EPA United States Environmental Protection Agency

Computational research methods/models/ tools/databases for health and ecological risk assessments – continued

Jennifer Olker
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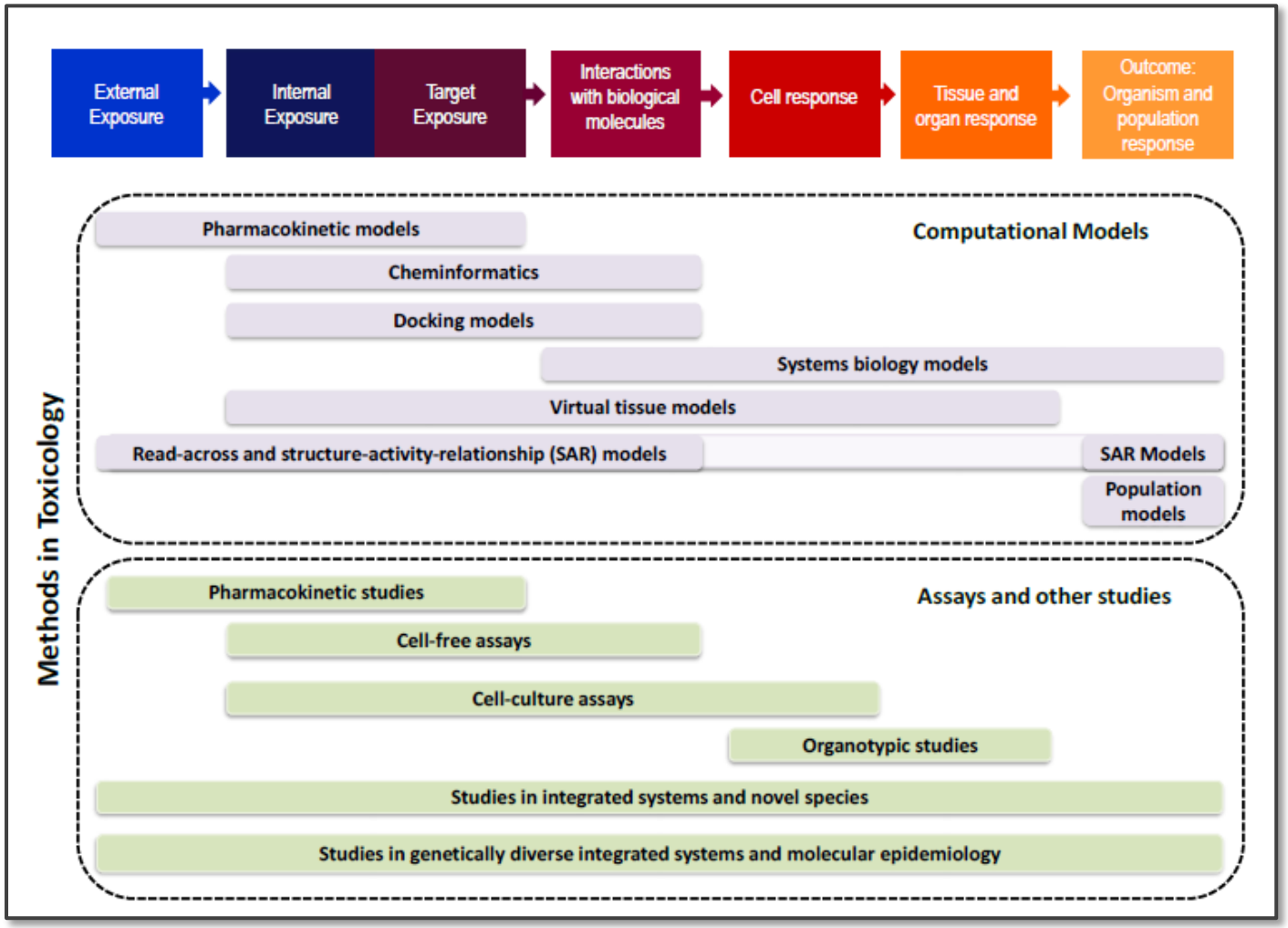
Center for Computational Toxicology & Exposure
US EPA Office of Research and Development (ORD)

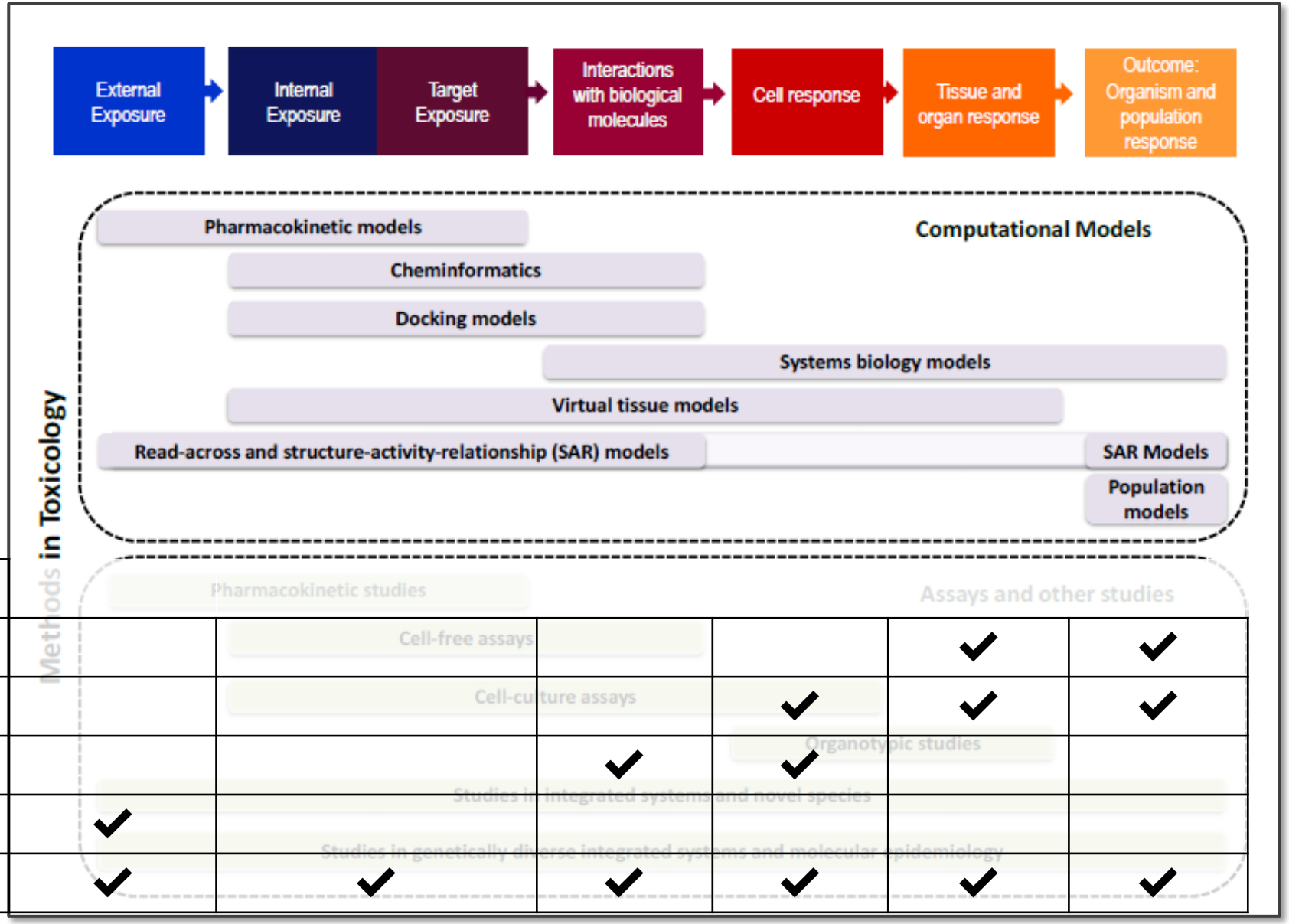
Georgetown University
EMAP Program
April 2021

Toxicology Moving to Embrace 21st Century Methods

https://www.nap.edu/catalog/24635/using-21st-century-science-to-improve-risk-related-evaluations



Data Sources and Tools

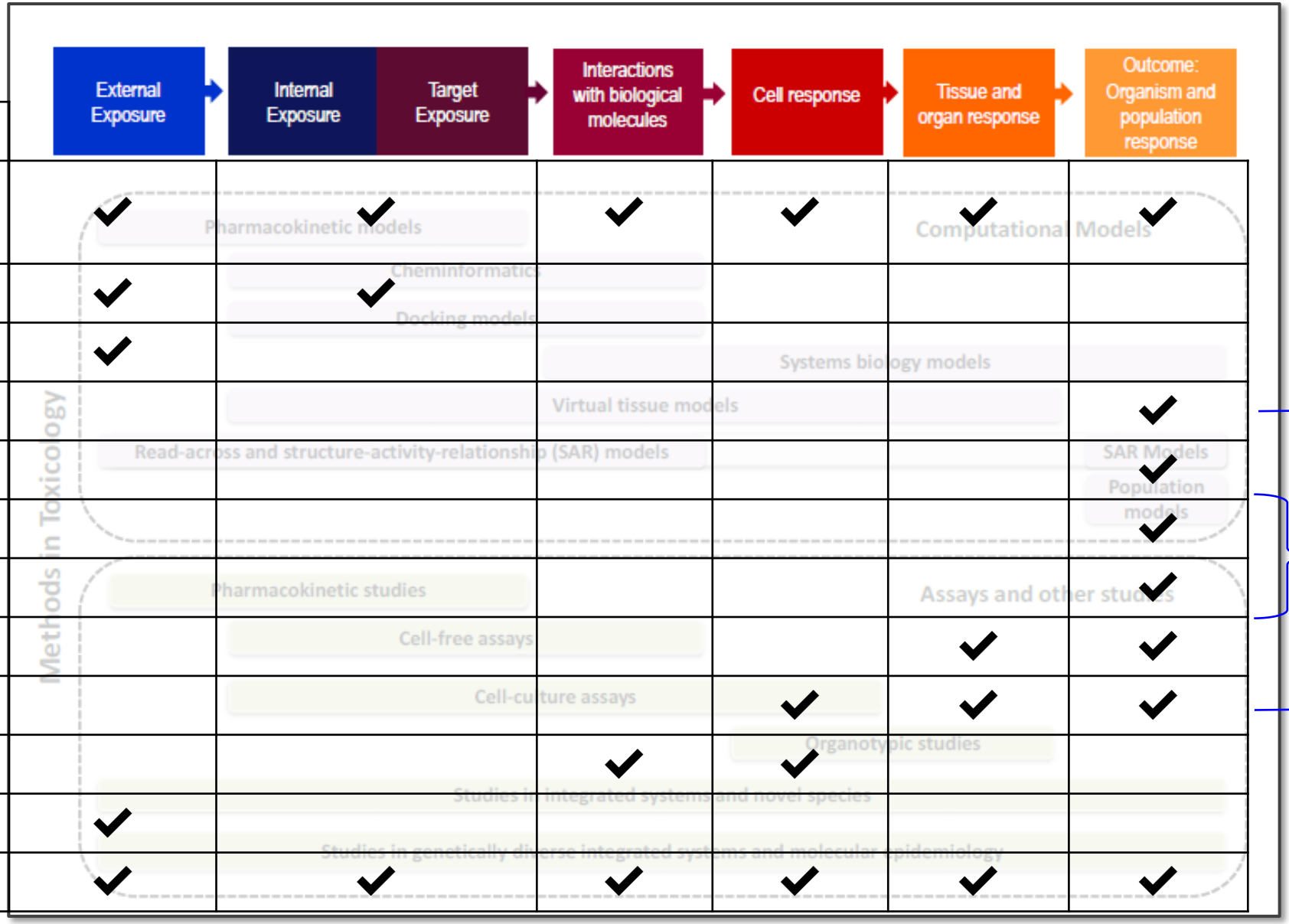


Source						
ToxRefDB					✓	✓
ECOTOX KB				✓	✓	✓
InVitro DB			✓	✓		
CPDat	✓					
Open Literature	✓	✓	✓	✓	✓	✓

