Feedback from the EPAA Partner Forum: Possibilities to address the area of long-term aquatic toxicity

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EPAA PARTNERS FORUM 2023

Use of Alternatives to Animal Testing for Environmental Safety Assessment

13-14 November 2023, CEFIC offices, Rue Belliard 40, 1040 Brussels

Presentations:

- European Commission - Joint Research Centre
- European Chemicals Agency
- CEFIC – chemicals
- AISE - detergents
- IFRA - fragrances
- Cosmetics Europe – cosmetic ingredients
- Crop Life Sciences Europe - pesticides
- EFPIA – human pharmaceuticals
- Animalhealth Europe – veterinary medicines

Round table discussion

- ECETOC
- CONCAWE
- HESI
- SETAC
- NC3Rs
- ICCS
- PARC
- ACPRA

Five priority areas of common interest identified:

- Fish acute toxicity
- Fish bioaccumulation
- Fish chronic toxicity
- Endocrine disruption assessment, covering all modalities
- New Systems-based approach to Environmental Safety Assessment

Fish chronic toxicity: current endpoints

Generic "Hazard Characterization" endpoints:

- Growth
- Development, hatching, survival
- Reproduction

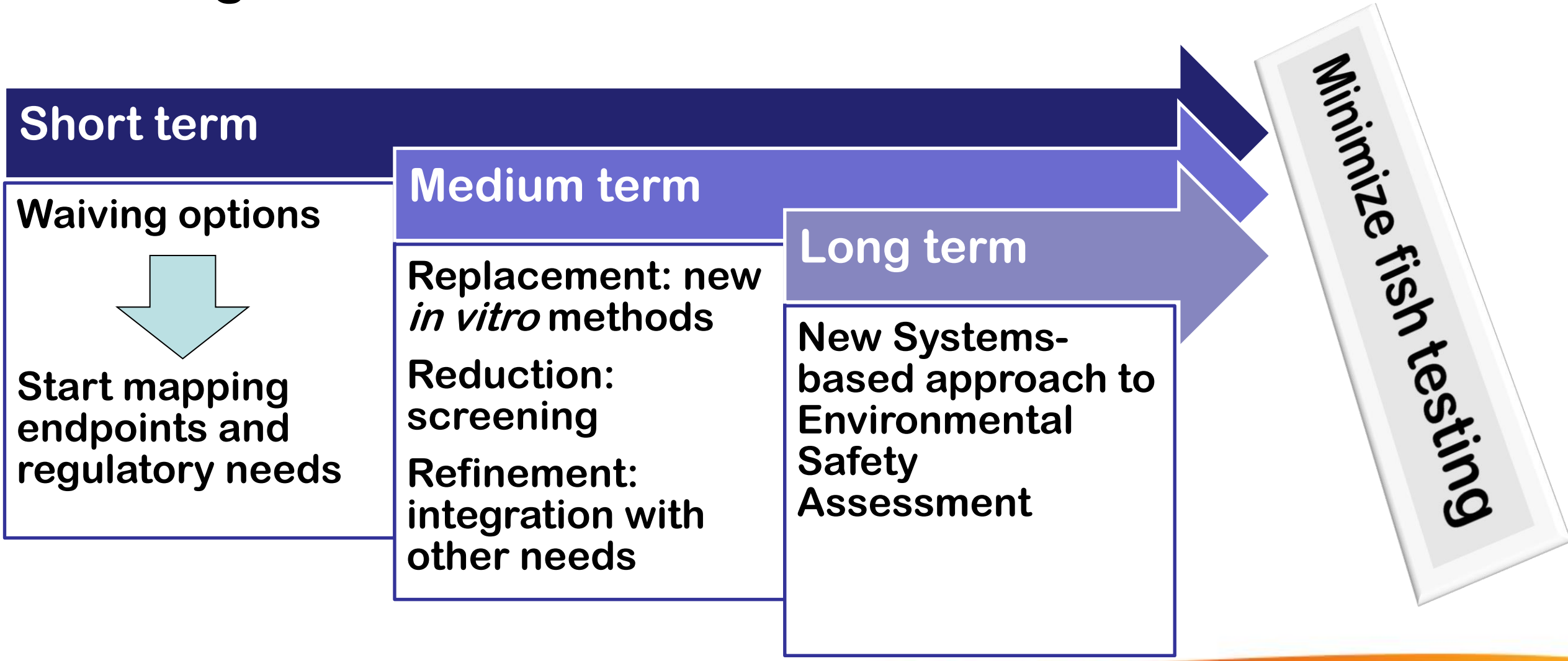
Procedure: Integration with other chronic toxicity test for C&L and estimation of PNECs or equivalent

