2_P...	signaling	log2_fold_induction
20	10	APR_HepG2_p53Act_1hr	1	1	Data from the assay component APR_HepG2_p...	signaling	log2_fold_induction
22	11	APR_HepG2_StressKinase_1hr	1	1	Data from the assay component APR_HepG2_S...	signaling	log2_fold_induction
24	12	APR_HepG2_CellCycleArrest_24hr	1	1	Data from the assay component APR_HepG2_C...	signaling	log2_fold_induction
26	13	APR_HepG2_CellLoss_24hr	1	1	Data from the assay component APR_HepG2_C...	viability	log2_fold_induction
28	14	APR_HepG2_MicrotubuleCSK_24hr	1	1	Data from the assay component APR_HepG2_M...	signaling	log2_fold_induction
30	15	APR_HepG2_MitoMass_24hr	1	1	Data from the assay component APR_HepG2_M...	signaling	log2_fold_induction

Demo

Madison Feshuk

Demo

- Toxicity Forecasting (ToxCast) home page <https://www.epa.gov/comptox-tools/toxicity-forecasting-toxcast>
 - Exploring ToxCast Data → Download Database Package
- Tcpl CRAN: <https://cran.r-project.org/web/packages/tcpl/index.html>
- Tcpl GitHub: <https://github.com/USEPA/CompTox-ToxCast-tcpl>
- CCD: <https://comptox.epa.gov/dashboard/>
 - Single Chemical Search "BPA" >Navigate to ToxCast tab>
 - ToxCast Summary plot (AC50 vs Scaled Top (max modeled response/cutoff), cytotoxicity burst median and lower bounds)
 - Bioactivity grid (Adding additional fields like Annotations, Inspecting plots)
 - Search by gene "estrogen"
 - Search by assay "ACEA_ER_80hr"
 - Lists of Assay vs Chemicals > Send to Batch
 - Batch Search Export of ToxCast AC50 values
- CCTE APIs home <https://api-ccte.epa.gov/docs/> (Must request API key to access)
- Bioactivity APIs <https://api-ccte.epa.gov/docs/bioactivity.html>
 - Overview of different request types
- ccdR for accessing APIs <https://cran.r-project.org/web/packages/ccdR/index.html>
- EE2 Case Study
 - Single Chemical Search>ToxCast Summary
 - Filter for SeqAPASS linkages and sort for lowest AC50 value
 - Consider TOX21_ERa_LUC_VM7_Agonist_10nM_ICI182780
 - TOX21_ERa_LUC_VM7_Agonist_10nM_ICI182780 was designed to measure changes to bioluminescence signals produced from an enzymatic reaction involving the key substrate [One-Glo] in the presence of an ER antagonist. Changes are indicative of transcriptional gene expression that may not be due to direct regulation by the human estrogen receptor 1

CompTox Chemicals Dashboard (CCD)

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

- CCD's ToxCast bioactivity module presents a view of potency and relative efficacy metrics across ToxCast endpoints for chemicals of interest
- Users can easily sort, filter, and export ToxCast results and assay descriptions
- Notable updates in the CCD v2.3 release (December 2023) include:
 - Data was refreshed to invitrodb v4.1
 - ToxCast Summary tab is now a single tab that combines the previous ToxCast Summary and ToxCast Conc. Response tabs
 - Bioactivity Summary Grid includes v4.1 information in new columns, including benchmark dose (BMD), benchmark response (BMR), and Continuous Hitcall

• *Example on right: Bisphenol A*

<https://comptox.epa.gov/dashboard/chemical/invitrodb/DTXSID7020182>



Filtering ToxCast Data on the CCD CompTox Chemicals Dashboard:

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

- CCD's ToxCast bioactivity module presents a view of potency and relative efficacy metrics across ToxCast endpoints for chemicals of interest
- Users can easily sort, filter, and export ToxCast results and assay descriptions
- Example: Consider BPA [DTXSID7020182](#)
 - Select ☰ in Bioactivity Summary Grid column headers to add additional annotation columns ☰☰☰
 - Explore!
 - Below shows results filtered to **Actives in human ESR1 cell-based assays**

<input type="checkbox"/>	Name ↑	Hit Call ↓↑	Assay Lists ▾ ↓↑	Gene Symbol ▾ ↓↑ ☰	Organism ▾ ↓↑	Tissue ↓↑	Cell Format ▾ ↓↑	Intended Target Family ↓↑
	<input type="text"/>	<input type="text"/>	(1) EDSP ER ▾	ESR1	human	<input type="text"/>	cell line	<input type="text"/>
<input type="checkbox"/>	ACEA_ER_80hr	Active	EDSP ER	ESR1	human	breast	cell line	nuclear receptor
<input type="checkbox"/>	ATG_ERE_CIS	Active	EDSP ER	ESR1	human	liver	cell line	nuclear receptor
<input type="checkbox"/>	ATG_ERa_TRANS	Active	EDSP ER	ESR1	human	liver	cell line	nuclear receptor
<input type="checkbox"/>	OT_ER_ERaERa_0480	Active	EDSP ER	ESR1	human	kidney	cell line	nuclear receptor
<input type="checkbox"/>	OT_ER_ERaERa_1440	Active	EDSP ER	ESR1	human	kidney	cell line	nuclear receptor
<input type="checkbox"/>	OT_ER_ERaERb_0480	Active	EDSP ER	ESR1 ESR2	human	kidney	cell line	nuclear receptor

ToxCast data are publicly accessible from the CompTox Chemicals Dashboard

Search by gene, vendor name, etc.

CompTox Chemicals Dashboard v2.2.1 Home Search Lists About Tools Submit Comments Search all data

Assay Endpoints List

Search Assay Lists

Showing 2205 of 2205 Records

Assay Component Endpoint Name	Multi Conc. Actives	Single Conc. Active	Description	Gene Symbols
ACEA_AR_agonist_80hr	161/1830 (8.80%)	-	Data from the assay component ACEA_AR_agonist_80hr was analyzed in the positive fitting direction relative to DMSO as the negative control and baseline of activity. Using a type of growth reporter, measures of the cells for gain-of-signal activity can be used to understand the signaling at the pathway-level as they relate to the gene AR. Furthermore, this assay endpoint can be referred to as a primary readout, because this assay has produced multiple assay endpoints where this one serves a signaling function. To generalize the intended target to other reliable targets, this assay endpoint is annotated to the "nuclear receptor" intended target family, where the subfamily is "steroidal".	AR
ACEA_AR_agonist_AUC_viability	609/1830 (33.28%)	-	Data from the assay component ACEA_AR_AUC_viability was analyzed in the negative fitting direction relative to DMSO as the negative control and baseline of activity. Using a type of growth reporter, loss-of-signal activity can be used to understand changes in the viability. Furthermore, this assay endpoint can be referred to as a secondary readout, because this assay has produced multiple assay endpoints where this one serves a viability function. To generalize the intended target to other reliable targets, this assay endpoint is annotated to the "cell cycle" intended target family, where the subfamily is "cytotoxicity".	
ACEA_AR_antagonist_80hr	743/1835 (40.49%)	-	Data from the assay component ACEA_AR_antagonist_80hr was analyzed in the positive fitting direction relative to DMSO as the negative control and baseline of activity. Using a type of growth reporter, measures of the cells for loss-of-signal activity can be used to understand the signaling at the pathway-level as they relate to the gene AR. Furthermore, this assay endpoint can be referred to as a primary readout, because this assay has produced multiple assay endpoints where this one serves a signaling function. To generalize the intended target to other reliable targets, this assay endpoint is annotated to the "nuclear receptor" intended target family, where the subfamily is "steroidal".	AR
ACEA_AR_antagonist_AUC_viability	707/1835 (38.53%)	-	Data from the assay component ACEA_AR_antagonist_AUC_viability was analyzed in the negative fitting direction relative to DMSO as the negative control and baseline of activity. Using a type of growth reporter, loss-of-signal activity can be used to understand changes in the viability. Furthermore, this assay endpoint can be referred to as a secondary readout, because this assay has produced multiple assay endpoints where this one serves a viability function. To generalize the intended target to other reliable targets, this assay endpoint is annotated to the "cell cycle" intended target family, where the subfamily is "cytotoxicity".	

Rows: 2,205 Total Rows: 2,205

Many users are accustomed to viewing data per substance (as identified by a DSSTox identifier, or DTXSID), but you can also identify assay endpoint data by entering from Lists > Lists of Assays. These data can be exported after loading the data for the assay.

<https://comptox.epa.gov/dashboard/assay-endpoints>

Application Programming Interfaces (APIs)

<https://api-ccte.epa.gov/docs/bioactivity.html>

Computational Toxicology and Exposure Data APIs - Bioactivity

Authentication

OPERATIONS

Bioactivity Assay Resource

- GET Get annotation by aeid
- GET Get all assays

Bioactivity Data Resource

- GET Get summary by aeid
- GET Get data by spid
- GET Get data by m4id
- GET Get data by dtxid
- GET Get data by aeid

BIOACTIVITY DATA RESOURCE

Get summary by aeid

GET /bioactivity/data/summary/search/by-aeid/{aeid}

REQUEST

PATH PARAMETERS

* aeid int32 1386

Numeric assay endpoint identifier
Examples: 1386

API Server <https://api-ccte.epa.gov>

Authentication Required (None Applied)

FILL EXAMPLE CLEAR TRY

```
curl -X GET "https://api-ccte.epa.gov/bioactivity/data/summary/search/by-aeid/1386" -H "accept: application/hal+json"
```

- APIs provide data for various use cases, including research and applications with user interfaces
- Users can avoid large data downloads by accessing invitrodb programmatically via an API
- This is a great read-only solution for users who require more flexibility than the CCD can provide
- For additional documentation, check out the [CCTE API Home Page](#) or [ccdR R package](#). More integration with tcpl is coming soon

ToxCast Data Downloads

<https://www.epa.gov/comptox-tools/exploring-toxcast-data>

- Data downloads allow users to set up their own personal instance of the invitrodb MySQL database and interact with the data directly via the tcpl R package
- This is a preferred option for more customized or programmatic ToxCast data needs, or if users want to do their own data processing

tcpl: ToxCast Data Analysis Pipeline

A set of tools for processing and modeling high-throughput and high-content chemical screening data. The package was developed for the the chemical screening data generated by the US EPA ToxCast program, but can be used for diverse chemical screening efforts.