Data Sources and Tools

Source	External Exposure	Internal Exposure	Target Exposure	Interactions with biological molecules	Cell response	Tissue and organ response	Outcome: Organism and population response
CompTox Chemicals Dashboard	✓	✓		✓	✓	✓	✓
httk	✓	✓					
OPERA	✓						
SSD Toolbox							✓
EcoSAR							✓
McNest							✓
Toxicity Translators							✓
ToxRefDB						✓	✓
ECOTOX KB					✓	✓	✓
InVitro DB				✓	✓		
CPDat	✓						
Open Literature	✓	✓		✓	✓	✓	✓

Data Sources and Tools



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EcoSAR							✓
McNest							✓
Toxicity Translators							✓
ToxRefDB						✓	✓
ECOTOX KB					✓	✓	✓
InVitro DB				✓	✓		
CPDat	✓						
Open Literature	✓	✓		✓	✓	✓	✓

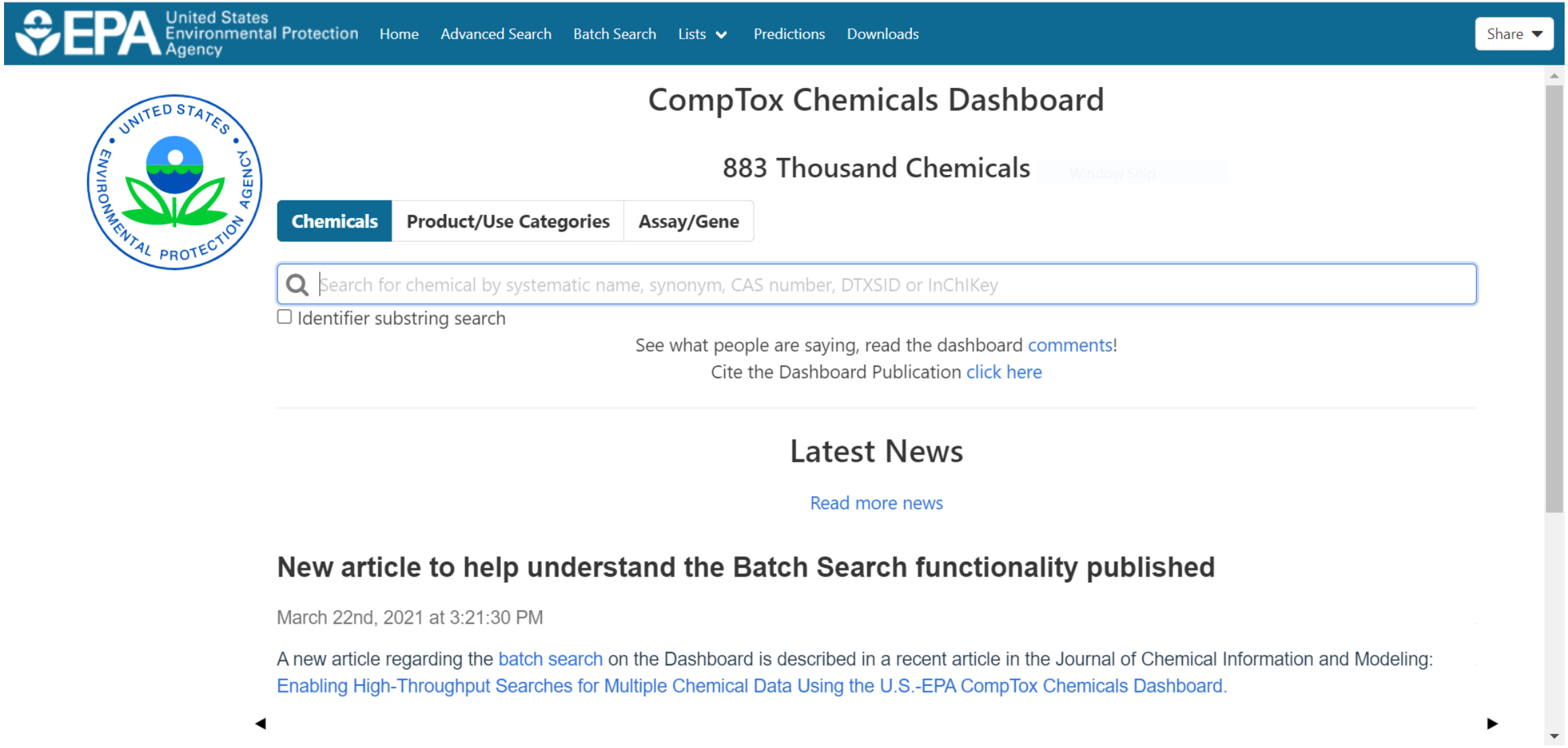
Multiple Species

Populations

Multiple Species

CompTox Chemicals Dashboard

https://comptox.epa.gov/dashboard



CompTox Chemicals Dashboard

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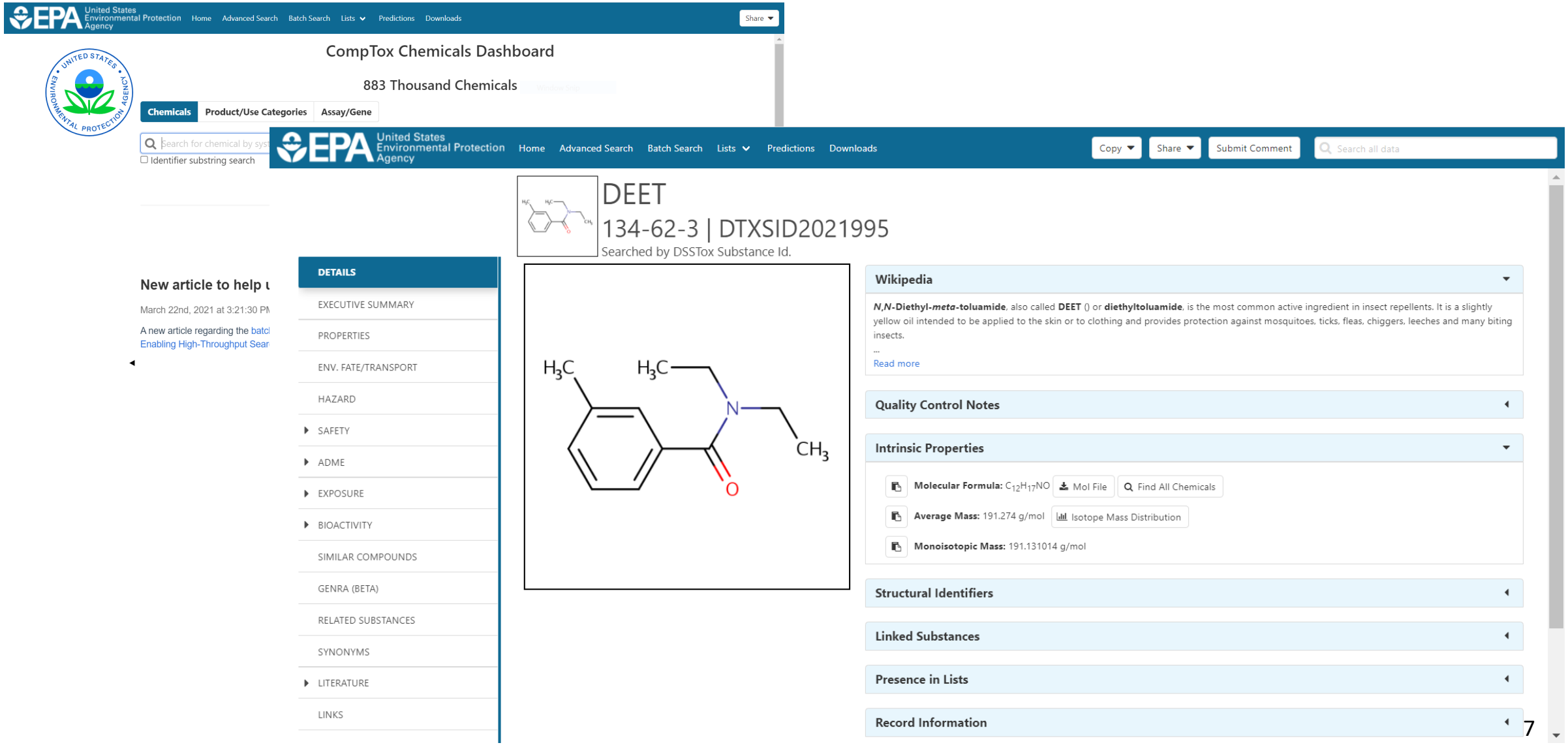
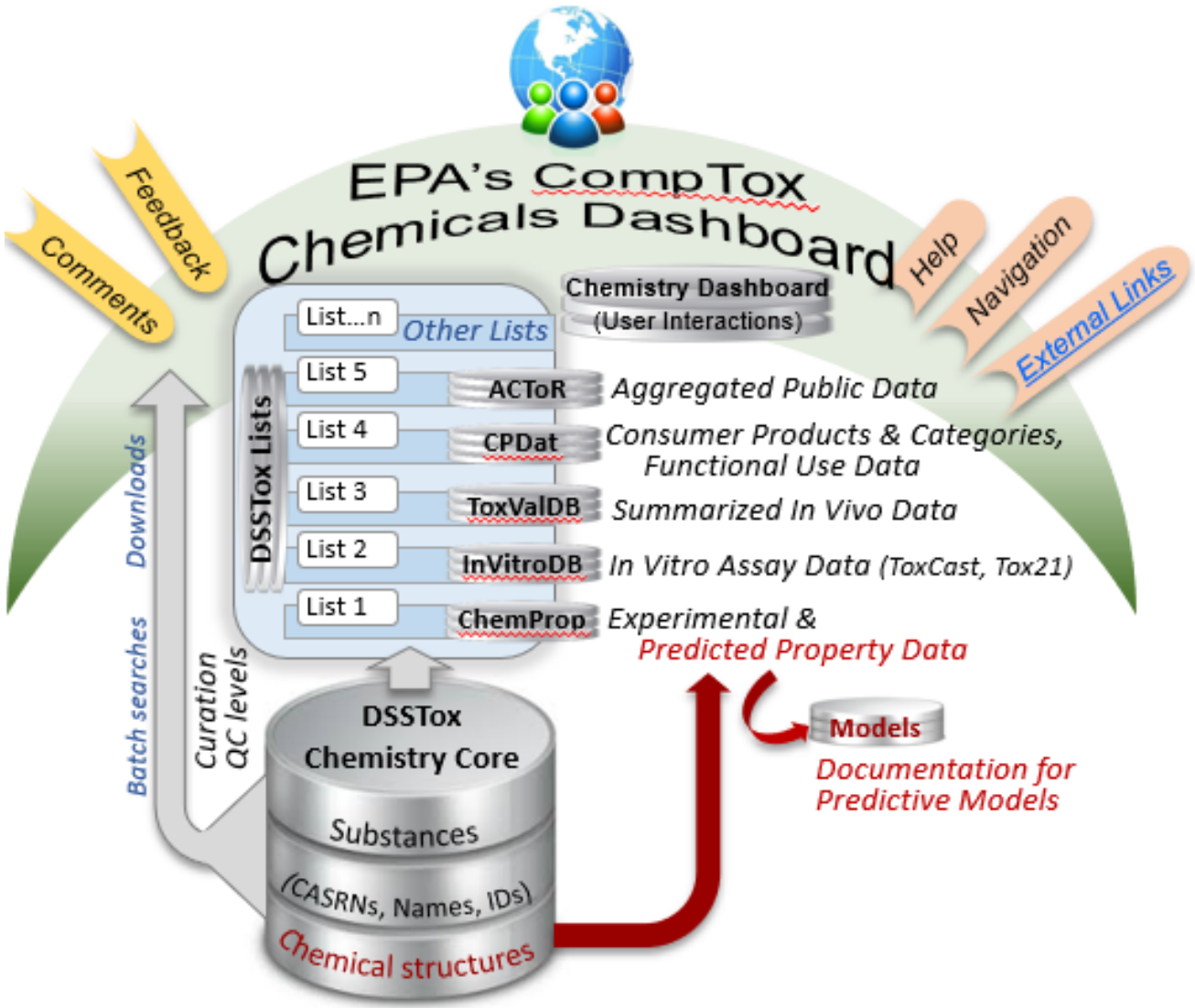


