EUROPEAN
COMMISSION

Brussels, 15.6.2016
SWD(2016) 211 final

PART 2/16

COMMISSION STAFF WORKING DOCUMENT

IMPACT ASSESSMENT

Defining criteria for identifying endocrine disruptors in the context of the implementation of the plant protection products regulation and biocidal products regulation

Annex 1 out of 16

Accompanying the document

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on endocrine disruptors and the draft Commission acts setting out scientific criteria for their determination in the context of the EU legislation on plant protection products and biocidal products

{COM(2016) 350 final}
{SWD(2016) 212 final}

ANNEX 1: PROCEDURAL INFORMATION

Contents

1. ORGANISATION AND TIMING

The European Commission decided in 2013 to perform an impact assessment with DG ENV and DG SANCO (now DG SANTE, Health and Food Safety) co-responsible for it. The corresponding Roadmap was published in June 2014.

Since November 2014, DG SANTE is the lead DG in the preparation of this initiative as an immediate consequence of the internal re-organisation of the European Commission and as the responsibility for the BP Regulation was transferred from DG ENV to DG SANTE.

Other DGs contributed to the preparation of this impact assessment via an IA Steering Group set up in 2013. The IA Steering Group (IASG) comprised members of DGs AGRI, CLIMA, COMP, CNECT, ENV, EMPL, GROW, JRC, LS, MARE, RTD, TRADE, SANTE and SG. The IASG discussed all aspects related to the preparation of the impact assessment. A total of 11 IASG meetings took place on the following dates:

IASG MEETINGS	**ISSUES DISCUSSED**
20 January 2014	▪ Scope of the roadmap ▪ Scope and details on the IA
22 February 2014	▪ Roadmap
23 July 2014	▪ Public consultation draft questionnaire
12 September 2014	▪ Public consultation draft questionnaire
10 December 2014	▪ Transfer of biocides file to DG SANTE ▪ Update on court case T- 521/14 ▪ Update on planned IA studies
19 March 2015	▪ Update on on-going and planned IA studies ▪ Presentation of the draft JRC methodology (1st study) ▪ Communication events foreseen (round-tables, conference)
21 May 2015	▪ Update on communication events ▪ Update on the progress of the public consultation report ▪ Update on the on-going and planned IA studies
17 July 2015	▪ Endorsement of the public consultation report ▪ Update on the on-going and planned IA studies
19 January 2016	▪ Update on the screening of substances (1st study) ▪ 2nd phase of the IA (presentation of the MCA-methodology) ▪ Timeline and general planning ▪ Follow up to the ruling of the General Court
1 February 2016	▪ Update on the general planning ▪ Discussion on the MCA-criteria
4 April 2016	▪ IA report

The initiatives under the PPP and BP Regulations are included in Agenda Planning under the references 2015/SANTE/001 (Implementing Regulation on Plant Protection Products to specify criteria to identify endocrine disruptors) and 2016/SANTE/045 (Delegated act biocides endocrine-disruptors), respectively. Moreover, in the European Commission Work

Programme for 2016, the European Commission has committed to "*conclude the complex preparatory work already under way to protect Europeans from the dangers of endocrine disruptors and follow up on it*."[1]

In July 2014 Sweden sued the Commission for failure to act (case T-521/14) regarding setting new scientific criteria for defining EDs in the Biocidal Products Regulation (EU) No 528/2012 by end of 2013. The European Parliament, the Council and individual Member States such as France, the Netherlands, Finland and Denmark intervened in favour of Sweden during the case. In its judgement of 16 December 2015, the EU General Court ruled that the European Commission breached EU law by failing to set criteria to identify EDs. The Court stated that according to the Biocides Regulation, the Commission had a clear, precise and unconditional obligation to adopt delegated acts as regards the criteria by December 2013.

2. EXTERNAL EXPERTISE AND SUPPORTIVE EVIDENCE

This impact assessment builds on preparatory work – listed below - which focused on EDs and which was carried out over the last few years by the European Commission or mandated by the European Commission to EU agencies or external contractors via public procurement rules.

