

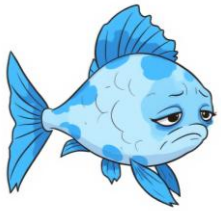
3Rs for chronic fish toxicity – a stakeholder view (I)

Case studies – ECETOC, HESI, ICCS

Heike Laue

Givaudan
Human by nature

Chronic fish toxicity – why and why now?

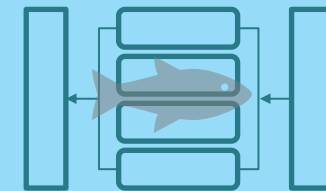


CONTEXT

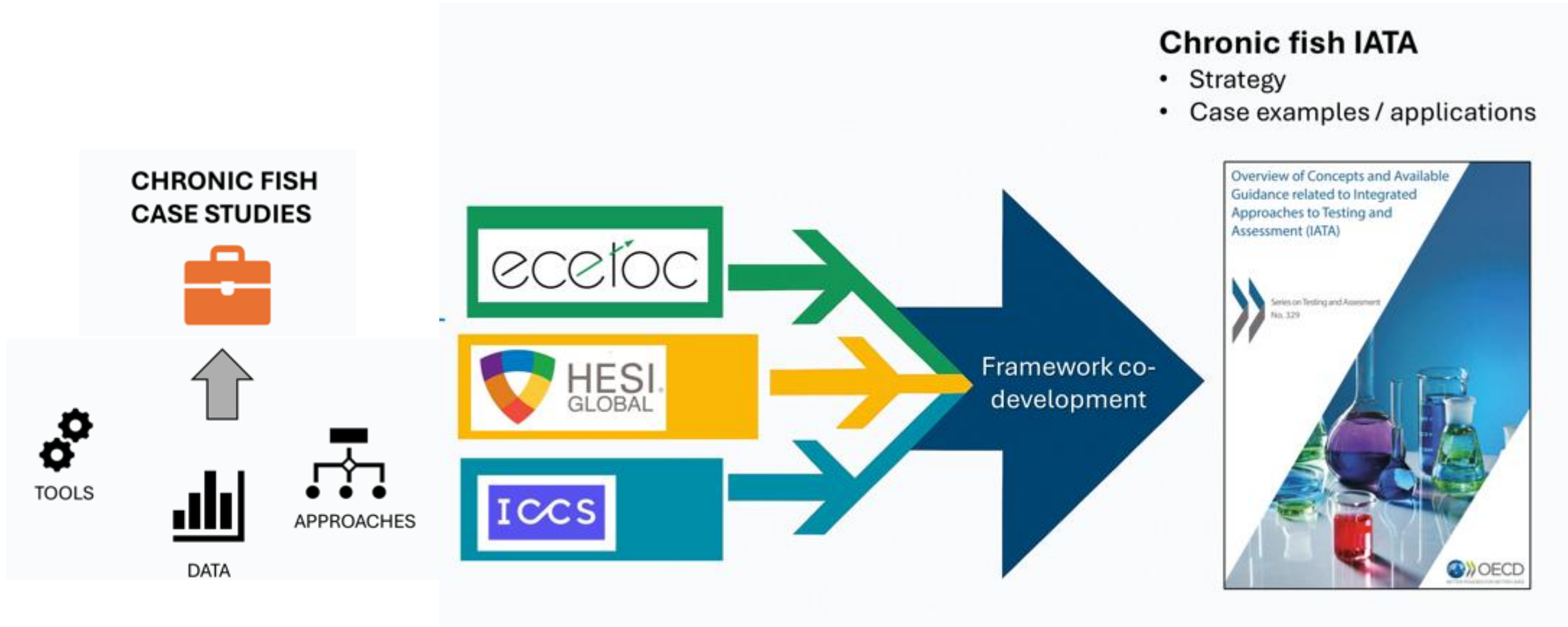
- Tiered testing frameworks and integrated testing strategies (ITS) exist for assessing fish toxicity.
- *In vitro* methods for chronic fish toxicity under development.
- Many methods/NAMs available, but integration for chronic toxicity is still limited.
- An Integrated Approach to Testing and Assessment (IATA) lacking.

DESIRED OUTCOME

- Develop case studies to inform integrative strategies for predicting chronic effects.
- Illustrate methods for intelligent, fit-for-purpose, testing strategies
- Provide guidance on leveraging NAMs in chemical hazard and risk assessment.
- Support future IATA development for assessment of chronic fish toxicity.



A Combined Effort



- EPAA Environmental Safety Assessment Team, including [EPAA Partners Forum 2023](#)
- [‘CRACK IT Challenge SAFE’](#) (NC3Rs)
- Commission [Roadmap](#)
- RIFM data generation

ECETOC Case Studies

OBJECTIVES:

- Develop case studies to inform a future IATA for chronic fish toxicity.
- Case studies to integrate multiple lines of evidence to conclude on chronic fish toxicity.

