POSITION PAPER
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CropLife Europe Position on the Draft Guidance Document on the impact of water treatment processes on residues of active substances or their metabolites in water abstracted for the production of drinking water

KEY MESSAGES

CropLife Europe would like to bring to the attention of the EU Commission and Member States that we consider the Draft Guidance Document (GD) on the impact of water treatment processes not fit for purpose in its current form and see a need for major revisions. CLE provided substantial comments to the draft version of the GD in September 2022, and we believe that these comments are essential to be considered in the final version. We also collected additional information on the potential impact of the GD that underlines our case.

The GD would trigger the generation of a substantial amount of new data, including experimental studies for more than 500 substances, and subsequent toxicity evaluation for potentially thousands of transformation products (TPs) within two years after entry into force. Considering the general lack of realism of the GD and the absence of evidence that the predicted TPs would occur under realistic conditions of drinking water pro-duction, CLE strongly advocates for a more targeted, realistic, and proportionate approach focusing on real concerns for public health, as stipulated in the Commission mandate to ECHA and EFSA.

- **The GD fails to focus on substances with a realistic potential to reach waterworks, thus leading to unnecessary experimental testing of active substances and metabolites. CLE strongly advocates for an improved screening scheme, based on a more realistic exposure assessment, to focus experimental work on substances at risk of occurring in raw water.**
- **The substantial amount of necessary new experimental data raises the question of the timeframe for data generation. A 2-year time window after entry into force of the GD, as stipulated by existing confirmatory data requests in the most recent renewal decisions of many active substances, is clearly not feasible. CLE's timeline estimate for data generation is 15-36 months in a simple case (active ingredient with 1 metabolite to test) and 18-48 months in a more complex case (active ingredient with 4 metabolites to test). This includes laboratory studies, synthesis of test material and toxicity studies.**
- **The proposed experimental test procedures are not suitable for use in a regulatory assessment framework due to the lack of detailed and validated testing guidelines. The new required studies are also not covered by the data requirements stipulated under e.g., Regulation (EC) 1107/2009. More importantly, the suggested experimental tests are isolated laboratory screens that do not reflect reality in waterworks. They present a very high risk of producing "artificial" TPs, formed under laboratory settings but not occurring under realistic conditions. These "artificial" TPs will require synthesis and toxicity testing, including animal testing, even though their presence in real water samples would not have been confirmed.**
- **Considering that more than 500 substances trigger experimental testing and taking a cautious assumption of 2 TPs per substance, the GD would trigger the evaluation of at least a thousand TPs, including toxicity studies, potentially animal testing, and human risk assessments within 2 years after entry into force of the GD. This is a significant obstacle given the limited capacities in laboratories and at Member State authorities. CLE questions whether this is a proportionate approach and advocates for a more efficient use of all stakeholders' capacities.**
- **The regulatory process and the human risk assessment needs a clearer description to avoid legal uncertainty. There is a need for a more realistic exposure calculations and alignment with the still ongoing OECD discussions on toxicological assessment of dietary metabolites before any animal tests are performed and the risk assessment is conducted. CLE developed a proposal for the toxicity evaluation and risk assessment of TPs in a dedicated position paper (POS/23/SN/36426).**

In September 2022, a draft *Guidance Document on the impact of water treatment processes on residues of active substances or their metabolites in water abstracted for the production of drinking water* was published for commenting. The Guidance aims to assess whether harmful transformation products (TPs) may be formed during drinking water treatment from residues of plant protection products (PPPs) and proposes a scheme to assess their safety.

CLE welcomes the development of a Guidance on this topic. It should enable applicants to address the question of TPs, thus increasing the confidence in the safety of our products. However, we wish to raise awareness with the EU Commission and Member States that, in our opinion, the Draft Guidance as seen during public commenting is not fit for purpose.

1. The Guidance will lead to a substantial amount of experimental testing of active substances and metabolites as it fails to focus on substances with realistic potential to reach waterworks.

According to the Guidance, all substances with estimated concentrations above 0.1 µg/L in raw water must be tested experimentally. While CLE agrees with the trigger for further evaluation, we disagree with the unrealistic, overly conservative dilution factors used to estimate concentrations in raw water from predicted environmental concentrations (PEC) in groundwater or surface water.

For groundwater, no dilution factors are proposed which implicitly assumes that raw water for drinking water production is abstracted at 1 m depth directly below an agricultural field. This is an unrealistic assumption which neglects any dilution by the hydrogeological conditions in soil and groundwater as well as mixing of leachate from different fields. Experimental data show that there is significant dilution towards drinking water abstraction wells that always receive water from a larger area with different uses and treatments[1].

For surface water, the dilution factors proposed are based on wastewater effluent dilution into surface waters and ignore other major aspects relevant for PPPs, e.g., landscape factors, such as the slope and proximity of the input area to the rivers, or diverse land use and the relative area treated. In addition, no higher-tier exposure assessment options are considered. It is possible and technically feasible to derive at an EU scale upstream surface water catchments that are relevant for raw water abstraction points. Modelling tools and data (e.g., on land use and relative area treated) are available for this purpose[2,3]; such refinements are already included in e.g, the established Dutch regulatory tool DROPLET[4]. This not only allows consideration of the factors that drive dilution from the edge-of-field surface water body towards a potential drinking water abstraction location, but also for higher-tier modelling or use of monitoring data to derive realistic (e.g., substance-specific) dilution factors.