Additional sector-specific data sources were used for the assessment of the impacts in some sectors, and are detailed in the corresponding Annexes.

2.1. Scientific Committees and Expert Groups chaired by the European Commission

In 2010, two expert groups were established with the aim of exchanging information on various scientific and policy aspects related to EDs. Both groups included representatives of industry associations, non-governmental organisations, European Commission Services, European Agencies and Member States.

The "***EDs Expert Advisory Group*", chaired by the JRC**, was set up to provide advice on scientific criteria for the identification of endocrine disrupting substances. The outcome is summarised in the two reports summarised below.

- **JRC Expert Advisory Group Report "Key scientific issues relevant to the identification and characterisation of endocrine disrupting substances" (2013)** [2]**.** The aim of the report is to capture the expert opinions expressed in the Expert Group. It acknowledges that consensus was not required and different views were presented. For instance, the report summarises that agreement was not reached on whether elements of hazard characterisation (potency, severity, lead toxicity, irreversibility) should be considered or not when identifying EDs of real concern. Those who

[1] Annex II: REFIT Initiatives. Annex to Commission Work Programme 2016; No time for business as usual. Retrieved from: http://ec.europa.eu/atwork/pdf/cwp_2016_annex_ii_en.pdf

[2] JRC Scientific and policy reports. Key scientific issues relevant to the identification and characterisation of endocrine disrupting substances. Report of the Endocrine Disrupters Expert Advisory Group. Retrieved from: http://www.fhi.no/dokumenter/623e53f70d.pdf

disagreed with such consideration were of the opinion that these elements can only be considered in the context of risk assessment. Others believed that, when decision making is based on hazard assessment, these elements should be considered altogether at the step of hazard identification/assessment to prioritise substances of higher concern. As regards availability of test methods, the Working Group agreed that existing standardised assays are mainly available only for the four modalities: estrogenic, androgenic, thyroid and steroidogenic (EATS). The Working Group also agreed that overall tests were lacking for birds and invertebrates.

- **JRC Expert Advisory Group Report "Thresholds for EDs and Related Uncertainties" (2013)** [3]**.** The Expert Group was asked to gather views on the likelihood of existence of thresholds for a biological adverse response of an organism to an ED. The question was posed in relation to a review of the REACH Regulation concerning the treatment of EDs under authorisation, but it was also considered of general relevance to the evaluation of an ED. Consensus was welcome but not necessary. The experts could not reach a consensus on whether a threshold or non-threshold approach was to follow in the evaluation of EDs. There were both points of agreement and disagreements.

  Experts agreed that lack of consensus exists regarding the evidence for low-dose effects and on occurrence and relevance of non-monotonic dose-response curves. Most experts agreed that thresholds of adversity are likely to exist for EDs but may be very low for certain EDs and during foetal development. Several experts also agreed that, although thresholds may exist, they might be difficult to measure with the current available test methods. Some experts considered that, even during foetal development, a threshold for adversity must exist and can be estimated with appropriate testing. Other experts considered that uncertainties in estimating thresholds would be higher for EDs than for other non-genotoxic toxicants.

  Some experts supported a "non-threshold approach" because: 1) endocrine related endpoints are missing in current test guidelines; 2) using additional dose groups in animal testing may help but it is hindered by animal welfare considerations; 3) potential additional effects of mixtures will increase uncertainty in estimating thresholds.

  Other experts considered a "threshold approach" appropriate and justified because: 1) test guidelines can be updated with relative sensitive endocrine-related endpoints; 2) appropriate dose spacing in animal testing can increase confidence in threshold estimates; 3) case-by-case assessment is the most appropriate approach, as thresholds can be estimated when adverse effects and mode of action are identified.

