federal public service
HEALTH, FOOD CHAIN SAFETY AND ENVIRONMENT

Endocrine Disruptors

Implementation of the new legislation

Biocide Forum

Brussels – 24 October 2019

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EU REGULATION – What is an ED

Regulation (EU) 2017/2100 setting out scientific criteria for determination of endocrine-disrupting properties under Regulation (EU) N°528/2012

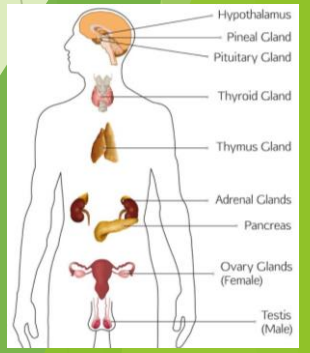
- A substance is considered as having ED properties if it meets the following criteria:

  a) Shows an adverse effect in an intact organism or its progeny, which is a change in morphology, physiology, growth, development, reproduction or life span of an organism, system or (sub)population resulting in an impairment of functional capacity or of the capacity to compensate for additional stress or an increase in susceptibility to other influences

  b) Has an endocrine mode of action, i.e. it alters the function(s) of endocrine system

  c) The adverse effect is a consequence of the endocrine mode of action

- These criteria apply **since <u>7 June 2018</u>**



EU REGULATION – How does ED criteria apply

- The assessment of potential ED properties is mandatory since 7 June 2018 for active substances & biocidal products
- A conclusion must be reached for both HUMANS & NON-TARGET ORGANISMS

- If the substance meets ED criteria, considered as a Substance of Concern
- Other legal consequences outlined in BPR apply

- **How to practically apply the ED criteria:**

  - **CA-September18.Doc.7.5.a-final** : Implementation of scientific criteria to determine the endocrine-disrupting properties of already approved active substances

  - **CA-March18.Doc.7.3.a- Final** : Implementation of scientific criteria to determine the endocrine-disrupting properties of active substances currently under assessment

  - **CA-March18-Doc.7.3.b-final** : The implementation of scientific criteria for the determinatio endocrine-disrupting properties in the context of biocidal product authorisation

ACTIVE SUBSTANCES

CA-September18.Doc.7.5.a-final : Already approved active substances

- EU Commission may review the approval of an active substance at any time
  - Where significant indications that conditions laid down in Article 4(1) are no longer met
  - At the request of a Member State, if indications that the use of the a.s. in biocidal products or treated articles raises significant concerns about their safety

- Implementation of ED scientific criteria may in many cases lead to requests for additional data

- For renewal applications submitted after 6 June 2018, these data should be generated, if possible, before submission of the dossier

  (Certain studies may take more than 2 years, e.g. long-term studies)

ACTIVE SUBSTANCES

CA-September18-Doc.7.5.a-final: Active substances identified as possible ED in the screening study performed by the Commission and triggered for an early review

Active substance	Expiry Date of approval	Remarks
Cypermethrin	PT18 : 30/06/2026 PT08 : 31/05/2025	Decision on early review depends on outcome of ED assessment under PPP-legislation **PPP-approval expires 31/10/2018 - ED assessment on-going**
Pyriproxyfen	PT18 : 31/01/2025	Decision on an early review depends on outcome of ED assessment under PPP-legislation **PPP-approval expires 31/12/2018 - ED assessment on-going**
Tebuconazole	**PT08 : 31/03/2020** PT07 : 30/06/2025 PT10 : 30/06/2025	ED assessment at renewal of PT08 & PPPs **PPP approval expires 31/08/2019** Decision on early review for PT07 & 10 depends on outcome for PT08
Propiconazole	**PT08 : 31/03/2020** PT09 : 30/11/2025 PT07 : 30/11/2026	Decision on early review for PT07 & 09 depends on outcome for PT08
Iodine	PT01 -PT03 -PT04 & PT 22: 31/8/2025	**Triggering early review**
PVP iodine	PT01 -PT03 -PT04 & PT 22: 31/8/2025	**Triggering early review**
Zineb	PT21 : 01/10/2026	**Triggering early review**

