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IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

SAN FRANCISCO DIVISION

FOOD & WATER WATCH, INC, et al., Plaintiffs, v. U.S. Environmental Protection Agency, et al., Defendants.	Case No.: 17-cv-02162-EMC FEDERAL DEFENDANTS' NOTICE OF MOTION AND MOTION TO DISMISS DATE: November 30, 2017 TIME: 1:30 pm Courtroom: 5, 17th Floor

NOTICE OF MOTION

Please take notice that on November 30, 2017 at 1:30 p.m. or as soon thereafter as counsel can be heard, Defendants United States Environmental Protection Agency ("EPA") and Scott Pruitt, EPA Administrator, in his official capacity, will move this Court, located in Courtroom 5, 17th Floor, United States Court House located at 450 Golden Gate Avenue, San Francisco, California, to dismiss all claims in the present litigation.

RELIEF REQUESTED

The relief Defendants seek is dismissal of all claims in the present matter.

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MEMORANDUM OF POINTS AND AUTHORITIES

Pursuant to Federal Rule of Civil Procedure 12(b)(6) and Local Civil Rule 7-2, defendants United States Environmental Protection Agency and Scott Pruitt, Administrator, in his official capacity (collectively "EPA") respectfully submit this Motion to Dismiss.

I. INTRODUCTION

Plaintiffs in this action seek an order compelling EPA to initiate a rulemaking pursuant to section 6(a) of the Toxic Substances Control Act ("TSCA"), 15 U.S.C. § 2605(a), to ban the introduction of "fluoridation chemicals" into drinking water. This action is brought pursuant to TSCA section 21, 15 U.S.C. § 2620, which provides that any person may petition EPA to commence a section 6(a) rulemaking, and further provides that, if EPA denies the petition, the petitioner may commence an action in district court for de novo review of its administrative petition.[1] If the Court finds that the plaintiff has demonstrated by a preponderance of the evidence that the chemical substance poses "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," it shall order EPA to initiate the requested rulemaking.

This case should be dismissed for failure to state a claim on which relief can be granted because Plaintiffs' administrative petition on its face does not provide sufficient information for either EPA or the Court to determine that a chemical substance poses an unreasonable risk under the conditions of use of the substance because (1) the petition, as submitted to EPA, fails to identify a specific "chemical substance," and (2) it does not address any conditions of use of "fluoridation chemicals" other than in drinking water. Accordingly, Plaintiffs' petition does not meet the minimum legal standards for the

[1] As described in the parties' Joint Case Management Statement, EPA believes that the Court's review of Plaintiffs' administrative petition is limited to the administrative record. DE 23 at 4-5.

evaluation of chemical substances under TSCA and, therefore, as a matter of law, cannot provide a basis for a determination that "fluoridation chemicals" pose an unreasonable risk under the conditions of use, which is a prerequisite for relief.

A. Statutory and Regulatory Background

1. TSCA Section 6

Section 6 of TSCA, 15 U.S.C. § 2605, as amended in 2016, establishes a three-step process by which EPA is to evaluate and manage the risk posed by "chemical substances."[2] *See* https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/how-epa-evaluates-safety-existing-chemicals. The amended statute also requires EPA to promulgate regulations to govern the process. 15 U.S.C. §§ 2605(b)(1)(A), (b)(4)(B). The first step in the process is for EPA to screen chemical substances and classify them as high-priority or low-priority. 15 U.S.C. § 2605(b); *see* https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/prioritizing-existing-chemicals-risk-evaluation. EPA must complete a prioritization decision on a chemical within 9-12 months of initiating the prioritization process for that chemical. 15 U.S.C. § 2605(b)(1)(C). Chemical substances classified as high-priority move on to the second step in the process.

The second step is a risk evaluation of the high-priority chemical substance. *Id.* § 2605(b)(4). In conducting a risk evaluation, EPA is required to, among other things, integrate and assess available information on hazards and exposures, including exposures

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[2] Subject to specified exceptions, a "chemical substance" is "any organic or inorganic substance of a particular molecular identity, including -- (i) any combination of such substances occurring in whole or in part as a result of a chemical reaction or occurring in nature and (ii) any element or uncombined radical." 15 U.S.C. § 2602(2). TSCA section 26(c) gives EPA broad discretion to group chemical substances into categories and authorizes EPA to take any actions authorized by statute – including the section 6 prioritization, risk evaluation and regulatory actions described above – by category, rather than by individual chemical substance. 15 U.S.C. § 2625(c)(1). EPA may categorize chemical substances based on similarity in molecular structure, similarity in use, or any other basis suitable for purposes of TSCA. *Id.* § 2625(c)(2)(A).

to potentially exposed or susceptible subpopulations identified as relevant by EPA, for the conditions of use of the chemical substance; not consider costs or other nonrisk factors; and take into account where relevant the likely duration, intensity, frequency, and number of exposures under the conditions of use of the chemical substance. *Id.* § 2605(b)(4)(F). The objective of the risk evaluation is to determine whether the chemical substance "presents an unreasonable risk of injury to health or the environment, without consideration of costs or other nonrisk factors . . . under the conditions of use." *Id.* § 2605(b)(4)(A). A risk evaluation must be completed within 3 years of initiation, although EPA may extend this deadline by up to six months. *Id.* § 2605(b)(4)(G).

If EPA determines that the chemical substance does not present an unreasonable risk under the conditions of use, EPA must issue an order incorporating that determination. 15 U.S.C. § 2605(i)(1). On the other hand, if EPA determines that a chemical does present an unreasonable risk under the conditions of use, step 3 of the process is triggered, in which EPA is required to promulgate a regulation imposing those requirements that EPA determines will eliminate the unreasonable risk. *Id.* § 2605(a). A section 6(a) rulemaking must be completed within two years of completion of the risk evaluation; EPA may extend this deadline for up to two years, although the total length of extensions of the deadlines for the risk evaluation and section 6(a) rulemaking for a chemical may not exceed two years. *Id.* § 2605(c)(1).