The "***Ad hoc working group of Commission Services, EU Agencies and Member States", chaired by DG ENV***, focussed on policy issues. In February 2013, a first draft for criteria was proposed by DG ENV to the Ad-Hoc Working Group. This draft working document did

[3] JRC Scientific and policy reports. Thresholds for Endocrine Disrupters and related uncertainties. Report of the Endocrine Disrupters Expert Advisory Group. Retrieved from: http://publications.jrc.ec.europa.eu/repository/bitstream/JRC83204/lb-na-26-068-en-n.pdf

not reach consensus among Commission Services, Member States and stakeholders and a formal Inter Service Consultation was not started.

Further, the **Scientific Committee on Consumer Safety (SCCS) issued a "Memorandum on EDs"** in 2014 [4]. The Memorandum supports the EFSA Opinion on use of risk assessment to assess EDs for decision making. The SCCS adds that "*due to the ban on animal testing for cosmetic ingredients effective since 2013, it will be extremely difficult in the future to differentiate between a potential ED and an ED, if the substance is registered solely for use in cosmetics products. The replacement of animal test methods by alternative methods in relation to complex toxicological endpoints (such as endocrine disruption) remains scientifically difficult, despite the additional efforts launched at various levels. With regard to substances with endocrine activity (potential EDs), the assessment of their impact to human health without the possibility to use animal data remains a challenge*."

2.2. European Commission mandates to agencies

In August 2012, the European Commission mandated the European Food Safety Authority (EFSA) to issue a **"*Scientific Opinion on the Hazard Assessment of EDs*"**, which was published on March 2013[5].

The EFSA opinion supports the WHO/IPCS definition for EDs and a case-by-case risk assessment approach to assess EDs for decision making. EFSA states that "*to inform on risk and level of concern for the purpose of risk management decisions risk assessment (taking into account hazard and exposure data/predictions) makes best use of available information. EDs can therefore be treated like most other substances of concern for human health and the environment, i.e. be subject to risk assessment and not only to hazard assessment*".

Further, EFSA clarified that for mixtures, critical windows of susceptibility and non-monotonic dose-response curves were general issues applicable to all chemicals (and not specific to EDs). The EFSA Opinion also concluded that "*a reasonably complete suite of standardised assays for testing the effects of EDs is (or will soon be) available for the estrogenic, androgenic, thyroid and steroidogenic (EATS) modalities in mammals and fish, with fewer tests for birds and amphibians".* There are no standardised mechanistic assays for any modalities in invertebrates. Although some apical tests[6] are available for invertebrates, none of these apical tests is able to provide a firm diagnosis of a specific endocrine activity linked to a given adverse effect.

In 2016 the European Commission requested the European Centre for Disease Prevention and Control (ECDC) to **provide information of certain diseases** for public health and the

[4] 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

[5] 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. [84 pp.] doi: 10.2903/j.efsa.2013.3132.

[6] Apical test: A test or assay aimed at detecting/measuring apical endpoints: generally in vivo testing describing a response by the organism as a whole (e.g. generally death, reproductive failure, or developmental dysfunction). For apical endpoints see the glossary.

importance of biocidal products to prevent them. The request focused on 1) infectious diseases in healthcare facilities (in particular hospitals), 2) infectious diseases (e.g. respiratory tract viruses and norovirus outbreaks) in community settings (e.g. schools, day care centers and childcare facilities), and 3) mosquito-borne diseases (West Nile Fever, Dengue, Chikungunya and Malaria). The request concerns only the situation of health in the Union. The provided information served as basis for Annex 10 (human health, transmissible diseases and food safety.

2.3. European Commission public procurement projects

The "State of the Art Assessment of EDs" Report (Kortenkamp, 2011)[7]

In 2009, the project "State of the Art Assessment of EDs" was commissioned through public procurement by the European Commission.

