

**From:** [D'Souza, Rena \(NIH/NIDCR\) \[E\]](#)  
**To:** [Levine, Rachel \(HHS/OASH\)](#); [Iademarco, Michael \(HHS/OASH\)](#); [Boateng, Sarah \(HHS/OASH\)](#)  
**Cc:** [Simon, Dina \(NIH/OD\) \[C\]](#); [Calsyn, Maura \(HHS/OASH\)](#); [Handley, Elisabeth \(OS/OASH\)](#); [Oh, Kathy \(OS/OASH\)](#); [Lee, Kinbo \(HHS/OASH\)](#); [Gray, Oneika \(HHS/OASH\)](#); [Fisher, Megan \(HHS/OASH\)](#); [Schwetz, Tara \(NIH/OD\) \[E\]](#); [Woychik, Rick \(NIH/NIEHS\) \[E\]](#); [States, Leith \(HHS/OASH\)](#)  
**Subject:** Re: Fluoride Discussion  
**Date:** Wednesday, June 29, 2022 6:08:22 AM  
**Attachments:** [image001.png](#)  
[RDS Fluoride summary 2022-06 \(v3a\).docx](#)

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Thank you for this summary VADM Iademarco.  
Minor edits and 2 comments from me for you to consider.

Best, Rena

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**From:** Levine, Rachel (HHS/OASH) <Rachel.Levine@hhs.gov>

**Date:** Tuesday, June 28, 2022 at 8:15 PM

**To:** Iademarco, Michael (HHS/OASH) <Michael.Iademarco@hhs.gov>, Boateng, Sarah (HHS/OASH) <Sarah.Boateng@hhs.gov>

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**Subject:** RE: Fluoride Discussion

RADM Iademarco, Sounds good, Thanks, RLL

**Rachel L. Levine, M.D.**

ADM, United States Public Health Service

Assistant Secretary for Health

Office of the Assistant Secretary for Health

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[hhs.gov/ash](https://hhs.gov/ash)

#### Summary of OASH, NIH meeting, June 7, 2022

1. A draft sent to NASEM to review, which combined the content and an earlier version of the meta-analysis, is on the FAN website, and therefore, the information is in the public domain.
2. NAM identified significant concerns twice and indicated that the data did not support a “hazard classification,” and we just learned that, with an earlier version of the meta-analysis, the Editor indicated that the manuscript would have to be updated with more recent work before it would be sent out for peer review. ~~Therefore, it wasn’t officially rejected because it was never peer reviewed at (b)(5).~~
3. The NTP BSC has not taken up this issue previously.
4. The NIEHS/NTP scientist authors for both products are intramural within the Division of the National Toxicology Program at NIEHS. The meta-analysis was pulled out of the monograph (due to concerns raised in the NAM review) and has been updated since the NAM review.
5. There are reviews with constructive criticisms with NIEHS from NIDCR, CDC, and FDA. (I still have not been able to ascertain whether there are two from OASH.) NIH has written comments from NIDCR, CDC and the FDA for the meta-analysis paper, and we have written comments from NIDCR for the SoS monograph, but we have not seen written comments from CDC and FDA for the monograph. OASH submitted comments on both documents after the meeting.
6. We all agreed that we cannot agree to disagree, and the ASH asked NIH to come up with a consensus approach.
7. The NIH consensus approach is for Rick with NIH OD support to request a BSC review of the monograph (qualitative systematic review) and separately the manuscript (meta-analysis and quantitative systematic review) asking for recommendations that a) primarily assess the sufficiency of the authors adjudication of the intra-HHS comments) and b) secondarily any additional insights into the quality of the work.
8. The choice of the BSC workgroup members is important and will aim to be representative of toxicology, epidemiology, statistical disciplines and will include experts in fluoride (fluoride metabolism) with consideration for inclusion of an oral health expert. Rick will seek suggestions of WG members (i.e., the experts) from OASH, CDC, FDA, and NIDCR and work with the BSC chair to finalize a list of WG members. This list will be vetted by OASH, NIH (OD and NIDCR), CDC, and FDA. The experts can be government or outside of government.
9. Both are NTP products. The SoS is the NTP monograph, and the meta-analysis is proposed as a peer reviewed paper that would be resubmitted to (b)(5). Rick will use the BSC recommendations as input to decide a) whether to publish a revised version of the monograph on the official NTP web site after vetting with Drs. Tabak and Schwetz and with the ASH and b) whether and how - to resubmit a revised version of the meta-analysis manuscript to a peer reviewed journal.
10. NIH will keep CDC (NIOSH and (b)(5)), FDA, and OASH updated regularly.
11. Iademarco thinks it is unresolved as to whether the monograph could be published before or without the meta-analysis, but agrees a simultaneous option is acceptable. Simultaneous posting of the monograph on the official NTP web site and resubmission of the meta-analysis to a peer reviewed journal is preferable to NIH.
12. Before publication of either product, an OASH-NIH leadership group would reconvene to formulate a communication strategy that at a minimum addresses the balance between the toxicology findings and oral health and overall well-being.

