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Quality Review Comments from SAB Members on the SAB Draft Report: *Review of the EPA’s Draft Fifth Contaminant Candidate List (CCL 5)*

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As of July 17, 2022**

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Comments from Lead Reviewers

Comments from Dr. Barbara Beck

Overall, I found the SAB report well-written and clear, and that it addresses the 4 charge questions well. There were several places, listed below, where clarification was needed or where certain statements were not well-supported. My most substantive comment relates to the scientific basis of the manganese (Mn) discussion in Section 2.3.1. Specific comments are provided below.

Cover letter to Administrator Regan

p. 2, (noting cover letter pages are not numbered), lines 25 - 26. I think it would be helpful to provide some more clarity on what is meant by “impacts the regulatory process”, in terms of grouping contaminants. For example, could this mean grouping chemicals for purposes of setting regulatory criteria?

p. 3, lines 2 - 3. The document appears to request the use of “risks” *versus* “health effects” for microbial, but not chemical contaminants. Is this the intent? In any case, it seems that risk would also be the appropriate terminology for chemical contaminants.

Response to charge questions

Section 2.1

p. 2, line 14. It would be useful to note how CCL 5 relates to CCL 4, *e.g.*, was the earlier list used in developing the CCL5, and what are the key new approaches and new chemicals/microbes?

Section 2.1.1

p. 3, lines 20 – 24. I think that this point regarding uncertainty in health risks based on the quality of the underlying literature is likely to be relevant to chemical contaminants. Suggest broadening this comment to include chemical contaminants

Section 2.1.3

p. 5, line 34 – 35. Same question as above - could this mean grouping chemicals for purposes of setting regulatory criteria?

Section 2.2.1

p. 7, Line 14. Define NORMAN.

Section 2.2.3

p. 9, line 1. Same point as above. Ensure that risk (and not effect) terminology is also used for chemical contaminants.

p. 9, lines 18 – 21. Provide date that NAWQA ends to help understand priority of the replacement effort.

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Section 2.3.1

p. 10, lines 38 – 43, **p. 11**, lines 1 – 9. This section presents certain points to support the suggestion that EPA consider moving Mn from the Draft to the Final CCL 5. One of the key supporting documents is a review by O’Neal and Zheng (2015); however, the article provides limited scientific support for the proposition. Many of the epidemiological studies of manganese in drinking water and health effects cited in the review are of cross-sectional design. Cross-sectional studies cannot be used to draw conclusions on causality because the exposure and the endpoint are determined at the same time. Examples of cross-sectional studies in the review include Hafeman¹ *et al.* (2007); Bouchard *et al.* (2011); and Khan *et al.* (2012). Similarly, caution is needed when associating symptoms of Mn exposure, especially from water ingestion, with symptoms similar to Parkinson’s. Mn-induced parkinsonism, a condition observed mainly in certain worker populations exposed *via* inhalation to high levels of manganese in air in the workplace, shares some similarities with Parkinson’s; however, as noted in a recent review comparing the two conditions, there are “striking differences in the clinical and pathologic manifestations between both disorders” (Kwakye *et al.*, 2015). Not only is it important to distinguish the two conditions in terms of disease processes, but also the relevance of the high level inhalation worker studies to the low level general population ingestion studies is limited, especially considering the differences in the pharmacokinetics of inhaled versus ingested Mn, and the role of homeostatic mechanisms associated with ingestion exposure of Mn (Yoon *et al.*, 2019).

While I agree that there is merit to the suggestion that EPA consider whether current literature supports moving the Mn from the Draft to the Final CCL 5, I don’t think that this section (especially pp. 10, lines 38 – 43, p. 11, lines 1 – 9) really supports the proposal. I recommend removing that specific text and adding the following points:

- Much research has been conducted on Mn since the Mn RfD (1995) and the associated Health Advisory Level (2004) were developed.
- Physiologically-based pharmacokinetic (PBPK) models are available that correlate exposure to Mn in food and water to Mn in different body compartments, including the globus pallidus of the brain, in potentially susceptible populations (*e.g.*, breast feeding infants, and young children) (see for example, Yoon *et al.*(2019). These models can help in the interpretation of epidemiological studies of Mn in drinking water and in understanding the impact of different concentrations of Mn in drinking water on body burden.
- The epidemiological literature continues to evolve, with some cohort studies of the general population now being available. The Health Canada (2019) report would be a good startingpoint. Note that Health Canada recommends a health-based maximum

¹ Note this was misspelled as Hefeman in the SAB report.

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allowable concentration of Mn in drinking water of 0.12 mg/L based on neurobehavioral findings in rats, with qualitative support from the epidemiological studies, due to limitations in the human studies. This value of 0.12 mg/L may be compared with the EPA Lifetime Health Advisory Level of 0.3 mg/L.