ACTIVE SUBSTANCES

CA-March18.Doc.7.3.a- Final : Active substances currently under assessment

1. **Assessment Report submitted before 1 September 2013 but Standing Committee on Biocidal Products did not deliver an opinion**

- Substance must be evaluated in accordance with BPD provisions & principles (BPR, Article 90(2))
- No assessment of ED properties according to the NEW criteria

BUT assessment according to INTERIM criteria (classified as Carc. Cat. 2 and/or Repr. Cat. 2)

- If a.s. fulfill interim criteria, only a 5-year approval period is granted
- Products containing an a.s. fulfilling the interim criteria is only authorised if one of the conditions of Article 5(2) of the BPR are met

- Applicant is informed if data is lacking to conclude on ED properties
- Can submit additional data within the time limits set by eCA

ACTIVE SUBSTANCES

CA-March18.Doc.7.3.a- Final : Active substances currently under assessment

2. **Assessment Report is submitted after 1 September 2013 : new ED criteria apply**

- RMS must conclude whether the a.s. has ED properties or not (EAST-mediated effects)
- Assessment of ED properties according to the "*Guidance for the identification of endocrine disruptors in the context of Regulations (EU) N°528/2012 and (EC) N°1107/2009*" (06/2018)

ADVERSITY	HUMAN & MAMMALS	OTHER NON-TARGET ORGANISMS
E-mediated A-mediated S-mediated	• OECD 443 - with cohort 1a/1b including the mating of cohort 1b to produce F2 generation • OECD 416 according to latest version of 01-2001	• OECD 240 (MEOGRT) • OPPTS 850.1500 (FLCTT)
T-mediated	• OECD 407 • OECD 408 • OECD 409 &/or One-year dog study (if available) • OECD 416 • OECD 443, if available • OECD 451-3	• OECD 241 (LAGDA) • OECD 231 (AMA)

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ACTIVITY	HUMAN & MAMMALS	OTHER NON-TARGET ORGANISMS
E-mediated	• ToxCast ER Bioactivity Model • OECD 440	• OECD 229 (FSTRA) • OECD 230 • Parameters investigated in OECD 229 or OECD 234
A-mediated	• OECD 441	
S-mediated	• OECD 456 • OPPTS 890.1200	
T-mediated	• See adversity	• OECD 231 (AMA)

ACTIVE SUBSTANCES

CA-March18.Doc.7.3.a- Final : Active substances currently under assessment

2. **Assessment Report is submitted after 1 September 2013 : new ED criteria apply**

- RMS must conclude whether the a.s. has ED properties or not (EAST-mediated effects)

- RMS can require additional data to conclude, during both evaluation phase or during peer review process in the BPC

- If required information not submitted within required timeframe with valid justifications, BPC may propose a non-approval (Article 4(1) not met)

ACTIVE SUBSTANCES

CA-March18.Doc.7.3.a- Final : Active substances currently under assessment

- An a.s. showing ED properties with regard to humans fulfills Exclusion criteria
- Not be approved, unless fulfills conditions of Article 5(2) and
  - Comparative Assessment needs to be carried out
  - Products containing this a.s. cannot be authorised for use by General Public
  - Products containing this a.s. are not eligible for simplified procedure authorization
- An a.s. showing ED properties with regard to non-target organisms is considered as Candidate for Substitution and as a Substance of Concern
  - Comparative Assessment needs to be carried out
  - Products containing this a.s. are not eligible for simplified procedure authorization
  - Authorisation only granted for 7 years maximum

PRODUCTS – EU LEVEL

CA-March18-Doc.7.3.b-final : ED assessment of biocidal products

- For authorisation of a product, RMS must conclude whether a biocidal product has ED properties (BPR, Articles 19 & 25)

- ED properties of ACTIVE SUBSTANCES are assessed in the context of their approval or renewal, except for those identified as possible ED by the Commission

- Active substances are <u>not</u> evaluated in the context of product authorization

- Co-formulants are assessed in the context of product authorization

- Assessment must be performed according to **CG-34 (2019-02)** :