Specific "Hazard Identification" endpoints:

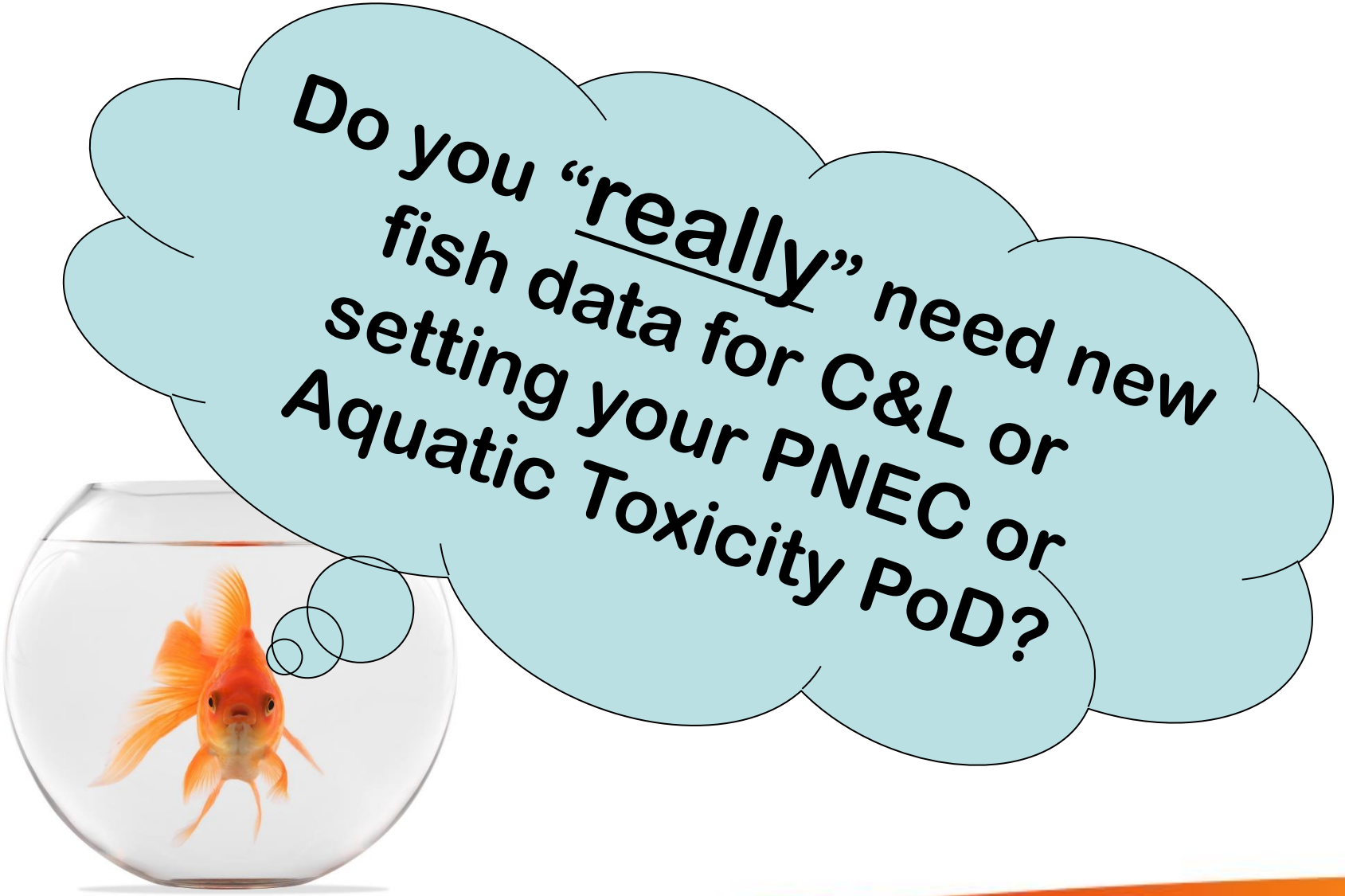
- Endocrine disruption (oestrogen and androgen receptors)

Procedure: Integration with other studies to cover ED modalities

Proposed pathway for fish chronic toxicity: Long-term vision with short & medium-term actions