Central to this scheme is the concept of "conditions of use." The conditions of use of a chemical substance are "the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." 15 U.S.C. § 2602(4). In promulgating the regulations required by the 2016 TSCA Amendments to implement the new risk evaluation procedure, EPA concluded that the statute gives the Agency some discretion to limit the conditions of use included within the scope of its evaluation. However, the Agency explained that, "[a]s EPA interprets the statute, the Agency is to exercise that discretion consistent with the objective of conducting a

technically sound, manageable evaluation to determine whether a chemical substance – *not just individual uses or activities* – presents an unreasonable risk." 82 Fed. Reg. 33,726, 33,729 col. 1 (July 20, 2017) (emphasis added).

The statute also establishes minimum throughput requirements for this 3-step process. EPA was required to have ten risk evaluations ongoing by December 2016, 15 U.S.C. § 2605(b)(2)(A),[3] and must maintain a steady state of at least 20 high-priority chemicals undergoing risk evaluation beginning in December 2019. *Id.* §§ 2605(b)(2)(B)-(C), 2605(b)(3)(C). In addition, TSCA section 6 authorizes manufacturers to request risk evaluations, and if EPA receives a sufficient number of compliant requests, EPA must be conducting between five and ten such risk evaluations beginning in December 2019. *Id.* §§ 2605(b)(4)(C)(ii), 2605(b)(4)(E).

2. TSCA Section 21

Section 21 of TSCA provides, in relevant part, that "[a]ny person" may petition EPA to initiate a proceeding to promulgate a regulation under section 6(a). 15 U.S.C. § 2620(a). The petition must "set forth the facts which it is claimed establish that it is necessary to issue . . . a rule under . . . section [6]." 15 U.S.C. § 2620(b)(1). Such a petition, in effect, asks EPA to jump immediately to step 3 of the statutory process described above and promulgate a regulation concerning the manufacture, processing, distribution in commerce, use, or disposal of a chemical substance. Accordingly, EPA has determined that TSCA section 21 requires a petition for a section 6(a) rule to present a scientific basis for action that is reasonably comparable, in its quality and scope, to a risk evaluation under TSCA section 6(b), such that it would provide the basis for a regulation that fully complies with the requirements of section 6(a). 82 Fed. Reg. 11,878, 11,880 col. 2 (Feb. 27, 2017).

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[3] These ongoing first ten risk evaluations are for 1,4-Dioxane, 1-Bromopropane, Asbestos, Carbon Tetrachloride, Cyclic Aliphatic Bromide Cluster, Methylene Chloride, N-methylpyrrolidone, Pigment Violet 29, Tetrachloroethylene, and Trichloroethylene. 81 Fed. Reg. 91,927, 91,928 col. 2 (Dec. 19, 2016).

Section 21 further provides that if EPA denies the petition, the petitioner may commence a civil action to compel EPA to initiate the requested rulemaking. 15 U.S.C. § 2620(b)(4)(A). In such an action "the petitioner shall be provided an opportunity to have such petition considered by the court in a de novo proceeding." *Id*. § 2620(b)(4)(B). If the plaintiff demonstrates by a preponderance of the evidence that the chemical substance or mixture presents an unreasonable risk to health or the environment under the conditions of use, the Court shall order EPA to commence the requested rulemaking. *Id*.

Congress made important corresponding changes to sections 6 and 21 in the 2016 TSCA Amendments. Prior to the Amendments, TSCA, including section 6(a), did not contain the phrase or concept of "conditions of use." Rather, section 6(a) authorized rulemaking upon an EPA determination that "there is a reasonable basis to conclude that . . . a chemical substance or mixture presents or will present an unreasonable risk of injury to health or the environment." 15 U.S.C. § 2605(a) (1976) (amended 2016). Correspondingly, pre-amendment section 21 authorized a court to compel section 6(a) rulemaking if the petitioner demonstrated that "there is a reasonable basis to conclude that the issuance of [a section 6(a)] rule . . . is necessary to protect against an unreasonable risk of injury to health or the environment." 15 U.S.C. § 2620(b)(4)(B)(ii) (1976) (amended 2016).

As described above, the amended section 6(a) authorizes rulemaking if EPA determines "in accordance with subsection [6](b)(4)(A)" (the risk evaluation provision described above as step 2 of the 3-step process) that a chemical substance presents an unreasonable risk of injury to health or the environment. 15 U.S.C. § 2605(a). Section 6(b)(4)(A), in turn, requires EPA to conduct risk evaluations to determine "whether a chemical substance 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 identified as relevant to the risk evaluation by the Administrator, under the conditions of use." *Id*. § 2605(b)(4)(A). Congress correspondingly amended the judicial petition portion of section 21 to align it

with these section 6 provisions, so that the finding a court must make to compel EPA action tracks verbatim with this section 6(b)(4)(A) risk evaluation standard.[4] 15 U.S.C. § 2620(b)(4)(B)(ii).