CompTox Chemicals Dashboard

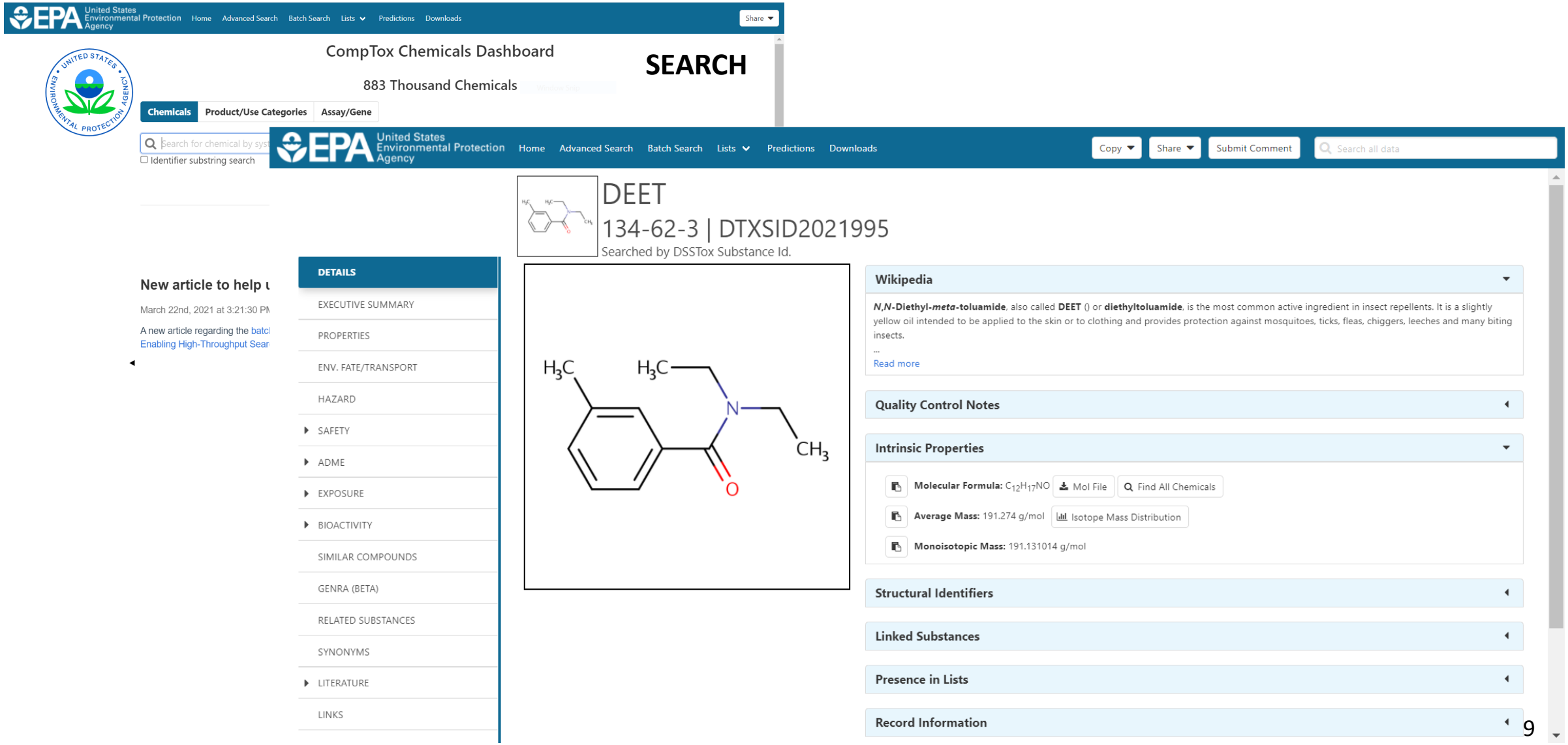


- Integration of multiple databases
  - DSSTox substance database
  - ToxValDB (includes ToxRef & ECOTOX)
  - CPCat and CPDat consumer products
  - InvitroDB (ToxCast/Tox21)
  - Property Database
  - QSAR predicted data
- Integrated to other Sources
  - Toxics Release Inventory
  - IRIS Reports
  - PPRTV Reports
  - ChemView
  - EPA Substance Registry Service
  - AOP-Wiki
- Links to ~80 public sites & services

Williams et al. 2017. https://doi.org/10.1186/s13321-017-0247-6

CompTox Chemicals Dashboard

https://comptox.epa.gov/dashboard



CompTox Chemicals Dashboard

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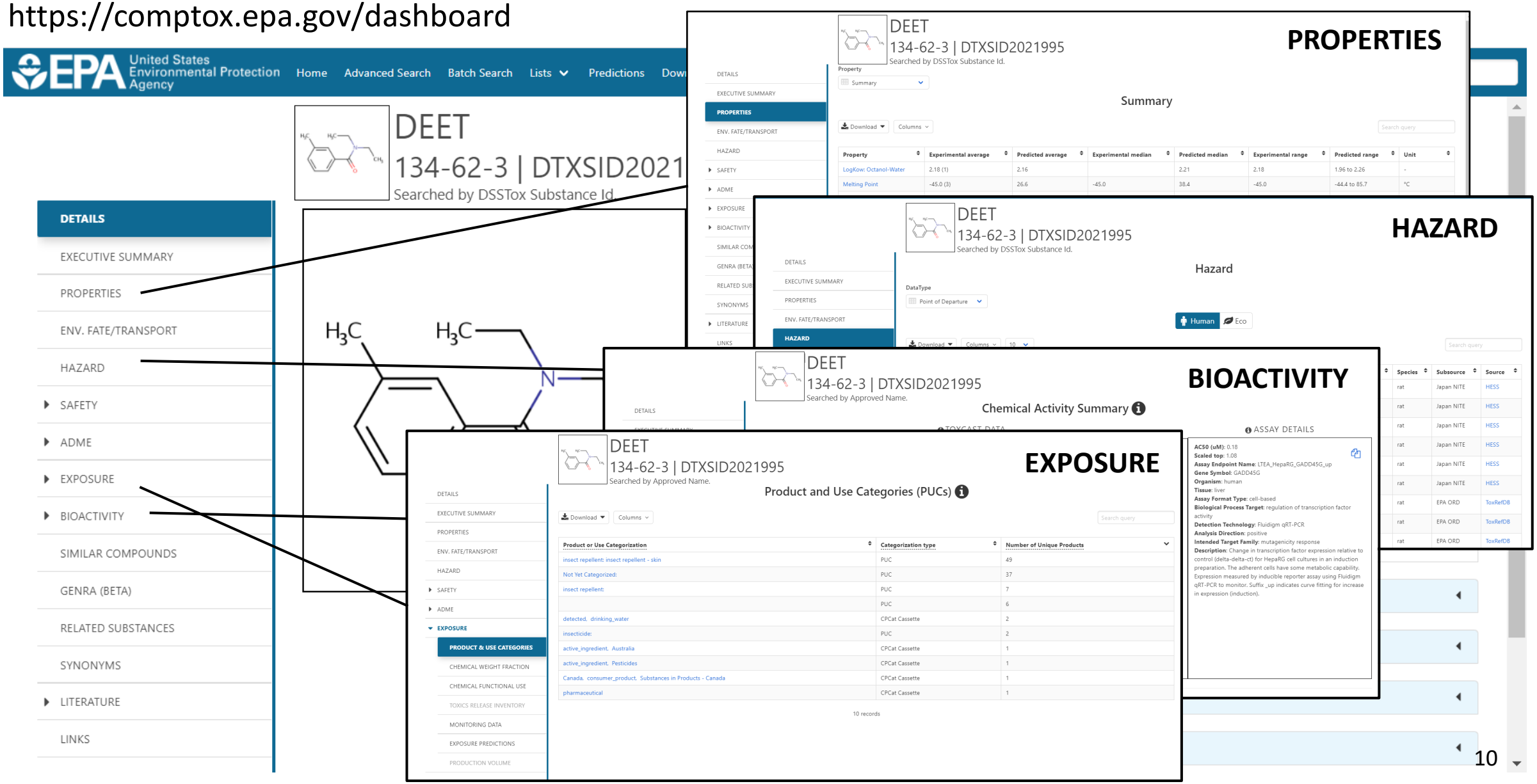

