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

Mark Bonnell (Environment and Climate Change Canada)
Dr. Aude Kienzle (European Commission, Joint Research Centre)
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)
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)
Connie Mitchell, MS (cmitchell@hesiglobal.org)

2020 Committee Highlights

Participating Organizations

7 government/regulatory agencies, **12** academic/research institutes, **9** industry, and **2** others

Publications

1 published, **2** submitted, and **5** in progress

Scientific Meetings and Trainings

1 workshop

- Collaboration with National Centre for the 3Rs (NC3Rs) on "Investigating Endocrine Disrupting Properties in Non-Mammalian Vertebrates: Opportunities to Apply the 3Rs" (February 2020, London, UK)

Web Tools and Assays

1 web tool

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

Outreach

4 poster presentations

- **2** at Society of Environmental Toxicology and Chemistry (SETAC) Europe 30th Annual Meeting (May 2020, virtual): posters presented on the effluent research project and "Quantifying Conservatism in ecoTTC and CTD"
- **2** at SETAC North America Meeting 2020 (November 2020, virtual): posters presented on the endocrine disrupting chemicals (EDC) project and ecoTTC predicted no effect concentration (PNEC) work

Collaborations

1 external

- Co-project with NC3Rs on endocrine disruption

Geographic Representation

Canada, Denmark, France, Germany, Italy, Japan, 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 (https://envirotoxdatabase.org) and refine and further develop applicable tools. Ongoing work is focused on development of case studies and updating/augmenting the database. Recent efforts have focused on developing manuscripts to describe and document the approaches and tools within EnviroTox, including a focus on algal acute to chronic ratios as well as PNECs.

- **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 2021 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.
- NEW **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.
- NEW **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.
- NEW **HESI/NC3Rs Workshop Follow-Up Team.** This group is developing a manuscript based on the output and critical discussions from the February 2020 workshop.
- NEW **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 (€250,000 for 2 years) to develop a Bayesian network model with collaboration from HESI and committee members. The kick-off meeting for the project was held in Spring 2020, and work is underway. HESI will receive a total of $20,000 to support staff time on this project over the next 2 years.

Areas of Focus for 2021

EnviroTox/ecoTTC

- A small group is continuing to work on augmenting and updating the EnviroTox database with additional data sources. Discussions are ongoing with the US Environmental Protection Agency (USEPA) Ecotox database group on how to more seamlessly include new relevant studies. In addition, inclusion of European Chemicals Agency (ECHA) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) data (via the OECD Toolbox) and USEPA High Production Volume Information System (HPVis) data is ongoing.
- A case study ("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 2020 once the database updates have been integrated into EnviroTox.
- A manuscript describing the platform's tools will be part of a special issue of *Frontiers in Toxicology* that is focused on the TTC. The issue should be published in 2021.
- There are several ongoing dialogues and collaborations related to the EnviroTox database, with more anticipated in 2021. This includes discussions with the National Oceanic and Atmospheric Administration's CAFÉ database as well as the USEPA Ecotox database group.

Effluent Assessment

- Plans for data/information collection are underway, with scoping for a virtual meeting format to initiate in Fall 2020.

Endocrine

- The two major working groups (alternatives and *in vivo*) are collecting assay information and plan to perform analyses and develop several manuscripts in late 2020/early 2021. The manuscript topics are as follows: (1) New Approach Methodologies (NAMs) in the Ecological Endocrine Activity Toolbox, (2) Analysis of Amphibian Metamorphosis Assay Data, (3) Dose-Setting in *In Vivo* Endocrine Assays, and (4) Analysis of Historical Control Data From Existing *In Vivo* Tests to Evaluate Endocrine Disruption.

SWIFT

- Work on this project began in 1Q 2020, and ongoing efforts are and will continue to focus on collection of relevant data and information to inform the development of 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.

2020 Awards, Grants, and Recognition

- The EnviroTox database was highlighted in a 2019 European Commission Science Update, "New Online Tool to Improve the Environmental Risk Assessment of Chemicals."
- The European Commission called the EnviroTox database "a valuable resource," considering it a "credible way of filling data gaps." The committee's paper "Creation of a Curated Aquatic Toxicology Database: EnviroTox" (Connors et al. 2019) was one of *Environmental Toxicology and Chemistry's* most downloaded papers in 2019.

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.* 263:127804. doi: 10.1016/j.chemosphere.2020.127804.

Submitted

Belanger SE, Beasley A, Brill JL, Krailler J, Connors KA, Embry M, Barron MG, Otter R, Kienzler A (2020) Comparisons of PNEC derivation logic flows under various regulatory schemes and implications for ecoTTC. (anticipated submission 4Q 2020)

Burden N, Embry MR, Hutchinson TH, Lynn SG, Maynard SK, Mitchell CA, Pellizzato F, Thorpe KL, Weltje L, Wheeler JR (2020) Investigating endocrine disrupting properties of chemicals in fish and amphibians: opportunities to apply the 3Rs. (anticipated submission to *Integrated Environmental Assessment and Management*, 4Q 2020)

In Progress

Analysis of amphibian metamorphosis assay data (EDC *In Vivo* Group). (anticipated submission mid-2021)

Barron MG, Otter R, Connors KA, Kienzler A, Embry MR. Ecological thresholds of toxicological concern: History, development, and application. Invited paper for special issue of *Frontiers in Toxicology*. (anticipated submission 4Q 2020)

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. (anticipated submission early 2021)

Existing *in vivo* tests to evaluate endocrine disruption. (anticipated submission mid-2021)

New approach methodologies (NAMs) in the Ecological Endocrine Activity Toolbox. (anticipated submission mid-2021)

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)
Research Institute for Fragrance Materials
St. Cloud State University
Texas Christian University
University of Aarhus
University of Guelph
University of Heidelberg
University of Plymouth
University of Saskatchewan

Industry

Chevron
DuPont
ExxonMobil Biomedical Sciences, Inc.
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)
Watchfrog (France)