Version: 3.1.0
Depends: R (≥ 3.5.0)
Imports: [data.table](#) (≥ 1.9.4), [DBI](#), [RMariaDB](#), [numDeriv](#), [RColorBrewer](#), [utils](#), [stats](#), [methods](#), [graphics](#), [grDevices](#), [sqldf](#), [dplyr](#), [tidyr](#), [plotly](#), [tcplfit2](#), [ggplot2](#), [gridExtra](#), [stringr](#)
Suggests: [roxygen2](#), [knitr](#), [prettydoc](#), [rmarkdown](#), [htmlTable](#), [testthat](#) (≥ 3.0.0), [reshape2](#), [viridis](#), [kableExtra](#), [colorspace](#), [magrittr](#), [vdiffr](#)
Published: 2023-10-06
Author: Richard S Judson [ctb, [ths](#)], Dayne L Filer [aut], Jason Brown [cre], Sarah E Davidson-Fritz [ORCID](#) [ctb], Madison Feshuk [ORCID](#) [ctb], Lori Kolaczowski [ctb], Kurt Dunham [ctb], Carter Thunes [ctb], Ashley Ko [ctb], Todd Zurlinden [ctb], Parth Kothiyia [ctb], Woodrow R Setzer [ctb], Matthew T Martin [ctb, [ths](#)], Katie Paul Friedman [ORCID](#) [ctb]
Maintainer: Jason Brown <brown.jason@epa.gov>
License: [MIT](#) + file [LICENSE](#)
URL: <https://github.com/USEPA/CompTox-ToxCast-tcpl>
NeedsCompilation: no
Materials: [NEWS](#)
CRAN checks: [tcpl results](#)

CompTox Tools

[CompTox Tools Home](#)

[ChemExpo](#)

[Cheminformatics](#)

[CompTox Chemicals Dashboard](#)

[ECOTOX Knowledgebase](#)

[GenRA](#)

[SeqAPASS](#)

[CompTox and Exposure Data APIs](#)

[Downloadable Computational Toxicology Data](#)

[CONTACT US](#)

Exploring ToxCast Data

On this page:

[Download ToxCast Data](#) | [ToxCast Results and Processing](#) | [Explore Use of ToxCast Data](#) | [Citations](#)

ToxCast data, once generated by labs and processed by EPA through the pipeline, can be downloaded from our website and is also available in the CompTox Chemicals Dashboard. The most recent ToxCast data is available in the [invitroDBv4.1 database](#). The database was released in September 2023. Data files from previously published ToxCast data releases are still [available for download](#). This page provides links to all relevant ToxCast chemical and assay data.

[ToxCast Chemicals](#) | [ToxCast Assays](#)

Resources

[About ToxCast](#)

[ToxCast Publications](#)

[Downloadable Computational Toxicology Data](#)

[Example Use Cases](#)

Download ToxCast Data

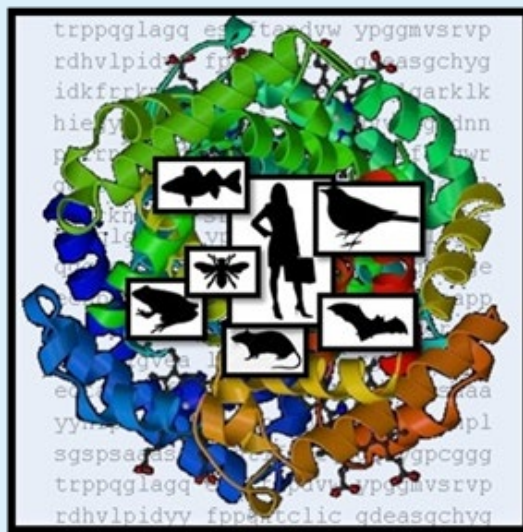
- **Most Recent InVitro Database Release (invitroDBv4.1) and Data Processing Package:** EPA's analysis of chemicals screened through high-throughput screening assays. The database release includes a MySQL database, release notes, summary files, assay information and concentration response plots. In conjunction, the ToxCast Pipeline for storing, transforming, normalizing, curve-fitting, and activity hit-calling is available as an R package, library(tcpl). Tcpl and invitrodb provide a standard for consistent and reproducible curve-fitting and data management for diverse, targeted in vitro assay data with readily available documentation, thus enabling sharing and use of these data in myriad toxicology applications.
 - [Download Database Package](#)
 - Download the tcpl R package:
 - [GitHub](#)
 - [CRAN](#)

Conclusions

- Hazard NAMs are being developed as alternatives to traditional hazard methods
- Many hazard NAM data are available in the CompTox Chemicals Dashboard, download, or API
- Each assay technology may have specific limitations, which may require user discretion for more complex interpretations of the data
- Hazard NAM data may be qualitatively and quantitatively informative in different contexts

SeqAPASS (Sequence Alignment to Predict Across Species Susceptibility)

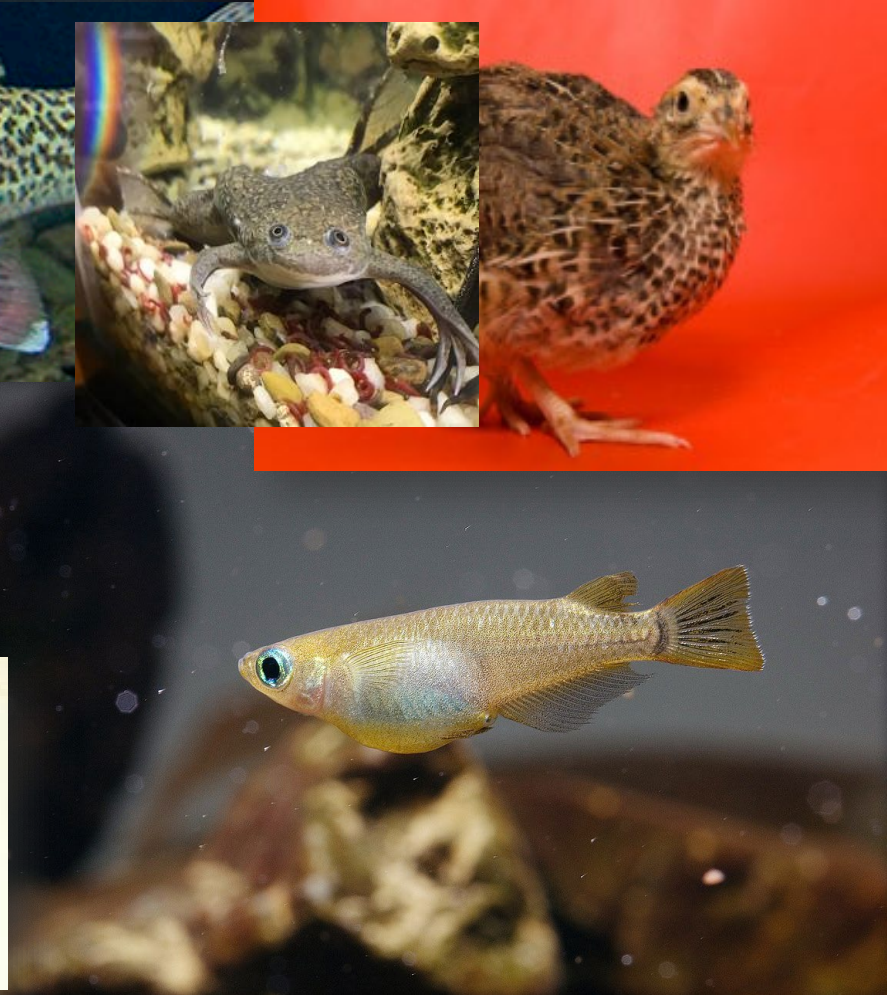
Marissa Brickley (Jensen), Carlie Lalone





Toxicity Testing to Understand Chemical Safety

- **US EPA Examples:**
- *Clean Air Act*
- *Clean Water Act*
- *Resource Recovery Act*
- *Endangered Species Act*
- *Food Quality Protection Act*
- *Endocrine Disruptor Screening Program*
- *Federal Insecticide, Fungicide, and Rodenticide Act*
- *Frank R. Lautenberg Chemical Safety for the 21st Century Act*
- *Comprehensive Environmental Response, Compensation, and Liability Act*
- *Guidelines for Deriving Numerical National Water Quality Criteria for the Protection of Aquatic Organisms and Their Uses*



