Best Practices for in-situ applications [and remaining issues]

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Good Bacteria
Lactococcus
Lactobacillus
Lactobacillus bifidus
Bad Bacteria
Clostridium perfringens
Staphylococcus
Escherichia coli

Subjects to be treated

- In-situ development before re-definition 2015
- In-situ development after re-definition 2015
- How to deal with products
- System approach [role of devices]
- Art 54 BPR & Cluster formation
- Free radicals

History and background – Regulatory status BPD vs. BPR

Result of a lack of a clear guidance for the regulation of in-situ generated active substances under the BPD:

- **Either the precursor was notified** (e.g. ammonium sulphate for the generation of monochloroamine from sodium hypochlorite; the in-situ generated active substance monochloroamine was not notified; [*sodium hypochlorite is an active substance on its own and was notified and supported*]

History and background – Regulatory status BPD vs. BPR

Result of a lack of a clear guidance for the regulation of in-situ generated active substances under the BPD:

- or **only the in-situ generated active substance was notified** (e.g. peracetic acid generated from TAED and sodium percarbonate; the precursors were identified, not notified).
- Result: In all of these cases, **the notifications per-formed were honored** and the precursor(s) were allowed to remain on the market until a decision was made on Annex I listing (i.e. approval) for the active substance generated in-situ from the concerned precursor(s).

ISG and precursors – definitions, reaction types and examples

1. In-situ generation of the biocidal active substance during use:

Principle: The biocidal active substance is generated in-situ **as a result of a decomposition or reaction from a single precursor** under use conditions such as heating, combustion e.g.
The **precursor** may be a biocidal active substance in its own right or may not have itself any significant biocidal effect on the target organisms.

Examples:

Aluminium/Magnesium phosphide **releasing → phosphane**
Various Substances **releasing →formaldehyde**

ISG and precursors – definitions, reaction types and examples

2. Hydrolysis to form an acid-base pair

- The biocidal active substance is formed in-situ only as an immediate consequence of the addition or dilution of the precursor to water **= hydrolysis →** The precursor and in-situ active substance are related as an acid-base pair.
- In such cases, the formation of an in-situ substance active may be an unavoidable consequence of the use of the precursor in water **at a given concentration, temperature and pH. This adds a kinetic dimension to the substance definition (peer review by APCP WG necessary)**

ISG and precursors – definitions, reaction types and examples

<u>Examples</u> of Hydrolysis to form an acid-base pair:

Sodium percarbonate releasing **hydrogen peroxide**
Chlorine / **hypochlorous acid** / hypochlorite
Substituted hydantoins hydrolysing to **hypohalous species**

ISG and precursors – definitions, reaction types and examples

3) Chemical reaction:

- **Principle: Two or more substances (precursors) are reacting with each other** prior to or during the application to generate other biocidal active substances in-situ.

- The initial substances may or may not possess biocidal activity and are placed on the market with the **intention** of generating the active substance(s) in-situ.

ISG and precursors – definitions, reaction types and examples

Examples of chemical reaction*

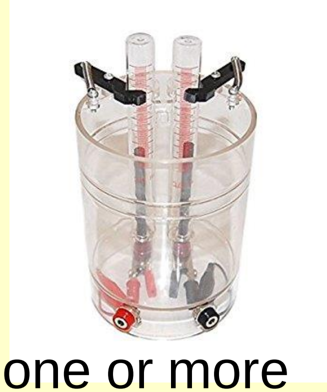
Ammonium salts and sodium hypochlorite → **chloramines**
Tetraacetylethylenediamine (TAED) and peroxygens → **peracetic acid**

Halide salts and oxidants generating → **hypohalous species**

Sodium chlorite reaction with a strong acid → **chlorine dioxide**
Sodium chlorate, with hydrogen peroxide and presence of a strong acid, → **chlorine dioxide**
Sodium chlorite reacting with Potassiumperoxomonosulphate → **chlorine dioxide**

*(with or without device)

ISG and precursors – definitions, reaction types and examples



4) Electrolysis and electrical generation:

- The biocidal active substance is generated in-situ from one or more substances by the action of electricity (= electrolysis).

- If the generating **equipment** is supplied with a biocidal claim or used as such and the substance(s) for generating the biocidal is supplied explicitly for use in the equipment generator the biocidal active substance are considered as a biocidal product.

- **How about Art 54 of BPR in the case of equipment ?**

ISG and precursors – definitions, reaction types and examples

<u>Examples</u> of electrolysis and electrical generation:

Sodium chloride generating **hypochlorous acid** via electrolysis
Sodium chlorite generating **chlorine dioxide** via electrolysis
Ozone via electrical discharge in air
Ozone via electrical discharge in oxygen
Ozone via electrolysis of water

Re-definition ISG 2013-2015

Core message(s) of CA proposals of “CA-July13-Doc.5.1.1” and “CA-March15-Doc.5.1-Final, Revised on 23 June 2015” (2):

- All in-situ generated active substances should be notified/defined with the respective precursor(s) they are generated from → all possible in-situ active substance/precursor combinations would have to be notified. → **CA-March15 documents!**

- In case of other precursor systems/combinations: An application would also have to be submitted for precursors **not covered by the in-situ dossier currently under examination for the respective active substance**.

