SETAC

Goals
Advance environmental science
Promote science-based decision making

Principles
• Multidisciplinary
• Multistakeholder engagement
• Science-based objectivity

setac.org/webinars
The Future of Environmental Health Sciences

- New approach methodologies
- Animal alternative testing
- Bioinformatics
- Big data
- One health approaches
International Consortium to Advance Cross-Species Extrapolation (ICACSER)

Global, cross-sector consortium includes researchers, regulators, and other advocates working to integrate bioinformatics approaches.
SETAC and ICACSER

Science Corner webpage
• www.setac.org/scixspecies

Resources and tools

Publications

Webinar Series
Society of Toxicology: Risk Assessment Specialty Section

- The Risk Assessment Specialty Section has over 700 members and has expressed an interest in participating in the Consortium’s activities.

- RASS’s Executive Committee (RASS EC) has agreed to provide support to the Consortium:
  - Publicizing events
  - Identifying members with an interest in the Consortium activities
Why the Interest in ICACSER?

Integral piece in human health and ecological risk assessment
- RA drives regulatory compliance
- Reduces animal use
- Addresses inadequate past practices
- Data-driven
- Promising new tools
Overview

- Meet the Steering Committee
- What was the motivation behind creating ICACSER?
- What are the primary challenges in extrapolation?
- What do we aim to accomplish?
- Who should be involved?
- What are the next steps?
Steering Committee

Carlie LaLone  
US EPA  
Co-founder

Fiona Sewell  
NC3Rs

Steve Edwards  
RTI

Patience Browne  
OECD

Michelle Embry  
HESI

Nil Basu  
McGill University

Geoff Hodges  
Unilever  
Co-founder

Established: March 2020
Chemicals make up the world around us – necessary for our modern society

Collectively protect human health and the environment
Motivation for ICACSER

- **Mutual goals** in translating science for regulatory use
- Eliminating or greatly **reducing the use of animals** in toxicology
- **Changing** regulatory landscape
  - Greater use of mechanistic, cell-based, and computationally derived information [New approach methods (NAMs)]
- Establish **confidence in mechanistic data** and provide evidence as to how it relates to apical level changes
  - Aid decision-makers in understanding **strengths and weaknesses for application**
    - Domain of applicability
- Establish **criteria/guidance for use** of NAMs
Reduce Animal Use

Merge human and eco health: Pathways
Need for Advances in Species Extrapolation

Define the taxonomic domain of applicability in AOP development

Use of historic toxicity data

High throughput transcriptomics

High-throughput screening assays (ToxCast)

Knowledge of a few surrogates representing the diversity of species in the environment
Species Extrapolation

What is it?
• Using existing knowledge about one species to **estimate, predict, project, or infer** the effect, impact, or trajectory of another species
  • For chemical safety typically dealing with toxicity
Why the need to extrapolate?

• **Impractical to generate new data** for all species
  • Limited or no toxicological data for the animal or plant species of interest – reliance on surrogate (model organisms)
  • Immense diversity of species in the wild
  • Important challenge for species listed under the Endangered Species Act

• Testing **resources are limited**
  • Ever-increasing demand to evaluate more chemicals in a timely and sometimes expedited manner

• International interest to **eliminate/reduce animal use**
  • Sensitivity of species must be estimated based on scientifically-sound methods of cross-species extrapolation
  • Ethical considerations
Historically applied methods for extrapolation

- Safety factors to extrapolate from toxicity in laboratory test species to all species representing the taxonomic group in the environment/ ecosystem

Concentration of chemical

Increasing knowledge about chemical + Reducing Assessment Factor

Predicted No-Effect Concentration

Acute Chronic

ECOSYSTEMS

Artificial Natural

Confidence limits
The Challenge

TOXICOKINETICS
- Absorption
- Distribution
- Metabolism
- Elimination

TOXICODYNAMICS
- Target site conservation
- Pathway conservation

Bioinformatics
Systematic literature review
Toxicokinetics/toxicodynamics modeling
Bioinformatics

• Combines mathematics, information science, and biology to answer biological questions

• Developing methodology and analysis tools to explore large volumes of biological data
  • Query, extract, store, organize, systematize, annotate, visualize, mine, and interpret complex data
  • Usually pertains to DNA, RNA, and amino acid sequences

