



EUROPEAN COMMISSION

Brussels, XXX
[...](2013) XXX draft

COMMISSION RECOMMENDATION

of XXXX

Defining criteria for endocrine disruptors

(Text with EEA relevance)

COMMISSION RECOMMENDATION

of XXX

on defining criteria for endocrine disruptors

(Text with EEA relevance)

THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Article 292 thereof,

Whereas:

- (1) The 1999 Community Strategy for Endocrine Disruptors¹ identifies for the first time in the EU the problem of endocrine disruption, as well as appropriate policy action on the basis of the precautionary principle in order to respond quickly and effectively to the problem of endocrine disruptors, hence alleviating public concern.
- (2) The Commission carried out a review² in 2013 of the Community Strategy for Endocrine Disruptors which identified the lack of agreed criteria for the identification of endocrine disruptors as one of the greatest obstacles in the implementation of policy measures aiming to protect human health and the environment from exposure to endocrine disruptors. The review concluded that horizontal scientific criteria for the identification of endocrine disruptors applicable across all relevant pieces of legislation are essential to ensure legal coherence and certainty, regulatory consistency and predictability to all players.
- (3) The Plant Protection Product Regulation³ requires the Commission, by 14 December 2013, to present to the Standing Committee of 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.
- (4) The Biocidal Product Regulation⁴ mandates the Commission, by 13 December 2013, to adopt delegated acts specifying scientific criteria for the determination of endocrine-disrupting properties.
- (5) The Water Framework Directive⁵ and REACH⁶ have a need for horizontal criteria for identification of endocrine disruptors for controlling the risks posed by some

¹ COM (1999) 706 final of 17.12.1999. *Community Strategy for Endocrine Disruptors - a range of substances suspected of interfering with the hormone systems of humans and wildlife*

² SWD(2013) XXX. *Critical Review of the Community Strategy for Endocrine Disruptors*

³ Regulation (EU) No 1107/2009

⁴ Regulation (EU) No 528/2012

substances. This is applicable to any future legislation with provisions on endocrine disruptors.

- (6) The Council of the European Union in its conclusions of 11 June 2012 urges the Commission to *inter alia* ensure the continuation and enhancement of policies to protect human health and the environment by addressing endocrine disruptors.
- (7) The European Parliament in its resolution of 14 March 2013 on the protection of public health from endocrine disruptors⁷ called *inter alia* for overarching horizontal criteria for endocrine disruptors based on science and in particular on the World Health Organisation's International Programme on Chemical Safety (WHO/IPCS) definition, with different categories based on weight of evidence.
- (8) The European Parliament considered that the weight of evidence approach implies that no single criterion should be seen on its own as decisive for the identification of an endocrine disruptor. It also considered that a socio-economic assessment should then be carried out in accordance with the relevant legislation when addressing the risks of endocrine disruptors.
- (9) The European Parliament further took the view that the criteria for defining endocrine disruptors should be based on criteria for defining 'adverse effect' and 'endocrine mode of action', being the WHO/IPCS definition the appropriate basis for that purpose. The Parliament considered that both 'adverse effect' and 'endocrine mode of action' must be examined and considered in parallel in a comprehensive assessment. The Parliament considers that observed effects should be assumed to be harmful when there is scientific data indicating so. It stressed that any possible combination effects, such as mixtures or cocktail effects, should be taken into consideration.
- (10) The joint United Nation Environmental Programme (UNEP) and WHO report on the state of the science of endocrine disrupting chemicals - 2012⁸ found as one of the future needs *'to develop weight-of-evidence approaches that allow effective consideration of research from all levels – from in vitro mechanistic data to human epidemiological data'*.
- (11) The Scientific Committee of the European Food Safety Authority (EFSA) in its opinion of 20 March 2013 on the scientific criteria for identification of endocrine disruptors and appropriateness of existing test methods⁹ concluded that *"an endocrine disruptor is defined by three criteria: i) the presence of an adverse effect in an intact organism or a (sub)population, ii) the presence of an endocrine activity, and iii) a plausible causal relationship between the endocrine activity and the adverse effect."* No specific criteria for endocrine disrupting effects were identified. The committee further concluded that *"expert judgement is required to assess on a case-by-case basis*

⁵ Directive 2000/60/EC

⁶ Regulation (EU) 1907/2006

⁷ P7_TA(2013)0091

⁸ WHO/UNEP, 2013 <http://www.who.int/ceh/publications/endocrine/en/index.html>

⁹ EFSA Scientific Committee; 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.

the (eco)toxicological relevance of changes at the molecular to individual and/or (sub)population level following exposure to an endocrine active substance."

