Current status of the OECD project on IATAs for acute fish toxicity

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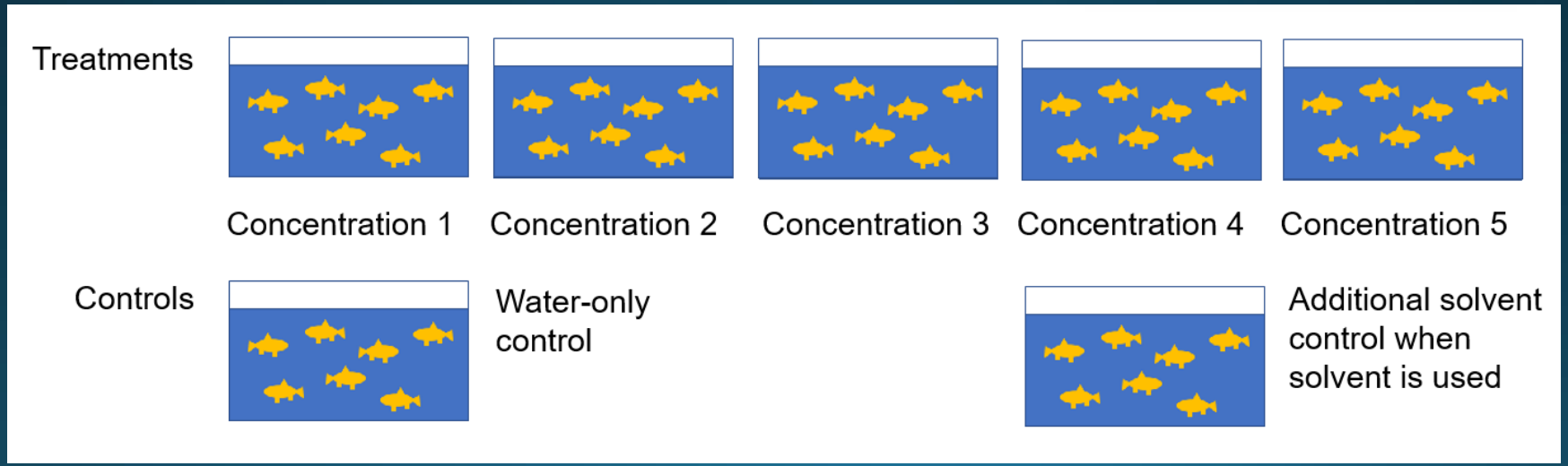
Outline

- Background
  - OECD TG 203
  - 3Rs in acute fish toxicity assessment
- Development of an IATA
  - Flexible IATA
  - Bayesian network IATA

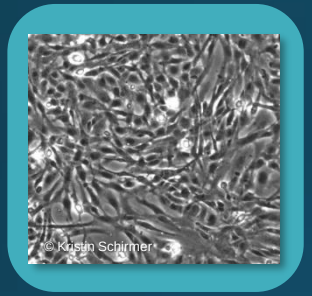
Method to be replaced:

OECD TG 203 on the acute fish toxicity test



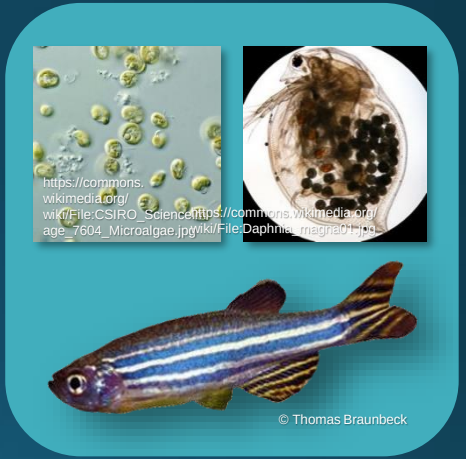
3Rs in acute fish toxicity assessment

In silico methods



OECD TG 249 RTgill-W1 cytotoxicity assay

OECD TG 236 ZFET / FET



OECD GD 126 Threshold Approach

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Concept Article

Limitations and Uncertainties of Acute Fish Toxicity Assessments Can Be Reduced Using Alternative Methods

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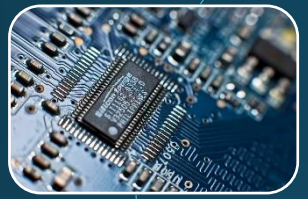
Abstract