CompTox Chemicals Dashboard

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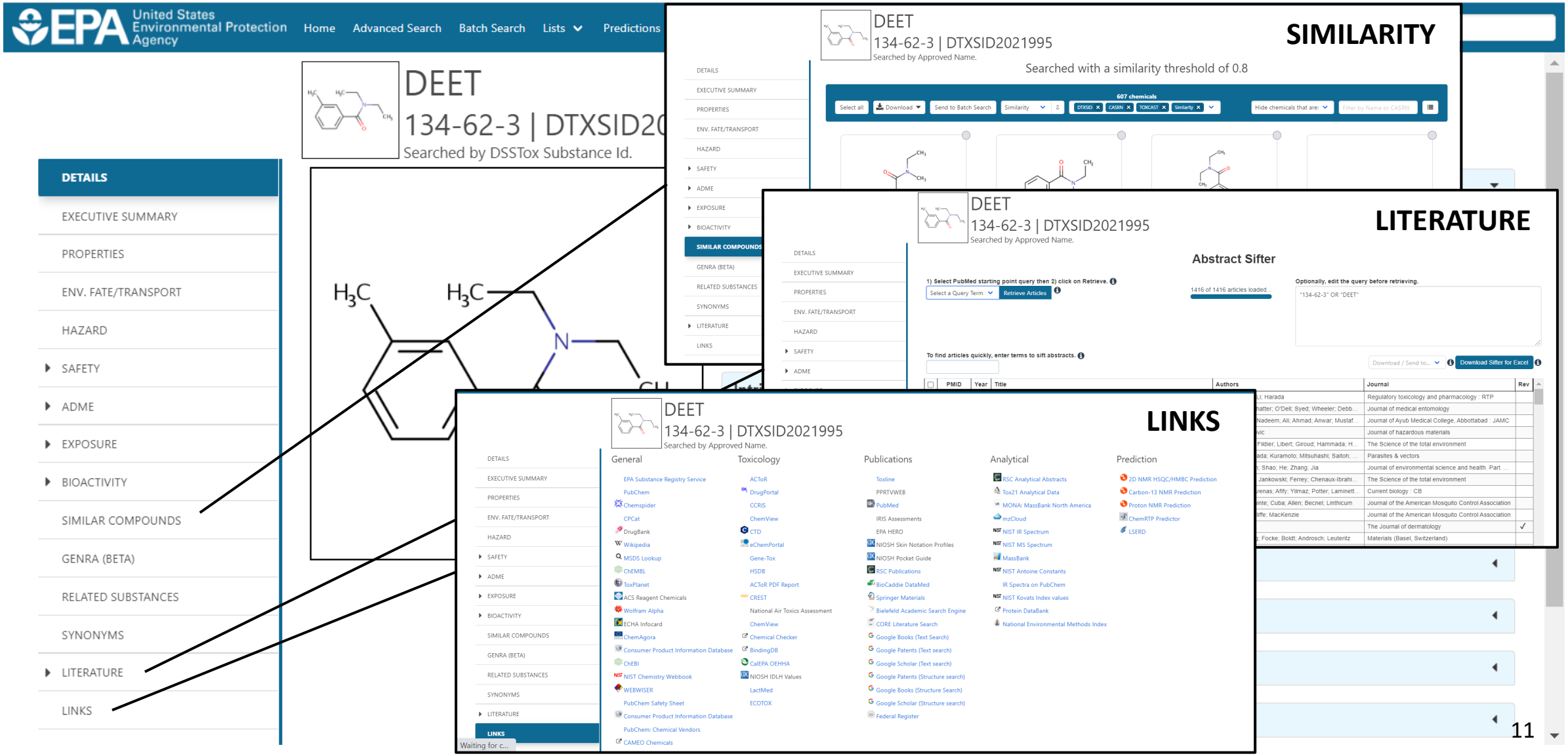

CompTox Chemicals Dashboard

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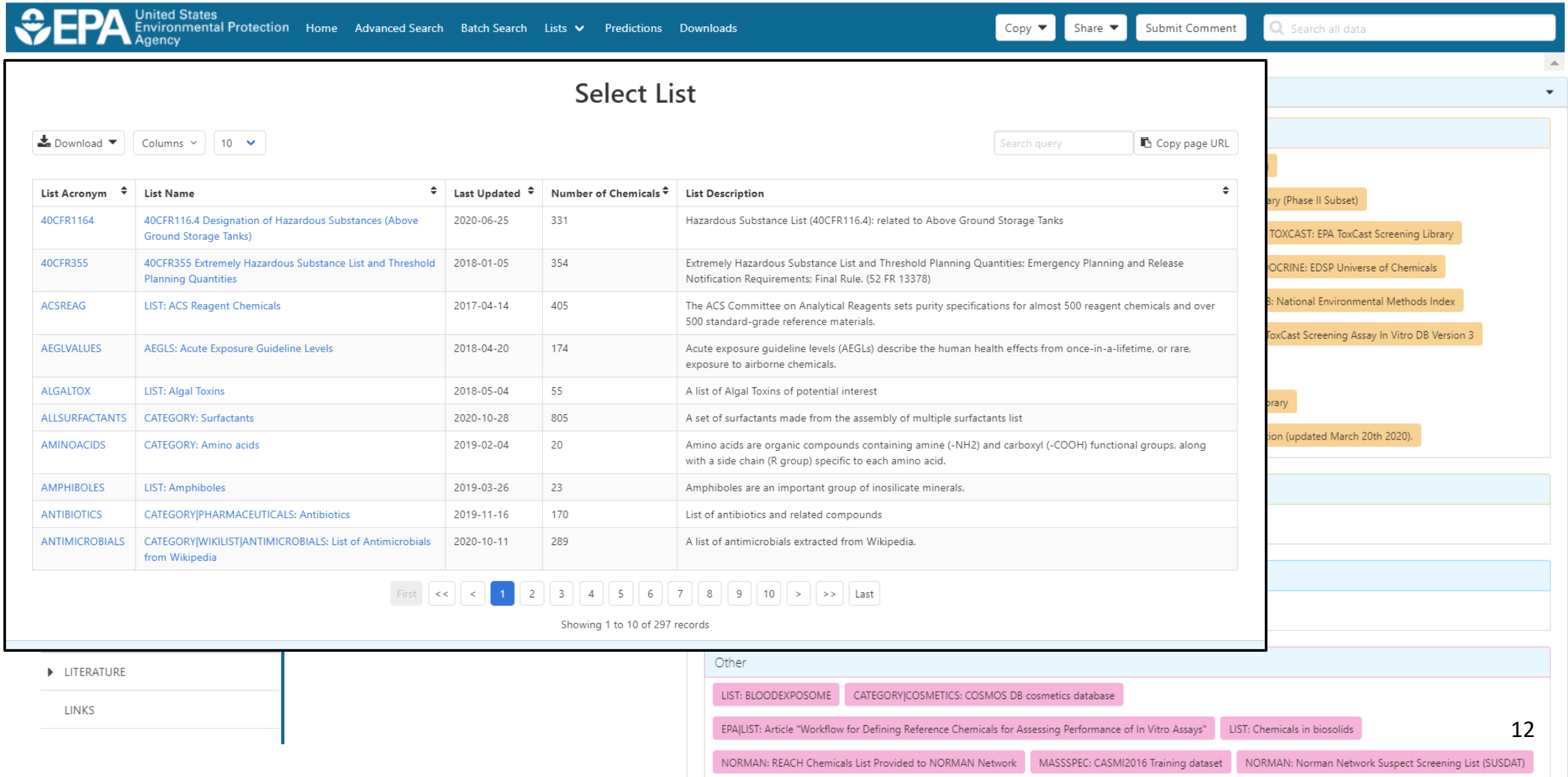
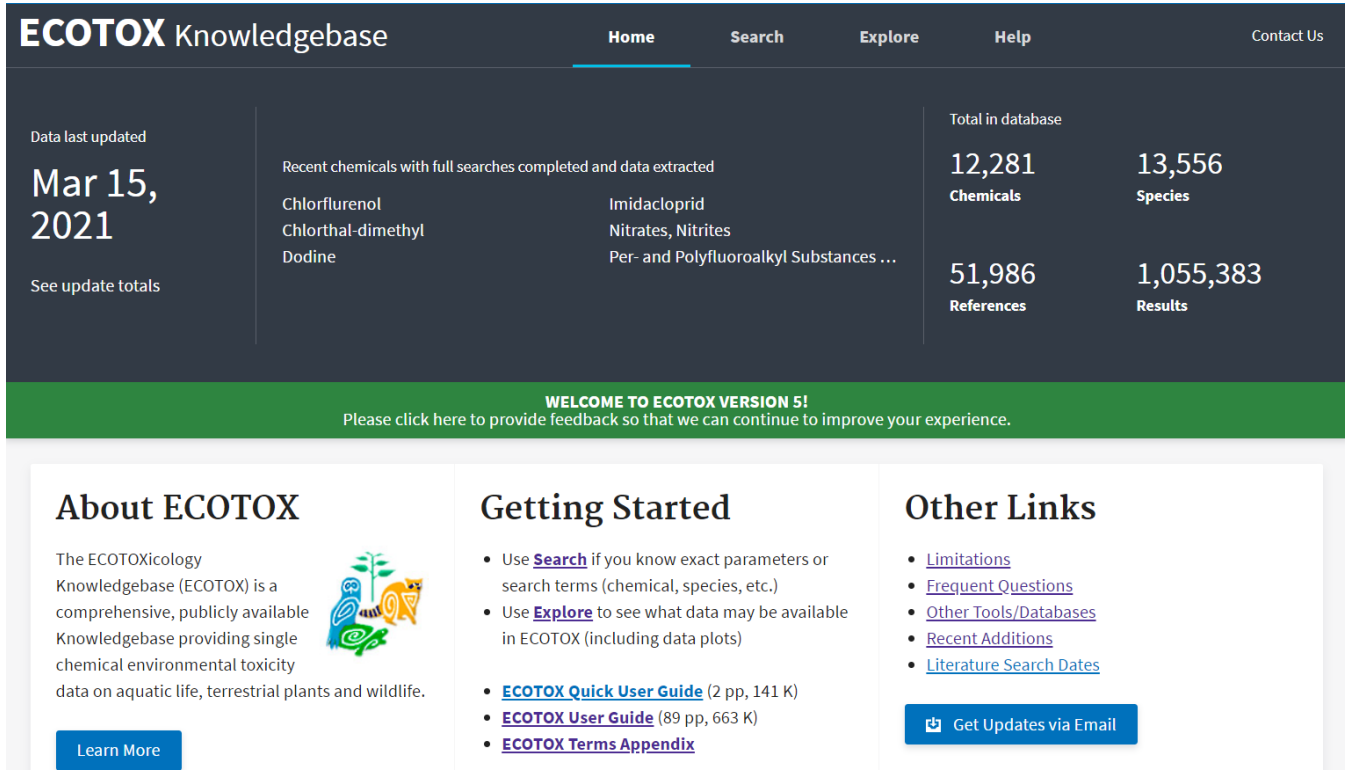


ECOTOX Knowledgebase

Publicly available, curated database providing toxicity data from single-chemical exposure studies to aquatic life, terrestrial plants and wildlife

- From comprehensive search and review of open and grey literature
  - Data extracted from acceptable studies, with up to 250 fields
  - Updated quarterly to public website
- 30+ year history
  - Originated in the early 1980s
  - Developed at US EPA's Office of Research and Development in Duluth
- Current user statistics
  - 8,000 distinct hosts search the Knowledgebase each month



www.epa.gov/ecotox

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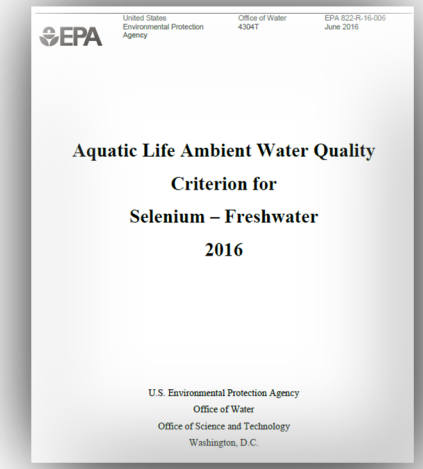
EPA Program and Regional Office Applications: Use in environmental decision making

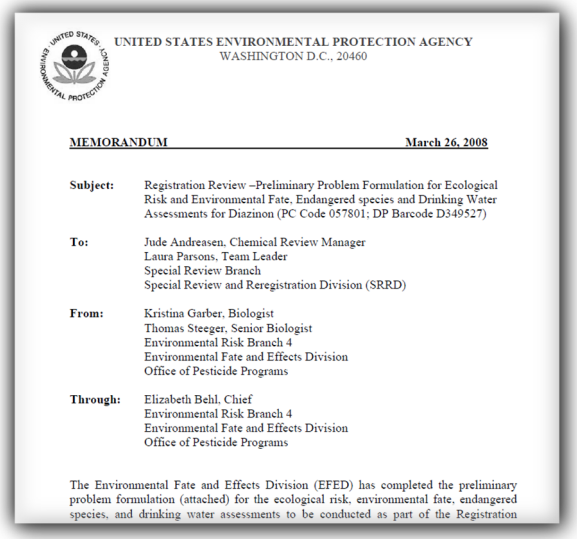

United States Environmental Protection Agency | Office of Water 4304T | EPA 822-R-16-006 June 2016

Aquatic Life Ambient Water Quality Criterion for Selenium – Freshwater 2016

U.S. Environmental Protection Agency
Office of Water
Office of Science and Technology
Washington, D.C.

