21th December 2017

Product authorisation in case of *in situ* generation

Introduction

At the **74th CA meeting** (27-29 September 2017), Aqua Europa and ECA Consortium presented their concerns and proposals on the management of the product authorisation stage for 'in situ generation' cases (CA-Sept17-Doc.4.8-a and CA-Sept17-Doc.4.8-b). They indicated the diversity of *in situ* systems/devices on the market and proposed a generic approach, identifying the worst case(s) scenario(s) to be evaluated in the risk assessment.

By October 20th, 2017, three **comments** were received on this proposal:

- Aqua Europa & ECA: thoughts and ideas on potential next steps:

- Implement a working group with representatives from interested CAs and industry stakeholders for the development of a guidance document. Input from industry: expert knowledge and practical experience;
- Support offered to eventual questions from CAs for commenting on position paper;
- Suggested milestones and responsibilities:
    - to determine key parameters for the definition of an "output and performance envelope";
    - to further assess and consider existing regulations and technical standards against the background of the requirements for biocidal product authorisation;
    - to develop a draft guidance beginning of 2018.

- Ctgb (CA, the Netherlands):

- An important question is whether reference can be made to the device in the SPC and how to do that;
- For complex *in situ* systems (ISS) using generally available precursors or precursors that cannot be authorised: Need for connection of the device that is used for generation in some way to the authorisation. Or: the biocidal product must be labelled and the only way to do that is by putting the **label on the device**;
- For inspection after authorisation, it is necessary that it can be recognised that a product is authorised and that the *in situ* product that is used in practice is the same as the product that is authorised (Output range of reaction is specified in the SPC);
- Not up to the CA's to decide on the standardisation that Aqua Europa is asking for;
- Up to industry to show whether it is possible to group ISS using existing standards;
- Important that the active substances, impurities and disinfection by-products that constitute the output of the system can be assessed for authorisation;

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- A specific variation in output is acceptable as long as it is possible that the "output envelop" can be defined clearly;
- The technical and other measures that can be taken to ensure that the output of all devices will fall within a "performance envelop", which has to be developed by industries themselves.

- KEMI (CA, Sweden):

- Supports the general principle that it should be possible to use a generic approach for authorisation of *in situ* generation systems;
- Start to discuss how *in situ* generated biocides will be authorised;
- As NL also mentions, an important question is whether reference can or should be made to the device in the SPC and if so, how to do that;
- Concern: How should ISS devices already placed on the market and in use, be regulated and authorised, especially when the company responsible for the placing on the market does not exist anymore?

At the **75th CA meeting** (23-24 November 2017) there was very limited discussion of the authorisation procedures of device-based ISS. The three comments received by 20th October 2017 were noted.

Proposal of EurO$_3$zon for product authorisation in case of *in situ* generation

EurO$_3$zon ivzw is an International Non-Profit Association dedicated to promoting the use of Ozone (O_3) in Europe. The member companies co-operate in matters concerning ozone applications that are regulated by the European Biocidal Products Regulation (BPR, Regulation (EU) No 528/2012). This is including ozone manufacturers, gas suppliers and other associations. Members of EurO$_3$zon are also initiating and supporting the development of technical standards in the field of ozone treatment. Additionally they are providing technological expertise to standardization bodies and related associations.

EurO$_3$zon would like to add their vision to the above discussion, from the viewpoint of ozone as an *in situ* generated active substance / biocidal product.

General position and proposal by **EurO$_3$zon:**

- The requirements for a safe and reliable operation of in situ system (ISS) devices are described already in widely acknowledged and applied European and national guidelines and standards.
- Above all for device-based ISS is important what comes out of these devices: "Technical active substance generated *in situ*"
- No obligation and no legal base exist to authorise devices (Article 17 BPR)

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- However, preferentially device manufacturers of ISS commit themselves to complete product authorisation and to become the authorisation holders.
- A connection between the devices (or a series of devices) and the authorisation dossier should however be made. As indicated by the Ctgb, this could be in the SPC.
- **EurO$_3$zon** would suggest to list at level 3 of the SPC of the BP family (see further 'BP family SPC: three level approach') all *in situ* devices by their generic brand and/or manufacturer names (no product-series names and model numbers), characterised by their output[1], and fitting to the output ranges defined in level 2 (meta-SPC). It should be able to add future devices that fall within the boundary envelope as an administrative change[2]. In case precursors are not subject of authorisation a product label is to be placed on the ISS device[3] in order to illustrate the authorization of the BP generated by that ISS device.
- Besides output characterisation and a short description of the *in situ* generation method, no other technical specification of the equipment is needed in the BP dossier.

