

Status of Current Work under OECD

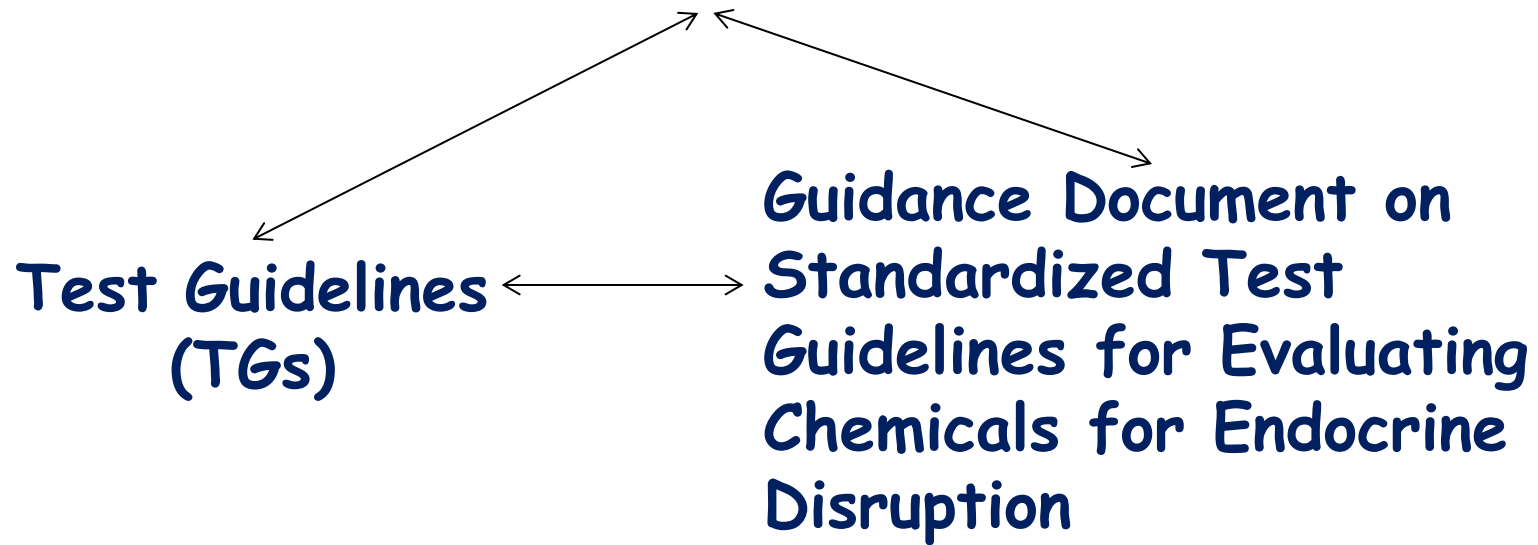
*EU Conference on endocrine
disruptors: Current challenges in
sciences and policy
11-12 June 2012*

Laurence Musset

**Environment, Health and Safety Division
Environment Directorate
Organisation for Economic Co-Operation and
Development**

Tools for testing and assessment

Conceptual Framework for Testing and Assessment of Endocrine Disruptors (EDs)



(Mechanism of action: Estrogen receptor, androgen receptor, thyroid hormone mediated; Steroidogenesis interference)

OECD Conceptual Framework for the testing and assessment of endocrine disruptors (CF)

CF is a toolbox including 5 Levels, which can be used to increase evidence that a chemical is /is not an ED:

- Level 1: existing data and non test information
- Levels 2, 3, 4, and 5: include assays that are available, under development or proposed

CF is a guide to the tests, which can provide information for endocrine disruptors' assessment

It is not a testing strategy; it does not include evaluation of exposure.