Used for every Ambient Water Quality Criteria for Aquatic Life since 1985.

Used for every Ecological Risk Assessment for Office of Pesticides for chemical registration and re-registration (FY20 – 27 chemicals).


UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C., 20460

MEMORANDUM March 26, 2008

Subject: Registration Review –Preliminary Problem Formulation for Ecological Risk and Environmental Fate, Endangered species and Drinking Water Assessments for Diazinon (PC Code 057801; DP Barcode D349527)

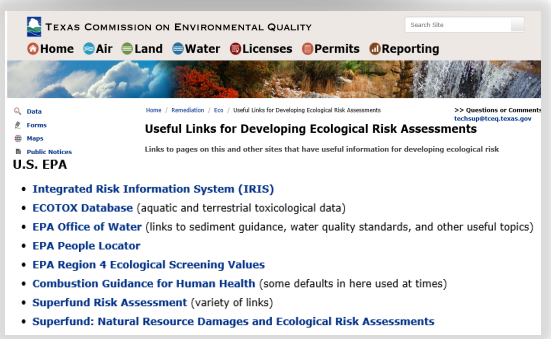
To: Jude Andreasen, Chemical Review Manager
Laura Parsons, Team Leader
Special Review Branch
Special Review and Reregistration Division (SRRD)

From: Kristina Garber, Biologist
Thomas Steeger, Senior Biologist
Environmental Risk Branch 4
Environmental Fate and Effects Division
Office of Pesticide Programs

Through: Elizabeth Behl, Chief
Environmental Risk Branch 4
Environmental Fate and Effects Division
Office of Pesticide Programs

The Environmental Fate and Effects Division (EFED) has completed the preliminary problem formulation (attached) for the ecological risk, environmental fate, endangered species, and drinking water assessments to be conducted as part of the Registration

Used by Office of Land and Emergency Management (Superfund and ORCR), HQ, Regions and States for site assessments and in emergency response.


TEXAS COMMISSION ON ENVIRONMENTAL QUALITY

Home | Air | Land | Water | Licenses | Permits | Reporting

Data
Forms
Maps
Public Notices

Home / Remediation / Eco / Useful Links for Developing Ecological Risk Assessments

>> Questions or Comments
tceqsup@tceq.texas.gov

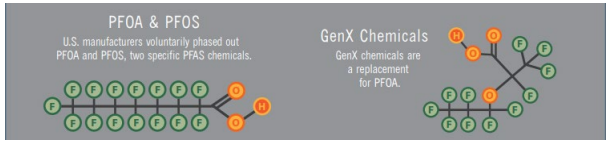
Useful Links for Developing Ecological Risk Assessments

Links to pages on this and other sites that have useful information for developing ecological risk

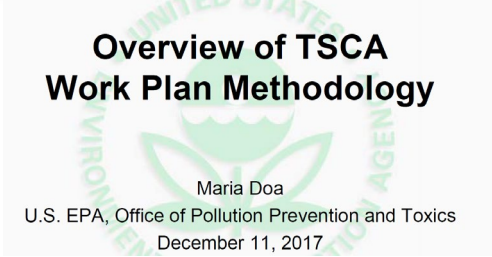
U.S. EPA

- **Integrated Risk Information System (IRIS)**
- **ECOTOX Database** (aquatic and terrestrial toxicological data)
- **EPA Office of Water** (links to sediment guidance, water quality standards, and other useful topics)
- **EPA People Locator**
- **EPA Region 4 Ecological Screening Values**
- **Combustion Guidance for Human Health** (some defaults in here used at times)
- **Superfund Risk Assessment** (variety of links)
- **Superfund: Natural Resource Damages and Ecological Risk Assessments**

Providing ecological hazard data for the prioritization and assessment of chemicals for TSCA/Lautenberg Act.



Providing ecological toxicity data for PFAS to researchers, EPA Eco Risk Assessment Forum, DoD Tri-Services ERA Work Group and others.


Overview of TSCA Work Plan Methodology

Maria Doa
U.S. EPA, Office of Pollution Prevention and Toxics
December 11, 2017

Ecological Hazard

Ecological hazard data are extracted from the EPA ToxValDB database where it had been compiled from the EPA ECOTOX database. Although data are available for a variety of species, only data for aquatic species are used in the current illustration. The data can come from any of the following study types: mortality:acute, mortality:chronic, reproductive:acute, reproductive:chronic, growth:acute, growth:chronic (all from ECOTOX). The types of effect levels are LDxx/LCxx/ECxx/EDxx where xx can range from 1% to 100%, and LOEL/NOEL/LOEC/NOEC. Values must be in units of mg/L. For each chemical, the lowest toxicity value was separately determined for acute and chronic studies, regardless of species. The

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Applications of ECOTOX

ECOTOX Knowledgebase

Chemical environmental toxicity data for aquatic life, terrestrial plants and wildlife

Interoperability with databases/tools

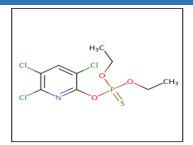
DTXSID/CASRN

Species ID; Protein ID

Integrated ontology

Reference ID

Chemicals Dashboard



SeqAPASS

Adverse Outcome Pathway WIKI

HERO
Health & Environmental Research Online

EPA Program Offices and Regions, States, Tribes, Other Federal Agencies and International Entities

Ecological Risk Assessments
Ambient Water Quality Criteria
Ecological Screening Values
Chemical Prioritization
Emergency Response

Tools and Applications

Species Sensitivity Distributions
(e.g., US EPA's WebICE, NOAA's CAFÉ)
PNECs and Eco Thresholds for Toxicological Concern
QSAR (e.g., ECOSAR, TEST, OECD QSAR Toolbox)
Bioaccumulation Factor modeling and validation
Adverse Outcome Pathway (AOP) development

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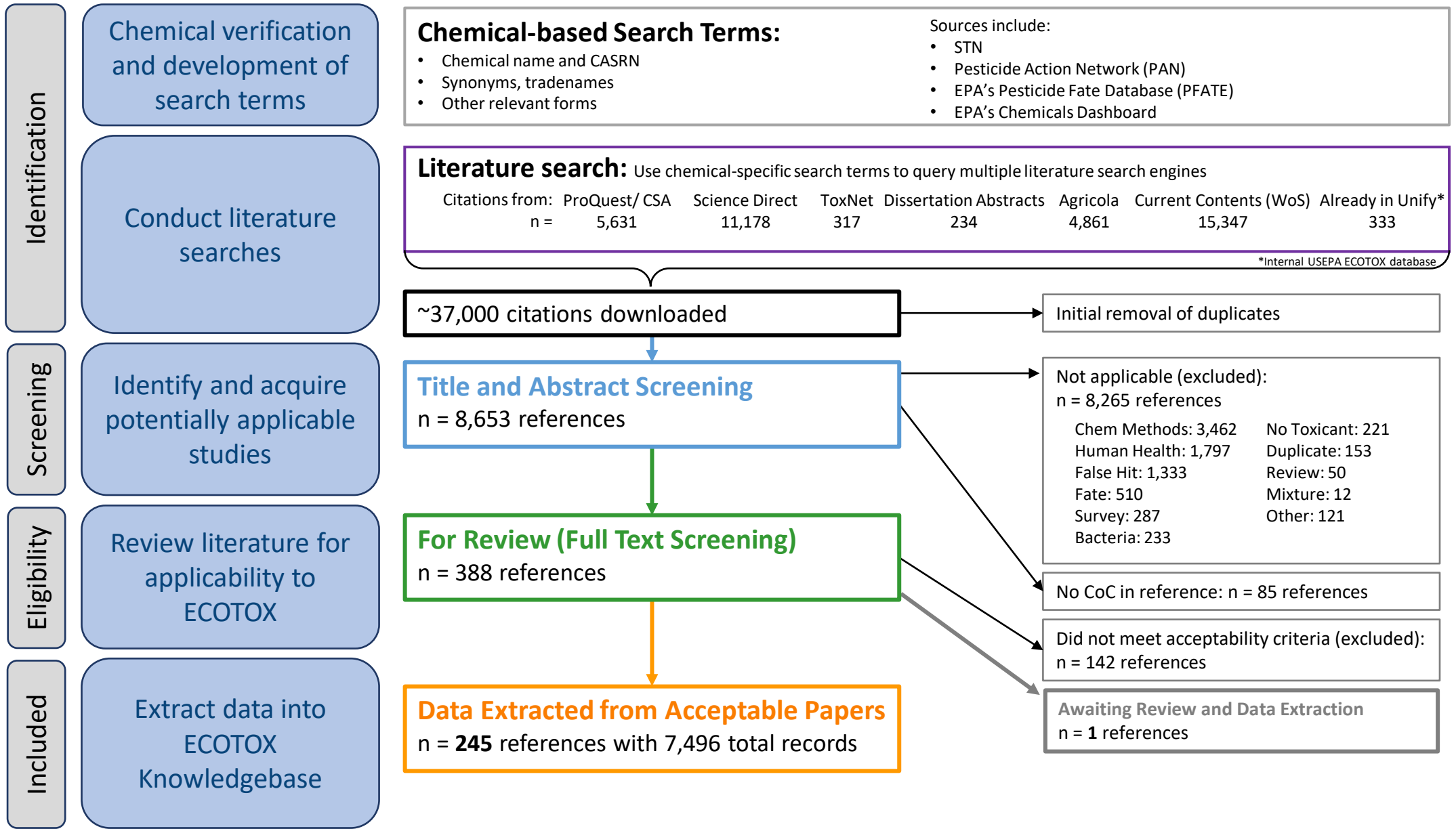
ECOTOX Pipeline: Systematic Review/Data Curation



