Overview of the International Consortium to Advance Cross Species Extrapolation in Regulation (ICACSER)

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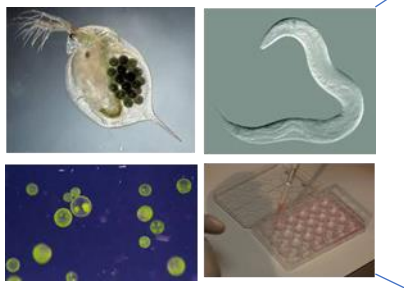
Established: March 2020

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

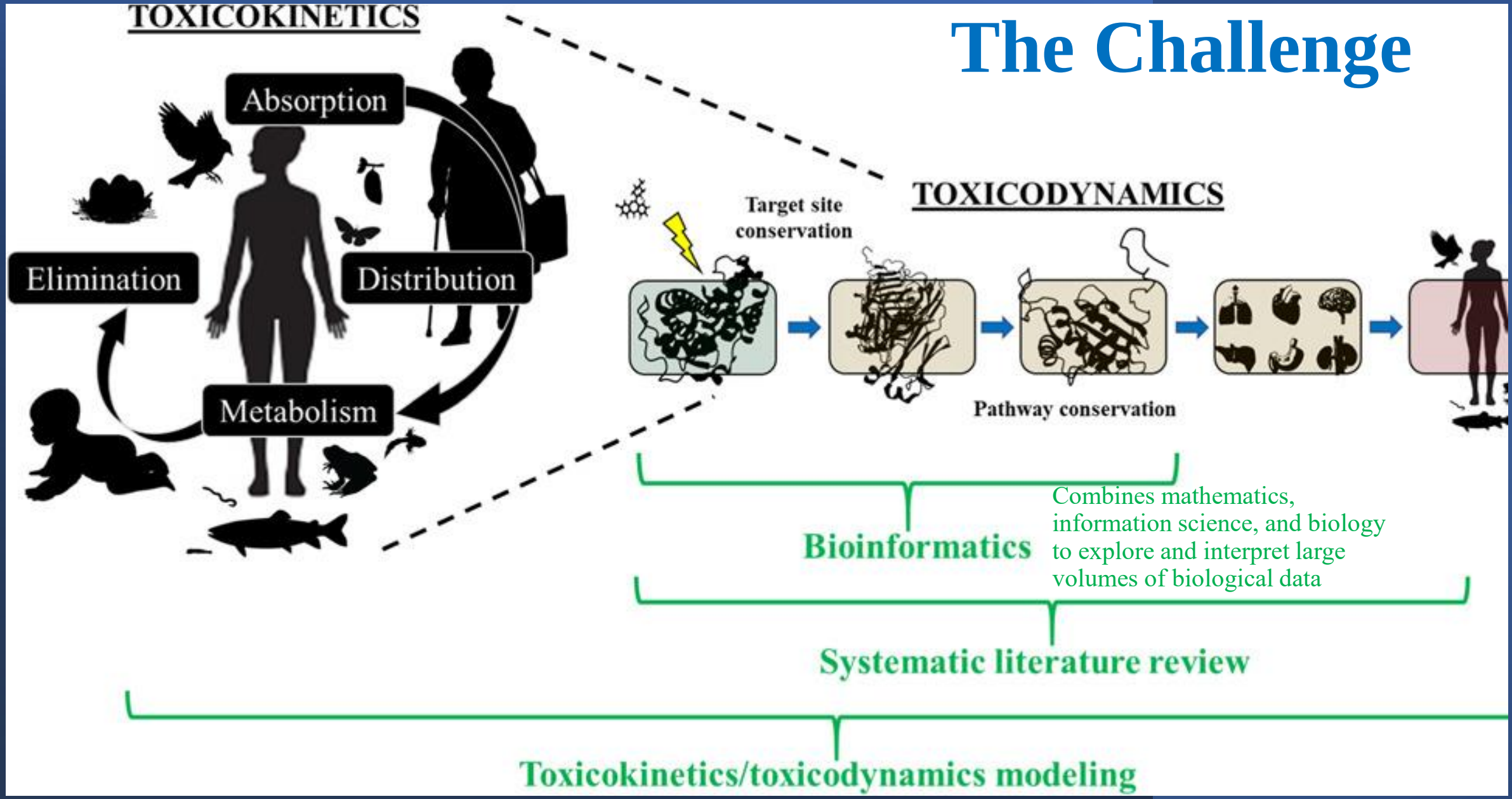
Species Extrapolation



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

The Challenge



Enviro Toxic and Chemistry, Volume: 40, Issue: 12, Pages: 3226-3233, First published: 22 September 2021, DOI: (10.1002/etc.5214)

A part of the solution

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

Mission

…to advance cross species extrapolation to inform a 21st century regulatory non animal testing agenda across HH and Env

….to deliver a platform for sharing and integrating data-streams from bioinformatic approaches

…toolbox creation aligned with existing knowledgebases

ICACSER
Vision to Move Forward

Teams

1. Global Regulatory Landscape 
2. Bioinformatics Toolbox Development 

3. Communicate a Shared Scientific Vision 

Global Regulatory Landscape

Supporting a policy and decision-making need

Objective:

Define the global regulatory landscape and the needs/ vision for exploiting cross species extrapolation of toxicity knowledge for supporting risk-based chemical safety decision making across both HH and the environment.

- Setting the direction
- Keeping track of the direction

Global Regulatory Landscape

Supporting a policy and decision-making need

Year 1

- Identify regulatory needs/ direction setting etc..

- Government organisations
- Regulatory agencies
- Decision-makers
- Policy-makers
- NGOs
- Organizations involved in developing standards/ standard approaches
- Etc..

Mapping

Survey

- Views on regulatory challenges
- Views on policy needs
- Views on opportunities
- Views on barriers
- Training needs
- Etc..

Shared in OECD network

Global Regulatory Landscape

Supporting a policy and decision-making need

Who?

All who are interested/have a vested interest. In particular:

- Government organisations
- Regulatory agencies
- Decision-makers
- Policy-makers
- NGOs with vested interest (e.g. NAT approaches)