- (12) The report State of the Art Assessment of Endocrine Disruptors¹⁰ commissioned by the Commission in 2009 provides a basis for the development of scientific criteria for the identification of endocrine disruptors.
- (13) The Commission set up in 2010 an Ad-hoc Group on the EU Community Strategy on Endocrine Disruptors comprised of representatives nominated from all relevant stakeholders, in particular from Member State regulatory authorities, European Union Agencies, industry associations and Non-Governmental Organisations to advise the Commission on regulatory matters concerning endocrine disruptors. The Endocrine Disruptors Expert Advisory Group was created in November 2011 as a sub-group of the Ad-hoc group to provide technical advice on the development of criteria for identification of endocrine disruptors.
- (14) The Endocrine Disruptors Expert Advisory Group undertook a 2 and a half year inclusive and comprehensive consultation process on endocrine disruptors, which is summarised in the Commission's Report¹¹ of 2013. As reflected in this report, the Endocrine Disruptors Expert Advisory Group agreed the identification of an endocrine disruptor relies on the *"demonstration of an adverse effect for which there is convincing evidence of a biologically plausible causal link to an endocrine disrupting mode of action and for which disruption of the endocrine system is not a secondary consequence of other non endocrine-mediated systemic toxicity. Relevance of the data to humans should be assumed in the absence of appropriate data demonstrating non-relevance. In relation to wildlife populations, data on all species are generally considered relevant. Relevance is instead applied in the context of identified adverse effects being relevant at population rather than individual level."*
- (15) The definition of endocrine disruptors in this Recommendation is the definition developed by the WHO/IPCS¹², necessitating the demonstration of an adverse effect caused through the endocrine disrupting mode of action.
- (16) Given the diversity of legislative acts addressing the hazards and risks of chemicals and in order to ensure a consistent, predictable and efficient identification of endocrine disruptors, it is necessary to take a horizontal approach by establishing horizontal criteria, encompassing overarching definitions and additional provisions as to how the criteria may be met, as was recognised in the Council conclusions of March 2000¹³.
- (17) The approach taken in this Recommendation limits the identification of endocrine disruptors to those endocrine active substances for which there is evidence of an adverse effect, *i.e.* endocrine activity on its own does not trigger identification and categorisation unless an adverse effect is observed.

¹⁰ Project Contract Number 070307/2009/550687/SER/D3 of Kortenkamp, 2012

¹¹ http://ihcp.jrc.ec.europa.eu/our_activities/food-cons-prod/endocrine_disruptors/LBNA25919ENN.pdf/view

¹² WHO/IPCS 2002, WHO/PCS/EDC/02.2

¹³ http://www.consilium.europa.eu/uedocs/cms_data/docs/pressdata/en/envir/07352.en0.html

- (18) The definition of the term "endocrine disruptor" and the criteria set for identifying them should be based on available scientific knowledge, be broadly applicable and not reflect specificities of sectorial policies or risk management practices.
- (19) The categorisation of endocrine disruptors in this Recommendation should be used as a reference for determining whether a substance should be considered as an "endocrine disruptor" or as a "suspected endocrine disruptor" for legislative and policy purposes in the Union.
- (20) The categorisation of endocrine disruptors in this Recommendation is based upon a weight of evidence approach, which takes its origin from the Commission report on key scientific issues relevant to the identification and characterisation of endocrine disrupting substances, the EFSA opinion on the hazard assessment of endocrine disruptors and the views of the European Parliament expressed in their own initiative report.
- (21) The UN Globally Harmonised System on Classification and Labelling (GHS), transposed into EU legislation by Regulation 1272/2008 of the European Parliament and of the Council¹⁴, is an overarching horizontal system of criteria and additional provisions as to how the criteria may be met for categories of adverse effects, some of which could be caused by the disruption of the endocrine system. Therefore, the criteria and the conditions under which the criteria may be met as set out in this recommendation uses the approaches and experiences from this system, benefiting from its experience, while it ensures legal certainty and consistency with the GHS and between the various regulatory frameworks that would implement the criteria.
- (22) The categorisation includes the application of expert judgement mirroring the GHS that also includes expert judgement to provide protection to the human health and the environment.
- (23) Cross-cutting and horizontally applicable guidance and testing methods as well as knowledge about developmental stages in- and ex-utero sensitive to exposure to endocrine disruptors should be developed by the Commission where feasible to facilitate the application of the definition, the criteria and additional provisions as to how the criteria are met in the various specific legislative frameworks.
- (24) Technological development and scientific progress continue. The definition should therefore be subject to a review by December 2019 to ensure that it corresponds to the needs. In particular, the review should assess whether lessons learned in the application of the criteria necessitate amending them, with the view of clarifying or codifying common practices.
- (25) The definition, the criteria and additional provisions as to how the criteria are met set out in this Recommendation should not prejudge nor reflect the scope of application of any piece of Union legislation or of any provisions potentially establishing additional requirements for those substances, including those relating to risk management.