Cross Species Extrapolation: Decisions based on available data

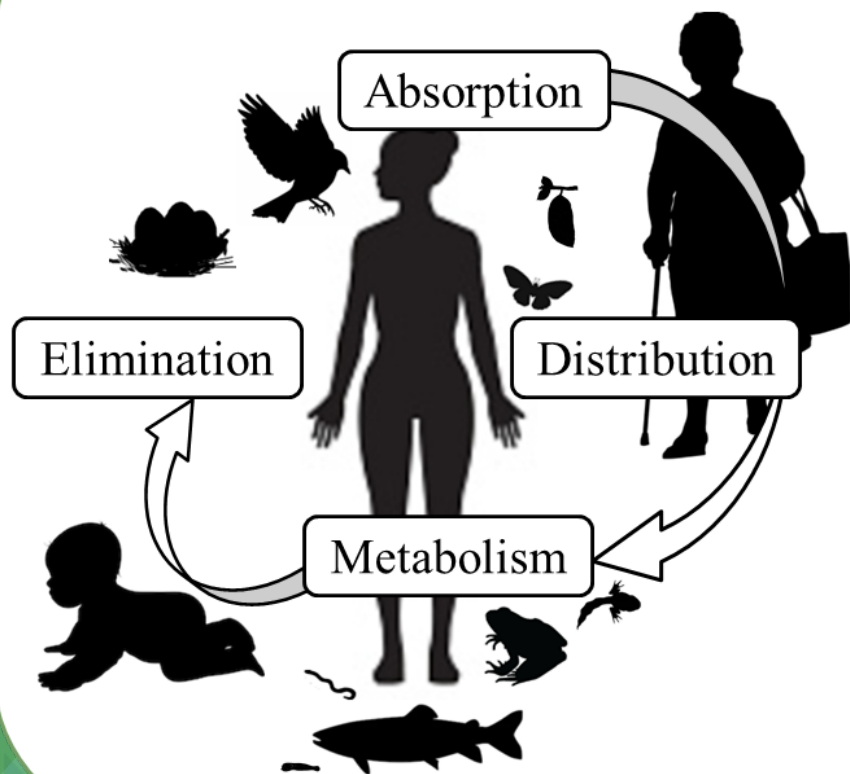
Available Toxicity Data



Protection Goal:
Amphibia

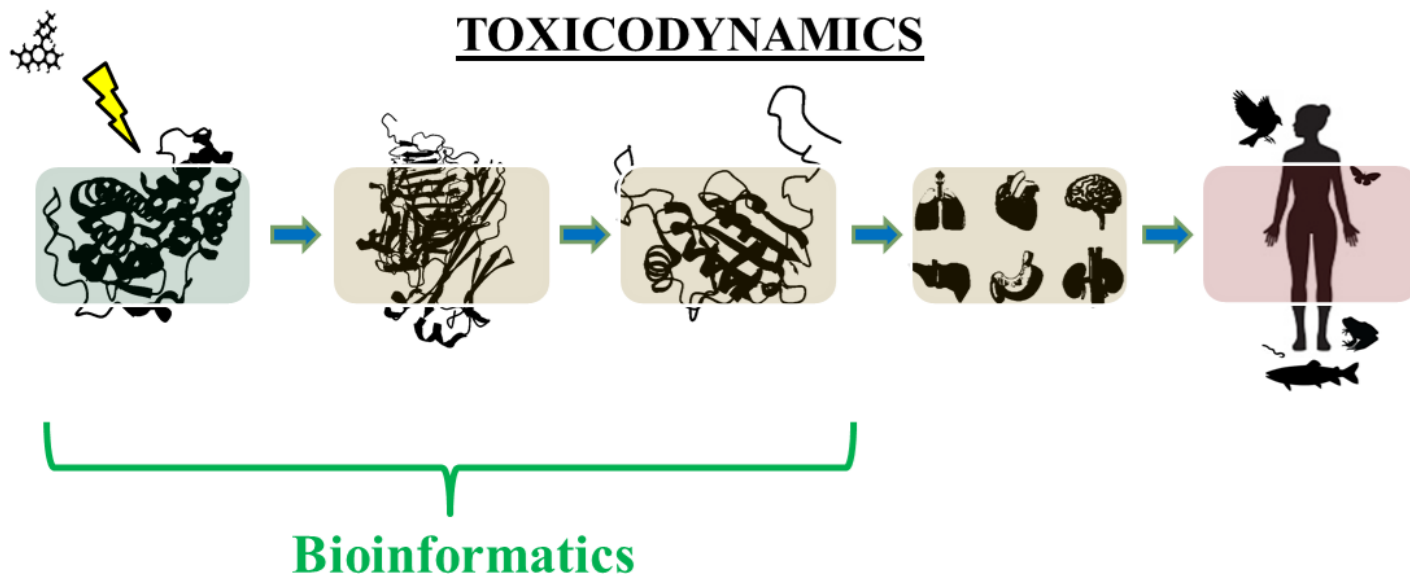
Sensitivity to Chemical Perturbation

TOXICOKINETICS



Cross Species Extrapolation

TOXICODYNAMICS

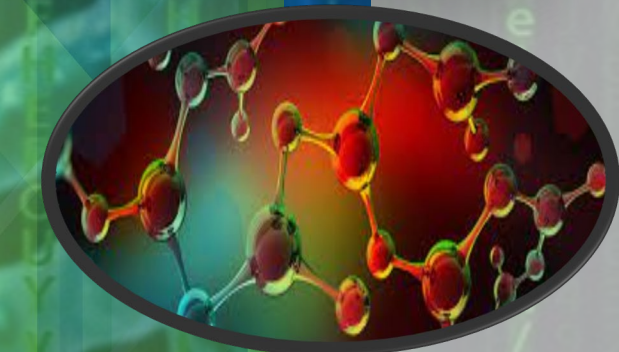
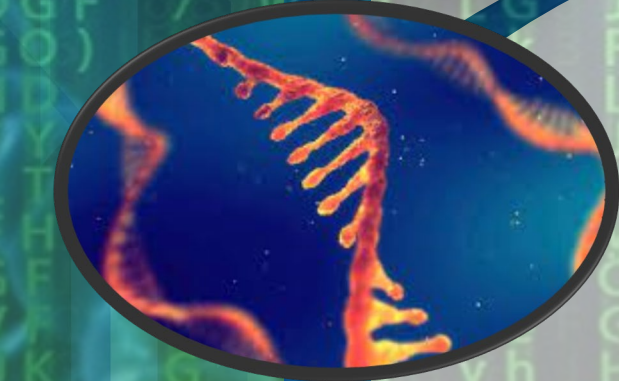


Simplify Complexity

Modified from LaLone et al., International Consortium to Advance Cross-Species Extrapolation of the Effects of Chemicals in Regulatory Toxicology. ET&C. 2021

BIOINFORMATICS

Query, extract, store, organize,
systematize, annotate, visualize, mine,
and interpret complex data



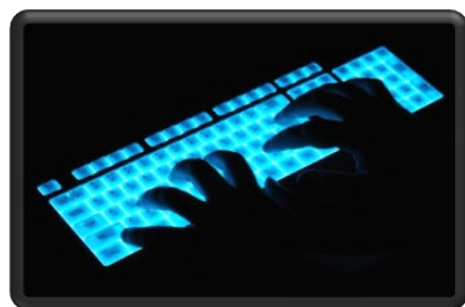


<https://seqapass.epa.gov/seqapass/>

Sequence Alignment to Predict Across Species Susceptibility (SeqAPASS): A Web-Based Tool for Addressing the Challenges of Cross-Species Extrapolation of Chemical Toxicity

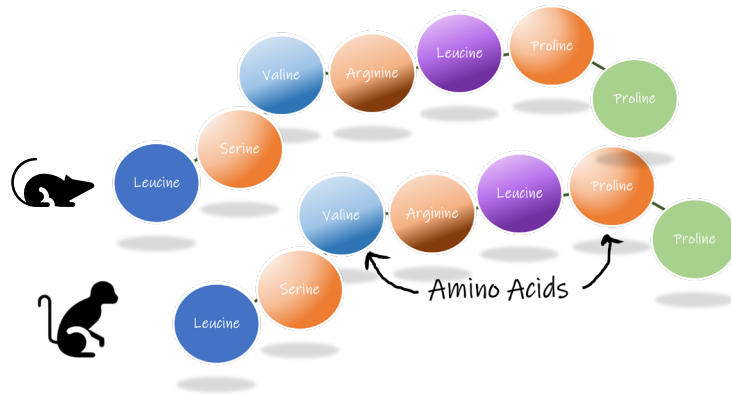
Carlie A. LaLone,^{*,1} Daniel L. Villeneuve,^{*} David Lyons,[†] Henry W. Helgen,[‡] Serina L. Robinson,^{§,2} Joseph A. Swintek,[¶] Travis W. Saari,^{*} and Gerald T. Ankley^{*}

Sequence Alignment to Predict Across Species Susceptibility (SeqAPASS)



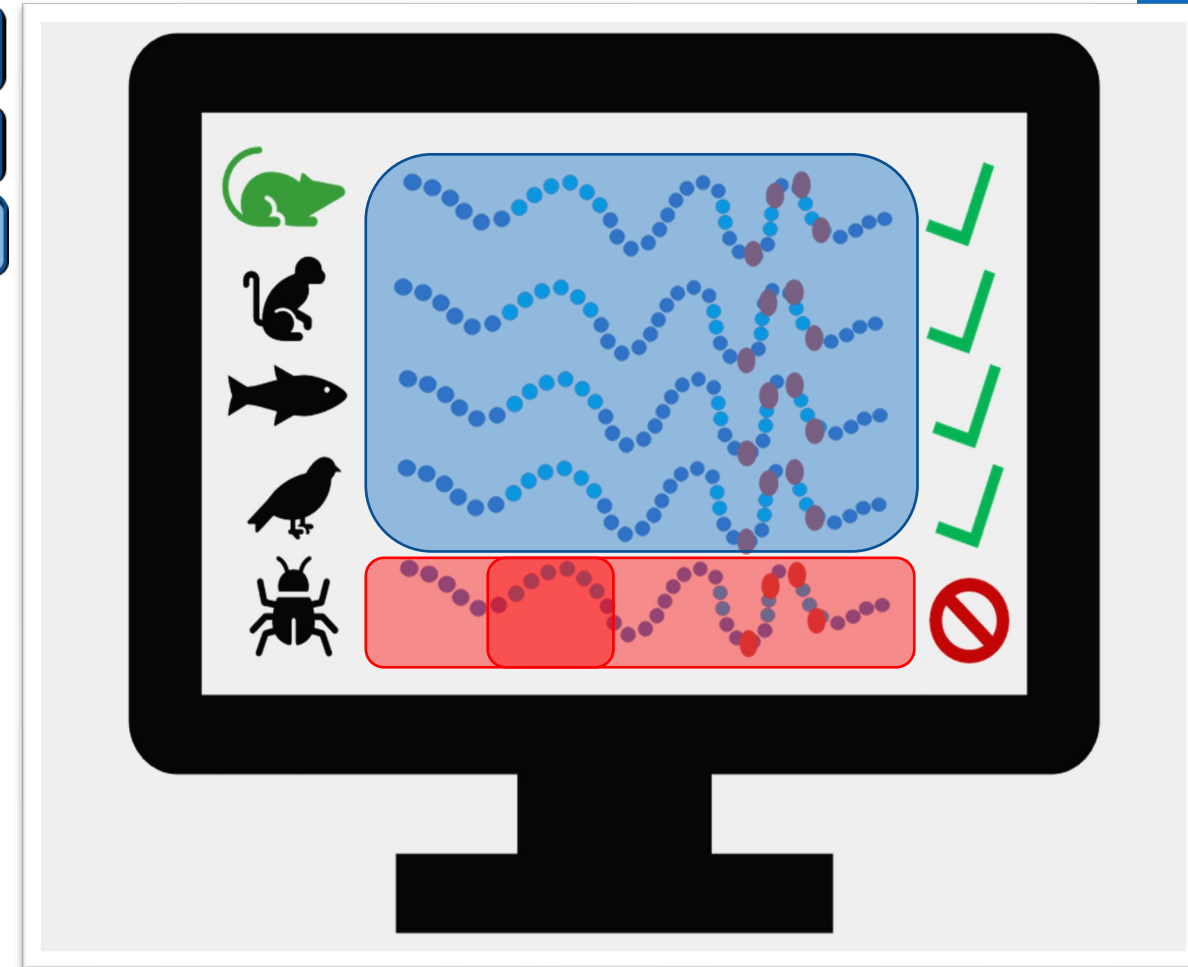
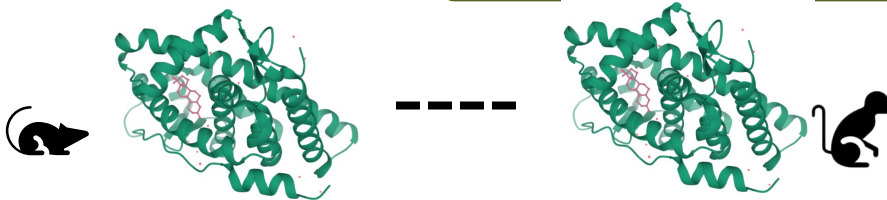
Flexible Analysis Based On Available Data

- Level 1 Primary Amino Acid Sequence Alignments
- Level 2 Conserved Functional Domain Alignments
- Level 3 Critical (Close Contact) Amino Acid Conservation



SeqAPASS v7.0
(Released 2023)