B. Factual Background

On November 23, 2016, EPA received a petition submitted by Plaintiffs pursuant to TSCA section 21 requesting that EPA ban the introduction of "fluoridation chemicals" into drinking water. Declaration of Norman L. Rave, Jr. ("Rave Decl."), Exhibit 1 (without attachments). EPA denied the petition on February 17, 2017. 82 Fed. Reg. 11,878 (Feb. 27, 2017) (Rave Decl. Exhibit 2). In denying the petition, EPA found that the petition, on its face, did not set forth facts that provided a basis to initiate the requested rulemaking. First, the petition requested that EPA regulate "fluoridation chemicals" but did not identify the specific chemical substances for which action was requested. *Id*. at 11,888 col. 1. Thus, it did not meet the basic requirement for requesting a rulemaking for a chemical substance under TSCA section 6(a), i.e., identification of the chemical substance. Nor did the petition provide the basic factual information required by EPA to determine whether it would be appropriate to regulate "fluoridation chemicals" as a category. Second, the petition did not provide any analysis of any conditions of use of the chemical substances covered by the petition other than use in fluoridating drinking water. *Id.* at 11,888 cols. 1-2. Thus, it did not provide a basis under the statute for regulation under section 6(a). In this regard, EPA determined that the authority in section 21(a) to petition the Agency for a rule under section 6(a) to regulate a chemical must be read as authorizing petitions for rules *that would actually comply with that section*, by eliminating any unreasonable risks presented by the chemical. 82 Fed. Reg. at 11,880 col. 2. In this regard, the statutory requirement to set forth the facts to establish that it is necessary to issue the requested rule must be interpreted to require the

[4] Because section 21 pertains to a citizen petition, and not a finding by the EPA Administrator, the language omits the phrase "identified as relevant to the risk evaluation by the Administrator" found in section 6. 15 U.S.C. §§ 2605(b)(4)(A), 2620(b)(4)(B)(ii).

presentation of facts sufficient to support such a statutorily-compliant rulemaking – which the petition did not do.

EPA also determined that, even if the petition were deemed to have met the threshold statutory requirements, the data presented by the petition were not of sufficient quality to demonstrate an unreasonable risk. *Id*. at 11,882-88. Specifically, EPA concluded that "[t]he petition has not set forth a scientifically defensible basis to conclude that any persons have suffered neurotoxic harm as a result of exposure to fluoride in the U.S. through the purposeful addition of fluoridation chemicals to drinking water or otherwise from fluoride exposure in the U.S." *Id*. at 11,887 col. 1.

Plaintiffs commenced this action by filing a Complaint on April 18, 2017. ECF No. 1.

ARGUMENT

I. STANDARD OF REVIEW

A motion to dismiss pursuant to Federal Rule of Civil Procedure 12(b)(6) tests the sufficiency of the complaint. *Christopher v. Harbury*, 536 U.S. 403, 406 (2002). A claim may be dismissed under Rule 12(b)(6) either because it asserts a legal theory that is not cognizable as a matter of law or because it fails to allege sufficient facts to support a cognizable legal claim. *Neitzke v. Williams*, 490 U.S. 319, 325, 327-28 (1989).

In reviewing an agency's construction of a statute it administers, courts must first decide "whether Congress has directly spoken to the precise question at issue." *Chevron, U.S.A., Inc. v. NRDC*, 467 U.S. 837, 842 (1984) ("*Chevron*"). If so, "that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress." *Id.* at 842-43. However, "if the statute is silent or ambiguous with respect to the specific issue, the question for the court is whether the agency's answer is based on a permissible construction of the statute." *Id.* at 843. Particular deference is due where the Agency's decision on the meaning of a statute involves reconciling conflicting policies committed to the Agency's care and expertise under the Act. *Rybachek v. EPA*, 904 F.2d 1276, 1284 (9th Cir. 1990). In addition, a

reviewing court must defer to EPA's interpretation of its own regulations unless that interpretation is "plainly erroneous or inconsistent with the regulation." *Kentuckians for the Commonwealth, Inc. v. Rivenburgh*, 317 F.3d 425, 439 (4th Cir. 2003) (quoting *Auer v. Robbins*, 519 U.S. 452, 461 (1997) (internal quotation marks omitted)). *See also United States v. Larionoff*, 431 U.S. 864, 872 (1977).

II. THE COMPLAINT SHOULD BE DISMISSED BECAUSE PLAINTIFFS' PETITION ON ITS FACE DOES NOT PRESENT A BASIS FOR EPA TO PROCEED WITH THE REQUESTED RULEMAKING AND THEREFORE THERE IS NO BASIS FOR GRANTING RELIEF

Congress amended TSCA sections 6(a)-(c) to require EPA to review chemical substances in commerce to ensure that they do not present an unreasonable risk of injury to health or the environment under the conditions of use. The result of the statutory process is that EPA either: (1) concludes, following risk evaluation, that the subject chemical substance does not present an unreasonable risk and issues an order to that effect under section 6(i)(1); or (2) regulates the chemical under section 6(a) to ensure that it no longer will present any unreasonable risks that are identified during the risk evaluation. Plaintiffs' section 21 petition does not provide enough information to allow the Agency or the Court to evaluate "fluoridation chemicals" under this statutory scheme because it does not identify the specific chemical substances at issue and does not present a scientific basis to conclude that any chemical substances present an unreasonable risk of injury to health or the environment under the conditions of use within the meaning of TSCA section 21(b)(4)(B)(ii), 15 U.S.C. § 2620(b)(4)(B)(ii). Because the petition on its face does not meet the minimum legal standards for the evaluation of chemical substances under TSCA, the Court cannot provide the relief Plaintiffs seek, and the Complaint should be dismissed.

To effectuate the statutory objective, in the 2016 TSCA Amendments, Congress made clear that EPA was to perform risk evaluations on high-priority chemical substances that would include evaluation of the conditions of use of the chemical substance needed to determine whether the chemical substance – not just individual uses

– presents an unreasonable risk of injury to health or the environment. Specifically, the statute requires that, in conducting a risk evaluation, EPA shall "integrate and assess available information on hazards and exposures for the *conditions of use* of the chemical substance . . . ." 15 U.S.C. § 2605(b)(4)(F)(i) (emphasis added). Furthermore, the Amendments specifically added a definition of "conditions of use" to the statute, which are "the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." 15 U.S.C. § 2602(4). The legislative history also makes clear that a risk evaluation must reach a determination of unreasonable risk on all conditions of use within the scope of the risk evaluation. 162 Cong. Rec. S3519 (June 7, 2016). Specifically, a colloquy between Senators Inhofe and Vitter makes clear that the scope of a risk evaluation under section 6 is intended to be comprehensive and include the conditions of use of the chemical substance except for those that EPA, in its discretion, has determined pose minimal risk or are already well controlled. *Id*. at S3519-20.

