UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

FOOD & WATER WATCH, INC., et al.,

Plaintiffs,

v.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY, et al.,

Defendants.

Case No. 17-cv-02162-EMC

**FINDINGS OF FACT AND CONCLUSIONS OF LAW**



## I. INTRODUCTION

In 2016, Congress amended the Toxic Substances Control Act ("TSCA"), empowering United States citizens to petition the Environmental Protection Agency ("EPA") to consider whether a chemical presents an unreasonable risk of injury to health. *See* Pub. L. No. 114-182, 114th Congress (Frank R. Lautenberg Chemical Safety for the 21st Century Act) (the "Act"). The Act addresses the modern day reality that "human beings and the environment are being exposed each year to a large number of chemical substances and mixtures," 15 U.S.C. § 2601(a)(1), and that, "among the many chemical substances and mixtures which are constantly being developed and produced, there are some whose manufacture, processing, distribution in commerce, use, or disposal may present an unreasonable risk of injury to health or the environment," *id.* § 2601(a)(2).

To this end, under TSCA, as amended by the Act ("Amended TSCA"), a citizen is entitled to judicial review of the EPA's denial of the citizen's petition, wherein a court considers whether the chemical poses an unreasonable risk *de novo*, *i.e.*, without deference to the EPA's decision. *See id.* § 2620(b)(4)(B). Amended TSCA sets up a system of judicial review that is remarkably different from the usual scope of judicial review of administrative actions under the Administrative Procedure Act, which confers substantial deference to administrative agencies. *See id.* Under Amended TSCA, the Court owes no deference to the EPA in assessing the risk posed by chemical substances. *See id.* If the Court finds anew that the chemical at issue presents

an unreasonable risk, it then orders the EPA to engage in rulemaking regarding the chemical. *See id.* The EPA is afforded in the first instance the authority to respond; regulatory actions can range from requiring a mere warning label to banning the chemical. *See id.* § 2605(a)(1)-(7). The EPA, in short, has options. *See id.*

The issue before this Court is whether the Plaintiffs have established by a preponderance of the evidence that the fluoridation of drinking water at levels typical in the United States poses an unreasonable risk of injury to health of the public within the meaning of Amended TSCA. For the reasons set forth below, the Court so finds. Specifically, the Court finds that fluoridation of water at 0.7 milligrams per liter ("mg/L") – the level presently considered "optimal" in the United States – poses an unreasonable risk of reduced IQ in children. It should be noted that this finding does not conclude with certainty that fluoridated water is injurious to public health; rather, as required by the Amended TSCA, the Court finds there is an unreasonable *risk* of such injury, a risk sufficient to require the EPA to engage with a regulatory response. This order does not dictate precisely what that response must be. Amended TSCA leaves that decision in the first instance to the EPA. One thing the EPA cannot do, however, in the face of this Court's finding, is to ignore that risk.

A. Context

Water fluoridation has a long history in the United States and has been a source of political discord, at times. *See, e.g.*, Dkt. No. 429-3, Trial Ex. 13 at 15.[1] In 1975 the EPA recommended adding fluoride to water, with an optimal level up to 1.2 mg/L for its dental health benefits. *Id.* at 16. Between 1981 and 1984, fluoride's association with adverse effects including osteosclerosis, enamel fluorosis, and psychological and behavioral problems was contested. *Id.* at 17-18. Still, as of 1986, up to 1.2 mg/L water fluoridation was considered optimal, and the maximum level was 4 mg/L. *Id.* at 14-18. After evidence increasingly established fluoride's connection to adverse

[1] Controversy over fluoridation of drinking water has even found its way into Hollywood. *See* DR. STRANGELOVE (Columbia Pictures 1964) (General Ripper characterizing fluoridation as a threat to our "precious bodily fluids" and "the most monstrously conceived and dangerous communist plot we've ever had to face").

effects, including severe enamel fluorosis, risk of bone fracture, and potential skeletal fluorosis, recommended levels were lowered in 2006. *Id.* at 10. Community water fluoridation has since continued at levels believed to be safe for its dental health benefits. At present, fluoride is added to tap water in the United States, with an optimal level of 0.7 mg/L.

However, scientific evidence has increasingly identified a link between fluoride exposure and adverse cognitive effects in children (reduced IQ). Accordingly, Plaintiffs exercised their power under Amended TSCA and petitioned the EPA to consider whether fluoride in drinking water presents an unreasonable risk of injury to human health. Notwithstanding the growing and robust body of evidence indicating an association between fluoride intake and cognitive impairment in children, the EPA denied Plaintiffs' petition. Plaintiffs filed suit in this Court, arguing that the EPA was wrong and that community water fluoridation at 0.7 mg/L (the "condition of use") poses an unreasonable risk of injury to human health.

B. Summary

To succeed in a suit brought under the Amended TSCA, Plaintiffs must prove, by a preponderance of the evidence, that a risk of injury to human health is present and that such risk is unreasonable. For a risk to be present, Plaintiffs must show that some segment of the United States population is exposed to the chemical at issue at levels that either exceed, or are too close to the dosage at which the chemical presents a hazard.[2] The reasonableness of the risk is informed by several factors, including *inter alia*, the size and susceptibility of impacted populations, severity of the harm at issue, and the frequency and duration of exposure.

There is little dispute in this suit as to whether fluoride poses a hazard to human health. Indeed, EPA's *own expert* agrees that fluoride is hazardous at some level of exposure. And ample evidence establishes that a mother's exposure to fluoride during pregnancy is associated with IQ decrements in her offspring. The United States National Toxicology Program ("NTP") – the federal agency regarded as experts in toxicity – undertook a systematic review of all available literature near the time of publication considering whether fluoride poses cognitive harm,

[2] The level at which the chemical presents a hazard is known as the "hazard level." The level at which human populations are exposed to the chemical is known as the "exposure level."

reviewing 72 human epidemiological studies considering this question. The NTP concluded that fluoride is indeed associated with reduced IQ in children, at least at exposure levels at or above 1.5 mg/L (*i.e.*, "higher" exposure levels). And notwithstanding inherent difficulties in observing effects at lower exposure levels, explained in further detail below, scientists have observed a statistically significant association between fluoride and adverse effects in children even at such "lower" exposure levels (less than 1.5 mg/L).

Notwithstanding recognition by EPA's expert that fluoride is hazardous, the EPA points to technicalities at various steps of the risk evaluation to conclude that fluoride does not present an unreasonable risk. Primarily, the EPA argues the hazard level and the precise relationship between dosage and response at lower exposure levels are not entirely clear. These arguments are not persuasive.

Importantly, the chemical at issue need not be found hazardous at the exposure level to establish that a risk is present under Amended TSCA. Instead, the EPA requires a *margin* exist between the hazard level and exposure level to ensure safety; if there is an insufficient margin then the chemical poses a risk. The trial evidence in this case establishes that even if there is some uncertainty as to the precise level at which fluoride becomes hazardous (hazard level), under even the most conservative estimates of this level, there is not enough of a margin between the accepted hazard level and the actual human exposure levels to find that fluoride is safe. Simply put, the risk to health at exposure levels in United States drinking water is sufficiently high to trigger regulatory response by the EPA under Amended TSCA.

To this end, as mentioned previously, the NTP compiled and analyzed all relevant studies it could find and concluded that, at least at dosages of 1.5 mg/L or higher, fluoride is associated with reduced IQ in children. Subsequently, toxicology experts endeavored to put a finer point on the impact of fluoride on children's IQ at "lower" exposure levels, *i.e.*, those below 1.5 mg/L, and conducted a pooled benchmark dose analysis to define the precise hazard level of fluoride. For reasons described below, this pooled benchmark dose analysis benefited from increased statistical power relative to the NTP's assessment due to its methodology (*i.e.*, the benchmark dose analysis used individualized, continuous data, while the NTP assessment did not, due to quantity and variety

of studies the NTP reviewed in that assessment). The pooled benchmark dose analysis concluded that **a 1-point drop in IQ of a child is to be expected for each 0.28 mg/L of fluoride in a pregnant mother's urine**. This is highly concerning, because maternal urinary fluoride levels for pregnant mothers in the United States range from **0.8 mg/L** at the median and **1.89 mg/L** depending upon the degree of exposure. Not only is there an insufficient *margin* between the hazard level and these exposure levels, for many, the exposure levels *exceed* the hazard level of 0.28 mg/L.

The EPA challenges, for a variety of reasons, whether this 0.28 mg/L hazard level (measured in maternal urinary fluoride) is appropriate for this risk evaluation. The EPA argues, among other things, that the hazard and exposure levels should not be expressed in maternal urinary fluoride because that metric reflects total fluoride exposure – not just exposure resulting from drinking fluoridated water from one's community. Fluoride may also be ingested through, *e.g.*, tea, fish, toothpaste, and commercial food and beverage made with fluoridated water. Nonetheless, the risk analysis should consider the *additive* effect of the chemical under the subjected condition of use (here, fluoridated community drinking water), especially where, as here, the fluoridated drinking water is a significant (and likely primary) contributor to aggregate exposure to fluoride. Indeed, the Amended TSCA, expressly contemplates that the *aggregate* exposure to a chemical will be considered when conducting a risk assessment. *See* 15 U.S.C. § 2605(b)(4)(F). In this sense, maternal urinary fluoride is not just an acceptable metric, it is highly useful in assessing the real-world end result of exposure from drinking fluoridated water along with other sources.

Even if urinary fluoride were not the appropriate metric in assessing health risk, or even if the toxicologically determined hazard level of 0.28 mg/L were deemed insufficiently substantiated, evidence in the record still establishes with little doubt that fluoridated drinking water presents a risk of injury to health. Using a highly conservative estimate of the hazard level of 4 mg/L measured in drinking water fluoride (well above the 1.5 mg/L identified as hazardous to children by the NTP) based on the consistent and repeated observation of adverse effects summarized in the NTP's assessment, a risk is present. There is little dispute that there is a

statistically significant association between IQ decrements in children and fluoride concentration levels at 4 mg/L.

The EPA's default margin of error requires a factor of 10 between the hazard level and exposure level due to variability in human sensitivities. Put differently, only an exposure that is below 1/10th of the hazard level would be deemed safe under Amended TSCA, given the margin of error required. Here, an even greater margin (100x) is owed because the methodology (which yields the 4 mg/L hazard level) uses the lowest observed adverse effect level ("LOAEL"); this methodology adds an additional level of uncertainty (and hence the application of a 100x rather than 10x margin). But even if only the default 10x margin is required, the safe level of fluoride exposure would be 0.4 mg/L (4 mg/L (hazard level) divided by 10). The "optimal" water fluoridation level in the United States of 0.7 mg/L is nearly double that safe level of 0.4 mg/L for pregnant women and their offspring.

In all, there is substantial and scientifically credible evidence establishing that fluoride poses a risk to human health; it is associated with a reduction in the IQ of children and is hazardous at dosages that are far too close to fluoride levels in the drinking water of the United States. And this risk is unreasonable under Amended TSCA. Reduced IQ poses serious harm. Studies have linked IQ decrements of even one or two points to *e.g.*, reduced educational attainment, employment status, productivity, and earned wages. Indeed, the EPA recognizes that reduction of IQ poses a serious community health issue. Moreover, highly susceptible populations are impacted, including over two million pregnant women and babies, a number far exceeding population size the EPA has looked to in determining whether regulatory action was warranted in other risk evaluations (*i.e.*, 500 people or less).

Thus, the Court finds Plaintiffs have met their burden in establishing, by a preponderance of the evidence, that community water fluoridation at 0.7 mg/L presents an unreasonable risk of injury to health under Amended TSCA and that the EPA is thus obliged to take regulatory action in response. The Court does not in this order prescribe what that response should be.

## II. BACKGROUND

A. Factual and Procedural Background

1. Section 6(a) of the Toxic Substances Control Act ("TCSA") requires Defendant United States EPA[3] to regulate the use of certain chemical substances that it determines pose an unreasonable risk to health or the environment. 15 U.S.C. § 2605(a).

2. The TSCA was initially passed in 1976, codified at 15. U.S.C. § 2601 *et seq.* Congress enacted the original TSCA, motivated by findings that "human beings and the environment are being exposed each year to a large number of chemical substances and mixtures," 15 U.S.C. § 2601(a)(1), and that, "among the many chemical substances and mixtures which are constantly being developed and produced, there are some whose manufacture, processing, distribution in commerce, use, or disposal may present an unreasonable risk of injury to health or the environment," *id.* § 2601(a)(2).

3. On June 22, 2016, the Frank R. Lautenberg Chemical Safety for the 21st Century Act was signed into law. *See* Pub. L. No. 114-182, 114th Congress. The Act amended the TSCA. *See id.*

4. Amended TSCA requires the EPA to regulate the use of certain chemical substances that pose an unreasonable risk of harm to health or the environment. 15 U.S.C. § 2605(a). If a chemical substance poses a risk of unreasonable harm, the EPA must promulgate a rule imposing one or more of a wide range of possible requirements. *See id.* § 2605(a)(2). Specifically, the rule adopted by the EPA must impose one or more of the following: a prohibition, restriction, or limitation of the amount of such substance that may be manufactured, processed, or distributed in commerce, *id.* § 2605(a)(1); a prohibition, restriction, or limitation upon such manufacture, processing, or use in connection with "a particular use" or "a particular use in a concentration in excess of a level specified by the Administrator," *id.* § 2605(a)(2); labeling requirements for such substance, *id.* § 2605(a)(3); record-keeping requirements for manufacturers or processors of the substance, *id.* § 2605(a)(4); commercial-use regulations, *id.* § 2605(a)(5); disposal requirements,

[3] Scott Pruitt, Administrator of the EPA is also named as a Defendant in his official capacity. Dkt. No. 372 (Supplemental Complaint ("FAC")) ¶ 1.

*id.* § 2605(a)(6); and/or notice requirements, *id.* § 2605(a)(7). The EPA may limit the application of such requirements to "specified geographic areas." *Id.* § 2605(a).

5. After the Act's amendment to TSCA, there are three pathways to obtain a Section 6(a) rule regulating a chemical: (1) an EPA's *sua sponte* designation of a chemical as "high priority," resulting in a finding that it presents an unreasonable risk,[4] 15 U.S.C. § 2605(c)(1); (2) an EPA risk evaluation of a chemical at the request of a manufacturer, *see id.* § 2605(b)(4)(C)(ii), which results in a finding of unreasonable risk; or (3) a successful Section 21 "citizen petition," *see id.* §§ 2620(a), (b)(3).

6. A Section 21 citizen's petition to the EPA to initiate Section 6(a) rulemaking is to be granted if the petitioner demonstrates a chemical substance poses an unreasonable risk of harm. *Id.* § 2620(a). Amended TSCA provides judicial review of a denial of such a petition to the EPA. *Id.* § 2620(b)(4). In contrast to the typical standard of judicial review under the Administrative Procedure Act, in considering a Section 21 citizen's petition, the Court considers the issue *de novo*; no deference is owed under to the EPA's denial of the petition. *See id.* § 2620(b)(4)(B).

7. Plaintiffs in the instant suit are non-profit advocacy organizations and associations and individuals suing on behalf of themselves and their children. FAC ¶ 1.[5]

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[4] To elaborate, Section 6(b) requires the EPA to perform its own evaluations of the risks posed by certain chemical substances. 15 U.S.C. § 2605(b)(4)(A). To this end, the EPA is required by Amended TSCA to designate chemical substances as "high-priority" or "low-priority" based on a risk screening process. *See id.* § 2605(b)(1). "High-priority" chemicals are those that "may present an unreasonable risk to health or the environment because of potential hazard and a potential route of exposure under the conditions of use." *Id.* § 2605(b)(1)(B)(i). A "low-priority" substance, in contrast, is one that the Administrator "concludes, based on information sufficient to establish . . . does not meet the standard" to be designated a high-priority substance. *Id.* § 2605(b)(1)(B)(ii). Once the EPA has designated a chemical substance "high-priority," it must initiate a Section 6(b) "risk evaluation." *Id.* §§ 2605(b)(3)(A), (4)(C)(i). A risk evaluation is not required for a "low-priority" substance. *Id.* § 2605(b)(1)(A). The EPA must pursue these risk evaluations at a minimum pace established by statute: within 6 months, risk evaluations must be underway on at least 10 substances drawn from the 2014 TSCA Work Plan for Chemical Assessments, *id.* § 2605(b)(2)(A); within three and a half years, risk evaluations must be underway on "at least 20 high-priority substances," *id.* § 2605(b)(2)(B); a new high-priority substance must be designated anytime a risk evaluation has been completed (other than those commenced at the request of a manufacturer), *id.* § 2605(b)(3)(C); and, generally, the EPA must continue designating substances and conducting evaluations "at a pace consistent" with its ability to meet the 3-year deadline to complete each risk evaluation, *id.* § 2605(b)(2)(C).

[5] Specifically, Plaintiffs are Food & Water Watch, Fluoride Action Network, and Moms Against Fluoridation ("Organizational Plaintiffs"), and Audrey Adams individually and on behalf of Kyle

8. On November 22, 2016, a group of organizations and individuals including Plaintiffs petitioned the EPA under Section 21 of Amended TSCA to regulate the fluoridation of drinking water supplies under Section 6(a). Dkt. No. 117-1, Ex. 1. Plaintiffs asserted that the ingestion of fluoride poses an unreasonable risk of neurotoxic harm to humans including IQ loss and other neurotoxic effects, particularly for infants, young children, and other subpopulations standing at elevated risk. *Id.*

9. On February 17, 2017, the EPA denied Plaintiffs' petition. Dkt. No. 28-1; 82 Fed. Reg. 11,878 (Feb. 27, 2017).

10. After the EPA denied Plaintiffs' petition, Plaintiffs filed this suit seeking judicial review of the EPA's denial pursuant to 15 U.S.C. § 2620. Dkt. No. 1 (Complaint ("Compl.")) ¶¶ 106-07.

11. Beginning on June 8, 2020, after the parties engaged in fact and expert discovery, the Court held a seven-day bench trial, which included expert testimony regarding the state of the scientific research on fluoride neurotoxicity ("Trial Phase 1"). *See* Dkt. Nos. 219, 238.

12. On August 10, 2020, the Court stayed the case due to concerns about Plaintiffs' standing and developments in scientific literature regarding fluoride. *See* Dkt. No. 262. The Court explained that the stay would allow EPA to consider new scientific studies published after EPA's denial of Plaintiffs' administrative petition and allow the Court to consider the imminent publication of the NTP systematic review "Monograph on the Systematic Review of Fluoride Exposure and Neurodevelopmental and Cognitive Health Effects." *Id.* at 3-5.

13. Thereafter, Plaintiffs filed a supplemental administrative petition for reconsideration to the EPA. Dkt. No. 270.

14. EPA again denied the petition. Dkt. No. 278.

15. On October 28, 2022, the Court granted Plaintiffs' motion to lift the stay and take the case out of abeyance, finding that Plaintiffs had standing and that there was new evidence that scientific developments had changed, including the fact that the aforementioned NTP's systematic review

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Adams, Kristen Lavelle individually and on behalf of Neal Lavell, and Brenda Staudenmaier individually and on behalf of Ko Staudenmaier and Hayden Staudenmaier ("Individual Plaintiffs") (collectively "Plaintiffs" or "FWW"). FAC ¶ 1.

had since undergone three additional rounds of peer review resulting in a near-final version of the document. *See* Dkt. No. 319 at 2-5.

16. Beginning on January 31, 2024, the Court held a second, ten-day bench trial ("Trial Phase 2") which included expert testimony regarding the updated state of the scientific research on fluoride neurotoxicity. *See* Dkt. Nos. 407-413, 422-424.

B. Relief Requested

17. Plaintiffs contend that the addition of fluoridation chemicals to drinking water at levels recommended in the United States (0.7 mg/L) presents an unreasonable risk of neurological harm when assessed under the risk evaluation framework that EPA uses under the Amended TSCA. Dkt. No. 378 (Joint Pretrial Conference Statement ("PTC Statement")) at 1-2.

18. Plaintiffs seek a declaration that fluoridation of water at 0.7 mg/L presents an unreasonable risk of injury to health and injunctive relief requiring the EPA to initiate the rulemaking proceeding requested by Plaintiffs in their Petition to the EPA. PTC Statement at 2. Specifically, Plaintiffs seek an order requiring the EPA to "initiate a proceeding for the issuance of a rule," but the order would not "prescribe the content of a rule or the outcome of such a proceeding." *Id.* In short, rulemaking would be left in the first instance to the EPA.

19. Plaintiffs also seek recovery of their costs of suit and reasonable fees for attorneys and expert witnesses, as permitted by 15 U.S.C. § 2620(b)(4)(C), and such further relief that the Court may deem just and proper. PTC Statement at 2.

C. Statutory Standard and Burden

20. Plaintiffs bear the burden of proving, by a preponderance of the evidence, that the chemical substance at issue presents an "unreasonable risk of injury to health or the environment, without consideration of costs or other nonrisk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation under the conditions of use." 15 U.S.C. § 2620(b)(4)(B)(ii). The Court considers the issue *de novo*; no deference is owed under TSCA to the EPA's denial of the petition. *Id.* § 2620(b)(4)(B).

21. If the Court determines that petitioner has met its burden, demonstrating unreasonable risk by a preponderance of the evidence, the Court "shall order the Administrator to initiate the action

requested by the petitioner." *Id.* Specifically, EPA would be directed to engage in rulemaking pursuant to Subsection 6(a) of TSCA wherein the EPA would consider applying one or more methods to neutralize the risk, ranging from requiring a notice be provided to the public of risks (*i.e.*, utilizing a warning label or disseminating a public advisory), *see id.* § 2605(a)(7), to prohibiting manufacturing or distributing the chemical at issue, *see id.* § 2605(a)(1).

