27 October 2022

EurEau comments on the EFSA/ECHA Guidance document on the impact of water treatment processes on residues of active substances

EurEau welcomes this Guidance document on the impact of water treatment processes on residues of active substances, enshrining the European Commission efforts to protect human health and the environment. The document outlines which environmental water residues have to be assessed, the identification of water treatment transformation products that are formed and how to complete a risk assessment that includes consumption of treated drinking water.

This proposal heralds good news for water operators: water suppliers need water resources that are protected from pollution so that tap water remains safe and affordable and the right to water is not jeopardised. Moreover, since each drinking water treatment in combination with its raw water is unique, the guidance document covers all commonly used water treatment methods across Europe, thus considering worst case approach at several levels, in line with the precautionary principle.

The Drinking Water Directive (DWD) (EU) 2020/2184 sets the legal framework to protect human health from the adverse effects of any contamination of water intended for human consumption. The relevant principles in this regard within the Directive are as follows:

1.- the efficiency of the disinfection applied is validated. Guidance on the Biocides Product Regulation -Vol. II Parts B+C- describes how to assess and evaluate the efficacy of biocidal products

2.- any contamination from disinfection by-products is kept as low as possible without compromising the disinfection,

3.- any contamination from treatment chemicals is kept as low as possible

The World Health Organization (WHO) Guidelines for drinking water quality include several recommendations about disinfection and disinfection by-products:

1. Disinfection should not be compromised in attempting to control disinfection byproducts.
2. The use of chemical disinfectants in water treatment usually results in the formation of chemical by-products. However, the risks to health from these by-products are extremely small in comparison with the risks associated with inadequate disinfection, and it is important that disinfection efficacy not be compromised in attempting to control such by-products

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3. Strategies for DBP control include source control, precursor removal, use of alternative disinfectants and removal of DBPs by technologies such as air stripping, activated carbon, UV light and advanced oxidation. These processes would need to be followed by a further disinfection step to guard against microbial contamination and to ensure a residual concentration of disinfectant within distribution.

Based on the above principles of the DWD and the WHO Guidelines, EurEau supports the exemption of Biocidal Products used in drinking water -PT5 from the scope of this document.

Chapter	Page	Line	Comment
Summary	2, 13, 27	63, 505, 1026	In this guidance, it seems that a difference is made between a metabolite and an environmental transformation product (eTP) while their difference is not clearly defined.
1.1	9	339	The Background of the Guideline can mention the Drinking Water Directive (EU) 2020/2184 and focus on the relevant scientific knowledge, summarized by the World Health Organization Guidelines for drinking water quality The DIRECTIVE (EU) 2020/2184 sets the legal framework to protect human health from the adverse effects of any contamination of water intended for human consumption. Any contamination from disinfection by-products must be kept as low as possible without compromising the disinfection. The Guidelines for drinking water quality -World Health Organization- include recommendations about disinfection and disinfection by-products: 1. Disinfection should not be compromised in attempting to control disinfection byproducts. 2. The use of chemical disinfectants in water treatment usually results in the formation of chemical by-products. However, the risks to health from these by-products are extremely small in comparison with the risks associated with inadequate disinfection, and it is important that disinfection efficacy not be compromised in attempting to control such by-products 3. Strategies for DBP control include source control, precursor removal, use of alternative