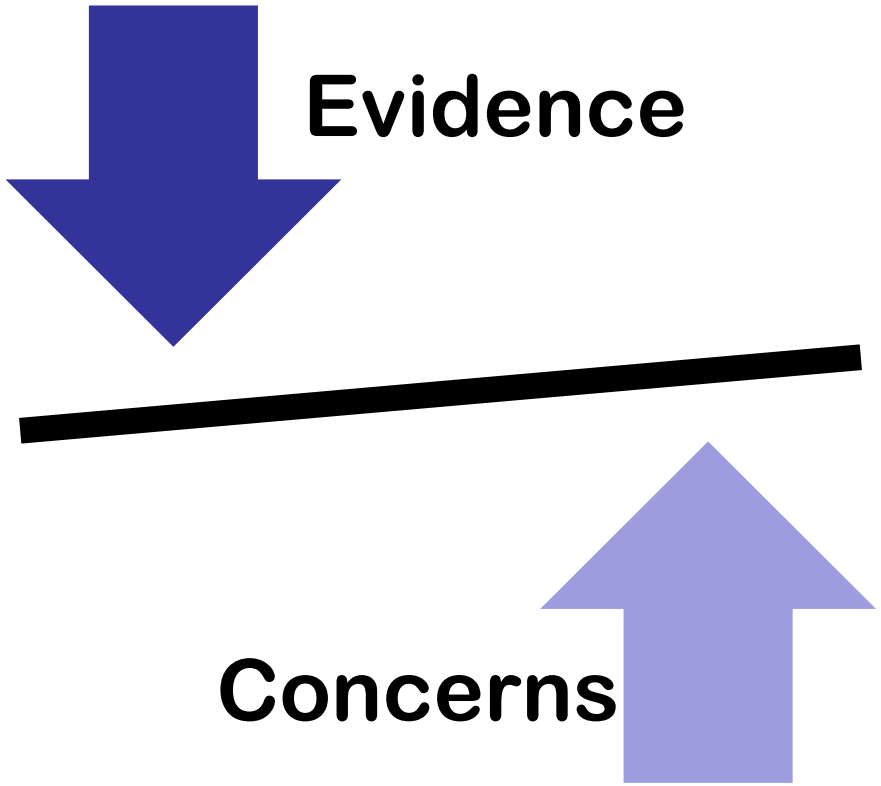
Phase one, 0-2 years: explore “all” waiving options



Fish chronic toxicity: possible waiving options

- Confirming higher sensitivity of other taxa
  - Experimental + *in silico* predictions
  - Based on mode/mechanism of action
- Acute to chronic extrapolation
- Threshold of ecotoxicological concern
- Exposure driven evidence
  - Low concern for chronic fish exposure
  - Environmental fate properties triggering other compartments
  - High margin of exposure
- …

Challenges and opportunities for waiving options



- *How to achieve "sufficient" confidence for concluding?*
- Combining different lines of evidence
- Guidance on Weight of Evidence
- Stakeholders' agreement on predictability/reliability principles

Phase two: A 3Rs way forward

- Replacement by *in silico & in vitro* methods
- Reduction/Refinement options
  - Screening approaches
  - Maximal use of *in vivo* studies
- Reconsidering the ESA paradigm

Replacement

In silico :

- new QSARs
- getting confidence in grouping and read-across

In vitro : planning ahead focusing on regulatory needs (consider lessons learnt from acute fish tox)

- Mapping current endpoints and regulatory needs (population effects)
- Ensure connectivity between developers and risk assessors, keep track of regulatory relevance and applicability
- Specific efforts for QIVIVE, internal exposure, and integration of TK

For both: consider substances with specific properties

- **UVCB including hydrocarbons, fragrances, …**
- **Surfactants, ionisable chemicals,..**

Reduction & Refinement

- IATA-based design, e.g. using “Points of Departure” from other taxa or *in silico* predictions

- Integration of different assays:
  - Combine toxicity, bioaccumulation and toxicokinetics
  - Measure internal concentrations in toxicity tests

- Mechanistic understanding:
  - Include OMIC-based endpoints
  - Explore integration with endocrine assessment

Reconsidering the ESA paradigm: A system-based approach

Aim: “Best use of science for achieving the protection goals”

- Mechanistic “eco”-drivers triggering environmental impacts
- A broader perspective: design ESA requirements under chemical legislations to support wider environmental protection policies: WFD, biodiversity protection, …
- Long-term goal, but should start already now, to progress in parallel with the other activities
- Is broader than fish (chronic) toxicity, but minimising, and when possible, avoiding animal testing is a key priority

Additional considerations and proposals

- Keep global perspective, facilitate exchange among jurisdictions, link with OECD and mutual recognition
- Further development of Weight of Evidence guidance
- Include studies conducted with alternative methods in regulatory dossiers
- Consider other taxonomic groups not captured in current ESAs
- Foster cooperation
  - Ongoing activities, including research projects
  - Human Health and Environment
  - Inter sectors, e.g., explore opportunities for case studies implementing the “One Substance One Assessment” approach

Thank you!