- Organizations involved in developing standards/ standard approaches, industry, professional societies (SETAC/ SOT/ BTS etc.)
- Academia with existing strong links with governmental organisations/ regulatory agencies etc.

Global Regulatory Landscape and Needs for Extrapolation:
Take home messages:

- Identify **current needs in regulation** and the **future opportunities**
- **Publication and case studies**
- Identify **training/guidance/ communication needs**
- **Engaging decision-makers** in development

from the start

- Define **recommendations/ roadmap for integration**

into regulation

  - OECD guidelines

Bioinformatics Toolbox Development

The right tools for the job

Objective:

Collaborative discussions

One Health (HH and Environment)

Integrating data streams to understand x-spp extrapolation of toxicity knowledge

A resource for regulatory decision-making

Consistent interpretation of x-spp knowledge

Task Team: 2. Bioinformatics Toolbox Development
The right tools for the job

Who:

- Developers
- Product owners
- Architects of the approaches/methods
- Authors of published tools/databases/methods
- Decision-makers that have vested interest
- Researchers that have vested interest
- Users of the tools/databases/methods
- Data curators

Task Team: Bioinformatics Toolbox Development

The right tools for the job

What:

1. Develop a bioinformatics toolbox for species extrapolation
2. Focus on coordination with the AOP-KB
3. Develop cross cutting case examples

Task Team: 2. Bioinformatics Toolbox Development

The right tools for the job

What:

1. Develop a bioinformatics toolbox for species extrapolation
    - Identification of published and accessible tools/databases/methods for species extrapolation (focus on bioinformatics approaches)
    - Develop criteria for tool/database/method development for inclusion
    - Draft criteria/guidance for development and application of bioinformatics approaches in regulatory decision-making
    - Understand limitations of the data (e.g., sequence availability, annotation) and working to fill gaps and advance/improve data quality and availability