In promulgating the regulations required by the Amendments to implement the new risk evaluation procedure, EPA explained that, while the statute gives the Agency some discretion to limit the conditions of use included within the scope of its evaluation, "[a]s EPA interprets the statute, the Agency is to exercise that discretion consistent with the objective of conducting a technically sound, manageable evaluation to determine whether a chemical substance – *not just individual uses or activities* – presents an unreasonable risk." 82 Fed. Reg. at 33,729 col. 1 (emphasis added). Accordingly, the Agency made clear that, while EPA could, in its discretion, exclude from the risk evaluation conditions of use that are de minimis or otherwise insignificant and therefore do not require evaluation, the evaluation must include those activities that are necessary

to determine whether the substance presents an unreasonable risk. *Id*. at 33,729 cols. 1-2.[5]

Because, the grant of a section 21 petition requesting a TSCA section 6(a) rule has the same effect as a finding of unreasonable risk by EPA under step 2 of the section 6 process, i.e., it requires EPA to commence a rulemaking to eliminate the unreasonable risk posed by the chemical substance, the statutory scheme would be substantially undermined if section 21 petitions were not required to present a scientific basis for action that is reasonably comparable, in its quality and scope, to a risk evaluation by EPA under TSCA section 6(b). At the very least, a petitioner must identify the chemical substance(s) at issue, address the conditions of use of the chemical substance(s), and either evaluate the risks associated with those conditions of use or explain why those conditions of use are insignificant or otherwise unnecessary to include within the scope of a risk evaluation. If a petition does not do so, it does not provide the basis for EPA to proceed with a section 6(a) rulemaking that complies with the statute.

The 2016 amendments to section 21 demonstrate that Congress intended that section 21 petitions requesting a section 6(a) rule present assessments of the risks of chemical substances that are comparable to those that would appear in EPA risk evaluations. As described above, Congress was careful to amend the section 21 provision for judicial action on section 6(a) petitions to track verbatim the section 6(b)(4)(A) provision setting out the determination that EPA must make upon completion of a risk evaluation. Thus, it is clear that Congress intended the finding a court must make to compel EPA action to be comparable to, and based on the same scope and quality of

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[5] EPA also determined that certain activities associated with chemical substances are generally not conditions of use within the meaning of TSCA section 6, and therefore would generally not be included within the scopes of risk evaluations. For example, EPA determined that the use of a product containing a chemical substance, such as use in previously installed insulation, is generally not a condition of use if the chemical substance is no longer, and is not reasonably foreseen to be, manufactured, processed or distributed for that use (so called "legacy uses"). 82 Fed. Reg. at 33,729 cols. 1-2.

information as, an EPA determination under section 6(b)(4)(A). Most relevant here, the finding must be based on an evaluation of the chemical substance under its conditions of use.

EPA's interpretation of these related provisions of TSCA is clearly reasonable and thus entitled to deference under *Chevron*.[6] Any other interpretation would be inconsistent with Congress' clear intention to establish an orderly process for comprehensive review and, as necessary, regulation of the risks posed by chemical substances. In order to meet the requirements of the statute, a section 6(a) rule must eliminate any unreasonable risks that have been identified through the risk evaluation process, so that the public is assured that the chemical substance does not present an unreasonable risk under *all* conditions of use assessed in the risk evaluation. If the statute were interpreted to allow petitioners to force a section 6(a) rulemaking based on analysis of a single condition of use, it would require EPA to conduct a "catch-up" risk evaluation addressing the conditions of use not addressed by the petition. Nothing in the statute authorizes the Court to impose that obligation on EPA. Moreover, to issue the required section 6(a) rule within the time required by section 6(c), EPA would have to conduct this "catch-up" evaluation without the benefit of the time period that TSCA section 6(b) would ordinarily afford EPA (*i.e.*, time to prioritize a chemical substance, conduct a careful review of its conditions of use, and receive the benefit of concurrent public comment). *See* 82 Fed. Reg. at 11,880 col. 2.

Congress could not have intended this result, i.e., that an administrative petition addressing only a single use could compel EPA to undertake a risk evaluation for a chemical substance that had not been through the risk prioritization process. The

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[6] While section 21 provides for "de novo" review of plaintiffs' claim of unreasonable risk, that standard does not apply to EPA's interpretation of the underlying provisions, particularly where Congress has specifically required EPA to interpret those provisions through regulations. *See Trumpeter Swan Society v. EPA*, 774 F.3d 1037, 1040 (D.C. Cir. 2014) (applying *Chevron* standard of review to EPA's interpretation of TSCA section 21).

prioritization process established in section 6(b) recognizes that a number of chemical substances may present an unreasonable risk of injury to health or the environment and charges EPA with prioritizing those that should be addressed first. As explained above, EPA was required to have ten chemical substances undergoing risk evaluation as of December 2016, and must have at least 20 high-priority substances undergoing risk evaluation by December 2019 (and as many as ten substances nominated for risk evaluation by manufacturers). 15 U.S.C. §§ 2605(b)(2)(A)-(B), 2605(b)(4)(E)(i). EPA is obligated to complete rulemakings to address any unreasonable risks identified in these risk evaluations within prescribed timeframes. 15 U.S.C. § 2605(c)(1). These required activities will place considerable demands on EPA resources. Indeed, Congress carefully tailored the mandatory throughput requirements of TSCA section 6, based on its recognition of the limitations of EPA's capacity and resources, notwithstanding the sizeable number of chemical substances that will ultimately require review.[7] Under this scheme, it is not reasonable to believe that Congress intended to empower petitioners to promote chemicals of particular concern to them above other chemicals that may well present greater overall risk, and force completion of expedited risk evaluations and rulemakings on those chemicals, based on risks arising from one condition of use. *See* 82 Fed. Reg. at 11,880 col. 3.

