The Director General

Maisons-Alfort, 1st of December 2016

SCIENTIFIC AND TECHNICAL SUPPORT NOTE of the French Agency for Food, Environmental and Occupational Health & Safety

concerning the request for an opinion on the new draft proposed by the Commission on ED criteria "2016-SA-0243"

On 15 November 2016, Anses received a formal request from the Directorate General for Risk Prevention (DGPR) to provide scientific and technical support for the following: Request for an opinion on the new draft proposed by the Commission on ED criteria (2016-SA-0243).

1. BACKGROUND AND PURPOSE OF THE REQUEST

On 15 June 2016, the European Commission (EC) published a proposal defining criteria for identifying endocrine disruptors (EDs), accompanied by a draft document proposing an amendment to the regulation in force concerning biocidal products (N° 528/2012) and a document proposing a draft amendment to the regulation concerning plant protection products N° 1107/2009). ANSES issued an opinion on 19 July 2016 to propose criteria for defining endocrine disruptors (EDs), as well as on these two documents, in response to a request from the Minister of the Environment, Energy and the Marine Affairs, responsible for International Climate Relations, in order to help clarify the French contribution to European Union discussions on this issue.

On 8 November 2016, the EC published new proposals for criteria for identifying EDs, contained in the following two documents, on which ANSES has been asked to provide scientific and technical support:

- The revised version of the draft delegated act[1] and its Article 5 defining the criteria for identifying endocrine disruptors under the Biocides Regulation (EU) No 528/2012.
- The revised version of the draft delegated act[2] and its Annex II defining the criteria for identifying endocrine disruptors under the Plant Protection Products Regulation (EU) No 1107/2009.

[1] *Revised Draft Commission Delegated Regulation (EU) No 528/2012. C(2016)3752 project & Annex 1*

[2] *Revised Draft Commission Regulation (EU) No 1107/2009. C(2016)3751 project & Annex 1*

2. ORGANISATION OF THE WORK

The expert appraisal was carried out in accordance with the French Standard NF X 50-110 “Quality in Expert Appraisals – General Requirements of Competence for Expert Appraisals (May 2003)”.

The response to this request was coordinated by the Risk Assessment Department with the contribution of the Regulated Products Assessment Department. The Agency also received support for its work from several experts.

3. ANALYSIS AND CONCLUSIONS

The ANSES comments presented below on the EC proposals of 8 November 2016 contained in the two documents are based on the above-mentioned ANSES Opinion of 19 July 2016.

The Agency notes a lack of convergence between the changes introduced by the Commission in these two texts, compared to the versions published on 15 June 2016 and the recommendations made by the Agency in its Opinion of 19 July 2016 concerning the criteria for identifying EDs.

ANSES hopes that, in the interest of transparency, the Commission will make public the process and choices that led to the drafting of the new proposals. The EC should therefore reveal their detailed analysis of the comments made by the various stakeholders; in particular those made by ANSES on the EC proposal defining criteria for endocrine disruptors published last June. To date, ANSES has received no explicit information enabling it to understand the justification which has brought the EC to change the proposed criteria.

After having analysed the Commission’s revised proposals concerning the criteria for identifying endocrine disruptors, ANSES considers that:

Concerning section A, point (1) (a) of the Biocides Regulation and 3.6.5.2.2 (1) of the Plant Protection Products Regulation, the terminology *"it shows an adverse effect"* to replace the term *"it is known to cause an adverse effect"* is not precise enough and introduces considerable uncertainty as to the level of evidence required to demonstrate that a substance is an ED. This formulation is contrary to the principle of ED categorisation recommended by the Agency in its Opinion of 19 July 2016, which recommends to apply the WHO/IPCS definition and breaks the EDs into three categories: "known", "presumed" or "suspected".

This approach therefore only stresses the continued lack of coherence and harmonisation with the regulation in force for classifying CMR substances (Regulation (EC) No 1272/2008 known as “CLP”).

In addition, point (1) expresses a strong conditional link (an adverse effect AND a mode of action AND an adverse effect secondary to the mode of action) requiring a level of evidence that seems unrealistic in the light of current scientific knowledge.

Concerning section A, point (1) (b) of the Biocides Regulation and 3.6.5.2.2 (2) of the Plant Protection Products Regulation, the terminology *"it has an endocrine mode of action, i.e. it alters the function(s) of the endocrine system",* reinforces the initial version of the Commission proposal of 15 June 2016. Indeed, for the substance to be recognised as an ED, this formulation means that evidence must be provided that the adverse effect *in vivo* is associated with the impairment of the endocrine function. Thus, the plausibility of a link between the occurrence of an adverse effect *in vivo* and exposure to a substance with an endocrine mode of action is not sufficient. ANSES considers that given the current state of knowledge and the available guidelines, it will be difficult to provide the level of evidence required for recognising that an ED’s mode of action is the cause of an observed adverse effect.

Concerning section A, point (2) (a) (i) of the Biocides Regulation and 3.6.5.2.3 (1) (a) of the Plant Protection Products Regulation, deletion of the expression *"and mechanistic studies"* reinforces the

already high level of evidence required to identify a substance as an ED by excluding certain scientific data such as the *in silico* studies and the QSAR.

Concerning the Commission's proposal on the weight of evidence: this terminology appears to apply to the adverse effect and to the mode of action. ANSES considers that the weight of evidence approach will be more difficult to apply to the mode of action than to the adverse effect, even though this is theoretically possible. For example, it is extremely rare to have studies demonstrating the reversibility of the effect with a specific inhibitor or specific antagonist, or a comparable response with a positive control. Most mechanistic studies describe a very limited part of certain modes of action.

Concerning point 3.8.2.2.3, (3) (a) of the Plant Protection Products Regulation, ANSES wishes to add the term "amphibian" to the list of taxonomic groups mentioned.

Concerning the endocrine system, ANSES wishes to reiterate that this system is not only found in vertebrates and that, although less evolved, the endocrine system also exists in invertebrates. ANSES considers this clarification important, in order to avoid restricting the scope of the endocrine system only to vertebrate organisms in the environment, and to include all non-target organisms.

In conclusion, ANSES reiterates and insists on the recommendations contained in its Opinion of 19 July 2016 aimed at identifying EDs according to three distinct categories: "known", "presumed" and "suspected" EDs as stated in the French National Endocrine Disruptor Strategy (SNPE). This option draws on the WHO/IPCS definition of an ED and reflects the level of uncertainty, outside any specific regulatory context. The Agency also recommends the application of categories in the criteria integrating the weight of evidence.

This categorisation should be applied horizontally independently of any regulatory context and independently of any risk management measures applicable within the context of each of the regulations, in order to provide a single classification which takes into account both humans and the environment. This identification process should be conducted by a single European-level authority.

Alongside the ED criteria definition and adoption process, ANSES also insists on the need to establish a methodological and technical guidance document that can be updated according to scientific progress rather than more binding texts such as regulations.

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KEYWORDS

Endocrine disruptors, biocides and phytopharmaceuticals substances, definition, criteria, classification, European Commission, humans, environment.

REFERENCES

ANSES, 2016. Opinion of 19 July 2016 on "the definition of scientific criteria for defining endocrine disruptors" (Request 2016-SA-0133), 11 p.

https://www.anses.fr/en/system/files/SUBCHIM2016SA0133EN.pdf