Task Team: 2. Bioinformatics Toolbox Development

The right tools for the job

What:

1. Develop a bioinformatics toolbox for species extrapolation
2. Focus on coordination with the AOP-KB
    - Coordinate toolbox development, tied into (Handbook Guidance, Gardening, and Internal Review (HGGIR) for domain of applicability)
    - Outline steps for interoperability with the AOP Knowledgebase and selected key 3rd party tools including agreeing common ontologies, funding etc.
    - Advances in data model
    - KB structure

Task Team: 2. Bioinformatics Toolbox Development

The right tools for the job

What:

1. Develop a bioinformatics toolbox for species extrapolation
2. Focus on coordination with the AOP-KB
3. Develop cross cutting case examples
    - Identify published case examples
    - Demonstrate utility of the toolbox for defined challenges in chemical risk assessment
    - Opportunities for define Accelerating the Pace of Chemical Risk Assessment (APCRA) case examples and OECD
    - International governmental collaboration
        - Development of new hazard, exposure, and RA methods for chemical evaluation

3. Communicate a Shared Scientific Vision

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

SETAC and ICACSER

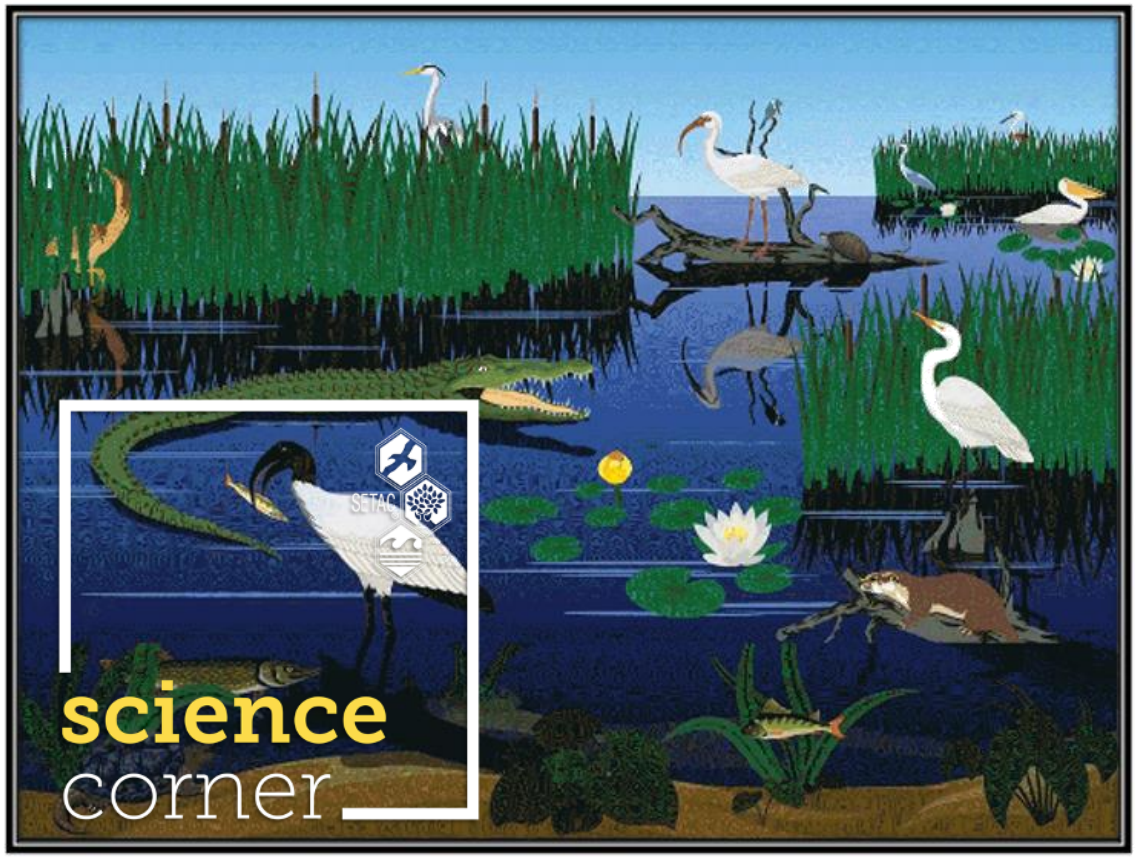
Science Corner webpage

- www.setac.org/scixspecies

Resources and tools

Publications

Webinar Series



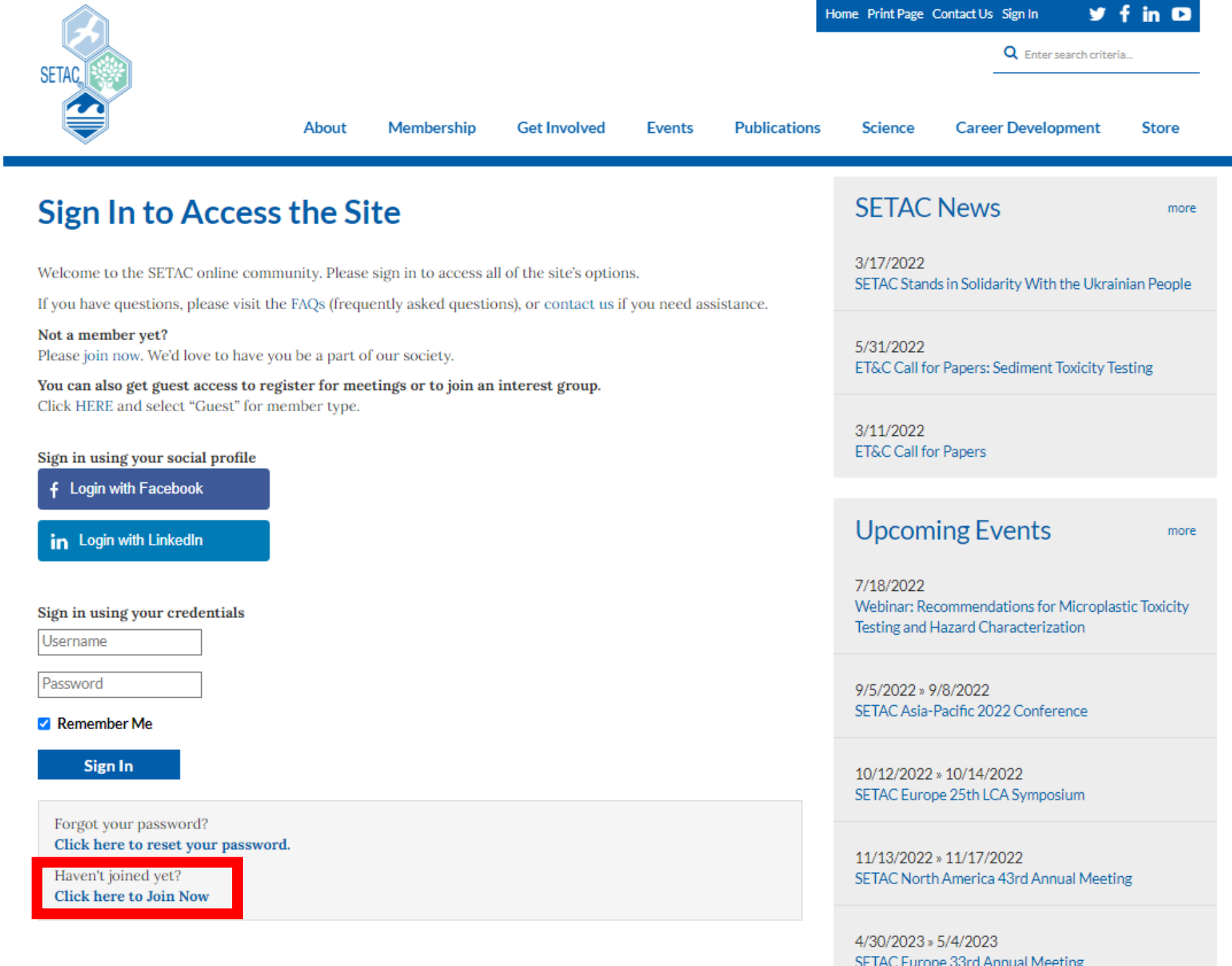
How to join a team?