D. Standing

22. The Court previously held, in lifting its stay on proceedings and allowing the case to proceed to phase two of trial, that Plaintiffs had standing. Dkt. No. 319 at 2-3. The Court reaffirms this finding. At a minimum, Organizational Plaintiff FWW has standing in a representative capacity. An association has standing to sue on behalf of its members when: "(1) its members would otherwise have standing to sue in their own right; (2) the interests it seeks to protect are germane to the organization's purpose; and (3) neither the claim asserted nor the relief requested requires the participation of individual members in the lawsuit." *Am. Unites for Kids v. Rousseau*, 985 F.3d 1075, 1096 (9th Cir. 2021) (citing *Hunt v. Wash. State Apple Advert. Comm'n*, 432 U.S. 333, 343 (1977)). Each prong is satisfied:

a. In its previous order, the Court found that Jessica Trader, a member of FWW, has standing. Dkt. No. 319 at 2-3. Article III standing requires: (1) an injury-in-fact that is concrete and particularized and actual or imminent, (2) a causal connection between the injury and the conduct complained of, and (3) probable redressability. *Id.* (citing *Lujan v. Defs. of Wildlife*, 504 U.S. 555, 560–61 (1992)). Ms. Trader became pregnant in November 2020 and gave birth in August 2021 (during the pendency of this lawsuit) and testifies that she plans to have several more children; she has taken steps to effectuate this goal including discontinuing her use of birth control medication. Dkt. No. 430-18, Trial Ex. 66 (Declaration of Jessica Trader) ¶¶ 5-8 & Ex. A. Ms. Trader has incurred costs and taken measures to avoid fluoridated water during her first pregnancy and continues to do so to protect her future children. *Id.* ¶¶ 9-16. As the Court previously explained, neurodevelopmental harm from fluoride exposure to Ms. Trader's child and future children is concrete and imminent; there is a credible causal connection between that neurodevelopmental harm and EPA's regulation of fluoride exposure or lack thereof; and the harm

would likely be redressed if EPA were to pass a rule prohibiting the addition of fluoridation chemicals to public drinking water supplies. Dkt. No. 319 at 2-3. Moreover, the EPA has conceded that standing would be satisfied by "someone who is an expectant parent who – who could be consuming fluoridated water, and, and – that could have potential effects on the baby she's carrying in utero. It could be a potential – a parent, someone with very young children." *Id.* (quoting Dkt. No. 133 at 14:9-17). Ms. Trader is such an individual. Thus, the first prong is satisfied; a member has standing.

b. As for the second prong, there is no dispute that FWW's mission is to ensure "clean, safe water for drinking" which it views as a "fundamental right that should be afforded to all people," and to "advocate for more government responsibility in protecting our drinking water resources." Dkt. No. 430-8, Trial Ex. 52 (Second Amended Declaration of Scott Edwards, Co-Director of FWW) ¶¶ 4, 6. Thus, the interests at stake in this suit – regulation of water fluoridation to protect public health – are germane to the organization's purpose. *See, e.g.*, *Am. Unites for Kids*, 985 F.3d at 1097 (explaining that where there is a close connection between the organization's mission and the interests of others it seeks to represent, organizational standing is appropriate); *G.G. by & through A.G. v. Meneses*, 638 F. Supp. 3d 1231, 1241 (W.D. Wash. 2022) (finding nonprofit disability rights organization had associational standing to bring claims on behalf of disabled members as rights of people with developmental disabilities was an interest the organization sought to protect).

c. The third prong is a "judicially fashioned and prudentially imposed" question, as opposed to a constitutional requirement of standing. *Or. Advocacy Ctr. v. Mink*, 332 F.3d 1101, 1109 (9th Cir. 2003). This suit is appropriately brought by a representative plaintiff; analysis under Amended TSCA focuses on scientific evidence substantiating the alleged risk to public health rather than focusing upon anecdotal evidence from plaintiffs. *See* ¶¶ 26-95; *accord Laborers Int'l Union Loc. 261 v. City & Cnty. of San Francisco*, 2022 WL 2528602, at *6 (N.D. Cal. July 6, 2022) (explaining that unlike claims seeking damages which require individualized proof, claims seeking injunctive relief are well-suited for adjudication by organizational plaintiff) (citing *Comm. for Immigrant Rts. of Sonoma Cnty. v. Cnty. of Sonoma*, 644 F. Supp. 2d 1177,

1194 (N.D. Cal. 2009)). The harm redressable herein is precisely the kind of harm that Amended TSCA is designed to address. For these reasons, the Court reaffirms its finding that requirements of standing have been satisfied.

## III. FINDINGS OF FACT

23. To discern whether a chemical substance presents an unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation, under the conditions of use, under TSCA section 6, the EPA engages in a TSCA risk evaluation process. 15 U.S.C. § 2605(b)(4); 82 Fed. Reg. 33,726 (July 20, 2017); Dkt. No. 434-18, Trial Ex. 544.

24. The TSCA risk evaluation is comprised of a risk assessment and risk determination. *See* Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 653:22-655:11 (Barone). The National Research Council (NRC, 1983) has defined risk assessment as including the following components: (1) hazard assessment (including hazard identification and quantitative dose response analysis); (2) exposure assessment; and (3) risk characterization. A risk evaluation under the Amended TSCA includes the three aforementioned steps of a risk assessment, as well as a fourth and final step: (4) a risk determination. *See id.* The "risk assessment" is the scientific technical evaluation, encompassing the first three parts of this process, resulting in an unbiased, transparent, and reproducible description of the risk. *See id.* The "risk determination" is the final step of the risk evaluation process, where EPA summarizes its findings and determines whether a chemical does or does not present unreasonable risk. *See id.*

25. The following is a summary of the risk evaluation steps. *See id.*; *accord* 15 U.S.C. § 2605(b)(4)(F)(i)-(v).

a. At step 1 (hazard assessment) the EPA determines if a chemical is considered hazardous and if so, the EPA endeavors to determine the point at which the chemical becomes hazardous ("point of departure" or "hazard level"). *See* Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 653:22-655:11 (Barone); *accord* 15 U.S.C. § 2605(b)(4)(F)(i)-(iii), (v).

b. At step 2 (exposure assessment) the EPA determines the level at which populations are exposed to the chemical. *See* Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 653:22-655:11 (Barone);

*accord* 15 U.S.C. § 2605(b)(4)(F)(i)-(iii), (v).

c. At step 3 (risk characterization), the EPA compares the point of departure with the exposure level to determine if a risk is present. *See* Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 575:8-583:13 (Barone). Because of uncertainty in data, the EPA establishes a margin between the point of departure and the community's exposure level. There must be a sufficient margin to find absence of risk. *See id.* The appropriate margin varies based upon how much uncertainty there is in the chosen point of departure. *See id.* The appropriate or required margin is referred to as the benchmark margin of exposure ("benchmark MOE"). *See id.* The actual margin is the actual margin of exposure ("actual MOE"). If there is an insufficient margin, *i.e.*, the actual MOE is less than the benchmark MOE, a risk has been identified. *See id.*

d. At step 4 (risk determination) if a risk is identified, the EPA will then determine if that risk is unreasonable, considering various factors such as the type of harm at issue and number of people exposed. *See* Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 653:22-655:11 (Barone); *accord* 15 U.S.C. § 2605(b)(4)(F)(iii)-(v). Each step of the risk assessment is discussed in turn below.[6]

A. Step 1: Hazard Assessment

26. The Hazard Assessment step is comprised of three subparts: (a) hazard identification; (b) weight-of-the-scientific evidence; and (c) dose-response assessment. *See* Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 654:19-655:11 (Barone). Each are addressed in turn below.

1. Step 1A: Hazard identification

a. *Framework*

27. The first component of the hazard assessment is hazard identification. Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 489:11-17 (Barone), 656:8-661:16 (Barone). At the hazard identification step of the risk evaluation framework, the reviewer determines if an adverse effect is associated with a chemical exposure. *See* Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 489:11-17 (Barone), 656:8-661:16 (Barone).

[6] The evaluation of fluoridation chemicals under TSCA follows the same standards for demonstrating hazard and risk that EPA uses for its evaluations of other industrial chemicals under TSCA; there is no justification for holding fluoridation chemicals to a higher burden. *See* Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 742:25-743:8 (Barone).

28. Proof of causation is not required to establish a hazard of neurotoxicity, only association between the chemical exposure and the adverse effect is required for a hazard to be identified. *See id.* at 490:1-5.

29. At this stage of the process EPA reviews, searches, screens, and evaluates all studies related to different hazards to determine whether the data are sufficient or insufficient for identified adverse effects. *Id.* at 492:24-494:9.

b. *Key finding*

30. The hazard identification step of the hazard assessment here is satisfied; exposure to the chemical fluoride is associated with the adverse effect of reduced IQ in children, and particularly in boys.

c. *Underlying findings*

31. The NTP is headquartered within the National Institute of Environmental Health Sciences ("NIEHS"). Dkt. No. 440, Feb. 13, 2024, Trial Tr. at 1425:23-1426:8 (Barone). By May of 2022, the NTP completed its systematic review of fluoride, titled *NTP Monograph on the State of the Science Concerning Fluoride Exposure and Neurodevelopmental and Cognitive Health Effects: A Systematic Review* (hereafter "NTP Monograph"). Dkt. No. 431-1, Trial Ex. 67. *See also* Dkt. No. 440, Feb. 13, 2024, Trial Tr. at 1427:5-8 (Barone); Dkt. No. 400, Feb. 4, 2024, Trial Tr. at 535:15-21 (Berridge). In August 2024, the NTP Monograph was formally published. *See* Dkt No. 442 (letter from parties recognizing publishing of document). The parties agree that there are no material differences between the published Monograph and the pre-publication version that was the subject of testimony and argument at trial (*i.e.*, Trial Exhibit 67). *Id.*[7]

[7] The parties originally filed a letter agreeing that the published version of the NTP Monograph was the same in all material respects as the Monograph this Court reviewed at trial. Dkt. No. 442. Subsequently, Plaintiffs filed a letter suggesting that certain aspects of the published NTP Monograph were modified in a way that lends *additional* support for their case. *See* Dkt. No. 443. In particular, Plaintiffs assert:

> Page 101 of the now-published version of the NTP Monograph summarizes the findings of the "in-press" meta-analysis as follows:
>
> The group-level meta-analysis of 59 studies (n = 20,932 children) used SMD as the effect measure and reported statistically significant

32. According to the EPA, a systematic review is "a scientific investigation that focuses on a specific question and uses explicit, pre-specified methods to identify, select, assess, and summarize the findings of similar but separate studies." Dkt. No. 255 (EPA Proposed Findings of Fact, Trial Phase 1) at 15 (citing 82 Fed. Reg. at 33,734). Moreover, "[t]he goal of systemic review methods is to ensure that the review is complete, unbiased, reproducible, and transparent." *Id.* The EPA explains that a systematic review is pertinent and is ideal in conducting a risk assessment under TSCA. *See id.* at 14-19 (arguing that during the first phase of trial, before the NTP Monograph was finalized, that Plaintiffs failed to meet their burden because they did not conduct a systematic review).

33. The NTP Monograph is a systematic review as the EPA has defined that term. The NTP Monograph is a scientific investigation, focusing on a specific question using explicit, pre-

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> inverse associations between fluoride exposure measures and children's IQ. There was also a significant dose response relationship between group-level fluoride exposure and IQ. **In stratified dose-response meta-analyses of the low risk-of-bias studies, the direction of association remained consistent when group-level exposure was restricted to <4mg/L, <2 mg/L, and <1.5 mg/L fluoride in drinking water and <4 mg/L, <2 mg/L, and <1.5 mg/L fluoride in urine.** The regression slopes meta-analysis of 13 studies (n = 4,475 children) with individual-level measures of fluoride found **a significant decrease in IQ of 1.63 points (95% CI: −2.33,−0.93; p-value <0.001) per 1-mg/L increase in urinary fluoride.** In subgroup analyses of both group-level and individual level data, the direction of the association remained inverse when stratified by study quality (high versus low risk of bias), sex, age group, outcome assessment, study location, exposure timing, and exposure metric.

Dkt. No. 443 (citing *NTP Monograph on the State of the Science Concerning Fluoride Exposure and Neurodevelopment and Cognition: A Systematic Review*, National Toxicology Program (August 2024), https://ntp.niehs.nih.gov/sites/default/files/2024-08/fluoride_final_508.pdf (emphases added)).

The EPA disputes whether the post-trial version of the NTP Monograph is properly considered by this Court. *See* Dkt. No. 444. Because the Court finds in Plaintiffs favor based upon the version of the NTP Monograph that the Court reviewed at trial, and because neither party suggests the aspects of the NTP Monograph that the Court reviewed therein have changed in a way that undermines Plaintiffs' case, the Court need not resolve this dispute. Instead, the Court bases its finding upon the version of the NTP Monograph reviewed at trial (Trial Exhibit 67), though noting that it has since been published formally, and that if it were considered, it would find the published Monograph even more supportive of the decision reached herein.

specified methods. Namely, the objective of the NTP Monograph was "[t]o conduct a systematic review of the human, experimental animal, and mechanistic literature to evaluate the extent and quality of the evidence linking fluoride exposure to neurodevelopmental and cognitive effects in humans." NTP Monograph at xii (Abstract). Regarding the methods: "[a] systematic review protocol was used following the standardized OHAT [referring to the Office of Health Assessment and Translation] systematic review approach for conducting literature-based health assessments. This monograph presents the current state of evidence associating fluoride exposure with neurocognitive or neurodevelopmental health effects and incorporated predefined assessments of study quality and confidence levels. Benefits of fluoride with respect to oral health are not addressed in this monograph." *Id.* Ultimately, the NTP Monograph analyzed all available studies assessing impacts of fluoride, including seventy-two human studies that assessed the association between fluoride exposure and IQ in children and integrated the findings in the studies to draw conclusions about the impact of fluoride to neurodevelopmental and cognitive effects in humans. *Id.* at xii-xiii. Moreover, the NTP Monograph's protocol underwent multiple rounds of peer review. *Id.* at G-1. And the Monograph's substance underwent multiple rounds of peer review, including assessment of technical accuracy, and the sufficiency of evidence supporting the NTP Monograph's conclusion. *Id.* at x. The peer review panel includes professors from Brown University School of Public Health, Columbia University Medical Center, Johns Hopkins Bloomberg School of Public Health, and other epidemiological experts. *See id.* The EPA does not dispute that the NTP Monograph is likely to have captured all relevant studies that were in existence as of the Monograph's literature cutoff date analyzing human data regarding neurodevelopmental impacts of fluoride. Dkt. No. 421 at 12-13. Even before the NTP Monograph was formally published, the EPA agreed that the NTP Monograph "followed the rules that have been developed by NTP for conducting systematic reviews" and utilized a "rigorous approach to assembling the evidence," "clearly defined rules for identifying and evaluating studies," and "a well-defined protocol for drawing inferences" from the studies. *Id.*[8] Indeed,

[8] Plaintiffs submitted evidence indicating that the delay in publication was highly irregular, and perhaps politically motivated. *See* Dkt. No. 385 at 12-13. The Court excluded evidence regarding

EPA's expert, Dr. Barone agreed that the NTP Monograph is a "high quality review." Dkt. No. 440, Feb. 13, 2024, Trial Tr. at 1427:2-4 (Barone). Accordingly, the Court finds that the NTP Monograph is probative and afforded significant weight in the risk evaluation analysis.

34. The NTP Monograph concludes that the majority of the 72 epidemiological studies on fluoride and IQ that had been published by April 2021 found an association between fluoride and reduced IQ in children, including 18 of the 19 studies the NTP Monograph deemed "high quality" and "low-risk-of-bias" as well as 46 of the 53 lower-quality studies. NTP Monograph at xii (NTP Monograph Abstract describing 46 of the 53 low-quality studies found an association between higher fluoride exposure and lower IQ in children and 18 of 19 high-quality studies reported an association between higher fluoride exposure and lower IQ in children including 3 prospective cohort studies and 15 cross-sectional studies); *accord* Dkt. No. 428-1, Trial Ex. 69 at 65 (NTP Board of Scientific Counselors Working Group Report agreeing that low-risk-of-bias studies were "consistent," meaning generating results in the same direction, in finding a negative association between fluoride exposure and children's IQ); Dkt. No. 396, Feb. 1, 2024, Trial Tr. at 313:25-314:5 (Grandjean) (summarizing and agreeing with NTP Monograph's finding that higher fluoride exposure (at or above 1.5 mg/L) was found to be associated with lower IQ scores in children in the majority of both low- and high-quality studies the NTP Monograph reviewed); Dkt. No. 414, Feb. 9, 2024, Trial Tr. at 1197:2-15 (Savitz) (expressing confidence in NTP's literature search strategy and its ability to identify all relevant studies on fluoride exposure published prior to the closing date of April 21, 2021, and confirming that the "vast majority of studies" that NTP reviewed identified an association between fluoride and reduced IQ), 1114:24-1115:1 (describing NASEM critique of adequate definition of the term "consistent" in NTP Monograph, but not disagreeing with characterization of NTP Monograph finding association between IQ and fluoride). The NTP Monograph explained its key finding regarding the impact of fluoride on children's IQ as follows:

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partisanship relating to publishing of the Monograph, in large part because the EPA did not argue the Monograph be afforded less weight for its draft status. *Id.* at 17. Eventually, the NTP Monograph was published, in August 2024. *See* Dkt. No. 442.

> ***In summary, the high-quality studies (i.e., studies with low potential for bias) consistently demonstrate lower IQ scores with higher fluoride exposure [e.g., represented by populations whose total fluoride exposure approximates or exceeds the WHO Guidelines for Drinking-water Quality of 1.5 mg/L of fluoride (WHO 2017)].*** The consistency in association is observed among studies of varying study designs, exposure measures, and study populations. Although some studies that conducted multiple analyses observed within-study variations in results (e.g., differences between subsets of IQ tests), these variations were unique to individual studies and did not detract from the overall consistency in the findings that higher fluoride is associated with lower IQ scores.

Trial Ex. 67 at 47 (emphasis added).

35. To come to this conclusion: the NTP Monograph identified 19 studies as being high-quality (*i.e.*, low risk-of-bias); all but one identified an association between fluoride and reduced IQ in children: Bashash et al. 2017; Choi et al. 2015; Cui et al. 2018; Ding et al. 2011; Green et al. 2019; Rocha-Amador et al. 2007; Saxena et al. 2012; Seraj et al. 2012; Sudhir et al. 2009; Till et al. 2020; Trivedi et al. 2012; Wang et al. 2012; Wang et al. 2020b; Xiang et al. 2003a; Xiang et al. 2011; Yu et al. 2018; Zhang et al. 2015b. NTP Monograph at 40, 29-39 (Table 6). To summarize these high-quality studies:

a. Bashash (2017): This study evaluated 211 mother-child pairs that were participants in The Early Life Exposures in Mexico to Environmental Toxicants Project ("ELEMENT Cohort")[9] and concluded that higher prenatal fluoride exposure was associated with statistically

[9] Bashash (2017) (like Green (2019) and Till (2020), discussed in subparagraphs (b) and (c)), is a longitudinal cohort study, evaluating fluoride in the urine of pregnant mothers. In such a cohort study design:

> [A] healthy group of people is assembled and followed forward in time and observed for the development of dysfunction. Such studies are invaluable for determining the time course for development of dysfunction (*e.g.*, follow-up studies performed in various cities on the effects of lead on child development). This approach allows the direct estimate of risks attributed to a particular exposure, since toxic incidence rates in the cohort can be determined. Prospective study designs also allow the study of chronic effects of exposure. One major strength of the cohort design is that it allows the calculation of rates to determine the excess risk associated with an exposure. Also, biases are reduced by obtaining information before the disease develops. This approach, however, can be very time-consuming and costly. In cohort studies information bias can be introduced when individuals provide distorted information about their health because they know their exposure status and may have been told of the expected health effects of the exposure under study.

significant lower scores on tests of cognitive function in offspring at ages 4 and 6-12 years; an increase in maternal urine fluoride of 0.5 mg/L predicted a 3.15 lower General Cognitive Index ("GCI") score and 2.50 lower IQ score of the offspring. Dkt. No. 432-2, Trial Ex. 106 at 1. ELEMENT collected urinary samples from women during pregnancy and from their children when the children were 6-12 years old (299 mother-child pairs) recruited from hospitals caring for low to moderate income populations in Mexico City. *Id.* at 1-2. The mean urinary fluoride in mothers and children was 0.90 mg/L (mothers) and 0.82 mg/L (children). *Id.* Child intelligence was measured via GCI for children at age 4 and IQ and from the Wechsler Abbreviate Scale of Intelligence ("WASI") at ages 6-12. *Id.* Fluoride exposure derived from fluoridated salt and naturally occurring fluoride in drinking water in Mexico City, ranging from 0.15 to 1.38 mg/L. *Id.* at 2. A second morning void ("spot") urine sample was targeted for collection during each trimester of pregnancy from mothers and the offspring children at time of measurements of intelligence. *Id.* A total of 1,484 prenatal samples was measured; after controlling for, *e.g.*, quality, duplicates, covariates, and outliers, 877 urine samples adjusted for creatinine were retained, stemming from 512 unique mothers. *Id.* at 3. A total of 287 mother-child pairs had complete data on exposure and outcome for children at 4 years and 211 for children at 6-12 years. Dkt. No. 434-27, Trial Ex. 656 (Savitz Summary of Methods in Key Studies of Fluoride Exposure and Neurodevelopment).

b. Green (2019): Green et al. (2019) studied mother-child pairs in Canada that were

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> More credence should be given to those studies in which both observer and subject bias are carefully controlled (*e.g.*, double-blind studies). A special type of cohort study is the retrospective cohort study, in which the investigator goes back in time to select the study groups and traces them over time, often to the present. The studies usually involve specially exposed groups and have provided much assistance in estimating risks due to occupational exposures. Occupational retrospective cohort studies rely on company records of past and current employees that include information on the dates of employment, age at employment, date of departure, and whether diseased (or dead in the case of mortality studies). Workers can then be classified by duration and degree of exposure.

Dkt. No. 429-7, Trial Ex. 17 at 17-18. Moreover, "[p]ositive or negative results from a properly controlled prospective study *should weigh heavily* in the risk assessment process." *Id.* (emphasis added).

participants in the Maternal-Infant Research on Environmental Chemicals program ("MIREC Cohort") and found a statistically significant, negative association between fluoride exposure and IQ in boys, but not girls. Dkt. No. 432-5, Trial Ex. 109 at 940, 944. The study concluded that 1 mg/L increase in maternal urinary fluoride was associated with a 4.49-point lower IQ score in boys and 1 mg higher daily intake of fluoride among pregnant women was associated with a 3.66 lower IQ score in boys and girls. *Id.* MIREC collected urinary spot samples and estimates of daily fluoride intake from water consumption for pregnant women recruited from cities across Canada (Vancouver, Montreal, Kingston, Toronto, Hamilton, Halifax). *Id.* at 941-942. Urinary samples from the women were collected across each trimester of pregnancy; the mean maternal urinary fluoride of mothers was 0.42 mg/L in fluoridated communities and 0.27 mg/L in non-fluoridated communities. *Id.* at 944. The mean estimated intake of water fluoride concentration was 0.39 mg/day; 0.43 mg for women in communities with fluoridated drinking water and 0.26 for those living in communities without fluoridated drinking water. *Id.* Children were between ages 3 and 4 years at testing. *Id.* at 940. Data on exposure and outcome was complete for 512 mother-child pairs measuring exposure through maternal urinary fluoride and 400 mother-child pairs estimating water fluoride intake. *Id.*

c. Till (2020): Till (2020) studied samples taken from 398 mother-child pairs that participated in the MIREC Cohort project (the cohort studied in Green (2019)), to evaluate IQ of children that were breastfed compared to formula-fed as infants in areas that had fluoridated and non-fluoridated water. Dkt. No. 432-19, Trial Ex. 123 at 1. This study found that an increase in fluoride intake from infant formula corresponded to an 8.8 decrement in performance IQ which was statistically significant, including after controlling for fetal fluoride exposure. *Id.*[10]

d. Cross-sectional studies[11] of children in China found significant inverse association

[10] Till (2020) and Green (2019) exemplify how the same samples from one cohort may be analyzed in multiple studies to either confirm results from a previous study or to extract different information from the same samples from a given cohort.

[11] Cross-sectional studies are afforded less weight than cohort studies. As the EPA guidelines explain:

> In cross-sectional studies or surveys, both the disease and suspected risk factors are ascertained at the same time, and the findings are

between fluoride and children's IQ score: Xiang (2003a) (finding significant inverse correlation between IQ and urinary fluoride; significant association of fluoride on IQ score based on drinking water levels); Ding (2011) (significant association between urinary fluoride and decrease in IQ score); Xiang (2011) (significant association between serum (blood-derived sample) fluoride and reduced IQ score in children); Wang (2012) (significant correlation between total fluoride intake and reduced IQ); Zhang (2015b) (significant correlation between reduced IQ score and children's serum fluoride, and urinary fluoride), Cui (2018) (significant association between IQ score and urinary fluoride); Yu (2018) (significant difference in mean IQ scores in high water fluoride areas compared to normal water fluoride areas); and Wang (2020b) (significant negative association between IQ and water and urinary fluoride and IQ in boys and girls). NTP Monograph at 29-33 (Table 6). One study, Cui (2020) identified a directionally negative, though not statistically significant decrease in mean IQ score with increasing fluoride levels. *Id.* at 32.

e. Rocha-Amador (2007), a cross-sectional study of children in Mexico found significant associations between fluoride and IQ scores. *Id.* at 33.

f. Cross-sectional studies of children in India found significant association between fluoride and intellectual impairment: Sudhir (2009) (found a significant increase in proportion of children with intellectual impairment with increasing drinking water fluoride levels); Saxena (2012) (significant correlations between reduced IQ and water fluoride and urinary fluoride levels); Trivedi (2012) (found significantly lower mean IQ scores in high fluoride villages compares to low-fluoride villages for boys and girls combined and separately). *Id.* at 38.

g. Siraj (2012), a cross-sectional study of children in Iran found a significant negative association between water fluoride and IQ score. *Id.* at 39.

