Endocrine Disruptor: theory and practice of the evaluation

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Disclaimer: Any views expressed cannot be regarded as stating an official position of SANTE or the European Commission.

Overview

PPP and BPR

- The implementation of the ED criteria
- The EFSA/ECHA guidance document
- Review of tests methods for data requirements
- Procedures foreseen for on-going evaluations
- First experiences for confirmatory informations

CPR

- Assessment of substances with ED properties under the Cosmetics Regulation

CLP

- Inclusion of ED in CLP/UN-GHS

REACH

- Update of REACH Information Requirements
- Update on Safety Data Sheets

Towards a comprehensive EU framework on endocrine disruptors

The Commission fulfilled its legal obligations in the PPP & BP Regulations

Adoption of criteria for the identification of substances with endocrine disrupting properties in:

- **Biocides**: *Commission Delegated Regulation (EU) 2017/2100 of 4 September 2017*
- **Plant Protection Products**: *Commission Regulation (EU) 2018/605 of 19 April 2018*

- The criteria are **harmonised** for biocidal products (BP) and plant protection products (PPP)

New scientific criteria for EDs

- **Biocides**:

  applicable from **7 of June 2018** to new and on-going applications

- **Plant protection products:**

  applicable from **10 November 2018** to new and on-going applications

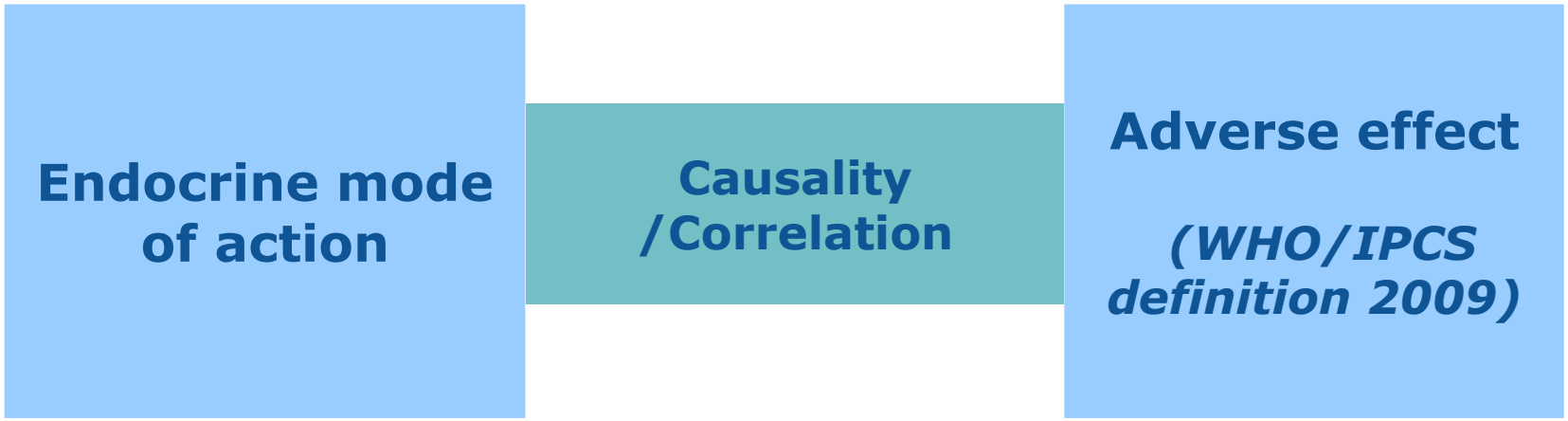
The criteria in the context of the mandates

- *The criteria are limited to **hazard identification***

  - They do NOT include hazard characterisation (*no potency*)
  - They do NOT define how to regulate EDs – this is already set out in the two Regulations
  - *No categories* – mandates in both Regulation are only to distinguish whether a substance is *ED/not ED* in the PPP/BP regulatory contexts

The criteria do protect human health & the environment

→ *Contain the **3 elements** of the 2002 WHO/IPCS definition of an endocrine disruptor:*



The criteria do protect human health & the environment

Principles:

- ***all*** *available scientific information: in-vivo, in-vitro, in-silico (read-across)*
  - standard studies (data requirements) & other scientific data (no hierarchy)
- *animal evidence considered relevant for humans (unless otherwise proven)*
- *weight of evidence*

Implementation of the ED-criteria

Further to the decision making on ED-criteria:

A. *A **joint EFSA/ECHA GD** to implement the criteria was published in June 2018*

B. *Review of test methods for **data requirements** for PPP and BP to align them with the new GD*

C. *Amendment of Regulations and Procedural Guidance for PPP and BP to specifically foresee implementation of the criteria for **on-going evaluations** of applications*

A. EFSA/ECHA ED GD

- Joint EFSA/ECHA GD with involvement of JRC
- Difficult task: EU is pioneering on ED identification for regulatory purposes
- Several consultations:
  - ✓ MS & stakeholders (April-May 2017; July-August 2017)
  - ✓ Public consultation (Dec 2017 – Jan 2018)
  - ✓ Workshop with MS & stakeholders on GD applicability (case-studies, Feb 2018)
  - ✓ Risk assessors PPP & BP sectors (Apr 2018)
  - ✓ Risk managers of PPP & BP sectors (May 2018)
  - ✓ Workshops with Risk assessors (2018-2019, Nov 27-28)
  - ✓ 1st Forum ED-8 Nov 2019;2nd forum 17.18 Dec 2020

A. EFSA/ECHA ED GD: applicability

- ScoPAFF PPP on 19-20 July 2018 notified that from 10 November 2018 the ED GD is to be used to apply ED criteria under PPP Regulation

  https://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1537782016257&uri=CELEX:52018XC0924(02)

- Competent Authorities for BP were informed at the 79th C.A. meeting on 5-6 July 2018 that the ED GD was published and available to apply ED criteria under BP Regulation

B. Review of test methods for data requirements for PPP and biocides

- The Communications listing the test methods for data requirements for PPP evaluations under Reg. (EC) No 1107/2009 is being reviewed in light of the ED EFSA/ECHA Guidance

- Similarly, the Annexes to Reg. (EU) No 528/2012 containing the data requirements for biocides are being updated & aligned to the ED EFSA/ECHA Guidance

B. BPR :Update of Data Requirements under the Biocidal Product Regulation

- Of biocidal active substances (BPR Annex II)
- Of biocidal products (BPR Annex III)

- Commission Delegated Regulation amending the BPR was adopted by the Commission last 19 October
- Currently under scrutiny of Parliament and Council (2 months)
- https://webgate.ec.europa.eu/regdel/#/delegatedActs/790
- https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=PI_COM%3AC%282020%296771

C. Assessment of ongoing evaluations

- As ED criteria applicable to ongoing evaluations: "stop the clock" at EFSA or COM level foreseen to obtain & assess additional data to conclude on ED criteria

- To this aim:
  - ✓ Procedural guidance for on-going procedures for the approval of biocidal active substances and the authorisation of **BP** was adopted in March 2018
  - ✓ Amendment Reg. 844/2012 setting procedures for **PPP** active substances renewals adopted on 24 October 2018

BP/PPP
Early review for approved BP & PPP active substances ?

- Screening study performed for ED Impact Assessment in 2016 identified BP and PPP active substances that may have ED properties under option 2

- COM analysed whether there can be any benefit in terms of timing to trigger an early review for those substances: only for 3 BP active substances, an early review would be needed

BPR : experience so far (updated 2019)

- 8 biocide active substances have been discussed for ED evaluation at BPC WGs

- 2 substances meet the ED criteria

- 4 substances required more data, 1 backlog, 1 waived potentially

- 14 active substances discussed by EDWG in ECHA (out of 78)

- 12 ED, 5 non-ED, many information required and assessment refinement ongoing

BPR: discussion ongoing on ED (1)

Non-active substances contained in biocidal products having indications for ED properties: bridging biocides with REACH

Non-active substances contained in biocidal products having indications for ED properties: whether including the name in BPC opinion, PAR and authorisations

Progression of evaluation of applications for approval as regards to the determination of ED properties

(discussion ongoing also at the next CA meeting on 8.9 December 2020)

BPR: discussion ongoing on ED (2)

Status of an active substance containing an impurity identified as an endocrine disruptor

Status of an active substance generating disinfection by products identified as an endocrine disruptor

(discussion ongoing also at the next CA meeting on 8.9 December 2020)

PPP

Implementing ED criteria for pending applications: amend Reg. 844/2012 setting procedures for PPP renewals

Objective:

- Obtain & assess additional data for pending applications to decide if new ED criteria are satisfied

- Amend Regulation 844/2012 to provide a "stop the clock" at the level of EFSA or Commission

PPP
Implementing ED criteria for pending applications

What are pending applications?

