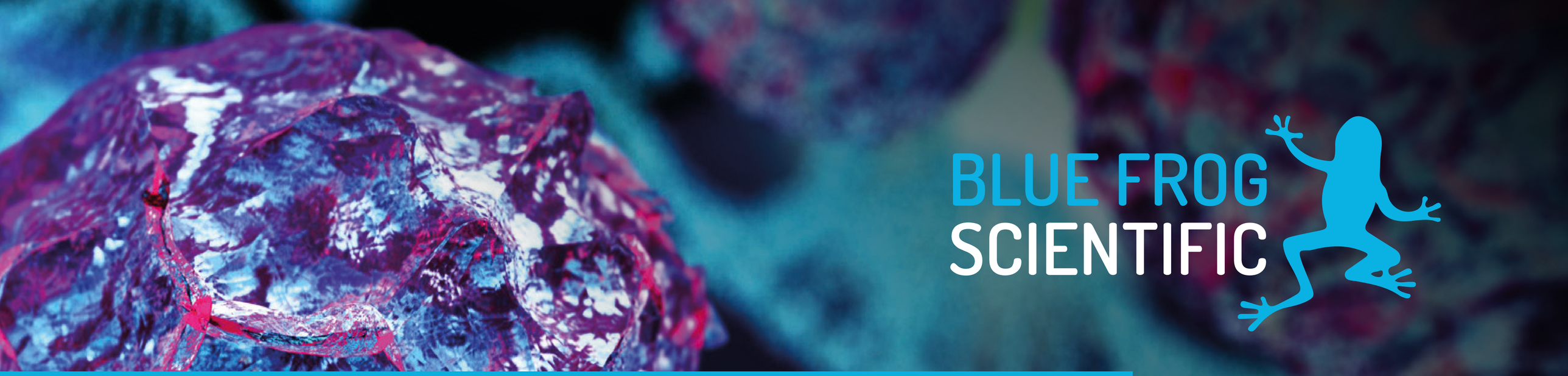


BLUE FROG SCIENTIFIC

SETAC EU 2026 - Presentation ID: 6.04.P-Mo388

A Desk-Based Approach to Determine the New CLP Endocrine Disruption Hazard Classes

Authors: Marianne Matzke[1], Pauline Remuzat[2], Kai Paul[1], Bryony Ross[1], John Miller[1], Jamie Marshall[1], Damien Carson[1]
Affiliation: [1]Blue Frog Scientific Limited, Edinburgh, United Kingdom; [2]Blue Frog Scientific SAS, Lyon, France
Contact Us: www.bluefrogscientific.com / marianne.matzke@bluefrogscientific.com

Blue Frog are exhibiting. (Booth 79)
Come & talk with us... we'd love to hear your views!

"An endocrine disruptor is an exogenous substance or mixture that alters the function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations."
WHO/IPCS (2002)

- Endocrine disruption (ED) is one of the newly implemented hazard classes under CLP regulation (EC) No 1272/2008.
- Increasing regulatory scrutiny under REACH (EU & UK), the Biocidal Products Regulation (BPR) and the Plant Protection Products Regulation (PPPR) demands proactive ED assessment to ensure compliance and (continuous) market access.
- The here presented stepwise approach - based on available or alternative information - ensures fulfilment of the requirements under the new CLP hazard classes, avoids additional animal testing and aligns with state of the art of scientific regulatory science.

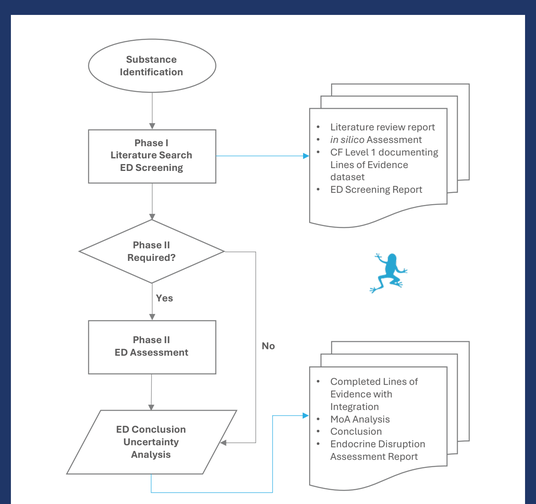


Figure 1: Overview ED assessment Blue Frog Scientific (BFS) approach – based on ECHA/EFSA, 2018 & OECD GD 150a

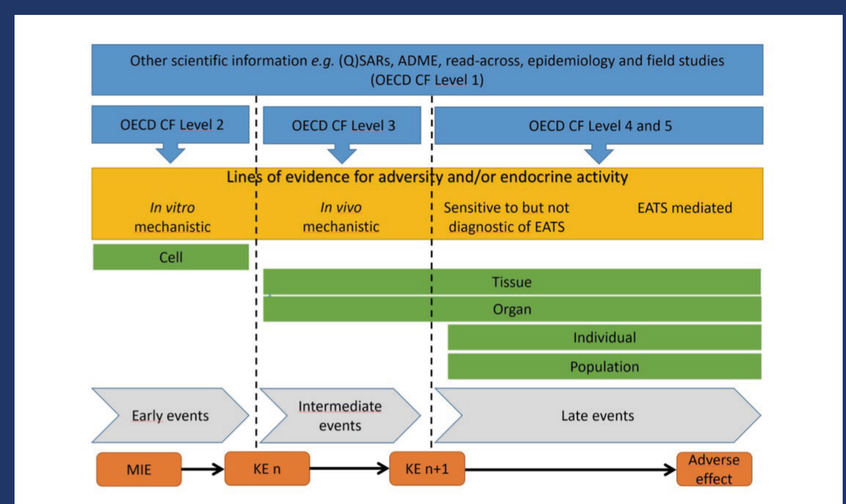


Figure 2: Conceptual Framework Level according to OECD GD 150 (OECD GD150, 2018; DOI:10.1787/9789264304741-en). KE: Key Event; MIE: Molecular Initiating Event. The arrows linking KEs represent KE relationships. It should be noted that borders between CF levels are not absolute in terms of parameters measured or their contribution to the weight of evidence.

