



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

DRAFT

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

of **XXX**

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

(Text with EEA relevance)

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

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**setting out scientific criteria for the determination of endocrine disrupting properties
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(Text with EEA relevance)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC¹, and in particular Article 78(1)(a) and second paragraph of point 3.6.5 of Annex II, thereof,

Whereas:

- (1) Scientific criteria for the determination of endocrine disrupting properties of active substances, safeners and synergists, should be developed taking into account the objectives of Regulation (EC) No 1107/2009, which are to ensure a high level of protection of both human and animal health and the environment, in particular ensuring that substances or products placed on the market have no harmful effect on human or animal health or unacceptable effects on the environment, and to improve the functioning of the internal market while improving agricultural production.
- (2) In 2002, the World Health Organisation (WHO) through its International Programme for Chemical Safety proposed a definition for endocrine disruptors² and in 2009 a definition of adverse effects³. Those definitions have by now reached the widest consensus among scientists. The European Food Safety Authority ('the Authority') endorsed those definitions in its Scientific Opinion on endocrine disruptors adopted on 28 February 2013⁴ (hereinafter "the Scientific Opinion of the Authority"). It is also the view of the Scientific Committee on consumer Safety⁵. It is therefore appropriate to

¹ OJ L 309, 24.11.2009, p. 1.

² WHO/IPCS (World Health Organization/International Programme on Chemical Safety), 2002. Global Assessment of the State-of-the-science of Endocrine Disruptors. WHO/PCS/EDC/02.2, publicly available at http://www.who.int/ipcs/publications/new_issues/endocrine_disruptors/en/.

³ WHO/IPCS (World Health Organization/International Programme on Chemical Safety), 2009. Principles and Methods for the Risk Assessment of Chemicals in Food. Environmental Health Criteria 240, publicly available at <http://www.who.int/foodsafety/chem/principles/en/index1.html>.

⁴ "Scientific Opinion on the hazard assessment of endocrine disruptors: Scientific criteria for identification of endocrine disruptors and appropriateness of existing test methods for assessing effects mediated by these substances on human health and the environment", EFSA Journal 2013;11(3):3132, doi: 10.2903/j.efsa.2013.3132.

⁵ Scientific committee on Consumer Safety, Memorandum on Endocrine disruptors, 16.12.2014 (SCCS/1544/14).

base the criteria to identify substances with endocrine disrupting properties on those WHO definitions.

- (3) In order to implement those criteria, weight of evidence should be applied following in particular the methodology provided for in Regulation (EC) No 1272/2008 of the European Parliament and Council⁶ on the weight of evidence. Previous experience with the Guidance document on standardised test guidelines for evaluating chemicals for endocrine disruption of OECD⁷ should also be considered. In addition, the implementation of the criteria should be based on all relevant scientific evidence, in particular studies based on internationally agreed study protocols.
- (4) As the specific scientific criteria laid down by this Regulation reflect the current scientific and technical knowledge and are to be applied instead of the criteria currently set out in point 3.6.5 of Annex II to Regulation (EC) No 1107/2009, they should be provided for in that Annex.
- (5) In addition, the first subparagraph of point 3.6.5 and point 3.8.2 of Annex II to Regulation (EC) No 1107/2009 currently provide that substances, safeners and synergists meeting the criteria to be identified as having endocrine disrupting properties may be approved in the case the exposure of humans or non-target organisms, respectively, to the substances, safeners or synergist is negligible under realistic proposed conditions of use.
- (6) However the Scientific Opinion of the Authority states that endocrine disruptors may be assessed like most other substances of concern for human health and the environment, that is to say be subject to risk assessment and not only to hazard assessment. The Authority specifies that the approach concerning substances with endocrine disrupting properties is to be based on a level of concern and whether or not this level of concern is reached, can only be determined by risk assessment. The Scientific Committee on Consumer Safety (SCCS) supports the use of risk assessment to assess endocrine disruptors in their Memorandum⁸ issued in 2014.
- (7) Experience gained during the application of other Union provisions on endocrine disrupting properties of chemical substances which entered into force later than Regulation (EC) No 1107/2009 should be also taken into consideration, in particular as regards the application of similar criteria set out in Regulation (EU) No 528/2012 of the European Parliament and of the Council.
- (8) Considering recitals 6 and 7, it is necessary to ensure that the level of residues of active substances having endocrine disrupting properties to be approved or renewed do not, taking account of the most recent relevant opinion of the Authority, present an unacceptable risk to humans and, where relevant, to animals, and are kept as low as possible in accordance with good agricultural practice for each pesticide with a view to protecting vulnerable groups such as children and the unborn, in accordance with Regulation (EC) No 396/2005 of the European Parliament and of the Council.

