Applications for the approval of free radicals and other *in situ* generated substances: experiences and challenges

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Outline of presentation

- What are *in situ* generated substances
- *In situ* generated substances in Review Programme and Art. 93
- Challenges Art. 93 in situ generated substances
- Challenges & experiences free radicals
- Practical recommendations

What are *in situ* generated substances (1)

In situ **generated active substance (CA-May12-Doc.6.2a):**

- **active substance that is not directly supplied to the user**
- **generated intentionally via a chemical reaction, or other means such as electrolysis and electrical generation, as a result of direct manipulation on the site of use prior to or during its intended application, from one or several other substances, called precursor substances.**
- **In situ generation ≠ on site formulation**

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What are *in situ* generated substances (2)

Methods for the *in situ* generation of active substances:

- **Chemical reaction**

  monochloramine from ammonium sulphate and a chlorine source

- **Electrolysis and electrical generation**

  sodium chlorite generating chlorine dioxide via electrolysis

- **Formation of the *in situ* generated active substance during use**

  Single precursor under use conditions such as heating

  aluminium phosphide released from phosphine

- **Hydrolysis to form an acid-base pair**

  - addition or dilution of the precursor to water

  - precursor and a.s. are related as an acid-base pair.

  Substituted hydantoins hydrolysing to hypophalous species

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What are *in situ* generated substances (3)

Precursor 1

Precursor 2

Precursor 3, ...

In situ generated a.s. (pure a.s.)

Unreacted precursors 1,2,3,...

Reaction by-products

Other impurities

- Recommendation of the BPC Working Groups
  In situ generated active substances – Risk assessment and implications on data requirements for active substances generated *in situ* and their precursors

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Review Programme: re-definition (1)

- **Substances that were already included in the Review Programme have been re-defined (CA-March15-Doc.5.1-Final)**

precursor => a.s. generated from precursor

Bromine chloride => Active bromine generated from bromine chloride

precursor 1 => a.s. generated from precursor 1 and precursor 2/3

Sodium bromide: => Active bromine generated from sodium bromide and sodium hypochlorite/ calcium hypochlorite/chlorine/ by electrolysis.

a.s. => a.s. from precursor with acid

Chlorine dioxide => chlorine dioxide generated from sodium chlorate and hydrogen peroxide in the presence of a strong acid

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Review Programme: re-definition (2)

- New precursor/active substance combinations could be added to the existing ones
- New PT's could be added to the existing ones
- Notification deadline: 27 april 2016
- Dossier submission of dossier max. 2 yrs after acceptance
- Overview of notifications: https://echa.europa.eu/documents/10162/17287015/list_compliant_notifications_en.pdf/e39a07ea-52dd-4562-a8e5-eab6be898312

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BPR Article 93 (1)

- **Substances that did not fall within the scope of the BPD (9/8/EC), but do fall under the scope of the BPR**
- **“Art. 93 substances”:**

  - Free radicals (ambient air/water/coating) incl. singlet oxygen

  - Ozone from ambient air

  - Active chlorine from (sea)water

  - Monochloramine from ammonia/ ammonium salts + 2nd precursor

  - Reaction mass of TiO2 and silver chloride

  - Silver phosphate glass

‘Article 93 list’ published by ECHA
https://echa.europa.eu/documents/10162/17287015/Art93_2017-05-08_en.pdf/0bafa033-c600-aa87-9811-f383e20e26ac

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BPR Article 93 (2)

- A.s.-dossier submitted by 1 Sept 2016:
  - products remain under transitional law (deadlines Art. 89)
  - new products: LoA to a.s. dossier needed
  - LoA needed for BPR authorisation (after a.s. approval)

- No a.s. dossier submitted by 1 Sept 2016:
  - transitional law until 1 Sept. 2017

