Animal Alternatives in Environmental Risk Assessment

Our Mission

The committee's mission is to ensure the development of a sound technical basis for alternative test methods as a means to reduce, refine, or replace standard ecotoxicity test procedures around the globe.

Steering Team

Public Steering Team Members

Mr. Mark Bonnell (Environment and Climate Change Canada)
Dr. Adam Lillicrap (Norwegian Institute for Water Research, NIVA)
Dr. Ryan Otter (Middle Tennessee State University)
Dr. Marlo Jeffries (Texas Christian University)
Dr. Kristin Schirmer (Swiss Federal Institute of Aquatic Science and Technology, Eawag)
Dr. Teresa Norberg-King (US Environmental Protection Agency)

Private Steering Team Members

Dr. Peter Wilson (Sanofi)
Dr. Marc Leonard (L'Oréal Corporation)
Dr. Kristin Connors (Procter & Gamble Company)
Dr. Sarah Hughes (Shell Chemicals, Ltd.)

HESI Staff

Dr. Michelle R. Embry (membry@hesiglobal.org)
Ms. Connie Mitchell, MS (cmitchell@hesiglobal.org)
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Webpage

https://hesiglobal.org/animal-alternatives-in-environmental-risk-assessment

2021 Committee Highlights

Participating Organizations

7 government/regulatory agencies, **12** academic/research institutes, **8** industry, and **3** others

Publications

4 published, **1** accepted, and **7** in progress

Web Tools and Assays

1 web tool

- EnviroTox (envirotoxdatabase.org), a curated, publicly available aquatic toxicity database that includes several analysis tools

Outreach

1 poster presentation, **6** oral presentations, **1** guest lecture, and **1** webinar

- **1** poster presentation and **2** oral presentations at the Society of Environmental Toxicology and Chemistry (SETAC) Europe 31st Annual Meeting (May 2021, virtual)
- **1** oral presentation at the "1st Workshop for Risk Assessment: Successes and Challenges for Safety Assessment" organized by the Federal University of Paraná (Brazil), University of São Paulo (Brazil), and University of Washington (January 2021, virtual)
- **1** oral presentation at the 11th World Congress on Alternatives and Animal Use in the Life Sciences (August 2021, virtual)
- **2** oral presentations at the SETAC Latin America 14th Biennial Meeting (September 2021, virtual)
- **1** guest lecture for the George Mason University Environmental Toxicology Course on "ecoTTC and the EnviroTox Database and Tools: Applications for Ecological Risk Assessment" (March 2021, virtual)
- **1** webinar co-organized by HESI, Eawag, and AquaTox Solutions on "New OECD Test No. 249: Fish Cell Line Acute Toxicity - The RTgill-W1 Cell Line Assay" (September 2021, virtual)

Collaborations

1 external

- Co-project with NC3Rs on endocrine disruption

Geographic Representation

Canada, Denmark, France, Germany, Italy, Netherlands, Norway, Switzerland, United Kingdom, and United States

Working Groups

- **EnviroTox Database and Tools/ecoTTC.** This group is tasked with developing a strategy to update and augment the EnviroTox database (envirotoxdatabase.org) and refine and further develop applicable tools. In 2021, the database added 900+ chemicals with 5,000 datapoints and removed 10,000+ duplicate entries. Ongoing work is focused on the development of case studies and applications.
- **Effluent Assessment.** Plans for a 2020 meeting with key stakeholders to help develop a comprehensive testing and evaluation plan for effluent NAMs were put on hold due to COVID-19. However, work will progress in 2022 related to sharing of information and development of a template to collect existing effluent information, with plans for an in-person meeting when travel allows. An overview of the research proposal that was developed in 2019 was presented at the 2020 SETAC Europe Virtual Annual Meeting and discussions are ongoing to identify additional funding to support (and potentially expand) the research project
- **Ecotoxicology Endocrine Toolbox: Alternative Methods.** This team, a collaboration between HESI and NC3Rs, is assessing available *in vitro/in silico* methods (new approach methodologies [NAMs]) to evaluate chemicals that may act via an endocrine pathway in fish and amphibians.
- **Ecotoxicology Endocrine Toolbox: *In Vivo* Analysis.** This team, a collaboration between HESI and NC3Rs, is evaluating current *in vivo* EDC tests in fish and amphibians, focusing on analysis of historical control data. This will involve several efforts related to analysis and communication of available *in vivo* information. The overall purpose is to provide a foundation upon which new alternative methods will be evaluated and to critically assess existing *in vivo* test methods.
- **Weight-of-Evidence in Acute Fish Toxicity Assessment (SWIFT).** The initial work of this committee focused on the development and scientific issues surrounding the fish embryo test (FET) as an animal alternative. While accepted as an Organization for Economic Cooperation and Development (OECD) guideline, uptake and use in regulatory assessments has been hampered due to a lack of interpretational guidance. A new initiative to develop qualitative and quantitative weight-of-evidence frameworks for assessment of acute fish toxicity using a wide range of lines of evidence is proposed. A working group, led by Dr. Adam Lillicrap (NIVA), successfully received European Chemical Industry Council Long-Range Initiative (CEFIC-LRI) funding to develop a Bayesian network model with collaboration from HESI and committee members.