The report summarises advances in the state of the science from 2002 to 2011 and maps ways of addressing EDs in important pieces of EU chemicals legislation (e.g. PPP Regulation, BP Regulation, REACH). It warned that the data required in EU chemicals legislation did not capture the range of endocrine disrupting effects that can be measured with internationally agreed and validated test methods. However, the PPP data requirements have been updated since the publication of the report, including updated test guidelines which also consider EDs (Regulations 283/2013 and 284/2013 on data requirements for PPP active substances and PPP formulations and the respective Communications 2013/C 95/01 and 2013/C 95/02 listing relevant test methods and guidance documents)[8].

Overall the report considers critical windows of susceptibility a key issue for EDs, which would *justify consideration of EDs as substances of concern equivalent to carcinogens, mutagens, reproductive toxicants and PBT* (persistent, bioaccumulative and toxic) *chemicals*. However, as mentioned above the EFSA Opinion[5] clarified that mixtures, critical windows of susceptibility and non-monotonic dose-response curves are general issues applicable to all chemicals and not specific to EDs.

The report considers that EDs should be identified according to the 2002 WHO-IPCS definition[9] and using a weight of evidence approach which considers all the elements of hazard characterisation together, i.e. potency together with other factors such as severity, lead toxicity, specificity of effect and irreversibility. Rigid potency-based cut-off values as decisive decision criteria are not recommended.

[7] Kortenkamp, Martin, Faust, Evans, McKinlay, Orton, Rosivatz. 2011. State of the art assessment of endocrine disrupters. Final Report, Project Contract Number 070307/2009/550687/SER/D3. Retrieved from: http://ec.europa.eu/environment/chemicals/endocrine/pdf/sota_edc_final_report.pdf

[8] European Commission. Legislation on Plant Protection Products (PPP). Retrieved from: http://ec.europa.eu/food/plant/pesticides/legislation/index_en.htm

[9] WHO/IPCS. 2002. Definition of an Endocrine Disruptor: *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.*

Screening of chemicals to evaluate if they would be identified as EDs under each of the proposed options (on-going, results for PPP and BP available, see Annexes 3 to 5)

In order to provide robust evidence on the potential impacts, approximately 600 chemicals are being screened by an external independent contractor in order to evaluate if they would be identified as ED under each of the options identified in the Roadmap. The screening covers chemicals falling under the PPP, BP, REACH, Cosmetics or WFD in this sequential order. The rationale for selection of the chemicals has been published and it is available in Annex 4. The study is still on-going, but all the evidence for PPP and BP is already available and has been used in this impact assessment.

The screening is based on available evidence (desk work) and is being carried out by a contractor selected following public procurement rules using the Framework Contract (FWC) SANCO/2012/02/011. The work started in May 2015 and presented final results for PPP active substances in January 2016 and for BP active substances in February 2016. Remaining results are expected by the end of April 2016 for a subsample of chemicals falling under the legislation for REACH, cosmetics and the WFD.

As a basis for this exercise, the Joint Research Centre of the European Commission (JRC) developed a screening methodology, which is summarised in Annex 3. The JRC also monitored the progress of the screening in cooperation with DG SANTE. The European Chemicals Agency (ECHA) and the EFSA were consulted in the elaboration of the methodology.

The final report of the study is planned to be published together with this impact assessment report. The results cannot however be used for regulatory purposes as for this a more in depth assessment would be required following the respective EU legislations.

3. CONSULTATION OF THE REGULATORY SCRUTINY BOARD

A draft impact assessment report was submitted to the Regulatory Scrutiny Board (RSB) on 13 April 2016. The meeting with the RSB took place on 12 May 2016. A negative opinion was issued by the RSB on the ground that there were several shortcomings in the report, which would limit its contribution to an informed decision making.

Based on the revised report submitted the 3 June 2016 the RSB issued a positive option with recommendations to be integrated in the report. These recommendations and how they have been addressed in the report are summarised below.