Re-definition ISG 2013-2015

Core message(s) of CA proposals of "CA-July13-Doc.5.1.1" and "CA-March15-Doc.5.1-Final, Revised on 23 June 2015" (2):

- CA proposal also included timelines for submission of a declaration of intention and make a notification to ECHA to take over the role as participant as well as for the submission of an application to require the approval of the respective in-situ systems (i.e. the preparation of complete AS dossiers)

- **→ Notifications were only possible (but required) for precursor combinations not already covered by the re-defined identity!**

Re-definition ISG 2013-2015

Annex I

In situ generated active substances

	Current name	Current precursor(s)/active substance combinations	Additional precursor(s)/active substance combinations	RMS	Legal basis for taking over
3.1 Stabilised chlorine					
458	Ammonium sulphate	Monochloramine generated from ammonium sulphate and a chlorine source		UK 11, 12	n/a
			Monochloramine generated from ammonium sulphate and a chlorine source	2, 4, 5	Art. 93
			Monochloramine generated from a mixture of ammonium sulphate and diammonium hydrogenorthophosphate and a chlorine source	2, 4, 5, 11, 12	Art. 93
		Monochloramine generated from a chlorine source and a chlorine stabiliser	Monochloramine generated from ammonia and a chlorine source	2,5, 11	Art. 93

Management of ISG - Redefined systems

- In the BPR, **the data requirements on the active substance(s) and the biocidal product are provided for in Annexes II (a.s.) and III (b.p.).**
- Due to the lack of a clear-cut guidance, data requirements and the quality of data needed for in situ systems is not well defined/adopted yet.
- Discussions in the **CA** on data requirements for in situ generated active(s) and precursor(s) are **ongoing**.
- The **APCP WG** compiled recommendations for in-situ in April 2017
- The July 2018 **Guidance on TE** postponed in-situ

Product approval ISG after re-definition

Example of an in-situ generated active substances and the precursor system it is generated from:

- Peracetic acid (PAA) generated in-situ from the precursors TAED and sodium percarbonate:

  $2\ (2\ Na_2CO_3 \cdot 3\ H_2O_2) + 3\ TAED \rightarrow 4\ Na_2CO_3 + 3\ DAED + 6\ \mathbf{PAA}$

- **Precursor suppliers on Art 95 are not necessarily reference suppliers according to Art 54 !! Hence → TE (costly !)**
- Products formulators have to submit Technical Equivalence data in their product dossier if their supplier is not doing that himself
- In this in-situ system there is fortunately **no device** needed

ISG: Role of Devices under BPR

- Devices play a key role in particular for **oxidative** biocides
- The variable parameters in devices are very different and a function of the particular active substance which they are bound to produce
  - These parameters need to be well understood and described in the **PhysChem** part of the active substance dossier
  - If formation of **DBP's** is to be expected (frequently a function of pH and TOC of the water being used in **electrolytic** processes) testing series under worst case assumptions become necessary

ISG: Role of Devices under BPR

  - Depending on the kinetic behaviour of the system these worst case testing series may have to be repeated at several times during the generation reaction
- **Question:** Is the electrode material part of a reference in-situ product ? (relevant for electrolytically generated substances)

- **Question:** How to prevent the user from modifying important parameters ? (relevant for electrolytically generated substances <u>and</u> ISG via chemical reactions)
- **Clustering of devices must not make Article 54 of BPR superfluous**

ISG: Role of Devices under BPR

Devices itself should become subject to standardization by appropiate TCs of CEN

*In the alternative the fast technical progress in digitalization will cause European devices **users** to import this equipment from other parts of the world (resulting in no chance of control by national BPR enforcement)*

Free Radicals (FR) and Art 93

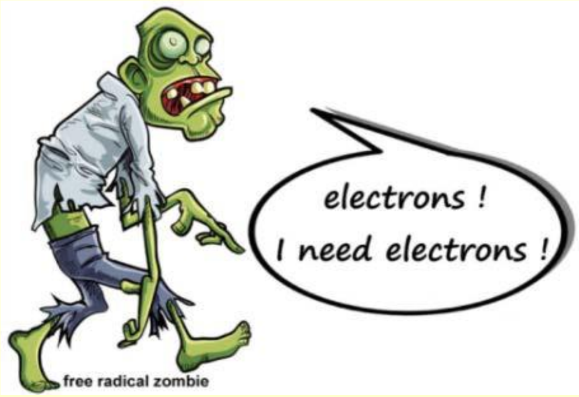
- Discussions at Competent Authority Meetings
  - 2003 - 2005 Barley Straw (photocatalyst)
  - 2005 - 2009 Ballast Water (TiO_2)
  - 2015 - ??? General Principles

- 2015 discussion centered around
  - FR and Disinfection By-Produts
  - What is different between FR and just re-defined in-situ actives ?

  - **The method by which FR are generated becomes decisive (case by case decision)**

Free Radicals (FR) and Art 93

- From **45** ISG substances dossier **23** were **FR**
- RMS are
    - 17 Netherlands
    - 4 Austria
    - 2 UK (before Brexit !)
- From **26** PT/a.s. combinations **9** were FR



Thank you for your attention!

It has been a pleasure to participate in the