- Level 4 (expert users only) Structure Alignments



Gather Lines of Evidence Toward Protein Conservation



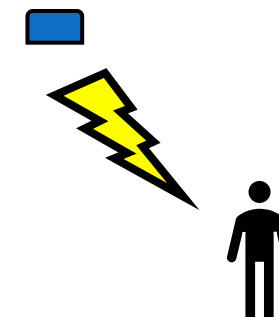
SeqAPASS Predicts Likelihood of Similar Susceptibility based on Sequence Conservation:

Demonstrated Application:

- Define the **taxonomic domain of applicability** for adverse outcome pathways
- Extrapolate high throughput **screening data**
- Predict relative intrinsic **susceptibility**
- Predict chemical **bioaccumulation** across species
- Generate **research hypotheses** prioritization strategies

Line(s) of evidence indicate

- The protein is **conserved**
- The protein is **NOT conserved**



Predictions for 100s to 1000s of species

Data and Connections in SeqAPASS

Guide the User to Sources to Identify Protein Targets:

- DrugBank - <https://www.drugbank.ca>
- VSDB: Veterinary Substances DataBase - <http://sitem.herts.ac.uk/aeru/vsdb/index.htm>
- Therapeutic Target Database - <http://db.idrblab.net/ttd/>
- The Toxin and Toxin-Target Database - <http://www.t3db.ca>
- AOP-Wiki - <https://aopwiki.org>
- **CompTox Chemicals Database** - <https://comptox.epa.gov/dashboard>

Provide Transparency for Source Data and Executables:

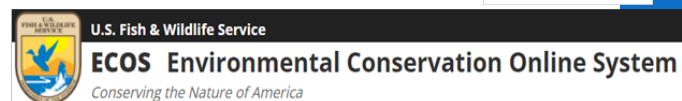
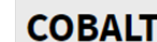
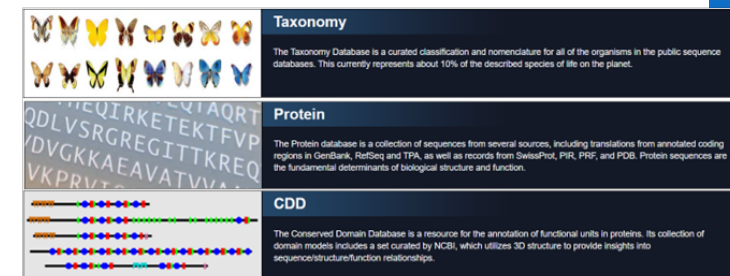
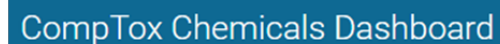
- NCBI Taxonomy Database - <http://www.ncbi.nlm.nih.gov/taxonomy>
- NCBI Protein Database - <http://www.ncbi.nlm.nih.gov/protein>
- NCBI Conserved Domain Database - <http://www.ncbi.nlm.nih.gov/Structure/cdd/>
- NCBI COBALT - <http://www.st-va.ncbi.nlm.nih.gov/tools/cobalt/>
- I-TASSER - <https://zhanggroup.org/I-TASSER/>
- TM-align - <https://zhanggroup.org/TM-align/>
- AlphaFold - <https://alphafold.ebi.ac.uk/>
- RCSB PDB - <https://www.rcsb.org/>

Guide the User to Appropriate Resources for Individual Amino Acid Comparisons:

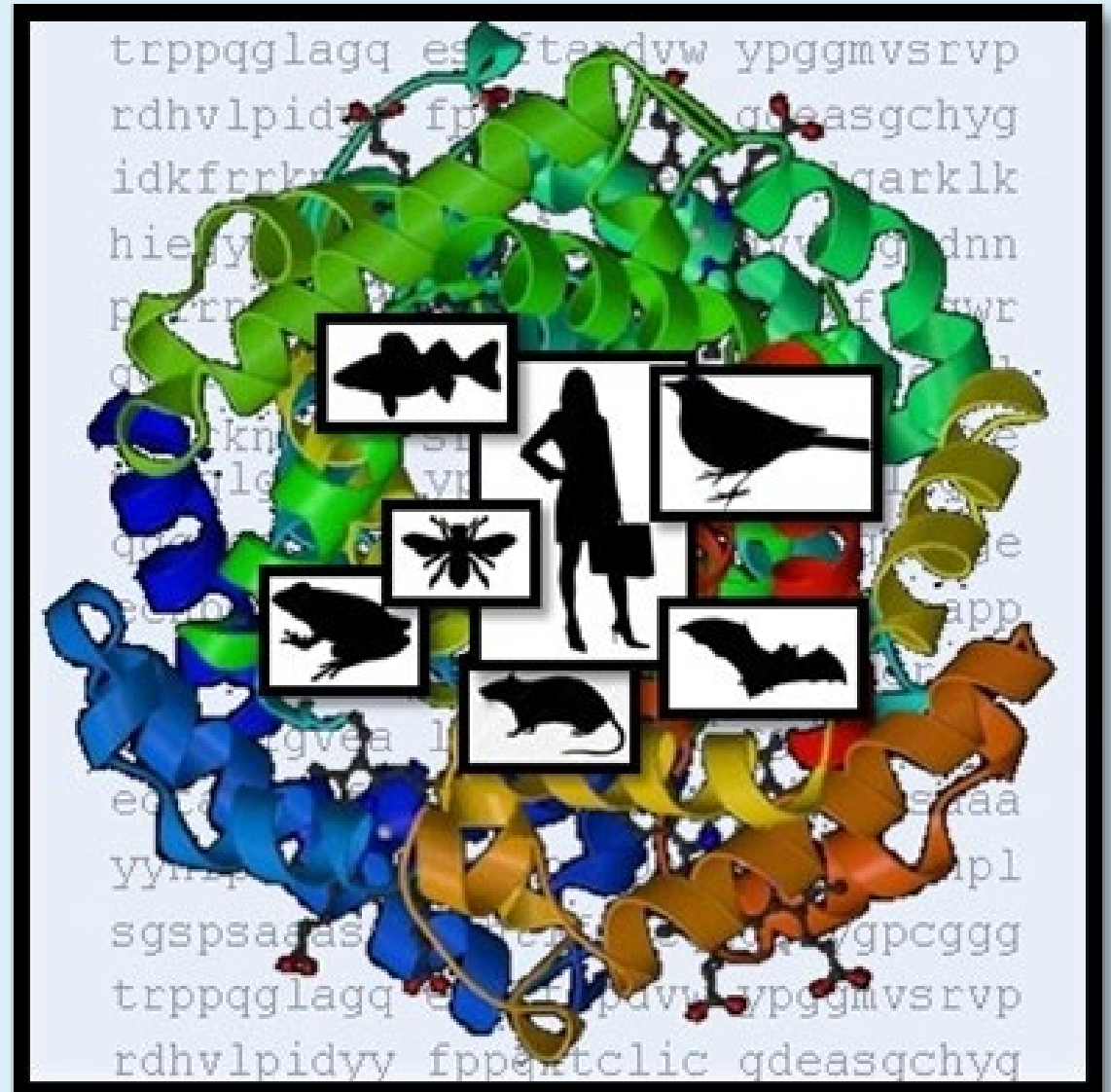
- Google Scholar - <https://scholar.google.com/>

Aids for Data Synthesis and Connection:

- **ECOTOX Knowledgebase** - <https://cfpub.epa.gov/>
- U.S. Fish & Wildlife Environmental Conservation Online System - <https://ecos.fws.gov/ecp/>



Demo





Related Topics: [SeqAPASS](#)

Sequence Alignment to Predict Across Species Susceptibility (SeqAPASS)



New to SeqAPASS Version 7.1 (See [user guide](#) for more details)

- Updated protein, taxonomy, and conserved domain data
- Updated BLAST executables
- Updated Threatened and Endangered species

Version 7.0

- Expert users can request Level 4 access for protein structure generation and alignment to gather additional lines of evidence toward conservation
- Automated filtering option for Level 3 sequence alignment selections based on annotations


[Log In to SeqAPASS](#)

Version 7.1

Welcome to SeqAPASS



[Login](#)

For optimal SeqAPASS performance use Chrome 

Instructions to create a SeqAPASS account and login can be found [here](#).

[About SeqAPASS](#)

Identify a Protein Target

SeqAPASS is designed to predict cross species chemical susceptibility based on a protein molecular target. The following resources have been identified to guide the user to an appropriate protein target based on the chemical, adverse outcome pathway (AOP), or high-throughput screening (HTS) assay target of interest. Click the help buttons below for descriptions of how to find relevant protein target information from these resources.

All links will open in a new tab.

The following links exit the site [EXIT](#)

Pharmaceutical protein targets:

Pesticides and other chemical protein targets:

AOP chemical initiators:

ToxCast HTS results by chemical:

Compare Primary Amino Acid Sequences

Select Search: By Species
 By Accession

SeqAPASS Submission

[NCBI Protein Database](#) [EXIT](#)

NCBI Protein Accession:

[Request Run](#) [Clear](#)

Identify a Protein Target

SeqAPASS is designed to predict cross species chemical susceptibility based on a protein molecular target. The following resources have been identified to guide the user to an appropriate protein target based on the chemical, adverse outcome pathway (AOP), or high-throughput screening (HTS) assay target of interest. Click the help buttons below for descriptions of how to find relevant protein target information from these resources.

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 By Accession

SeqAPASS Submission

[NCBI Protein Database](#) [EXIT](#)

NCBI Protein Accession:

[Request Run](#) [Clear](#)

Partial Protein Sequence

[Request Selected Report](#)

[Refresh Available Reports](#)

- View Report
- Save Report(s)


Available Reports

Search: NP_000116.2

	SeqAPASS Run Id	Data Version	Ortholog Count	Level 1 Query Accession	Query Protein Name	NCBI Taxonomy ID	Query Species Name	Query Common Name	Taxonomy	SeqAPASS End Time
<input type="radio"/>	3741	8	846	NP_000116.2	estrogen receptor isoform 1	9606	Homo sapiens	Human	Mammalia	2024 01 26 11:55:59
<input type="radio"/>	3711	7	712	NP_000116.2	estrogen receptor isoform 1	9606	Homo sapiens	Human	Mammalia	2022 06 08 11:11:58
<input type="radio"/>	2847	6	656	NP_000116.2	estrogen receptor isoform 1	9606	Homo sapiens	Human	Mammalia	2021 08 19 11:55:31
<input type="radio"/>	2519	5	410	NP_000116.2	estrogen receptor isoform 1	9606	Homo sapiens	Human	Mammalia	2020 08 28 10:00:50
<input type="radio"/>	1902	4	348	NP_000116.2	estrogen receptor isoform 1	9606	Homo sapiens	Human	Mammalia	2019 10 24 11:07:33
<input type="radio"/>	1410	4	348	NP_000116.2	estrogen receptor isoform 1	9606	Homo sapiens	Human	Mammalia	2019 05 16 11:04:08
<input type="radio"/>	1219	3	305	NP_000116.2	estrogen receptor isoform 1	9606	Homo sapiens	Human	Mammalia	2018 03 09 22:35:14
<input type="radio"/>	699	2	-	NP_000116.2	estrogen receptor isoform 1	9606	Homo sapiens	Human	Mammalia	2017 05 30 11:36:37
<input type="radio"/>	414	1	-	NP_000116.2	estrogen receptor isoform 1	9606	Homo sapiens	Human	Mammalia	2016 06 01 14:13:39

(1 of 1)

10

Download Table: 

Level 1 Query Protein Information

Hit proteins are identified for the following query protein. Use the main button to go back to the SeqAPASS Reports list.