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> useful in generating hypotheses. A group of people are interviewed, examined, and tested at a single point in time to ascertain a relationship between a disease and a neurotoxic exposure. This study design does not allow the investigator to determine whether the disease or the exposure came first, rendering it less useful in estimating risk. These studies are intermediate in cost and time required to complete compared with case reports and more complex analytical studies, but should be augmented with additional data.

Dkt. No. 429-7, Trial Ex. 17 at 16.

h. Soto-barreras (2019), a cross-sectional study of children in Mexico 9-10 years of age did *not* find a significant association between fluoride and IQ levels. *Id.* at 34.

36. In addition to the studies that the NTP Monograph deemed "high-quality," and thus most relevant to understanding impact of fluoride, the NTP Monograph explains that 46 of the 53 studies deemed low-quality by the NTP Monograph also found an association between fluoride exposure and reduced IQ in children. NTP Monograph at xii.

37. Several studies published after the NTP Monograph literature cut-off date (April 2021), *see* NTP Monograph at 5-12, 12 n.8, B-2, C-2-C-44, also found negative association between fluoride and IQ, and acutely, for boys – bolstering the NTP Monograph's finding of a negative association between IQ in children and fluoride exposure:

a. Goodman (2022a): studied samples from the ELEMENT cohort and concluded that an increase in maternal urinary fluoride predicated an average 2.12-point decrease in GCI scores of 4-year-olds and a 2.63 decrease in performance IQ of 6- to 10-year-olds. Dkt. No. 432-11, Trial Ex. 115 at 1-2. The study also found a marginal association with maternal urinary fluoride and verbal IQ across time. *Id.* at 2. The study concluded that visual-spatial and perceptual reasoning ability may be more impacted by prenatal fluoride exposure as compared to verbal abilities. *Id.*

b. Cantoral (2021): studied 103 mother-child pairs from the Programming Research in Obesity, Growth, Environment and Social Stressors ("PROGRESS Cohort") program. Dkt. No. 432-6, Trial Ex. 110 at 2. The PROGRESS Cohort collected data regarding dietary fluoride intake from mothers (via food and beverage) during pregnancy and neurodevelopmental testing from their offspring for 948 mother-child pairs from Mexico City. *Id.* at 2. Dietary fluoride intake was measured via food frequency questionnaires from mothers in trimesters two and three of pregnancy and children's cognitive, motor, and language outcomes were measured at 12 and 24 months. *Id.* at 1. Cantoral (2021) studied data from 103 mother-child pairs from the PROGRESS Cohort to understand if dietary fluoride intake during pregnancy is associated with toddlers' neurodevelopment. *Id.* The study found a statistically significant association between maternal fluoride intake and cognitive outcome in 24-month-old boys (0.5 mg/day increase in overall dietary fluoride intake associated with 3.5-point lower cognitive outcome). *Id.* There was no

statistical association for girls or boys at 12 months of age. *Id.* Averaging across the entire age group, a 0.5 mg/day increase was associated with a 3.46-point lower cognitive outcome in boys, which was statistically significant. *Id.* The study concludes: "[t]hese findings suggest that the development of nonverbal abilities in males may be more vulnerable to prenatal fluoride exposure than language or motor abilities, even at levels within the recommended intake range." *Id.*

c. Godebo (2023): this study assessed the association between chronic exposure to naturally occurring fluoride and drinking water and cognitive function in school-aged children, measured by two distinct assessments: a drawing test with familiar objects and the Cambridge Neuropsychological Test Automated Battery, Paired Associate Leaning ("CANTAB PAL")[12] test. Dkt. No. 432-14, Trial Ex. 118 at 15-16. The population studied was recruited from eight communities exposed to chronic fluoride ranging from 0.41 to 15.5 mg/L fluoride in water sources. *Id.* at 15. The study reported adverse associations of fluoride exposure in drinking water with children's drawing and CANTAB task performance, with the most significant negative impacts observed for more challenging drawing tasks (*i.e.*, drawing a donkey rather than a house or a person). *Id.* at 16. The study concluded that this may be indicative of a greater challenge "accessing working memory for this task." *Id.*

d. Adkins (2022): this study evaluated data collected from the Cincinnati Childhood Allergy and Air Pollution Study ("CCAAPS"). Dkt. No. 432-8, Trial Ex. 112 at 1. CCAAPS collected urine samples from children at 12 years of age and collected Behavior Assessment System for Children-2 which evaluates internalizing symptoms such as anxiety depression and somatization. *Id.* at 2. The study found that higher children's urinary fluoride concentrations were significantly associated with increased somatization, but not depression or anxiety. *Id.* The study found that male participants exhibited higher internalizing and somatization behaviors relative to female participants. *Id.* at 6. The study concluded that "[d]espite males and females having comparable urinary fluoride concentrations, males may be at greater risk for adverse effects of

[12] The tests present patterns and shapes on a screen and ask children to touch and recount the patterns to assess spatial memory and learning. Dkt. No. 432-14, Trial Ex. 118 at 10-11. Spatial memory and learning are linked to the medial temporal lobe *e.g.*, hippocampus, which the study reports is the brain region thought to be most affected by fluoride toxicity. *Id.* at 5.

fluoride exposure as the association between fluoride concentrations and internalizing symptoms was more robust among males." *Id.* at 9.

e. Risk Sciences International ("RSI"), under contract with Health Canada, also conducted an extensive systematic review of the fluoride neurotoxicity literature: Taher (2024). Dkt. No. 433-4, Trial Ex. 129; Dkt. No. 433-6, Trial Ex. 131 (Taher (2024) Supplementary Materials). Taher (2024) came to a similar conclusion as the NTP Monograph, finding a "moderate to strong magnitude (strength) of association between fluoride and neurocognitive effects with consistent evidence across studies for the impact on childhood IQ." Dkt. No. 433-4, Trial Ex. 129 at 21; Dkt. No. 433-6, Trial Ex. 131 at 1516 ("The overall evidence identified to date strongly suggests that fluoride can affect cognitive outcomes in children (specifically, reduction in IQ scores), at levels close to those currently seen in North American drinking water.").[13]

38. Other post-NTP Monograph studies did not find fluoride was associated with adverse cognitive outcomes in children:

a. Ibarluzea (2021): the study evaluated data from 316 to 248 mother-child pairs from the Infancia y Medio Ambiente cohort project ("INMA Cohort"). Dkt. No. 432-10, Trial Ex. 114 at 1. The INMA Cohort draws on data from mothers and children in Gipuzkoa, Spain (Basque Country) living in fluoridated and non-fluoridated water communities that supplied water with the mean fluoride level of 0.81 mg/L. *Id.* at 1, 3. The INMA study collected maternal urinary fluoride levels in the first and third trimesters of pregnancy, and children's cognitive domains and

[13] Unlike the NTP Monograph, Taher (2024) considered evidence relating to multiple endpoints (*i.e.*, a particular adverse effect, *see* Dkt. No. 434-15, Trial Ex. 535 at 43) aside from reduced IQ to decide which endpoints need be accounted for by regulators; endpoints considered included kidney dysfunction, sex hormone disruptions, and dental fluorosis, *see* Dkt. No. 433-4, Trial Ex. 129 at 21-23. Taher (2024) concluded that dental fluorosis and reduced IQ are critical endpoints; evidence supported the association between fluoride and those two adverse effects. *See id.* at 27. Taher (2024) did find that dental fluorosis should be the primary endpoint used by regulators because data regarding the association between dental fluorosis and fluoride was more certain than evidence regarding the association between IQ reduction and fluoride. *Id.* However, Taher (2024) explained that *both* dental fluorosis, and separately, IQ reduction in children should be considered by regulatory bodies, including the United States EPA, when assessing regulation of fluoride. *Id.* To this end, the review recommended that fluoride at 1.56 mg/L be deemed hazardous, explaining that this level should be utilized by regulators in its calculations to protect the public against *both* dental fluorosis *and* IQ reduction. *See id.* Thus, the findings of Taher (2024) are consistent with the NTP Monograph's finding that fluoride is associated with reduced IQ, particularly at exposure levels above 1.5 mg/L.

intelligence indexes, evaluated used the Bayley Scales (age 1) and McCarthy Scales (age 4). *Id.* at 1. The study concluded that per unit of maternal fluoride across the pregnancy was associated with a sizeable *increase* in IQ scores (15-point increase) and an increase in verbal, performance, numeric, and memory domains in boys. *Id.* For girls, there was no significant association between maternal fluoride and cognitive score. *Id.*

b. Dewey (2023): This study compared data collected from maternal-child pairs in Calgary, Canada pre- and post-May 19, 2011, when the city stopped fluoridating its drinking water (with a recommended level of 0.7 mg/L) to discern if fluoridated drinking water was associated with children's intelligence and executive function at 3-5 years of age. Dkt. No. 432-13, Trial Ex. 117 at 1. The study compared data from maternal-child pairs that were either fully exposed to fluoridated drinking water throughout pregnancy, exposed for part of the pregnancy, and those not exposed to fluoridated drinking water. *Id.* The study found no adverse associations between maternal exposure to fluoridated drinking water for intelligence. *Id.* at 7. The study observed that maternal exposure to fluoridated drinking water was associated with poorer executive function in preschool aged children and, particularly, girls. *Id.*

c. Do (2022): This study collected additional data from participants in Australia's National Child Oral Health Study 2012-14, which gathered data from children aged 5-10 years, and collected additional data from them again 7-8 years later but before the children turned 18 years of age. Dkt. No. 432-9, Trial Ex. 113 at 1. The study estimated lifetime exposure to fluoridated water based upon residential history and postcode-level fluoride levels in public tap water and measured children's emotional and behavioral development and executive functioning using questionnaires. *Id.* The study concluded that exposure to fluoridated water during the first 5 years of life (post-birth) was not associated with altered measures of child emotional and behavioral development and executive functioning by 18 years of age. *Id.*

39. For several reasons, the studies that did not find a negative association between fluoride and IQ, or that observed the association in some groups (boys) but not others (girls) do not undermine the significant evidence finding such an association, reflected in the NTP Monograph and studies published after the Monograph. The Court affords less weight to these studies finding

lack of an association due to various characteristics of those studies:

a. The reliability of Ibarluzea (2021) is questionable in several respects:

i. This study found that per one unit increase in the mg/L maternal urinary fluoride, there was an association with a 15-point increase in the IQ of boys associated with maternal urinary fluoride. Dkt. No. 432-10, Trial Ex. 114 at 1. Dr. Savitz, EPA's expert, agrees that this finding is an outlier and unexpected, insofar as no other study has reported a *positive* association between fluoride exposure upon IQ, and does not meaningfully support that fluoride is beneficial. *See* Dkt. No. 414, Feb. 9, 2024, Trial Tr. at 1067:2-1069:11 (Savitz) ("Again, based on what I know, I would doubt that that is an accurate reflection of the causal impact of fluoride on IQ."). Experts also testified that they were not aware of *any* other chemical known to increase the IQ of humans by 15 points. Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 372:14-16 (Grandjean); Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 111:4-6 (Hu). This association appears scientifically implausible and raises questions about the overall reliability of this study.

ii. Further, the 15-point increase in IQ disappeared to reflect a null finding when the maternal urinary fluoride was not adjusted for creatinine. Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 109:5-11 (Hu). Adjusting maternal urinary fluoride for creatinine is standard practice, and results from creatinine-adjusted urinary fluoride are considered the informative and reliable results of a study. Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 108:7-10 (Hu); Dkt. No. 414, Feb. 9, 2024, Trial Tr. at 1089:5-17 (Savitz), 1090:24-1091:2 (Savitz). However, adjusting for creatinine is expected to sharpen results, because the adjustment countervails for urinary dilution which might introduce noise into a study; the adjustment is *not*, however, expected to have any significant impact on the direction of results of the study. Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 108:11-22 (Hu); Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 372:25-373:22 (Grandjean), 376:15-378:24 (Grandjean). The results in the Ibarluzea (2021) study, which transitioned from a significant positive association to a null finding when urinary fluoride was adjusted for creatinine, was considered surprising and not a plausible result. Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 109:13-110:7 (Hu); Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 372:25-373:22 (Grandjean), 376:15-378:24 (Grandjean). Plaintiffs' experts credibly testified that this discrepancy suggests there was

an error when matching fluoride and creatinine data. Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 372:25-373:22 (Grandjean). EPA's experts at trial could not explain or account for this aspect of the study. Dkt. No. 414, Feb. 9, 2024, Trial Tr. at 1091:3-1093:8 (Savitz).

iii. Another concern with the Ibarluzea (2021) study is that it did not adjust for seafood as a covariate in the analysis of fluoride and IQ. Dkt. No. 397, Feb. 2, 2024, Trial Tr. at 453:12-17 (Grandjean). Seafood is both high in fluoride content and omega 3 fatty acids. Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 110:20-23 (Hu). This is problematic because omega 3 fatty acids have beneficial effects on cognition, and thus seafood may be a confounding factor, skewing results of a study if the population has a high seafood ingestion rate. Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 110:20-111:3 (Hu). The study did adjust for cord blood mercury levels, which could operate as an adjustment for fish consumption because fish often contain mercury. Dkt. No. 414, Feb. 9, 2024, Trial Tr. at 1073:20-1074:14 (Savitz). However, the bigger the fish, the more likely the accumulation of mercury; conversely, the smaller the fish, the less likely the accumulation of mercury. *Id.* at 1076:20-1078:9. Yet, in coastal Spain where the study was conducted, sardines and anchovies are popular, which are small fish that are lower on the food chain and accordingly low in mercury. *See* Dkt. No. 417, Feb. 2, 2024 at 458:23-459:17 (Grandjean); Dkt. No. 414, Feb. 9, 2024, Trial Tr. at 1269:24-1270:12 (Savitz). Thus, it is not clear that the adjustment for cord blood mercury levels is a sufficient proxy for seafood consumption. To this end, Dr. Savitz agreed that it is a reasonable hypothesis that fish consumption accounted for the beneficial results associated with IQ observed in the Ibarluzea (2021) study. Dkt. No. 414, Feb. 9, 2024, Trial Tr. at 1069:23-1070:18 (Savitz).

iv. Taher (2024) likewise concluded that Ibarluzea (2021) does not overcome evidence linking fluoride to reduced IQ in children. Namely, Taher (2024) concluded that "[t]he available evidence demonstrated a moderate to strong magnitude (strength) of association between fluoride and neurocognitive effects with consistent evidence across studies for the impact on childhood IQ at fluoride exposures relevant to current North American drinking water levels." Dkt. No. 433-4, Trial Ex. 129 at 21. This is because, "[f]ocusing on high quality cohort studies, most of the evidence suggests a reduction in childhood IQ scores associated with fluoride levels,

though results from one 2023 study in Spain (Ibarluzea et al. 2022) documented an improvement in specific cognitive domain scores in boys." *Id.*

b. Dewey (2023) is not strong evidence regarding the association between fluoride and reduced IQ because of the design of this study. The study attempted to take advantage of what was thought to be a naturally occurring cohort with an exposure contrast (*i.e.*, one cohort exposed to fluoride and one not exposed to fluoride) to see if there was a meaningful difference in cognitive outcomes amongst the two groups. Dkt. No. 397, Jan. 31, 2024, Trial Tr. at 368:22-369:7 (Grandjean). Specifically, the study looked at individuals from a Canadian community that, for a long time, fluoridated its water and stopped fluoridating the water; the study compared the cognition of children in fluoridated and non-fluoridated groups to discern the impact of fluoride. Dkt. No. 397, Jan. 31, 2024, Trial Tr. at 368:22-369:7 (Grandjean). However, the study did not collect data on the urinary fluoride levels of the mother or assess how long pregnant mothers lived in the area prior to their pregnancy. Dkt. No. 397, Jan. 31, 2024, Trial Tr. at 368:22-369:18 (Grandjean). This is relevant because women who live in a fluoridated area throughout their lives will have fluoride which accumulates in her bones from consumption of fluoridated water, along with other sources; for several years after cessation of fluoride exposure she is likely to release accumulated fluoride from her bones into blood due to skeletal breakdown. Dkt. No. 397, Jan. 31, 2024, Trial Tr. at 370:6-371:12 (Grandjean); Dkt. No. 402, Feb. 8, 2024, Trial Tr. at 932:16-20 (Thiessen). This skeletal breakdown is particularly present during pregnancy, as the maternal skeleton dissolves itself to provide calcium to the growing fetal skeleton. Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 121:10-20 (Hu). Accordingly, the group that was considered non-fluoridated in the study, thus creating an exposure contrast between the two groups allowing for a potential association to be observed, may have in fact exposed the child to fluoride during pregnancy if she lived in a fluoridated area prior to the study (a phenomenon that is not reported or considered by the study). This could lessen the exposure contrast and calls the results of the study into question. *See* Dkt. No. 397, Jan. 31, 2024, Trial Tr. at 368:22-369:18 (Grandjean). EPA's expert witnesses did not account for this concern regarding the study design. Thus, the Dewey study is accorded diminished weight.

c. Do (2022) assessed primarily behavioral outcomes rather than impact on IQ in children and, as Dr. Savitz testified, "doesn't stand out as definitive or more persuasive," relative to other studies directly on point to association of fluoride on the IQ of children. Dkt. No. 414, Feb. 9, 2024 Trial Tr. at 1106:22-1107:10 (Savitz). Plaintiffs' experts also expressed concerns with the study. The study utilized the "SDQ" test to measure impact of fluoride on children in Australia, which is a test that, for certain cultural or linguistic reasons, has been determined to be unreliable for Australians by another study conducted by the co-author of Do (2022). Dkt. No. 397, Jan. 31, 2024, Trial Tr. at 364:8-14, 365:15-366:4 (Grandjean). EPA's expert witness did not rebut evidence that there were significant problems with the validity of the SDQ test in Australia. Dkt. No. 415, Feb. 12, 2024, Trial Tr. at 1240:1-6 (Savitz). Further, the value of this study is weakened because it did not analyze individualized data, but instead measured exposure based on residence of the child and community-wide data on fluoride in that area. *See* Dkt. No. 396, Feb. 1, 2024, Trial Tr. at 240:17-19 (Lanphear) (explaining that individualized data is generally a strength of a study); Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 366:5-367:4, 367:15-368:4 (Grandjean). Lack of individualized data can lead to exposure imprecision, creating "noise" in the data, which may bias results toward the null, *i.e.*, noise makes it less likely to show an association between the chemical and a result. Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 106:18-107:16 (Hu); Dkt. No. 396, Feb. 1, 2024, Trial Tr. at 281:14-17 (Lanphear), 281:24-282:3 (Lanphear), 317:16-24 (Grandjean); Dkt. No. 414, Feb. 9, 2024, Trial Tr. at 1176:4-17 (Savitz) (agreeing with a statement made in his textbook that in general exposure misclassification tends to produce results with a bias towards the null). Thus, this study is not particularly probative evidence as to association between fluoride and IQ of children.

40. EPA experts agreed, in line with the NTP Monograph's conclusion, that fluoride is associated with adverse IQ in children at "higher" levels of exposure. Namely, Dr. Barone testified that he agreed that there is "something going on" at higher-dose levels, though unclear about where the threshold is. Dkt. No. 415, Feb. 12, 2024, Trial Tr. at 1372:9-1373:9 (Barone). Dr. Barone agreed that, at 4 mg/L of fluoride exposure and above, there is more data to support a finding of an adverse effect associated with fluoride. *Id.* at 1373:1-9 (Barone). Dr. Barone further

testified: "I agree with the NTP's conclusions that at some level above 1.5 mg/L that there is moderate evidence to support an association between fluoride and developmental IQ decrements." Dkt. No. 416, Feb. 12, 2024, Trial Tr. at 1428:4-11 (Barone).[14] The primary concern presented by EPA's experts relates to lack of clarity as to whether *lower* exposure levels of fluoride (below 1.5 mg/L) results in an adverse outcome and the precise relationship between dose and response. *See* Dkt. No. 415, Feb. 12, 2024, Trial Tr. at 1357:9-1360:10 (Barone). For example, Dr. Savitz (EPA's expert witness) did not opine that the NTP Monograph's main conclusion that fluoride is presumed to be a cognitive neurodevelopmental hazard to humans was incorrect, though expressing concerns as to a previous draft of the Monograph regarding whether its conclusion was well explained and qualified. Dkt. No. 414, Feb. 9, 2024, Trial Tr. at 1113:16-1115:23 (Savitz) ("Whether [a committee reviewing a draft of the NTP Monograph] agreed with [the NTP Monograph's conclusion] was not the issue. It was – the story that gets to the punchline at the end we did not find persuasive."). Indeed, Dr. Savitz explained that he does not have a basis to challenge the NTP's conclusion that, with moderate confidence, there is an association or appears to be an association between neurological decrements in fluoride concentrations above 1.5 mg/L. *Id.* at 1140:10-19 (Savitz) ("I don't have any reason to challenge [this conclusion], but I haven't corroborated it by going through the dozens of studies one-by-one to make my own assessment."). Dr. Savitz likewise made clear he did not undertake a complete review of the NTP Monograph, but testified his primary concern was the Monograph's "inferences regarding lower levels of fluoride exposure." *Id*. at 1129:11-1131:3 (Savitz).

41. The robust body of scientific literature systematically assessed by the NTP Monograph (described above, ¶ 35) and literature published after the NTP Monograph cutoff date (described above, ¶ 37), even considering some countervailing scientific literature (described above, ¶¶ 38-39) establishes by a preponderance of the evidence that fluoride is associated with reduced IQ in

[14] Dr. Barone testified that the NTP Monograph was helpful but not complete and thus insufficient to satisfy the hazard identification prong of TSCA hazard assessment. Dkt. No. 440, Feb. 13, 2024, Trial Tr. at 1428:22-1429:3 (Barone). That testimony is not credible because it directly contradicts Dr. Barone's prior testimony during his deposition that the literature the NTP reviewed through April 2021 was sufficient to satisfy the human evidence standard for identifying a hazard under the EPA's TSCA guidelines. *Id.* at 11-21.

children – at least at "higher" concentration levels, *i.e.*, above 1.5 mg/L (measured in either water fluoride levels or urinary fluoride levels). At the hazard identification step, the EPA does not require showing that an adverse effect is present at the level akin to the exposure in the community (*i.e.*, 0.7 mg/L) or require the establishment of a dose-response relationship of the chemical at "lower" levels. Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 493:16-495:12 (Barone). The evidence regarding the "higher" exposure levels is sufficient to satisfy the hazard identification step of the analysis.

42. Regardless, scientific literature in the record also indicates there is an association between fluoride and reduced IQ in children even at "lower" levels of exposure (*i.e.*, below 1.5 mg/L).

43. Two of the three high-quality studies that evaluated the effects of "lower" levels of fluoride exposure (below 1.5 mg/L) did observe an association between fluoride and reduced IQ in children or boys. Namely: (1) Bashash (2017), studied mother-child pairs from the ELEMENT Cohort (Mexican population) and observed a statistically significant decrement of 3.15 GCI score and 2.5 IQ score of offspring per an increase of 0.5 mg/L of maternal urinary fluoride where the mean maternal urinary fluoride in mothers was **0.9 mg/L**, Dkt. No. 432-2, Trial Ex. 106 at 1; and (2) Green (2019) studied mother-child pairs in the MIREC Cohort (Canadian population) and found a statistically significant decrement of 3.66 IQ score in boys only (3.66 IQ score decrement per a 1 mg/L per day increase in maternal urinary fluoride) where the mean maternal urinary fluoride of mothers was **0.42 mg/L**, Dkt. No. 432-5, Trial Ex. 109 at 1-3, 5.

