

## 14.0 GLOSSARY<sup>1</sup>

**Accuracy<sup>2</sup>:** A measure of test performance. (a) The closeness of agreement between a test result and an accepted reference value; (b) The proportion of correct outcomes of a method. Often used interchangeably with **concordance**.

**Activation (of genes):** The interaction of specific molecules or molecular complexes with specific genes to initiate their expression (i.e., transcription of mRNA).

**Affinity (high; low):** The strength of binding of a molecule to a receptor protein.

**Agonism:** The binding of a substance to a receptor to initiate effects similar to those produced by the natural ligand for the receptor.

**Agonist:** A substance that mimics the action of an endogenous hormone.

**Androgen:** A class of steroid hormones, which includes testosterone and 5 -dihydrotestosterone, responsible for the development and maintenance of the male reproductive system.

**Antagonism:** The binding of a substance to a receptor to inhibit or counteract the effects produced by the natural ligand for the receptor.

**Antagonist:** A substance that blocks or diminishes the activity of an **agonist**.

**Complex mixture:** A mixture containing many, generally uncounted substances, a majority of which are undefined (e.g., plant homogenates, fuels).

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<sup>1</sup> The definitions in this Glossary are restricted to their uses with respect to endocrine mechanisms and actions.

<sup>2</sup> Definition used by the Interagency Coordinating Committee on the Validation of Alternative Methods.

**Concordance<sup>2</sup>:** A measure of test performance. The proportion of all chemicals that are correctly classified as positive or negative. Often used interchangeably with **accuracy**. The concordance is highly dependent on the **prevalence** of positives in the population being examined.

**COS:** A monkey kidney cell line

**C-Terminal region:** The end of a protein molecule that contains a free carboxylic acid moiety.

**CV-1:** A monkey kidney cell line

**Cytoplasm:** The material inside the cell, excluding the nucleus, that contains the intracellular fluid, organelles, soluble enzymes, membrane components and other factors.

**Cytosol:** see Cytoplasm.

**Detoxification:** Reduction of the toxicity (of a substance) by metabolism to a less toxic form, or by removal of the substance from the affected cell or organism.

**Domain:** A region of a protein defined by its activity.

**Endocrine disruption:** Activity by an exogenous chemical substance that alters the structure or function(s) of the endocrine system and causes adverse effects at the level of the organism, its progeny, populations, or subpopulations of organisms.

**Endocrine disruptor:** A substance determined to cause endocrine disruption.

**Endocrine system:** Made up of glands located throughout the body, the hormones that are synthesized and secreted by the glands into the bloodstream, and the receptors in the various tissues and organs that recognize and respond to the hormones.

**Endogenous:** Originating within the organism of interest.

**Endpoint:** The biological process, response, or effect assessed by a test method.

**EPC:** A carp cell line derived from a skin tumor.

**Estrogen:** A class of steroid hormones, which includes 17 -estradiol, responsible for regulation of specific female reproductive functions and for development and maintenance of the female reproductive system.

**Exogenous:** Originating outside the organism of interest.

**False negative<sup>2</sup>:** An active substance incorrectly identified as negative by a test.

**False negative rate<sup>2</sup>:** The proportion of all positive (active) substances falsely identified as negative. A measure of test performance.

**False positive<sup>2</sup>:** An inactive substance incorrectly identified as positive by a test.

**False positive rate<sup>2</sup>:** The proportion of all negative (inactive) substances falsely identified as positive. A measure of test performance.

**Frog metamorphosis assay:** A test method that measures the ability of a substance to affect the metamorphosis of frog larvae (tadpoles) to adults.

**Gonadal recrudescence assay:** A test method that measures the ability of a substance to produce effects in estrogen- and androgen-dependent accessory sex organs or gonad maturation in fish. A test method for potential estrogen- and androgen-related endocrine disruption.

**Half-life:** The time it takes for a chemical or radioactive substance to lose half its activity.

**Hazard:** An adverse health or ecological effect.

**HeLa:** A human cell line derived from a cervical cancer.

**HepG2:** A human cell line derived from a hepatoma.

**Hershberger assay:** Measures the ability of a substance to alter the weight of androgen-dependent accessory sex organs (e.g., ventral prostate or seminal vesicles) or tissues in castrated rats or mice. A test method for potential androgen and anti-androgen related endocrine disruption activity.

**Hormone:** A chemical substance produced in specific cells, or glands, that can either act locally or be released into the bloodstream to act on an organ or tissue in another part of the body.

**Hypospadias:** A clinical condition in newborns that manifests itself as a displaced opening of the urethra. Occurs in males only and is considered a fetal developmental anomaly.

**Interlaboratory reproducibility<sup>2</sup>:** A measure of whether different laboratories using the same protocol and test chemicals can produce qualitatively and quantitatively similar results. See **reliability**.

**Intralaboratory reproducibility<sup>2</sup>:** A measure of whether the same laboratory can successfully replicate results using a specific test protocol at different times. See **reliability**.

**In vitro:** In glass. Refers to assays that are carried out in an artificial system (e.g., in a test tube or petri dish) and typically use single-cell organisms, cultured cells, cell-free extracts, or purified cellular components.

**In vivo:** In the living organism. Refers to assays performed in multicellular organisms.

**Ligand:** A substance that is capable of binding to a specific receptor protein.

**Ligand-binding domain:** The area within a receptor molecule that is designed to attract and hold a ligand.

**LnCaP-FGC:** A cell line established from a supraclavicular lymph node removed from a patient with metastatic prostatic adenocarcinoma.