References

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Yoon, M; Ring, C; Van Landingham, CB; Suh, M; Song, G; Antonijevic, T; Gentry, PR; Taylor, MD; Keene, AM; Andersen, ME; Clewell, HJ. 2019. "Assessing children's exposure to manganese in drinking water using a PBPK model." *Toxicol. Appl. Pharmacol.* 380 :114695. doi: 10.1016/j.taap.2019.114695

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Comments from Dr. Aimin Chen

The CCL5 Review Panel was charged to answer four charge questions: 1) Transparency in approach; 2) Process used to derive the draft CCL5; 3) Contaminants that should not be listed; 4) Contaminants that should be added.

1) Were the charge questions to the Committee adequately addressed?

The charge questions to the committee are adequately addressed, using three tiers of responses: Tier 1 for short term actions; Tier 2 for suggestions; and Tier 3 for future considerations/long-term actions. Each of the charge questions have been analyzed and the responses are well reasoned.

2) Are there any technical errors or omissions or issues that are not adequately dealt with in the draft report?

I did not find any technical errors or omissions or issues that are not adequately dealt with.

3) Is the draft report clear and logical?

The draft report is clear and logical.

4) Are the conclusions drawn or recommendations provided supported by the body of the draft report?

The conclusions drawn and recommendations provided are supported by the body of the draft report. These include providing similar approach for expert opinion weighing for microbials and for chemicals, expanding definition for PFAS, removing *Shigella sonnei* from the Final CCL5, and adding additional bisphenols and other saxitoxins to the Final CCL5.

Comments from Dr. Gloria Post

My responses to the quality review questions, as well as a few additional editorial suggestions, are below. Please note that the page and line numbers in my comments refer to the draft dated June 21, 2022 that is posted on the EPA SAB website.

1. *Were the charge questions to the Panel adequately addressed?*

The charge questions were adequately addressed.

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2. *Are there any technical errors or omissions or issues that are not adequately dealt with in the draft report?*

I recommend that the following technical information on 1,4-dioxane and manganese be considered when finalizing the draft report:

1,4-Dioxane

Section 2.2.3 of the draft report (*Prioritizing Contaminants with the Greatest Public Health Concern*; p. 9, lines 7-9) states that “Compounds like 1,4-dioxane, a byproduct that was included in the Draft CCL 5 through nomination, might not be adequately captured in the universe using existing data sources.” This statement does not appear to adequately capture the uses and drinking water occurrence for 1,4-dioxane, and it is suggested that this discussion be clarified and/or expanded.

While it is true that 1,4-dioxane can be formed as a byproduct of surfactants used in consumer products, 1,4-dioxane is also used as a solvent, component or additive in the manufacture of various products (reviewed in NJ DWQI, 2021, <https://www.state.nj.us/dep/watersupply/pdf/14dioxane-rec-sum-appendixa.pdf>). As stated in NJ DWQI (2021), “historically, 90% of 1,4-dioxane was used as a stabilizer for chlorinated solvents in industrial processes, particularly 1,1,1-trichloroethane,” and this use is a major source of groundwater contamination with 1,4-dioxane.

1,4-Dioxane is also known to occur frequently in drinking water, including at levels exceeding the EPA health-based Reference Concentration. 1,4-Dioxane was included in the EPA Unregulated Contaminant Monitoring Rule 3 (UCMR3) for which sampling occurred in 2013-15. In UCMR3, 1,4-dioxane was detected above the Minimum Reporting Level of 0.07 µg/L in 21.9% of the 4,915 public water systems tested and above the EPA health-based Reference Concentration (1 x 10⁻⁶ cancer risk level) of 0.35 µg/L in 6.9% of these water systems. See <https://www.epa.gov/sites/default/files/2017-02/documents/ucmr3-data-summary-january-2017.pdf>

Manganese

The discussion of manganese in Section 2.3.1 (p. 10-11) does not appear to consider a substantial body of information that is relevant to determining whether manganese should be included in the final CCL 5. It is recommended that revisions to the manganese discussion should be considered based on the additional information summarized below:

As stated in the draft SAB CCL5 report, manganese occurs naturally, has beneficial uses, and is an essential element in the diet. The draft report also states that the risks and benefits of regulating manganese should be carefully examined, and that serious health concerns were not identified for manganese. However, numerous human epidemiology and animal toxicology studies, including studies not considered in the draft CCL 5 report, indicate that developmental (i.e., infant) exposures to manganese at levels that occur in drinking water can cause neurobehavioral toxicity. These human and animal studies are reviewed and cited in NJDEP (2021, memo submitted for posting with these

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comments), WHO (2021, <https://apps.who.int/iris/rest/bitstreams/1403892/retrieve>), and Scher et al. (2021, <https://ehp.niehs.nih.gov/doi/epdf/10.1289/EHP7901>).

The draft CCL 5 report (p. 10, lines 33-35) states that the World Health Organization (WHO) set a health-based drinking water standard for manganese of 400 ug/L in 2004. However, WHO (2021) reviewed more recent human and animal studies and established an updated provisional health-based guideline value of 80 µg/L in 2021. Bottle-fed infants were identified as the sensitive subpopulation, and the critical effect was neurodevelopmental toxicity in four well-conducted rat studies.

