ED assessment for active substances where the CAR was submitted before entry into force of the BPR: literature review

Date: 26 February 2019

Agreed at BPC-29

1. Introduction

The criteria[1] for the identification of ED properties stipulates in the Annex section A, point 2 (and similarly in Annex section B, point 2), that the assessment will take into account, among others, 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 particular those referred to in Annexes II and III of Regulation (EU) No 528/2012;*

   ii. *other scientific data selected applying a systematic review methodology*

On the other hand, the COM note[2] indicates that, for active substances for which the assessment report is submitted before 1 September 2013, the assessment will be done "*on the basis of information already submitted in the current dossier and/or provided by the applicant*". The affected active substances are indicated in the Annex below. With this respect, it is noted that:

1) The COM note should not be read as limiting the information to be taken into account in the assessment, but it informs of the rights and obligations of the applicant, including the opportunity to provide further information.
2) The eCA should inform the applicant that a literature review is required in order to conclude on the ED properties. The applicant does not have the obligation to perform and submit this information but can choose to provide it if they wish ("*the applicant will be informed about the data that is lacking in order to conclude on ED properties of the active substance and must be given the opportunity to submit additional information*").
3) It should be noted that, as for any hazard property, the evaluating CA would be expected to take into account all information readily available, including by means of a literature review[3].
4) Endocrine disruption was not specifically mentioned in the data requirements under the Biocidal Products Directive (BPD) although the consideration of endocrine effects was referred to in Annex VI of the BPD. For CARs submitted before entry into force of the BPR on 1 September 2013, the dossiers are expected to be unlikely to contain sufficient information to enable concluding on the ED properties.

[1] COMMISSION DELEGATED REGULATION (EU) 2017/2100.
[2] CA-March18.Doc.7.3.a- Final – Implementation of scientific criteria to determine the endocrine-disrupting properties of active substances currently under assessment.
[3] See Article 14(1) of Regulation EC 1451/2007: "*Without prejudice to Article 12 of Directive 98/8/EC, the Rapporteur Member State may take into account other relevant technical or scientific information regarding the properties of the active substance, metabolites or residues.*"

According to the COM note, in case the information is not sufficient for the BPC to reach a conclusion, the BPC opinion will inform "*that the necessary data was not submitted and that no conclusion could be drawn on the ED properties*".

2. Proposal

The following approach is proposed for substances where the CAR was submitted before entry into force of the BPR:

1. As indicated in the COM note[2], "*the applicant will be informed about the data that is lacking in order to conclude on ED properties of the active substance and must be given the opportunity to submit additional information*". Accordingly, the eCA will inform the applicant that a systematic literature review is needed in order to conclude on the ED properties.
2. The applicant may provide a systematic literature review but is not obliged to do so. The applicant shall inform the eCA of its decision as soon as possible. The COM note clarifies that the eCA can proceed without having received information of the applicant.
3. If the applicant does not perform a systematic literature review, the eCA would have to perform an initial literature review that could be less extensive than a systematic literature review in accordance with the ED criteria[1] and guidance[4].
    a. No further elaboration of this initial literature review is necessary if the outcome of the eCA's assessment is that there are no indications of ED properties and/or it is not possible to conclude. The BPC opinion should indicate that 1) the necessary data was not submitted and no conclusion could be drawn on the ED properties based on the information available, and 2) a systematic literature review would be required at the renewal stage.
    b. The eCA should perform a systematic literature review in accordance with the ED criteria[1] and guidance[4] if the likely outcome of the eCA's assessment is that the substance should be considered to have ED properties.

oOo

[4] Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009; https://efsa.onlinelibrary.wiley.com/doi/10.2903/j.efsa.2018.5311

3. Annex: the dossiers affected

The Table below presents a list of backlog dossiers for which the CAR was submitted before 1 September 2013. The information was extracted from CA-Nov18-Doc.5.1.

	eCA	Substance	PTs
1.	DE	Carbendazim	7, 9, 10
2.		Cyanamide	3, 18
3.		Formaldehyde	2, 3
4.	DK	Icaridin	19
5.	EL	Polymeric Betaine	8
6.		Prallethrin	18
7.		Ethanol	1, 2, 4
8.	ES	Chrysanthemum cinerariaefolium extract from open and mature flowers of Tanacetum cinerariifolium obtained with supercritical carbon dioxide	18, 19
9.		Chrysanthemum cinerariaefolium extract from open and mature flowers of Tanacetum cinerariifolium obtained with hydrocarbon solvent	18, 19
10.		1,2-benzisothiazolin-3H-one (BIT)	6, 13
11.		AEM 5772	2, 7, 9
12.	FR	MBT	12
13.	IT	BARDAP	2, 4
14.		DDAC	1, 2, 3, 4
15.		BKC	1, 2, 3, 4
16.	MT	ADBAS	2, 4
17.	NL	Sodium bromide - Hypobromous acid generated from sodium bromide	2
18.		Bromochlorodimethylhydantoin	2
19.		Hypobromous acid generated from sodium bromide	11, 12
20.		DCDMH	11
21.		DCEMH	11
22.	PL	DMDM Hydantoin	6, 13
23.		Magnesium-monoperoxyphthalate-Hexahydrate	2
24.	PT	N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine	8
25.	SE	Bromide activated chloramines, BAC, generation in situ with ammonium bromide	12
26.		Silver zinc zeolite	2, 4, 7, 9
27.	SK	Active chlorine generated from sodium chloride by electrolysis	1, 2, 3, 4, 5
28.		Active chlorine released from hypochlorous acid	1, 2, 3, 4, 5