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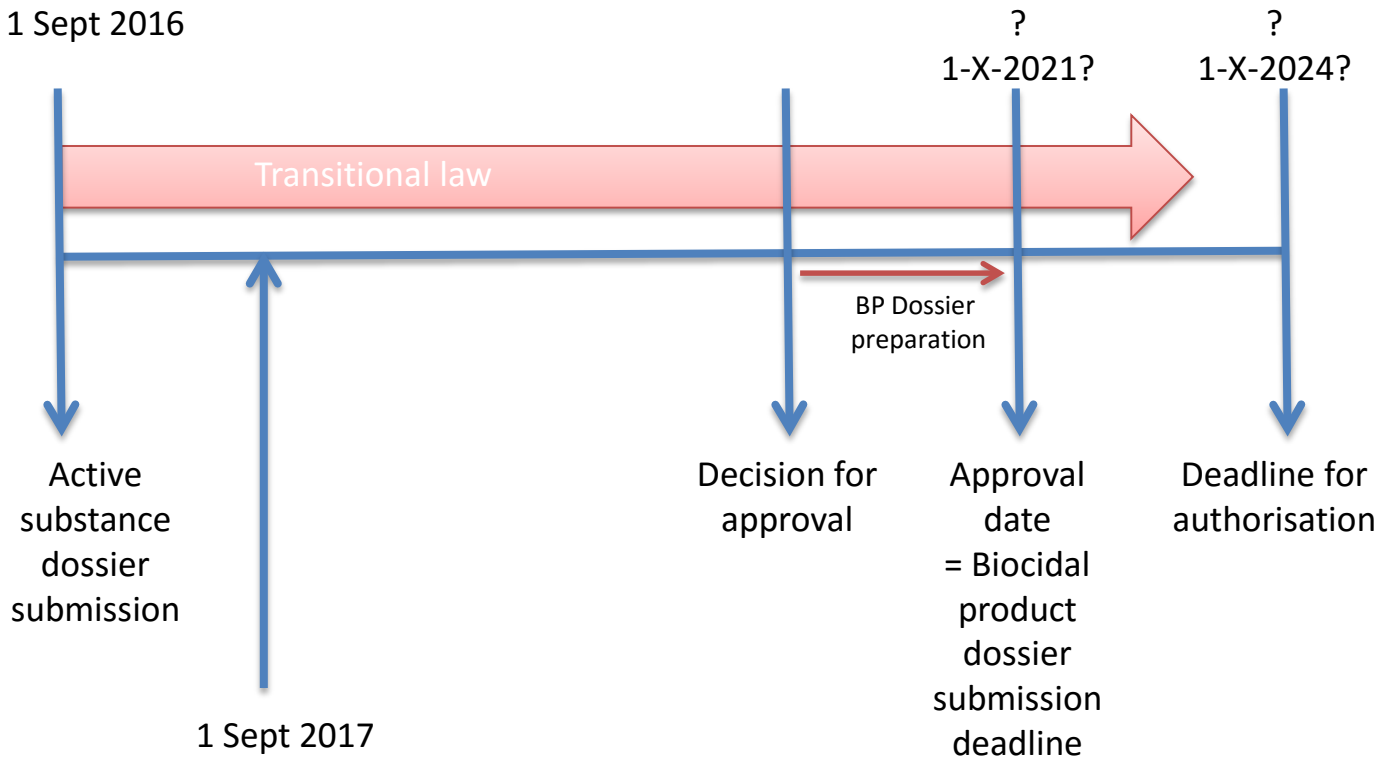
BPR Article 93 (3)

Timelines Art. 93 substances



No product dossier
=> grace period
max. 180 /365 d

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Art. 93 in situ generated substances: applications

Article 93 active substance applications	
# applications a.s./ PT / applicant	45 *free radicals: 23*
# Active substances	12
# PT/a.s. combinations	26 *free radicals: 9*
PT	2, 3, 4, 5, 6, 7, 9, 11, 12, 13, 21 *free radicals: 2, 3, 4, 5, 7, 9, 11, 12, 13, 21*
eCA (# appl.)	AT (6), DE (5), FR (1), NL (23), SE (5), UK (5) *free radicals: AT (4), NL (17), UK (2)*