Areas of Focus for 2022

New Approach Technologies for Understanding Risk in the Environment (NATURE). HESI will be merging the Animal Alternavites and Bioaccumulation Committees in 2022 to create the New Approach Technologies for Understanding Risk in the Environment (NATURE) Committee. The committee's mission will be to develop, refine, and communicate the scientific tools and approaches needed to suport ecological risk assessment around the globe. This committee will address (but is not necessarily restricted to) the following topical areas: (a) tools to evaluate the toxicokinetics of organic chemicals that facilitate the connection between exposure and hazard (e.g., ADME and bioaccumulation) and (b) the use and development of new approach methodologies (NAMs) and animal alternative methods for ecological assessment in various contexts (e.g., screening, prioritization, C&L, risk assessment) sectors (e.g., pharmaceutical, agrochemical, chemical, personal care/cosmetics), and regulatory jurisdictions.

- **EnviroTox Database and Tools/ecoTTC.** Work will continue to identify a sustainable process to augment and update the EnviroTox database on a yearly basis. A case study on "Exploring conservatism in ecoTTC and CTD: case study of chemicals with regulatory water quality values" is nearing completion. This example was presented at the 2020 SETAC Europe Virtual Annual Meeting and includes neurotoxicants, benzenes, and phthalates as examples. It is anticipated that this case study will be completed in late 2021, with journal submission in 1Q 2022.
- **Effluent Assessment.** Plans for data/information collection are underway, with scoping for a series of informational/training webinars beginning in 4Q 2021.
- **Ecotoxicology Endocrine Toolbox.** The two major working groups (alternatives and *in vivo*) are completing several manuscripts to be submitted in late 2021/early 2022. These include (a) New approach methodologies (NAMs) in the ecological endocrine activity toolbox, (b) Analysis of amphibian metamorphosis assay data, (c) Dose setting in *in vivo* endocrine assays, and (d) Analysis of historical control data from existing *in vivo* tests to evaluate endocrine disruption.
- **Weight-of-Evidence in Acute Fish Toxicity Assessment (SWIFT).** The project is continuing to pull together data sources and refine the Bayesian Network.

Strategic Impact Areas

Enhanced Efficiency and Accuracy in Safety Assessment Practice

The EnviroTox database has pulled together a curated resource of existing information that will allow for development and evaluation of new methods in a more straight-forward manner. The tools associated with the database allow for novel analysis approaches, particularly with regard to risk-based prioritization. The committee's database and tools were recently highlighted in a European Commission Report, and the ecoTTC concept was invited to be part of a forthcoming special issue of *Frontiers in Toxicology* dedicated to the TTC concept more broadly.

Catalysis of New Science

The initial work of this committee was focused on the FET test, which has led to various initiatives, including the recently funded CEFIC-LRI SWIFT project. SWIFT is working to develop qualitative and quantitative weight-of-evidence frameworks for assessment of acute fish toxicity using a wide range of lines of evidence. This project will develop a Bayesian network model with collaboration from HESI and various committee members and is led by researchers at NIVA in Norway.

Enhancement of the Societal Knowledge Base on Environmental or Ecological Processes of Relevance for Protecting the Health of the Environment

The totality of this committee's work is dedicated to environmental protection. In particular, this group's work is focused on developing and evaluating alternative strategies that can be used to maximize resource use while providing sufficient levels of protection. The effluent subgroup is working to identify approaches and strategies that can reduce the use of *in vivo* fish tests, coupling scientific advancements with considerations and needs of various stakeholders at the national, state/provincial, and local levels.