Support for the generic approach as proposed by Aqua Europa and ECA (CA-Sept17-Doc.4.8-a and CA-Sept17-Doc.4.8-b):

  - Identify worst case conditions considering existing regulations and standards for the precursor sources, devices and use scenarios of application and use.
  - Cluster *in situ* devices by implementing an integrated, generic approach, in terms of exposure scenarios for human health and environment.
  - Demonstrate for a group of device-based ISS, using different precursor sources/qualities, (different water qualities) and different devices, that the *in situ* generated active substance quality is within the pre-defined specifications.
  - To deliver and/or produce relevant data in accordance with the BPR provisions for this integrated, generic approach.
- Older systems/devices installed before approval:
  - If manufacturer still exists: The manufacturer – only on request of the owner and/or operator of these older devices and if there is no need to replace yet said device –, makes sure the device falls within the boundary envelope defined in product authorisation and provides any necessary labels.
  - If "orphan" device (manufacturer responsible for bringing the device on the market does not exist anymore): the responsibility for regulatory compliance of biocidal product generated by such orphan devices belongs to the end-user, the national authorities or any third party that is willing to take up responsibility. It is however, in general, unlikely that the individual end-user will manage this by himself.

[1] instead of having individual "biocidal products", which cannot be defined for ISS generated biocidal products
[2] E.g. in case a new portfolio of generators (new brand names) is developed
[3] This also applies if the use of authorized precursors is not sufficient to ensure that the output of the device complies with the SPC

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Specific proposal of EurO$_3$zon for devices for generating ozone *in situ*:

- **EurO$_3$zon** wants to ensure the continuation of ozone-based disinfection at feasible / reasonable effort for authorities and ozone device manufacturers.
- Precursors for ozone: no precursors with biocidal claim exist on the market, only:
  - available generic precursors (liquid oxygen)
  - precursors that cannot be authorised (air, oxygen made *in situ* from air, water)
- Therefore, the **biocidal product** to be authorised **is (equal to) the technical active substance ozone generated *in situ***.
- As far as the active substance and the biocidal product are to be considered equivalent, there are ultimately no further authorisation requirements deemed necessary as a safe use has already been proven as part of the active substance approval.
- The ozone *in situ* devices are designed such that, depending on various operational factors (such as precursor identity, quality/composition) and settings (specific energy, …), the devices themselves are able to produce a wide range of technical ozone concentrations within a boundary envelope.
- There is a wide variety of ozone devices, each able to produce a variety of technical *in situ* ozone – a situation that is comparable with ISS devices generating other active substances.
- Therefore, it is impossible to define individual ozone "products" that are characterised by a fixed percentage of ozone content and link them to a device.
- It is the output of the ozone ISS what receives authorisation as BP and in the SPC the following is defined (1) a boundary output envelope of ozone, and (2) ozone use concentration ranges for the individual uses, for ozone typically based on efficacy results obtained in simulated use or field testing. (1) and (2) are taken over in the authorisation act and the product label. This product label is placed on the device.
- Definition of "Ozone output" *vs* "Ozone use concentration":
  - "Ozone output": expresses the **pure ozone content** in the technical ozone generated *in situ* (ozone in gas or ozone in water), at the time of generation (% w/w). More specific, ozone output can mean:
    - a) Ozone concentration (in gas-phase / air or oxygen as wt% or g/Nm^3_{gas})
    - b) Ozone capacity = g or kg ozone generated per hour
  - "Ozone use concentration" is the **applied ozone** in the media (water or air) expressed in g ozone/$m^3_{water\ or\ air}$. This is not the actual measured or finally found, residual or dissolved ozone concentration.
  - "Ozone use concentration" is actually a better characterisation of the "product" in use, since for efficacy and risk assessment the actually applied ozone is of prime importance.
- The aspect of "use concentration" ("use case" in Aqua Europa/ECA doc) forms indeed an important aspect in the worst case exposure scenarios. In Germany there is an existing norm, DIN 19627 ("Ozonerzeugungsanlagen zur Wasseraufbereitung"), defining safe operation scenarios for ozone. The norm is planned to be upgraded to an EN standard.

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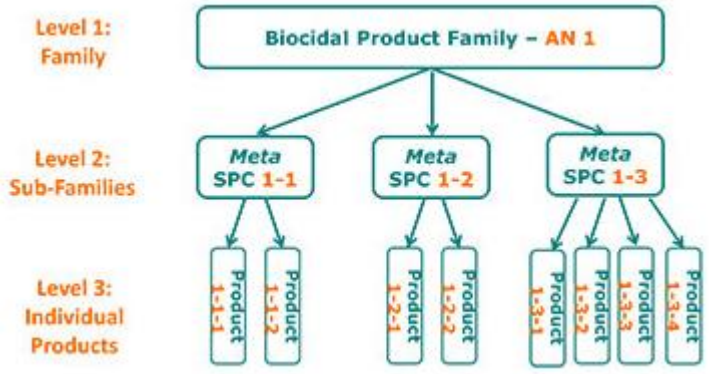
BP family SPC: three level approach

- Level 1: BP Family
- Level 2: Meta-SPCs
- Level 3: individual products



→ on level 2, the generic approach can result in definition of clusters of device output ranges (content of active substance, content of non-active substances), taking into account authorised uses and corresponding worst case scenarios for risk assessment. Ideally, such a cluster is then defined in a meta-SPC. Several clusters / meta-SPCs will make up the family (level 1).

→ on level 3, instead of individual "products", which cannot be defined for ISS based biocidal products, it would be an option to list all ISS devices, characterised by their output, and fitting to the output ranges defined in level 2.

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