CropLife Europe expects that at least 500 substances (active substances and metabolites) will be triggered into experimental testing. This is the result of a survey conducted by CLE among its members in April 2023 and based on responses by 10 companies. According to this survey, 760 substances (active substances and metabolites) will require the submission of an assessment of the impact of water treatment processes, resulting in 506 substances needing experimental studies. Considering the magnitude of this task and the fact that it does not address a real concern, we strongly advocate for a more differentiated screening scheme focusing experimental testing on substances truly at risk of occurring in raw water.

2. The significant amount of new data raises the question of the timeframe for data genera-tion. A 2-year time window after entry into force of the GD is clearly not feasible.

CLE's estimate of the timeline to satisfy the requirements of the GD is presented below:

	Simple case (active substance + 1 metabolite to be tested)	**Complex case** (active substance + 4 metabolites to be tested)
Laboratory experiments, including: - treatments simulation*, - structure elucidation, - TP quantification**	~ 6 months	~ 12 months
Synthesis of reference material	~ 3-6 months	~ 3-6 months
Toxicity evaluation and risk assessment	~ 6-12 months in best case ~ 12-24 months in case of higher tier animal testing	
TOTAL	**~ 15-36 months**	**~ 21-42 months**

* chlorination with NaOCl, chlorination with NH_2Cl, oxidation with ClO_2, combined processes ClO_2 followed by NaClO or NH_2Cl, ozonation, UV disinfection, biodegradation during sand filtration.
** TP quantification is only possible once reference material has been synthesized.

The timeline estimation for the laboratory experiments is about 6 months for a simple case and 12 months for a more complex case. This includes experiments for the 7 treatment methods foreseen in the Guidance (see table footnote), structure elucidation, and TPs quantification (only possible once reference material has been synthesized). Around 3 to 6 months are required for TP synthesis and 6 to 12 months in a best case for toxicity testing or up to 12 to 24 months in case of higher tier animal testing. This leads to a total of 15-36 months for a simple case and 21-42 months for a complex case.

3. The experimental test procedures proposed to simulate water treatment in the laboratory present a high risk of producing "artificial" TPs as they do not reflect reality in waterworks.

The proposed experimental test procedures fail to consider that a combination of treatments is standard practice for drinking water treatment across Europe. Oxidative treatments are typically combined with pre-treatments such as filtration or flocculation, to remove precursors, and post-treatments, such as activated carbon filtration or sand filtration, to remove TPs[5,6,7]. Pre- and post-treatment steps are implemented to reduce the occurrence of harmful disinfection by-products (DBPs) formed from natural organic matter during oxidation (independent of the presence of PPP residues in raw water). This was one of the requests formulated in the Commission mandate to ECHA and EFSA, and CLE feels that this is not adequately fulfilled by the GD.

The proposed experimental test procedures are small, laboratory-scale batch experiments. We question whether such laboratory experiments realistically simulate actual drinking water treatment conditions at the scale of water treatment plants. Unrealistic laboratory test procedures increase the risk of producing "artificial" TPs that would not occur under real-world conditions.

Beyond that, it is essential that test procedures for regulatory purposes are aligned with the data requirements of the relevant assessment frame and are described in sufficient detail, validated and

(ring-)tested to ensure they yield results that are consistent, reliable, and suitable under the rules of Good Laboratory Practice (generally, OECD-approved guidelines are used in a regulatory context). While agreeably promising and powerful, "non-target analytics" is still an emerging methodology. To our knowledge, no EU-agreed guidance is available, particularly on the crucial point of data processing and filtering algorithms. It appears problematic to apply such a methodology in a regulatory context without appropriate guidelines and testing conditions to ensure consistency of their application, leaving the burden of assessment and acceptance with the evaluating authority.

The proposed experimental test procedures are not suitable for use in a regulatory context and do not reflect reality in waterworks. They will generate "artificial" TPs that are formed under laboratory conditions but would not occur in realistic water treatment and processing environments. The multitude of "artificial" TPs will require synthesis, toxicity testing, potentially including animal testing, even though their presence in real water samples is not confirmed. "Artificial" TPs would also inappropriately raise public concern about the perceived quality of drinking water.

4. More than a thousand new TPs could be generated and require evaluation with toxicity studies, potentially animal testing, and human risk assessment.

Considering more than 500 substances are triggered into experimental testing, and taking a cautious assumption of 2 TPs per substance, more than a thousand new substances will need to be evaluated at EU level, with toxicity studies - potentially including animal testing - and human risk assessment. This is an unprecedented number of new substances, leading to a considerable volume of new data to be evaluated, presenting a challenge for the limited resources of Members State authorities and testing facilities.

CLE questions whether this is a proportionate approach and advocates for a more efficient use of all stakeholders' capacities. Harmful TPs formed from PPPs residues have only been reported in very rare instances, despite considerable research in this field in the last decades. More-over, harmful TPs are known to be formed (even at relatively high concentrations) from natural substances or other contaminants present in the raw water[8]. Addressing TPs potentially formed from PPPs is a meaningful step but will not solve the question of TPs formed from other contaminants or disinfection by-products (DBPs) formed from natural substances.

Conclusion

CLE supports initiatives promoting the safety of drinking water, provided they address true concerns. Based on the arguments developed above, CLE considers that the GD is not fit for purpose and strongly advocates for a more targeted, realistic, and proportionate approach focusing on real concerns for public health.

Sources

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