SeqAPASS ID: 3741 Query Accession: [NP_000116.2](#) [EXIT](#) Ortholog Count: 846

Query Species: Homo sapiens

Query Protein: estrogen receptor isoform 1

Protein and Taxonomy Data: 01/11/2023

BLAST Version: 2.15.0

Software Version: 7.1

Susceptibility Cut-off [+](#)

Primary Report Settings [i](#) [+](#)

Visualization [i](#) [+](#)

Level 2 [i](#) [+](#)

Level 3 [i](#) [+](#)

[Refresh Level 2 and 3 Runs](#)

Level 4 [i](#) [+](#)

[Refresh Level 4 Runs](#)

- Partial Hit Protein Sequence [i](#)
- Primary Report
- Percent Similarity > 100%
- Full Report
- Susceptible = Y, Ortholog Count = 0
- Show Only Eukaryotes

[View Level 1 Summary Report](#) [i](#)

[Push Level 1 To DS Report](#) [i](#)

Level 1 Data - Primary

The following links exit the site [EXIT](#)

[Download Current Level 1 Report Settings](#) [i](#)

[ECOTOX Widget](#) [i](#)

Search: [i](#)

<input type="checkbox"/>	Data Version	NCBI Accession ↕	Protein Count ↕	Species Tax ID ↕	Taxonomic Group ↕	Filtered Taxonomic Group ↕	Scientific Name ↕	Common Name ↕	Protein Name ↕	BLASTp Bitscore ↕	Ortholog Candidate ↕	Ortholog Count
--------------------------	--------------	----------------------------------	---------------------------------	----------------------------------	-----------------------------------	--	-----------------------------------	-------------------------------	--------------------------------	-----------------------------------	--------------------------------------	----------------

Decision Summary Report

Level 1 Report

Select Taxonomic Groups (CLASS)	
<input type="checkbox"/> select All	Taxonomic Group
<input type="checkbox"/>	Mammalia
<input type="checkbox"/>	Testudinata
<input type="checkbox"/>	Aves
<input type="checkbox"/>	Crocodylia
<input type="checkbox"/>	Lepidosauria
<input type="checkbox"/>	Amphibia
<input type="checkbox"/>	Chondrichthyes
<input type="checkbox"/>	Dipnomorpha
<input type="checkbox"/>	Coelacanthiformes
<input checked="" type="checkbox"/>	Actinopteri
<input type="checkbox"/>	Cladistia
<input type="checkbox"/>	Hvveroartia

<input checked="" type="checkbox"/>	Korean striped bitterling
<input checked="" type="checkbox"/>	Pengze crucian carp
<input checked="" type="checkbox"/>	Burton's mouthbrooder
<input checked="" type="checkbox"/>	Mandarinfish
<input checked="" type="checkbox"/>	Derbio
<input checked="" type="checkbox"/>	Zebrafish
<input checked="" type="checkbox"/>	Cichlids
<input checked="" type="checkbox"/>	Plateau loaches
<input checked="" type="checkbox"/>	Bluefin trevally
<input checked="" type="checkbox"/>	Carps and others
<input checked="" type="checkbox"/>	Tanaka's snailfish
<input checked="" type="checkbox"/>	Carps and others
<input checked="" type="checkbox"/>	Pufferfishes and others
<input checked="" type="checkbox"/>	Plateau loaches

Common Name
 Scientific Name

Level 1 Info

Level 1 Query Protein Information
 SeqAPASS ID: 3741
 Query Species: Homo sapiens
 Query Protein: estrogen receptor isoform 1
 Query Accession: [NP_000118.2](#) EXON
 Ortholog Count: 848
 Protein and Taxonomy Data: 01/11/2023
 BLAST Version: 2.15.0
 Software Version: 7.1

Report Settings
 Report Type: Primary
 E-Value: 0.01
 Sorted By Taxonomic Group: CLASS
 Common Domains: 1
 Species Read-Across: Y
 Cut-off %: 34.43
 Show Only Eukaryotes: Y

Optional Components

Component	Add to Report
Level 1 Info	<input checked="" type="checkbox"/>
Level 1 Visualization	<input type="checkbox"/>

Level 2 Report

Select Level 2 Domains		Optional Components		
Domain		Add To Report Table	Add Info to Report	Add Visualization to Report
(310) cd06949, NR_LBD_ER, Ligand binding domain of Estrogen receptor, which are activated by the hormone 17beta-estradiol (estrogen)		<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Level 3 Report

Level 3 Info

SeqAPASS ID: 3741
 Template Species: Homo sapiens
 Template Protein: [NP_000118.2] estrogen receptor isoform 1
 Protein and Taxonomy Data: 01/11/2023
 BLAST Version: 2.15.0
 Software Version: 7.1

Selected Amino Acids
 351D,353E,362K,364V,394R,524H

Optional Components

Component	Add to Report
Level 3 Report	<input checked="" type="checkbox"/>
Level 3 Info	<input checked="" type="checkbox"/>

Final Decision Summary Report



Search:

Data Version	NCBI Accession	Filtered Taxonomic Group	Species	Protein	Level 1 Susceptible (Y/N)	(310) cd06949, NR_LBD_ER, Ligand binding domain of Estrogen receptor, which are activated by the hormone 17beta-estradiol (estrogen)	Level 3 Template	Level 3 Amino Acids (Y/N)
8	NP_000116.2	Mammalia	Human	estrogen receptor isoform 1	Y	Y	Homo sapiens	Y
8	MBN3300166.1	Actinopteri	Bowfin	ESR1 protein	Y	Y	Homo sapiens	Y
8	BAG82653.1	Actinopteri	Tropical gar	estrogen receptor alpha	Y	Y	Homo sapiens	Y
8	MBN3320116.1	Actinopteri	Alligator gar	ESR1 protein	Y	Y	Homo sapiens	Y
8	XP_006625908.1	Actinopteri	Spotted gar	PREDICTED: estrogen receptor	Y	Y	Homo sapiens	Y
8	RXM34939.1	Actinopteri	Sterlet	Estrogen receptor	Y	Y	Homo sapiens	Y
8	KAK1171545.1	Actinopteri	Atlantic sturgeon	estrogen receptor-like isoform X1	Y	Y	Homo sapiens	Y
8	XP_041108348.1	Actinopteri	Mississippi paddlefish	estrogen receptor	Y	Y	Homo sapiens	Y
8	BAG82650.1	Actinopteri	Amur sturgeon	estrogen receptor alpha1	Y	Y	Homo sapiens	Y
8	XP_028809450.1	Actinopteri	Denticle herring	estrogen receptor	Y	Y	Homo sapiens	Y
8	CUH82767.1	Actinopteri	European eel	estrogen receptor 1	Y	Y	Homo sapiens	Y
8	KAJ8009573.1	Actinopteri	Alaska blackfish	hypothetical protein DPEC_G00090280	Y	Y	Homo sapiens	NA
8	XP_056150700.1	Actinopteri	Smalleye Pacific opah	estrogen receptor	Y	Y	Homo sapiens	Y
8	XP_029983893.1	Actinopteri	Orbiculate cardinalfish	estrogen receptor isoform X1	Y	Y	Homo sapiens	Y
8	XP_061097150.1	Actinopteri	European conger	estrogen receptor isoform X1	Y	Y	Homo sapiens	Y
8	TMS12676.1	Actinopteri	Large yellow croaker	Estrogen receptor	Y	Y	Homo sapiens	Y
8	XP_017548048.1	Actinopteri	Red-bellied piranha	estrogen receptor isoform X1	Y	Y	Homo sapiens	Y
8	XP_060907966.1	Actinopteri	Cuckoo wrasse	LOW QUALITY PROTEIN: estrogen receptor	Y	Y	Homo sapiens	NA
8	XP_018586825.1	Actinopteri	Asian bonytongue	estrogen receptor isoform X1	Y	Y	Homo sapiens	Y
8	XP_036437904.1	Actinopteri	Tambaqui	LOW QUALITY PROTEIN: estrogen receptor	Y	Y	Homo sapiens	NA

(1 of 15)

1 2 3 4 5 6 7 8 9 10

20

Download Table:



Download DS Report





Select Species



Select Taxonomic Groups (CLASS)

Select All	Taxonomic Group
<input checked="" type="checkbox"/>	Mammalia
<input checked="" type="checkbox"/>	Testudinata
<input checked="" type="checkbox"/>	Aves
<input checked="" type="checkbox"/>	Crocodylia
<input checked="" type="checkbox"/>	Lepidosauria
<input checked="" type="checkbox"/>	Amphibia
<input checked="" type="checkbox"/>	Chondrichthyes
<input type="checkbox"/>	Dipnomorpha
<input type="checkbox"/>	Coelacanthiformes
<input checked="" type="checkbox"/>	Actinopteri

Max number of species: 500
Number of Species Selected: 564

Select Species

Select All	Species
<input checked="" type="checkbox"/>	Human
<input type="checkbox"/>	Western gorilla
<input type="checkbox"/>	Western lowland gorilla
<input type="checkbox"/>	Chimpanzee
<input type="checkbox"/>	Pygmy chimpanzee
<input type="checkbox"/>	Bornean orangutan
<input type="checkbox"/>	Sumatran orangutan
<input type="checkbox"/>	Pere David's macaque
<input type="checkbox"/>	Crab-eating macaque
<input type="checkbox"/>	Pig-tailed macaque

Common Name
 Scientific Name

Push NCBI Tax IDs

Select Species

Select Taxonomic Groups (CLASS)

Select All	Taxonomic Group
<input type="checkbox"/>	Mammalia
<input type="checkbox"/>	Testudinata
<input type="checkbox"/>	Aves
<input type="checkbox"/>	Crocodylia
<input type="checkbox"/>	Lepidosauria
<input type="checkbox"/>	Amphibia
<input type="checkbox"/>	Chondrichthyes
<input type="checkbox"/>	Dipnomorpha
<input type="checkbox"/>	Coelacanthiformes
<input checked="" type="checkbox"/>	Actinopteri

Max number of species: 500
Number of Species Selected: 155

Select Species

Select All	Species
<input checked="" type="checkbox"/>	Homo sapiens
<input type="checkbox"/>	Gorilla gorilla
<input type="checkbox"/>	Gorilla gorilla gorilla
<input type="checkbox"/>	Pan troglodytes
<input type="checkbox"/>	Pan paniscus
<input type="checkbox"/>	Pongo pygmaeus
<input type="checkbox"/>	Pongo abelii
<input type="checkbox"/>	Macaca thibetana thibetana
<input type="checkbox"/>	Macaca fascicularis
<input type="checkbox"/>	Macaca nemestrina

Common Name
 Scientific Name

Push NCBI Tax IDs



Select Chemicals (Optional) ?