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			disinfectants and removal of DBPs by technologies such as air stripping, activated carbon, UV light and advanced oxidation. These processes would need to be followed by a further disinfection step to guard against microbial contamination and to ensure a residual concentration of disinfectant within distribution. Based on the above principles of the DWD and the WHO Guidelines, Biocidal Products used in drinking water -PT5 are excluded from the scope of this guidance document. <u>References</u> DIRECTIVE (EU) 2020/2184 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 December 2020 on the quality of water intended for human consumption Guidelines for drinking-water quality: fourth edition incorporating the first addendum. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO.
2.3.2	29	1132	According to SANCO/221/2000 Rev 11, a non-relevant eTP must not comply to 0,1 µg/L in groundwater, and a limit at 0,75 µg/L is even mentioned in the assessment. Nevertheless, this relevance assessment can only be applied to define the relevance of a eTP, not to assess the risk resulting from its transformation after water treatment. A non-relevant eTP at concentration lower than 0,75 µg/L could lead to the formation of tTP toxicologically relevant. Therefore, this guidance document must not consider differently relevant and non-relevant eTP as defined by SANCO/221/2000 Rev 11, both should be assessed according to this guidance once above 0,1 µg/L.
3.4	39	1342 Figure 5	For groundwater, the paragraph states that a relevant metabolite can be toxicologically non relevant. According to SANCO/221/2000 Rev 11, a relevant metabolite is toxicologically relevant. This wording is confusing and should be removed or adapted.
4.2	44 51	1488 1695	A high concentration defined as 1000 times the limit of quantification (LOQ) is not a suitable criteria, for example if the LOQ is 1 ng/L the high concentration will be equal to 1 µg/L, which represents the range of environmental relevant concentrations chosen in this guidance. A high chemical concentration could be defined as 0,1 mg/L.
4.2	44 56	1504 1904	An environmental relevant concentration could be set at 10 µg/L of the chemical to be tested, to avoid

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			different results associated to the initial concentration.
4.2	44	1508	When testing at an environmental concentration of 1 to 10 µg/L, an unobserved signal should be ensured to be < 0,075 µg/L, in agreement with the genotoxicity criteria defined on page 63 line 2120, otherwise the formation of genotoxic compounds could be underestimated.
4.2.3	49	1639 (Table 3)	Ozonation can lead to the formation of N-Nitrosodimethylamine. The column "Some examples of TP" could include this compound in the ozonation process. Andrzejewski P, Kasprzyk-Hordern B, Nawrocki J. N-nitrosodimethylamine (NDMA) formation during ozonation of dimethylamine-containing waters. Water Res. 2008 Feb;42(4-5):863-70. doi: 10.1016/j.watres.2007.08.032. Epub 2007 Sep 7. PMID: 17904190.
4.2.4	51	1723	Standard water is prepared by dissolving natural organic matter Suwannee River DOC. This NOM consists of humic and fulvic acids -high molecular weight, high hydrophobicity, high ultraviolet absorbance, and high reactivity with chlorine to form THM-. Thus, the standard water contains some precursors of a tTP -THM. Scientific evidence supports the same behavior concerning to other tTP (Haloacetic acids-HAA). Coagulation processes partially remove this NOM. So, this experimental procedure might avoid the addition of Natural Organic Matter because interferes with the interpretation of the results. Maybe the NOM addition comes from the biocidal efficacy assessment. The evaluation of the efficacy of a biocidal product is carried out following the ECHA guidance on efficacy. This guidance includes the addition of natural organic matter to simulate soiling conditions and to assess the interference of this natural organic matter on the disinfectant efficacy. But the addition of NOM -soiling conditions- leads to the tTP formation. It is not recommended when dealing with the impact of DWT processes on residues of active substances. Guidance on the BPR: Volume II Parts B+C Version 3.0 April 2018 Reference: ECHA-18-G-02-EN Archer, Aaron D., and Philip C. Singer. "An Evaluation of the Relationship between SUVA and NOM Coagulation Using the ICR Database." Journal (American Water Works Association), vol. 98, no. 7, 2006, pp. 110–23. JSTOR, http://www.jstor.org/stable/41313741. Tseng, T. and Edwards, M. (1999), Predicting full-scale TOC removal. Journal - American Water Works Association, 91: 159-170. https://doi.org/10.1002/j.1551-8833.1999.tb08622.x Golea, Dan & Upton, Andrew & Jarvis, Peter & Moore, G. & Sutherland, S. & Parsons, S.A. & Judd, Simon. (2017). THM and HAA formation from NOM in