Level 1

- Physical & chemical properties
- All available (eco)toxicological data from standardized or non-standardized tests
- Read across, chemical categories, QSARs and other *in silico* predictions, and ADME model predictions

Level 2: *In vitro* assays providing data about selected endocrine mechanism(s)/ pathway(s)

Mammalian and non mammalian toxicology

Estrogen or androgen receptor binding affinity

Estrogen receptor transactivation (TG 455)

Androgen or thyroid transactivation (If/when TGs are available)

Steroidogenesis *in vitro* (TG 456)

MCF-7 cell proliferation assays (ER antagonist/agonist)

Other assays as appropriate

Level 3: *In vivo* assays providing data about selected endocrine mechanism(s)/ pathway(s)

Mammalian toxicology	Non mammalian toxicology
Uterotrophic assay (TG 440)	Xenopus embryo thyroid signalling assay (When/if TG is available)
Hershberger assay (TG 441)	Amphibian metamorphosis assay (TG 231)
	Fish reproductive screening assay (TG 229)
	Fish screening assay (TG 230)
	Androgenized female stickleback screen (GD 140)

Level 4: *In vivo* assays providing data on **adverse effects** on endocrine relevant endpoints (1)

Mammalian toxicology	Non mammalian toxicology
Repeated dose 28-day study (TG 407)	Fish sexual development test (TG 234)
Repeated dose 90-day study (TG 408)	Fish reproduction partial lifecycle test (when/If TG is available)
1-Generation reproduction toxicity study (TG 415)	Larval amphibian growth & development assay (when TG is available)
Male pubertal assay / Female pubertal assay (US TGs)	Avian reproduction assay (TG 206)
Intact adult male endocrine screening assay (US TG)	Mollusc partial lifecycle assays (when TG is available)

Level 4: *In vivo* assays providing data on adverse effects on endocrine relevant endpoints (2)

Mammalian toxicology	Non mammalian toxicology
Prenatal development toxicity study (TG 414)	Chironomid toxicity test (TG 218-219)
Chronic toxicity and carcinogenicity studies (TG 451-3)	Daphnia reproduction test (with male induction) (TG 211)
Reproductive screening test (TG 421 if enhanced)	Earthworm reproduction test (TG 222)
Combined 28 day/reproductive screening assay (TG 422 if enhanced)	Enchytraeid reproduction test (TG 220)
Developmental Neurotoxicity study (TG 426)	Other invertebrate assays (TG 225, TG 226, TG 232)

Level 5: *In vivo* assays providing more comprehensive data on adverse effects on endocrine relevant endpoints over extensive parts of the life cycle of the organisms

Mammalian toxicology	Non mammalian toxicology
Extended one-generation reproductive toxicity study (TG 443)	FLCTT (Fish life-cycle toxicity test) (when TG is available)
2-generation reproductive toxicity study (TG 416 most recent update)	Medaka multigeneration test (MMGT) (when TG is available)
	Sediment water chironomid life cycle toxicity test (TG 233)
	Avian 2-generation reproductive toxicity assay, Mysid life cycle toxicity test, Copepod reproduction and development test, Mollusc full life cycle assays, Daphnia multigeneration assay (when TGs are available)

Guidance Document on Standardized TGs for Evaluating Chemicals for Endocrine Disruption (1)

Objectives

- To support regulatory authorities' decisions on the hazard of specific chemicals and relevant metabolites **when they receive results from an OECD Test Guideline** for the screening/testing of chemicals for endocrine disruption;
- To provide guidance on how to interpret the outcome of individual tests and **how to increase evidence** on whether or not a substance may be an ED

Guidance Document on Standardized TGs for Evaluating Chemicals for Endocrine Disruption (2)

Benefits

- 1/ provides guidance for assessing results of individual tests, together with existing information on mechanisms/effects, according to different scenarios, in a weight-of-evidence approach
- 2/ recommends a test method that may be performed if regulatory authorities need more evidence on whether or not a substance may be an endocrine disrupter

Harmonisation of testing and assessment will minimise animal testing

Three case studies using example chemicals

To evaluate whether the conclusions and next steps recommended in the Guidance Document are sensible and helpful

- Prochloraz
- 4-tert-octylphenol
- Perchlorate

Detailed Review Paper: State of the Science on Novel *in Vitro* and *in Vivo* Screening and Testing Methods and Endpoints for Evaluating Endocrine Disruptors

- Other hormonal pathways besides oestrogen, androgen, thyroid (EAT), or non conventional interaction with EAT hormonal systems
- Identification of endocrine-specific screening and testing methods and endpoints (protocol standardisation and protocol status)

Conclusions

- **Eleven Test Guidelines** for *in vitro* and *in vivo* assays have been developed or updated **specifically** for detecting potential endocrine disruptors
- Other less specific Test Guidelines and **approximately 50 ED-related** guidance documents, detailed review papers, validation reports, peer review reports, and workshop reports also provide useful information for testing and assessment of endocrine disruptors

www.oecd.org/env/testguidelines