Other authoritative agencies have also developed drinking water guidance values for manganese specific to exposures to infants. The basis for the four drinking water guidelines mentioned below is reviewed in NJDEP (2021).

The following three drinking water guidance values are based on neurodevelopmental effects in rat studies:

- Minnesota Department of Health (2012) – 100 µg/L. <https://www.health.state.mn.us/communities/environment/risk/docs/guidance/gw/manganese.pdf>
- Health Canada (2016) – 120 µg/L. <https://www.canada.ca/en/health-canada/services/publications/healthy-living/guidelines-canadian-drinking-water-quality-guideline-technical-document-manganese.html>
- INSPQ (Province of Quebec, 2017) - 60 µg/L. https://www.inspq.qc.ca/sites/default/files/publications/2637_guide_sanitaire_manganese_eau_potable.pdf; See also, Valcke et al. (2018) <https://www.mdpi.com/1660-4601/15/6/1293>

Additionally, the New Hampshire Department of Environmental Services (NHDES, 2020; memo submitted for posting with these comments) developed a manganese drinking water guideline protective for infants of 100 µg/L using a different approach than was used for the three other drinking water guidelines mentioned above.

Finally, it is stated on p. 10, lines 34-36, that ATSDR set a maximum manganese intake of 5 mg/day. However, no citation for this statement is provided, and I was unable to locate the source of this information.

Note: NJDEP (2021) and NHDES (2020) are publicly available memos that are not posted online. They were submitted to EPA along with these comments.

3. *Is the draft report clear and logical?*

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Most of the information in the draft report is clear and logical. The comments below are intended to improve the clarity and logic of specific sections of the draft report:

- Section 2.1.1 of the draft report (*Selection Process for Contaminants*; p. 2, lines 23-26) states: “The SAB suggests that the EPA explicitly list the criteria for screening chemical contaminants from the initial universe of contaminants to form the PCCL (i.e., before the point-based scoring is applied). The rationale for selecting 250 chemicals to be included on the Draft CCL 5 is not evident in the FRN or supporting documents.” This suggestion is then provided as a Tier 1 recommendation (p. 3, lines 29-30) as follows: “Provide an explicit list of the criteria used to screen chemical contaminants from the initial universe to form the PCCL before the point-based scoring is applied.”

The basis for this statement and recommendation is unclear to me since the *EPA Technical Support Document for the Draft Fifth Contaminant Candidate List (CCL 5) - Chemical Contaminants* states (p. 18) that “EPA applied the point-based screening system across all chemical contaminants in the CCL 5 Universe to determine which of the approximately 22,000 universe chemicals warranted further consideration during the time- and resource-intensive classification process...” This statement in the EPA document appears to indicate that criteria were not used to screen the 22,000 chemical contaminants in the initial universe prior to applying the point-based scoring. Rather, the point-based scoring was applied to all 22,000 contaminants, and (as discussed in Section 3.5 of the *EPA Technical Support Document for the Draft Fifth Contaminant Candidate List (CCL 5) - Chemical Contaminants*) the 250 contaminants with the highest scores were included in the PCCL.

- Section 2.1.3 of the draft report (*Use of Groups in the Draft CCL 5*; p. 5, lines 33-34) recommends that a table listing the specific PFAS considered by EPA be provided. However, later in the same paragraph of the draft report, it is acknowledged that EPA may be considering PFAS as a whole, rather than as individual compounds, as follows: “There are also multiple methods for bulk organofluorine analysis that can quantify concentrations of aggregated PFAS without indicating which specific chemicals are present (McDonough et al., 2019). These methods may be useful if the EPA prioritizes broader occurrence and exposure of PFAS, rather than individual compounds.”

Regarding this issue, the *EPA Technical Support Document for the Draft Fifth Contaminant Candidate List (CCL 5) - Chemical Contaminants* states that “more than 4,000 PFAS have been manufactured and used... which would make listing PFAS individually on the Draft CCL 5 difficult and challenging” and that it “proposes to list PFAS as an all-inclusive group (except for PFOA and PFOS).” This EPA document also states that “listing [PFAS and other chemicals as groups] on the Draft CCL 5 does not necessarily mean EPA will make subsequent regulatory decisions for the entire group. Rather, EPA will evaluate scientific data on the listed groups, subgroups, and individual contaminants to inform any regulatory determinations for the group, subgroup, or individual contaminants in the group.”

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As such, it is unclear whether it is possible for EPA to provide a table that lists the specific PFAS that it considered. Additionally, this recommendation does not appear to be consistent with the related Tier 1 recommendation at the end of this section (p. 5, lines 37-38): “Provide information on the criteria for grouping the individual PFAS... within CCL 5.”

Finally, Section 2.4.1 of the draft report (*Chemical Contaminants Recommended for Consideration or Inclusion*; p. 14, lines 44 – p. 15, line 3) recommends that EPA use an expanded definition of PFAS, such as the definition established by OECD which defines PFAS as any compound with at least one fully fluorinated methyl or methylene carbon atom (Wang et al., 2021). The draft report states that this definition would encompass more than 9,500 compounds. Recommendation of this expanded definition, which includes even more compounds than the current EPA definition, does not appear to be consistent with recommending that EPA provide a table listing the PFAS that it considered (Section 2.1.3).