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			raw and treated surface waters. Water Research. 112. 10.1016/j.watres.2017.01.051.
4.2.4	52	1726	The Guidance could clarify that these experiments should be carried out only to determine which TP may be formed. Genotoxicity of transformation products must be assessed from testing the pure substance. Some interferences could arise if genotoxicity is assessed from the experimentals procedures of the 4.2.4. For example In the case in vivo tests are mandatory, and experiment 4.2.4.1 Chlorinantion with NaOCl is carried out, Chlorate could interfere with the in vivo Genotoxicity tests due to the oxidative stress resulting in damage to Red Blood Cells. Fresh NaOCl solution should be sourced at least every two weeks (chlorate may otherwise have formed in the concentrated NaOCl solution). The NaOCl should be stored cold (between 2 and 8°C) and in the dark.
4.2.4	52	1748	Specify mg_Cl_2/L for chlorine concentration.
4.2.4	52	1769	Specify mg_Cl_2/L for monochloramine concentration.
4.2.4	52	1769	Concentration of 0.5 mg/L is very low. The DWD 2020/2184 Spanish transposition regulates combined chlorine -monochloramine to 2.0 mg_Cl_2/L) Several tests to detect the tTP formation potential use much higher concentrations of the disinfectant. Chlorine:3 mg_Cl_2/L Standard Methods Committee of the American Public Health Association, American Water Works Association, and Water Environment Federation. 5710 formation of trihalomethanes and other disinfection byproducts In Standard Methods For the Examination of Water and Wastewater. Lipps WC, Baxter TE, Braun-Howland E, editors. Washington DC: APHA Press. DOI: 10.2105/SMWW.2882.112 Stevens, Alan A., and James M. Symons. "Measurement of Trihalomethane and Precursor Concentration Changes." Journal (American Water Works Association), vol. 69, no. 10, 1977, pp. 546–554. JSTOR, http://www.jstor.org/stable/41268826. Eaton AD, Clesceri LS, Greenberg AE. editors. Standard methods for the examination of water and wastewater,20th ed. Washington DC: American Public HealthAssociation, American Water Works Association, WaterEnvironment Federation Publishers, 1998 Chloramine: Some tests like the gold standard test for NDMA formation potential $NDMA_{FP}$ (Mitch-2003) specify much higher [concentration x time] (55mM·h). The Guidance [concentration x time] is 0.169 mM·h. If a contact time of 240 hours is proposed (Mitch-2003) monochloramine concentration should be 16.3 mg_Cl_2/L *Cit. Even when the chloramine contact time is doubled, the NDMA concentration shows no significant increase after the initial 55mMh exposure.*