Volunteer!

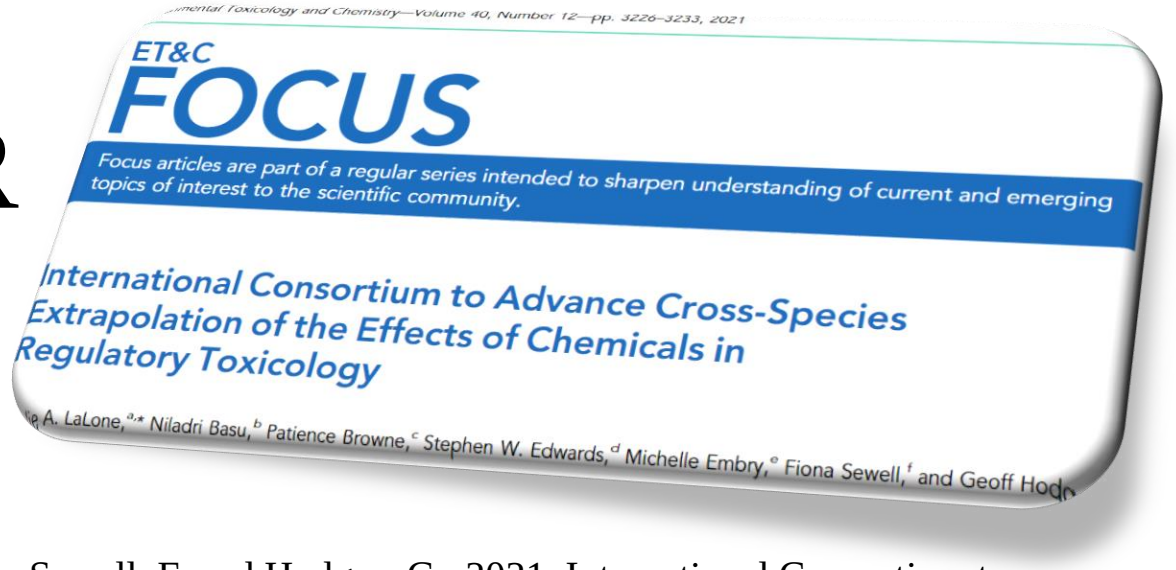
https://www.setac.org/group/ICACSER

If you **are a SETAC member**
You can **use your credentials**

You DO NOT need to be a **SETAC member**
Can create an account to access **ICACSER Team information**



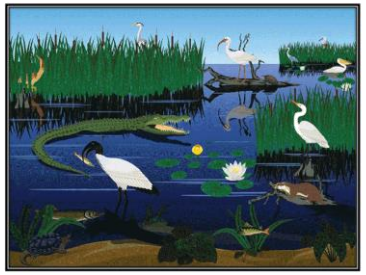
Resources for ICACSER



- Join ICACSER by emailing:
  - LaLone.Carlie@epa.gov
  - Geoff.Hodges@unilever.com
- Publication:
  - LaLone, C.A., Basu, N., Browne, P., Edwards, S.W., Embry, M., Sewell, F. and Hodges, G., 2021. International Consortium to Advance Cross-Species Extrapolation of the Effects of Chemicals in Regulatory Toxicology. Environmental Toxicology and Chemistry https://doi.org/10.1002/etc.5214
- SETAC Websites:
  - https://www.setac.org/general/custom.asp?page=scixspecies
- Professional meeting sessions:
  - May 2023 SETAC EU Training Course *Application of Bioinformatics for Species Extrapolation (TC07)*
  - November 2022 SETAC NA
  - June 2022 OECD Working Group on Hazard Assessment *Introduction to ICACSER*
  - 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*

