AADOCR
American Association for Dental, Oral, and Craniofacial Research

April 28, 2023

Kathleen M. Gray, Ph.D.
Chair, NTP Board of Scientific Counselors
c/o Office of Policy, Review, and Outreach

National Institute of Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, NC 27709

**Re: National Toxicology Program Monograph on the State of the Science Concerning Fluoride Exposure and Neurodevelopmental and Cognitive Health Effects: A Systematic Review.**

*via website:*
*https://tools.niehs.nih.gov/webforms/index.cfm/main/formViewer/form_id/341/contentid/954127*

The American Association for Dental, Oral, and Craniofacial Research (AADOCR) is the leading professional community for multidisciplinary scientists who advance dental, oral, and craniofacial research. We appreciate the opportunity to share our thoughts on the National Toxicology Program's (NTP) Monograph on the State of the Science Concerning Fluoride Exposure and Neurodevelopmental and Cognitive Health Effects: A Systematic Review report. AADOCR recognizes the NTP's efforts toward the testing, research, and analysis of agents of concern to identify toxic and biological effects, provide information that strengthens the science base, and inform decisions by health regulatory and research agencies to safeguard public health. AADOCR also commends the Board of Scientific Counselors (BSC) for their efforts to determine whether the NTP adequately addressed concerns regarding the methodology, conclusions, clarity, and transparency of the monograph.

There is a large body of research – over 7 decades' worth – pointing to the safety and effectiveness of fluoride to prevent tooth decay. Dental caries (tooth decay) remains the most prevalent chronic disease in both adults and children and fluoridated water is a simple, equitable, and effective strategy that can help millions of people[1,2]. An especially higher prevalence of tooth decay has been observed among children from low-income and/or minority families[2]. The Oral Health in America: Advances and Challenges report affirms that community water fluoridation (CWF) is "a cost-effective community-based mode of prevention, benefits everyone, including children in low-income families"[3]. It also advocates for the expansion of CWF that intentionally targets lower income counties as it could yield greater benefits in reducing both dental caries and income disparities in dental caries[3]. As recent as December 2021, the United States

T +1.703.548.0066 | F +1.703.548.1883 | 1619 Duke Street, Alexandria, VA 22314-3406, USA | www.aadocr.org

Preventative Services Task Force (USPSTF) continued to recommend that primary care clinicians prescribe oral fluoride supplementation starting at age 6 months for children whose water supply is deficient in fluoride[4] – providing support for the use of fluoride at appropriate doses. Therefore, it is crucial that the NTP monograph clearly and accurately communicates any risks associated with fluoride exposure as communicated an unsubstantiated risk may further exacerbate oral health challenges in lower socio-economic communities.

**AADOCR supports the NTP completing the peer review process with the National Academies of Science, Engineering, and Medicine (NASEM)**. NASEM's consensus study process is considered the gold standard of independent, nonpartisan, evidence-based advice[5]. They traditionally enlist the best available expertise across disciplines to examine the evidence, reach consensus, and identify a path forward on some of society's most pressing challenges. NASEM provided several recommendations after twice reviewing the report that remains inadequately addressed in the current draft of the monograph by the NTP[6,7,8]. On each occasion of their review, the NASEM Committee deduced that the monograph "**fell short of providing a clear and convincing argument that supported its assessment**". In their reviews, the NASEM Committee had difficulty in following various aspects of the reported methods, identified a few worrisome inconsistencies, was not able to find some key data used in the meta-analysis, and had concerns about the wording of some conclusions[6,7]. They noted that there are several issues associated with the general methods of NTP's systematic review process that reduced the transparency of the process and probability of reproducing the findings and did not align with some general best practices or systematic review. Therefore, it is critical that NTP return to the NASEM review process to address the concerns expressed.