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			Mitch, W.A., Gerecke, A.C., Sedlak, D.L., 2003. A N-nitrosodimethylamine (NDMA) precursor analysis for chlorination of water and wastewater. Water Res. 37 (15), 3733-3741.
4.2.4	52	1770	The formation of dichloramine is expected at this pH. Usually, the pH for the monochloramine disinfection is over 8.0. So the experiment should be carried out at pH ≥8.0.
4.2.4	52	1773	Chloramine: Guideline proposes 24 hours. Some tests like the gold standard test for NDMA formation potential $NDMA_{FP}$ (Mitch-2003) specify much higher [concentration x time] (55mM·h). 10 days *Cit. These results indicate that, under the conditions of the standard NDMA precursor analysis, the NDMA concentration plateaus within 10 days because organic precursors have been consumed.* Mitch, W.A., Gerecke, A.C., Sedlak, D.L., 2003a. A Nnitrosodimethylamine (NDMA) precursor analysis for chlorination of water and wastewater. Water Res. 37 (15), 3733-3741.
4.2.4.3	53	1781	A concentration of 0,5 mg/L chlorine dioxide could be recommended instead of a ratio ClO2/DOC, ensuring a large molar excess of ClO2 compared to the chemical to be tested.
4.2.4.7	55	1895	An activated sludge process is working under aerobic conditions, therefore removing the oxygen through bubbling nitrogen is not to be recommended.
5.1	57	1929	This guidance also introduces the notion of relevance, but different from the relevance defined by SANCO/221/2000 Rev 11 for the metabolite of a pesticide. This can bring some confusion between relevance of a metabolite of pesticide and of a transformation product formed after water treatment.
5.2	58	1965-1966	Mention if the Ames Test must be carried on with metabolic activation.
5.2	59	1997-2011	Agreed that Positive in vitro tests listed in this Guidance must be followed by In vitro Genotoxicity assays because In vitro tests do not always address molecular (DNA) binding. (ECHA,2017a p287). We suggest clarifying the kind of in vivo tests required. Now ECHA is requesting a battery of in vivo tests for the biocidal active substance evaluation for PT-5: In vivo mammalian alkaline comet assay in several tissues (OECD 489) combined with in vivo mammalian erythrocyte micronucleus test (OECD 474). Some concerns arise from these kinds of tests:

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			1. tTP from disinfectant (ie. chlorate from sodium hypochlorite- see comment on 1742\) could interfere with the in vivo genotoxicity tests, and 2. oral gavage will be problematic because gastric acids will react with the product and the disinfectant ECHA, 2017a. Guidance on Information Requirements and Chemical Safety Assessment, 2587 Chapter R.7a: Endpoint specific guidance, Version 6.0, July 2017, 610 pp. Available online: 2588 Guidance on IR&CSA – Chapter R.7a (europa.eu)
5.2	59	2016	Maybe an erratum (against line 1952) Incorrect: TTC value of 0.15 μg/kg/day (0.075 μg/L) Correct: TTC value of 0.15 μg/person/day (0.075 μg/L)
6.2	61	2058	Flowchart. **TIER 2**: Stage 1→Stage 1A→ Stage 2→ Does the exposure to tTP exceed the acceptable overall TTC? In case "NO" the flowchart point to Proceed to Tier 2 risk assessment. Likely it is *No further assessment*

6.2	61	2058	Flowchart. **TIER 2**: Stage 1→Stage 1B→ Stage 2→ Does the tTP have toxicological properties other than genotoxicity based on repeated dose study? There is not a link with the following process in the flowchart Stage 2: What is the total exposure of consumer to tTP? Likely it is *NO* ↓
6.2	63	2113	The maximal concentrations proposed by this guidance are derived from threshold values of the TTC approach considering 100% allocated to from drinking water. Other parts of this guidance mention that a total exposure must be considered (line 2091), taking into account all sources of oral exposure (line 2243). Therefore, an allocation factor of 20% for drinking water should be adopted in the calculation of any maximal concentration based on threshold values of the TTC approach, as recommended by WHO for a drinking water allocation factor.
7.2	68	2336	Effect-based monitoring most often needs sample pre-concentration by extraction, such as SPE, to measure a biological effect. As extraction of a water sample is ineffective for several very polar and soluble

			chemicals, the measured biological effect can be underestimated, e.g. nitrosamines are difficult to extract while these are genotoxic. Therefore, extraction should be avoided and effect-based monitoring should be performed at high chemical concentration (0,1 mg/l for example) with sample dilution allowing biological effect to be measured on the whole mixture without loss of any chemical.
B4	130	3576	Ozonation can lead to the formation of N-Nitrosodimethylamine Andrzejewski P, Kasprzyk-Hordern B, Nawrocki J. N-nitrosodimethylamine (NDMA) formation during ozonation of dimethylamine-containing waters. Water Res. 2008 Feb;42(4-5):863-70. doi: 10.1016/j.watres.2007.08.032. Epub 2007 Sep 7. PMID: 17904190.

About EurEau

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