#### Additional Background added after the meeting

- The first draft NTP monograph (Sept 2019) did not contain the meta-analysis.

**Commented [DR([1]:** If a manuscript is not sent out for peer review it is considered ‘rejected’ as Editors are authorized to assess quality prior to further processing.

**Commented [DR([2]:** It would be good to present a firm rationale for why a BSC review is being conducted following 2 successive reviews provided by the Academies. The latter is accepted as the highest level of unbiased review available in the scientific community.

- The NASEM comments on the draft NTP monograph suggested that a meta-analysis be conducted.
- NASEM report, Summary Human Evidence, page 5. "The committee notes that NTP did not conduct a meta-analysis. Given that meta-analysis is a useful tool for aggregating and summarizing data and analyzing comparable studies, the committee strongly recommends that NTP reconsider its decision not to perform one."
- The decision was made to separately publish the SoS monograph and meta-analysis. The SoS monograph is a broad compilation of the literature (i.e., a systematic review) and provides a **qualitative** assessment of the association between fluoride exposures and cognitive effects in adults and the association with IQ and with neurodevelopment and other cognitive outcomes in children. The meta-analysis only applies to the subset of studies that evaluated fluoride exposure and children's IQ, provides a **quantitative** assessment, and goes beyond the initial scope of the project. Therefore, the meta-analysis was removed from the monograph and expanded and is being submitted for publication in a peer-reviewed journal.
- The SoS monograph differs from the Sept 2019 NTP monograph submitted to NASEM in that it (1) is revised based upon comments from NASEM on both the Sept 2019 and 2020 drafts and (2) it no longer applies hazard classification to the scientific evidence on fluoride exposure and neurodevelopmental and cognitive health effects in adults or children. It provides a qualitative rating of the confidence in the scientific evidence for fluoride exposure and neurocognitive health effects.

Drafted from Iademarco notes

Review and finalized by Schwetz

2022-06

**From:** Iademarco, Michael (HHS/OASH) <Michael.Iademarco@hhs.gov>

**Sent:** Tuesday, June 28, 2022 3:26 PM

**To:** Levine, Rachel (HHS/OASH) <Rachel.Levine@hhs.gov>; Boateng, Sarah (HHS/OASH) <Sarah.Boateng@hhs.gov>

**Cc:** Simon, Dina (NIH/OD) [C] <(b)(6)>; Calsyn, Maura (HHS/OASH) <Maura.Calsyn@hhs.gov>; Handley, Elisabeth (OS/OASH) <Elisabeth.Handley@hhs.gov>; Oh, Kathy (OS/OASH) <Kathy.Oh@hhs.gov>; Lee, Kinbo (HHS/OASH) <Kinbo.Lee@hhs.gov>; Gray, Oneika (HHS/OASH) <Oneika.Gray@hhs.gov>; Fisher, Megan (HHS/OASH) <Megan.Fisher@hhs.gov>; Schwetz, Tara (NIH/OD) [E] <(b)(6)>; D'Souza, Rena (NIH/NIDCR) [E] <(b)(6)>; Woychik, Rick (NIH/NIEHS) [E] <(b)(6)>; States, Leith (HHS/OASH) <Leith.States@hhs.gov>

**Subject:** RE: Fluoride Discussion

ADM Levine, Attached is a meeting summary that Tara and I worked out, just to capture the approach. Anyone copied, should let me know if there are any concerns. Based on communications with the NIH, these steps are underway. V/r, Michael

-----Original Appointment-----

**From:** Levine, Rachel (HHS/OASH) <[Rachel.Levine@hhs.gov](mailto:Rachel.Levine@hhs.gov)>

**Sent:** Thursday, June 2, 2022 8:02 PM

**To:** Levine, Rachel (HHS/OASH); Levine, Rachel (HHS/OASH); Schwetz, Tara (NIH/OD) [E]; D'Souza, Rena (NIH/NIDCR) [E]; Woychik, Rick (NIH/NIEHS) [E]; Iademarco, Michael (HHS/OASH); Boateng, Sarah (HHS/OASH)

**Cc:** Simon, Dina (NIH/OD) [C]; Calsyn, Maura (HHS/OASH); Handley, Elisabeth (OS/OASH); Oh, Kathy (OS/OASH); Cure, Kelly (OS/OASH) (CTR); Lee, Kinbo (HHS/OASH); Gray, Oneika (HHS/OASH); Fisher, Megan (HHS/OASH)

**Subject:** Fluoride Discussion

**When:** Monday, June 6, 2022 5:30 PM-6:00 PM (UTC-05:00) Eastern Time (US & Canada).

**Where:** <https://hhsgov.zoomgov.com> (b)(6)

(b)(6)

ADM Rachel Levine is inviting you to a scheduled ZoomGov meeting.

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