Applications for the renewal of an active substance

- submitted **before** 10 November 2018

- AND where the relevant Committee has not voted on a draft Regulation concerning the renewal or non-renewal

PPP : I. Application pending at the level of the rapporteur Member State (RMS)

Additional Article 11a

- Where the RMS considers that some information is missing in order to assess whether the ED criteria (points 3.6.5 and/or 3.8.2 of Annex II) are satisfied

- RMS shall propose in the draft renewal assessment report which additional information is necessary in order to reach these conclusions (including the "type" of the additional information to be submitted)

- If agreed during the peer review, the stop of the clock will be at EFSA level

PPP : II. Application pending at EFSA level

Additional Article 13(3)a

- *EFSA decides, also taking into account the draft assessment report, that some information is missing in order to assess whether the ED criteria (points 3.6.5 and/or 3.8.2 of Annex II) are satisfied*
- *EFSA consults RMS & decides which information should be submitted*
- *EFSA sets a period for the submission of this information after consulting RMS and the applicant*
  - *The period must not exceed 30 months + be justified in relation with the type of information needed*
  - *RMS evaluates the new information within 60 days*
  - *Deadline for submission of EFSA conclusions is extended*

PPP : III. Application pending at COM level

Additional Article 14(1)a

- *COM decides that some information is missing to assess whether the ED criteria (points 3.6.5 and/or 3.8.2 of Annex II) are satisfied*
- *EFSA consults RMS & decides which information should be submitted*
- *EFSA sets a period for the submission of this information after consulting RMS and the applicant*
  - *The period must not exceed 30 months + be justified in relation with the type of information needed*
  - *RMS evaluates the new information within 60 days*
  - *EFSA sends its conclusions within 90 days*

PPP : Other provisions

When the stop the clock takes place *the applicant can also within the same period of time:*

- submit information to address the conditions of approval in point 3.6.5 and point 3.8.2 of Annex II to Reg. 1107/2009 (negligible exposure)

and/or

- apply for a derogation under Article 4(7) of Reg. 1107/2009

PPP : Confirmatory information about ED

- 24 Active substances requested to submit ED confirmatory information 2 year after the application of the requirements (deadline : 10 November 2020)

- 4 not supported for renewal

- 6 renewal ongoing

- 7 with renewal expiration in late 2020 or 2021

- 7 out 20 submission received within /around the deadline

PPP: Experience so far

- all decisions taken @ PAFF since 10 Nov 2018 under consideration of the new ED criteria; in some cases mandates to EFSA, in some cases decision taken (no ED)

- EFSA considering ED criteria; several dossiers are currently under "stop the clock"

- RMS are applying new ED criteria

- 2 BTSF trainings for PPP and BP risk assessors of MS (Feb 2019, November 2019)

PPP: Experience so far active substances and ED evaluation (updated 2019)

- From late 2018, 43 active substances have been evaluated for HH and 41 for non-target organisms (NTO)

- For HH: 17 additional data required, 11 non-ED, 7 ED waived, 7 ED, 1 still pending

- For NTO: 33 additional data required, 4 non-ED, 1 ED waived, 3 ED,2 still pending

- For 8 substances, same conclusions have been reached for both HH and NTO

PPP : Some active substances not renewed, due to their ED properties or not finalized for ED properties

Among others:

- *Mancozeb*
- *Thiophanate-methyl*
- *Benalaxyl*
- *Propineb*
- *Desmedipham*

PPP : Review Clause

- The Regulations setting the criteria foresee that an evaluation of the experience with their application will be provided at the latest in 7 years (Art. 3 of the criteria)

- The guidance and/or test methods can be complemented or revised even beforehand in the light of scientific progress

CPR : Assessment of EDs under the Cosmetics Products Regulation

- On 7 November 2018, the Commission adopted the review on EDs under CPR
- Commitment of Commission to establish a priority list of potential EDs in cosmetics for further assessment by Scientific Committee on Consumer Safety(SCCS)
- A list of 14 + 14 substances was established (Group A high priority, Group B lower priority)
- SCCS was mandated in beginning of 2020 to provide opinion on first five Group A substances

