

Cross-species extrapolation in (eco-)toxicity testing – lessons learnt from the ERGO project

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The current OECD testing strategy for endocrine disruptors requires the use of extensive animal testing for both, human and environmental health assessment. The ERGO project aims at breaking down the wall between mammalian and non-mammalian vertebrate regulatory testing by identifying, developing and aligning thyroid hormone (TH) system sensitive biomarkers and endpoints for linkage of effects between different vertebrate classes. A part of this work is dedicated to development and validation of potential TH system sensitive endpoints in fish and the use of alternative models (new approach methodologies, NAMs), such as fish embryonic stages. The TH system regulates a wide range of measurable molecular and morphological endpoints in fish, including swim bladder inflation, thyroid- and eye-related gene expression, and the development of thyroid follicles and eyes. ERGO and a recently initiated OECD validation aim to investigate whether these endpoints are suitable for detecting TH system disruption in fish embryo models. Based on the resulting data, we are now working on a broader network of thyroid AOPs to support cross-vertebrate extrapolation of mechanisms and effects of TH system disruption for informing both on environmental and human health. The endorsement and publication of these AOPs by OECD supports the addition of new endpoints to existing OECD fish test guidelines (TGs). Such refined TGs will improve the evaluation of THSDCs and will be included in the development of approaches for extrapolation of TH system disruption effects across vertebrate species.