In its current form, **AADOCR supports NTP providing clear statements that define that the monograph cannot be used to draw any conclusions regarding low fluoride exposure concentrations**, including those typically associated with drinking-water fluoridation. This should be explicitly stated in the abstract and all other relevant sections of the report. NASEM's reviewers cautioned that "**the monograph cannot be used to draw conclusions about low fluoride exposure concentrations (less than 1.5 mg/L), including those in fluoridated drinking water systems**"[6,7]. This is attributed to the fact that much of the evidence presented comes from studies that involve relatively high fluoride concentrations. However, the current draft of the monograph concludes "*with moderate confidence* in the body of evidence that higher fluoride exposure is consistently associated with lower IQ in children"[8]. Taken independently, this could lead to the erroneous conclusion that fluoride is presumed to be a cognitive neurodevelopmental hazard to humans although not supported by the body of scientific evidence. However, there are many confounding factors - socioeconomic, physical, familial, cultural, genetic, nutritional, and environmental

confounders - that affect IQ. The evaluation of confounding was insufficient and applied inconsistently throughout the report and therefore conclusions may be inaccurate, incomparable, or ungeneralizable. Therefore, addressing the recommendations by the NASEM Committee is paramount to ensure accurate and clear scientific communication by the NTP. **AADOCR supports clear statements that state the statistical associations observed should not be construed as high fluoride exposure caused IQ deficits.** NTP has acknowledged this by removing the *presumed neurodevelopmental hazard* assessment statement, but this assessment is not reflected in this monograph. Therefore, the research recommendation should focus on studies to understand if there is a causal association between high levels of fluoride and IQ deficits.

The current draft of the monograph has also not sufficiently addressed NASEM's concerns regarding their meta-analysis. As shown in Figure 1.2 of the BSC review, the BSC found that the NTP did **not** adequately address 13% of reviewer comments and another 16% needed further suggestions[9]. And for the Meta-analysis, the BSC found that the NTP did **not** adequately address 35% of reviewer comments and another 22% needed further suggestions[9]. NASEM stated that there was a lack of rigorous statistical review and improper evaluation of the meta-analysis[6,7]. In the current draft, there is still a failure to examine the studies included in the meta-analysis in greater depth - to determine whether each study properly accounted for its design[10] – as not doing so could invalidate the meta-analysis results). Additionally, several studies included in the report fail to clearly define their sampling design, clustering approach, and statistical analysis methodology[10]. In the current draft, there is also a need to review the process used to exclude study results from the meta-analysis to ensure consistency across all studies. **AADOCR supports the NTP adequately addressing the concerns related to the statistical review and evaluation of the meta-analysis** to ensure that the data that attributes to the conclusions within the monograph have been well-vetted. Although published after NTP's evaluation period, a more recent meta-analysis on the association between low fluoride exposure and children's intelligence showed show that fluoride exposure relevant to community water fluoridation is not associated with lower IQ scores in children[11].

The NTP monograph states within its results that "The current bodies of experimental animal studies and human mechanistic evidence do not provide clarity on the association between fluoride exposure and cognitive or neurodevelopmental human health effects"[10]. Several statements within the discussion section affirm these results: i). existing animal studies provide little insight into the question of whether fluoride exposure affects IQ, ii). studies that evaluated fluoride exposure and mechanistic data in humans were too heterogenous and limited in number to make any determination on biological plausibility and iii). there is also some evidence that fluoride exposure is associated with other neurodevelopmental and cognitive effects in children; although,

because of the heterogeneity of the outcomes, there is low confidence in the literature for these other effects[10]. Therefore, **AADOCR supports the NTP revisit its results and discussion sections to craft a conclusion that more closely aligns with the statements within those sections**.

AADOCR appreciates the opportunity to provide comments on the request for comments on the NTP Monograph on the State of the Science Concerning Fluoride Exposure and Neurodevelopmental and Cognitive Health Effects: A Systematic Review report. AADOCR stands ready to work with NTP and the BSC to address the contextual and clarity challenges within the monograph.

If you have any further questions, please contact Dr. Makyba Charles-Ayinde, Director of Science Policy, at mcayinde@iadr.org.

Sincerely,

Christopher H. Fox, DMD, DMSc
Chief Executive Officer

Alexandre Vieira, DDS, MS, PhD
President

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