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 ICASCER
- 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



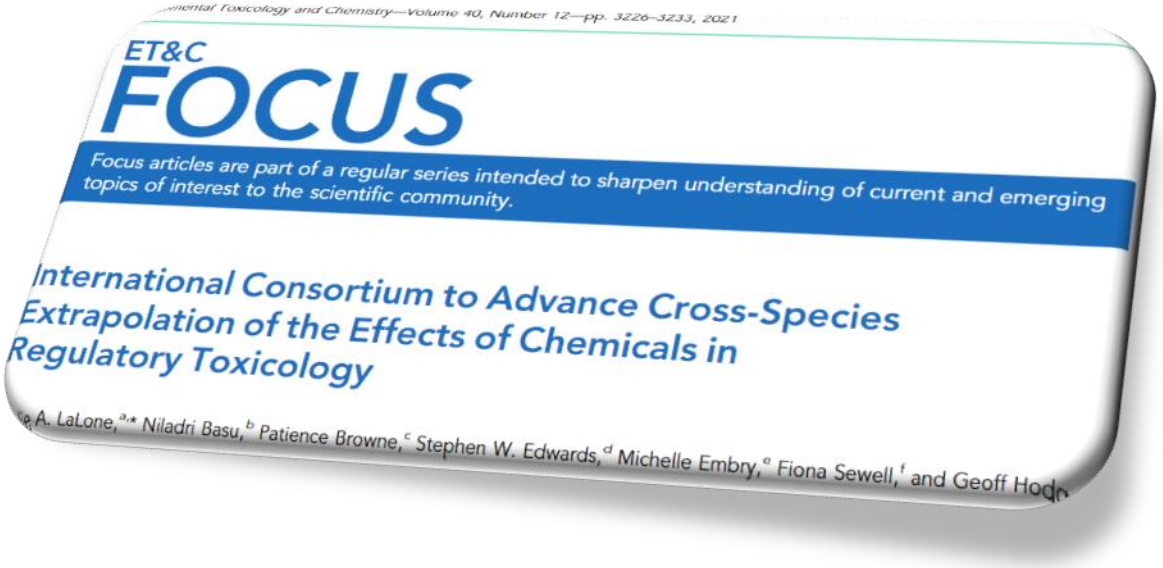
www.setac.org/scixspecies

- Active teams progress activities, training, communication:
- Training Course SETAC Dublin, May 2023: Application of Bioinformatics for Species Extrapolation (TC07)
- SETAC Webinar series during 2023

ICACSER

Supporting a policy and decision-making need

Thank you



Initiating the International Consortium to Advance Cross-Species Extrapolation in Regulation (ICACSER)

9 March 2022 | Categories: 2022, Science and Publications, Volume 23 Issue 3

Carlie LaLone, U.S. Environmental Protection Agency, and Geoff Hodges, Unilever

It is now uncommon to partake in discussions surrounding topics in toxicology without acknowledging new approach methods (NAMs) and their role in the future of chemical regulation. Notably, this conversation is on a global scale with all major regulatory bodies exploring opportunities for reduction, refinement and replacement (i.e., 3Rs) of whole-animal toxicity testing. With this evolving outlook comes an opportunity to advance and enhance mechanism-based and computational methods for use in chemical safety evaluations. Since NAMs encompass in vitro, in chemico, in silico, high-throughput, systems biology, -omics, etc., researchers and decision-makers are trying to better understand the utility and domain of applicability for such methods in regulation. Clearly, there is much work going on to demonstrate the utility of NAMs and to engage regulatory partners to play an active role in developing and integrating such approaches in