- Section 2.1.4 of the draft report (*Control of Communicable Disease Manual*; p. 6, lines 22-26) and the related Tier 1 recommendation (p. 6, lines 31-33) recommend that EPA verify the accuracy of the content of the 18th (2005) edition of the Control of Communicable Disease Manual against the 20th (2014) or 21st (2022) editions. It is unclear why it is not recommended that information from the most recent (2022) edition be used by EPA in the finalize CCL 5 and that the 2022 edition be cited instead of the older (2005) edition.
- Section 2.2.1 of the draft report (*Assessment of potential drinking water exposure*; p. 7, lines 8-9) and the related Tier 1 recommendation (p. 7, lines 35-36) request clarification of the process for “selecting contaminants for monitoring under the UCMR” for contaminants with “either health effects or occurrence data (but not both).” It is my understanding that the process for developing the list of contaminants to be included in UCMR is separate from the process for developing a CCL. As such, the relevance of this recommendation to development of CCL 5 should be clarified in the SAB report.

4. *Are the conclusions drawn or recommendations provided supported by the body of the draft report?*

In general, the conclusions and recommendations are supported by the body of the draft report.

However, clarification is needed as to whether the following sentence (in the recommendation at the top of p. 3 of the cover letter for the SAB CCL 5 report) applies only to microbial contaminants or to both microbial and chemical contaminants: “The SAB recommends renaming “health effects” to “health risks” in the CCL 5 documents.”

In the body of the report (p. 8, line 43 – p. 9, line 2), the use of the term “health risks” rather than “health effects” is recommended, but it is not stated that this applies specifically to microbial

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contaminants. However, the Tier 1 recommendation on this topic (p. 9, line 28) specifies that this recommendation applies to microbial contaminants.

Additionally, in the same recommendation (top of p. 3 of the cover letter), the first two sentences of the recommendation are about prioritization based on health risks and renaming “health effects” to “health risks.” The next two sentences are about adding or removing specific contaminants in CCL 5. These two parts of the recommendation do not appear to be directly related, and it is suggested that this recommendation be divided into two separate recommendations.

Additional editorial suggestions:

- Throughout the report, it is suggested that consistent units be used, especially within a discussion of a specific contaminant. For example, both µg/L and mg/L are used in the section on manganese on p. 10-11.
- p. 6, line 1-2. Suggest adding the words “occurrence at” as follows: “Thus, occurrence at concentrations relevant to human health effects may often not be captured in the UCMR 5 approach.”
- p. 16, lines 14-15. Regarding microplastics (MPs), suggest changing “MPs can absorb organics, particularly polycyclic aromatic hydrocarbons (PAHs). . .” to “MPs can absorb organics such as polycyclic aromatic hydrocarbons (PAHs). . .” to convey that other types of organics may also be highly absorbed.
- p. 16, lines 25-26. (*Nanoparticles* section). This sentence does not appear to be correctly worded and needs to be revised (“...considered at very least in the PCCL.”)

Comments from Dr. Peter Thorne

1. Were the charge questions to the Panel adequately addressed?

Yes, the Panel did a comprehensive job and addressed the charge questions thoroughly.

2. Are there any technical errors or omissions or issues that are not adequately dealt with in the draft report?

None that I saw.

3. Is the draft report clear and logical?

In the cases where there is no specific recommendation for a tier 1, 2, or 3, the document could simply not list that tier instead of stating there is no recommendation for that tier.

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It is not clear to this reviewer why the text in the report on *Legionella pneumophila* being unregulated contaminants is insufficient.

What can the EPA do to replace the USGS NAWAQ monitoring effort?

Replace “developing infant” with “fetus” in Organophosphate Esters page 15, line 16.

The Panel suggests specifically listing other saxitoxins. Should it also be recommended to include the full suite of 50+ microcystins? Could the request be to list “saxitoxins”.

4. Are the conclusions drawn or recommendations provided supported by the body of the draft report?

Yes, in most cases.

I note that the text regarding exclusion of Mn does not appear to draw any conclusion.

Comments from other SAB Members

Comments from Dr. Joseph Arvai

1. Were the charge questions to the Panel adequately addressed?

In my opinion, yes.

I particularly agree with the comments made under heading 2.2.2 (Consideration of sensitive populations). In order to adequately and defensibly evaluate the risks from unregulated contaminants, the potential (negative) consequences for affected populations needs to be assessed.

And, given our own research on the matter, I also agree with the recommendation that EPA consider the inclusion of microplastics in future contaminant candidate list (CCLs).

2. Are there any technical errors or omissions or issues that are not adequately dealt with in the draft report?

Many of the toxicological concepts and recommendations discussed in the SAB CCL5 report fall well outside of my areas of expertise. However, in my view, the report was clearly written and thoughtfully contextualized. Thus, to the best of my ability, I did not detect any (a) technical errors or (b) omissions or (c) issues that required additional attention in the draft report.