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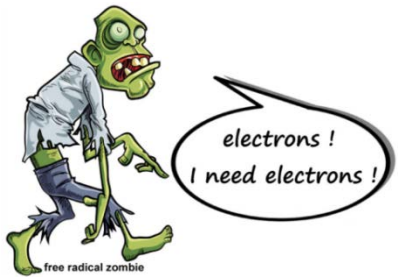
Free radicals: status in NL

- Pre-submission meetings with applicants
- Most validations finalised, evaluations started
- Active substance part
  mainly empty (data waivers)
- Evaluation and discussion
  needed to determine data gaps



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Art. 93 substances: Challenges (1)

- Several applicants for one substance in several countries
- Example: 'Free radicals generated in situ from ambient air or water'
  - 1 substance approval
  - 3 eCA's
  - 9 PT's
  - 10 applicants with very different systems

- Similar cases for ozone, active chlorine from (sea)water
- Only one CAR
- Coordinated by ECHA project manager
- Free radicals: 1st telcon in May

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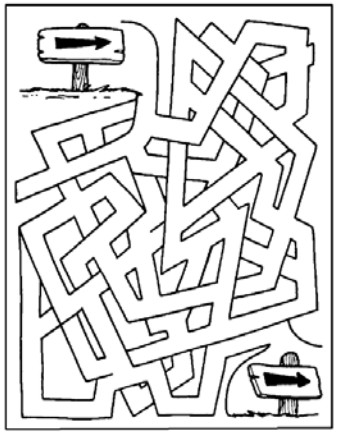
Challenges (2)

- What is to be assessed at a.s. level/ at product level
  - No precursors
  - Different systems
  - approval should also cover/allow future new system
  - treated articles

- ~~Assessment of precursors~~
- Composition of ambient air or water

Challenges (3)

- **Disinfection By-Products (DBP)**
  Guidance on the Biocidal Products Regulation Volume V, Guidance on Disinfection By-Products (January 2017)
- **Classification:**
  Exclusion, substitution/Annex I listing: based on properties of the in situ generated active substance only



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Challenges (4)

- **What should be authorised at product level?**
  - substance(s) or mixture generating the active substance
  - the a.s. generated from substances/mixtures which cannot themselves be authorised as biocidal products

  (CA-March15-Doc.5.1-Final)

- **Equipment?**

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Challenges: free radicals (1)

- Levels and identity of free radicals:
  Information needed about the relation between electric discharge/coating concentration/…. and the amount of radicals/oxidising potential
- How is over- and underdosing prevented/ specification of apparatus?
- Humidity, temperature, light intensity, composition of ambient air or water/pollution

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Challenges: free radicals (2)

- Disinfection By-Products (DBP): theoretical approach possible?
- Analysis of air outlet; of filters?
- Efficacy: few standard tests for these types of applications (no European standards)

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Practical recommendations

- Always include data or data waivers
- Include a clear description of the system
- If a.s. application for several PT's, indicate differences between dossiers
- Reports in English
- Draft assessment in Word
- Do not delete paragraphs/annexes from template: explain why not relevant
- Include study reports in IUCLID

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Guidance

- See ECHA website 'In situ generated substances'
- New: Recommendation of the BPC Working Groups *In situ* generated active substances – Risk assessment and implications on data requirements for active substances generated *in situ* and their precursors
- In preparation:
  BSM (new annex): How to report, in IUCLID, active substance(s) generated in situ

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Thank you for your attention!

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Free radicals: guidance (bonus)

- Guidance: CA-May16-Doc.5.1 – Final
- Definition: free radicals generated in situ from ambient air or water
- No further definition of the radicals
- - Water treatment
  - Air treatment
  - Surface treatment/ coated articles
- Testing in most cases not necessary/possible
- Risk assessment:
  - DBP
  - emission during handling/application of product
  - emission during handling of treated articles

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