Plaintiffs' petition, on its face, clearly fails to present a scientific basis for action that is reasonably comparable, in its quality and scope, to a risk evaluation under TSCA section 6(b) that would provide the basis for a compliant rule under section 6(a). It thus provides an inadequate basis for EPA to grant the petition or for the Court to compel EPA to undertake a rulemaking. While the petition is based on the alleged neurological effects of exposure to unspecified "fluoridation chemicals," Rave Decl. Exhibit 1 at 29, it addresses only the use of such fluoridation chemicals in drinking water. As Plaintiffs'

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[7] There are more than 85,000 chemicals on the TSCA Chemical Substance Inventory subject to this prioritization, risk evaluation, and regulation scheme. https://www.epa.gov/tsca-inventory/about-tsca-chemical-substance-inventory.

Complaint acknowledges, ECF No. 1 at ¶ 2, several different chemicals are used for this purpose, and by failing to distinguish between them, the petition provides no basis for EPA or the Court to determine whether there are any differences among the chemicals that could affect the level of risk they pose. While EPA has discretion to act on chemicals as a category under TSCA section 26(c), 15 U.S.C. § 2625(c), the petition contains inadequate information about the properties or conditions of use of the individual chemical substances for EPA or the Court to determine whether they should be considered as a category for purposes of risk evaluation and any necessary regulation.

Further, Plaintiffs' petition provides no information about any other conditions of use of fluoridation chemicals, which is clearly not sufficient information to perform a risk evaluation that could support a statutorily-compliant section 6(a) rule. Under Congress' clearly stated intent, an acceptable risk evaluation must consider the conditions of use of each chemical substance subject to the evaluation. 82 Fed. Reg. at 11,888 col. 2. Plaintiffs' petition does not meet this test. The petition provides no information about the uses of fluoridation chemicals other than as a drinking water additive, and makes no attempt to evaluate the risk from these other uses, or to demonstrate that such risks are insignificant or otherwise unnecessary to completion of a risk evaluation. Without such an analysis, there is no way for EPA to promulgate a rule that comprehensively addresses whatever risk fluoridation chemicals might pose. Thus, Plaintiffs' petition does not set out the facts that would enable the Court to determine that any chemical substance presents an unreasonable risk of injury under the conditions of use within the meaning of TSCA section 21(b)(4)(B)(ii), 15 U.S.C. § 2620(b)(4)(B)(ii).

In sum, because a petition under section 21 acts as a substitute for steps 1 and 2 of the process Congress mandated for rules under section 6, a legally sufficient section 21 petition requesting a section 6(a) risk management rule must provide EPA with all of the information required for the Agency to initiate that rulemaking. Plaintiffs' petition fails this test because it does not identify the specific chemicals at issue, nor any conditions of use of "fluoridation chemicals" other than as an additive to drinking water. Petitioners'

attempt to compel EPA to take one prescribed action, i.e., ban the introduction of "fluoridation chemicals" into drinking water, is clearly inconsistent with Congress' intent that EPA rulemaking under section 6 should comprehensively regulate the risk posed by chemical substances.[8]

CONCLUSION

Because Plaintiffs' administrative petition on its face fails to provide a basis for a regulation under TSCA section 6, there is no basis for the Court to compel EPA to commence such a proceeding to promulgate such a regulation, which is the only relief available under section 21. Accordingly, the Complaint should be dismissed for failure to state a claim on which relief can be granted.

Dated: September 25, 2017

Respectfully submitted,

JEFFREY H. WOOD
Acting Assistant Attorney General

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[8] As EPA stated in its denial of Plaintiffs' petition, Plaintiffs are free to submit a petition that clearly identifies the chemical substances at issue and addresses the other conditions of use those chemical substances. 82 Fed. Reg. at 11,888 col. 2.

[PROPOSED] ORDER

Before the Court is Defendants' Motion to Dismiss. Upon due consideration and for good cause shown, the Motion is GRANTED and Plaintiffs' Complaint is hereby dismissed.

IT IS SO ORDERED.

DATED this _____ day of _____, 2017.

_____
EDWARD M. CHEN
United States District Court Judge

CERTIFICATE OF SERVICE

I hereby certify that a true and correct copy of the foregoing was served by Notice of Electronic Filing this 25th day of September, 2017, upon all ECF registered counsel of record using the Court's CM/ECF system.

/s/ *Norman L. Rave, Jr.*
Norman L. Rave, Jr., Trial Attorney

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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN FRANCISCO DIVISION

FOOD & WATER WATCH, INC, et al., Plaintiffs, v. U.S. Environmental Protection Agency, et al., Defendants.	Case No.: 17-cv-02162-EMC **DECLARATION OF NORMAN L. RAVE, JR.**

I, Norman L. Rave, Jr., declare as follows:

1. I am an attorney for the United States Department of Justice and am counsel of record for Defendants, United States Environmental Protection Agency and Administrator Scott Pruitt. I submit this declaration in support of EPA's Motion to Dismiss.

2. Exhibit 1 is a true and correct copy of an administrative petition submitted by Michael Connett on behalf of the Fluoride Action Network, et al., to Lisa P. Jackson, Administrator dated November 22, 2016 (without attachments).

3. Exhibit 2 is a true and correct copy of Federal Register notice titled "Fluoride Chemicals in Drinking Water; TSCA Section 21 Petition; Reasons for Agency Response," published at 82 Fed. Reg. 11,878 (Feb. 27, 2017).