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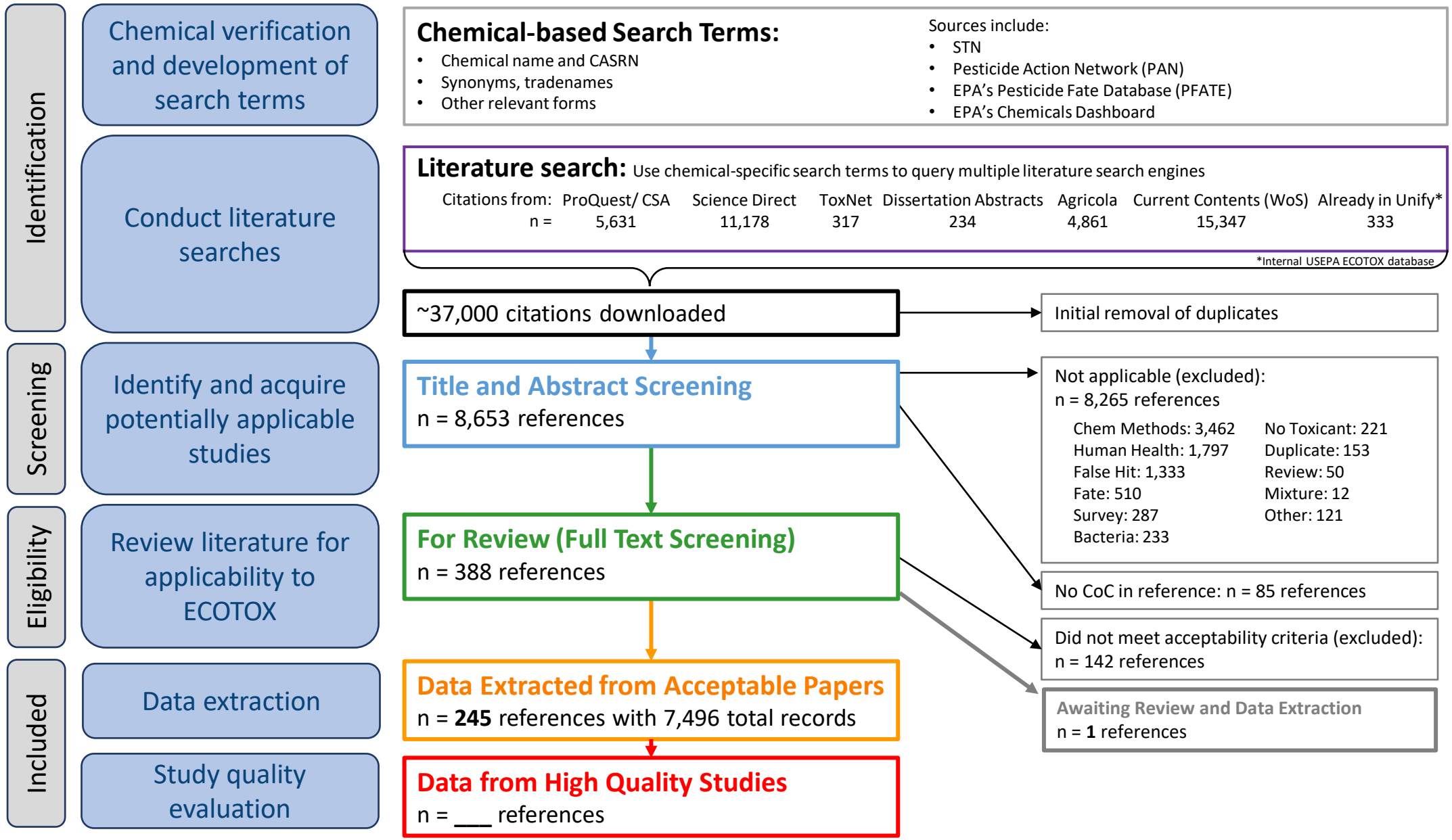
ECOTOX Pipeline: Systematic Review/Data Curation



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ECOTOX Pipeline: Systematic Review/Data Curation

Identification

Chemical verification and development of search terms

Conduct literature searches

Screening

Identify and acquire potentially applicable studies

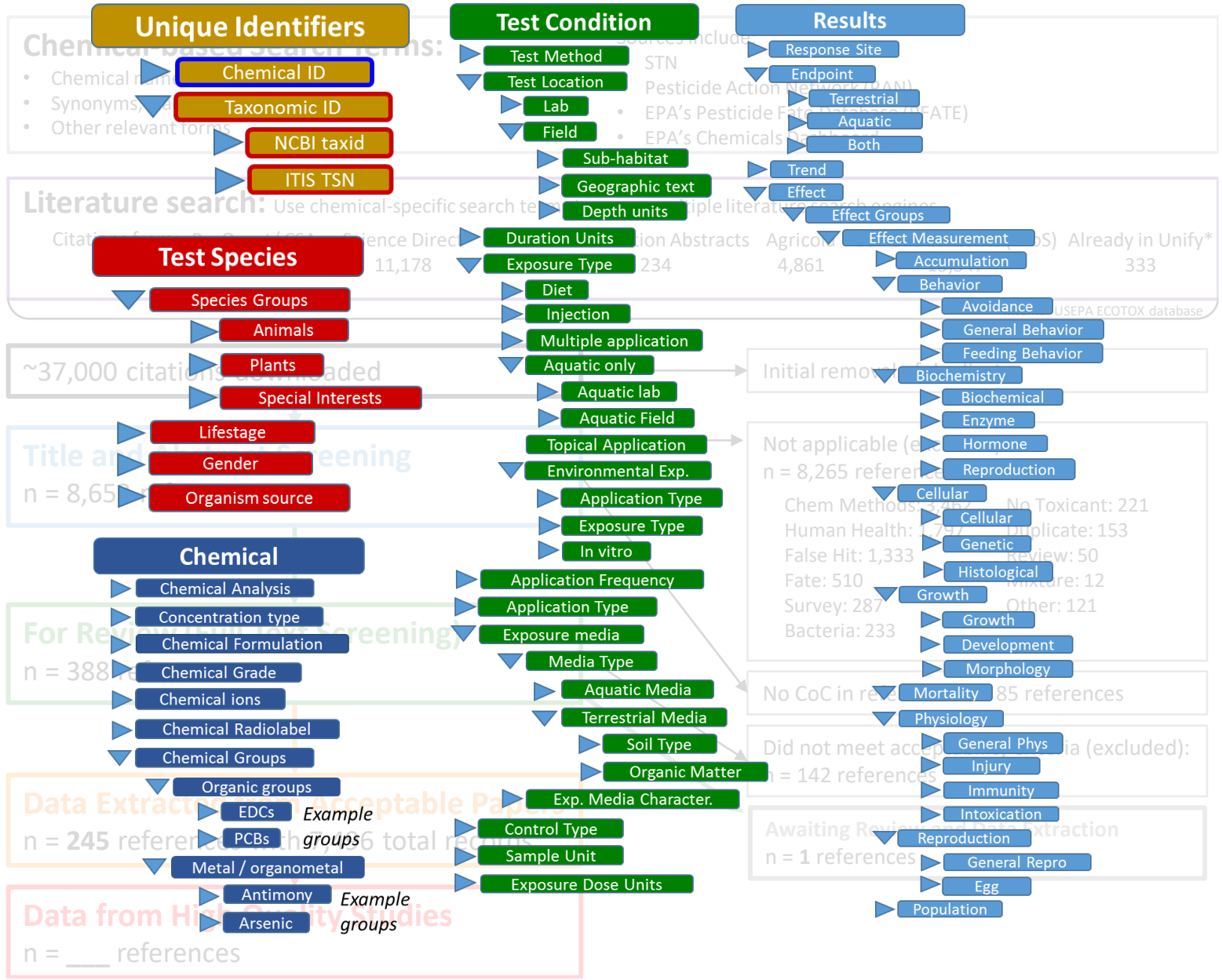
Eligibility

Review literature for applicability to ECOTOX

Included

Data extraction

Study quality evaluation



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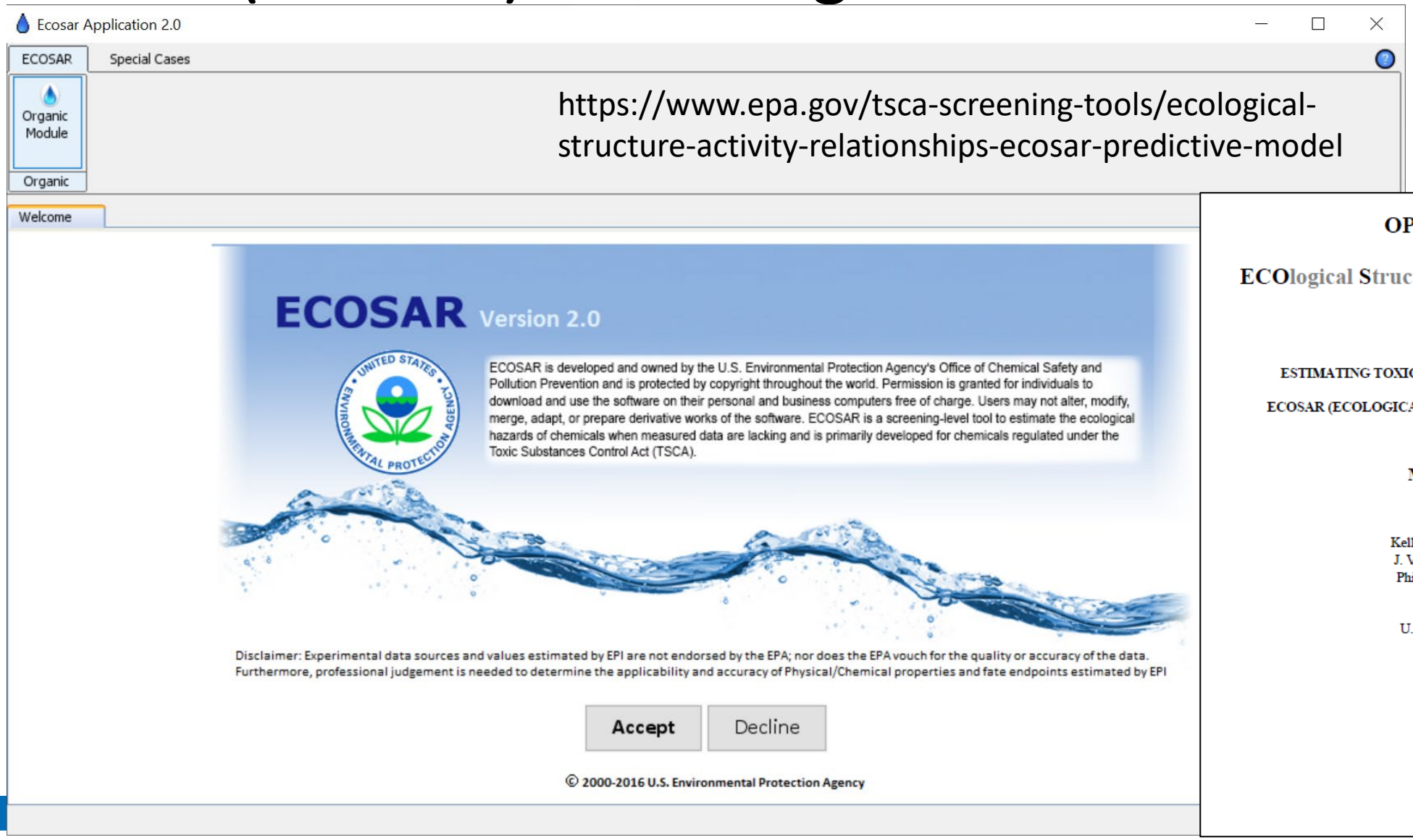
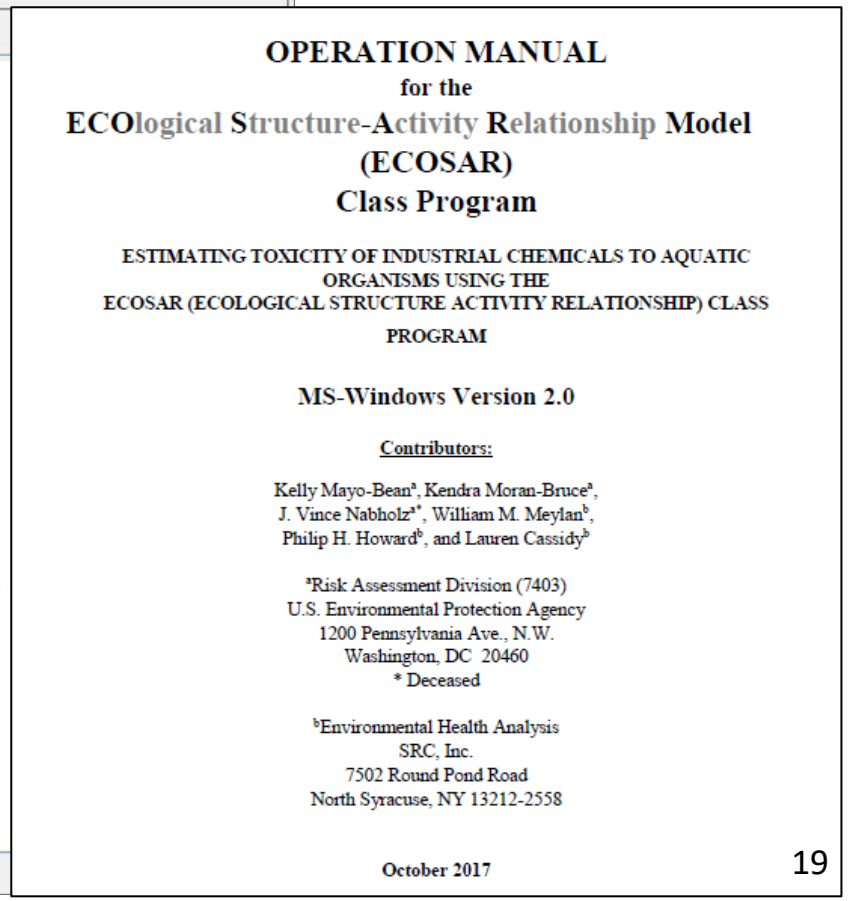
ECOlogical Structure-Activity Relationship Model (ECOSAR) Class Program



https://www.epa.gov/tsca-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model



