Endocrine disruptors

Update on legislation

Biocides Forum

Brussels - 19 May 2022

EU REGULATION - Application of the criteria

- Mandatory assessment of ED properties since **7 June 2018** for active substances (AS) and biocidal products
- Conclusion must be reached for both humans AND non-target organisms

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

  - Active substances already approved
  - Active Substances currently under assessment
  - Renewal of AS already approved or new AS
  - Specific cases: impurities and disinfection by-products (DBP)
  - ED criteria at product level (national and EU)

Active substances already approved

CA-September18.Doc.7.5.a

- The European Commission may review the approval of an active substance at any time (*early review*)
  - Where significant indications that the conditions set out in Article 4(1) are no longer met
  - At the request of a Member State, if indications that the use of the AS in biocidal products or treated articles raises significant concerns about their safety

- In most cases, new data will need to be generated in order to make a decision

Active substances currently under assessment

CA-March18.Doc.7.3.a

1. **Assessment Report submitted prior to 1 September 2013 but for which the Standing Committee has not yet delivered an opinion**

- Substance assessed according to **BPD** criteria (Directive 98/8/EC)
- Conclusion based upon **interim criteria**:

Classification Carc. Cat. 2 and/or Repr. Cat. 2

- A substance classified as such is considered an ED
  - Approved for an initial period of 5 years
  - Products authorised ONLY IF one of the conditions set out in Article 5(2) is met

Active substances currently under assessment

CA-March18.Doc.7.3.a

2. **Assessment Report submitted after 1 September 2013**

- **New criteria apply** to determine whether the AS has ED properties

- Additional data needed to make a decision: can be requested during evaluation phase or peer review process in the BPC

- If the information is not submitted in time along with a valid justification, the BPC can suggest a non-approval (conditions set out in Article 4(1) are not met)

Renewal of approved AS or new AS

- Renewals submitted after 6 June 2018 and new AS
- **New criteria apply** to determine whether the AS has ED properties
- Mandatory data have to be generated **PRIOR** to submission

!!Some studies can take more than 2 years!!

- eCA can request additional data in order to make a decision (stop-clock)
- **NOT intended to complete the dossier if some mandatory data are missing !**
- If the information is not submitted in time along with a valid justification, the BPC can suggest a non-approval (conditions set out in Article 4(1) are not met)

Assessment of ED properties

- eCA must decide whether the AS meets the ED criteria for humans AND non-target organisms (NTOs)

- Assessment of ED properties according to following guidance:

  "*Guidance for the identification of endocrine disruptors in the context of Regulations (EU) N°528/2012 and (EC) N°1107/2009*" (06/2018)

- Two-step assessment:

  1. **Humans**

  - Tests on mammals + literature review in order to make a decision with regard to humans

  2. **Environment**

  - Can we use data on mammals to make a decision?
  - If not, test on NTOs + literature review in order to make a decision with regard to the environment

Assessment of ED properties

- *"Guidance for the identification of endocrine disruptors in the context of Regulations (EU) N°528/2012 and (EC) N°1107/2009"* (06/2018)

1. **Human health assessment**

	ADVERSITY (core data package)	ACTIVITY (investigate mode of action)
E-mediated	• OECD 414 • OECD 426 • OECD 443 Or OECD 416 according to the latest version of 2001	• ToxCast ER Bioactivity Model • OECD 440 • OECD 455
A-mediated		• OECD 441 • OECD 458
S-mediated		• OECD 456 • OPPTS 890.1200
T-mediated	• OECD 407 • OECD 408 • OECD 409 and/or One-year dog study • OECD 414 • OECD 416 and/or OECD 443 (if available) • OECD 451-3	• OPPTS 890.1500

Assessment of ED properties

- *"Guidance for the identification of endocrine disruptors in the context of Regulations (EU) N°528/2012 and (EC) N°1107/2009"* (06/2018)

2. **Environmental assessment**

	ACTIVITY (screening)	ADVERSITY (further investigation)
E-mediated	• OECD 229 (FSTRA) Or OECD 230 Or parameters investigated in OECD 234	• OECD 240 (MEOGRT) Or OPPTS 850.1500 (FLCTT)
A-mediated		
S-mediated		
T-mediated	• OECD 231 (AMA)	• OECD 241 (LAGDA) Or OECD 231 (AMA)

When the AS meets the ED criteria

- AS having ED properties for **humans**: meets the **exclusion criteria**
- Not approved, unless it meets at least one of the conditions set out in Article 5(2) AND
  - Products not authorised for use by the general public
  - Candidate for Substitution (Article 10)

- AS having ED properties for **non-target organisms**: **Candidate for Substitution** and **Substance of concern**

- When an AS is a **Candidate for Substitution**:
  - Approval for 7 years maximum
  - Mandatory *comparative assessment* for products
  - Products not eligible for the simplified authorisation procedure
  - Use of products authorised for 5 years, renewed for a period not exceeding 5 years (Article 23)
  - Risk mitigation measures (RMM) to ensure that exposure of humans and the environment is minimised