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct.

Executed on September 25,, 2017 in Washington, D.C.

/s/ *Norman L. Rave, Jr.*

EXHIBIT 1

November 22, 2016

Lisa P. Jackson, Administrator
Environmental Protection Agency
Ariel Rios Building
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460

Dear Administrator Jackson:

Pursuant to section 21 of the Toxic Substances Control Act ("TSCA"), 15 U.S.C. § 2620, the Fluoride Action Network, Food & Water Watch, Organic Consumers Association, American Academy of Environmental Medicine, International Academy of Oral Medicine and Toxicology, Moms Against Fluoridation, and undersigned individuals (collectively, "Petitioners") hereby petition the U.S. Environmental Protection Agency to protect the public and susceptible subpopulations from the neurotoxic risks of fluoride by banning the addition of fluoridation chemicals to water.

Under Section 6 of TSCA, EPA is invested with the authority to prohibit the "particular use" of a chemical substance if the use presents an unreasonable risk to the general public or susceptible subpopulations. 15 U.S.C. § 2605(a). EPA has recognized that its authority to regulate chemical substances under TSCA includes the authority to prohibit *drinking water additives*.

EPA should exercise its authority under TSCA to prohibit fluoridation additives because application of the Agency's own *Guidelines for Neurotoxicity Risk Assessment* to the existing database on fluoride shows that (1) neurotoxicity is a hazard of fluoride exposure, and (2) the reference dose that would reasonably protect against this hazard is incompatible with the doses now ingested by millions of Americans in fluoridated areas. In fact, the amount of fluoride now regularly consumed by many people in fluoridated areas *exceeds* the doses *repeatedly* linked to IQ loss and other neurotoxic effects; with certain subpopulations standing at elevated risk of harm, including infants, young children, elderly populations, and those with dietary deficiencies, renal impairment, and/or genetic predispositions.

The risk to the brain posed by fluoridation additives is an unreasonable risk because, *inter alia*, it is now understood that fluoride's predominant effect on tooth decay comes from *topical* contact with teeth, not *ingestion*. Since there is little benefit in *swallowing* fluoride, there is little justification in exposing the public to *any* risk of fluoride neurotoxicity, particularly via a source as essential to human sustenance as the public drinking water and the many processed foods and beverages made therefrom. The addition of fluoridation chemicals to water thus represents the very type of unreasonable risk that EPA is duly authorized to prohibit pursuant to its powers and responsibilities under Section 6 of TSCA, and Petitioners urge the Agency to exercise its authority to do so.

THE PETITIONERS

ORGANIZATIONS:

American Academy of Environmental Medicine (AAEM) was founded in 1965, and is an international association of physicians and other professionals that provides research and education in the recognition, treatment and prevention of illnesses induced by exposures to biological and chemical agents encountered in air, food and water.

Fluoride Action Network (FAN), was founded in 2000 as a project of the American Environmental Health Studies Project, Inc. FAN is an organization of scientists, doctors, dentists, environmental health researchers, and concerned citizens working to raise awareness about the impact of current fluoride exposures on human health.

Food & Water Watch (FWW) is a national non-profit public interest consumer organization, based in Washington, D.C. that works to ensure safe food and clean water. FWW has worked on many emerging technologies that impact our food supply, by educating consumers, the media, and policymakers about the impact on the food system and public health and by calling for appropriate regulation.

The **International Academy of Oral Medicine & Toxicology** (IAOMT) has been dedicated to its mission of protecting public health through the practice of biological dentistry since it was founded in 1984. A worldwide organization of over 800 dentists, physicians, and research professionals in more than 14 countries, IAOMT's mission is accomplished by funding and promoting relevant research, accumulating and disseminating scientific information, investigating and promoting non-invasive scientifically valid therapies, and educating medical professionals, policy makers, and the general public.

Moms Against Fluoridation is a national nonprofit with a mission to increase awareness of the unsafe and unethical practice of artificial water fluoridation in America today.

Organic Consumers Association is a nationwide grassroots public interest organization dealing with issues of food safety, industrial agriculture, and genetic engineering while promoting organic and sustainable agriculture.

INDIVIDUALS:

Audrey Adams, a resident of Renton, Washington (individually and on behalf of her son Kyle Adams); **Jacqueline Denton**, a resident of Asheville, North Carolina (individually and on behalf of her children Tayo Denton and Rumi Denton); **Valerie Green**, a resident of Silver Spring, Maryland (individually and on behalf of her children Joseph Scribner, Paxton Scribner, Savannah Scribner, Talia Scribner, and Violet Scribner); **Kristin Lavelle**, a resident of Berkeley, California (individually and on behalf of her son Neal Lavelle); and **Brenda Staudenmaier** from Green Bay, Wisconsin (individually and on behalf of her children Ko Staudenmaier and Hayden Staudenmaier).

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I. INTRODUCTION

The addition of industrial-grade fluoride chemicals at a concentration of 0.7 to 1.2 mg/L to public water supplies for the purpose of preventing tooth decay is a common practice in the United States, with approximately 200 million Americans now consuming artificially fluoridated water. This practice, known as "water fluoridation," is hailed as an effective practice by public health institutions in the U.S., but has been rejected by most of continental Europe without any demonstrable adverse effect on childhood caries rates.[1]

Water fluoridation began in the U.S. in the 1940s on the premise that fluoride's primary benefit to teeth comes from *ingestion*. (Fejerskov 2004). The consensus among dental researchers today, however, is that fluoride's predominant benefit is *topical* not systemic. (NRC 2006, at 13; CDC 2001, at 4; Featherstone 2000). It is also now recognized that fluoride is not an essential nutrient. (NRC 1993, at 30; NRC 1989, at 235). Fluoride does not need to be swallowed, therefore, to prevent any disease, including tooth decay. By contrast, fluoride's risks to health come from ingestion, including the spectrum of neurotoxic effects discussed below. Accordingly, a reasonable use of fluoride for caries prevention would aim to maximize its topical contact with teeth, while minimizing its ingestion. Topical fluoride products like toothpaste are compatible with this goal; fluoridating water supplies is not.