44. Another program collected samples from 837 mother-child pairs from the Odense municipality in Denmark: the Odense Child Cohort ("OCC Cohort"). Dkt. No. 432-15, Trial Ex. 119 at 1. The OCC Cohort measured maternal urinary fluoride during pregnancy and the IQ of school-aged offspring of those mothers. *Id.* The maternal urinary fluoride concentrations averaged at **0.58 mg/L** per day. *Id.* at 2. The study, when accounting for covariables did **not** observe a statistically significant association between maternal urinary fluoride and child Full-Scale IQ score, with no clear interaction between sex and fluoride exposure. *Id.*

45. The result of the OCC Cohort does not negate the findings regarding the MIREC and ELEMENT cohorts. It is inherently more difficult to observe an adverse effect of a chemical at

lower exposure levels because of reduced exposure contrast[15] at those levels. Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 113:2-25 (Hu), 114:8-14 (Hu); Dkt. No 396, Feb. 1, 2024, Trial Tr. at 213:5-25 (Lanphear); Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 525:9-526:13 (Berridge). EPA's expert, Dr. Savitz, agreed. Dkt. No. 402, Feb. 8, 2024, Trial Tr. at 1009:7-23 (Savitz) ("[Y]ou could think of the worst cases, if we all had the exact same value, everybody in the population had the same exposure, you could not do an informative study of the association of exposure with a disease. And if it's very narrow, of course, you're only able to study – if you're only able to study, let's say, the contrast of, you know, .4 and .5 milligrams per liter fluoride, you're going to have a tough time, even if there were an effect, it's going to be difficult to find because you have a very limited contrast. As you spread that out more, of course, you are – you have a larger contrast and you're able to address a more informative range of exposure."). It is particularly difficult to observe effects of fluoride at lower exposure levels because of challenges in finding a control group with zero or very little fluoride exposure. Dkt. No 396, Feb. 1, 2024, Trial Tr. at 212:7-213:25 (Lanphear). This is because fluoride exposure is prevalent. Some common sources aside from fluoridated water include naturally occurring fluoride in food and beverage, fluoride in food and beverage made with fluoridated water, and other products, like toothpaste. *Id*. at 212:10-19 (Lanphear). Thus, it is difficult to find a control group without any fluoride exposure; the "noise" created by background fluoride exposure tends to obscure the contrast between those who consume fluoridated water and those who do not. *Id*. at 212:19-23 (Lanphear) ("And so if we wanted to ask a question . . . is there a difference in children who are unexposed to fluoride? Well, we really can't find children who are unexposed to fluoride versus kids who have levels in a nonfluoridated community or a fluoridated community."). It is thus more challenging to observe

[15] Exposure contrast refers to the difference between exposure of a chemical in one group (a control group) and another group (the group exposed to the chemical). Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 113:6-22 (Hu). For example, an observer would compare a group with less or no fluoride exposure to a group with more exposure to determine if there is a meaningful difference in the group with more exposure. *See* Dkt. No 396, Feb. 1, 2024, Trial Tr. at 212:10-23 (Lanphear). When trying to observe effects of a chemical at lower levels, there is less "exposure contrast" between the control group and exposed group. *See id.* at 212:10-213:25. Dr. Hu provided an illustration: "It's sort of like looking at, you know, a picture and trying to determine whether this shade is different from that shade. If you increase the contrast, it's easier to see." Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 114:12-14 (Hu).

effects at lower concentration levels of fluoridated water. *Id*. at 212:24-213:25 (Lanphear). Accordingly, the Court finds convincing and credible the expert testimony that studies analyzing the OCC Cohort are not inconsistent with studies analyzing the ELEMENT and MIREC Cohorts; the lower exposure levels account for some difficulty in repeating observed effects. Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 116:24-117:4 (Hu).[16] In short, the association between intake of water at lower fluoridated levels and IQ is likely harder to detect. Inconsistent results between studies are not unexpected. The two high-quality studies which detected such an association at lower concentration levels of fluoride remain significant and are not undermined by the OCC Cohort study.

46. In conclusion, Plaintiffs have established by a preponderance of the evidence that exposure to fluoride is associated with the adverse effect of reduced IQ in children, and particularly, young boys. Hence, the hazard identification step of the analysis is satisfied.

2. Step 1B: Weight of the scientific evidence

a. *Framework*

47. Once a hazard has been identified, the EPA assesses the weight of the scientific evidence, wherein the risk assessor considers the weight of that evidence, determining which adverse effects (endpoints) are to be assessed, and which studies are appropriate for use in quantifying the relationship between the dose of the chemical and adverse effect(s) (response) at issue (the "dose-response" assessment). Dkt. No. 400, Feb. 4, 2024, Trial Tr. at 661:18-666:14 (Barone). To this end, not all studies are appropriately utilized in the dose-response assessment. *See* Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 494:17-495:12 (Barone). Rather, the EPA identifies the studies from the hazard identification step that are generally of high or medium quality, and thus are deemed permissible to use in the dose-response assessment. *Id.* at 494:17-495:12; Dkt. No. 421 at 5 (undisputed fact).

[16] Expert witnesses also testified credibly that there are some possible explanations for the differing study results; for example, it is possible that Denmark has higher iodine consumption, accounting for the discrepancy, as iodine deficiency is theorized to be an aggravating factor for impacts of fluoride on neurodevelopment. *See* Dkt. No. 396, Feb. 1, 2024, Trial Tr. at 248:10-250:3 (Lanphear).

48. The parties disagree as to precisely how the weight-of-the-scientific evidence analysis intersects with the subsequent step of the analysis: the dose-response assessment wherein a point of departure[17] is identified (Step 1C, discussed in Section III.A.3.). *See* Dkt. No. 421 at 22-23. Plaintiffs assert that the weight-of-the-scientific evidence analysis is a distinct, qualitative characterization of the evidence regarding a "chemical's potential to produce neurotoxicity," separate from the quantitative dose-response assessment wherein a point of departure is calculated (Step 1C, discussed in Section III.A.3). *Id.* The EPA asserts that there is not a clear distinction between the qualitative and quantitative dose-response assessment. *See id.* Dr. Barone, EPA's expert does recognize that risk evaluation includes a "quantitative track wherein the agency is doing a quantitative measurement, deriving a point of departure, and a qualitative track where [the assessor is] assessing whether that evidence is appropriate for that purpose." *See* Dkt. No. 400, Feb. 4, 2024, Trial Tr. at 666:9-14 (Barone). Moreover, Dr. Barone stated that: "in this weight of the scientific evidence evaluation . . . [we ask] how much data do we actually have for that particular endpoint or that particular outcome, and are there a series of outcomes that are related to neurotoxicity that we should consider as an example or reproductive toxicity. So we may have multiple endpoints to consider and multiple studies within that, that can be ***carried forward*** to dose response." *Id.* at 662:2-19 (emphasis added). This testimony intimates that the weight-of-scientific-evidence analysis occurs prior to, and separately from, the quantitative dose-response assessment wherein a point of departure is calculated. *See id.* However, to avoid any doubt, the Court assesses the weight-of-the-scientific evidence both as a standalone, qualitative issue, characterizing the weight of the evidence assessing the association between the chemical and endpoint (in this section of the analysis (Section III.A.2., as Step 1B)) and also assesses the weight-of-the-scientific-evidence, as part of the quantitative dose-response assessment wherein a point of departure is identified (Section III.A.3, as Step 1C, discussed below).

b. *Key finding*

49. The weight of the scientific evidence regarding fluoride's association with reduced IQ is

[17] As explained in depth in Section III.A.3., the point of departure represents the level at which the chemical at issue becomes hazardous.

sufficient to proceed to the dose-response assessment; the evidence in the record is appropriate for use in calculating a point of departure.

c. *Underlying findings*

50. The term "weight of the scientific evidence" is supported by EPA's systematic analysis of the related information to support the Agency's findings. *Id.* at 651:22–652:5; *accord* 40 CFR 702.33. The assessor uses the "best available science," in the analysis, which means that TSCA risk evaluations need to be unbiased and objective, and the methodologies employed must be transparent and reproducible and generally peer reviewed. Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 652:6-16 (Barone); *accord* 40 C.F.R. 702.33.

51. In the weight-of-the-scientific-evidence analysis, generally, high- or medium-quality studies are adequate to move to the dose-response determination. Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 494:17-495:12 (Barone); Dkt. No. 421 at 5 (undisputed fact). Still, the EPA sometimes carries over low-quality studies into the dose-response analysis as well. Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 494:21-495:1 (Barone). In this weight-of-the-scientific-evidence analysis, some or all factors referred to as the "Bradford Hill" factors may be considered. Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 626:8-24 (Barone). The nine Bradford Hill factors are: (1) strength of the association, (2) consistency of the association; (3) specificity of the association; (4) temporality of the association; (5) biological gradient (*i.e.*, dose response) of the association; (6) plausibility of the association; (7) coherence of the association, (8) experimental support for the association, and (9) analogies for the association. *See* Dkt. No. 198-3, Grandjean Trial Decl. ¶¶ 111-125. However, there is no mandate that each of the Bradford Hill factors be considered in the weight-of-the-evidence assessment in a non-cancer TSCA risk evaluation such as this one. *See* Dkt. No. 437-1, Trial Ex. 96 (hereinafter "PCE Risk Evaluation") at 326 (considering only consistency of association factor); Dkt. No. 437-7, Trial Ex. 102 (hereinafter "Methylene Risk Evaluation") at 285-95 (considering some, but not all, of the Bradford Hill factors).

52. As discussed previously, not every epidemiological study on fluoride has found associations with reduced IQ in children. *See* ¶¶ 35, 38. However, the evidence at issue is overall **consistent** as to the finding that fluoride is associated with reduced IQ in children, and there is a

vast amount of **experimental support** for the association:

a. The NTP Monograph studied a robust amount of literature regarding fluoride's impact on children's IQ: 72 epidemiological studies – 19 of which were deemed "high quality" and "low-risk-of-bias," and 53 lower-quality studies – a large majority of which identified an association between fluoride and reduced IQ. NTP Monograph at xii (describing that 46 of the 53 low-quality studies found an association between higher fluoride exposure and lower IQ in children and 18 of 19 high-quality studies reported an association between higher fluoride exposure and lower IQ in children including 3 prospective cohort studies and 15 cross-sectional studies). Indeed, when narrowing evidence to view only 19 studies that are high quality and low risk-of-bias, all but one identified an association between fluoride and reduced IQ: Bashash et al. 2017; Choi et al. 2015; Cui et al. 2018; Ding et al. 2011; Green et al. 2019; Rocha-Amador et al. 2007; Saxena et al. 2012; Seraj et al. 2012; Sudhir et al. 2009; Till et al. 2020; Trivedi et al. 2012; Wang et al. 2012; Wang et al. 2020b; Xiang et al. 2003a; Xiang et al. 2011; Yu et al. 2018; Zhang et al. 2015b). NTP Monograph at 29-40 (Table 6).

b. The findings of the NTP Monograph are properly afforded substantial weight. The NTP is headquartered within NIEHS, which is "is one of the premier environmental health sciences research institutions in the world." Dkt. No. 440, Feb. 13, 2024, Trial Tr. at 1425:23-1426:2 (Barone). The EPA does not dispute this fact. Dkt. No. 421 at 10. Even before the NTP Monograph was formally published, the EPA agreed the NTP Monograph is a high-quality review, followed rules that have been developed by NTP for conducting systematic review, had a "rigorous approach to assembling the evidence," "clearly defined rules for identifying and evaluating studies," and "a well-defined protocol for drawing inferences" from the studies. Dkt. No. 440, Feb. 13, 2024, Trial Tr. at 1427:9-21 (Barone), 1427:2-8 (Barone).

c. Though there were some critical peer review comments on earlier drafts of the NTP Monograph, the core conclusion of the NTP Monograph regarding the high-quality studies was not called into question by reviewers. *See, e.g.*, Dkt. No. 438-1, Trial Ex. 69 at 65 (NTP Board of Scientific Counselors Working Group Report agreeing that low-risk-of-bias studies were "consistent," meaning generating results in the same direction, in finding a negative association

between fluoride exposure and children's IQ); Dkt. No. 414, Feb. 9, 2024, Trial Tr. at 1114:24-1115:1 (Savitz) (describing NASEM critique of adequate definition of the term "consistent" in NTP Monograph, but not disagreeing with characterization of NTP Monograph finding association between IQ and fluoride). Indeed, EPA's experts at trial expressed confidence in the NTP Monograph's methodologies. Dkt. No. 414, Feb. 9, 2024, Trial Tr. at 1197:2-15 (Savitz) (expressing confidence in NTP's literature search strategy and its ability to identify all relevant studies on fluoride exposure published prior to the closing date of April 21, 2021, and agreeing that the "vast majority of studies" that NTP reviewed identified an association between fluoride and reduced IQ). *See also* Dkt. No. 414, Feb. 9, 2024, Trial Tr. at 1140:10-19 (Savitz) ("I don't have any reason to challenge [this conclusion], but I haven't corroborated it by going through the dozens of studies one-by-one to make my own assessment."). Further, Dr. Savitz, the expert called by the EPA herein, acknowledged he is not an expert in conducting risk assessment, and particularly not under Amended TSCA. Dkt. No. 415, Feb. 9, 2024, Trial Tr. at 1264:2-6 (Savitz). Formal publication of the NTP Monograph affirms its quality. *See also* ¶ 33.

d. As explained previously, studies published after the NTP Monograph's literature cut-off date likewise observed a negative association between fluoride and children's cognition: Goodman (2022(a)), Cantoral (2021), Godebo (2023), and Adkins (2022)). *See* ¶ 37.

e. Further, notwithstanding difficulties in observing effects of a chemical at lower levels, *see* ¶ 45, adverse outcomes have even been observed at those levels with statistical significance: Green (2019) and Bashash (2017), ¶¶ 42-43.

f. As explained previously, some studies have not observed an association between fluoride and reduced IQ: Soto-barreras (2019), ¶ 35(h); Ibarluzea (2021), ¶ 38(a); Dewey 2023, ¶ 38(b); Do (2022), ¶ 38(c); and the OCC Cohort, ¶ 44. However, complete consistency amongst studies is not expected. Dkt. No. 414, Feb. 9, 2024, Trial Tr. at 1172:23-1173:6 (Savitz). To this end, various co-factors or susceptibilities can influence the impact or manifestation of neurotoxicants, and as such, it is to be expected that there will be some variability in results across studies of different populations. *See id.* What may appear to be a discrepant result may, in fact, reflect unmeasured differences in cofactors that influence the course of a chemical's

neurotoxicity. *See* Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 102:22-104:24 (Hu); Dkt. No. 417, Feb. 1, 2024, Trial Tr. at 242:21-243:9 (Lanphear), 328:14-23 (Grandjean). And, as also explained previously, particular characteristics of these studies finding null outcomes render them less probative here. *See* ¶ 39. Namely, Ibarluzea (2021) found an unrealistic 15-point IQ benefit, included unexplained and implausible results regarding creatinine adjustments, and failed to control for seafood, ¶ 39(a); Dewey (2023) did not account for previous residence of mothers or continued excretion of fluoride from skeletal breakdown during pregnancy in the control group, ¶ 39(b); Do (2022) utilized an unreliable IQ test and did not analyze individualized data, ¶ 39(c); and the OCC Cohort measured lower exposure levels which makes it more difficult to observe adverse effects, ¶ 45.

53. Though not definitive, there is additional evidence that supports the **plausibility** of the association by assessing potential *mechanisms* for fluoride to impact IQ. Specifically, studies have endeavored to consider explanations for the observed association between fluoride and IQ and hypothesize that thyroid disruption may be the mechanism by which fluoride impacts cognitive function:

a. Goodman (2022b) studied samples from the MIREC Cohort to assess the three-way interplay between prenatal fluoride exposure, maternal iodine status, and child IQ. Dkt. No. 432-12, Trial Ex. 116 at 1, 8. The study found that the negative association between fluoride exposure and IQ observed in Green (2019) was exacerbated by low maternal iodine in pregnancy among boys. *Id.* The study hypothesized that change in thyroid function may be a mechanism by which fluoride impacts cognition; iodine impacts thyroid function. *Id.* at 1-2.

b. Hall (2023): studied samples from the MIREC Cohort and concluded that fluoride in drinking water was associated with increased risk of hypothyroidism in pregnant women, and that thyroid disruption may contribute to developmental neurotoxicity of fluoride. Dkt. No. 432-16, Trial Ex. 120 at 1-2.

54. A lack of a dose-response relationship in the data may suggest that the effect is not related to the putative neurotoxic effect or that the study was not appropriately controlled. Dkt. No. 429-7, Trial Ex. 17 (Guidelines for Neurotoxicity Risk Assessment, Fed. Reg. 63(93):26926-26954

(hereinafter "EPA Guidelines"))[18] at 50. As discussed in the next section regarding the dose-response assessment, there is some lack of clarity as to the precise dose-response relationship at lower exposure levels of fluoride. However, evidence indicates that there is no **threshold** by which fluoride and adverse IQ cease to be associated. *See* ¶¶ 42-43.

55. In conclusion, this evidence is sufficient to proceed to the dose-response assessment of the analysis. *Cf.* Methylene Risk Evaluation at 262 (conducting dose-response analysis for Methylene under Amended TSCA based upon one animal study).

3. Step 1C: Dose-response assessment

a. *Framework*

56. The point at which the chemical ceases to be safe is known as the "point of departure" (*i.e.*, "POD") or "hazard level." *See* Dkt. No. 429-20, Trial Ex. 38 at 1; Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 495:9-14 (Barone); Dkt. No. 421 at 5. To this end, the dose-response assessment describes the relationship between dosage of the chemical and a response, and endeavors to identify the dosage at which a chemical is safe, and conversely, becomes hazardous; this is the point of departure. *See* EPA Guidelines at 57. *See also* Dkt. No. 429-20, Trial Ex. 38 at 1 (describing that the objective of the dose-response assessment is to "document the relationship between dose and toxic effect").

57. There are different points of departure that can be used in a risk assessment. EPA Guidelines at 57-58. The first approach is the NOAEL/LOAEL approach. *See* Dkt. No. 429-19, Trial Ex. 38 at 3-4. A No-Observed-Adverse-Effect Level ("NOAEL") is the "highest exposure level at which no statistically or biologically significant increases are seen in the frequency or severity of adverse effect between the exposed population and its appropriate control population." *Id.* at 4. In cases in which a NOAEL cannot be identified, the term lowest-observed-adverse-effect level ("LOAEL") is used, which is the lowest dose tested at which an adverse effect is detected.

[18] These Guidelines were published in April 1998 and are the currently applied guidelines for EPA Neurotoxicity Risk Assessment according to the EPA's website. *See Guidelines for Neurotoxicity Risk Assessment*, UNITED STATES ENVIRONMENTAL PROTECTION AGENCY (last visited September 12, 2024), https://www.epa.gov/risk/guidelines-neurotoxicity-risk-assessment.

*Id.* at 4. Alternatively, when possible, the benchmark dose ("BMD") approach can be used to arrive at a point of departure. *Id.*

58. The BMD approach is preferred over the NOAEL/LOAEL approach, and use of a NOAEL is preferred over the LOAEL. *Id. See also* Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 495:23-496:25 (Barone); EPA Guidelines at 2-3, 57-58; Dkt. No. 421 at 5 (undisputed fact). The NOAEL/LOAEL approach derives the point of departure from a dosage and corresponding response in subjects that was actually observed. *See* EPA Guidelines at 57-59. *See also* Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 672:1-11 (Barone) ("So generally a NOAEL or LOAEL, as we described earlier, comes directly from what is the observed concentration for an effect or no effect. So it's directly coming from the study of where that threshold for non-cancer – generally gets a threshold – where does that concentration occur. And that's describing, generally speaking, a single dose. It's within the dose continuum of how many doses were employed in the study, what concentration did they measure an effect."). *See also* EPA Guidelines at 57-59. The NOAEL/LOAEL is thus limited to only dosages observed in the study. *See* EPA Guidelines at 57-59. Other limitations of the NOAEL/LOAEL approach include that this approach is highly dependent upon sample size of a study (*e.g.*, where a sample size is limited, it might present a higher point of departure than the true point of departure), and it does not account for the shape of the dose-response curve from the experiment at issue. *Id*. Because of these limitations, the BMD approach is preferred if the data set is appropriate for such modeling. *See* Dkt. No. 429-20, Trial Ex. 38 at 4; Dkt. No. 400, Feb. 5, 2024, Trial Tr. at at 479:14-580:9 (Barone).

59. In utilizing the BMD approach, a benchmark dose, *i.e.*, BMD or benchmark concentration ("BMC") is identified. *See* Dkt. No. 429-20, Trial Ex. 38 at 4. The BMD/BMC is the dose of a substance that produces a "predetermined change in the response rate of an adverse effect." *Id*. The benchmark dose level ("BMDL") or benchmark concentration level ("BMCL") is the lower end of the statistical confidence limit on the dose that produces the selected response. *Id.* In other words, there is a statistical confidence interval on either side of the BMD/BMC; the BMDL/BMCL is the point at the lower side of that confidence interval. *See id.* Like the NOAEL/LOAEL, the BMCL/BMDL can be used as the point of departure. *Id.*

b. *Key findings*

60. 0.28 mg/L, or alternatively, 0.768 and/or 1.536 mg/L measured in maternal urinary fluoride is associated with a 1-point decrease in IQ of girls and boys and is a legitimate point of departure (BMCL) to use in this risk evaluation.

61. Alternatively, 4 mg/L measured in either urinary fluoride or water fluoride, is a legitimate, conservative point of departure (LOAEL) to use in the risk evaluation.

62. Regarding the weight of the scientific evidence, the quality and weight of the evidence in the record substantiates points of departure derived from either BMD modeling of the data or from a LOAEL/NOAEL approach.

c. *Underlying findings*

(a) POD: 0.28 mg/L BMCL (Grandjean (2023)) or in the alternative, 0.768 mg/L and/or 1.536 mg/L BMCL (Grandjean (2022))

63. Dr. Philippe Grandjean ("Grandjean") was the lead author of two pooled BMCL analyses, one published in 2022 and another in 2023. Dkt. No. 432-20, Trial Ex. 124. (hereinafter "Grandjean (2022)"); Dkt. No. 432-15, Trial Ex. 119 (hereinafter "Grandjean (2023)").

64. Dr. Grandjean and his co-authors are well-regarded for their benchmark dose analyses. To this end, EPA cited a pooled benchmark dose analysis authored by Grandjean as an example of how to perform such an analysis in its Benchmark Dose Technical Guidance Manual, and EPA has relied upon the authors' benchmark dose analysis work in its assessment of other chemicals. Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 287:16-288:18 (Grandjean), 479:25-5 (Grandjean); Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 748:19-750:6 (Barone).

65. Grandjean (2022) analyzed data from two cohorts, the ELEMENT Cohort and the MIREC Cohort to conduct its BMCL analysis. Grandjean (2022) at 1-2. Grandjean (2023) analyzed three cohorts: ELEMENT, MIREC, and the OCC cohorts. Grandjean (2023) at 1.

66. The pooled BMCL analyses of the birth cohorts sought to determine the level of fluoride in maternal urine ("MUF") that is associated with a 1-point drop in the IQ of the mothers' offspring. Dkt. No. 417, Feb. 1, 2024, Trial Tr. at 339:13-23 (Grandjean). As described by RSI, "[t]he choice of a BMR of 1 IQ point (corresponding to a 1% reduction from a mean IQ of 100)

has been adopted as an appropriate benchmark on this endpoint by several regulatory bodies, including the US EPA and EFSA." Dkt. No. 433-4, Trial Ex. 129 at 27. Pooled analyses are also particularly useful because a pooled analysis benefits from heightened statistical power and precision that comes from large samples sizes. Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 111:9-112:16 (Hu).

