OECD Conceptual Framework for Testing and Assessment of Endocrine Disrupters (as revised in 2012)

This document presents the revised Conceptual Framework for Testing and Assessment of Endocrine Disrupters, as included in the Guidance Document 150 (Annex 1.4) published in the OECD Series on Testing and Assessment in August 2012. Very few editorial changes were necessary to be able to post it on the public website as a standalone document.

The OECD Conceptual Framework for Testing and Assessment of Endocrine Disrupters (as revised in 2012) lists the OECD Test Guidelines and standardized test methods available, under development or proposed that can be used to evaluate chemicals for endocrine disruption. The Conceptual Framework is intended to provide a guide to the tests available which can provide information for endocrine disrupters' assessment but is not intended to be a testing strategy. Furthermore, this Conceptual Framework does not include evaluation of exposure; however this should be included when deciding whether further testing is needed. Further information regarding the use and interpretation of these tests is available in Guidance Document No. 150.

Mammalian and non mammalian Toxicology	
Level 1 Existing Data and Non-Test Information	• Physical & chemical properties, e.g., MW reactivity, volatility, biodegradability • 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) / pathways(s) (Mammalian and non mammalian methods)	• Estrogen or androgen receptor binding affinity • Estrogen receptor transactivation (OECD TG 455 – OECD TG 457) • Androgen or thyroid transactivation (If/when TGs are available) • Steroidogenesis in vitro (OECD TG 456) • MCF-7 cell proliferation assays (ER ant/agonist) • Other assays as appropriate

	Mammalian Toxicology	**Non-Mammalian Toxicology**
Level 3 *In vivo* assays providing data about selected endocrine mechanism(s) / pathway(s)[1]	• Uterotrophic assay (OECD TG 440) • Hershberger assay (OECD TG 441)	• Xenopus embryo thyroid signalling assay (When/if TG is available) • Amphibian metamorphosis assay (OECD TG 231) • Fish Reproductive Screening Assay (OECD TG 229) • Fish Screening Assay (OECD TG 230) • Androgenized female stickleback screen

		(GD 140)
Level 4 *In vivo* assays providing data on adverse effects on endocrine relevant endpoints [2]	• Repeated dose 28-day study (OECD TG 407) • Repeated dose 90-day study (OECD TG 408) • 1-generation reproduction toxicity study (OECD TG 415) • Male pubertal assay (see GD 150, Chapter C4.3)[3] • Female pubertal assay (see GD 150, Chapter C4.4)[3] • Intact adult male endocrine screening assay (see GD 150, Chapter Annex 2.5) • Prenatal developmental toxicity study (OECD TG 414) • Chronic toxicity and carcinogenicity studies (OECD TG 451-3) • Reproductive screening test (OECD TG 421 if enhanced) • Combined 28-day/reproductive screening assay (OECD TG 422 if enhanced) • Developmental neurotoxicity (OECD TG 426)	• Fish sexual development test (OECD TG 234) • Fish Reproduction Partial Lifecycle Test (when/If TG is Available) • Larval Amphibian Growth & Development Assay (when TG is available) • Avian Reproduction Assay (OECD TG 206) • Mollusc Partial Lifecycle Assays (when TG is available) [4] • Chironomid Toxicity Test (TG 218-219) [4] • Daphnia Reproduction Test (with male induction) (OECD TG 211) [4] • Earthworm Reproduction Test (OECD TG 222) [4] • Enchytraeid Reproduction Test (OECD TG 220) [4] • Sediment Water Lumbriculus Toxicity Test Using Spiked Sediment (OECD TG 225) [4] • Predatory mite reproduction test in soil (OECD TG 226) [4] • Collembolan Reproduction Test in Soil (TG OECD 232) [4]
Level 5 *In vivo* assays providing more	• Extended one-generation reproductive toxicity study (OECD TG 443)[5]	• FLCTT (Fish LifeCycle Toxicity Test) (when TG is available)

comprehensive data on adverse effects on endocrine relevant endpoints over more extensive parts of the life cycle of the organism [2]	• 2-Generation reproduction toxicity study (OECD TG 416 most recent update)	• Medaka Multigeneration Test (MMGT) (when TG is available) • Avian 2 generation reproductive toxicity assay (when TG is available) • Mysid Life Cycle Toxicity Test (when TG is available)[4] • Copepod Reproduction and Development Test (when TG is available)[4] • Sediment Water Chironomid Life Cycle Toxicity Test (OECD TG 233) [4] • Mollusc Full Lifecycle Assays (when TG is available) [4] • Daphnia Multigeneration Assay (if TG is available) [4]

[1] Some assays may also provide some evidence of adverse effects.

[2] Effects can be sensitive to more than one mechanism and may be due to non-ED mechanisms.

[3] Depending on the guideline/protocol used, the fact that a substance may interact with a hormone system in these assays does not necessarily mean that when the substance is used it will cause adverse effects in humans or ecological systems.

[4] At present, the available invertebrate assays solely involve apical endpoints which are able to respond to some endocrine disrupters and some non-EDs. Those in Level 4 are partial lifecycle tests, while those in Level 5 are full- or multiple lifecycle tests.

[5] The Extended one-generation reproductive Toxicity Study (OECD TG 443) is preferable for detecting endocrine disruption because it provides an evaluation of a number of endocrine endpoints in the juvenile and adult F1, which are not included in the 2-generation study (OECD TG 416) adopted in 2001

Notes to the OECD Revised Conceptual Framework

Note 1: Entering at all levels and exiting at all levels is possible and depends upon the nature of existing information and needs for testing and assessment.

Note 2: The assessment of each chemical should be made on a case by case basis, taking into account all available information.

Note 3: The framework should not be considered as all inclusive at the present time. At levels 2, 3, 4 and 5 it includes assays that are either available or for which validation is under way. With respect to the latter, these are provisionally included.