Let the computers do the work
Bioinformatics: Conserved Biology
Sequence Alignment to Predict Across Species Susceptibility (SeqAPASS)
Tool development cannot be done in a silo:
ICACSER
Vision to Move Forward

What we plan to accomplish
Define the Global Regulatory Landscape and Needs for Extrapolation

• Where is species extrapolation currently applied in regulation?
  • What are the differences in regulations?
• What are the criteria for validation/confirmation/development?
• What are training/communication needs?
• How to engage decision-makers in development from the start?
• Define a roadmap for integration in regulation
  • OECD guideline
Developing a Bioinformatics Toolbox: The right tools for the job

• Identify **available** tools/databases/methods
  • Ideally developers join ICACSER
• Define **standards** for inclusion
• Development for **interoperability**
• Create case studies to **demonstrate applicability**
• **Engage** decision-makers
• **Create toolbox** and make available for all
  • Workshop(s) to meet objectives
Communicate a Shared Scientific Vision

- Develop and provide training
- Communicate Bioinformatics Pipeline – Using the toolbox
  - Publications,
  - Sessions/meetings/workshops
Expand Focus Beyond Bioinformatics

TOXICOKINETICS
- Absorption
- Distribution
- Metabolism
- Elimination

TOXICODYNAMICS
- Target site conservation
- Pathway conservation

Bioinformatics
Systematic literature review

Toxicokinetics/toxicodynamics modeling
Progress and Next Steps

• Create Steering Committee ✓
• Develop initial mission statement and define objectives ✓ ✓
• Define relationships with appropriate professional societies ✓ ✓
• Publish article describing the Consortium ✓ ✓
• Create website for ICASCR ✓ ✓
• Introduce topics at SETAC and SOT professional meetings ✓ ✓
• Develop invited participant list ✓ ✓
• Develop a webinar series to introduce tasks more broadly
  • Self nomination of presenters ✓ ✓
• Kickoff teams to work on tasks – June 22, 2022, 9-10:00 AM CDT
  • Invite or Self nomination ✓ ✓
  • Develop meeting schedules for Task Teams and ICACSER ✓ ✓
Upcoming Webinars

June
• Extrapolation in the Current Regulatory Landscape

September
• The Adverse Outcome Pathway Framework to Capture Knowledge Across Species

October
• Needs for Advances in Species Extrapolation; use of biomedical data/knowledge for chemical safety

December
• Vision for bioinformatics in decision-making

setac.org/webinars
Who should be involved

• The consortium aims to incorporate a diversity of expertise that represent the tripartite nature of the challenges faced in species extrapolation. Participants will be those motivated to advance this area of science in a collaborative and inclusive manner. It is anticipated that participants will be representatives from government (researchers, regulators, policy-makers), academia, industry, non-government organizations, communicators and social scientists.
Members: Invitations and self-identified interest

Teams:
• Define the global regulatory landscape/need
• Develop a bioinformatics toolbox
• Communicate a shared scientific vision

March 2022
Kickoff Webinar

April 2022
Identify members

May-June 2022
Team meetings

SETAC Pittsburgh
ICACSER Face to Face

Case Examples
Publications
Presentations
Training
What motivates you?

• Is your research so exciting that you can’t wait to get to the office in the morning to get to work?
• Are you passionate about evaluating the risk of chemicals and protecting the environment?
• Do you enjoy taking on difficult scientific challenges?
• Do you find it rewarding to ensure that quality science reaches the hands of regulators?
• Are you most productive in your research working with other motivated individuals with a variety of expertise?
Resources for ICACSER

• Join ICACSER by emailing:
  • Lalone.Carlie@epa.gov
  • Geoff.Hodges@unilever.com

• Publication:

• SETAC Websites:
  • https://www.setac.org/general/custom.asp?page=scixspecies

• Professional meeting sessions:
  • May 2022 SETAC EU Computational new approach methods (NAMs) supporting regulatory decision making for chemical safety
  • March 2022 SOT Roundtable Cross Species Extrapolation: opportunities in a 21st century regulatory non-animal testing world
  • November 2021 SETAC NA SciCon4 Bioinformatics to inform cross species extrapolations in regulatory toxicology: What tools are available?
  • May 2021 SETAC EU SciCon2 Cross Species Extrapolation: opportunities in a 21st century regulatory non-animal testing world