ECETOC Advisory Panel

[27 experts - industry, academia, regulatory, policy & NGOs]

- Select case studies
- Review draft MS



Consultant

(ECT Oekotoxikologie)

- Develop case studies
- Peer-reviewed manuscript

Specific MoA

PPP:

- Fungicide; CYP P450 inhibition
- Insecticide (pyrethroid); Neurotox
- Insecticide, incl veterinary applications; Neurotox
- Herbicide

Pharma:

- Immunosuppressant
- Antihistamine

Narcotic MoA

REACH Chemicals:

- Fuel ether
- Fragrance ingredient
- Chelating agent



Four case studies to be selected

- Different mode of action (ED MoA excluded).
- Different species sensitivity, different levels of toxicity
- *In vivo* data as cross-comparison of WoE outcome



HESI Case Studies

1) Identify suitable chemical(s)



- Herbicides (SER 264 binders 1°)
- 3,4-DCA
- Others TBD

2) Problem contexts



Analogues for read-across

3) Assess Line of Evidence relevance

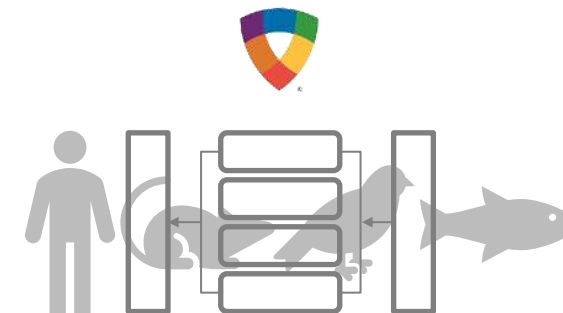


Identify an estimated point of departure for risk assessment to determine if an *in vivo* FELS is needed

4) Data quality assessment

5) Weights of evidence:

- With only pre-existing information (e.g., QSARs, read-across)
- With previous, plus *in vitro* data
- With previous, plus *in vivo* data



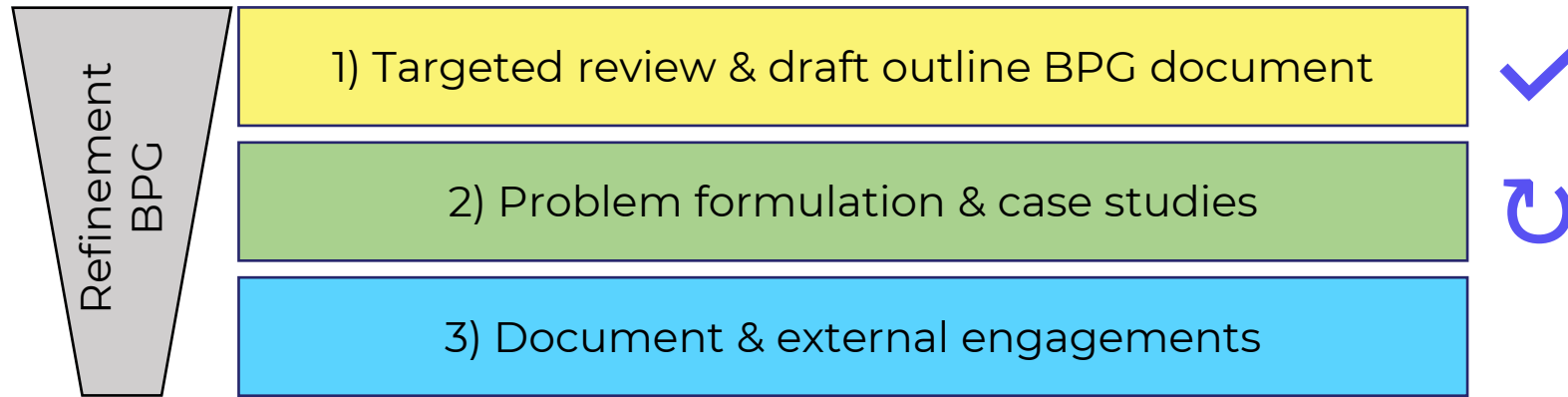
ICCS Case Studies

Project with ToxStrategies and Markus Hecker, University of Saskatchewan

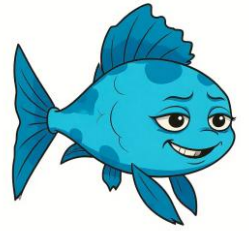
- Case studies with 2 – 3 cosmetic ingredients
- Consolidated into [ICCS Best Practice Guidance \(BPG\) document](#)

Objective BPG:

Provide safety assessor with best practices to approach chronic fish toxicity assessment for cosmetic ingredients using NAMs



CONCLUSIONS



Chronic fish IATA



For different regulatory frameworks

Case studies:

- REACH chemicals
incl. cosmetic ingredients
- Plant Protection Products
- Pharmaceuticals



eceloc
WE ARE THE CENTER FOR CHEMICAL SAFETY ASSESSMENT

Lucy Wilmot, Heike Laue



Michelle Embry, Julie Krzykwa

ICCS

Amelie Ott/Ryan Heisler,
Adriana Wigh