



Brussels, **XXX**
C(2016) 3751 projet

ANNEX 1

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to the

COMMISSION REGULATION (EU) .../...

**setting out scientific criteria for the determination of endocrine disrupting properties
and amending Annex II to Regulation (EC) 1107/2009**

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Annex II to Regulation (EC) No 1107/2009 is amended as follows:

(1) Point 3.6.5. is replaced by the following:

"3.6.5. Endocrine disrupting properties

~~4.1.1.1.~~3.6.5.1. An active substance, safener or synergist shall only be approved if, on the basis of the assessment of Community or internationally agreed test guidelines or other available data and information, including a review of the scientific literature, reviewed by the Authority, it is not considered to have endocrine disrupting properties that may cause adverse effect in humans, unless the exposure of humans to that active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with point (b) of Article 18(1) of Regulation (EC) No 396/2005.

By 14 December 2013, the Commission shall present to the Standing Committee on the Food Chain and Animal Health a draft of the measures concerning specific scientific criteria for the determination of endocrine disrupting properties to be adopted in accordance with the regulatory procedure with scrutiny referred to in Article 79(4).

Pending the adoption of these criteria, substances that are or have to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as carcinogenic category 2 and toxic for reproduction category 2, shall be considered to have endocrine disrupting properties.

In addition, substances such as those that are or have to be classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as toxic for reproduction category 2 and which have toxic effects on the endocrine organs, may be considered to have such endocrine disrupting properties.

~~4.1.1.2.~~3.6.5.2. From [date of EIF], the following shall apply instead of the first, the third and the fourth paragraph of point 3.6.5.1.

3.6.5.2.1. An active substance, safener or synergist shall only be approved if, on the basis of the assessment of the available evidence carried out in accordance with the data requirements for the active substances, safeners or synergists and other available data and information, it is not ~~identified as having endocrine disrupting properties considered, in accordance with respect to humans according to~~ the criteria specified in point 3.6.5.2.2, to have endocrine disrupting properties that may cause adverse effect in humans, unless the risk to humans from exposure to that active substance, safener or synergist in a plant protection product, under realistic worst case proposed conditions of use, is negligible, in particular where the product is used in closed systems or in other conditions which aim at excluding contact with humans, and where maximum residue levels of the active substance, safener or synergist concerned in or on food and feed can, taking account of the latest opinion of the Authority with respect to that active substance, synergist, safener, be set in accordance with Regulation (EC) No 396/2005, which ensure a high level of consumer protection.

3.6.5.2.2. An active substance, safener or synergist shall be considered as having endocrine disrupting properties ~~with respect to that may cause adverse effect in humans if, based on points (1) to (4) of point 3.6.5.2.3., it is a substance that meets all of the following criteria, unless there is information demonstrating that the adverse effects identified are not relevant to humans:~~

- (1) it ~~is known to cause~~shows an adverse effect ~~relevant for human health 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;
- (2) it has an endocrine mode of action~~;~~, ~~i.e. it alters the function(s) of the endocrine system;~~
- (3) the adverse effect ~~relevant for human health~~ is a consequence of the endocrine mode of action.

3.6.5.2.3. The identification of an active substance, safener or synergist as having endocrine disrupting properties ~~that may cause adverse effect in humans~~ in accordance with point ~~3.6.5.2.2.~~ shall be based on all of the following:

- (1) all available relevant scientific ~~evidence, data:~~
 - (a) ~~scientific data primarily performed~~generated in accordance with ~~according to~~ 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~~, or~~ in vitro ~~and mechanistic studies informing about endocrine modes of action,~~ ~~in~~). ~~In particular, on those internationally agreed study protocols listed in the Commission Communications in the framework of setting out the data requirements for active substances and plant protection products, in accordance with Regulation (EC) No 1107/2009, shall be considered.~~
 - (b) ~~other relevant scientific data selected~~ applying a systematic review methodology, in particular following guidance listed in the Commission Communications in the framework of setting out the data requirements for active substances and plant protection products, in accordance with Regulation (EC) No 1107/2009, ~~to analyse other relevant scientific information,~~
- (2) ~~An assessment of the available relevant scientific data based on a comparison of the weight of the scientific evidence approach in order to establish whether on endocrine mediated adverse effects with the criteria set out in point 1, considering whether or not the effects are adverse, the mode of action, together with the biological plausibility of the causal link between the adverse effect and the endocrine mode of action~~3.6.5.2.2 are fulfilled.
- (3) ~~in applying the weight of evidence determination, using expert judgement and internationally agreed guidelines, the following elements shall be considered:~~
- (4)(3)The assessment of quality, reliability, reproducibility and consistency of the scientific evidence shall, in particular, consider all of the following factors:
 - (a) ~~Both~~both positive and negative results ~~shall be considered together in a single weight of evidence determination.~~

- (b) ~~ii. — The weight of evidence should consider~~ the relevance of the study designs, for the assessment of adverse effects and ~~for the evaluation of mechanistic information. For the assessment of adverse effects, generally adequate reliable and representative data on humans shall have precedence over other data; but positive results from well-conducted animal studies are not necessarily negated by the lack of positive human experience of the endocrine mode of action.~~
- (c) ~~iii. — The~~ biological plausibility of the link between the adverse effects and the endocrine mode of action.
- (d) ~~iv. — The~~ quality and consistency of the data ~~shall be given appropriate weight~~, considering the pattern and coherence of the results within and between studies of a similar design and across different species.
- (e) ~~v. — The~~ route of exposure, toxicokinetic and metabolism studies ~~are assumed to be relevant to humans, unless convincing evidence exists to explain the differences between test animals and humans.~~
- (f) ~~vi. — The~~ concept of the limit dose, and international guidelines on maximum recommended doses and for assessing confounding effects of excessive toxicity.