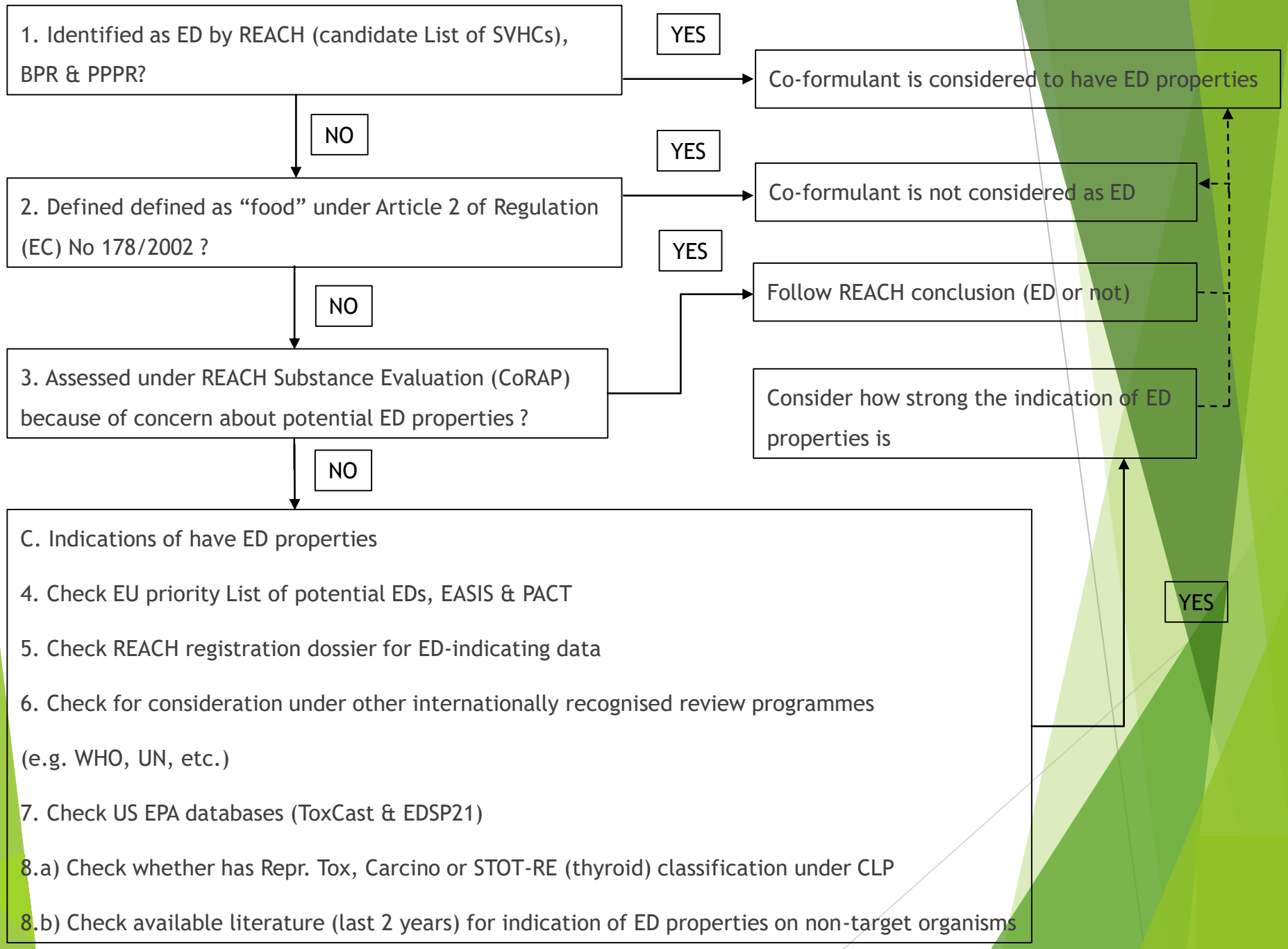
  "*Assessment of endocrine disruption (ED) properties of co-formulants in biocidal products – Instructions for applicants*"

PRODUCTS – EU LEVEL

Assessment of endocrine disruption (ED) properties of co-formulants (CG-34_2019-02)