67. Grandjean (2023) concluded that "[t]he joint analysis of all three cohorts showed a statistically significant association between urine-fluoride and IQ, with a BMC of 0.45 mg/L (BMCL, 0.28 mg/L)." Grandjean (2023) at 1-2. Specifically, Grandjean (2023) found that the BMCL associated with a 1-point decrease in IQ scores of boys and girls was 0.28 mg/L maternal urinary fluoride; this BMCL was adjusted for creatinine and derived from use of a linear dose-response model. Grandjean (2023) at 1-2, 9. This BMCL is a legitimate point of departure to use in the risk evaluation for fluoride.

68. When determining whether the point of departure can be derived using the BMD or BMC approach, as opposed to identifying a LOAEL or NOAEL, it is necessary to consider whether the data set is appropriate for use in the BMD/BMC modeling. *See* Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 658:9-659:10 (Barone) (explaining that in identifying studies and key endpoints to "carry forward to the dose-response analysis," the assessor considers whether "are [the studies] amenable to BMDS, benchmark dose modeling? Are they amenable to a LOAEL/NOAEL approach? Should we use some other type of approach?"). To this end, the EPA's technical guidance provides that the following should be considered as to whether the data set is appropriate for BMD modeling: (1) whether there is a statistically or biologically significant dose-related trend in the selected endpoint; (2) whether a response is not only seen at a high dose; and (3) where there are adequate model fits. *See* Benchmark Dose Technical Guidance, U.S. ENVIRONMENTAL PROTECTION AGENCY (June 2012) available at https://www.epa.gov/sites/default/files/2015-01/documents/benchmark_dose_guidance.pdf (hereinafter "EPA's Benchmark Dose Technical Guidance") at 12-18.[19]

[19] This document was not submitted as an exhibit, but the EPA's witnesses rely on the document for their testimony. *See, e.g.*, Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 745:9-25 (Barone) ("Q:

69. For the reasons discussed below, the data that Dr. Grandjean analyzed is appropriate for use in BMD modeling, and for similar reasons, his point of departure is supported by the weight of the scientific evidence. *See* ¶ 51 (discussing weight-of-scientific-evidence factors). It is demonstrated by a preponderance of the evidence.

70. As explained previously, there is a well-supported and documented, statistically significant dose-related trend in the selected endpoint (reduced IQ). *See* ¶¶ 52-53 (discussing the robust body of evidence establishing the relationship between fluoride and reduced IQ, including studies observing this relationship at "lower" exposure levels).

71. Dr. Grandjean rests his BMCL analysis upon studies observing the ELEMENT, MIREC, and OCC cohorts. Grandjean (2023) at 1-2. These high-quality studies are appropriate for use in BMD modeling, particularly because they include data regarding dose-response at "lower" exposure levels, *i.e.*, 0.9 mg/L (mean maternal urinary fluoride in ELEMENT cohort), 0.42 mg/L (mean maternal urinary fluoride in MIREC cohort), and 0.58 mg/L (average maternal urinary fluoride in the OCC cohort). *See* ¶¶ 42-44. Thus, rather than observing only a response at high dosages, the data set utilized by Dr. Grandjean observes dose-response at low exposure levels. The data set are thus appropriate for BMD modeling. To this end, RSI found that the MIREC and ELEMENT cohorts represent a "high quality of evidence partly based on Canadian population, conducted within a context relevant to Canadian drinking water fluoride exposure levels.[20] Both studies included prospective data collection, with prenatal exposure assessment (maternal urine collection over successive trimesters) and follow-up during the early life of the infants and children." Dkt. No. 433-4, Trial Ex. 129 at 23. And the ELEMENT and MIREC cohort studies

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Now, moving beyond semantics, I wanted to ask you about your testimony about benchmark dose, okay? You made comments in your testimony about Dr. Grand[j]ean's BMCL analysis, correct? A. Yes, I did. Q. You based your comments on EPA's BMD guidance technical manual, correct? A. Yes, I did."). The Court thus considers this technical guidance document.

[20] The United States and Canada take a similar approach to water fluoridation; this finding is applicable to United States drinking water fluoride exposure levels. *See* Tr. Ex. 129, Dkt. No. 433-4 at 16 (describing optimal water fluoride levels in Canada of 0.7 mg/L). *See also* Dkt. No. 396, Feb. 1 , 2024 Trial Tr. at 245:1-22 (Lanphear) (describing optimal 0.7 mg/L water fluoride standard in Canada).

are strong for their extensive control for covariates and individualized measurements of fluoride exposure during the prenatal period. Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 95:2-96:5 (Hu).

72. The model fits of the data utilized by Grandjean's BMCL are also adequately supported. On this point, the EPA takes issue with the fact that Dr. Grandjean's BMCL of 0.28 mg/L was derived by applying a linear model of the dose-response curve.[21] Grandjean (2023) at 1-2, 9. To discern the best model fit for a set of data, a model is used to find a fit to the data, and based upon that fit, an "AIC" score is generated; the lower the AIC score, the better the model fit. Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 421:20-21 (Grandjean). To EPA's point, Grandjean (2023) did not include a published table illustrating the AIC scores for all model fits, but did so only for the linear model and piece-wise model, though not the squared model. *See* Grandjean (2023) at 9 (Table S3). The government thus argued at trial that Dr. Grandjean improperly assumed, without testing the assumption, that the linear model was appropriate for the data set evaluated. However, the use of the linear model in Grandjean (2023) to generate the BMCL is sufficiently justified:

i. Dr. Grandjean testified, and the Court finds this testimony credible, that he did not assume that the linear model was the best fit, but rather that he and his co-authors compared various models and determined that the linear model was the preferred model for the data. Dkt. No. 396, Feb. 1, 2024, Trial Tr. at 333:6-19 (Grandjean). Dr. Grandjean did state that "[i]n my communications with the EPA, I was told that the default curve function was the linear one." *Id.* at 333:8-9. However, Dr. Grandjean clarified that this default was only a starting point

[21] When a curve is linear, generally the dose and effect increase or decrease in a somewhat uniform fashion, *i.e.*, when the dose increases, the effect increases; when the dose decreases, the effect decreases. *See* EPA's Benchmark Dose Technical Guidance at 25-26, 77-78 (describing linear, quadratic, and other models), 71 (defining "Linear Dose-Response Model" as "[a] mathematical relationship in which a change in response is proportional to a fixed amount of change in dose, e.g., Response = a + b × Dose. This is in distinction from a more general linear mathematical model, which is a linear combination of parameters"). The shape of the dose-response curve is relevant, particularly because it is used to extrapolate to lower levels of exposure not observed in the study, and thus to calculate the BMCL. *See id.* at 5 ("The dose response assessment under the guidelines is a two-step process: (1) response data are modeled in the range of empirical observation — modeling in the observed range is done with biologically based or curve-fitting models; and then (2) extrapolation below the range of observation is accomplished by modeling, if there are sufficient data, or by a default procedure (linear, nonlinear, or both)."). The model will thus determine the BMCL identified. *See id.* at 5, 25-26, 77-78.

and that "what we've done in our work is to compare that to some variations and the statistical methods so that you can actually compare the fit if, let's say, curvilinear or a broken line fits better. And in our case the linear was actually – was the best fit." *Id.* at 333:10-14. And further, Dr. Grandjean testified that he also used "nonlinear methods to assess whether the dose-response relationship is linear," *id.* at 333:15-19. *See also id.* at 339:24-340:7 ("We started out with EPA's default recommendation, namely that linear association. But we then also looked at a curvilinear, for example, log 2 transformation of exposure. We also looked at broken lines of – and overall the linear association was not inferior to anything. It was sometimes clearly superior."); Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 440:23-419:1 (Grandjean) ("[W]e certainly did look at other models."). Dr. Grandjean and his co-authors did not simply assume that the linear model was the best fit for the data. It was chosen through an analytical process.

ii. Moreover, Grandjean (2022) includes a table that reports the AIC scores for squared models as they fit to data from the MIREC and ELEMENT cohorts and reveals comparable fit scores and supports Dr. Grandjean's testimony as to the validity of the linear model fit:

**Table 2.**

Benchmark Concentration Results (mg/L Urinary Fluoride, Creatinine-Adjusted) for a BMR of 1 IQ Point Obtained from the MIREC Study and the Two Cognitive Assessments from the ELEMENT Study as Well as the Joint Results. Two Concentration-Response Models are used, a Linear and One with the Squared Exposure Variable. For both Models, Sex-Specific and joint benchmark Results are Provided. The fit of the Regression models was Compared by the AIC (Where Lower Values Indicate a Better Fit)

| Study | | MIREC ($n$ = 407) | | ELEMENT IQ ($n$ = 211) | | ELEMENT GCI ($n$ = 287) | | MIREC and ELEMENT IQ ($n$ = 618) | | | MIREC and ELEMENT GCI ($n$ = 694) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Model | Sex | BMC | BMCL | BMC | BMCL | BMC | BMCL | BMC | BMCL | AIC | BMC | BMCL | AIC |
| Linear | Both | 0.497 | 0.228 | 0.200 | 0.122 | 0.159 | 0.099 | 0.326 | 0.201 | 4770.1 | 0.312 | 0.192 | 5491.3 |
| Linear | Boys | 0.201 | 0.125 | 0.275 | 0.130 | 0.148 | 0.084 | 0.222 | 0.144 | 4766.7 | 0.184 | 0.125 | 5488.4 |
| Linear | Girls | ∞ | 0.609 | 0.160 | 0.091 | 0.169 | 0.087 | 1.098 | 0.275 | 4766.7 | 2.972 | 0.315 | 5488.4 |
| Squared | Both | 1.545 | 0.896 | 0.614 | 0.496 | 0.611 | 0.467 | 1.008 | 0.768 | 4768.8 | 1.133 | 0.807 | 5493.9 |
| Squared | Boys | 0.840 | 0.622 | 0.684 | 0.496 | 0.581 | 0.435 | 0.787 | 0.619 | 4769.4 | 0.761 | 0.601 | 5493.7 |
| Squared | Girls | ∞ | 1.262 | 0.576 | 0.449 | 0.642 | 0.434 | 1.637 | 0.866 | 4769.4 | ∞ | 1.040 | 5493.7 |

Abbreviations: AIC, Akaike Information Criterion; BMC, benchmark concentration; BMCL, benchmark concentration level; BMR, benchmark response; GCI, Global Cognitive Index; IQ, Intelligence Quotient.

Grandjean (2022) at 17 (Table 2) (red annotation added). The AIC scores for the linear and squared models were comparable, with the best fit for boys and girls individually, measuring IQ, using a linear model (AIC 4766.7 linear compared to 4769.4 squared), and squared combined (AIC 4768.8 squared compared to 4770.1 linear). *See id.* For GCI (the General Cognitive Index

score), the linear model was a better fit than the squared model for all categories. *See id.* Even if not definitive, the comparable AIC fits for linear and squared models reflected in Grandjean (2022) support that the linear model is a justifiable model to apply to the MIREC and ELEMENT cohort data.

iii. Dr. Grandjean's analysis is also consistent with the NTP's analysis.

The NTP Meta-analysis did not publish AIC scores for models restricted to low-risk-of bias studies. *See* Dkt. No. 431-2, Trial Ex. 68 at 40-41 (eTable 4) (hereinafter "NTP Meta-analysis"). However, it did publish AIC scores for model fit of data in all studies, as reflected in the below table:

| Exposure Analysis | Parameters | Fluoride Exposure | | | |
|---|---|---|---|---|---|
| | | All data | <4 mg/L | <2 mg/L | <1.5 mg/L |
| **Urinary Fluoride – All Studies** | | | | | |
| No. Studies/No. Observations | | 18/32 | 13/26 | 7/11 | 5/8 |
| Number of Children | | 8,502 | 6,885 | 4,654 | 3,992 |
| Linear Model[b] | Beta (95% CI) | −0.16 (−0.24, −0.08) | −0.17 (−0.30, −0.05) | −0.06 (−0.14, 0.01) | −0.09 (−0.16, −0.01) |
| | p-value | p < 0.001 | p = 0.005 | p = 0.094 | p = 0.026 |
| | AIC | AIC = 73.8 | AIC = 68.0 | AIC = 1.2 | AIC= 2.8 |
| Quadratic Model[c] | Beta (95% CI); p-value | −0.10 (−0.31, 0.11); p = 0.360 | 0.07 (−0.23, 0.38); p = 0.645 | −0.22 (−0.65, 0.20); p = 0.303 | 0.65 (−1.46, 2.76); p = 0.548 |
| | Beta (95% CI); p-value | −0.01 (−0.05, 0.02); p = 0.496 | −0.07 (−0.16, 0.01); p = 0.071 | 0.08 (−0.13, 0.30); p = 0.456 | −0.66 (−2.11, 0.80); p = 0.379 |
| | AIC | AIC = 84.3 | AIC = 75.8 | AIC = 9.2 | AIC = 8.3 |
| | p-value* | p* = 0.14 | p* = 0.08 | p* = 0.42 | p* = 0.10 |
| Restricted Cubic Splines Model[d] | Beta (95% CI); p-value | −0.12 (−0.28, 0.04); p = 0.150 | −0.03 (−0.22, 0.16); p = 0.741 | −0.14 (−0.32, 0.04); p = 0.130 | −0.52 (−1.65, 0.62); p = 0.371 |
| | Beta (95% CI); p-value | −0.10 (−0.43, 0.23); p = 0.545 | −0.24 (−0.47, −0.002); p = 0.048 | 0.13 (−0.17, 0.43); p = 0.395 | 0.63 (−1.32, 2.59); p = 0.524 |
| | AIC | AIC = 79.6 | AIC = 73.3 | AIC = 8.5 | AIC = 6.7 |
| | p-value* | p* = 0.13 | p* = 0.07 | p* = 0.37 | p* = 0.07 |

*Id.* Using urinary fluoride as the exposure metric, the linear model reflected the lowest AIC score unilaterally. *See id.* And although the linear model did not generate a statistically significant inverse association at all exposure levels, the linear model generated a statistically significant inverse association at <1.5 mg/L (in line with Grandjean (2023)'s finding relating to lower-exposure levels as noted above), and the findings remained directionally negative at all levels which also supports Grandjean (2023)'s use of the linear model. *See* Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 115:16-25 (Hu) ("In fact, epidemiology is moving away from a simple reliance on just P values and saying 'this is significant, this is not significant.' It's really important to also look at the so-called directionality of the relationships."). Additionally, as explained in more detail below, some of the loss of association observed in the NTP Meta-analysis may be explained by the

use of the means effect method in the Meta-analysis, which results in loss of statistical power and sensitivity in the data. *See* ¶ 74(b). Ultimately, the authors of the NTP Meta-analysis concluded that "[b]ased on the AIC and likelihood ratio tests, the best model fit was achieved when quadratic or restricted cubic spline exposure levels were added to the linear models for drinking water (eFigure 17); ***the linear model was the best fit for urinary fluoride*** (eFigure 18)." NTP Meta-analysis at 10 (emphasis added). This further bolsters the legitimacy of Grandjean (2023)'s use of a linear model to generate the BMCL, expressed in maternal urinary fluoride.

73. Assuming, in the alternative, that the squared model is a more appropriate fit for this data set, as EPA suggested at trial, a BMCL of 0.768 mg/L and/or 1.536 mg/L is appropriately used to conduct the risk assessment. Though Grandjean (2023) did not identify a BMCL using the squared model, Dr. Grandjean's 2022 BMCL analysis did identify a BMCL of 0.768 mg/L utilizing a squared model. Grandjean (2022) at 17 (Table 2); Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 423:12-21 (Grandjean). It is true that this BMCL is derived from the ELEMENT and MIREC cohort data only and excludes data from the OCC Cohort. This is relevant because inclusion of the OCC Cohort data is likely to increase the BMCL; when the OCC cohort data was added to the BMCL analysis in Grandjean (2023), the BMCL increased by 0.08 mg/L, or forty percent[22] (from 0.20 mg/L (MIREC and ELEMENT alone) to 0.28 mg/L (MIREC, ELEMENT and OCC cohort data)). *See* Grandjean (2023) at 3 ("The joint BMC was found to be 0.45 mg/l (BMCL, 0.28 mg/l), *i.e.* slightly higher than previously found (BMC, 0.33 mg/l; BMCL, 0.20 mg/L) for the two North American cohorts alone."). But a preponderance of the evidence indicates the inclusion of the OCC Cohort data would not make a material difference. To be highly conservative, the BMCL of 0.768 mg/L can be *doubled*, to account for any discrepancy caused by the omission of the OCC data: 1.536 mg/L (0.768 mg/L times two). This could be used conservatively as an alternative point of departure implied from the data if the squared model is used. As discussed below, even using this higher point of departure, the ultimate finding of an unreasonable risk would not change.

[22] ((.08 / .20) * 100).

74. One additional concern with Dr. Grandjean's BMCL calculation is that it, at first glance, appears to be in tension with the NTP Monograph's conclusion that "[m]ore studies are needed to fully understand the potential for lower fluoride exposure [i.e., below 1.5 mg/L] to affect children's IQ." NTP Monograph at xiii.[23] However, this ultimately does not undermine the validity of the BMCL identified in Grandjean (2023) for the following reasons:

a. Though the authors of the NTP Monograph recognized some lack of clarity in the precise relationship between fluoride and reduced IQ at lower exposure levels, NTP Monograph at xiii, given the strength of the association between fluoride and reduced IQ, the authors of the NTP Monograph refused to limit the applicability of its findings in the systematic review to higher exposure levels and made clear that its confidence assessment also considered fluoride exposures "that are similar to, or lower than, those associated with optimally fluoridated water supplies in the United States," *i.e.*, 0.7 mg/L. Dkt. No. 438-1, Trial Ex. 69 at 24-25 (comments and responses from NTP Monograph authors and evaluators of the NTP Monograph).

b. The NTP also conducted a Meta-analysis, integrating all of the studies assessed in the NTP Monograph to analyze the dose-response relationship between fluoride and reduced IQ. The findings of the NTP Meta-analysis first appear to be in tension with Dr. Grandjean's findings but are, in fact, consistent with those findings because of the methodologies used. Namely, the NTP Meta-analysis concluded that "the consistency of the data supports an inverse association between fluoride exposure and children's IQ." NTP Meta-analysis at 3. However, the Meta-analysis reported somewhat mixed results regarding the dose-response relationship, particularly at

[23] Regarding "lower" fluoride exposure levels – both Grandjean (2023) and the NTP Monograph analyzed data from the ELEMENT and MIREC cohorts though Grandjean (2023) also analyzed data from the OCC Cohort, another lower-exposure level study.

lower levels of fluoride exposure:

| Exposure Analysis | Parameters | Fluoride Exposure | | | |
|---|---|---|---|---|---|
| | | All data | <4 mg/L | <2 mg/L | <1.5 mg/L |
| Linear model | Beta (95% CI)<br>p-value<br>AIC | −0.15 (−0.23, −0.07)<br>p < 0.001<br>AIC = 74.5 | −0.16 (−0.28, −0.04)<br>p = 0.011<br>AIC = 68.6 | −0.05 (−0.14, 0.04)<br>p = 0.259<br>AIC = 1.3 | −0.08 (−0.16, −0.01)<br>p = 0.036<br>AIC = 3.0 |
| Urinary Fluoride – Low Risk-of-bias Studies | | | | | |
| No. Studies/No. Observations<br>Number of Children | | 9/15<br>5,713 | 9/15<br>5,713 | 5/8<br>4,141 | 4/7<br>3,952 |
| Linear model | Beta (95% CI)<br>p-value<br>AIC | −0.10 (−0.21, 0.01)<br>p = 0.082<br>AIC = 5.9 | −0.10 (−0.21, −0.01)<br>p = 0.082<br>AIC = 5.9 | −0.05 (−0.17, 0.08)<br>p = 0.472<br>AIC = 2.8 | −0.08 (−0.16, −0.01)<br>p = 0.028<br>AIC = 2.5 |

*Id.* at 41 (eTable 4) (red annotation added). In reviewing all studies and measuring exposure of fluoride per urinary fluoride the NTP Meta-analysis found a statistically significant inverse association between children's urinary fluoride exposure and IQ at <4 mg/L urinary fluoride. *Id.* When restricted to <2 mg/L and <1.5 mg/L urinary fluoride, there was still an inverse association. *Id.* This finding is consistent with Grandjean (2023). However, when analyses were restricted to low risk-of-bias publications, the associations at <2 mg/L and <1.5 mg/L became smaller in magnitude and were only statistically significant at <1.5 mg/L, but not at <2 mg/L. *Id.* That finding of an adverse association at <1.5 mg/L is consistent with the conclusion in Dr. Grandjean's pooled benchmark dose analysis (though appearing somewhat anomalous compared to the finding at <2 mg/L). Dr. Grandjean's pooled benchmark analysis uses a method with more statistical precision than the NTP Meta-analysis, and thus could account for the more specific findings as to the relationship between fluoride and IQ at lower exposure levels. Specifically, the NTP Meta-analysis used a "means effect analysis," which is useful for its ability to compare different types of studies with varied methodologies and metrics (72 total and 19 low-risk-of-bias studies) – but it loses sophistication and precision in the underlying data of each study when it converts the findings into standard, comparable metrics. Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 469:3-471:6 (Grandjean). Specifically, so that different studies using different exposures or result metrics could be compared, the data was grouped into buckets (*e.g.*, high exposure, low exposure) and analyzed. *Id.* at 471:6-15. Accordingly, each of the underlying studies lose some of its statistical power when data is simplified to allow for cross-study, like-to-like comparison. *See id.* at 471:6-473:24. On the other hand, the pooled benchmark analysis maintains individualized, continuous

data and does not simplify that data for meta-analysis comparison; the benchmark analysis maintains increased sophistication and statistical sensitivity. *Id.* at 473:18-24. Thus, the findings of the NTP Meta-analysis are not inconsistent with Dr. Grandjean's pooled benchmark analysis.

75. Ultimately, TSCA does not require complete certainty as to the threshold level at which a chemical produces the hazard; indeed, such certainty is very difficult to obtain from epidemiologic studies of human populations. Dkt. No. 440, Feb. 13, 2024, Trial Tr. at 1440:18-23 (Barone); Dkt. No. 414, Feb. 9, 2024, Trial Tr. at 1173:7-13 (Savitz). Either BMCL of 0.28 mg/L (linear model per the MIREC, ELEMENT, and OCC cohort data) or 0.768 mg/L (squared model per the MIREC and ELEMENT cohort data) identified by Dr. Grandjean and his co-authors are legitimate points of departure to utilize in a risk analysis. So is the implied BMCL of 1.536 mg/L (were the OCC study taken into account). The Court finds, though not with absolute certainty, Dr. Grandjean's BMCLs are supported by a preponderance of the evidence.[24]

(b) POD: 4 mg/L urinary or water fluoride (LOAEL)

76. As described previously, use of the BMD approach is preferred in identifying a point of departure because of limitations of a NOAEL or LOAEL, but where data is not amenable to benchmark dose modeling, a NOAEL or LOAEL may be utilized instead. *See* ¶¶ 57-59. The Court thus examines this alternative approached to establishing a point of departure.

77. Again, notwithstanding the limitations of the NOAEL/LOAEL approach, this approach is properly used, and has been used by the EPA, with the application of uncertainty factors, to determine the point of departure where datasets are, for various reasons, not amenable to BMD modeling. *See* Dkt. No. 429-20, Trial Ex. 38 at 4. For example, the EPA conducted a risk evaluation of Perchloroethylene ("PCE"), pursuant to Amended TSCA, and utilized NOAEL/LOAELs as PODs because it was unable to use BMD modeling. *See* PCE Risk Evaluation at 351 ("For this risk evaluation, non-cancer PODs were all based on NOAELs and LOAELs because the data for the selected endpoints was unable to be BMD modeled. This results

[24] The government also takes issue with the use of maternal urinary fluoride ("MUF") as the metric of the exposure or hazard level utilized in the risk assessment analysis. The validity of maternal urinary fluoride as a metric is taken up subsequently in Section III.B (Exposure Assessment).

in reduced precision in POD estimates because the POD is dependent on the dose selection of the study as opposed to the response rate/level for the effect of interest."); Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 772:3-11 (Thiessen).