3. Is the draft report clear and logical?

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In my opinion, yes.

4. Are the conclusions drawn or recommendations provided supported by the body of the draft report?

In my opinion, yes.

Comments from Dr. Roland Benke

CCL 5 responses to quality review questions:

1. Yes.
2. One minor question on units was transmitted separately as a comment in the margin.
3. Yes. Very few editorial suggestions were provided separately. Nicely done!
4. Yes.

Editorial comments have been provided separately.

Comments from Dr. Tami Bond

I note that the CCL 5 and the SAB draft report on its contents do not lie within my field of expertise. Thus, I read the report mainly with attention to the process and logic used by the evaluating subcommittee that developed the draft.

1. Were the charge questions to the Panel adequately addressed?

To the best of my ability to assess, the charge questions to the Panel were well covered.

2. Are there any technical errors or omissions or issues that are not adequately dealt with in the draft report?

To the best of my knowledge, there are no technical errors, and the evaluation in the draft report provides sufficient justification for addressing and resolving any remaining issues between the EPA SAB and the authors of the CCL5 report.

3. Is the draft report clear and logical?

I find that the draft report is well-organized and that the logic of the evaluating subcommittee is particularly well explained.

4. Are the conclusions drawn or recommendations provided supported by the body of the draft report?

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I agree with the recommendations in the draft report.

Comments from Dr. Mark Borsuk

1. *Were the charge questions to the Panel adequately addressed?*

Yes, the Panel adequately addressed all the charge questions presented to them,

2. *Are there any technical errors or omissions or issues that are not adequately dealt with in the draft report?*

No, I could not find any technical errors, omissions, or inadequately handled issues.

3. *Is the draft report clear and logical?*

Yes, the report is clearly written and logical. I did find a few typos and word omissions, which I can send along separately.

4. *Are the conclusions drawn or recommendations provided supported by the body of the draft report?*

Yes, however I do feel that the Panel could provide more detail on what they are recommending with regard to “machine learning.” It is mentioned in the last bullet point of the cover letter and in section 2.2.1 of the draft report. Machine learning represents a broad set of tools for data analysis that generally speaking focuses on the identifications of patterns in data, rather than revealing causality or mechanisms. Therefore, it is not clear to me why it is being proposed over more conventional data analysis or model-based statistical inference as a complement to expert judgement.

Comments from Dr. Sylvie Brouder

Preliminary Quality Review Comments submitted by S.M.Brouder

Quality Review of EPA’s Draft Fifth Contaminant Candidate List (CCL 5)

1. Were the charge questions to the Committee adequately addressed?

Yes although see comments 3 and 4 for some suggestions on clarifications for text and recommendations.

2. Are there any technical errors or omissions of issues that are not adequately dealt with in the draft report?

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Yes. (Please make sure the list of acronyms and abbreviations is complete – UCMR is missing.)

3. Is the draft report clear and logical?

In general, yes. There is occasional use of language that may be jargon and/or that seems overly vague. For example, the 2nd paragraph on occurrence data ends with a sentence that requests more information on the use of “production values” (pg 4/L25). From the preceding text, it appears that “production values” are a form of occurrence data but an additional sentence or two on what these values are and why there is concern that point assignments for these data are on the lower end of the range would add clarity. Likewise, in the subsequent paragraph, is there a need for the SAB to specify what should be considered “standard methods” (pg4/L32) versus “other methods” or are these terms sufficiently specific for those with expertise in contaminants to be able to address the SAB’s concern. A couple of other methods are identified in the Tier 1 recommendations (pg 5/L12) but is this sufficient for clarity regarding the expectation for the standard methods.

Occasionally, paragraphs end in or are largely declarative statements and it is unclear what the SAB wants EPA to do. For example, the last sentence regarding including cyanotoxins as a group (pg6/L1-2) could be interpreted as the SAB stating its assumption about EPA’s justification and we just want to make sure they spell this out. Or it could be interpreted as a statement suggesting that EPA had other data beyond the UCMR for the listing. Some specificity to this request for clarification might be helpful to EPA. Similarly, in section 2.2.1 (pg7), there is a statement on limitation for occurrence estimates for pesticides (L26-28) but no particular suggestion. In the text on recommendations for reconsideration/removal of chemicals, the section on vanadium does conclude with a sentence summarizing SABs analysis/recommendation (pg 12, L13-15) that is then reflected in the Tier 2 recommendation. However, text on Mn and W do not end with summary statements on SAB perspectives and seem a missed opportunity to help the EPA focus on next steps.

Finally, the suggestion to “use machine learning” for contaminant identification seems oddly juxtaposed against expert judgement (pg7/L10). Are there other statistical approaches that should be explored? What is the rationale for specifying ML versus other analytical/computational approaches? Is it about the sheer volume of data or is it about the search for patterns? Is there a reference or two that can be cited in support of this suggestion or details regarding the outcome of the application that might be useful to EPA?