Case Study

Heterocyclic organic chemical with multiple legacy studies & one ED specific study (REACH)

ED concerns for the environment: structural characteristics potentially interacting with the hypothalamus-pituitary-thyroid axis, i.e. interfering with the mechanism converting T4 to T3; not biodegradable; wide dispersive use resulting in potentially significant environmental exposure.

Dataset: Four studies: one short-term fish, one short-term daphnia, one long-term daphnia and one algal study; following a request for further information one AMA (OECD TG 231).

Screening Outcome

- **EAS modality**: no experimental data in the current data set permitting further investigation of EAS activity in environmental species.
- **Adverse effects**: effects on metamorphosis of Xenopus laevis recorded (AMA OECD TG 231).
- **Endocrine activity**: direct mechanistic evidence such as hormonal level changes (T3, T4, TSH) or effects on gene expression of the thyroid hormone synthesis is missing – only data available for structurally similar compounds (potential read-across).
- **Endocrine disrupting mode of action**: linking observed effects (metamorphosis) with very distinct histological changes of the thyroid in the AMA is indicative of an altered function of the HPT axis.

Overall ED Conclusion: ED Category 2; lacking direct mechanistic evidence and some uncertainties regarding the applicability domain of AMA for substances with potential effects on liver clearance needs further investigation.

Endocrine Disruption Assessment in Practice

Phase I ED Screening

Literature Search
- Literature Search & Sift.
- Literature Evaluation.

DB Searches & In Silico Profiling
- Generate CF Level 1 data & *in silico* profile.
- Establish initial evidence base for subsequent stages of the ED assessment and ensure consistency with the regulatory conceptual framework.

Screening for Endocrine Relevant
- Existing data subject to targeted review by CF level, with the aim of screening for adverse effects which may be plausibly linked with any EATS or non-EATS endocrine modes of action.
- Screening should consider any relevant impurities or transformation products in line with the cut-off values used for PBT/ SVHC assessments.

ED Screening
- Summarises available data, interpretation & any conclusions that can be drawn at screening level
- Existing data will be organised into relevant CF levels in the report to assist.

Phase II ED Screening

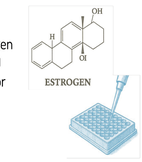
Study Monitoring
- Provide scientific and organisational support for studies to be conducted at external contract laboratories, should any new testing activities be planned as part of the project strategy.

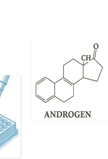
ED Assessment
- Conduct a full Endocrine Disruption Assessment in accordance with relevant regulatory requirements and specific guidance (e.g. OECD GD 150, ECHA/EFSA 2018 and CLP guidance v5.0 2024).

ED Assessment Report
- Prepare report, documenting available data in detail, interpretation & conclusions on classification.
- Describes data sources & quality; assesses endocrine activity & adversity; integrates lines of evidence & evaluates biological plausibility, clearly distinguishing between empirical findings, mechanistic interpretation, and weight-of-evidence reasoning.

Examples for Test Systems According to CF Level

❖ **CF level 2** – *in vitro* endocrine mechanistic screening: androgen receptor (OECD TG 458) and estrogen receptor (OECD TG 455) transactivation assay; H295R steroidogenesis (OECD TG 456) or estrogen receptor binding (OECD TG 493)





❖ **CF level 3** – *in vivo* short-term mechanistic: amphibian metamorphosis (OECD TG 231); fish short-term reproduction for estrogen/androgen activity (OECD TG 229); fish 21-day steroidogenesis etc. (OECD TG 230); *Xenopus* eleuthero embryonic thyroid assay (OECD TG 248)

❖ **CF level 4** – *in vivo* adverse endocrine-relevant effects: fish sexual development (OECD TG 234); fish early-life stage toxicity (OECD TG 210); *Daphnia magna* reproduction test (OECD TG 211); earthworm reproduction (OECD TG 222) or chironomid toxicity (OECD TG 218/219)

❖ **CF level 5** – *in vivo* full life cycle/ multigenerational studies: *Medaka* extended one-generation reproduction test (OECD TG 240); avian reproduction (OECD TG 206)

Challenge

Available data are either old (no GLP, different validity criteria) and/or not the required endpoints for a meaningful assessment; so far vertebrate data are preferred & invertebrate data supportive; more ED specific TG under development; different species might be required in different regulations for assessment.

Outlook & Conclusion

Refine & rethink approaches for future proofing for more challenging compounds such as biopesticides (e.g. peptides); *in silico* methods & read-across are a valuable tools to support the overall conclusion.

Achievements

This structured flow of activities allows to support pragmatic assessment of complex datasets allowing to generate a robust & coherent strategy to support conclusions on ED compliant with the new CLP requirements for hazard communication and longevity of applicant's registration.

LinkedIn: #SETAC2026 #CLP #EndocrineDisruption

www.bluefrogscientific.com

References :
- ECHA/EFSA (2018). Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009. EFSA Journal 2018 ; 16(6):5311.
- OECD (Organisation for Economic Cooperation and Development) (2018). Revised Guidance Document 150 on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption. Series: OECD Series on Testing and Assessment. ISBN 978- 92-64-30474-1