Identifying and Curating Ecologically-Relevant Toxicity Data with the ECOTOXicology Knowledgebase Literature Search and Review Process

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What is the ECOTOX Knowledgebase?

The ECOTOXicology Knowledgebase is a comprehensive, publicly available, curated database that provides environmental toxicity data from single chemical exposure studies on aquatic life, terrestrial plants and wildlife.

ECOTOX originated in the early 1980s and is maintained by U.S. EPA ORD, available at: www.epa.gov/ecotox

ECOTOX was developed to meet the need for:

1) an ***authoritative source of toxicological data*** for regulators, and
2) an efficient way for the regulated community and researchers to ***document literature searches and acquisition of data*** used for risk assessments, risk management and research.

Annually, comprehensive search and data extraction is done for 35-50 chemicals to meet the needs of EPA ORD and Program Offices.

As of September 2019, ECOTOX has curated ecological data for:

11,756 chemicals
12,906 species
49,153 references
952,634 test results

Each quarter ~7,500 new records added.

ECOTOX Pipeline: Systematic Review/Data Curation

Comprehensive search and review of toxicity data in open and grey literature (e.g., government documents), with transparent standard operating procedures that meet requirements for systematic review protocols.

Data curated for >200 fields of information (see Table 2) as reported by authors.

- Streamlines the cost for literature searches and data curation within the Agency and provides all information in public format for States, Tribes, Industry, and International governmental entities.
- Continuous update of protocols and annual evaluation of most applicable sources to ensure inclusion of relevant publications

Literature search and study selection flow diagram with ECOTOX pipeline

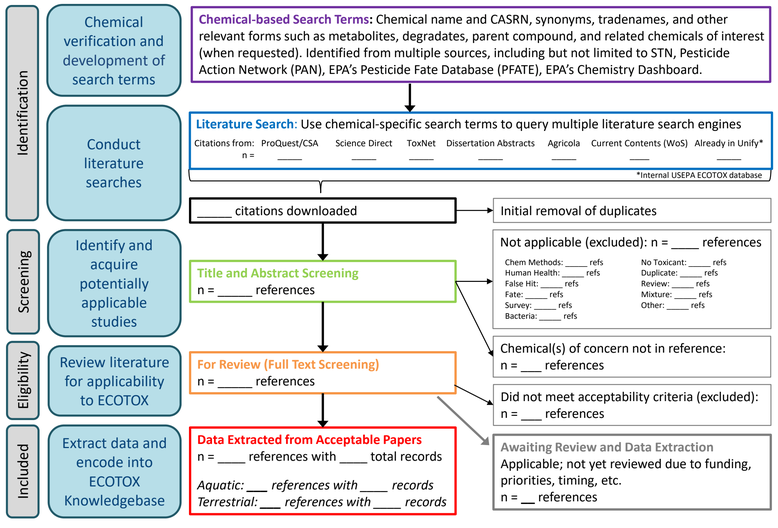

Figure 1. Literature search and study selection flow diagram, with general steps on left from PRISMA (grey) and ECOTOX pipeline (blue). Criteria for inclusion are listed in Table 1.

Criteria for inclusion in ECOTOX

Table 1. Criteria for inclusion in ECOTOX, with recently-developed PECO statement and requirements in well-established ECOTOX SOPs.