The RSB asked to further clarify in the report that (i) the criteria for the identification of EDs should be specified only on the basis of the relevant scientific evidence and irrespective of the economic and social impacts and that (ii) the proposed analysis of impacts is provided only with a view to informing about the implications of the different options for the specification of EDs in a given regulatory context and not to influencing the selection of the preferred option for the criteria to identify EDs. As a response to this recommendation, clarifications have been added to the impact assessment report on sections 1.1, 4, 6 and 6.3, as well as to the Annexes 6 to 15 to clarify that the impact assessment is not concluding on any preferred

option for setting scientific criteria to identify endocrine disruptors, but aims at providing additional information to decision makers.

The RSB recommends discarding Option 4 from the impact assessment in view of the emerging scientific consensus according to which potency is not relevant for the identification of a substance as endocrine disruptor. The emerging scientific consensus refers to the consensus paper signed by scientists as a consequence of the meeting carried out the 11 and 12 of April 2016. This consensus paper has been referenced throughout the report, including a citation of its most relevant parts and a particular consideration on the final discussion of the options to set scientific criteria to identify EDs. However, it has to be considered that the impact assessment report was submitted on 13 April 2016 and that the consensus paper was made available via the BfR website on the 4 May 2016 but has not yet been published in a scientific peer reviewed journal. Discarding retroactively an option of the impact assessment, which is the preferred option for some stakeholders including some Member States, on the basis of a scientific publication which has not yet been published, does not seem appropriate at this stage. However, in particular in Sections 1.2.1, 4.1.2, 4.1.4, and 6.3, clear reference to the emerging scientific consensus has been introduced and strengthened.

The RSB recommends clarifying the potential regulatory changes in the derogations under the PPP Regulation foreseen under Option B. In response to this, Figure 2 has been added to Section 4.2.2, as well as cross references to Section 1.5 (main report) and Annex 8, where the derogations under the PPP and BP Regulations are explained in detail. These amendments quote the corresponding parts of the regulations and explain in particular the different derogation approach between the BP Regulation (substances shall not be approved unless the risk from exposure is negligible) and the PPP Regulation (substances shall not be approved unless the exposure is negligible).

The RSB recommends clarifying further the methodology used for comparing the options, in particular Options A and B. Additional clarifications were added to Sections 5.1.2, 5.1.4, 5.4. The two-step procedure for assessing the impacts (screening study + Multi Criteria Analysis (MCA)) was better explained, as well as why the MCA methodology mentioned in the Better Regulation Guidelines Toolbox was chosen to evaluate the impacts. It was also further clarified in Section 5.1.3 how the MCA-criteria were developed: considering Tools #8 and #16 of the Better Regulation Toolbox, the availability of evidence, responses received via the public consultation (see Annex 2), and discussions between the General Directorates involved in the Impact Assessment Steering Group. An overview table with the evidence available for each MCA-criterion – in addition to the screening study results which played an important role in the assessment - was added (Table 2 in Section 5.1.4). It was also emphasised that the MCA was carried out sequentially in 2 steps: one MCA focusing on the impacts expected when implementing the criteria to identify EDs (Options 1 to 4) under the current regulatory framework (Option A), and a 2nd MCA where it was assessed whether these expected impacts would remain the same or not under consideration of different regulatory implementations (Options A to C; Option C was discarded but kept for methodological reasons). For this 2nd MCA, assumptions played a more prominent role due to the fact that the evaluation could only be done qualitatively in the context of the impact assessment. In addition, Section 6, including its subsections 6.1, 6.2 and 6.3, was adapted and details of the MCA only

mentioned in the corresponding Annexes (Annexes 6 and 7). Finally, a clarification was added to each of the Annexes 6 to 15, giving an overview of the application of the MCA methodology and, where applicable, its link with the assessment of the impacts (i.e. "performance" of the options).

A clarification regarding the selection of supporting evidence mentioned in Section 1.2.1. was added, as recommended by the RSB. The relevant WHO reports, including the WHO 2012 report, were/are mentioned at the very beginning of the impact assessment report (2nd paragraph of section 1). An additional section listing the cited literature has been added to the main report, and a summary of the literature cited in the main report and the Annexes has been added to Annex 16.

Editorial comments were fully taken over.