4. Are the conclusions drawn or recommendations provided supported by the body of the draft report?

In general, yes. From my perspective, the only recommendation for which the text might require some expansion is that concerning adding a group of antimicrobial resistance genes (pg 15). These are indicators but not themselves contaminants. Why are these in a separate category from

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microbial contaminants? Presumably the genes would be indicators of the microbial contaminants. Does the CCL already include non-contaminants that are simply indicators of contaminants and/or even genes? The SAB notes that these can be important indicators and useful input to the PCCL process but the justification for the leap to including them on the CCL 5 is not obvious.

I offer the following minor points for consideration for improvement of text in support of recommendations.

- Recommendations for Transparency of Approach (2.1.1; pg. 3). The last Tier 1 suggestion refers to 250 chemicals on the CCL 5 as a “threshold.” The first paragraph of 2.1.1, suggests that 250 was the total number selected and not necessarily a threshold number. Is the recommendation to explain why only 250 were selected or why a minimum of 250 had to be selected?
- The Tier 2 recommendation for clarification on valid data for CISs (pg5/L18), seems an important part of the overall request for clarification on rejection/inclusion of occurrence data. Simply clarifying which data are considered valid would seem in keeping with the Tier 1 requests. However, the preceding text suggests that the literature review might not be complete and elaborating on process for an expanded literature review might be a Tier 2 level effort or even a Tier 3 effort?
- Concerning recommendations for Microbial Contaminants for Consideration, it seems that simply creating a group for pathogenic mycobacteria would not be a heavy lift although populating it might be. Given the clarity and direction offered by creating that grouping, this recommendation might warrant a Tier 1 designation rather than Tier 2.

Comments from Dr. Alison Cullen

Initial Comments regarding SAB Quality Review of “Review of the EPA’s Draft Fifth Contaminant Candidate List (CCL5).

I commend the SAB panel for its careful review of the EPA’s Draft Fifth Contaminant Candidate List. Below are the quality review questions with responses.

1) Were the charge questions to the Committee adequately addressed?

The panel has addressed the charge questions fully and adequately.

2) Are there any technical errors or omissions or issues that are not adequately dealt with in the draft report?

The included content is technically sound.

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One area where additional detail and attention would be helpful is with respect to sensitive subpopulations. The Review report suggests that EPA further clarify the approach applied in identifying and considering sensitive subpopulations.

Charge Question 2 reads

“Please comment on the process used to derive the Draft CCL 5, including but not limited to, the CCL 5 improvements to assess potential drinking water exposure, consider sensitive populations, and prioritize contaminants that represent the greatest potential public health concern.”

The Report notes that EPA considers the effect of contaminants on sensitive populations such as infants, children, pregnant women, the elderly, and individuals with a history of serious illness or other subpopulations. The language here would benefit from being more explicit regarding the *other* subpopulations. In particular, are overburdened communities considered specifically through an environmental justice lens?

3) Is the draft report clear and logical?

Yes, the draft report is clear and logical.

4) Are the conclusions drawn or recommendations provided supported by the body of the draft report?

Yes, the conclusions and recommendations provided are well supported by the body of the draft report.

Comments from Dr. John Guckenheimer

Edits on the SAB CCL5 report:

P12,L31: "W" should be "V".

P13, L7: Replace "logs" by "orders of magnitude".

Comments from Dr. David Keiser

1) Were the charge questions to the Committee adequately addressed?

- Yes. It appears that these questions were thoroughly addressed.

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2) Are there any technical errors or omissions or issues that are not adequately dealt with in the draft report?

- I did not see any technical errors or omissions.

3) Is the draft report clear and logical?

- Yes. The draft is well written and easy to follow. I have three comments:
 - In the introductory/summary comments, SAB recommends removing *Shigella sonnei* and adding additional bisphenols and other saxitoxins. However, in the more detailed recommendations, SAB mentions several other contaminants for reconsideration/removal or contaminants that should be added. I suggest that SAB consider whether any of these other contaminants should be highlighted in the introduction.
 - On page 4, the report discusses the possibility of considering urban runoff data. The report states that EPA should “provide a rationale or justification for not including these data.” On page 5, the report seems to take a stronger stance and says that “the SAB suggests that the EPA include urban runoff occurrence data in parallel with wastewater occurrence data.” I lean towards the first stance (suggesting that EPA consider), but happy to hear from the report authors if the statement should be stronger. I would also like to hear from the authors if a broader statement should be included that includes urban and non-urban runoff (i.e., agricultural runoff).
 - I believe there is a typo on line 26 of page 9 in the sentence “Clarify the reason for using a 10-year timeframe the supplemental literature review...” Perhaps missing a word between timeframe and the supplemental?

4) Are the conclusions drawn or recommendations provided supported by the body of the draft report?

- Yes. The conclusions appear supported by the body of the draft report.