78. To the extent that the BMD approach is not appropriate based upon the present data set, in the alternative, 4.0 mg/L (using exposure measurement of water fluoride intake) is a legitimate and highly conservative LOAEL to utilize as a point of departure to conduct a risk assessment of fluoride per the findings of the NTP Meta-analysis. Utilizing 4.0 mg/L as the LOAEL is especially conservative in view of the NTP Monograph's conclusion with moderate confidence that exposure to fluoride concentration in drinking water at or above 1.5 mg/L is associated with lower IQ in children. One could reasonably take 1.5 mg/L as a LOAEL. Nonetheless, the Court uses the more conservative 4.0 mg/L based on a close analysis of the NTP Meta-analysis which establishes with consistency an association with reduced IQ at that level. Specifically, the NTP Meta-analysis observed a statistically significant inverse association between fluoride and reduced IQ at 4 mg/L measured in water fluoride, based on low-risk-of-bias/high quality studies (*i.e.*, 6 epidemiological studies deemed high quality), which is reflected in the below table from the Meta-

analysis summarizing the NTP's dose-response analysis:[25]

eTable 4. Dose-Response Meta-analysis Using Mean Effects—Model Selection[a]

| Exposure Analysis | Parameters | Fluoride Exposure | | | |
|---|---|---|---|---|---|
| | | All data | <4 mg/L | <2 mg/L | <1.5 mg/L |
| **Water Fluoride – All Studies** | | | | | |
| No. Studies/No. Observations | | 29/39 | 21/27 | 7/9 | 7/7 |
| Number of Children | | 11,656 | 8,723 | 2,971 | 2,832 |
| Linear Model[b] | Beta (95% CI)<br>p-value<br>AIC | −0.15 (−0.20, −0.11)<br>p < 0.001<br>AIC = 53.8 | −0.22 (−0.27, −0.17)<br>p < 0.001<br>AIC = 16.1 | −0.15 (−0.41, 0.12)<br>p = 0.274<br>AIC = 11.8 | 0.05 (−0.36, 0.45)<br>p = 0.816<br>AIC = 8.2 |
| Quadratic Model[c] | Beta (95% CI); p-value<br>Beta (95% CI); p-value<br>AIC<br>p-value* | −0.27 (−0.34, −0.21); p < 0.001<br>0.02 (0.01, 0.03); p < 0.001<br>AIC = 48.8<br>p* < 0.001 | −0.12 (−0.35, 0.11); p = 0.318<br>−0.04 (−0.10, 0.03); p = 0.280<br>AIC = 21.2<br>p* = 0.012 | 0.79 (−0.01, 1.58); p = 0.052<br>−0.56 (−0.97, −0.16); p = 0.006<br>AIC = 12.5<br>p* = 0.007 | 0.30 (−0.53, 1.14); p = 0.477<br>−0.23 (−1.01, 0.55); p = 0.561<br>AIC = 11.3<br>p* = 0.04 |
| Restricted Cubic Splines Model[d] | Beta (95% CI); p-value<br>Beta (95% CI); p-value<br>AIC<br>p-value* | −0.29 (−0.39, −0.20); p < 0.001<br>0.48 (0.18, 0.78); p = 0.002<br>AIC = 42.3<br>p* < 0.001 | −0.14 (−0.34, 0.06), p = 0.162<br>−0.23 (−0.66, 0.20), p = 0.295<br>AIC = 16.9<br>p* = 0.009 | 1.15 (0.07, 2.22) p = 0.037<br>−1.20 (−2.03, −0.36)<br>p = 0.005<br>AIC = 10.5<br>p* = 0.010 | 0.49 (−0.50, 1.47) p = 0.334<br>−0.69 (−2.40, 1.02) p = 0.428<br>AIC = 10.2<br>p* = 0.05 |
| **Water Fluoride – Low Risk-of-bias Studies** | | | | | |
| No. Studies/No. Observations | | 6/11 | 6/9 | 3/4 | 3/3 |
| Number of Children | | 4,355 | 4,251 | 921 | 879 |
| Linear model | Beta (95% CI)<br>p-value<br>AIC | −0.19 (−0.34, −0.05)<br>p = 0.009<br>AIC = 10.3 | −0.22 (−0.36, −0.07)<br>p = 0.003<br>AIC = 3.9 | −0.34 (−0.72, 0.03)<br>p = 0.070<br>AIC = 4.5 | −0.32 (−0.91, 0.26)<br>p = 0.276<br>AIC = 4.1 |

Dkt. No. 431-2, Trial Ex. 68 at 39 (eTable4) (red annotation added). That value was derived from a linear model which, for this group of studies, had the lowest AIC score. *See id.* (identifying AIC of 16.1 (linear for all studies), 21.1 (quadratic for all studies), 16.9 (restricted cubic splines for all studies)).

[25] Note that where values in the parenthesis, which represent the confidence interval, are below zero, the finding is statistically significant. *See* Dkt. No. 417, Feb. 2, 2024, Trial Tr. at 394:2-14 (Grandjean).

79. Further, the NTP Meta-analysis observed an association between fluoride and reduced IQ at <4 mg/L measured in urinary fluoride, based on low-risk-of-bias/high-quality studies (9 epidemiological studies deemed high quality):

| Exposure Analysis | Parameters | Fluoride Exposure | | | |
|---|---|---|---|---|---|
| | | All data | <4 mg/L | <2 mg/L | <1.5 mg/L |
| **Urinary Fluoride – All Studies** | | | | | |
| No. Studies/No. Observations | | 18/32 | 13/26 | 7/11 | 5/8 |
| Number of Children | | 8,502 | 6,885 | 4,654 | 3,992 |
| Linear Model[b] | Beta (95% CI) | −0.16 (−0.24, −0.08) | −0.17 (−0.30, −0.05) | −0.06 (−0.14, 0.01) | −0.09 (−0.16, −0.01) |
| | p-value | p < 0.001 | p = 0.005 | p = 0.094 | p = 0.026 |
| | AIC | AIC = 73.8 | AIC = 68.0 | AIC = 1.2 | AIC= 2.8 |
| Quadratic Model[c] | Beta (95% CI); p-value | −0.10 (−0.31, 0.11); p = 0.360 | 0.07 (−0.23, 0.38); p = 0.645 | −0.22 (−0.65, 0.20); p = 0.303 | 0.65 (−1.46, 2.76); p = 0.548 |
| | Beta (95% CI); p-value | −0.01 (−0.05, 0.02); p = 0.496 | −0.07 (−0.16, 0.01); p = 0.071 | 0.08 (−0.13, 0.30); p = 0.456 | −0.66 (−2.11, 0.80); p = 0.379 |
| | AIC | AIC = 84.3 | AIC = 75.8 | AIC = 9.2 | AIC = 8.3 |
| | p-value* | p* = 0.14 | p* = 0.08 | p* = 0.42 | p* = 0.10 |
| Restricted Cubic Splines Model[d] | Beta (95% CI); p-value | −0.12 (−0.28, 0.04); p = 0.150 | −0.03 (−0.22, 0.16); p = 0.741 | −0.14 (−0.32, 0.04); p = 0.130 | −0.52 (−1.65, 0.62); p = 0.371 |
| | Beta (95% CI); p-value | −0.10 (−0.43, 0.23); p = 0.545 | −0.24 (−0.47, −0.002); p = 0.048 | 0.13 (−0.17, 0.43); p = 0.395 | 0.63 (−1.32, 2.59); p = 0.524 |
| | AIC | AIC = 79.6 | AIC = 73.3 | AIC = 8.5 | AIC = 6.7 |
| | p-value* | p* = 0.13 | p* = 0.07 | p* = 0.37 | p* = 0.07 |
| **Urinary Fluoride – Sensitivity analysis including Ibarluzea et al. (2021)[87] Bayley MDI scores** | | | | | |
| No. Studies/No. Observations | | 19/33 | 14/27 | 8/12 | 6/9 |
| Number of Children | | 8,815 | 7,445 | 4,967 | 4,305 |
| Linear model | Beta (95% CI) | −0.15 (−0.23, −0.07) | −0.15 (−0.28, −0.03) | −0.04 (−0.14, 0.05) | −0.08 (−0.15, −0.003) |
| | p-value | p < 0.001 | p = 0.015 | p = 0.371 | p = 0.043 |
| | AIC | AIC = 75.0 | AIC = 69.0 | AIC = 1.7 | AIC = 3.6 |
| **Urinary Fluoride – Sensitivity analysis including Ibarluzea et al. (2021)[87] McCarthy GCI scores** | | | | | |
| No. Studies/No. Observations | | 19/33 | 14/27 | 8/12 | 6/9 |
| Number of Children | | 8,749 | 7,445 | 4,901 | 4,239 |

| Exposure Analysis | Parameters | Fluoride Exposure | | | |
|---|---|---|---|---|---|
| | | All data | <4 mg/L | <2 mg/L | <1.5 mg/L |
| Linear model | Beta (95% CI) | −0.15 (−0.23, −0.07) | −0.16 (−0.28, −0.04) | −0.05 (−0.14, 0.04) | −0.08 (−0.16, −0.01) |
| | p-value | p < 0.001 | p = 0.011 | p = 0.259 | p = 0.036 |
| | AIC | AIC = 74.5 | AIC = 68.6 | AIC = 1.3 | AIC = 3.0 |
| **Urinary Fluoride – Low Risk-of-bias Studies** | | | | | |
| No. Studies/No. Observations | | 9/15 | 9/15 | 5/8 | 4/7 |
| Number of Children | | 5,713 | 5,713 | 4,141 | 3,952 |
| Linear model | Beta (95% CI) | −0.10 (−0.21, 0.01) | −0.10 (−0.21, −0.01) | −0.05 (−0.17, 0.08) | −0.08 (−0.16, −0.01) |
| | p-value | p = 0.082 | p = 0.082 | p = 0.472 | p = 0.028 |
| | AIC | AIC = 5.9 | AIC = 5.9 | AIC = 2.8 | AIC = 2.5 |

Dkt. No. 431-2, Trial Ex. 68 at 39 (eTable 4) (red annotation added). That value was also derived from a linear model which, for this group of studies, likewise had the lowest AIC score. *See id.* (identifying 68 (linear for all studies), 75.8 (quadratic for all studies), 73.3 (restricted cubic splines for all studies)).

80. Even if there may be some uncertainty about the dose-response relationship below that exposure level (4 mg/L), significant data supports that there is an adverse effect *at or above the specified level*. *See* Dkt. No. 415, Feb. 12, 2024, Trial Tr. at 1373:1-9 (Barone) (testimony from

Dr. Barone agreeing that at 4 mg/L of fluoride exposure and above there is relatively more data to support a finding of an adverse effect associated with fluoride.), 1428:4-11 (Barone) ("I agree with the NTP's conclusions that at some level above 1.5 that there is moderate evidence to support an association between fluoride and developmental IQ decrements."). Again, TSCA does not require absolute certainty as to the threshold level at which a chemical produces the hazard, and indeed as noted above such certainty is very difficult to obtain from epidemiologic studies of human populations. Dkt. No. 440, Feb. 13, 2024, Trial Tr. at 1440:18-23 (Barone); Dkt. No. 414, Feb. 9, 2024, Trial Tr. at 1173:7-13 (Savitz). In view of the record evidence, 4 mg/L as the lowest-observed-effect-level would be a conservative point of departure to utilize in the analysis; it is certainly well-supported by scientific evidence as described in the conclusion of the NTP Monograph: "the high-quality studies (*i.e.*, studies with low potential for bias) consistently demonstrate lower IQ scores with higher fluoride exposure [*e.g.*, represented by populations whose total fluoride exposure approximates or exceeds the WHO Guidelines for Drinking-water Quality of 1.5 mg/L of fluoride (WHO 2017)]." NTP Monograph at 47.

81. The EPA has identified a LOAEL based upon far less evidence than that in the record before this Court. In the EPA's risk evaluation of Methylene, conducted pursuant to Amended TSCA, it used a LOAEL for developmental neurotoxicity, derived from the analysis of ***one study conducted upon mouse pups*** (Fredriksson et al., 1992). *See* Methylene Risk Evaluation at 262. Here, there are between six and nine[26] high-quality, epidemiological studies of human populations underlying the point of departure. Dkt. No. 431-2, Trial Ex. 68 at 39, 41 (eTable 4).

82. To restate, in conclusion, either the LOAEL of 4.0 mg/L, measured either in urinary fluoride or water fluoride, or the BMCL of 0.28 mg/L, 0.768 mg/L, or even 1.536 mg/L measured in maternal urinary fluoride, is a well-supported point of departure to utilize in the risk evaluation. Each of these measures of the point of departure is supported by a preponderance of high-quality evidence.

[26] Six studies measuring fluoride exposure by way of water fluoride and nine studies measuring urinary fluoride. Dkt. No. 431-2, Trial Ex. 68 at 39, 41 (eTable 4).

B. Step 2: Exposure Assessment

a. *Framework*

83. At this step, the EPA conducts an exposure assessment to identify the exposure level under the conditions of use for the chemical at issue. Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 567:18-568:2 (Barone); 15 U.S.C. § 2605(b)(4)(F)(iv) ("In conducting a risk evaluation under this subsection, the Administrator shall . . . take into account, where relevant, the likely duration, intensity, frequency, and number of exposures under the conditions of use of the chemical substance."). Namely, the EPA identifies sources of exposure to the chemical (*e.g.*, food or water), estimates what the intake level of exposure is, and endeavors to understand and characterize the population that is exposed. Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 694:4-695:11 (Barone).

84. To understand the level of exposure, the EPA estimates a range of exposure levels for a condition of use from the central tendency exposure (*e.g.*, 50th percentile) to high-end exposure (*e.g.*, 95th percentile). Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 649:1-650:10 (Barone), 697:15-698:6 (Barone); *see also* EPA Guidelines at 64 (describing consideration of upper percentile exposure and highest-exposed individuals in risk assessment).

85. As discussed in depth in the next section (Section III.C), the exposure level is important because it is used to calculate whether the chemical presents a risk to humans. Specifically, in the next step of the analysis (risk characterization), the exposure level is compared to the point of departure to determine if a risk is present. *See* Dkt. No. 401, Feb. 6, 2024, Trial Tr. (Barone) at 705:7-706:21. At that step, the EPA determines the appropriate margin that needs to exist from the point of departure (*i.e.*, point at which the chemical becomes hazardous). *See id.* This is the benchmark Margin of Exposure ("MOE"). *See id.* The benchmark MOE is calculated by multiplying the point of departure by Uncertainty Factors ("UFs") to account for assumptions or uncertainty in the data. *See id.* The benchmark MOE is then compared to the actual MOE, *i.e.*, the existing margin between the exposure level and the point of departure, to determine if that margin is sufficient. *See id.*

b. *Key findings*

86. For reasons discussed below, **maternal urinary fluoride** is an appropriate metric to use in conducting the risk evaluation of fluoride under the condition of use, *i.e.,* community water fluoridation at 0.7 mg/L.

87. Pregnant mothers in fluoridated communities in the United States have a median exposure level to fluoride of **0.8 mg/L**, measured in **maternal urinary fluoride**; at the 95th percentile,[27] pregnant mothers have an exposure level to fluoride of **1.89 mg/L**, measured in **maternal urinary fluoride**. Approximately half of these maternal urinary fluoride levels is attributed to community water fluoridation.

88. Alternatively, the exposure levels of **0.7 mg/L,** or **0.56 mg/L** measured in **water fluoride**, is an appropriate exposure level to use in this risk evaluation.

c. *Underlying findings*

89. Two studies are highly probative in assessing exposure levels in this risk evaluation: Till (2018), and Malin (2023). To summarize these studies:

a. Till (2018) studied samples collected from the MIREC Cohort (1,566 pregnant women in Canada) to assess the relationship between maternal urinary fluoride in pregnant women and water fluoride concentrations and concluded that "[c]ommunity water fluoridation is a major source of fluoride exposure" for the pregnant women studied. Dkt. No. 432-4, Trial Ex. 108 at 1. Specifically, the study observed that the mean urinary fluoride values were almost two times higher for pregnant women living in fluoridated regions compared to non-fluoridated regions, and "significantly lower" for women living in non-fluoridated regions. *Id.* at 6. The median concentration of fluoride in drinking water in Canada was 0.56 mg/L in fluoridated areas. *Id.* at 8 (Table 2). Given that the United States fluoridates its water levels at an optimal 0.7 mg/L (higher than the median in Till (2018)), the urinary fluoride levels in this sample are lower, if anything, relative to the condition of use at issue (fluoridation at 0.7 mg/L). The findings of Till (2018),

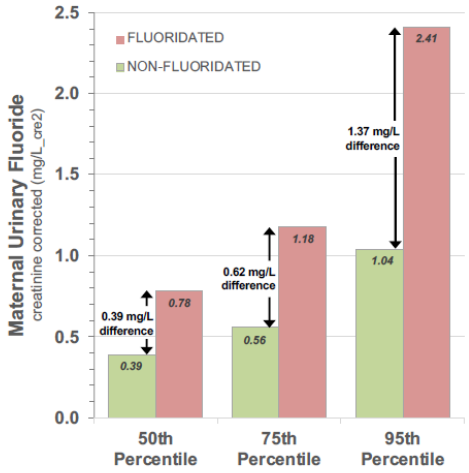
[27] The 95th percentile reflects individuals that have exposure levels greater than 95 percent of the population. *See* Dkt. No. 108 at 6. The median, on the other hand, reflects individuals at the mid-point of exposure. *See id.*

comparing the maternal urinary fluoride levels of pregnant women in fluoridated compared to non-fluoridated reasons are exemplified in the below tables, summarizing the key results of this study:

**Table S4.** Fluoride concentrations in the urine of pregnant women from the MIREC cohort living in fluoridated versus non-fluoridated communities.

| | Trimester | N | Arith Mean | Arith SD | Geo Mean | Geo SD | Min | 5% | 25% | 50% | 75% | 95% | Max |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **NON-FLUORIDATED** | | | | | | | | | | | | | |
| MUF_Unadjusted | 1 | 541 | 0.24 | 0.29 | 0.15 | 2.65 | 0.01 | 0.03 | 0.08 | 0.15 | 0.30 | 0.69 | 3.56 |
| | 2 | 509 | 0.32 | 0.33 | 0.23 | 2.22 | 0.03 | 0.06 | 0.13 | 0.22 | 0.38 | 0.90 | 3.54 |
| | 3 | 476 | 0.47 | 0.39 | 0.36 | 2.05 | 0.04 | 0.11 | 0.22 | 0.36 | 0.60 | 1.23 | 3.77 |
| $MUF_{SG}$ | 1 | 541 | 0.31 | 0.39 | 0.20 | 2.56 | 0.01 | 0.04 | 0.12 | 0.20 | 0.35 | 0.84 | 4.67 |
| | 2 | 507 | 0.39 | 0.32 | 0.31 | 1.89 | 0.04 | 0.12 | 0.21 | 0.29 | 0.46 | 0.96 | 2.44 |
| | 3 | 475 | 0.48 | 0.32 | 0.40 | 1.78 | 0.08 | 0.17 | 0.28 | 0.38 | 0.56 | 1.09 | 2.71 |
| $MUF_{CRE\_1}$ | 1 | 533 | 0.50 | 0.50 | 0.35 | 2.40 | 0.01 | 0.08 | 0.22 | 0.37 | 0.60 | 1.41 | 4.5 |
| | 2 | 502 | 0.58 | 0.44 | 0.48 | 1.85 | 0.06 | 0.19 | 0.31 | 0.46 | 0.69 | 1.47 | 3.31 |
| | 3[a] | 386 | 0.67 | 0.47 | 0.56 | 1.75 | 0.12 | 0.24 | 0.40 | 0.54 | 0.79 | 1.45 | 4.61 |
| $MUF_{CRE\_2}$ | 1 | 534 | 0.41 | 0.45 | 0.29 | 2.42 | 0.01 | 0.06 | 0.18 | 0.30 | 0.49 | 1.15 | 4.81 |
| | 2 | 502 | 0.43 | 0.32 | 0.35 | 1.85 | 0.04 | 0.14 | 0.23 | 0.34 | 0.51 | 1.08 | 2.43 |
| | 3[a] | 386 | 0.48 | 0.33 | 0.40 | 1.75 | 0.08 | 0.17 | 0.29 | 0.39 | 0.56 | 1.04 | 3.29 |
| **FLUORIDATED** | | | | | | | | | | | | | |
| MUF_Unadjusted | 1 | 762 | 0.57 | 0.49 | 0.40 | 2.57 | 0.02 | 0.06 | 0.23 | 0.43 | 0.79 | 1.48 | 3.98 |
| | 2 | 728 | 0.71 | 0.53 | 0.56 | 2.03 | 0.04 | 0.17 | 0.35 | 0.56 | 0.89 | 1.68 | 3.77 |
| | 3 | 712 | 0.82 | 0.60 | 0.63 | 2.04 | 0.11 | 0.19 | 0.39 | 0.64 | 1.06 | 1.99 | 4.36 |
| $MUF_{SG}$ | 1 | 762 | 0.52 | 0.46 | 0.37 | 2.44 | 0.01 | 0.07 | 0.25 | 0.4 | 0.64 | 1.30 | 3.84 |
| | 2 | 728 | 0.71 | 0.47 | 0.59 | 1.84 | 0.03 | 0.23 | 0.40 | 0.58 | 0.87 | 1.63 | 3.78 |
| | 3 | 711 | 0.88 | 0.55 | 0.74 | 1.81 | 0.08 | 0.27 | 0.51 | 0.77 | 1.08 | 1.89 | 3.97 |
| $MUF_{CRE\_1}$ | 1 | 757 | 0.83 | 0.68 | 0.60 | 2.44 | 0.01 | 0.12 | 0.39 | 0.65 | 1.09 | 2.19 | 4.89 |
| | 2 | 723 | 1.13 | 0.77 | 0.93 | 1.91 | 0.05 | 0.32 | 0.61 | 0.91 | 1.42 | 2.63 | 4.89 |
| | 3[a] | 546 | 1.30 | 0.82 | 1.10 | 1.86 | 0.12 | 0.41 | 0.72 | 1.08 | 1.63 | 3.10 | 4.63 |
| $MUF_{CRE\_2}$ | 1 | 759 | 0.68 | 0.58 | 0.49 | 2.46 | 0.01 | 0.09 | 0.31 | 0.53 | 0.88 | 1.80 | 4.61 |
| | 2 | 727 | 0.85 | 0.60 | 0.69 | 1.92 | 0.04 | 0.24 | 0.45 | 0.67 | 1.05 | 2.00 | 4.66 |
| | 3[a] | 553 | 0.97 | 0.68 | 0.80 | 1.90 | 0.09 | 0.29 | 0.52 | 0.78 | 1.18 | 2.41 | 4.78 |

*Id.* at 25 (Table S4) (red annotations added). This data is reflected in the below bar graph, illustrating that Till (2018) found that fluoride levels were approximately two times higher in fluoridated vs. non-fluoridated areas:[28]




[28] Though not in evidence, the Court includes this demonstrative bar graph (presented to the Court

b. Malin (2023) studied the maternal urinary fluoride levels of pregnant women in Los Angeles, California (*i.e.*, samples collected from the Maternal and Developmental Risks from Environmental and Social Stressors cohort ("MADRES Cohort")) to discern if those levels of American women were comparable to levels observed amongst pregnant women in Mexico and fluoridated communities in Canada. Dkt. No. 432-18, Trial Ex. 122 at 9. Malin (2023) concluded that the maternal urinary levels observed in Los Angeles were comparable to those found in pregnant women in Mexico and Canada. *Id.* at 1, 9. These findings corroborate the conclusions of Till (2018), and further support that water intake is an important contributor to maternal urinary fluoride levels.