Recently developed PECO statement for ECOTOX		Requirements/Inclusionary Criteria from ECOTOX SOP
P (Population)	Animal: Aquatic and terrestrial species (live, whole organism) of any lifestage (including preconception, in utero, lactation, peripubertal, and adult stages). Include wild mammals (e.g. Peromyscus sp.), insects, spiders, amphibians, birds, crustaceans, fish, molluscs, reptiles, worms and invertebrates. Bacteria and viruses are not included. Plants: Aquatic and terrestrial species (live), all plants including algal, moss, lichen and fungi species	• Ecologically-relevant species • Live, whole organisms • Organism taxonomic information verifiable against standard taxonomic sources • Priority species are wild (test results for terrestrial domestic and laboratory species are used to fill data gaps when needed) • NOT: humans, monkeys, bacteria, viruses, yeast • In vitro studies (with viable cells or tissue) flagged for possible inclusion as requested by Programs.
E (Exposure)	Relevant forms: Chemical of Concern, name and CASRN (plus synonyms, tradenames); when requested: Metabolites, degradants, parent compound and related chemicals Animal: Any exposure to relevant forms of the chemical of concern including via water, injection, diet, and dermal, with reported concentration and duration. Inhalation studies are excluded unless this is the primary route of environmental exposure (e.g., for volatile compounds). Plants: Exposure to relevant forms of the chemical of concern via water or soil, with reported concentration and duration. * Studies involving exposures to mixtures will be included only if they include exposure to a relevant form for the chemical alone. * Chemical exposures for aquatic organisms where only sediment concentrations are reported from field studies are excluded (unless porewater concentration measured); laboratory-based sediment studies are retained.	• Verifiable Chemical Abstract Services (CAS) number • Single chemical exposure • Relevant to environmental exposure • Report exposure concentration, dose or application rate • Report duration of exposure • Sediment studies must have a water concentration reported to be included • NOT: Air pollution studies related to CO2 and ozone
C (Comparison/ Control)	A concurrent control group exposed to vehicle-only treatment and/or untreated control (control could be a baseline measurement).	• Must have a control treatment
O (Outcome)	All biological effects (including bioaccumulation from laboratory studies with concurrently measured water and tissue concentrations).	• Biological effect measured • Effect concurrent with associated chemical exposure • Adverse effects are priority (beneficial, nutritional effects are lower priority)
Publication/ Data Format		• Primary source of the data • Study must be a full article in English • NOT: Reviews or abstract only

Data extraction fields in ECOTOX

Table 2. Types of data extracted from each reference (if applicable and reported), with category, example data fields, and examples of how ECOTOX fields can inform study evaluation questions.

Category	Data Fields (not all inclusive)	Select study evaluation questions with relevant ECOTOX field(s)
Chemical	Chemical Name, CASRN, Grade, Purity, Formulation, Carrier *Test Specific*: Analysis, Application Type and Rate/Frequency, Number of Doses, Doses, Concentration Type (e.g., active ingredient or formulation), Concentration/Dose associated with each effect and/or endpoint	Is test substance identified? **Required for inclusion in ECOTOX inclusion** Is the purity of test substance reported? Chemical Purity Were chemical concentrations verified? Chemical Analysis (e.g., nominal versus measured concentrations)
Species	Scientific and Common Name, Taxonomy, Lifestage, Age, Initial and Final Weight, Gender, Source	Is the species given? **Verifiable species (Scientific Name, etc.) required for inclusion in ECOTOX** Are the organisms well described? Organism Source, Lifestage, Age, Gender, Initial and Final Weight
Test Conditions	Test Method, Media Type, Test Location, Exposure and Study Duration, Control, Experimental Design, Physical and Chemical Soil and Water Parameters	Are appropriate controls performed? **A control is required for inclusion in ECOTOX**, type described in Control Is a guideline method (e.g., OECD) used? Test Method Are the experimental conditions appropriate and acceptable for the test substance and organism? Test Method, Media Type, Test Location, Experimental Design, Physical and Chemical Soil and Water Parameters (e.g., pH, Temperature, Dissolved Oxygen)
Test Results	Effect (observation of a response): general effect groups and specific effect measurements, Endpoint (quantification of an observed effect, e.g., LC50), Trend, Response Site, Effect %, Statistical Significance and Level, Observed Duration (exposure Duration when result observed), Bioconcentration (BCF or BAF) with units	Are the reported effects and endpoints appropriate for the purpose, test substance and organism? Effect Measurement, Endpoint Is the response/effect statistically significant? Statistical Significance, Significance Level

Recent Updates for Requested Chemicals – 4 examples

Per- and Polyfluoroalkyl Substances (PFAS)

Requested by Office of Research and Development

Literature search for >300 PFAS
title/abstract and full-text review, inclusionary criteria applied, data extraction from 1st set completed June 2019, with on-going quarterly updates

13,208 total data records from 437 references for 264 species

96 PFAS with ecological toxicity data

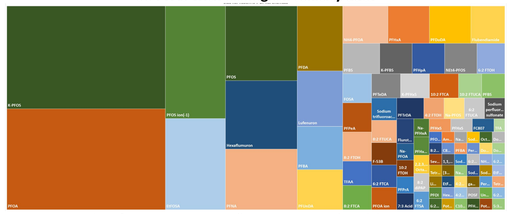

Figure 2. Box plot of 96 PFAS in ECOTOX (by unique CASRN), with box size representing number of references that include relevant and acceptable ecological toxicity data.