OPERATION MANUAL
for the
ECOlogical Structure-Activity Relationship Model
(ECOSAR)
Class Program

ESTIMATING TOXICITY OF INDUSTRIAL CHEMICALS TO AQUATIC ORGANISMS USING THE ECOSAR (ECOLOGICAL STRUCTURE ACTIVITY RELATIONSHIP) CLASS PROGRAM

MS-Windows Version 2.0

Contributors:

Kelly Mayo-Bean[a], Kendra Moran-Bruce[a], J. Vince Nabholz[a*], William M. Meylan[b], Philip H. Howard[b], and Lauren Cassidy[b]

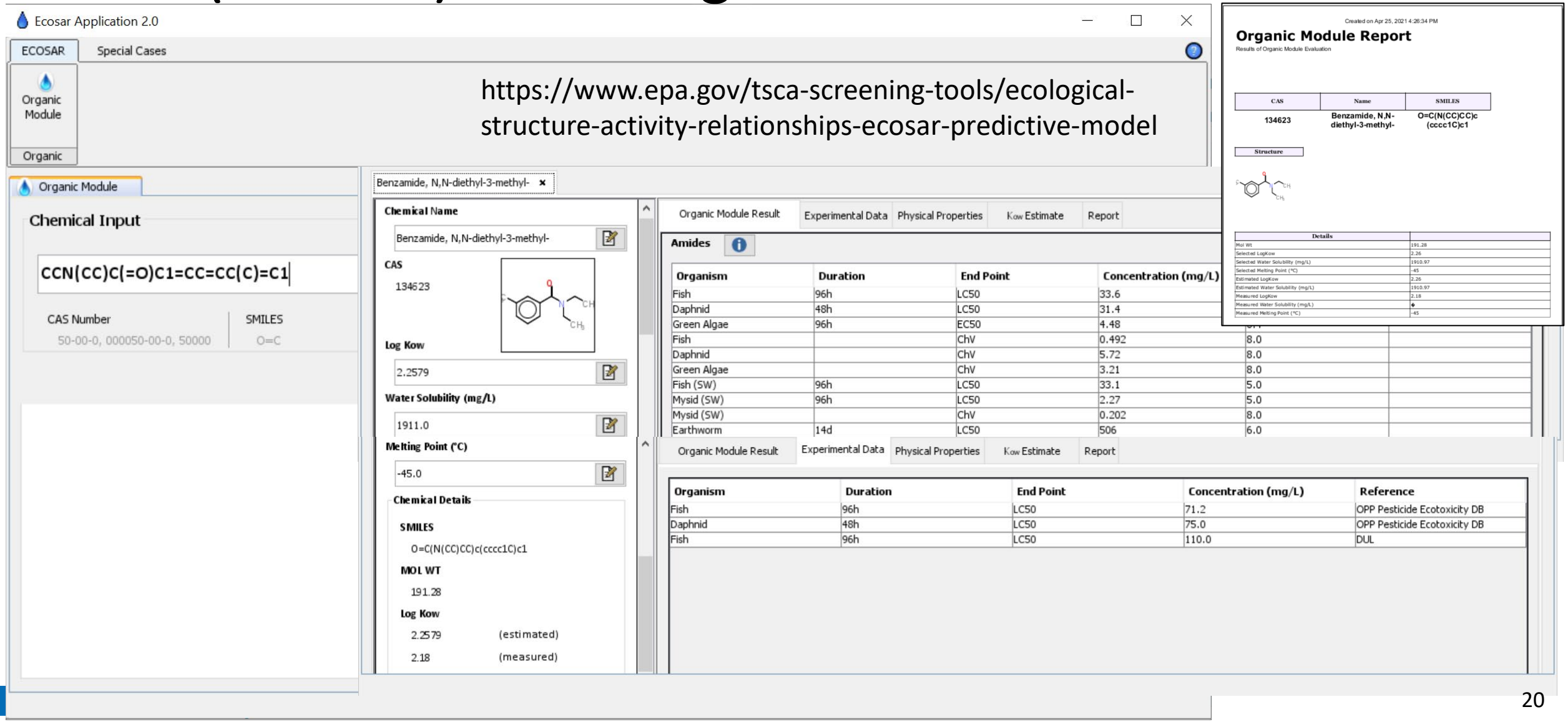
[a]Risk Assessment Division (7403)
U.S. Environmental Protection Agency
1200 Pennsylvania Ave., N.W.
Washington, DC 20460
* Deceased

[b]Environmental Health Analysis
SRC, Inc.
7502 Round Pond Road
North Syracuse, NY 13212-2558

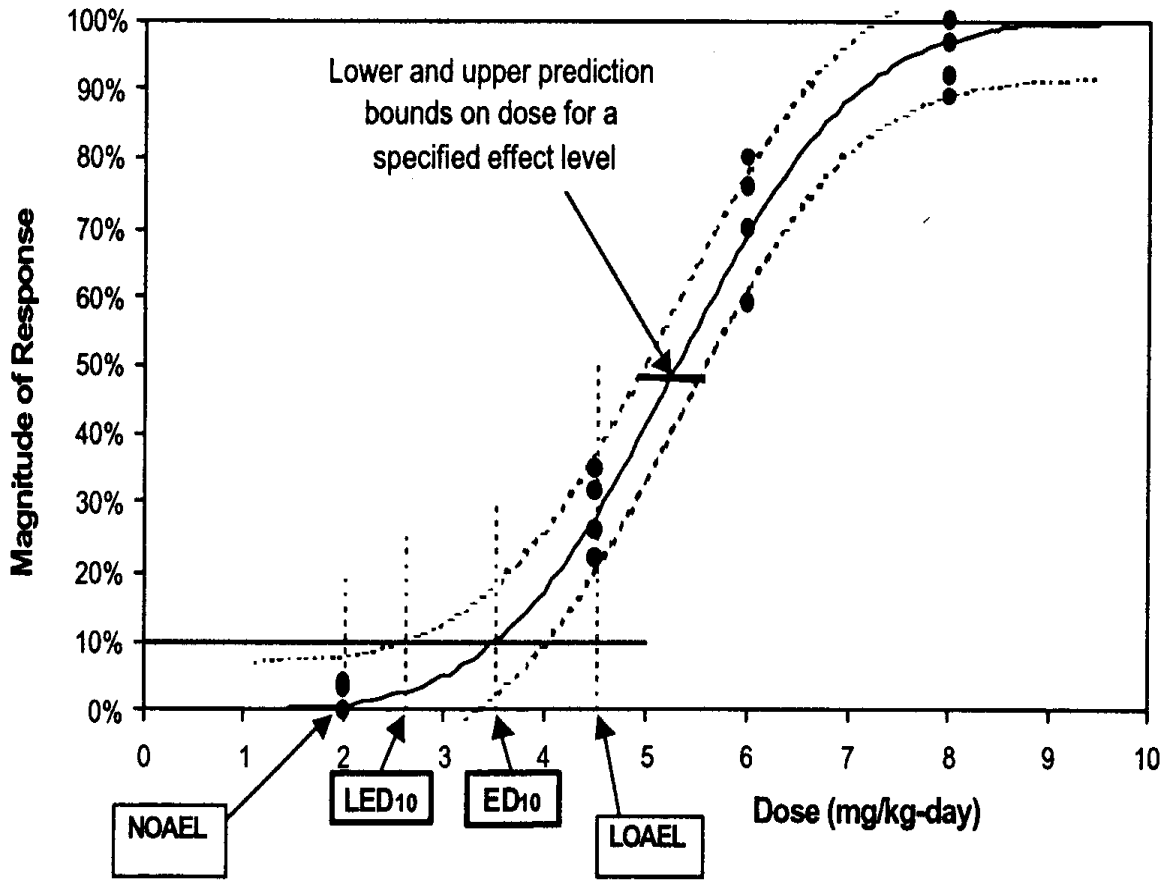
October 2017

ECOlogical Structure-Activity Relationship Model (ECOSAR) Class Program

https://www.epa.gov/tsca-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model

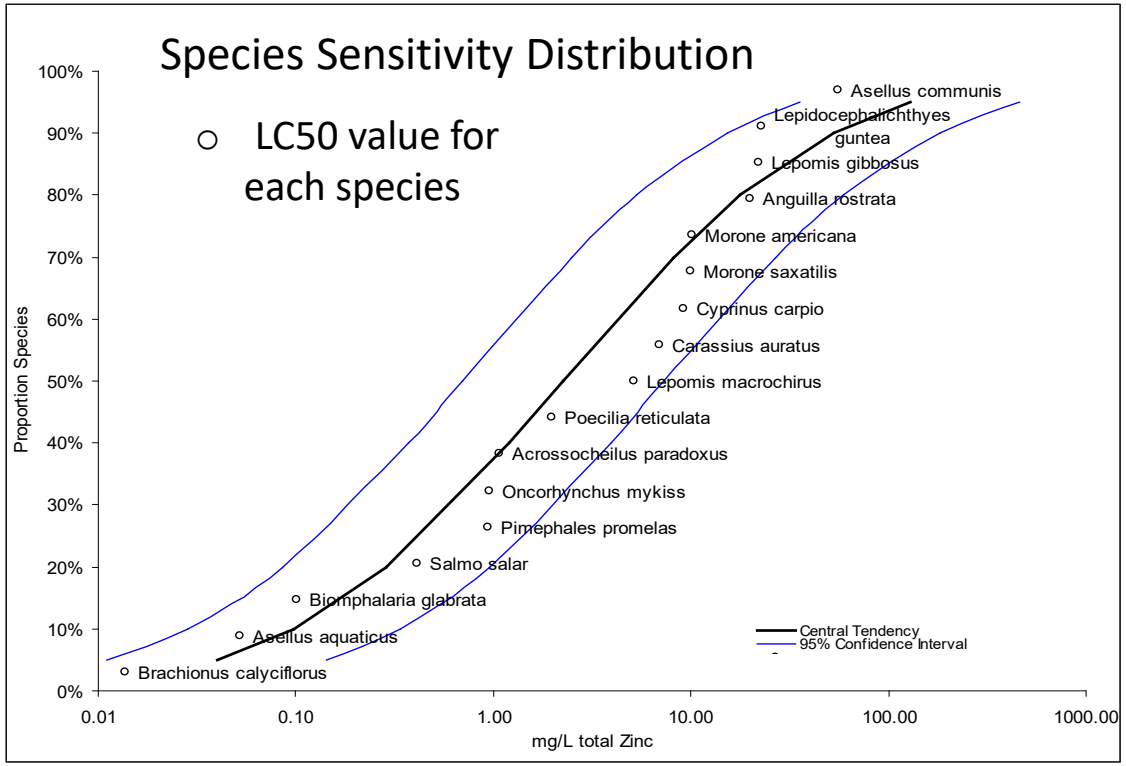


Hazard: Individual Species



Increasing proportion of species affected (LC_{50})