Comments from Dr. Angela Leung

1. Were the charge questions to the Panel adequately addressed? YES
2. Are there any technical errors or omissions or issues that are not adequately dealt with in the draft report? NO
3. Is the draft report clear and logical? YES
4. Are the conclusions drawn or recommendations provided supported by the body of the draft report? YES

Comments from Dr. John Morris

The review document is clearly written, provides logical rationales for its recommendations and is internally consistent with respect to the summary recommendations and the text supporting

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them. I offer only a few comments. These are not reflective of substantive concerns but would be better described as editorial comments to improve clarity. My comments are organized relative to the four quality review questions that were identified in the Chair's memo.

Question 1) The review adequately addressed the charge questions. The review provided thoughtful text that focused on: the clarity and transparency of the EPA report; the process through which the EPA derived its recommendations; the possibility that certain contaminants should not be included in the CCL 5 listing (including peer reviewed information); possible contaminants that should be added to the CCL 5 list (with peer-reviewed information). Overall, the review was highly responsive to the charge questions. I concur with all the recommendations, including the recommendations for contaminants that should be considered for inclusion.

Question 2) I am not aware of any technical errors or omissions in the draft report.

Question 3). Overall, the draft report is clear and logical. I offer a few comments which are aimed at enhancing clarity of the draft report.

From an editorial sense, it is somewhat confusing that the recommendation for explaining the rationale for carrying over most of the microbial contaminants from prior CCLs is listed as a Tier 2 item rather than Tier 1 (bottom of p3). The confusion lies from the fact that the earlier text p3, line 6 says that the "EPA provided an incomplete explanation of the rationale...". Most of the other descriptions in the text rely on less "harsh" wording, such as "would enhance clarity" or the like, the other descriptions do not state something is incomplete. Perhaps line 6 should merely state "greater clarity would be provided if..." or something similar.

The section on criteria for inclusion or rejection of occurrence data is well conceived and clearly written, identifying both general concerns and also listing specific examples. I note that the text of this section clearly indicates the needed for the EPA document to more clearly clarify its acceptance/rejection criteria, but also avoids making any specific recommendations on what would or would not be a problematic practice. For example, the draft review text highlights that the EPA should indicate whether or not state agency reports that aren't peer reviewed should be included in the CCL evaluation, but the draft review makes no indication whether or not including a non-peer reviewed report would be problematic. Presumably this is intentional.

With respect to the grouping of contaminants for regulatory purposes (p5-6) I would note that from a toxicological perspective it makes little sense to group compounds with "diverse modes for action and potencies, as well as widely varying occurrence" (p5, line 35-36). The draft review text does state that the "SAB finds that it is useful to have some contaminants listed as groups" but provided no perspectives on when grouping may or may not be useful. Perhaps this is intentional, however, it might enhance general clarity of some perspectives (or perhaps some examples) of when grouping might be useful versus when it is not.

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In addressing the assessment of potential drinking water exposure section, the draft review suggests the employment of machine learning (p7, line 10). Is this recommendation adequately specific? Machine learning, in my view, is a fairly broad term.

There may be a subtle inconsistency in the issue of limits of detection in the text of section 2.2.1 (p7, line28) versus the recommendations (p8, line 7). The text simply states there are uncertainties in method detection whereas the recommendations indicate the need for range and median method detection limits. These two statements are not inconsistent with each other, but the recommendation is considerably more specific than the preceding text and it may catch the reader by surprise.

There may be an inconsistency in the terminology used to describe transformation products. On page 9, lines 5-6, transformation products are indicated to include metabolites and degradates. Many other portions of the text describe the need to assess metabolites and degradates (e.g., p4, p9), but on p4, line6, the text refers to, "the likelihood of..pesticides to degrade into longer-lived metabolites." Is the exclusion of degradates from this description intentional? If so, it might be explicitly stated. Might it be preferable to use the term "transformation products" uniformly throughout the text because it is the more generic term?

Another terminology question deals with the use of antimicrobial versus antibiotic. A section on p15 is entitled "Antimicrobials" yet the subsequent text focusses only on antibiotics. This is somewhat confusing.

Although perhaps poorly relevant to the review, the indication that bisphenols, OP esters and phthalates can adhere onto microplastics raises the question of whether the analytical methodologies for these compounds will detect compound adsorbed onto plastics. If this is known with certainty than including this information in the review might be useful.

Question 4). In general, the conclusions that are drawn and recommendations provided are well supported by the body of the draft report. The specific recommendations provided at the end of each suggestion flow from the preceding text of that section (except for the small concern about detection limits that I highlighted above). The cover letter to the Administrator lists several key findings. These are well supported in the subsequent text and the text appropriately highlights the findings that are listed in the cover letter as key.

One minor concern deals with the section on manganese and whether or not it should be included in the CCL 5 listing (p 10-11). The point of this section (e.g. the bottom line) doesn't stand out. The fundamental conclusions relative to Tungsten and Vanadium are quite clear. Is the fundamental issue relative to manganese that the newer information that is highlighted in the draft review text should be included in the EPA evaluation? I so, a concluding sentence such as that at the end of the Vanadium section ("...SAB recommends careful consideration..and incorporating the information provided..") would greatly aid in clarifying intent.

