EUROPEAN
COMMISSION

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ANNEX 1

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ANNEX

to the

COMMISSION DELEGATED REGULATION (EU) …/...

setting out scientific criteria for the determination of endocrine-disrupting properties pursuant to Regulation (EU) No 528/2012

ANNEX

A substance shall be considered as having endocrine disrupting properties with respect to humans or non-target organisms, where it meets the criteria set out in section A or section B.

Section A - Endocrine disrupting properties with respect to humans

(1) A substance shall be considered as having endocrine disrupting properties that may cause adverse effect in humans if, based on points (a) to (e) of point (2), it is a substance that meets all of the following criteria, unless there is ~~information~~ evidence demonstrating that the adverse effects identified are ~~clearly~~ not relevant to humans:

(a) it shows an adverse effect in an intact organism or its progeny, which is a change in the morphology, physiology, growth, development, reproduction or life span of an organism, system or (sub)population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress or an increase in susceptibility to other influences;

(b) it has an endocrine mode of action , i.e. it alters the function(s) of the endocrine system;

(c) the adverse effect is a consequence of the endocrine mode of action.

(2) The identification of a substance as having endocrine disrupting properties that may cause adverse effect in humans in accordance with point (1) shall be based on all of the following:

(a) all available relevant scientific data (in vivo studies or adequately validated alternative test systems predictive of adverse effects in humans or animals; as well as in vivo, in vitro , or, if applicable, in silico studies informing about endocrine modes of action):

(i) scientific data generated in accordance with internationally agreed study protocols ~~(in vivo studies or adequately validated alternative test systems predictive of adverse effects in humans or animals; as well as in vivo, in vitro , or, if applicable, in silico studies informing about endocrine modes of action)~~.

(ii) other scientific data selected applying a systematic review methodology.

(b) an assessment of the available relevant scientific data based on a weight of evidence approach in order to establish whether the criteria set out in point (1) are fulfilled.

(c) in applying the weight of evidence determination the assessment of the scientific evidence shall, in particular, consider all of the following factors:

(i) both positive and negative results.

(ii) the relevance of the study designs for the assessment of adverse effects and of the endocrine mode of action.

(iii) the biological plausibility of the link between the adverse effects and the endocrine mode of action.

(iv) the quality and consistency of the data, considering the pattern and coherence of the results within and between studies of a similar design and across different species.

(v) the route of exposure, toxicokinetic and metabolism studies.

(vi) the concept of the limit dose, and international guidelines on maximum recommended doses and for assessing confounding effects of excessive toxicity.

(d) adverse effects that are non-specific secondary consequences of other toxic effects shall not be considered for the identification of the substance as endocrine disruptor.

~~(e) Where there is information demonstrating that the adverse effects are clearly not relevant for humans the substance should not be considered a human endocrine disruptor.~~

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Section B - Endocrine disrupting properties with respect to non-target organisms

(1) A substance shall be considered as having endocrine disrupting properties that may cause adverse effects on non-target organisms if, upon the application of points (a) to (e) of point (2), it is a substance that meets all of following criteria, unless there is ~~information~~ evidence demonstrating that the adverse effects identified are not relevant at the (sub)population level for non-target organisms:

(a) it shows an adverse effect in non-target organisms, which is a change in the morphology, physiology, growth, development, reproduction or life span of an organism, system or (sub)population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress or an increase in susceptibility to other influences;

(b) it has an endocrine mode of action, i.e. it alters the function(s) of the endocrine system;

(c) the adverse effect is a consequence of the endocrine mode of action.

(2) The identification of a substance as having endocrine disrupting properties that may cause adverse effects on non-target organisms in accordance with point (1) shall be based on all of the following:

(a) all available relevant scientific data (in vivo studies or adequately validated alternative test systems predictive of adverse effects in humans or animals; as well as in vivo, in vitro or, if applicable, in silico studies informing about endocrine modes of action):

(i) scientific data generated in accordance with internationally agreed study protocols. ~~(in vivo studies or adequately validated alternative test systems predictive of adverse effects in humans or animals; as well as in vivo, in vitro or, if applicable, in silico studies informing about endocrine modes of action). I~~ in particular, guidance on the implementation of Regulation ~~(EU) No 528/2012, issued by the European Chemicals Agency shall be considered.~~

(ii) other scientific data selected applying a systematic review methodology.

(b) an assessment of the available relevant scientific data based on a weight of evidence approach in order to establish whether the criteria set out in point 1 are fulfilled.

(c) in applying the weight of evidence determination, the assessment of the scientific evidence shall consider all of the following factors:

(i) both positive and negative results, discriminating between taxonomic groups (e.g. mammals, birds, fish, amphibians) where relevant.

(ii) the relevance of the study designs for the assessment of the adverse effects and its relevance at the (sub)population level, and for the assessment of the endocrine mode of action.

(iii) the adverse effects on reproduction, growth/development, and other relevant adverse effects which are likely to impact on (sub)populations. Adequate, reliable and representative field or monitoring data and/or results from population models shall as well be considered where available.

(iv) the biological plausibility of the link between the adverse effects and the endocrine mode of action.

(v) the quality and consistency of the data, considering the pattern and coherence of the results within and between studies of a similar design and across different taxonomic groups.

(vi) the concept of the limit dose and international guidelines on maximum recommended doses and for assessing confounding effects of excessive toxicity.

(d) adverse effects that are non-specific secondary consequences of other toxic effects shall not be considered for the identification of the substance as endocrine disruptor with respect to non-target organisms.

(e) If the intended biocidal mode of action of the active substance being assessed, as defined under point 6.5 of Annex II of Regulation (EU) No 528/2012~~point 3.6 of Part A of the Annex to Commission Regulation (EU) No 283/2013~~, ~~acts by~~consists of ~~regulating moulting and/or growth of~~controlling ~~harmful~~ target harmful organisms via their endocrine system, ~~it~~ this mode of action shall not be considered for the identification of the substance as endocrine disruptor with respect to non-target organisms of the same taxonomic phylum that is targeted to be controlled.

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