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

Supported by the Society of Environmental Toxicology and Chemistry

Steering Committee: Carlie LaLone (US EPA), Nil Basu (McGill University), Patience Browne (OECD), Steve Edwards (RTI), Michelle Embry (HESI), Fiona Sewell (NC3Rs), Geoff Hodges (Unilever)

SETAC and SOT Support

- Bringing membership together to advance the science and input from decision-makers

Overview

- Meet the Steering Committee
- What was the motivation behind creating ICACSER?
- What do we plan to accomplish?
- Who should be involved?
  - Why you were initially identified as a potential participant
  - Role of Professional Societies in support of the consortium
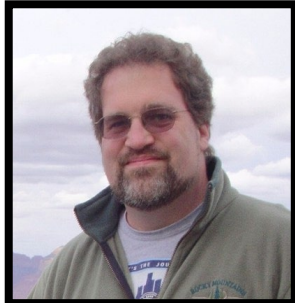- What are the next steps?

Steering Committee

Carlie LaLone
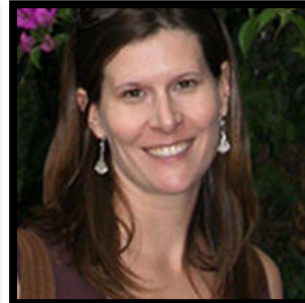**US EPA**

Fiona Sewell
NC3Rs

Steve Edwards
RTI

Patience Browne
OECD

Michelle Embry
HESI

Nil Basu
McGill University

Geoff Hodges
Unilever

Initiated Discussions: March 2020

Motivation for ICASCER

- Changing regulatory landscape
  - Greater use of mechanistic, cell-based, and computationally derived information
- New approach methods (NAMs)
- Eliminating or greatly reducing the use of animals in toxicology
- 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

What we plan to accomplish

Theme	Objective	Key activities	Benefit/ expected outcome
1. Define the taxonomic domain of applicability	Develop an overview of available tools for defining the taxonomic domain of applicability and a proposal to integrate data streams that inform challenges in species extrapolation.	Identify key research areas that are prime to contribute to efforts to define the taxonomic domain of applicability	Publication outlining developed research areas that could redefine the landscape for extrapolating pathway knowledge across species.
2. Define the global regulatory landscape/ need	Define the global regulatory landscape and the needs/ vision for exploiting x-species extrapolation of toxicity knowledge for supporting risk-based chemical safety decision making across both HH and the environment.	Engage champions within organizations to inform and guide consortium activities (ED focus to start as proof of principle)	Global agreed approach to developing and using x-species extrapolation of toxicity knowledge for supporting chemical risk safety decisions (across HH and Environment)
		Capture regulatory drivers and needs to scope and define the scientific charge	Publication regarding needs and recommendations
		Identify and work with partners for case study proposal to present to regulator partners (i.e. via Accelerating the Pace of Chemical Risk Assessment; APCRA)	Developed case study examples to demonstrate how methods can be used in regulation for input b y regulators to share with APCRA

What we plan to accomplish

Theme	Objective	Key activities	Benefit/ expected outcome
3. Develop a bioinformatics toolbox	Through collaborative discussions and partnership develop tangible actions toward the delivery of a bioinformatics toolbox that integrates data-streams for consistent interpretation in understanding cross species extrapolation of toxicity knowledge in a One Health (HH and Environment) context	Identify available key tools/ method architecture for integration	The development of a bioinformatics toolbox that is interoperable with the AOP Knowledgebase that enables/ facilitates: 1.Access by decision makers and researchers to interrogate x-species toxicity knowledge across HH and Environment. 2.A platform for hosting new tools.
		Outline steps for interoperability with the AOP Knowledgebase and selected key 3rd party tools including agreeing common ontologies, funding etc.	
		Coordinate toolbox development, tied into (Handbook Guidance, Gardening, and Internal Review (HGGIR) for domain of applicability)	
		Update OECD guidance document(s) for the domain of applicability in the use of bioinformatic approaches	Updated OECD guidance including input from members and provision of expert review of taxonomic relevance
		Identify steps for tool development/data-stream integration for incorporation of developing and future applications for species extrapolation	Guidance document on maintenance and new tool development/ integration

What we plan to accomplish

Theme	Objective	Key activities	Benefit/ expected outcome
4. Communicate a shared scientific vision	Disseminate the agreed shared vision across academia/ regulators/ industry/ NGOs for the use of integrated bioinformatic approaches exploiting cross species extrapolation of toxicity knowledge for decision making in HH and Environmental chemical safety assessment.	Prepare publications	Develop awareness and acceptance. Initial publications: 1. case study for ED that demonstrate strengths in interoperability 2. regulatory use/application

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.

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
- Introduce ICACSER to invited participants
- Identify teams to work on various tasks
  - Self nomination
- Develop a webinar series to introduce tasks more broadly
  - Self nomination of presenters
- Develop meeting schedules for Task Teams and ICACSER

Resources for ICACSER

- Steering Committee Communication:
  - 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 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*

What we are asking of you…..

1. Do you see the value of this area of science in your specialty groups and in SOT?

2. Do you see ICACSER as a useful addition to support the development of this area of science?

3. Do you think that a shared SETAC_SOT vision and working together would be valuable?

4. Do you want to be involved to help shape this?

5. Do you have any thought on how to progress if so?

SETAC and SOT Support

- Bringing membership together to advance the science and input from decision-makers
  - Joint sessions at professional meetings
  - Joint communications to membership
  - Joint webinar series
  - Linked websites
  - Shared files for ICACSER
  - Joint publications across society journals
  - Joint workshops