Uranium

Requested by Office of Land and Emergency Management

Literature search for 13 CASRNs (e.g., Uranium, Uranium nitrate, Uranyl sulfate, Uranyl nitrate, Schoepite)
title/abstract and full-text review, inclusionary criteria applied, and data extraction completed in 2019

4955 total data records from 195 references for 144 species

Terrestrial data for multiple uranium compounds, with a range of effects

Figure 4. Data for uranium compounds in Terrestrial organisms by exposure concentration and type of Effect, data for 9 CASRNs, 7 plottable (all endpoints included).

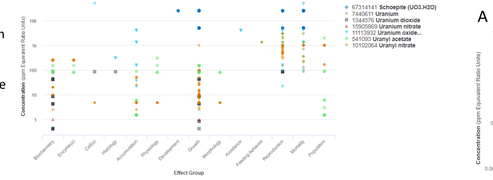

Table 3. Number of references by CASRN for each species groups.

algae	trees/shrubs	amphibians	crustacean	reptiles	birds	fish	insect/spider	mammals	molluscs	other inverts	worms
6	45	0	29	0	1	31	7	0	6	1	8
4	3	0	4	0	0	8	1	0	4	5	0
1	5	0	3	0	1	9	0	0	3	1	4
2	5	1	0	0	0	9	1	0	0	3	1
3	3	0	2	0	0	1	2	0	1	0	0
0	3	0	1	0	0	1	0	0	0	0	0
0	0	0	1	0	0	0	0	0	0	0	2
0	2	0	0	0	0	0	0	0	0	0	0
1	1	0	0	0	0	0	0	0	0	1	0

Ziram

Requested by OCSPP's Office of Pesticide Programs

Literature search for CASRN: 137-30-4
title/abstract and full-text review, inclusionary criteria applied, and data extraction completed in 2019

1,211 total data records (786 terrestrial, 425 aquatic) from 102 references

Data for 75 Terrestrial Species from 15 Classes | **Data for 41 Aquatic Species from 12 Classes**

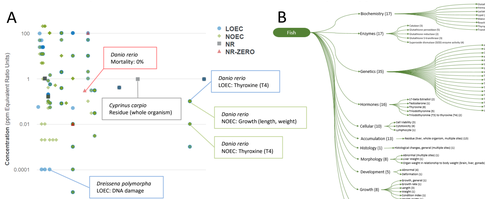

Figure 3. Distribution of data records in ECOTOX for Ziram by Species Group and general type of Effect, for [A] Terrestrial species and [B] Aquatic species.

Decabromodiphenyl ether (DCBE)

Requested by Risk Assessment Division in OCSPP's OPPT

Literature search for CASRN: 1163-19-5 (BDE209)
title/abstract and full-text review, inclusionary criteria applied, data extraction completed in 2019

651 total data records from 43 references for 31 species

Aquatic data demonstrate the diversity in types of effects

Figure 5. BDE209 data for: [A] Aquatic species by exposure concentration and duration of exposure, with all endpoints included, and [B] Effects observed in fish species from 18 studies showing types of effects and effect measurements, with respective number of data records for endpoints with LOEC or NR (no effect data excluded).

Advances for ECOTOX: Recent and Upcoming

- Increased variety of toxicological effects and endpoints curated, including biochemistry, enzymes, hormones, and genetics effect measures
- Risk assessor default output focusing on critical data requested
- Updated user interface with improved functionality to the EXPLORE feature, and new interactive tools for data exploration and visualization
- Integration of EPA's Toxic Substances Control Act (TSCA) systematic review protocols into ECOTOX, including expanded literature searches, *in vitro* data, HERO reference IDs, and study evaluation protocols
- Mapping of ECOTOX terms to Open Biological and Biomedical Ontology (OBO) class identifiers for advanced query capabilities and interoperability
- Enhanced interoperability across tools and databases, including CompTox Chemistry Dashboard, AOPWiki, SeqAPASS, and environmental contaminant databases

U.S. Environmental Protection Agency
Office of Research and Development

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

SETAC North America 40th Annual Meeting, November 5, 2019, Toronto, Ontario, Canada

For further information on the ECOTOX Knowledgebase, contact ECOTOX Support: ecotox.support@epa.gov