CPR : Assessment of EDs under the Cosmetics Products Regulation

- Benzophenone-3
- Kojic acid
- 4-methylbenzylidene camphor
- Propylparaben
- Triclosan
- Resorcinol
- Octocrylene
- Triclocarban
- Butylated hydroxy-toluene (BHT)
- Benzophenone
- Homosalate
- Benzyl salicylate
- Genistein
- Daidzein

In red: substances for which opinion was requested

CPR: Assessment of EDs under the Cosmetics Products Regulation

- Draft opinions published by SCCS and open for commenting until:
  - Homosalate → 4 January 2021
  - Propylparaben → 4 January 2021
  - Resorcinol → 22 December 2022
  - Benzophenone-3 → opinion under development
  - Octocrylene → opinion under development

- https://ec.europa.eu/health/scientific_committees/consumer_safety/opinions_en#fragment0

CPR : Assessment of EDs under the Cosmetics Products Regulation

→ Calls for data and other substances to be subsequently assessed

- Further information/websites

https://ec.europa.eu/growth/sectors/cosmetics/products/endocrine_en

https://ec.europa.eu/growth/content/call-data-ingredients-potential-endocrine-disrupting-properties-used-cosmetic-products_en

https://ec.europa.eu/health/scientific_committees/consumer_safety/opinions_en#fragment0

Assessment of BPA in clothing articles

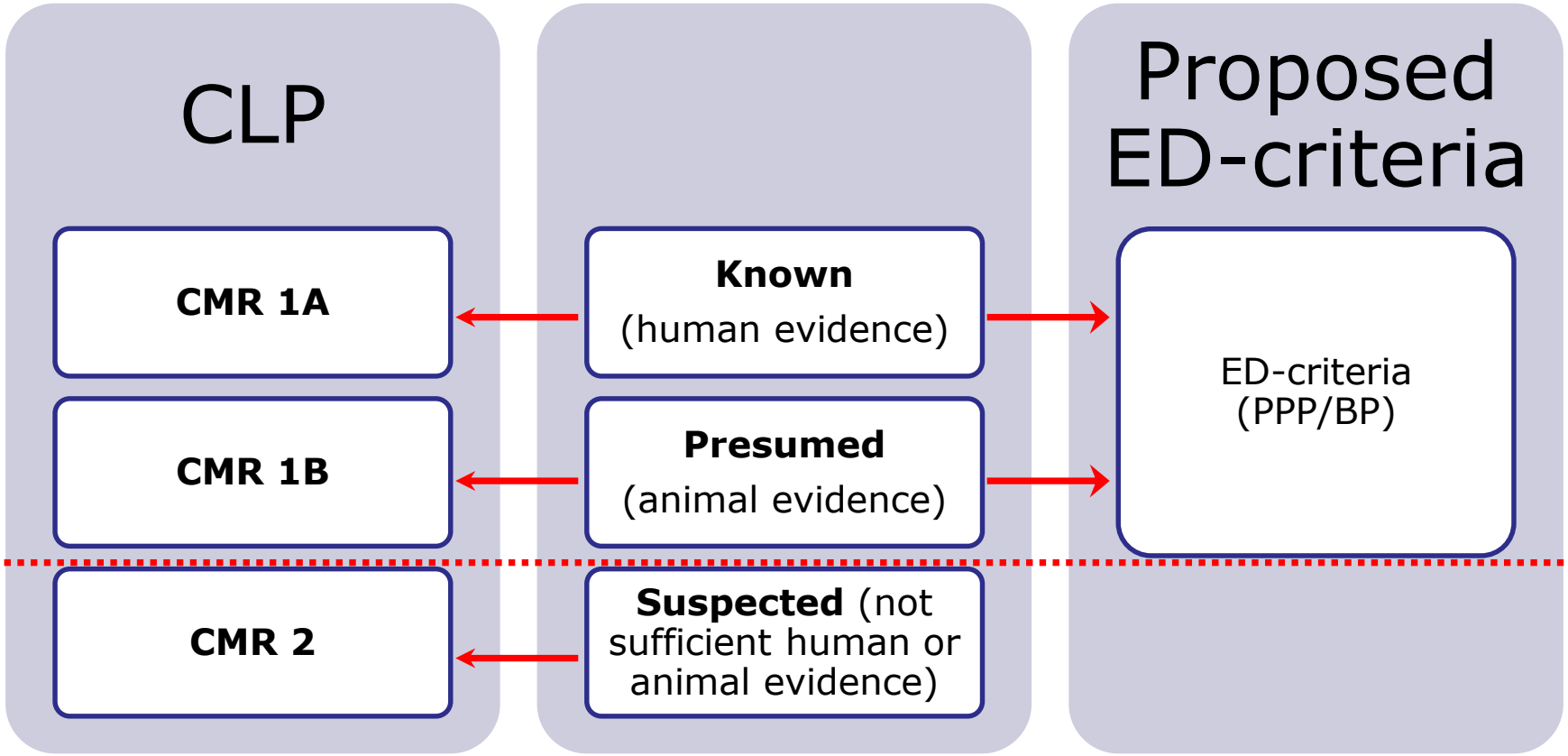
→ Other draft opinions of the Scientific Committee on Consumer Safety (SCCS)