¹⁴ OJ L 353, 31.12.2008, p. 1.

HAS ADOPTED THIS RECOMMENDATION

1. This Recommendation concerns the definition of the term 'endocrine disruptor' and the categorisation of the substances falling under such definition as used in Union policies applied within the Community and the European Economic Area.
2. Member States, the Union agencies and economic operators are invited to comply with the following definition of the term 'endocrine disruptor' as well as the categories for endocrine disruptors in the adoption and implementation of legislation, policy and research programmes concerning chemicals.
3. 'Endocrine disruptor' means an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations.
4. For the purpose of categorisation for endocrine disruption, substances which comply with the definition of endocrine disruptor are allocated to one of two categories based on strength of evidence and additional considerations in a weight of evidence approach. Categories for endocrine disruptors are:
 - Category 1: Endocrine disruptors
 - Category 2: Suspected endocrine disruptors
5. Criteria for Category 1 – Endocrine disruptors

Substances are placed in category 1 when they are known or presumed to have caused endocrine-mediated adverse effects in humans or population-relevant endocrine-mediated adverse effects in animal species living in the environment or when there is evidence from experimental studies (*in vivo*), possibly supported with other information (e.g.(Q)SAR, analogue and category approaches), to provide a strong presumption that the substance has the capacity to cause endocrine-mediated adverse effects in humans or population-relevant endocrine-mediated adverse effects on animal species living in the environment.

Basis of Category 1

The experimental studies shall provide clear evidence of endocrine-mediated adverse effects in the absence of other toxic effects, or if occurring together with other toxic effects, the endocrine-mediated adverse effects should not be a secondary non-specific consequence of other toxic effects.

Where there is (e.g. mechanistic) information demonstrating that the effects are clearly not relevant for humans and not relevant at population level to animal species living in the environment, then the substance should not be considered an endocrine disruptor.

Substances can be allocated to the category 1 based on:

- Convincing evidence from humans or from animal species living in the environment where it is plausible that the observed adverse effects are endocrine-mediated, or

- Experimental studies where it is plausible that the observed adverse effects are endocrine-mediated, or
- Experimental studies showing endocrine activity *in vivo* predicted to have (e.g. through (Q)SAR, analogue and category approaches) adverse effects *in vivo*

6. Criteria for Category 2 – Suspected endocrine disruptors

Substances are placed in category 2 when there is some evidence for endocrine-mediated adverse effects from humans, animal species living in the environment or from experimental studies, and where the evidence is not sufficiently strong to place the substance in category 1. If, for example, limitations in the study (or studies) make the quality of evidence less convincing, category 2 could be more appropriate.

Basis of Category 2

Endocrine disrupting effects should be observed in the absence of other toxic effects, or if occurring together with other toxic effects, the endocrine disrupting effects should not be a secondary non-specific consequence of other toxic effects.

Substances can be allocated to this category based on:

- Evidence from humans or from animal species living in the environment where it is suspected that the observed adverse effect is endocrine-mediated, or
- Experimental studies where it is suspected that the observed adverse effects are endocrine-mediated but where, for example, specific weaknesses in study design or execution weaken this conclusion, or
- Experimental studies *in vivo* where it is suspected that the observed adverse effects are endocrine-mediated.
- Experimental studies showing endocrine activity *in vivo* which is suspected to be linked to adverse effects *in vivo* (e.g. through (Q)SAR, analogue or category approaches), or
- Experimental studies *in vivo* showing endocrine activity but for which the link to an adverse effect is uncertain, or
- Experimental studies *in vitro* showing endocrine activity, combined with toxicokinetic *in vivo* data, linked to adverse effects *in vivo* (e.g. through Q(SAR), analogue and category approaches but for which the link is suspected.

7. General considerations by categorisation

Categorisation of a substance for endocrine disruption is made on the basis of evidence from reliable and relevant studies. The evaluations shall be based on all existing data, including peer-reviewed published studies and additional acceptable data.

The allocation to categories follows from a step by step procedure:

- Gather all available data
 - Consider adversity and mode of action together
 - Assess the data quality, reliability, reproducibility and consistency
 - Evaluate whether endocrine disruption is due to a specific endocrine-mediated mode of action and not non-specific secondary consequences of other toxic effects
 - Evaluate human and wildlife relevance
 - Final (eco)toxicological evaluation and categorisation
8. This Recommendation is addressed to the Member States, Union agencies and economic operators.

Done at Brussels, [...]

For the Commission

[...]

Member of the Commission