

Note: Document prepared by the Secretariat of the Test Guidelines Programme based on the agreement reached at the 6th Meeting of the EDTA Task Force

OECD Conceptual Framework for the Testing and Assessment of Endocrine Disrupting Chemicals

<p style="text-align: center;">Level 1</p> <p>Sorting & prioritization based upon existing information</p>	<ul style="list-style-type: none"> - physical & chemical properties, e.g., MW, reactivity, volatility, biodegradability, - human & environmental exposure, e.g., production volume, release, use patterns - hazard, e.g., available toxicological data 		
<p style="text-align: center;">Level 2</p> <p><i>In vitro</i> assays providing mechanistic data</p>	<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none; vertical-align: top;"> <ul style="list-style-type: none"> - ER, AR, TR receptor binding affinity - Transcriptional activation - Aromatase and steroidogenesis <i>in vitro</i> - Aryl hydrocarbon receptor recognition/binding - QSARs </td> <td style="width: 50%; border: none; vertical-align: top;"> <ul style="list-style-type: none"> - High Through Put Prescreens - Thyroid function - Fish hepatocyte VTG assay - Others (as appropriate) </td> </tr> </table>	<ul style="list-style-type: none"> - ER, AR, TR receptor binding affinity - Transcriptional activation - Aromatase and steroidogenesis <i>in vitro</i> - Aryl hydrocarbon receptor recognition/binding - QSARs 	<ul style="list-style-type: none"> - High Through Put Prescreens - Thyroid function - Fish hepatocyte VTG assay - Others (as appropriate)
<ul style="list-style-type: none"> - ER, AR, TR receptor binding affinity - Transcriptional activation - Aromatase and steroidogenesis <i>in vitro</i> - Aryl hydrocarbon receptor recognition/binding - QSARs 	<ul style="list-style-type: none"> - High Through Put Prescreens - Thyroid function - Fish hepatocyte VTG assay - Others (as appropriate) 		
<p style="text-align: center;">Level 3</p> <p><i>In vivo</i> assays providing data about single endocrine Mechanisms and effects</p>	<table style="width: 100%; border: none;"> <tr> <td style="width: 60%; border: none; vertical-align: top;"> <ul style="list-style-type: none"> - Uterotrophic assay (estrogenic related) - Hershberger assay (androgenic related) - Non-receptor mediated hormone function - Others (e.g. thyroid) </td> <td style="width: 40%; border: none; vertical-align: top;"> <ul style="list-style-type: none"> - Fish VTG (vitellogenin) assay (estrogenic related) </td> </tr> </table>	<ul style="list-style-type: none"> - Uterotrophic assay (estrogenic related) - Hershberger assay (androgenic related) - Non-receptor mediated hormone function - Others (e.g. thyroid) 	<ul style="list-style-type: none"> - Fish VTG (vitellogenin) assay (estrogenic related)
<ul style="list-style-type: none"> - Uterotrophic assay (estrogenic related) - Hershberger assay (androgenic related) - Non-receptor mediated hormone function - Others (e.g. thyroid) 	<ul style="list-style-type: none"> - Fish VTG (vitellogenin) assay (estrogenic related) 		
<p style="text-align: center;">Level 4</p> <p><i>In vivo</i> assays providing data about multiple endocrine Mechanisms and effects</p>	<table style="width: 100%; border: none;"> <tr> <td style="width: 60%; border: none; vertical-align: top;"> <ul style="list-style-type: none"> - enhanced OECD 407 (endpoints based on endocrine mechanisms) - male and female pubertal assays - adult intact male assay </td> <td style="width: 40%; border: none; vertical-align: top;"> <ul style="list-style-type: none"> - Fish gonadal histopathology assay - Frog metamorphosis assay </td> </tr> </table>	<ul style="list-style-type: none"> - enhanced OECD 407 (endpoints based on endocrine mechanisms) - male and female pubertal assays - adult intact male assay 	<ul style="list-style-type: none"> - Fish gonadal histopathology assay - Frog metamorphosis assay
<ul style="list-style-type: none"> - enhanced OECD 407 (endpoints based on endocrine mechanisms) - male and female pubertal assays - adult intact male assay 	<ul style="list-style-type: none"> - Fish gonadal histopathology assay - Frog metamorphosis assay 		
<p style="text-align: center;">Level 5</p> <p><i>In vivo</i> assays providing data on effects from endocrine & other mechanisms</p>	<table style="width: 100%; border: none;"> <tr> <td style="width: 60%; border: none; vertical-align: top;"> <ul style="list-style-type: none"> - 1-generation assay (TG415 enhanced)¹ - 2-generation assay (TG416 enhanced)¹ - reproductive screening test (TG421 enhanced)¹ - combined 28 day/reproduction screening test (TG 422 enhanced)¹ </td> <td style="width: 40%; border: none; vertical-align: top;"> <ul style="list-style-type: none"> - Partial and full life cycle assays in fish, birds, amphibians & invertebrates (developmental and reproduction) </td> </tr> </table> <p style="font-size: small; margin-top: 5px;">¹ Potential enhancements will be considered by VMG mamm</p>	<ul style="list-style-type: none"> - 1-generation assay (TG415 enhanced)¹ - 2-generation assay (TG416 enhanced)¹ - reproductive screening test (TG421 enhanced)¹ - combined 28 day/reproduction screening test (TG 422 enhanced)¹ 	<ul style="list-style-type: none"> - Partial and full life cycle assays in fish, birds, amphibians & invertebrates (developmental and reproduction)
<ul style="list-style-type: none"> - 1-generation assay (TG415 enhanced)¹ - 2-generation assay (TG416 enhanced)¹ - reproductive screening test (TG421 enhanced)¹ - combined 28 day/reproduction screening test (TG 422 enhanced)¹ 	<ul style="list-style-type: none"> - Partial and full life cycle assays in fish, birds, amphibians & invertebrates (developmental and reproduction) 		

Notes to the Framework

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

Note 2: In level 5, ecotoxicology should include endpoints that indicate mechanisms of adverse effects, and potential population damage

Note 3: When a multimodal model covers several of the single endpoint assays, that model would replace the use of those single endpoint assays

Note 4: The assessment of each chemical should be based on a case by case basis, taking into account all available information, bearing in mind the function of the framework levels.

Note 5: The framework should not be considered as all inclusive at the present time. At levels 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. Once developed and validated, they will be formally added to the framework.

Note 6: Level 5 should not be considered as including definitive tests only. Tests included at that level are considered to contribute to general hazard and risk assessment.