- 3 main sources of information
  A. Checking EU Decisions on ED properties
  B. Excluding from further assessment co-formulants which are food or foodstuff materials
  C. Checking information on 'Indications' of ED properties

- Result of co-formulants assessment is presented in the Assessment Report:
  - Public PAR : Executive summary with the conclusion for both humans & non-target organisms
  - Confidential annex : Complete report with all data used to reach the conclusion


1. Identified as ED by REACH (candidate List of SVHCs), BPR & PPPR?
YES
Co-formulant is considered to have ED properties
NO
2. Defined defined as “food” under Article 2 of Regulation (EC) No 178/2002 ?
YES
Co-formulant is not considered as ED
NO
3. Assessed under REACH Substance Evaluation (CoRAP) because of concern about potential ED properties ?
YES
Follow REACH conclusion (ED or not)
Consider how strong the indication of ED properties is
NO
C. Indications of have ED properties
4. Check EU priority List of potential EDs, EASIS & PACT
5. Check REACH registration dossier for ED-indicating data
6. Check for consideration under other internationally recognised review programmes
(e.g. WHO, UN, etc.)
7. Check US EPA databases (ToxCast & EDSP21)
8.a) Check whether has Repr. Tox, Carcino or STOT-RE (thyroid) classification under CLP
8.b) Check available literature (last 2 years) for indication of ED properties on non-target organisms
YES

PRODUCTS – EU LEVEL

- If the co-formulant is subject to examination under another legal framework regarding its ED properties (REACH, step 5) AND not possible to conclude with the legal deadlines

- Post-authorisation condition to, if necessary, reconsider the autorisation once the conclusion of ED status is agreed

- Responsibility of the Applicant to inform the RMS about any new relevant information in relation to ED properties of the substance

(e.g. conclusion by REACH or PPPR, inclusion in WHO list, etc.)

PRODUCTS – EU LEVEL

- A co-formulant having ED properties is considered as a Substance of Concern
- Qualitative & quantitative composition of the SoC must be listed in the SPC
- Environment: a complete assessment is needed (mixture toxicity)

- Other legal consequences outlined in BPR & 'CA March 18-Doc.7.3.b_final' apply
  - A Comparative Assessment needs to be carried out
  - Not authorised for use by General Public
  - Product not eligible for simplified procedure authorization
  - RMM may be needed to protect humans & environment
  - May affect the composition of a family (all products with ED in the same meta-SPC)
  - Etc.

- Product with an a.s. 'Candidate for Substitution' is only authrorized for 5 years & renewed for a period not exceeding 5 years (BPR, Article 23)

PRODUCTS – NATIONAL LEVEL

- BE apply REGULATION (EU) 2017/2100 & REGULATION (EU) No 528/2012 for national authorisation
- Database gathering data from
  - EU legislation (REACH, BPR, PPP, etc.)
  - National screening programs on ED (EU MS, USA, Japan, etc.)
  - Internationally recognised non-EU organisations (WHO, UN, etc.)
  - Relevant database (SIN list, TEDX list, TOXCast, etc..)
- Cross the data to establish whether co-formulants has ED properties or not
- Legal consequences outlined in REGULATION (EU) No 528/2012 are applied
  - No use by General Public
  - RMM may be needed to protect humans (professional users) & environment
  - Closed circuit (specific to BE)

PRODUCTS – NATIONAL LEVEL

- A standard phrase is automatically added on the act:

- *In overeenstemming met artikel 24 van het KB van 4/04/2019, is de registratiehouder verplicht om de bevoegde dienst onmiddellijk in kennis te stellen indien het biocide stoffen bevat die officieel erkend worden als hormoonverstoorder door ECHA.*

- *Conformément à l'article 24 de l'AR du 4/04/2019, le détenteur d'enregistrement est dans l'obligation d'informer le service compétent immédiatement s'il s'avère que le produit biocide contient des substances qui sont officiellement reconnues comme perturbateurs endocriniens par l'ECHA.*

- Relevant for active substances AND co-formulants

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Thank you for your attention