90. Plaintiffs have shown, by a preponderance of the evidence, that a pregnant mother in the United States, under the condition of use (community water fluoridation of 0.7 mg/L, which is higher than the median water fluoridation levels in the Till (2018) data set of 0.56 mg/L found in Canada) produces a maternal urinary fluoride concentration level of at least **0.8 mg/L** for median water consumption or **1.89 mg/L** for 95th percentile water consumption.

a. As explained above, Till (2018) studied urinary fluoride levels in fluoridated areas of Canada, and identified a median (specific gravity adjusted) urinary fluoride level of 0.77 mg/L and a 95th percentile urinary fluoride level of 1.89 mg/L. Dkt. No. 432-4, Trial Ex. 108 at 25-26 (Table S4); Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 118:5-20 (Hu). Malin (2023) studied pregnant mothers living in Los Angeles, California, a fluoridated city, and similarly observed that those mothers had a median (specific gravity-adjusted) urinary fluoride level of 0.8 mg/L, and a 95th percentile level of 1.89 mg/L, in the third trimester. Dkt. No. 432-18, Trial Ex. 122 at 5 (Table 2); Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 124:1-16 (Hu). Dr. Hu testified credibly that the Malin (2023) cohort is representative of mothers in the United States as a whole, though if anything, this cohort would present *lower* fluoride exposure levels relative to other populations because data indicates Hispanic communities have a greater distrust of tap water relative to other communities, in part due to immigration from Mexico where tap water is distrusted. Dkt. No. 395,

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as Plaintiff's Demonstrative No. 4 at trial) to illustrate fully the trial testimony.

Jan. 31, 2024, Trial Tr. at 118:11-119:9 (Hu). Canada and the United States each take a similar approach to water fluoridation; both countries identify 0.7 mg/L as the optimal fluoridation level. *See* NTP Monograph at 1; Dkt. No. 396, Feb. 1, 2024, Trial Tr. at 245:1-22 (Lanphear). It follows that pregnant woman in the United States, exposed to fluoride under the condition of use at issue (community water fluoridation at a typical or optimal level of 0.7 mg/L) have an exposure level of **0.8 mg/L measured in maternal urinary fluoride** (median water intake) and **1.89 mg/L measured in maternal urinary fluoride** (95th percentile water intake), urinary fluoride levels that reflect the real world results of drinking water fluoride levels at the condition of use at issue in this case.

b. To be sure, maternal urinary fluoride reflects not only fluoride that a pregnant woman is exposed to from drinking fluoridated water from her community (the condition of use at issue), but also fluoride from other sources such as food and beverage and household items such as toothpaste; it reflects aggregate exposure to fluoride. *See* Dkt. No. 395, Jan 31, 2024, Trial Tr. at 105:10-25 (Hu); Dkt. No. 416, Feb. 12, 2024, Trial Tr. at 1404:19-21 (Barone); Dkt. No. 198-1 (Hu Trial Decl.). The EPA argues that because maternal urinary fluoride reflects *aggregate* fluoride exposure, rather than exposure attributed solely from community water fluoridation, maternal urinary fluoride is an inappropriate metric to use in assessing the risk of community water fluoridation. However, exposure level of fluoride expressed in the metric of maternal urinary fluoride is properly used in this risk assessment because:

i. Maternal urinary fluoride, though not a perfect metric in all respects, is a valuable metric in assessing risk associated with water fluoridation since it is a comprehensive metric, reflecting the true aggregate exposure to the chemical at issue. As Dr. Hu explained: "[T]he primary benefit [of using urinary fluoride as the metric of fluoride exposure] is that you're integrating fluoride exposure from whatever exposure source there is. So if it's dietary, if it's in the water, it's in the food, it's in the food that was cooked with the fluoridated water; if you happen to swallow toothpaste or if you're using other sources of fluoride, it will integrate all of it and express it in terms of what is the level of fluoride that's circulating in your blood and then gets filtered out into the kidneys. And that ultimately is the component of fluoride in the body that's

available to cross the blood-brain barrier to the brain and also to go to other target organs in the body." Dkt. No. 395, Jan. 31, 2024, Trial Tr. at 105:13-25 (Hu). Put differently, this metric reflects that water fluoridation does not occur in a vacuum; in the real world, fluoridating water means exposing women to fluoride *in addition to* the exposure a woman has to fluoride via other sources. Because dosage matters, it makes good sense to consider other sources of exposure to fluoride in deciding if adding to that exposure level presents a risk. *See* Dkt No. 400, Feb. 5, 2024, Trial Tr. at 676:12-21 (Barone) (recognizing that exposure and point of departure can be expressed in urine content in a risk assessment); Dkt. No. 402, Feb. 8, 2024, Trial Tr. at 1015:9-1020:13 (Savitz) (discussing pros and cons of using urinary fluoride as a measurement of water fluoridation and recognizing that urinary fluoride has a "number of positive features," including integrating exposure from different sources, that it is a measurement reflecting not just what is in that body on a given day but for a longer period of time, and explaining that he has used urinary fluoride as a metric in assessing another chemical, PFAS); Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 790:8-12 (Thiessen) ("there's no scientific reason why [the exposure level and hazard level] have to be milligrams per kilogram per day. They could also be milligrams per liter in the drinking water, they could also be milligrams per liter *in the urine*") (emphasis added).

ii. The EPA permits considering the *additive* risk posed by a chemical under the condition of use at issue when conducting a risk evaluation. To this end, Dr. Barone explained that in a situation where the condition of use is additive to other background sources, "you want to be able to understand, well, what's the background, be able to subtract the background; you want to be able to say what's the dietary component and what is the actual water intake component. And then if you have information on the other sources, potential sources, whether it's pharmaceutics or other inhaled or overly ingested pollutants having a similar kind of exposure, additive exposures, *you want to be able to capture that to the best of your ability*." Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 678:6-21 (Barone) (emphasis added). *See also* Dkt. No. 400, Feb. 5, 2024, Trial Tr. (Barone) at 567:18-568:2 ("Q. And the point of the exposure assessment is to identify what the human exposure level is under the specific conditions of use of the chemical being evaluated, right? A. It is – it is condition-of-use specific. Q. Now, it is condition-of-use

specific, but TSCA specifically permits EPA to consider aggregate exposures to the chemical, correct? A. *TSCA specifically allows for consideration of aggregate exposures*. It doesn't require us to quantify based upon aggregate exposures") (emphasis added). Indeed, rather than preventing a risk evaluator from considering aggregate exposure to a chemical in evaluating risk, Amended TSCA expressly identifies that a risk evaluator should describe whether *aggregate exposure* was considered and explain why, or why not. *See* 15 U.S.C. § 2605(b)(4)(F). Specifically, the statute provides: "[i]n conducting a risk evaluation under this subsection, the Administrator shall . . . describe *whether aggregate or sentinel exposures to a chemical substance under the conditions of use were considered*, and the basis for that consideration." 15 U.S.C. § 2605(b)(4)(F) (emphasis added).

iii. If water fluoridation was a minor contributor to overall exposure to fluoride, then it may be less appropriate to utilize an aggregate exposure metric in assessing risk of water fluoridation. If that were the case, much of the risk at issue would not derive from water fluoridation but another source; regulating water fluoridation would be of little consequence to the total exposure. But that is not the case. Instead, as described in depth below at ¶ 91(a), water fluoridation accounts for more than half of a pregnant woman's aggregate exposure level (*i.e.*, maternal urinary fluoride level). To this end, Dr. Thiessen credibly testified that fluoride content of the urine "will be driven by the fluoride content of the water," as "for most individuals, the intake is driven by the fluoridated water." Dkt. No. 402, Feb. 8, 2024, Trial Tr. at 934:18-22 (Thiessen). Drinking water fluoridation is highly consequential to a pregnant woman's overall exposure level and so it is wholly appropriate to use maternal urinary fluoride as the metric of exposure in assessing the risk of community water fluoridation. *See also* Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 790:8-12 (Thiessen) ("[T]here's a consistent association between urinary fluoride and drinking water fluoride concentrations. As the concentration of fluoride in the drinking water increases, the fluoride concentration in the urine will increase."), 792:19-2793:16 ("[I]n most cases, the primary driver of the total fluoride intake [is fluoride concentration in the

drinking water]. So you can still make that hazard-to-exposure comparison.").[29]

91. To the extent that risk assessment requires determining the exposure level attributed solely to the condition of use (community water fluoridation), Plaintiffs have shown, by a preponderance of the evidence, that at least half of the maternal urinary fluoride levels observed, **0.4 mg/L** (median) (*i.e.*, 0.8 mg/L divided by two) maternal urinary fluoride and **0.945** mg/L (95th percentile) (*i.e.*, 1.89 mg/L divided by two) maternal urinary fluoride can be attributed to the condition of use (community water fluoridation):

a. As explained above, ¶ 89(a), Till (2018) observed that the maternal urinary fluoride levels were approximately **two-times higher** for pregnant women living in fluoridated regions compared to non-fluoridated regions. Dkt. No. 432-4, Trial Ex. 108 at 6, 25-26 (Table S4). Dr. Thiessen credibly testified that it is reasonable to conclude from Till (2018) that the 2x increase in maternal urinary fluoride levels in fluoridated areas can be attributed to community water fluoridation in those areas. *See* Dkt. 401, Feb. 6, 2024, Trial Tr. at 784:1-16 (Thiessen) ("The primary difference and the only main group difference that we're aware of is that one group is fluoridated and one is not. So a difference in the urinary fluoride would be attributable to the fluoride in the drinking water."); Dkt. No. 402, Feb. 8, 2024, Trial Tr. at 934:18-22 (Thiessen). And the EPA's expert witness agreed that the increase in maternal urinary fluoride levels can largely be attributed to intake of fluoridated water. Dkt. No. 416, Feb. 13, 2024, Trial Tr. at 1408:10-1409:11 (Barone) (explaining that the "parsimonious" explanation as to the 2x increase of maternal urinary fluoride levels observed in Till (2018) is that it is "due to intake, total intake,

[29] In Thippeswamy (2021), the researchers compared fluoride concentrations in urine, serum, and cord blood of women consuming water with designated "low" and "optimum" concentrations of fluoride to understand the relationship of these metrics. Dkt. No. 432-7, Trial Ex. 111 at 1. Thippeswamy (2021) did not observe a one-to-one correlation between urinary fluoride and water fluoride concentration, but concluded that "the low/optimum fluoride concentration in drinking water compared to urine . . . correlated significantly." *Id.* The strong relationship between the fluoride concentration in water and urinary fluoride is further corroborated by Green (2019). Green (2019) studied samples collected from the MIREC Cohort (Canadian women and offspring) and identified a moderate correlation between maternal urinary fluoride intake and water fluoride concentration. Dkt. No. 432-5, Trial Ex. 109 at 1, 5 ("The MUF, was moderately correlated with fluoride intake ($r = 0.49$; $P < .001$) and water fluoride concentration ($r = 0.37$; $P < .001$)."). Though not a one-to-one comparison, the correlation observed in these studies further corroborates Dr. Thiessen's testimony as to the relationship between water fluoride and urinary fluoride.

and that's probably both food and water . . . [a]nd water is a significant portion . . . of that"). Moreover, water fluoridation also contributes to fluoride exposure indirectly because commercial food and beverages are made using fluoridated water; this is known in the scientific community as the "halo effect" of water fluoridation. *See, e.g.*, Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 799:7:800:13 (Thiessen) (describing the "halo effect" of water fluoridation wherein individuals ingest water that has been fluoridated by way of beverages such as colas, juices, beer and wine, that were made using water from a fluoridated community); Dkt. No. 396, Feb. 1, 2024, Trial Tr. at 212:7-23 (Lanphear) (describing the "halo effect" of communities that fluoridate water, causing exposure of fluoride in surrounding areas by way of food and beverage). *See also* Dkt. No. 432-4, Trial Ex. 108 at 6-7 (describing the "diffusion or halo effect" . . . "which refers to the extension of fluoridation to residents of nonfluoridated communities as a result of foods and beverages that are commercially processed in fluoridated areas and consumed in nonfluoridated communities") (citing Griffin et al. 2001; Ripa 1993). Accordingly, it is appropriate to infer conservatively that approximately **half** of the maternal urinary fluoride observed in a pregnant woman's urine is attributed to community water fluoridation.[30] Here, that is **0.4 mg/L** (0.8 mg/L divided by two) (median) maternal urinary fluoride and **0.945 mg/L** (1.89 mg/L divided by two) (95th percentile) maternal urinary fluoride.

b. One concern regarding extrapolating water intake from maternal urinary fluoride is that fluoride intake is not necessarily equivalent with fluoride excretion; the absorption and excretion process adds complexity. For example, a pregnant woman will experience the breakdown of her own skeleton during pregnancy to form the fetal skeleton, releasing fluoride absorbed in her bones, resulting in an increase in excretion of urine not tied to additional fluoride consumption. *See* Dkt. No. 395, Jan. 1, 2024, Trial Tr. at 121:10-20 (Hu). To this end the EPA argues that because of the complexities regarding absorption and excretion of fluoride, use of a physiologically based pharmacokinetic ("PBPK") modeling[31] is necessary to convert maternal

[30] As noted below in Paragraph 91(b)(i), the EPA allows for assumptions, including, *e.g.*, absorption rates, when specific data is not available.

[31] PBPK model is "a computer model that estimates concentrations of a substance in other parts of

urinary fluoride levels to estimate the fluoride intake level. Because Plaintiffs have not done PBPK modeling, EPA argues, it is inappropriate to estimate exposure attributed to the condition of use from maternal urinary fluoride. *See* Dkt. No. 402, Feb. 8, 2024, Trial Tr. at 943:1-7 (Thiessen) (recognizing that PBPK models have not been identified to predict maternal urinary fluoride concentrations based on drinking water exposures.). The Court rejects the EPA's argument for the following reasons.

i. While PBPK modeling may be useful and perhaps ideal, it is not essential to conduct a risk evaluation. The Amended TSCA does not expressly mandate use of a PBPK model, but instead affords ample discretion in the methodologies and modeling the risk assessor may employ in assessing risk. *See* 15 U.S.C. § 2625(h) (describing factors to be considered determining the methodologies or models to employ when assessing risk and omitting any reference to a PBPK model).[32] And the EPA Guidelines expressly recognize that pharmacokinetic data may not always be available and instructs a risk assessor to be aware of

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the body based on physiological parameters like absorption" and is used to convert from excretion level to intake level. *See* Dkt. No. 402, Feb. 8, 2024, Trial Tr. at 943:1-7 (Thiessen).

[32] This section provides in full:

> In carrying out sections 2603, 2604, and 2605 of this title, to the extent that the Administrator makes a decision based on science, the Administrator shall use scientific information, technical procedures, measures, methods, protocols, methodologies, or models, employed in a manner consistent with the best available science, and shall consider as applicable – (1) the extent to which the scientific information, technical procedures, measures, methods, protocols, methodologies, or models employed to generate the information are reasonable for and consistent with the intended use of the information; (2) the extent to which the information is relevant for the Administrator's use in making a decision about a chemical substance or mixture; (3) the degree of clarity and completeness with which the data, assumptions, methods, quality assurance, and analyses employed to generate the information are documented; (4) the extent to which the variability and uncertainty in the information, or in the procedures, measures, methods, protocols, methodologies, or models, are evaluated and characterized; and (5) the extent of independent verification or peer review of the information or of the procedures, measures, methods, protocols, methodologies, or models.

15 U.S.C. § 2625(h).

uncertainties posed by lack of such data. Specifically, the EPA Guidelines provide: "If data to be used in a risk characterization are from a route of exposure other than the expected human exposure, then pharmacokinetic data should be used, if available, to make extrapolations across routes of exposure. If such data are not available, the Agency makes certain assumptions concerning the amount of absorption likely or the applicability of the data from one route to another (U.S. EPA, 1992)." EPA Guidelines at 62. This is an implicit recognition that a risk evaluation can proceed without pharmacokinetic modeling when such data is not available. *See also* EPA Guidelines at 47 ("Pharmacokinetic data *may* be helpful in defining the dose-response curve, developing a more accurate basis for comparing species sensitivity (including that of humans), determining dosimetry at sites, and comparing pharmacokinetic profiles for various dosing regimens or routes of administration. The correlation of pharmacokinetic parameters and neurotoxicity data *may* be useful in determining the contribution of specific pharmacokinetic processes to the effects observed.") (emphasis added). Dr. Barone likewise testified that the EPA has conducted risk evaluations under Amended TSCA without PBPK modeling as such models are not always available, explaining: "[w]e used PBPK models in five of the first [ten] risk evaluations. And to varying degrees . . . In some cases we actually had the ability to . . . incorporate studies that included oral exposures, inhalation exposures and dermal exposures . . . so we could look at a wider range of exposures and to do that aggregation of exposures across routes. That's not always available to us, we don't always have those kinds of models available to us." Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 675:9-676:7 (Barone). *See also* Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 576:12-17 (Barone), 578:8-10 (Barone) ("Q. And in EPA's 10 risk evaluations under TSCA, EPA has only departed from using the default uncertainty factor of 10 for intraspecies variability when it had an acceptable physiologically-based pharmacokinetic model for the chemical, correct? A. In the first ten that is a true statement."). Put simply, this lack of PBPK modeling is not fatal to Plaintiffs' proof.

ii. Though Plaintiffs do not present a PBPK model, Till (2018) and Malin (2023) provide real-world, observational data as to the exposure level of for the population at issue under the condition of use at issue. *See* ¶ 90. *See also* Dkt. No. 400, Feb. 5, 2024, Trial

Tr. at 678:6-21 (Barone) (describing that in assessing risk under a condition of use one endeavors to subtract the background exposure from the water intake component to understand the risk at issue, ideally through modeling, but ultimately "to the best of your ability"). And uncertainties posed by lack of modeling may be accounted for in subsequent steps of the analysis (*i.e.*, assessing overall confidence in data in the risk characterization, *see* ¶¶ 112-13 and when determining the appropriate uncertainty factor to employ when assessing the margin of exposure, *see* ¶ 101(b)). Under the present circumstances, there is sufficient data to support the exposure levels identifies notwithstanding lack of PBPK modeling.[33]

iii. As stated above, Till (2018) observed an approximately 2x increase in maternal urinary fluoride levels comparing the mothers in fluoridated relative to non-fluoridated communities across three trimesters of pregnancy. *See* Trial Ex. 108, Dkt. No. 432-4 at 6-7, 8-9; Dkt. No. 432-18, Trial Ex. 122 at 5-6 (Table 2 and Fig. 1). However, Till (2018) and Malin (2023) also observed that pregnant women's maternal urinary fluoride levels increased in *both* fluoridated and non-fluoridated areas in the third trimester of pregnancy relative to the first trimester. *See* Dkt. No. 432-4, Trial Ex. 108 at 8-9, Table 3; Dkt. No. 432-18, Trial Ex. 122, at 5-6 (Table 2 and Fig. 1). This would, at first blush, suggest that something other than fluoridated water contributed to increased maternal urinary fluoride levels in the third trimester, undermining the assumption that fluoridated water is a significant contributor to those levels. However, this observation is well accounted for. As explained previously, the increase in maternal urinary fluoride across both populations in the third trimester of pregnancy is believed to be caused by the breakdown of the maternal skeleton in later trimesters of pregnancy to facilitate the formation of the fetal bone – a process that releases fluoride. *See, e.g.*, Dkt. No. 395, Jan. 1, 2024, Trial Tr. at 121:10-20, 121:25-123:8 (Hu). This observation thus does not undermine the probative value of

[33] Though EPA does not bear the burden of proof in this context the Court does note that EPA has not explained why, if PBPK modeling is necessary to understand risk associated with water fluoridation and appropriate models are available, the EPA has not itself conducted this PBPK modeling. This is not legally relevant given the statutory framework, and does not bear on the Court's findings. However, to the extent that the EPA determines that PBPK modeling is necessary to engage in rulemaking, it may conduct this assessment to put a finer point on risk posed by the condition of use before taking regulatory action; there is nothing preventing EPA from doing so.

Till (2018) and Malin (2023).

92. The present recommended water fluoride concentration in the United States is 0.7 mg/L fluoride. NTP Monograph at 1. It follows that pregnant women living in a fluoridated community in the United States are typically exposed to fluoride levels of **0.7 mg/L** fluoride, measured in water fluoridation. Even more conservatively, the Till (2018) median water fluoride level of **0.56 mg/L** measured in water fluoride is also an appropriate, conservative exposure level to utilize in the risk evaluation. This is because the United States and Canada (where data for Till (2018) was collected) take a similar approach to water fluoridation. *See* Dkt. No. 433-4, Trial Ex. 129 at 16 (describing optimal water fluoride levels in Canada of 0.7 mg/L); Dkt. No. 396, Feb. 1, 2024 Trial Tr. at 245:1-22 (Lanphear) (describing optimal 0.7 mg/L water fluoride standard in Canada). Moreover, urinary fluoride levels in mothers from Los Angeles observed in Malin (2023) and Till (2018) are highly similar. *See* Dkt. No. 432-18, Trial Ex. 122 at 1, 9.

93. The EPA often expresses exposure and hazard level in mg/kg/day, but this is not necessary. What is vital, however, is that the exposure level and hazard level is in the same unit. Dkt. No. 400, Feb. 5, 2024, Trial Tr. (Barone) at 672:22-673:4 (testifying that what matters is that the "[e]xposure concentration in the denominator has to be in the same units as the hazard point of departure or hazard level in the numerator[;] [t]hey have to match up"). Dr. Thiessen likewise testified that "there's no scientific reason why [the hazard and exposure levels] have to be milligrams per kilogram per day. They could also be milligrams per liter in the drinking water, they could also be milligrams per liter in the urine. What matters is comparison of a hazard level and exposure level that are in the same units." Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 790:18-791:16 (Thiessen). Thus, the exposure and hazard level need not be expressed in mg/kg/day, but the units for each must match when conducting subsequent steps of the analysis.

94. For the reasons stated above, and in view of the record evidence, Plaintiffs have shown by a preponderance of the evidence that:

a. Pregnant mothers in fluoridated communities in the United States are typically exposed to fluoridation of drinking water at a concentration level of **0.7 mg/L**, or conservatively, **0.56 mg/L**. They have a median exposure level to fluoride of **0.8 mg/L** (measured in maternal

urinary fluoride), and at the 95th percentile have an exposure level to fluoride of **1.89 mg/L** (measured in maternal urinary fluoride).

b. To the extent that the exposure level used in this risk assessment must reflect exposure attributed solely to the condition of use of the chemical, approximately half of the maternal urinary fluoride levels discussed in Paragraph 87 are attributed to water fluoridation.

C. Step 3: Risk Characterization

a. *Framework*

95. At this step, the EPA calculates the risk presented by the chemical at issue by comparing the point of departure (*i.e.*, hazard level) with the human exposure level. *See* Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 705:7-706:21 (Barone). To ensure a risk is not present, the EPA utilizes a Margin of Exposure (MOE) equation that compares a safe margin from the point of departure (benchmark MOE) with the actual margin between the exposure level and point of departure (MOE). *See id.* at 707:13-708:19.