2021 Awards, Grants and Recognition

- HESI was awarded $20,000 over two years from Cefic-LRI to support staff time for the Weight-of-Evidence in Acute Fish Toxicity (SWIFT) program.
- The manuscript "Recommendations for improving methods and models for aquatic hazard assessment of ionizable organic chemicals" (Escher et al., 2020) was recently recognized as one of *Environmental Toxicology and Chemisty*'s Top 10 Exceptional Papers of 2020. The concepts for the publication were initiated in an "Experts Workshop on the Ecological Risk Assessment of Ionizable Organic Chemicals" that was co-sponsored by HESI, Environment and Climate Change Canada, Cefic, and SETAC.

Publications

Published

Brill JL, Belanger SE, Barron MG, Beasley A, Connors KA, Embry M, Carr GJ (2021) Derivation of algal acute to chronic ratios for use in chemical toxicity extrapolations. *Chemosphere.* doi: 10.1016/j.chemosphere.2020.127804.

Barron MG, Otter RR, Connors KA, Kienzler A, Embry MR (2021) Ecological thresholds of toxicological concern: a review. *Frontiers in Toxicology*. doi: 10.3389/ftox.2021.640183.

Belanger SE, Beasley A, Brill JL, Krailler J, Connors KA, Carr GJ, Embry M, Barron MG, Otter R, Kienzler A (2021) Comparisons of PNEC derivation logic flows under example regulatory schemes and implications for ecoTTC. *Regulatory Toxicology and Pharmacology*. doi: 10.1016/j.yrtph.2021.104933.

Burden N, Embry MR, Hutchinson TH, Lynn SG, Maynard SK, Mitchell CA, Pellizzato F, Sewell F, Thrope KL, Weltje L, Wheeler JR (2021). Investigating endocrine disrupting properties of chemicals in fish and amphibians: opportunities to apply the 3Rs. *Integrated Environmental Assessment and Management*. doi: 10.1002/ieam.4497.

Accepted

Kuo DTF, Rattner BA, Marteinson SC, Letcher RJ, Fernie KJ, Treu G, Deutsch M, Johnson M, Deglin S, Embry M (2021) A review on bioaccumulation and biotransformation of organic chemicals in birds. *Reviews of Environmental Contamination and Toxicology*. Accepted.

In Progress

Mitchell CA et al. New approach methodologies (NAMs) in the endcorine activity toolbox: environmental assessment for fish and amphibians. In preparation.

Authors TBD. Critical evaluation of existing *in vivo* tests for endocrine modes of action. In preparation.

Wheeler et al. Control of performance of amphibian metamorphosis assays with xenopus laevis. In preparation.

Authors TBD. Concentration setting for *in vivo* ecotoxicology studies. In preparation.

Embry MR, Barron MG, Bejarano A, Connors KA, Fay K, Kienzler A, Mitchell CA et al. Quantifying conservatism in ecoTTC and CTD: case study of chemicals with regulatory water quality criteria values. In preparation.

Authors TBD. Analysis of amphibian metamorphosis assay data. In preparation. Anticipated submission mid-2022.

Authors TBD. Existing *in vivo* tests to evaluate endocrine disruption. In preparation. Anticipated submission mid-2022.

Participating Organizations

Government/Regulatory Agencies

Environment and Climate Change Canada
European Commission, Joint Research Centre
National Institute for Public Health and the Environment (RIVM, The Netherlands)
Norwegian Institute for Water Research (NIVA)
Ontario Ministry of the Environment, Conservation, and Parks
Swiss Federal Institute of Aquatic Science and Technology (Eawag)
US Environmental Protection Agency

Academic/Research Institutes

George Mason University
Helmholtz Centre for Environmental Research (UFZ)
Middle Tennessee State University
National Institute for Basic Biology (Japan)
St. Cloud State University
Texas Christian University
University of Aarhus
University of Bern
University of Guelph
University of Heidelberg
University of Plymouth
University of Saskatchewan

Industry

Chevron
DuPont
FMC Corporation
L'Oréal Corporation
Procter & Gamble Company
S.C. Johnson & Son, Inc.
Sanofi
Shell Chemicals, Ltd.

Others

National Centre for the Replacement, Refinement, and Reduction of Animals in Research (NC3Rs, UK)
Research Institute for Fragrance Materials (RIFM)
Watchfrog (France)