II. THE TOXIC SUBSTANCES CONTROL ACT (TSCA)

Section 6 of the Toxic Substances Control Act (TSCA) invests EPA with the authority and duty to take certain actions if it determines that "the manufacture, processing, distribution in commerce, use, or disposal of a chemical substance . . . presents an unreasonable risk of injury to health." 15 U.S.C. § 2605(a). In making this determination, TSCA commands that EPA consider not only risks to the general public, but to "susceptible subpopulation[s]" as well. 15 U.S.C. § 2605(b)(4)(A). Further, TSCA commands that EPA conduct the risk evaluation "without consideration of costs or other nonrisk factors." *Id.*

If EPA determines that a chemical substance presents an unreasonable risk to the general public or susceptible subpopulation(s), the Agency "shall" take action "to the extent necessary to protect adequately against such risk using the least burdensome requirements." 15 U.S.C. § 2605(a). The actions that EPA may take include: (1) a complete prohibition on the manufacture, processing, and distribution of the substance or (2) a prohibition on a "particular use" of the substance. 15 U.S.C. § 2605(a)(1)–(3).

EPA's authority to prohibit and regulate the use of chemical substances under TSCA encompasses drinking water additives. EPA recognized this in its June 12, 1979 Memorandum of Understanding with the FDA, in which the Agency stated unequivocally that it has authority "to regulate direct and indirect *additives to drinking water* as chemical substances and mixtures under TSCA."[2] (EPA/FDA 1979)

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[1] Tooth decay rates declined precipitously throughout the western world during the second half of the twentieth century, in both the *minority* of western countries that fluoridate water (e.g., Australia, Canada, Ireland, New Zealand, and the U.S.), and the majority of western countries that do not. (Cheng et al. 2007; Pizzo et al. 2007; Neurath 2005; Bratthall et al. 1996; Diesendorf 1986).

[2] As EPA explained, "[a]lthough Section 3(2)(B) of TSCA excludes from the definition of 'chemical substance' food and additives as defined under FFDCA, the implicit repeal by the [Safe Drinking Water Act] of FDA's authority over

EPA may not consider costs when determining whether a risk exists, but it must do so when determining the appropriate course of action to protect against the risk. Specifically, EPA must consider: (1) "the effects of the chemical substance," (2) "the magnitude of the exposure of human beings," (3) "the benefits of the chemical substance," and (4) "the reasonably ascertainable economic consequences of the rule." 15 U.S.C. § 2605(c)(2)(A). The EPA shall also consider "whether technically and economically feasible alternatives . . . will be reasonably available as a substitute when the proposed prohibition or other restriction takes effect." 15 U.S.C. § 2605(c)(2)(C).

Finally, EPA is authorized to take action under TSCA, *even if it has authority under other laws to address the risk*, so long as "it is in the public interest" to do so. 15 U.S.C. § 2608(b)(1). In determining whether it is in the public interest to take action under TSCA, EPA "*shall* consider . . . all relevant aspects of the risk and *a comparison of the estimated costs and efficiencies* of the action to be taken under [TSCA] and an action to be taken under such other law to protect against such risk." 15 U.S.C. § 2608(b)(2) (emphases added).

Although EPA has certain authorities to regulate fluoride in drinking water under the Safe Drinking Water Act (SDWA), there is an important distinction between TSCA and SDWA that permits EPA to take the requested action under TSCA in a more targeted, efficient, and less expensive manner than would be the case under SDWA. Namely, TSCA permits the EPA to differentiate between fluoride that is *added* to water versus fluoride that is *naturally occurring*. As explained in Section XII below, prioritizing regulatory action against fluoridation *additives* is further justified on policy and scientific grounds. It is therefore in the public interest for EPA to take the requested action under TSCA, instead of SDWA.

III. FLUORIDE IN DRINKING WATER: RECENT REGULATORY BACKGROUND

In 2003, the EPA asked the National Research Council (NRC) to review the scientific merits of EPA's Maximum Contaminant Level Goal (MCLG) for fluoride, which then and now is set at 4 mg/L. In response, the NRC reviewed the existing research on fluoride toxicity and concluded, in March 2006, that the MCLG is not protective of public health and should be lowered. (NRC 2006). The NRC's conclusion was based on fluoride's adverse effects on bone and teeth, but the NRC also raised numerous concerns about the potential for fluoride to cause other systemic harm, particularly to the nervous and endocrine systems.

With respect to the nervous system, the NRC concluded: "On the basis of information largely derived from histological, chemical, and molecular studies, it is apparent that fluorides have the ability to interfere with the functions of the brain." (NRC 2006, at 222). The NRC's conclusion about fluoride's interference with the brain rested primarily on its review of animal studies, since—at the time of NRC's review—few human studies were available. The situation today, however, is much different as many studies linking fluoride exposure to cognitive deficits in humans have now been published. The number of human studies published subsequent to the NRC review that have found significant relationships between fluoride and adverse cognitive outcomes (n = 46) dwarfs the number of such studies that were available to the NRC (n = 5).[3]

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drinking water enables EPA to regulate direct and indirect additives to drinking water as chemical substances and mixtures under TSCA." (EPA/FDA 1979)

[3] The 46 post-NRC human cognitive studies are cited in Appendix A. The five human cognitive studies that NRC cited are: Li et al. (1995); Zhao et al. (1996); Lu et al. (2000); Xiang et al. (2003a,b); and Qin et al. (1990).