[CompTox Chemical Dashboard](#)

Chemical Search:

Add Selected Chemical

Selected Chemicals:

- 17alpha-Ethinylestradiol (CASRN:57636)**
- 17alpha-Estradiol (CASRN:57910)
- 17alpha-Ethinylestradiol acetate (CASRN:21221294)

Remove Selected Chemical

Remove All Chemicals

(0/5) CAS Numbers Selected

Back to Tax IDs

Open in ECOTOX

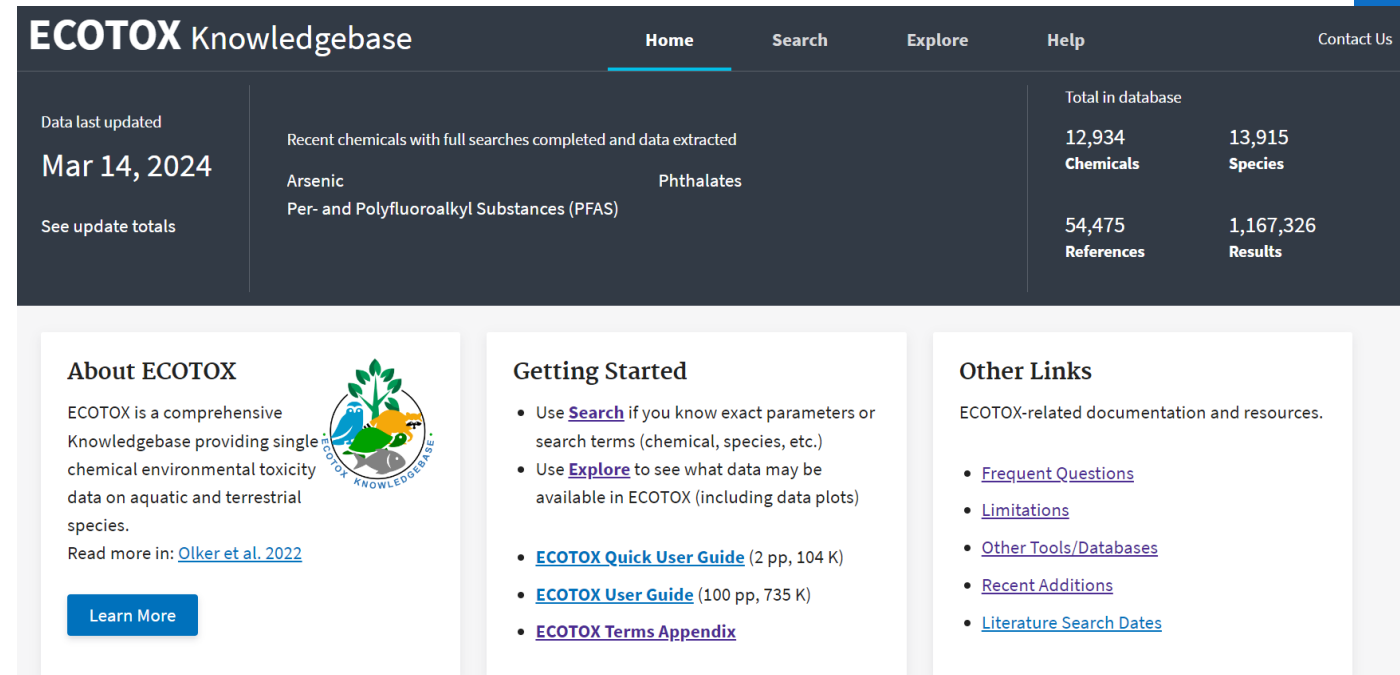


ECOTOX Knowledgebase

Jennifer Olker

What is the ECOTOX Knowledgebase?

- From comprehensive search and review of open and grey literature
- Chemical-based literature searches
- Accessible, structured empirical data from *in vivo* toxicity tests
- Updated quarterly to public website
- 30+ year history



The screenshot shows the ECOTOX Knowledgebase website. At the top, there is a navigation bar with links for Home, Search, Explore, Help, and Contact Us. Below the navigation bar, there is a summary section with the following data:

ECOTOX Knowledgebase		Total in database	
Data last updated	Recent chemicals with full searches completed and data extracted	12,934	13,915
Mar 14, 2024	Arsenic Per- and Polyfluoroalkyl Substances (PFAS)	Chemicals	Species
See update totals		54,475	1,167,326
		References	Results

Below the summary section, there are three main content areas:

- About ECOTOX:** ECOTOX is a comprehensive Knowledgebase providing single chemical environmental toxicity data on aquatic and terrestrial species. Read more in: [Olker et al. 2022](#). A "Learn More" button is provided.
- Getting Started:** Includes links for [Search](#), [Explore](#), [ECOTOX Quick User Guide](#) (2 pp, 104 K), [ECOTOX User Guide](#) (100 pp, 735 K), and [ECOTOX Terms Appendix](#).
- Other Links:** Includes links for [Frequent Questions](#), [Limitations](#), [Other Tools/Databases](#), [Recent Additions](#), and [Literature Search Dates](#).

www.epa.gov/ecotox

ECOTOX Overview: Olker et al. 2022 <https://doi.org/10.1002/etc.5324>

ECOTOX Pipeline



Planning and Identification

Screening

Eligibility

Included

Chemical verification & search term development

Conduct literature searches

Identify & acquire potentially applicable studies

Review literature for applicability

Extract study and toxicity data

Provide toxicity results and study details

Chemical-based Search Terms*

- Chemical name and CASRN
- Synonyms, tradenames
- Other relevant forms

Literature Search

Use chemical-specific search terms to query multiple literature search engines.

* 40-90 searches conducted per year, not possible to update data for all chemicals each year

Title/Abstract Screening

- Established applicability (inclusion) criteria
- Documentation of exclusion reason

Full Text Review

Data Extraction

- ECOTOX-specific Controlled Vocabularies
 - Test chemical
 - Test organism
 - Study methods and test conditions
 - Toxicity results
- Updated to public website, with downloadable outputs

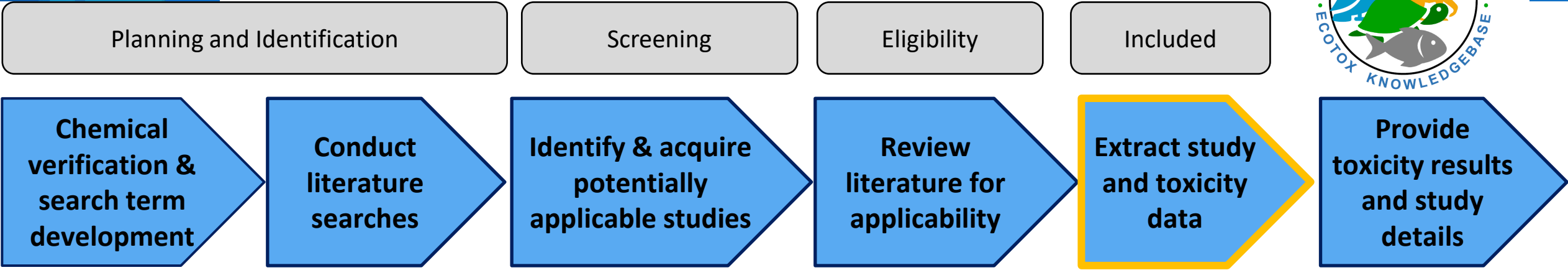
Inclusion Criteria

Identify and
acquire potentially
applicable studies

Review
literature for
applicability

Category	Key Area	Data Requirement
P (Population)	Species	<ul style="list-style-type: none"> Taxonomically verifiable, ecologically-relevant organisms (including cells, organs, gametes, embryos, plant cuttings) [NOT bacteria, humans, monkeys, viruses, or yeast]
E (Exposure)	Chemical	<ul style="list-style-type: none"> Single, verifiable chemical toxicants, administered through an acceptable route
	Exposure Amount (Concentration)	<ul style="list-style-type: none"> Exposure amount is quantified, either as a concentration in the environment when administered via soil or water, or as a dosage when introduced directly into or on the organism, via injection, orally, or topically
	Exposure Duration	<ul style="list-style-type: none"> Known duration from the time of initial exposure to the time of measurement
C (Comparator/ Control)	Control	<ul style="list-style-type: none"> Must have a control treatment
O (Outcome)	Effect	<ul style="list-style-type: none"> Biological effect measured Effect concurrent with associated chemical exposure
	Publication Type	<ul style="list-style-type: none"> Primary source of the data [NOT a Review] Study must be a full article in English

ECOTOX Pipeline



Data Extraction

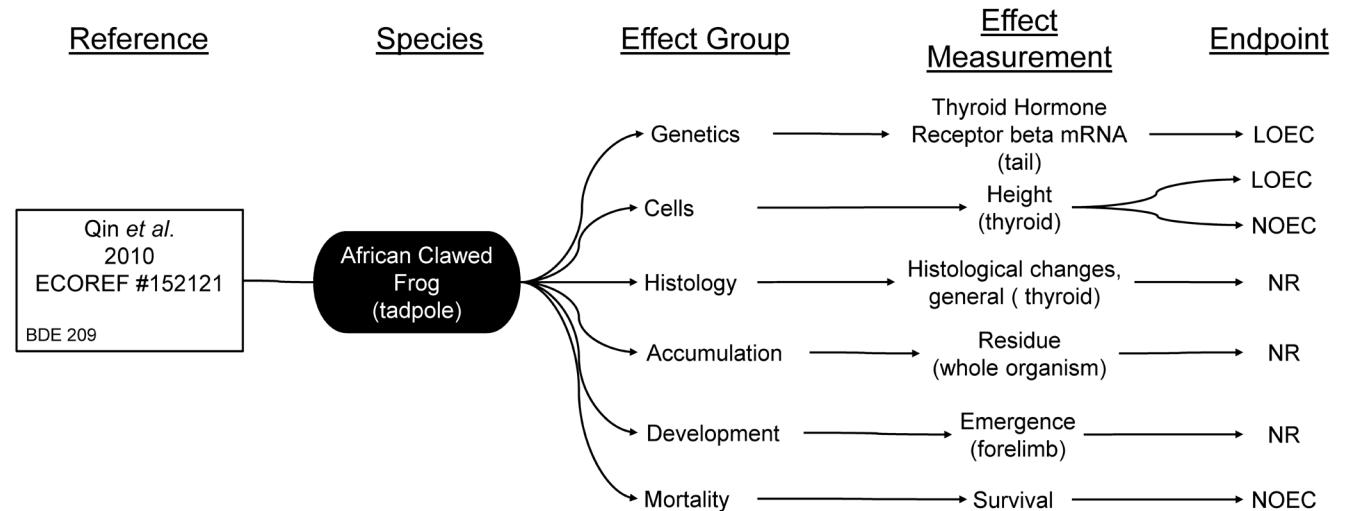
Example of multiple ECOTOX records from a single study:



Journal of Environmental Sciences
Volume 22, Issue 5, 2010, Pages 744-751



Thyroid disruption by technical decabromodiphenyl ether (DE-83R) at low concentrations in *Xenopus laevis*



NOEC = No Observed Effect Level LOEC = Lowest Observed Effect Level NR = Not Reported

ECOTOX Data Fields

Extract study
and toxicity
data

Category	ECOTOX data fields (examples)
Chemical	<ul style="list-style-type: none"> • Chemical identifier (CASRN, DTXSID) • Chemical Analysis • Chemical Formulation & Grade • Concentration(s)/Dose(s) tested
Species	<ul style="list-style-type: none"> • Species identifiers (ITIS TSN, NCBI TaxID, Taxonomy) • Life stage, Age, Sex • Organism Source
Study Methods & Test Conditions	<ul style="list-style-type: none"> • Experimental design • Control(s) • Test location and method • Exposure type, route, and media • Study and exposure duration • Physical and Chemical Soil and Water Parameters (e.g., pH, Temperature, Dissolved Oxygen)
Test Results	<ul style="list-style-type: none"> • Specific Effect Measured (with higher-level groups) • Calculated Endpoint • Concentration associated with effect and endpoint • Response site (e.g., whole organism, specific organ or body part) • Statistical significance and level of response

* **ECOTOX Data Fields**
<https://cfpub.epa.gov/ecotox/help.cfm?sub=wi-definitions>

* **ECOTOX Vocabularies:**
<https://cfpub.epa.gov/ecotox/help.cfm?sub=term-appendix>

ECOTOX: www.epa.gov/ecotox

ECOTOX Knowledgebase

[Home](#)[Search](#)[Explore](#)[Help](#)[Contact Us](#)

Data last updated

Mar 14, 2024

[See update totals](#)

Recent chemicals with full searches completed and data extracted

Arsenic

Phthalates

Per- and Polyfluoroalkyl Substances (PFAS)

Total in database

12,934

Chemicals

13,915

Species

54,475

References

1,167,326

Results

About ECOTOX

ECOTOX is a comprehensive Knowledgebase providing single chemical environmental toxicity data on aquatic and terrestrial species.

Read more in: [Olker et al. 2022](#)

[Learn More](#)



Getting Started

- Use [Search](#) if you know exact parameters or search terms (chemical, species, etc.)
- Use [Explore](#) to see what data may be available in ECOTOX (including data plots)
- [ECOTOX Quick User Guide](#) (2 pp, 104 K)
- [ECOTOX User Guide](#) (100 pp, 735 K)
- [ECOTOX Terms Appendix](#)

Other Links

ECOTOX-related documentation and resources.

- [Frequent Questions](#)
- [Limitations](#)
- [Other Tools/Databases](#)
- [Recent Additions](#)
- [Literature Search Dates](#)

www.epa.gov/ecotox

ECOTOX: Explore

 Aquatic Terrestrial[Group Summary](#)[Records](#)[Plot View](#)[Send Query Filters to Search](#)

Query Filters

Select one or more of each filter to reduce the records.

Chemicals (2)

2 Selected

Species Group (8)

All

Class (12)

All

Order (16)

All

Family (17)

All

Genus (22)

All

Species (31)

All

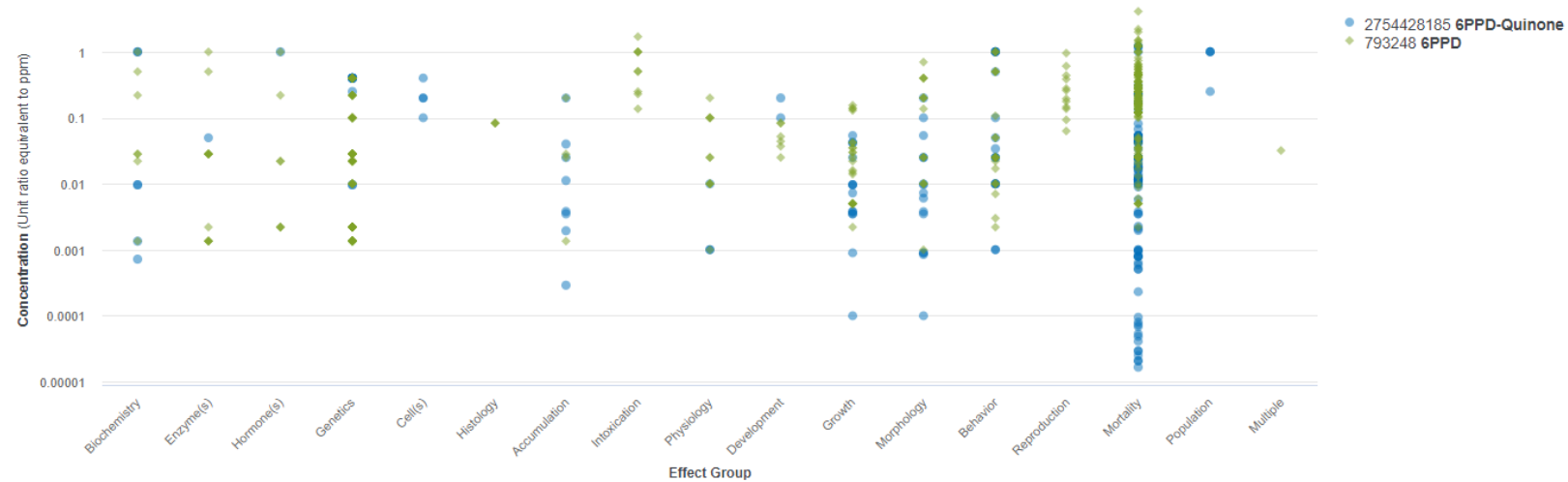
539 Plottable Records — 847 Total Records

Records are plotted if they can be converted to **Standardized Concentration Units**. Ordered by **Concentration (low-high)**.

[Effect × Chem](#)[Dur × Chem](#)[Dur × Endpt](#)[Custom](#)[Export](#)

Y-axis scale: Linear Logarithmic

Click and drag to zoom in. Hold down shift key to pan.



Showing all 539 records

ECOTOX: Search

Parameters



Aquatic

Terrestrial

Customize Output Fields

All Chemicals



All Effects



All Endpoints



All Species



All Test Conditions



All Publication Options



CAS Number	Chemical Name	Chemical Grade	Chemical Analysis	Chemical Purity	Species Scientific Name	Species Common Name	Organism Lifestage	Organism Age	Age Units	Exposure Type	Media Type	Test Location	Number of Doses
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Measured	>95	Salvelinus leucomaenis	Whitespotted Char	Juvenile	<1	Year(s)	Renewal	Fresh water	Lab	6	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Measured	>95	Salvelinus leucomaenis	Whitespotted Char	Juvenile	<1	Year(s)	Renewal	Fresh water	Lab	6	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Measured	>95	Salvelinus leucomaenis	Whitespotted Char	Juvenile	<1	Year(s)	Renewal	Fresh water	Lab	6	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Measured	>95	Salvelinus leucomaenis	Whitespotted Char	Juvenile	<1	Year(s)	Renewal	Fresh water	Lab	6	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Measured	>95	Oncorhynchus masou ssp.	Cherry Salmon	Juvenile	<1	Year(s)	Renewal	Fresh water	Lab	2	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Measured	>95	Oncorhynchus masou ssp.	Cherry Salmon	Juvenile	<1	Year(s)	Renewal	Fresh water	Lab	2	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Measured	>95	Salvelinus leucomaenis	Whitespotted Char	Juvenile	<1	Year(s)	Renewal	Fresh water	Lab	6	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Measured	>95	Salvelinus leucomaenis	Whitespotted Char	Juvenile	<1	Year(s)	Renewal	Fresh water	Lab	6	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Measured	>95	Salvelinus curilus	Southern Dolly Varden	Juvenile	<1	Year(s)	Renewal	Fresh water	Lab	2	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Measured	>95	Salvelinus curilus	Southern Dolly Varden	Juvenile	<1	Year(s)	Renewal	Fresh water	Lab	2	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Unmeasured	>95	Salvelinus leucomaenis	Whitespotted Char	Juvenile	<1	Year(s)	Static	Fresh water	Lab	3	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Measured	>95	Salvelinus leucomaenis	Whitespotted Char	Juvenile	<1	Year(s)	Renewal	Fresh water	Lab	6	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Unmeasured	>95	Salvelinus curilus	Southern Dolly Varden	Juvenile	<1	Year(s)	Static	Fresh water	Lab	3	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Measured	>95	Salvelinus curilus	Southern Dolly Varden	Juvenile	<1	Year(s)	Renewal	Fresh water	Lab	2	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Measured	NR	Salvelinus alpinus	Arctic Char	Juvenile	~3	Year(s)	Renewal	Fresh water	Lab	2	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Measured	>95	Oncorhynchus masou ssp.	Cherry Salmon	Juvenile	<1	Year(s)	Renewal	Fresh water	Lab	2	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Unmeasured	>95	Oncorhynchus masou ssp.	Cherry Salmon	Juvenile	<1	Year(s)	Static	Fresh water	Lab	3	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Measured	>95	Salvelinus leucomaenis	Whitespotted Char	Juvenile	<1	Year(s)	Renewal	Fresh water	Lab	6	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Unmeasured	>95	Salvelinus leucomaenis	Whitespotted Char	Juvenile	<1	Year(s)	Static	Fresh water	Lab	3	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Unmeasured	>98.0	Danio rerio	Zebra Danio	Embryo	<16	Cell stage	Renewal	Culture	Lab	10	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Unmeasured	>98.0	Danio rerio	Zebra Danio	Embryo	<16	Cell stage	Renewal	Culture	Lab	10	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Unmeasured	>98.0	Danio rerio	Zebra Danio	Embryo	<16	Cell stage	Renewal	Culture	Lab	10	
2754428185	2-[(1,3-Dimethylbutyl)amino]-5-(phenylamino)2,5-cyc	Unmeasured	>98.0	Danio rerio	Zebra Danio	Embryo	<16	Cell stage	Renewal	Culture	Lab	10	

ECOTOX: Help

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Welcome to the U.S. EPA ECOTOX Web site!