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Comments from Dr. Amanda Rodewald

Review of the EPA's Draft Fifth Contaminant Candidate List (CCL 5)

1) Were the charge questions to the Committee adequately addressed?

Yes.

2) Are there any technical errors or omissions or issues that are not adequately dealt with in the draft report?

Two minor points:

The section discussing the Adenovirus on page 13 opens with the statement that "The SAB is concerned about the EPA potentially overstating the health risks of adenovirus," but the remainder of the paragraph did not seem to provide justification or evidence for that statement. Instead, the paragraph focused on resistance and disinfectants without explicit link to the opening statement. There also was no mention of adenovirus in the Tier recommendations.

Page 5, line 7 – remove colon between from and water

3) Is the draft report clear and logical?

Yes. I especially liked how the committee used Tiers to categorize recommendations. That seemed very helpful.

Regarding 2.2.2 Consideration of sensitive populations, I want to be sure that my understanding is correct. It seems that the committee is not recommending that immunocompromised individuals be considered but rather only that the Agency should clarify why they are not considered. If that is not the case, then the wording is unclear.

4) Are the conclusions drawn or recommendations provided supported by the body of the draft report?

Yes

Comments from Dr. Emma Rosi

This Committee Review Report is thorough and provides useful recommendations to the EPA to improve the draft CCL 5. I agree with the Committee Report that the EPA documentation adequately described the processes used to generate the CCL 5. The approaches used by the EPA are clear and thorough and the improvements suggested by the committee will strengthen the draft CCL 5 documentation. The recommendations for Charge Question 1 will strengthen the transparency of the approach used by the EPA. I also agree with the need for more

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information on the rationale for excluding urban run-off. I agree with the recommendations associated with Charge Question 2 and concur with the committee that the EPA should include language about the ending of the NAWQA program. The approach used to develop the CCL 5 relies on data collected by the NAWQA program and the implications of the cessation of this monitoring program should be addressed. This may represent a future potential data gap that may hamper future CCLs. There is a typo in Tier 3 (page 12), it should be V not W, in the phrase “Mn and W on future CCLs”. I agree with the suggestion to expand the list to include other Bisphenols compounds that are being used to replace BPA. I strongly agree with the committee that the EPA needs to clarify how they are considering PFAS, because this represents such a large group of compounds. It is not clear how these PFAS compounds will be prioritized for monitoring and reporting. I also agree that it would be valuable to consider including both antimicrobials and antimicrobial resistant genes and consider microplastics in future CCLs.

Comments from Dr. Godfrey Uzochukwu

1. Were the charge questions to the Panel adequately addressed?

• ***Charge Question 1: Transparency in approach***

Please comment on whether the Federal Register Notice (FRN) published on July 19, 2021 (86 FR 37948) (Docket ID Number EPA-HQ-2018-0594) and associated support documents are clear and transparent in presenting the approach used to list contaminants on the Draft CCL 5. If not, please provide suggestions on how EPA could improve the clarity and transparency of the FRN and the support documents.

Response: The CCL development process and documentation are clear and transparent. Decisions used to generate the universe of potential contaminants, the screening process used to generate the Preliminary CCL (PCCL), and the ranking and prioritization of contaminants to produce the Draft CCL 5 were clearly presented. Over 22,000 compounds which were screened for health effects and occurrence.

This reviewer concurs with SAB’s suggested selection process for contaminants and recommendations for Tiers 1, 2 and 3; listing contaminants as groups and recommendations for Tiers 1 and 2 and verification of the accuracy of content citing in the 18th edition against the 20th (Heymann, 2014) or 21st (Heymann, 2022) editions in the Control of Communicable Disease Manual.

• ***Charge Question 2: Process used to derive the Draft CCL 5***

Please comment on the process used to derive the Draft CCL 5, including but not limited to, the CCL 5 improvements to assess potential drinking water exposure, consider sensitive populations, and prioritize contaminants that represent the greatest potential public health concern.

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Response: This reviewer concurs with SAB's assessment of potential drinking water exposure and recommendations for Tiers 1, 2 and 3; consideration for sensitive populations and recommendations for Tiers 1, 2; prioritizing contaminants with the greatest public health concern and recommendations for Tiers 1, 2 and 3.

- **Charge Question 3: Contaminants that should not be listed**

Based on your expertise and experience, are there any contaminants currently on the Draft CCL 5 that should not be listed? Please provide peer-reviewed information or data to support your conclusion.

Response: This reviewer concurs with listing tungsten, manganese, vanadium; recommendations for Tiers 2 and 3 and microbial contaminants recommended for reconsideration or removal and recommendations for Tiers 1 and 2.

Question: Why was Iron (Fe) not included on the list?

- **Charge Question 4: Contaminants that should be added**

Based on your expertise and experience, are there any contaminants which are currently not on the Draft CCL 5 that should be listed? Please provide peer-reviewed information or data to support your conclusion.

Response: None. Are there any technical errors or omissions or issues that are not adequately dealt with in the draft report?

None

2. Is the draft report clear and logical?

Yes

3. Are the conclusions drawn or recommendations provided supported by the body of the draft report?

Yes