Impurities identified as ED

CA-March21-Doc.5.1 : AS containing impurities identified as ED

- Definition according to BPR & REACH: an **'active substance'** includes **its impurities**

- AS identified as ED if (one of) its impurities identified as ED (no threshold value like REACH)

  EXCEPT IF the AS, including its impurities (present during the (eco)toxicological tests), does not meet the ED criteria

- No need to determine whether each impurity has ED properties

DBP identified as ED

CA-March21-Doc.5.2: AS having a DBP identified as ED

- **Disinfection by-product (DBP)** considered as **residues** because
  - Not present in the product itself prior to use
  - Only generated during or after use of product

- BPR: NOT considered to be part of the active substance or the product
- Not assessed at active substance level BUT at product level

DBP identified as ED

CA-March21-Doc.5.2: AS leading to a DBP identified as ED

- **Article 19(1) of BPR**: The product must have **no unacceptable effects** itself, or as a result of **its residues**, on human health and on the environment

- DBP having ED properties: product **NOT authorised** for use by the **general public** EXCEPT IF
  - No human exposure OR
  - A threshold value can be proven AND no risk occurs

!!A product is **NOT** considered having ED properties if one of its DBPs has such properties!!

!!A DBP registered as a biocidal AS is assessed as an AS!!

Biocidal products - EU level

CA-March18-Doc.7.3.b : ED assessment of biocidal products (BP)

- Prior to BP authorisation, eCA must conclude whether it has ED properties
  - AS **NOT** assessed during product authorisation process: assessed during approval or renewed approval
  - **Only the co-formulants** are checked during assessment of biocidal products

Biocidal products - EU level

Assessment according to document **CG-50-2022-05 AP 16.6** (replaces document CG-34-2019-02 AP 16.5)

"*ED assessment of co-formulants by applicants*"

- 3 main sources of information

A. Check decisions at European level on ED properties of substances (BPR, PPPR & REACH)

B. Exclude co-formulants considered as food or foodstuff materials

C. Check whether substances have "indications" of ED properties

- REACH (registry of SVHC intentions, EDEG, PACT, CoRAP, REACH registration dossier)
- Classification, US database, literature review

All necessary links available in the document

Biocidal products - EU level

Literature review has to cover at least the last two years

- The report has to include:
  - **The date** on which the review was conducted
  - **The names of the databases** used to conduct the review (e.g. ScienceDirect, PubMed, etc.)
  - **Key words** used (see CG-34-2019-02 AP 16.5)
  - The criteria for assessing the **relevance** and **reliability** of the articles
  - **All articles found have to be assessed for relevance and reliability**
    1) Remove irrelevant articles (title and summary)
    2) Read and assess relevant articles to decide whether there are indications of ED effects

For more details, EFSA guidance: EFSA Journal 2011;9(2):2092

Biocidal products - EU level

- Indications of ED properties:

CA-March21-Doc.4.4:

- Significant indication if and only if there is an **registry intention to propose the substance as SVHC** due to its ED properties
  - The substance is reported in the public version of the PAR and in the confidential annex (and in the BPC's opinion with regard to UA)

- If there are other indications of a potential ED effect, **NOT** mentioned in the public version of the PAR, only in the confidential annex.

Biocidal products - EU level

- Co-formulant is under review by REACH and not possible to decide within the legal deadlines:

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

- **Responsability of the applicant** to inform the eCA of any **new relevant information** with regard to ED properties of co-formulants present in his product

Co-formulant meeting the ED criteria

- **CA March 18-Doc.7.3.b**: a co-formulant meeting the ED criteria is considered a **Substance of Concern (SoC)**

  - Product **NOT authorised** for use by the **general public**
  - Toxicology and Ecotoxicology: Complete assessment of the substance needed
  - Physical chemistry: May have an influence on the required analytical methods
  - SPC: must include the qualitative & quantitatve composition of the SoC
  - Can affect family composition (all products having ED properties need to be in a meta SPC reserved for professionals)
  - Mandatory comparative assessment
  - Products not eligible for the simplified authorisation procedure
  - Risk mitigation measures (RMM) to ensure that exposure of humans and the environment is minimised

Biocidal products - National level

- EU rules apply to national authorisations:
  - REGULATION (EU) 2017/2100 for already approved active substances
  - CG-50-2022-05 AP 16.6 for co-formulants
- Legal consequences outlined in REGULATION (EU) No 528/2012 apply:
  - Product **NOT authorised** for use by the **general public**
  - Risk mitigation measures (RMM) to ensure that exposure of humans and the environment is minimised
  - Closed circuit (specific to BE)

Biocidal products - National level

- Co-formulant currently being assessed at REACH and impossible to decide within the legal timeframe

- **Responsability of the applicant** to inform us of any **new relevant information** with regard to ED properties present in his product and of its consequences

- A standard phrase is automatically added to the authorisation Act:

- *Pursuant to Article 24 of the Royal Decree of 4 April 2019, the registration holder has to immediately inform the agency in charge if it turns out that the biocidal product contains substances that are officially recognised as endocrine disruptors by the ECHA.*

- Applies to active substances and co-formulants

Thank you for your attention