~~(5)(4) Adverse~~ ~~adverse~~ effects ~~or endocrine modes of action~~ that are non-specific secondary consequences of other toxic effects shall not be considered for the identification of the substance as endocrine disruptor."

~~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."~~

(2) Point 3.8.2. is replaced by the following:

"3.8.2. Endocrine disrupting properties

3.8.2.1. An active substance, safener or synergist shall only be approved if, on the basis of the assessment of Community or internationally agreed test guidelines, it is not considered to have endocrine disrupting properties that may cause adverse effects on non-target organisms unless the exposure of non-target organisms to that active substance in a plant protection product under realistic proposed conditions of use is negligible.

3.8.2.2. From [date of EIF] the following shall apply instead point 3.8.2.1.

3.8.2.2.1 An active substance, safener or synergist shall only be approved if it is not considered, in accordance with the criteria specified in point 3.8.2.2.2, to have endocrine disrupting properties that may cause adverse effects on non-target organisms~~1-~~, unless the risk to the non-target organisms from exposure to that active substance, safener or synergist in a plant protection product, under realistic worst case proposed conditions of use, is negligible.

3.8.2.2.2 As of [Date of EIF], a ~~an~~ active substance, safener or synergist shall be ~~identified~~considered as having endocrine disrupting properties ~~with respect to that may cause adverse effects on non-target organisms if, based on points (1) to (4) of point 3.8.2.2.3, it is a substance that meets all of the following criteria, unless there is~~

information demonstrating that the adverse effects identified are not relevant at the (sub)population level for non-target organisms:

- (1) ~~it is known to causes~~shows an adverse effect ~~for~~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, considered relevant at the (sub)population level;
- (2) it has an endocrine mode of action; ~~i.e. it alters the function(s) of the endocrine system;~~
- (3) the adverse effect ~~relevant for the non-target organism at the population level~~ is a consequence of the endocrine mode of action-

~~3.8.2.2.3 2-~~The identification of an active substance, safener or synergist as having endocrine disrupting properties that may cause adverse effects on non-target organisms in accordance with point ~~4~~3.8.2.2.2 shall be based on all of the following:

- (1) all available relevant scientific ~~evidence~~data:
 - (a) ~~scientific data primarily performed~~generated in accordance with according to 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 ~~or~~ in vitro ~~and mechanistic studies informing about endocrine modes of action~~), ~~in~~ In particular, ~~on~~ those internationally agreed study protocols listed in the Commission Communications in the framework of setting out the data requirements for active substances and plant protection products, in accordance with Regulation (EC) No 1107/2009, ~~shall be considered.~~
 - (b) other relevant scientific data selected applying a systematic review methodology, in particular following guidance listed in the Commission Communications in the framework of setting out the data requirements for active substances and plant protection products, in accordance with Regulation (EC) No 1107/2009, ~~to analyse other relevant scientific information.~~
- (2) 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 3.8.2.2 are fulfilled ~~a comparison of the weight of the scientific evidence on endocrine mediated adverse effects with the criteria set out in point 1, considering whether or not the effects are adverse, the mode of action, together with the biological plausibility of the causal link between the adverse effect and the endocrine mode of action.~~

~~1-~~ in applying the weight of evidence determination referred in point 2, using expert judgement and internationally agreed guidelines, all of the following elements shall be considered:

~~2.~~(3) ~~The~~ assessment of quality, reliability, reproducibility and consistency of the scientific evidence shall consider all of the following factors:

- ~~3.~~(a) ~~Both~~both positive and negative results ~~shall be considered together in a single weight of evidence determination,~~ discriminating between taxonomic groups (e.g. mammals, birds, fish) where relevant.

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~~4.(b) ii. — The weight of evidence should consider the relevance of the study designs, design for relevance—the assessment of the adverse effects and its relevance at the (sub)population level,; and for the evaluation of mechanistic information. Generally, evidence from field studies shall have precedence over other data. Nevertheless positive results from well-conducted laboratory studies shall be considered even in the case of lack of positive results in field studiesassessment of the endocrine mode of action.~~

~~5.(c) iii. —The adverse consequenceseffects on reproduction and growth/development, as these are the effects most likely to impact on (sub)populations. Adequate, reliable and representative higher-tier experimental studiesfield or monitoring data and/or results from reliable population models shall be considered where available—for assessing the relevance of the adverse effect at the population level.~~

~~6.(d) iv. —The biological plausibility of the link between the adverse effects and the endocrine mode of action,—and its relevance for populations of non target organisms.~~

~~7.(e) v. —The quality and consistency of the data—shall be given appropriate weight, considering the pattern and coherence of the results within and between studies of a similar design and across different taxonomic groups.~~

~~8.(f) vi. —The concept of the limit dose and international guidelines on maximum recommended doses and for assessing confounding effects of excessive toxicity.~~

~~9.(4) Adverse effects—or endocrine modes of action 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:—"~~

~~Where there is information demonstrating that the adverse effects are clearly not relevant at the population level for non target organisms, the substance should not be considered a endocrine disruptor with respect to non target organisms.~~

~~3. An active substance, safener or synergist shall only be approved if it is not identified as having endocrine disrupting properties according to the criteria specified above, unless the risk from exposure of the non target organisms to that active substance, safener or synergist in a plant protection product, under realistic worst case proposed conditions of use, is negligible."~~

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