**MCF-7:** A cell line from a human breast adenocarcinoma.

**MDA (all variations):** A human cell line derived from a breast carcinoma.

**Metabolic activation:** Metabolism by an organism or a cell-free extract of a chemical to a biologically active form.

**Negative predictivity<sup>2</sup>:** The proportion of correct negative responses among substances testing negative.

**N-Terminal region:** The end of a protein molecule that contains a free amino acid moiety.

**PC-3:** A human cell line derived from a prostate adenocarcinoma.

**Peer review:** Objective review of data, a document, or proposal, and provision of recommendations, by an expert individual or group of individuals having no conflict of interest with the outcome of the review.

**pH:** A measure of the acidity or alkalinity of a solution. pH 7.0 is neutral; higher pHs are alkaline, lower pHs are acidic.

**Placental aromatase assay:** Measures the ability of a substance to induce or inhibit the activity of the aromatase enzyme which converts testosterone to estradiol. A test method for potential anti-estrogen related endocrine activity.

**Positive predictivity<sup>2</sup>:** The proportion of correct positive responses among substances testing positive.

**Protocol<sup>2</sup>:** The precise, step-by-step description of a test, including the listing of all necessary reagents, criteria and procedures for the evaluation of the test data.

**Pubertal female assay:** Measures the ability of a substance to induce or inhibit the onset of puberty in immature female rats and mice, measured as an early or late opening of the vagina. A test method for potential estrogenicity and anti-estrogenicity.

**Pubertal male assay:** Measures the ability of a substance to induce or inhibit prepubertal separation in immature male rats and mice. At recovery (53 days), various tissues are weighed and the thyroid examined histologically. A test method for potential androgen- and anti-androgen related endocrine disruption.

**R1881:** Methyltrienolone

**Receptor:** A protein or protein complex which binds to specific molecules for the purpose of transporting them elsewhere in the cell, or for producing a chemical signal.

**Receptor binding assay (competitive):** An assay to measure the ability of a substance to bind to a hormone receptor protein, which is typically performed by measuring the ability of the substance to displace the bound natural hormone.

**Receptor superfamily:** A family of related receptors with similar composition and reactivity (e.g., the estrogen, androgen, and glucocorticoid receptors).

**Relevance (of an assay)<sup>2</sup>:** The relationship of a test to the effect of interest and whether a test is meaningful and useful for a particular purpose. The extent to which an assay will correctly predict or measure the biological effect of interest. A measure of assay **performance**.

**Reliability (of an assay)<sup>2</sup>:** Reliability is a measure of the degree to which a test can be performed reproducibly within and among laboratories over time.

**Repression (of genes):** The interaction of specific molecules or molecular complexes with specific genes to prevent their expression (transcription of mRNA).

**Reproducibility:** The variability between single test results obtained in a single laboratory (intralaboratory reproducibility) or in different laboratories (interlaboratory reproducibility) using the same protocol.

**Screen/Screening Test<sup>2</sup>:** A relatively rapid, simple test conducted for the purposes of a general classification of substances according to general categories of hazard. The results of a screen are generally used for preliminary decision making and to set priorities for more definitive tests. A screening test may have a truncated response range (e.g., provides a qualitative response only).

**Sensitivity<sup>2</sup>:** The proportion of all positive substances that are correctly classified as positive in a test.

**Specificity<sup>2</sup>:** The proportion of all negative substances that are correctly classified as negative in a test.

**Steroidogenesis assay:** Measurement of the ability of chemicals to inhibit steroid hormone biosynthesis in testicular tissue or cells *in vitro*.

**Test battery:** A series of tests, usually performed at the same time or in close sequence. Each test in the battery usually measures a different component of a multifactorial toxic effect, or a mechanistically related effect.

**Tier 1 assay:** An assay that is a component of the EDSP screening battery of tests.

**Tier 1 battery:** Defined by the EDSP as a series of *in vitro* and *in vivo* tests to determine the ability of substances to interact with the endocrine system.

**Tier 2 assay:** An assay that is a component of the EDSP testing battery.

**Tier 2 battery:** Defined by the EDSP as a series of *in vivo* tests designed to confirm the endocrine disrupting ability of substances in laboratory animals and wildlife species.

**Transcriptional activation (assay):** An assay to measure the initiation of mRNA synthesis in a gene in response to a specific chemical signal, such as an androgen-androgen receptor complex.

**Transcriptional regulatory protein:** A protein that binds to a specific DNA sequence resulting in a change in the regulation of mRNA synthesis.

**Transfection:** The process by which foreign DNA is introduced into a cell to change the cell's genotype.

**Uterotrophic assay:** Measures the ability of a substance to cause uterine enlargement in an immature or ovariectomized rat or mouse. A test method for potential estrogenicity and anti-estrogenicity.

**Valid method<sup>2</sup>:** A method determined to be acceptable for a specific use.

**Validated method<sup>2</sup>:** A method for which the reliability and relevance for a specific purpose has been established.

**Validation<sup>2</sup>:** Validation is the process by which the reliability and relevance of an assay for a specific purpose are established.

**Vector:** A small segment of DNA (frequently a plasmid or viral DNA) that is used to carry a foreign gene or DNA sequence into a cell's nucleus.

**Weight of evidence (process):** The strengths and weaknesses of a collection of information are used as the basis for a conclusion that may not be evident from the individual data.

**Xenobiotic:** A substance that is not produced by the organism of interest.

**Zinc finger motif:** A configuration of a DNA-binding protein that resembles a finger and binds a zinc ion for its activity.

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