The ECOTOXicology Knowledgebase (ECOTOX) is a source for locating single chemical toxicity data for aquatic life, terrestrial plants and wildlife. ECOTOX was created and is maintained by the U.S.EPA's [Center for Computational Toxicology and Exposure's \(CCTE's\) Great Lakes Toxicology Ecology Division \(GLTED\)](#).

ECOTOX integrates three previously independent databases - AQUIRE, PHYTOTOX, and TERRETOX - into a unique system which includes toxicity data derived predominately from the peer-reviewed literature, for aquatic life, terrestrial plants, and terrestrial wildlife, respectively.

You should review the [limitations](#) of ECOTOX data retrieval for an understanding of system and minimum data requirements prior to performing searches on this site.

You should consult the original scientific paper to ensure an understanding of the context of the data retrieved from ECOTOX.

ECOTOX Documentation

- [ECOTOX User Guide](#) (100 pp, 735 K)
- [ECOTOX Quick User Guide](#) (2 pp, 104 K)

ECOTOX: Search Planner

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[Search Planner \(PDF\)](#) (5 pp, 133 K, [About PDF](#))

Taxonomic Searching

Within ECOTOX you may conduct a search by entering the Species Name or number(s), Genus/Species Name(s), or Common Name or Other Taxonomic Name(s). The Contains and Exact Match radio buttons allow for partial or exact name matches. You can also search by Species Group. All data records within ECOTOX include a Scientific name for the test species. All names and predefined groups have been verified in [reliable taxonomic sources](#).

The ECOTOX species file includes historical synonyms for the species. If a search is conducted using a species name that is noted as a taxonomic synonym in our system, ECOTOX will present the results using the currently acceptable genus and species name.

Taxonomic Entry

Species Number: All species in ECOTOX have been assigned a unique number. You can include numbers and text information (either Scientific or common names) in one search. Species numbers are always searched as an exact match.

Example Taxonomic Search

The example below is the correct method of entering query text. You can enter a mix of numbers and species terms. Number will always be treated as exact matches by the ECOTOX query.

Example Genus/Species Name Query

ECOTOX SEARCH PLANNING FORM

Use this form to help plan your searches or to document searches for yourself or others to perform.

Chemicals

Chemical Names	CAS Numbers	Predefined Groups	
		Metal Compounds	Organic Compounds
		Aluminum	Conazoles
		Antimony	Cyanotoxins
		Arsenic	DDT and metabolites
		Barium	Dibenzofurans
		Beryllium	Explosives
		Cadmium	Glycol Ethers
		Chromium	Major Ions
		Cobalt	Neonicotinoids
		Copper	Nitrosamines
		Iron	Perchlorates
		Lead	Phthalate Esters
		Manganese	Polyaromatic Hydrocarbons (PAH)
		Mercury	Polychlorinated Biphenyls (PCB)
		Nickel	Polybrominated Diphenyl Ethers (PBDE)
		Organotin	Pharmaceutical Personal Care (PPCP)
		Selenium	Strobins
		Silver	
		Vanadium	Per- and Polyfluoroalkyl Substances (PFAS)
		Zinc	

Species

Scientific Names/ Taxonomic Levels	Common Names	Species ECOTOX Numbers or NCBI TaxIDs	Predefined Taxonomic Groups
			All Animals Amphibians Insects/Spiders Molluscs Birds Other Invertebrates Reptiles Crustaceans Mammals Worms Fish All Plants Algae Moss/Hornworts, Fungi, Flowers, Trees, Shrubs, Ferns Special Interest Standard Test Species US Threatened/Endangered Species US Exotic/Nuisance

Demo

Aquatic

 Terrestrial

Query Filters

Select one or more of each filter to reduce the records.

Chemical Group (1)

All

Chemicals (1)

17alpha-Ethinylestradiol - 57636

Class (1)

All

Order (11)

All

[Group Summary](#)
[Records](#)
[Plot View](#)
[Send Query Filters to Search](#) ⓘ
[Export CSV](#)

38 Species

Species are ordered by **Scientific Name (A-Z)**.

Showing all 38 species from *Anguilla anguilla* to *Zoarcetes viviparus*

SCIENTIFIC NAME ^	COMMON NAME	RECORDS	PUBLICATIONS	YEAR MIN	YEAR MAX	
<input type="text" value="type to filter..."/>	<input type="text" value="..."/>	<input type="text" value="..."/>	<input type="text" value="..."/>	<input type="text" value="..."/>	<input type="text" value="..."/>	
<i>Anguilla anguilla</i>	Common Eel	3	1	2004	2004	>
<i>Carassius auratus</i>	Goldfish	41	5	2005	2013	>
<i>Clarias gariepinus</i>	Zambezi Barbel	25	3	2006	2009	>
<i>Cyprinodon variegatus</i>	Sheepshead Minnow	20	3	2000	2001	>
<i>Cyprinus carpio</i>	Common Carp	41	8	1994	2012	>
<i>Danio rerio</i>	Zebra Danio	1137	86	2001	2022	>

 Export ▼

- Table as CSV
- Export Plot as Image

Effect Measurements **(425)**

All ▼

Endpoints **(21)**

All ▼

Duration (Observed) - Days **(118)**

All ▼

Duration (Observed) Range - Days

to

Publication Years

1915 to 2024

✕ Reset All

[View All Applied](#)

CAS NO.	CHEMICAL ...	SPECIES...	COMMO...	EFFECT	MEASURE...	ENDPOINT	DUR (STD)	CONC. T...	CONC. M... ^	CONC. U...
<i>type to filter.</i>
57636	17alpha-Ethinylestradiol Chemicals Dashboard	Danio rerio	Zebra Danio	Genetics	Cytochrome P450aromB mRNA	NOEC	3	Active ingredient	2.964094E-008	AI mg/L
57636	17alpha-Ethinylestradiol Chemicals Dashboard	Danio rerio	Zebra Danio	Genetics	Cytochrome P450aromB mRNA	NOEL	3	Active ingredient	2.964094E-008	AI mg/L
57636	17alpha-Ethinylestradiol Chemicals Dashboard	Rutilus rutilus	Roach	Growth	Length	NOEC	518	Active ingredient	4E-008	AI mg/L
57636	17alpha-Ethinylestradiol Chemicals Dashboard	Rutilus rutilus	Roach	Growth	Length	NOEC	518	Active ingredient	4E-008	AI mg/L
57636	17alpha-Ethinylestradiol Chemicals Dashboard	Rutilus rutilus	Roach	Growth	Weight	NOEC	518	Active ingredient	4E-008	AI mg/L

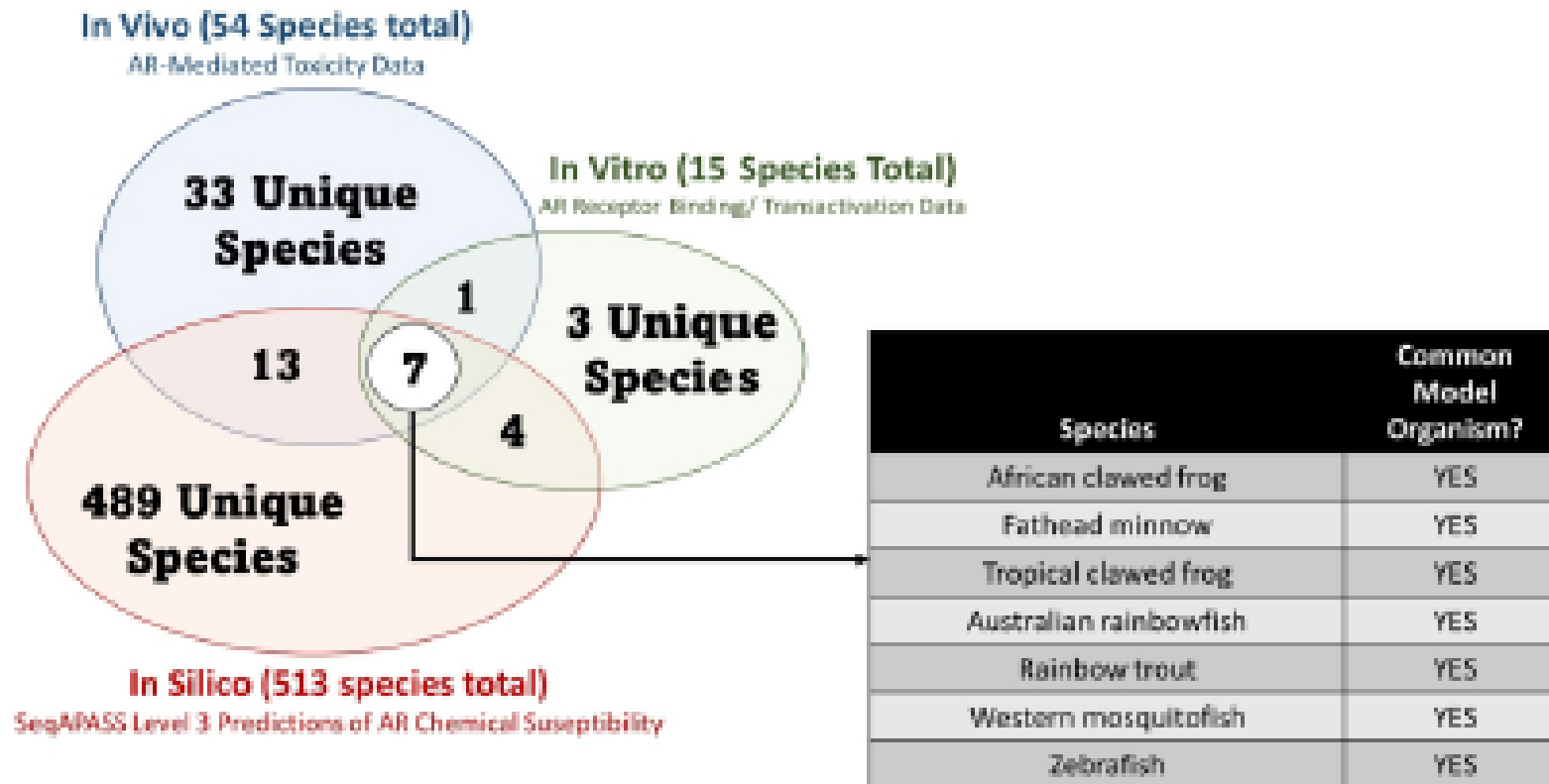


Figure 8. Species representation across tiers of evidence. (A) Venn diagram displays the number of unique species, as well as the number shared across the different tiers of evidence for in silico SeqAPASS evaluations, in vitro data for cross-species androgen receptors, and in vivo biological responses. (B) Seven species had data present at all tiers of analysis, all were commonly used fish species and model organisms.

Questions & Discussion