

At its meeting on May 4, 2023, the NTP Board of Scientific Counselors (BSC) voted to accept the BSC Working Group's report in full, with the exception of text related to an IQ statistic (8.P, page 323), that the BSC asked the Working Group to verify or correct. In its review, the Working Group determined that Table 2 of the Draft Meta-Analysis Manuscript (page II-36) presents the Standardized Mean Difference (SMD). Assuming a standard deviation of 15 points, a SMD of -0.46 would equate to a decrease of 7 points in IQ ( $-0.46 \times 15 = -6.9$ ). The example in the Discussion section of the Draft Meta-Analysis Manuscript that presents a 5-point decrease in IQ is reasonably consistent with the data, and thus the BSC Working Group's assessment is in error, because the Working Group incorrectly thought that the -0.46 was the mean difference in IQ points, not the Standardized Mean Difference. The BSC Working Group has revised its assessment of 8.P to delete text related to the IQ statistic.

**8.P:** Discussion section: "Although the estimated decreases in IQ may seem small, research on other neurotoxicants has shown that subtle shifts in IQ at the population level can have a profound impact on the number of people who fall within the high and low ranges of the population's IQ distribution."

**comment:** Does this imply that fluoride causes a shift in intelligence at all levels of exposure (e.g., including at 0.7 mg/L)? If that is not the intent, this passage could be misleading.

**Response: Disagree (no change)**

- We do not consider this statement to be misleading. Using [redacted] example, total fluoride exposure among individuals living in optimally fluoridated areas (0.7mg/L in drinking water) may be higher than 0.7mg/L, dependent on personal behaviors and habits. We discuss the potential for this type of variation in the manuscript.

**BSC WG Assessment:**

The BSC WG considers the NTP authors' response to the reviewer's comment inadequate.

The BSC WG agrees that subtle shifts in mean IQ at the population level could have a large impact. The BSC WG notes that fluoride exposure among individuals in optimally fluoridated areas could be higher or lower than 0.7 mg/L depending on personal behaviors and habits. ~~The BSC WG has concern about the next sentence in the Discussion section of the draft M-A Manuscript: "For example, a 5-point decrease in a population's IQ, would nearly double the number of people classified as intellectually disabled (reference 55)." Table 2 of the M-A Manuscript lists the Overall Mean Effect on IQ in 55 studies as -0.46 (-0.55, -0.37). Given that the mean effect size is ~ a half a point in mean IQ, that the studies included in the meta-analysis have very indirect measures of exposure (mean effects), and that the heterogeneity in this meta-analysis is very high, the BSC WG recommends that the authors present an example more consistent with their data.~~

**See Appendix II, page II-12.**