⁶ Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006 (OJ L 353, 31.12.2008, p. 1).

⁷ OECD Series on Testing and Assessment No. 150.

⁸ Scientific Committee on Consumer Safety (SCCS) Memorandum on Endocrine Disruptors. Retrieved from: http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_009.pdf.

- (9) In order to reflect current scientific and technical knowledge in accordance with Article 78(1)(a) of Regulation (EC) No 1107/2009, points 3.6.5 and 3.8.2 of Annex II to Regulation (EC) No 1107/2009 should be amended.
- (10) The criteria for the determination of endocrine disrupting properties reflect the current state of scientific and technical knowledge and allow identifying active substances having endocrine disrupting properties more accurately. The new criteria should therefore apply as soon as possible, except where the relevant Committee has voted on the draft Regulation presented to it without that Regulation having been adopted by the Commission by [Date of EIF]. The Commission will consider on a case-by-case basis the implications for each procedure pending under Regulation (EC) No 1107/2009 and, where necessary, take appropriate measures with due respect for the rights of the applicants. This may include a request for additional scientific input from the Authority and comments from the applicants.
- (11) The measures provided for in this Regulation are in accordance with the opinion of the Standing Committee on Plants, Animals, Food and Feed,

HAS ADOPTED THIS REGULATION:

Article 1

Annex II to Regulation (EC) No 1107/2009 is amended in accordance with the Annex to this Regulation.

Article 2

Point 3.6.5 and point 3.8.2 of Annex II to Regulation (EC) No 1107/2009, as amended by the present Regulation, shall apply as of [*date of EIF of the Regulation*], except for procedures where the Committee has voted on the draft Regulation presented to it without that draft Regulation having been adopted by [*date of EIF this Regulation*].

Article 3

This Regulation shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

This Regulation shall be binding in its entirety and directly applicable in all Member States.

Done at Brussels,

For the Commission
The President
Jean-Claude JUNCKER



EUROPEAN
COMMISSION

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ANNEX 1

DRAFT

ANNEX

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**

ANNEX

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

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.

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.

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 with respect to humans according to the criteria specified in point 3.6.5.2, 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.

2. An active substance, safener or synergist shall be considered as having endocrine disrupting properties with respect to humans if it is a substance that meets all of the following criteria:

- (1) it is known to cause an adverse effect relevant for human health, 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;
- (3) the adverse effect relevant for human health is a consequence of the endocrine mode of action.

3. The identification of an active substance, safener or synergist as having endocrine disrupting properties in accordance with point 1 shall be based on all of the following:

- (1) all available relevant scientific evidence,
 - (a) primarily performed 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, in vitro and mechanistic studies informing about endocrine modes of action), 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,
 - (b) 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) 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.
- (3) in applying the weight of evidence determination, using expert judgement and internationally agreed guidelines, the following elements shall be considered:
 - (a) The assessment of quality, reliability, reproducibility and consistency of the scientific evidence shall, in particular, consider all of the following factors:
 - i. Both positive and negative results shall be considered together in a single weight of evidence determination.
 - 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.
 - 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 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.
 - 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.
 - vi. The concept of the limit dose, and international guidelines on maximum recommended doses and for assessing confounding effects of excessive toxicity.
- (b) 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.
 - (c) 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

1. As of [Date of EIF], an active substance, safener or synergist shall be identified as having endocrine disrupting properties with respect to non-target organisms if it is a substance that meets all of the following criteria:

- (1) it is known to cause an adverse effect for 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 population level;
- (2) it has an endocrine mode of action;
- (3) the adverse effect relevant for the non-target organism at the population level is a consequence of the endocrine mode of action.

2. The identification of an active substance, safener or synergist as having endocrine disrupting properties in accordance with point 1 shall be based on all of the following:

- (1) all available relevant scientific evidence:
 - (a) primarily performed 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, in vitro and mechanistic studies informing about endocrine modes of action), 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,
 - (b) 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) 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.
- (3) 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:
 - (a) The assessment of quality, reliability, reproducibility and consistency of the scientific evidence shall consider all of the following factors:
 - i. 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.
 - ii. The weight of evidence should consider the relevance of the study designs, for relevance of the adverse effects at the 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 studies.
 - iii. The adverse consequences on reproduction and growth/development, as these are the effects most likely to impact on populations. Adequate, reliable and representative higher tier experimental studies and/or results from reliable population models shall be considered where available for assessing the relevance of the adverse effect at the population level.
 - 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.
 - 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.
 - vi. The concept of the limit dose and international guidelines on maximum recommended doses and for assessing confounding effects of excessive toxicity.
 - (b) 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.
 - (c) 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."