Information about acute fish toxicity is routinely required in many jurisdictions for environmental risk assessment of chemicals. This information is typically obtained using a 96-hour juvenile fish test for lethality according to OECD test guideline (TG) 203 or equivalent regional guidelines. However, TG 203 has never been validated using criteria currently required for new test methods including alternative methods. Characterization of the practicality and validity of TG 203 is important to provide a benchmark for alternative methods. This contribution systematically summarizes the available knowledge about limitations and uncertainties of TG 203, based on methodological, statistical, and biological considerations. Uncertainties stem from the historic flexibility (e.g. use of a broad range of species) and constraints of the basic test design (e.g., no replication). Other sources of uncertainty arise from environmental safety extrapolation based on TG 203 data. Environmental extrapolation models, combined with data from alternative methods, including mechanistic indicators of toxicity, may provide at least the same level of environmental protection. Yet, most importantly the 3R advantages of alternative methods allow a better standardization, characterization and an improved basic study design. This can enhance data reliability and thus facilitate the comparison of chemical toxicity, as well as the environmental classifications and prediction of no-effect concentrations of chemicals. Combined with the 3R gains and the potential for higher throughput, a reliable assessment of more chemicals can be achieved, leading to improved environmental protection.

https://commons.wikimedia.org/wiki/File:CSIRO_ScienceImage_7604_Microalgae.jpg



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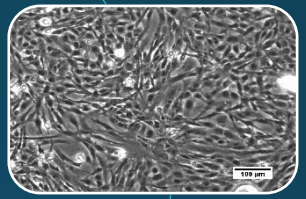

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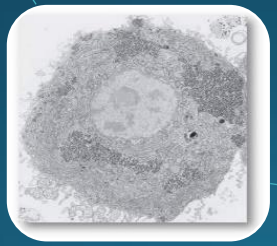
IATA



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Flexible IATA

AFT: acute fish toxicity test (TG 203)

FCT: fish cell test (TG 249)

IATA: Integrated Approach to Testing and Assessment

TC: threshold concentration

ZFET: zebrafish embro acute toxicity test (TG 236)

Collect existing reliable, relevant information; apply *in silico* approaches; and conduct weight-of-evidence analysis.

Each data element is characterised for its quality, relevance, and associated uncertainty. The TC is derived.

Internationally Standardised Information Sources

OECD TG 249: RTgill-W1 fish cell line test to predict acute fish toxicity

OECD TG 201: Freshwater Alga and Cyanobacteria, Growth Inhibition Test

OECD TG 202: *Daphnia* sp. Acute Immobilisation Test

OECD TG 236: Fish Embryo Acute Toxicity Test

Not Internationally Standardised Information Sources

In silico data, e.g. (Q)SARs, machine learning, grouping/read-across, bridging

Physical-chemical information, e.g. on molecular weight, bulkiness, charge

Additional *in vitro* and *in vivo* data relevant to acute fish toxicity, e.g. on metabolism and from high-throughput screening and other taxa (e.g. mammalians)

WoE inconclusive

WoE conclusive

No further testing

Conduct Core Tests to Predict Acute Fish Toxicity

= assessment questions

= testing

= conclusions

START Concern for neurotoxicity? e.g. (Q)SARs, *in vitro*, daphnids, *in vivo* data

No

Concerns for high molecular weight, 3D structure, and charge ?

Yes

FCT

FCT EC_{50} < TC ?

No

Yes

FCT LC_{50} ~ fish LC_{50}

Yes

AFT at TC

No

Preference and availability of models

ZFET at TC

ZFET mortality > 10% ?

Yes

Full ZFET

ZFET LC_{50} ~ fish LC_{50}

No

AFT mortality > 10% ?

No

Fish LC_{50} ≥ TC

ZFET at TC with touch-evoke response

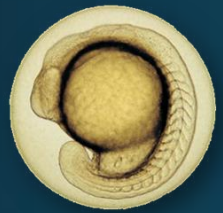
Yes

Full AFT

AFT LC_{50} ~ fish LC_{50}

Bayesian network-based IATA

Strengthening **W**eight of ev**i**dence for FET data to replace acute **F**ish **T**oxicity (SWiFT)



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Substance

Lines of evidence

- Physical and chemical properties / Mode of Action
- Toxicity of chemical category
- Toxicity to other species
- Toxicity of fish embryos
- Metabolism
- Gill cell cytotoxicity
- Neurotoxicity
- QSARs

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Toxicity to juvenile fish predicted

Thank you!

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