

New endpoints for thyroid hormone system disruptor testing with fish

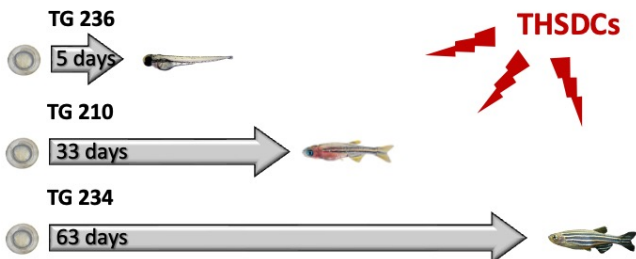
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Introduction

Major parts of early vertebrate development are regulated by **thyroid hormones (THs)** and can therefore easily be disrupted by environmental pollutants, which interact with the TH system (TH system disrupting chemicals, THSDCs). The **lack of THS-endpoints in fish tests** has been identified as serious gap in the currently available test battery for endocrine disruptor testing with non-target organisms. We aim to close this gap by **implementation of new endpoints into existing fish test guidelines (TGs)** like the TGs 210 (fish early life-stage test), 234 (fish sexual development test) or 236 (fish embryo toxicity test).

Methodology

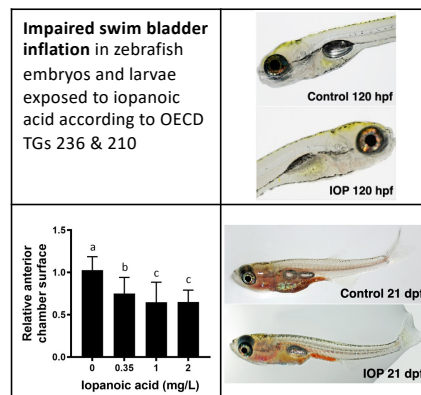
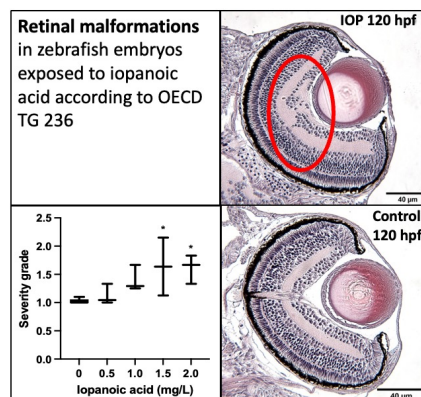
An extensive **literature research** was performed to evaluate the impact of THSDCs on fish and investigate which of their developmental processes could be disrupted by them. Based on the results, combined with data from amphibian tests, a **set of different model THSDCs** was selected to perform exposure experiments with fish according to the established OECD TGs 210, 234, 236. **Zebrafish (*Danio rerio*)** wildtype and a thyroid transgenic line were used. **Swim bladder inflation and eye development** were selected as most promising apical endpoints and were combined with analyses of **TH levels and thyroid follicle morphology**.



Exposure design using existing fish OECD TGs

Results

In our experiments, we observed **strong effects** of different THSDCs **on different endpoints** in different life-stages of zebrafish:



Applicability of different THS-sensitive endpoints in established OECD test guidelines with zebrafish:

	TG 236	TG 210	TG 234
TH levels	✓	✓	✓
Thyroid follicle morphology	✓	✓	✓
Eye morphology	✓	✓	✓
Swim bladder inflation	anterior	✗	?
	posterior	✓	?
Swimming behavior	✓	?	?

Conclusions

Based on **extensive literature analyses and our experimental test battery** with different model THSDCs we provide strong evidence that **eye development and swim bladder inflation**, combined with TH level measurements and analyses of thyroid follicle morphology can and should be implemented as THS-specific endpoints into existing TGs for endocrine disruptor testing with fish. **All investigated apical endpoints react sensitively** to different modes of action of THSDCs and can be seen as meaningful, population-relevant endpoints. Different **adverse outcome pathways (AOPs)** for swim bladder inflation and eye development in fish support our work:

AOP for swim bladder inflation: <https://aopwiki.org/aops/159>

AOP for eye development: <https://aopwiki.org/aops/363>

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