- The safety of presence of BPA in clothing articles

- Further information/websites

https://ec.europa.eu/health/scientific_committees/consumer_safety/opinions_en#fragment0

The current criteria to identify known & presumed EDs



CLP : CARACAL Subgroup on Endocrine Disruptors (CASG ED)

Mandate follows up on Commission Communication (2018)734 :

- Update of REACH annexes to include data requirements on endocrine disruption
- Explore possibilities to include endocrine disruption in the existing international system for classification (UNGHS) and in CLP
- 3 meetings of the CASG ED this year

CLP : Inclusion of in CLP/UNGHS

- Discussion document presented as CASG ED on 2 July with three options:

  I. Introducing (a) new ED hazard class(es)
  II. new supplemental hazard statement(s) (EUH),
  III. new or modified hazard statement code(s) to existing hazard classes.

- Conclusion of discussion document:
  - Option (I) is preferential option
  - Inclusion of two hazard classes, one for human health and one for the environment
  - Inclusion should be followed up by proposal at the UN-GHS

CLP : Inclusion of in CLP/UNGHS

- Further discussions needed on
  - Concrete proposal for hazard classes
  - Categories

- Timeline:
  - Proposal to amend CLP in 2021 (see Chemicals Strategy for Sustainability, COM(2020)667)
  - Proposal at the GHS level in 2022-2024

CLP : Update of the REACH Information Requirements

- Two options discussed on CASG ED on 19 October → thought-starter document
- Waiting for feedback from participants → revise options/come up with new options

- Timeline:
  - Finalise options in early 2021
  - Impact Assessment in course of 2021
  - Adoption in 2022

REACH : Implementation of actions of the Communication on endocrine disruptors (COM(2018)734)

- Update of Safety Data Sheets (REACH Annex II)

→ Published as Commission Regulation 2020/878 on 18 June 2020 in the Official Journal of the EU

→ Applicable as of 1 January 2021 on

→ Already available Safety Data Sheets can be provided until 31 December 2022

https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.L_.2020.203.01.0028.01.ENG&toc=OJ:L:2020:203:TOC

Towards a comprehensive EU framework on endocrine disruptors

most up-to-date science; commitment to invest in research:

- Fill knowledge gaps for ED
- Several relevant research strands under Horizon Europe

Inclusive

- Annual Forum on ED with all interested stakeholders (8th November 2019, 17.18 December 2020)
- Commitment to step up international work (OECD, international system for classification of chemicals)
- Launch of a web portal on ED
- Encourage MS to develop specific information and educational campaigns

Towards a comprehensive EU framework on endocrine disruptors

***Taking forward the EU's policy on EDs**; significant progress achieved in the past 20 years but more is needed*

***Comprehensive**; Fitness Check on ED*

First time for cross-cutting look at the legislation on endocrine disruptors

- Building on scientific evidence and data collected through finalised/on-ongoing evaluations (e.g. food contact materials, chemicals, etc.)

Towards a comprehensive EU framework on endocrine disruptors

- *Commission Communication - **Towards a comprehensive EU framework on endocrine disruptors** (COM 2018 734, 7 Nov 2018).*
- *Commission Staff Working Document Executive **Summary Of The Fitness Check On Endocrine Disruptors** of the Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions.*

  Chemicals strategy for sustainability towards a toxic-free environment

(https://ec.europa.eu/environment/pdf/chemicals/2020/10/Executive_summary_FC_EDC.pdf)

- *Horizon 2020 topic '**New testing and screening methods to identify endocrine disrupting chemicals**'*

Thank you for your attention!

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More information available at:

https://ec.europa.eu/health/endocrine_disruptors/overview_en