96. The actual MOE is calculated by discerning the ratio of the point of departure and the human exposure level, *i.e.,* the point of departure divided by the exposure level. Dkt. No. 429-7, Trial Ex. 17 at 65. The benchmark MOE (*i.e.*, the safe or requisite margin) is the product of the applicable uncertainty factors (UFs) (*i.e.*, UF x UF). *See id.* at 2-3; Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 575:17-576:24 (Barone), 580:10-13 (Barone) ("Q. Now, the benchmark MOE is the product of all uncertainty factors that are found to be applicable to a given – to a given hazard, correct? A. To a given hazard, that's correct."), 580:24-581:19 (Barone) ("We don't add them. We multiply – if the uncertainty factor is the default of 10 for human variability, then we use that and multiply is by any other uncertainty factors."). For example, if there is an uncertainty factor of 10 for intraspecies variability, and an uncertainty factor of 10 for using a LOAEL as the point of departure, the benchmark MOE is 100 (10 times 10). *Id.* at 581:12-582:11. As another example, if the first uncertainty factor is 10, and the second uncertainty factor is 3, the benchmark MOE is 30 (10 times 3). *Id.*

97. If the actual MOE is lesser (*i.e.*, there is a smaller margin) than the benchmark MOE, then there is a risk present; if the actual MOE is greater (*i.e.*, there is a bigger margin) than the

benchmark MOE then a risk is presumed not to be present. *See* Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 583:8-13 (Barone) (explaining that if the benchmark MOE exceeds the MOE between the hazard and exposure level a risk is present); Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 707:20-708:9 (Barone) (explaining the converse).

b. *Key findings*

98. A risk is present when using the BMCL of 0.28 mg/L (maternal urinary fluoride) as the point of departure, and whether calculating risk using either the median or high-end exposure levels; the exposure levels exceed the point of departure.

99. A risk is present when using the BMCL of 0.768 mg/L or even 1.536 mg/L (maternal urinary fluoride) as the point of departure, whether calculating risk using either the median or high-end exposure levels; the exposure levels exceed the point of departure.

100. Alternatively, a risk is present when utilizing the conservative 4 mg/L (water fluoride) as the point of departure; the actual MOE is less than the benchmark MOE.

c. *Underlying findings*

(a) BMCL: 0.28 mg/L and in the alternative, 0.768 mg/L and/or 1.536 mg/L (maternal urinary fluoride)

101. The appropriate benchmark MOE to use in calculating risk for the BMCLs identified by Dr. Grandjean is 10, which includes at least one UF of 10 to account for intraspecies variability:

a. A UF of 10 is utilized as a default practice in calculating risk to account for intraspecies variability, *i.e.*, the variability within the human species in reacting to chemicals.[34] *See* Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 712:12-713:22 (Barone).

b. Absent use of physiologically based pharmacokinetic (PBPK) modeling to account for those variabilities, which could allow for the reduction of the UF from 10 down to 3, the EPA applies the UF of 10 in calculating the benchmark MOE. *See id.* at 712:24-713:22; Dkt. No. 401,

[34] Intraspecies variability can be compared with interspecies variability, which accounts for variability between different species (*i.e.*, animals and humans) when extrapolating from animal studies. Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 713:6-10 (Barone).

Feb. 6, 2024, Trial Tr. at 576:12-17 (Barone), 578:8-10 (Barone) ("Q. So the default uncertainty factor that EPA uses to account for intraspecies variability and uncertainty is 10, correct? A. That is the default. Q. And in EPA's 10 risk evaluations under TSCA, EPA has only departed from using the default uncertainty factor of 10 for intraspecies variability when it had an acceptable physiologically-based pharmacokinetic model for the chemical, correct? A. In the first ten that is a true statement.").

c. A PBPK model has not been performed to assess fluoride intake in pregnant women. Dkt. No. 402, Feb. 8, 2024, Trial Tr. at 943:1-16 (Thiessen); Dkt. No. 440, Feb. 13, 2024, Trial Tr. at 1396:17-1397:2 (Barone), 1397:20-23 (Barone) ("Q. And so in the nearly four years since the first trial in this case, plaintiffs still have not performed a PBPK model to extract a urinary fluoride value to an intake value, right? A. No, they haven't.").

d. Because there is no PBPK model utilized here, which would decrease uncertainty and allow from a downward departure of the default UF of 10, the default UF of 10 is appropriately used as the benchmark MOE in the present risk evaluation.

102. The median exposure level for pregnant women measured in urinary fluoride is 0.8 mg/L, and the 95th percentile is 1.89 mg/L. *See* ¶ 87.

103. The actual MOE for the BMCL of 0.28 mg/L at the median exposure level is 0.35 (0.28 mg/L divided by 0.8 mg/L) and 0.148 at the 95th percentile exposure level (0.28 mg/L divided by 1.89 mg/L). The actual MOEs, 0.35 and 0.148, do not exceed the benchmark MOE of 10; thus, the MOE is below the benchmark MOE and a risk is present. *See* Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 707:20-708:9 (Barone) (explaining that a risk is not present where the actual MOE is *higher* than the benchmark MOE). Another way of looking at exposure/risk is taking the BMCL and adjusting it downward for risk factors. To account for a ten-fold risk factor of human variability, actual exposure should not exceed 1/10th of the BMCL of 0.28 mg/L – *i.e.*, 0.028 mg/L. However, the trial evidence establishes actual exposure of levels of 0.8 and 1.89 mg/L – this far exceeds that safety limit of 0.028 mg/L. *See also* Dkt. No. 198-4 at 75-77 (Thiessen Decl.) (providing MOE calculations).

104. The actual MOE for the BMCL of 0.768 mg/L at the median exposure level is 0.96

(0.768 mg/L divided by 0.8 mg/L) and 0.406 at the 95th percentile exposure level (0.768 mg/L divided by 1.89 mg/L). The actual MOEs, 0.96 and 0.406, do not exceed the benchmark MOE of 10; thus, the MOE is below the benchmark MOE and a risk is present. *See* Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 707:20-708:9 (Barone). *See also* Dkt. No. 198-4 at 75-77 (Thiessen Decl.) (providing MOE calculations). Put differently, 1/10th of this BMCL is 0.0768 mg/L (0.768 mg/L divided by 10). Both the median and upper exposure levels of fluoride found in mothers' urine exceed this amount.

105. Even using the higher 1.536 mg/L BMCL to account for omission of the OCC Cohort data, *see* ¶ 73 (discussing exclusion of OCC Cohort data in deriving 0.768 mg/L BMCL using squared model in Grandjean (2022)), a risk is present. Using this figure, the actual MOE at the median exposure level is 1.92 (1.536 mg/L divided by 0.8 mg/L) and 0.813 at the 95th percentile exposure level (1.536 mg/L divided by 1.89 mg/L). 1.92 and 0.813 do not exceed 10; thus, the actual MOE is below the benchmark MOE and a risk is present. *See* Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 707:20-708:9 (Barone). *See also* Dkt. No. 198-4 at 75-77 (Thiessen Decl.) (providing MOE calculations). Put differently, 1/10th of this BMCL is 0.1536 mg/L (1.536 mg/L divided by 10). Both the median and upper exposure levels in mothers' urine exceed this amount.

106. Even if the Court were to consider only half of the exposure level, directly attributable to water fluoridation, as opposed to other sources of fluoride (0.4 mg/L (0.8 mg/L divided by 2) (median) maternal urinary fluoride and 0.945 mg/L (1.89 mg/L divided by 2) (95th percentile) maternal urinary fluoride, a risk is still present. Both of these figures exceed the safe level using a BMCL of 0.28 mg/L (0.028 mg/L). *See* ¶ 103. And these figures also exceed the safe level considering the margin of error if the BMCL of 0.768 mg/L or 1.536 mg/L; the safe levels are 0.0768 mg/L and 0.1536 mg/L (1/10th of each BMCL), respectively. *See* ¶¶ 104-05.

(b) LOAL: 4 mg/L (water fluoride)

107. Alternatively, to the extent that the BMCLs identified previously are not appropriate points of departure, or maternal urinary fluoride is not an appropriate metric, a risk is present using a LOAL of 4 mg/L measured in water fluoride.

108. The appropriate UF applied in the benchmark MOE analysis using the LOAEL of 4

mg/L is 100 (10 x 10):

a. The UF of 10 is appropriately applied to account for intraspecies variability. *See* ¶ 101.

b. A second UF of 10 is also appropriately applied when using a LOAEL as the point of departure. Dkt. No. 440, Feb. 13, 2024, Trial Tr. at 1425:13-17 (Barone) ("Q. Right. If we were using a human study and only had a LOAEL, like was the case with PCE, you would, at that point, consider an additional uncertainty factor beyond the intraspecies variability uncertainty factor? A. Generally, yes. Yes, we would.").

c. Again, the benchmark MOE is calculated by multiplying the applicable UFs. Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 575:17-576:24 (Barone), 580:10-13 (Barone) (explaining that the benchmark MOE is the product of applicable UFs), 580:24-581:19 (stating that "[w]e don't add them[;] [w]e multiply").

109. Pregnant women in "optimally" fluoridated communities in the United States have an exposure level of at least 0.7 mg/L (water fluoride). *See* ¶ 86. Or conservatively, 0.56 mg/L derived from Till (2018), in the alternative. *See* ¶ 89(a).

110. The actual MOE for the LOAEL of 4 mg/L (water fluoride) is 5.71 (4 mg/L divided by 0.7 mg/L) or 7.14 (4 mg/L divided by 0.56 mg/L).

111. 5.71 and/or 7.14 do not exceed 100; the actual MOE is below the benchmark MOE and thus a risk is present. Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 583:8-13 (Barone) (explaining that if the benchmark MOE exceeds the MOE between the hazard and exposure level a risk is present). *See also* Dkt. No. 198-4 at 75-77 (Thiessen Decl.) (providing MOE calculations). Again, another way of looking at this is to take the LOAEL of 4 mg/L, and divide that by the two risk factors. To this end, 4 mg/L divided by 100 equals 0.04 mg/L, reflecting the tolerable concentration of exposure given the risk factors. Exposure to 0.7 mg/L in United States drinking water, or conservatively 0.56 mg/L (Till (2018)),[35] far exceeds that limit.

[35] The condition of use at issue in this suit is fluoridation of water at 0.7 mg/L. However, it is useful to consider the risk posed with the lesser exposure level of 0.56 mg/L given the findings of Till (2018). There, subjects in Canada – which has the same optimal level of water fluoridation as the United States – had a median community water fluoride level of 0.56 mg/L. It follows that

D. Step 4: Risk Determination

a. *Framework*

112. Once the risk has been identified, in the last step of the risk evaluation process the assessor determines if that risk is an *unreasonable* one. Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 735:11-19 (Barone).

113. In making the determination of whether the risk is unreasonable, the assessor considers several factors including: (1) severity of the hazard; (2) exposure-related considerations (*e.g.*, duration, magnitude, or frequency of the exposure, and size of the affected population); (3) other characteristics of the population that is exposed, including the susceptibility of subpopulations; (4) confidence in the information used to inform the hazard and exposure values; and relatedly, the (5) overall strength of the evidence and uncertainties and assumptions included throughout the risk assessment. *See* Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 735:11-736:19 (Barone); Dkt No. 437-1, Trial Ex. 96, at 500 (PCE Risk Evaluation); Dkt. No. 437-3, Trial Ex. 98 at 271 (1,4-Dioxane Risk Evaluation).

b. *Key finding*

114. Based on the aforementioned factors, and in view of the record evidence, the risk at issue – reduced IQ in children posed by water fluoridation at 0.7 mg/L – is an unreasonable risk.

c. *Underlying findings*

115. Given the seriousness of reduced IQ, and the ample support in the record that the United States population is at risk of experiencing IQ decrements of over four IQ points, the **severity** of the hazard at issue (reduced IQ in children, *see* Section III.A.1.), weighs in favor of finding the risk at issue unreasonable:

a. The EPA has recognized that cognitive deficits including reduced IQ are critical chronic health effects, as exemplified by its in its risk evaluation of PCE under the Amended TSCA which identified cognitive deficits as the hazard warranting regulatory action. Dkt. No.

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some communities in the United States may have similar median water fluoridation levels. Thus, it is worth considering if a risk is present at this lower level of exposure, to understand the risk of setting an optimal fluoridation level of 0.7 mg/L as is the standard in the United States.

400, Feb. 5, 2024, Trial Tr. at 597:9-13 (Barone). Moreover, according to the EPA's Clean Air Science Advisory Commission, in the context of its analysis of lead: "[a] population loss of 1-2 IQ points is highly significant from a public health perspective." Dkt. No. 430-1, Trial Ex. 42 at 67000. To this end, a 1-to-2 point loss in IQ was the hazard that supported the identification of lead as a substance posing an unreasonable risk. *Id.* *See also* Dkt. No. 433-4, Trial Ex. 129 at 27 (recognizing that one study found that a reduction of one IQ point "has been shown to be associated with reduced educational attainment, employment status, productivity, and earned wages, reflecting substantial public health concerns").

b. In risk assessments, the EPA evaluates not only the hazard presented at median exposures levels, but considered the hazard posed to the 95th percentile (*i.e.*, high exposure populations). Dkt. No. 430-1, Trial Ex. 42 at 67000. And the EPA considers impact upon smaller, susceptible subpopulations in assessing the risk at issue. *See* Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 587:7-18 (Barone) (testifying that the EPA considered impact on small, susceptible subgroup of population in regulating lead).

c. As Dr. Grandjean explained, women in the 95th percentile exposure level to fluoride exceed the BMCL for a 1-point loss in IQ by over a factor of four. *See* Dkt. No. 397, Feb. 2, 2024, Trial Tr. at 358:2-18 (Grandjean). Indeed, when considering high-end exposure levels, relative to Dr. Grandjean's BMCL identifying the dosage at which a 1-point IQ decrement is expected, fluoride presents a risk of a decrease in IQ ranging from 2.86 to 6.75 IQ points.[36]

116. **Exposure-related considerations** (*e.g.*, duration, magnitude, or frequency of the exposure, and size of the affected population) weighs heavily toward finding the risk at issue unreasonable; the exposure is continuous, and nearly all Americans are affected.

[36] According to Dr. Grandjean's analysis, an increase of 0.28 mg/L of fluoride exposure (measured in maternal urinary fluoride) is associated with a 1-point IQ loss in the mother's offspring (boys and girls). *See* Dkt. No. 432-15, Trial Ex. 119 (Grandjean (2023)) at 1-2, 9. Pregnant mothers in fluoridated communities in the United States have a median and 95th percentile exposure level to fluoride of 0.8 mg/L and 1.89 mg/L, respectively (measured in maternal urinary fluoride). *See* ¶¶ 86-88; Trial Ex. 122, Dkt. No. 432-18 at, Trial Ex. 122 at 9. Thus, fluoride presents a hazard of reduced IQ ranging from approximately 2.86 points at the median intake level,((0.8 mg/L (median exposure level) divided by 0.28 mg/L (dosage at which 1 IQ point decrease is observed)), *i.e.*, 2.857) to 6.75 points at the 95th percentile ((1.89 mg/L (95th percentile exposure level) divided by 0.28 mg/L (dosage at which 1 IQ point decrease is observed)), *i.e.*, 6.75).

117. The size of the affected population is vast. Approximately 200 million Americans have fluoride intentionally added to their drinking water at a concentration of 0.7 mg/L. *See* Dkt. No. 421 at 206-07 (undisputed). Other Americans are indirectly exposed to fluoridated water through consumption of commercial beverages and food manufactured with fluoridated water (*i.e.*, the "halo effect"). *See, e.g.*, Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 799:7:800:13 (Thiessen) (describing the "halo effect" of water fluoridation); Dkt. No. 396, Feb. 1, 2024, Trial Tr. at 212:7-23 (Lanphear) (similar). *See also* Dkt. No. 432-4, Trial Ex. 108 at 6-7 (describing the "diffusion or halo effect" . . . "which refers to the extension of fluoridation to residents of nonfluoridated communities as a result of foods and beverages that are commercially processed in fluoridated areas and consumed in nonfluoridated communities") (citing Griffin et al. 2001; Ripa 1993). Approximately two million pregnant women, and over 300,000 exclusively formula-fed babies are exposed to fluoridated water. Dkt. No. 421 at 209-210. *See also* Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 815:6-816:23 (Thiessen). The number of pregnant women and formula-fed babies alone who are exposed to water fluoridation each year exceeds entire populations exposed to conditions of use for which EPA has found unreasonable risk; the EPA has found risks unreasonable where the population impacted was less than 500 people. *See* Dkt. No. 400, Feb. 5, 2024, Trial Tr. at 588:11-15 (Barone) (testifying that under TSCA the EPA had made unreasonable risk determinations for conditions of use that involve less than 500 people, and that "many are less than 500 people"). *See also* Dkt. No. 421 at 209-210 (EPA agreeing that "the exposed population for the condition of use of community water fluoridation exceeds the exposed populations of the first ten risk evaluations under Amended TSCA").

a. Individuals are exposed to fluoride through water intake every day; the parties do not dispute that frequency of exposure for most people is several times daily (*i.e.*, through drinking tap water). Dkt. No. 421 at 207 (undisputed).

b. And the duration of exposure to fluoridated water is continuous with its effects long-lasting. *See* Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 813:18-20 (Thiessen) (describing that exposure to community water fluoridation is intended to be lifelong). To this end, fluoride remains in the body through years; for several years after cessation of fluoride exposure a woman

is likely to release fluoride into blood due to skeletal breakdown. Dkt. No. 397, Jan. 31, 2024, Trial Tr. at 370:6-371:12 (Grandjean); Dkt. No. 402, Feb. 8, 2024, Trial Tr. at 932:16-20 (Thiessen).

118. The **susceptibility** of exposed populations weighs heavily toward finding the risk at issue unreasonable. It is undisputed that large numbers of susceptible individuals are being exposed each year to fluoride through fluoridation, namely, approximately two million **pregnant women**, and over 300,000 exclusively formula-fed **babies**. Dkt. No. 421 at 209-210. *See also* Dkt. No. 401, Feb. 6, 2024, Trial Tr. at 815:6-816:23 (Thiessen).

119. The scientific literature in the record provides a high level of certainty that a hazard is present; fluoride is associated with reduced IQ. There are uncertainties presented by the underlying data regarding the appropriate point of departure and exposure level to utilize in this risk evaluation. But those uncertainties do not undermine the finding of an unreasonable risk; in every scenario utilizing any of the various possible points of departures, exposure levels and metrics, a risk is present in view of the applicable uncertainty factors that apply:

a. Regarding the point of departure, as discussed above, there is some uncertainty regarding the appropriate point of departure to utilize. Specifically, there is lack of certainty regarding the model fit to be utilized in the BMD modeling analysis, which determines the BMCL to utilize as a point of departure. *See* ¶ 72 (discussing use of linear vs. squared model to derive BMCL). However, under either scenario (whether using a linear or squared model), there is an insufficient safety margin between the exposure level and hazard level; a risk is present. *See* ¶¶ 102-106. Even assuming BMD modeling cannot be used for the data set and using a highly conservative LOAEL of 4 mg/L, a risk remains present by a substantial margin. *See* ¶¶ 107-111. Accordingly, the uncertainty regarding the point of departure (hazard level) is ultimately not consequential to the conclusion herein. The EPA has deemed a risk unreasonable even where it lacked high confidence in the hazard data. *See* Dkt. No. 421 at 211 (undisputed).

b. Regarding the exposure level, there is uncertainty presented by the fact that a PBPK model was not utilized to determine the precise amount of fluoride reflected in pregnant women's maternal urinary fluoride levels that derives from fluoridated water. *See* ¶ 91(b).

Uncertainty due to lack of modeling is offset by the fact that it is appropriate to view risk presented by water fluoridation in context of its additive effects on aggregate exposure, which is best reflected by real world maternal urinary fluoride levels. *See* ¶¶ 89-90. And this is particularly true where, as here, water fluoridation is known to be a significant contributor to maternal urinary fluoride levels, and indeed functions roughly as a 2x multiplier to those levels. *See id.* Further, here, there is real-world observational data showing what the maternal urinary fluoride levels of women that live in communities with fluoridation levels comparable to that of the United States; this data makes the PBPK model less critical to the analysis. *See* ¶¶ 89-91. The uncertainty from the lack of PBPK model weighs against finding the risk unreasonable, but not strongly so due to these mitigating circumstances. Moreover, when utilizing the conservative LOAEL as a point of departure, that metric is derived from water fluoride intake, and does not present the same uncertainty posed by using maternal urinary fluoride levels as the metric of hazard and exposure. Finally, the EPA has deemed a risk unreasonable even where it lacked high confidence in the exposure data. *See* Dkt. No. 421 at 211 (undisputed).

c. There is significant *certainty* in the data set regarding the association between fluoride and reduced IQ. Namely, there is a robust body of evidence finding a statistically significant adverse association between fluoride and IQ. A large majority of the 72 epidemiological studies assessed by the NTP Monograph observed this relationship including all but one of the 19 high-quality studies, *see* ¶¶ 34-36, and literature published after the NTP Monograph cutoff date observed the same relationship, *see* ¶ 37 – and countervailing evidence, for various reasons described previously, are of little impact on this repeated, and consistently observed association between fluoride and reduced IQ, *see* ¶ 39. Moreover, complete consistency amongst studies is not expected. *See* Dkt. No. 414, Feb. 9, 20240, Trial Tr. at 1172:23-1173:6 (Savitz). Notably, notwithstanding inherent difficulties in observing this association at lower exposure levels, studies assessing such levels still observed a statistically significant relationship between fluoride and reduced IQ. *See* ¶¶ 42-44. Again, to put the breadth of evidence supporting this finding in perspective, the EPA has identified a LOAEL based upon far less in other contexts. For instance, in the EPA's risk evaluation of Methylene, conducted pursuant to Amended TSCA,

the EPA used a LOAEL for developmental neurotoxicity, derived from the analysis of ***one study conducted upon mouse pups*** (Fredriksson et al., 1992). *See* Methylene Risk Evaluation at 262. Compare this with 6 (water fluoride) and 9 (urinary fluoride), high-quality, epidemiological studies of human populations underling the 4 mg/L LOAEL underlying the POD here. Dkt. No. 431-2, Trial Ex. 68 at 39, 41 (eTable 4). The scientific literature in the record provides a high level of certainty that a hazard is present; fluoride is associated with reduced IQ. The qualitative evidence is superior.

120. In sum, the first three factors weigh toward finding the risk unreasonable. Namely, the severity of the hazard weighs toward finding the risk unreasonable. The exposure-related considerations and exposure of susceptible populations weighs *strongly* toward finding the risk unreasonable; millions of susceptible individuals are exposed to fluoride and the exposure is frequent and long-lasting. The two final factors, confidence in hazard data and overall strength of the evidence and uncertainties, are largely neutral. Because the first three factors weigh strongly toward finding the risk unreasonable and the last two are largely neutral, the totality of the factors establish that the risk is unreasonable under the Amended TSCA. The Court thus finds that the Plaintiffs have established by a preponderance of the evidence that the risk at issue is **unreasonable**.

## IV. CONCLUSIONS OF LAW

121. Plaintiffs have proven, by a preponderance of the evidence, that water fluoridation at the level of 0.7 mg/L – the prescribed optimal level of fluoridation in the United States – presents an "unreasonable risk of injury to health or the environment, without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation under the conditions of use." 15 U.S.C. § 2620(b)(4)(B)(ii).

122. The Court thus orders the Administrator to initiate rulemaking pursuant to Subsection 6(a) of TSCA. *See id.* §§ 2605(a), 2620(a).

123. The Court defers ruling as to whether Plaintiffs are entitled to recovery of their costs of suit and attorneys and expert witness fees. Parties are ordered to submit a proposed supplemental briefing schedule regarding costs and fees within two weeks of the date of this order.

Defendant shall respond two weeks thereafter. The Court will take the matter under submission unless it orders a hearing.

The Clerk of Court is directed to enter judgment in Plaintiffs' favor.

**IT IS SO ORDERED**.

Dated: September 24, 2024

EDWARD M. CHEN
United States District Judge

United States District Court
Northern District of California