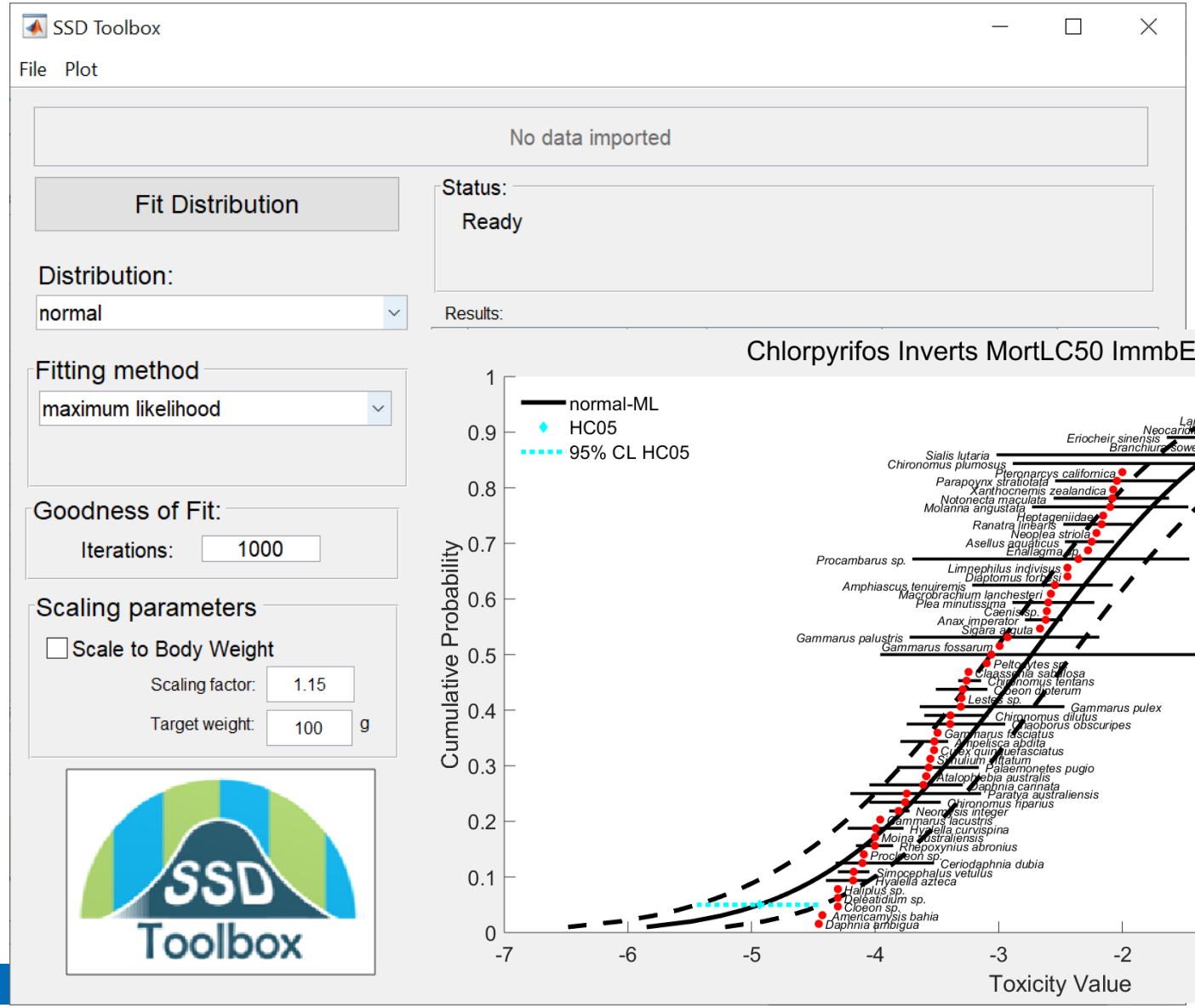
Hazard: Multiple Species

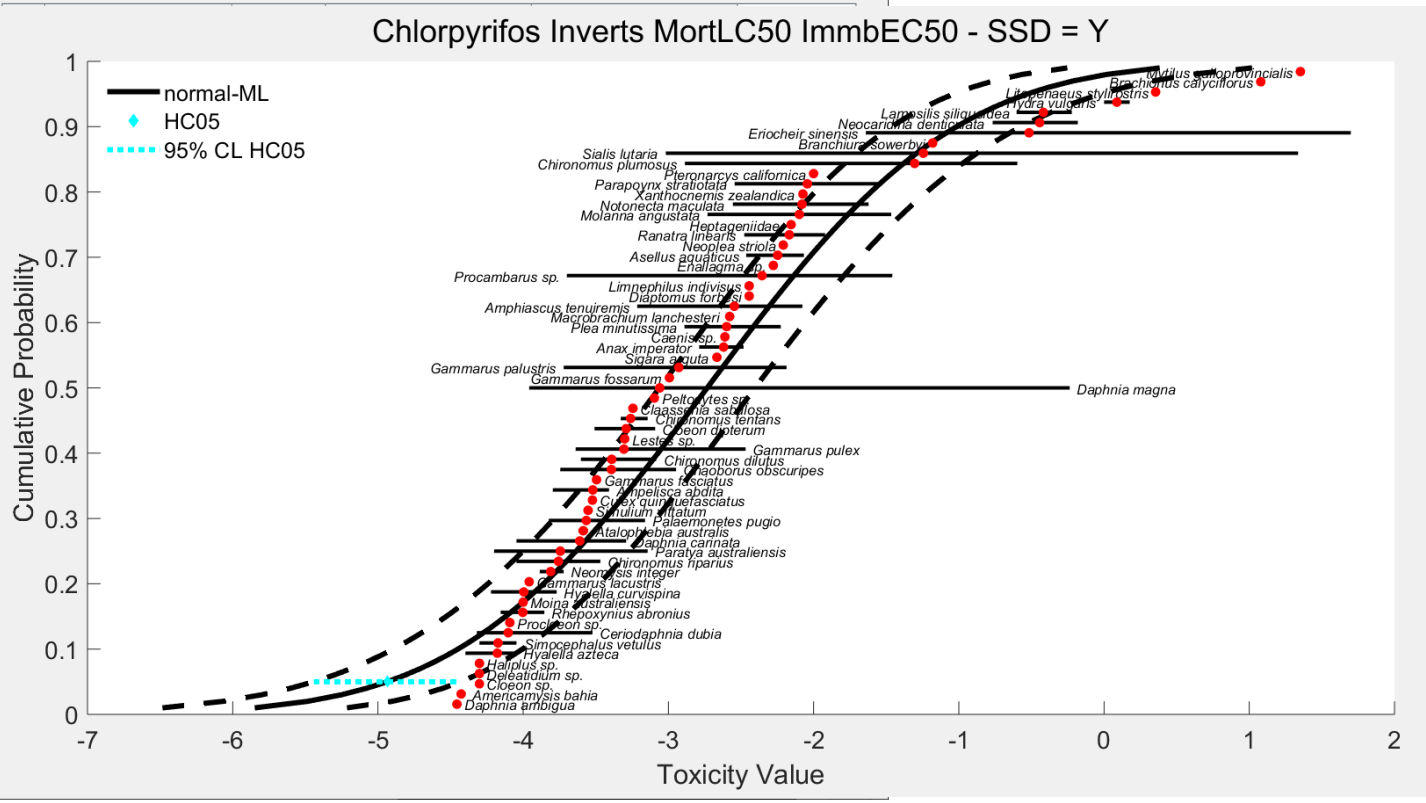


Increasing stressor intensity

Figures from Frithsen/Schofield 3/5/2021 lecture

Species Sensitivity Distribution Toolbox





https://www.epa.gov/chemical-research/species-sensitivity-distribution-ssd-toolbox

EPA/600/R-18/116

User's Manual: SSD Toolbox Version 1.0

v Etterson
l Protection Agency
n and Development
l Toxicology and Exposure
gy and Ecology Division
th, MN

SD
lbox

h 2020

Data Sources and Tools

- CompTox Chemicals Dashboard – A 'first-stop-shop' for chemical information. https://comptox.epa.gov/dashboard
  - Chemical Properties, Structure
  - Toxicity
  - Bioactivity
  - Exposure
  - Predictions
  - Links
- ToxRefDB (version 2) – Toxicity results from >5,000 in vivo studies, conducted largely to guidelines or specifications from the US EPA and National Toxicology Program. https://doi.org/10.1016/j.reprotox.2019.07.012
- ECOTOX Knowledgebase – Single chemical environmental toxicity data on aquatic life, terrestrial plants and wildlife. https://cfpub.epa.gov/ecotox/
- InVitroDB – ToxCast data from assays testing chemical activity. https://www.epa.gov/chemical-research/exploring-toxcast-data
- CPDat (Chemical and Products Database) – Information mapping more than 49,000 chemicals to usage or function in 16,000 consumer products. https://www.epa.gov/chemical-research/chemical-and-products-database-cpdat

Data Sources and Tools

- Read-Across and Quantitative Structure Activity Relationship models
  - OPERA (Open Structure-activity/property Relationship App) – Provide predictions of physicochemical properticies and chemical activity to non-animal approaches for predicting toxicity. https://ntp.niehs.nih.gov/whatwestudy/niceatm/comptox/ct-opera/opera.html
  - ECOSAR (Ecological Structure Activity Relationships) – Providing predictions of acute and chronic toxicity to aquatic organisms. https://www.epa.gov/tsca-screening-tools/ecological-structure-activity-relationships-ecosar-predictive-model
  - TEST (Toxicity Estimation Softward Tool) – Provide estimates of toxicity of chemicals using QSARs. https://www.epa.gov/chemical-research/toxicity-estimation-software-tool-test
- httk (High-Throughput Toxicokinetics) R Package – Includes models and databases to help researchers, risk assessors, and regulators understand how chemicals interact with the body. https://cran.r-project.org/web/packages/httk/index.html
- SSD Toolbox (Species Sensitivity Distribution Toolbox) – Simplifies the process of generating Species Sensitivity Distributions by gathering a variety of algorithms to support users in fitting, summarizing, visualizing and interpreting SSDs. https://www.epa.gov/chemical-research/species-sensitivity-distribution-ssd-toolbox
- McNest (Markov Chain Nest Productivity Model) – Predicts annual reproductive success of bird populations based on existing toxicity and species life history information. https://www.epa.gov/chemical-research/markov-chain-nest-productivity-model
- Fish Toxicity Translator – A mechanistic population model to estimate population-level effects of chemical exposure scenarios based on existing toxicity and life history characteristics on fish.
- SeqAPASS (Sequence Alignment to Predict Across Species Susceptibility) – Provides online screening tool to extrapolate toxicity information across species based on protein targets. https://seqapass.epa.gov/seqapass/
- AOPwiki – An Adverse Outcome Pathway (AOP) is a structured representation of biological events leading to adverse effect(s). The AOPwiki is a repository for AOPs developed and in development. https://aopwiki.org/