The evidence linking fluoride to neurotoxicity in humans, therefore, is far more compelling today than it was when NRC published its review. Indeed, in 2014, fluoride was added to the list of chemicals "*known* to cause developmental neurotoxicity in *human beings*" in a review published by *Lancet Neurology*. (Grandjean & Landrigan 2014, at 334, Tbl 2). Only 12 chemicals are on this list.

It has been 10 years since the NRC concluded that the MCLG for fluoride be lowered, but the EPA has yet to do so. Further, despite the voluminous post-2006 research on neurotoxicity, and despite the Safe Drinking Water Act's mandate that EPA protect against "known or *anticipated* adverse effects,"[4] EPA's Office of Water (EPA OW) has indicated that it will *not* be considering neurotoxicity as an endpoint of concern when promulgating the new MCLG. Specifically, in its December 2010 risk assessment of fluoride's non-cancer effects, EPA OW established a reference dose for fluoride based solely on severe dental fluorosis, and declined to add an uncertainty factor to account for the neurotoxicity hazard. (EPA 2010, at 3 & 106). EPA OW justified this decision on the grounds that NRC's 2006 review did not draw firm conclusions about the public health relevance of fluoride neurotoxicity. (EPA 2010, at 106). Nowhere in EPA OW's risk assessment, however, did it account for the neurotoxicity research published subsequent to NRC's review.

The cavalier manner in which EPA's OW dismissed the evidence of fluoride neurotoxicity stands in stark contrast to EPA's own *Guidelines for Neurotoxicity Risk Assessment* [hereafter *Guidelines*] that EPA has stated it "*will* follow in evaluating data on *potential* neurotoxicity associated with exposure to environmental toxicants." (EPA 1998, at 1). Petitioners submit that application of EPA's *Guidelines* to the existing database for fluoride shows that neurotoxicity is a hazard of fluoride exposure, that the weight of evidence indicates neurotoxicity is a more sensitive endpoint of fluoride exposure than severe dental fluorosis,[5] and, further, that the reference dose for fluoride that will protect the public and susceptible subpopulations against neurotoxicity is incompatible with the doses now ingested in fluoridated areas.

IV. FLUORIDE'S NEUROTOXICITY IS SUPPORTED BY OVER 180 STUDIES PUBLISHED SINCE NRC'S 2006 REVIEW

One of the striking features of the research on fluoride neurotoxicity is the large quantity of studies—animal, cellular, *and* human—that have reported an effect. In a recent review of developmental neurotoxins by EPA scientists, only 22% of suspected neurotoxins were found to have *any* supporting human data. (Mundy et al. 2015, at 25). The EPA team thus characterized chemicals, including fluoride, whose suspected neurotoxicity is backed by human data, as "gold standard" chemicals that warrant prioritization. (Mundy et al. 2015, at 27). In the case of fluoride, not only is there human data, the data is so extensive that fluoride has been classified alongside lead, mercury, and PCBs as one of only 12 chemicals "*known* to cause developmental neurotoxicity in *human beings*." (Grandjean & Landrigan 2014, at 334, Tbl 2). The existence of so many human studies on fluoride neurotoxicity highlights the urgent need for a diligent risk assessment, per EPA's *Guidelines*, to ensure that the general public, and sensitive subpopulations, are not ingesting neurotoxic levels.

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[4] 42 U.S.C. § 300g-1(b)(4)(A).

[5] The *Guidelines* state that: "If data are considered sufficient for risk assessment, and *if neurotoxicity is the effect occurring at the lowest dose level* (i.e., the critical effect), an oral or dermal RfD or an inhalation RfC, based on neurotoxic effects, is then derived." (EPA 1998, at 2)

Unlike EPA's 2010 risk assessment, a diligent evaluation of fluoride's neurotoxicity would consider the voluminous data that has been released since the NRC published its review in March 2006. Towards this end, Petitioners have attached an exhaustive list of human, animal, and cell studies of fluoride's neurotoxicity that have become available since NRC's review.[6]

In total, Petitioners have identified 196 published studies that have addressed the neurotoxic effects of fluoride exposure subsequent to the NRC's review, including 61 human studies, 115 animal studies, 17 cell studies, and 3 systematic reviews.

The post-NRC human studies include:

- 54 studies investigating fluoride's effect on cognition, including but not limited to IQ, with all but 8 of these studies finding statistically significant[7] associations between fluoride exposure and cognitive deficits.[8] (Appendix A)
- 3 studies investigating fluoride's effect on fetal brain, with each of the 3 studies reporting deleterious effects. (Appendix B)
- 4 studies investigating fluoride's association with other forms of neurotoxic harm, including ADHD, altered neonatal behavior, and various neurological symptoms. (Appendix C)

The post-NRC animal studies include:

- 105 studies investigating fluoride's ability to produce neuroanatomical and neurochemical changes, with all but 2 of the studies finding at least one detrimental effect in the fluoride-treated groups. (Appendix D)
- 31 studies investigating fluoride's effect on learning and memory, with all but one of the studies finding at least one deleterious effect in the fluoride-treated groups. (Appendix E)
- 18 studies investigating fluoride's impact on other parameters of neurobehavior besides learning and memory, with all but one of the studies finding effects. (Appendix F)

The post-NRC cell studies include:

- 17 studies, including 2 studies that investigated and found effects at fluoride levels that chronically occur in the blood of Americans living in fluoridated communities. (Appendix G)

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[6] Included among these studies are Chinese language studies that were originally published in Chinese journals prior to 2006 but were not translated and made available in the U.S. until after the NRC's review. Excluded from these studies are those that are only available in abstract form, and animal/cell studies that have not yet been published and/or translated into English.

[7] In 4 of the 8 studies not finding statistically significant associations, the IQs of the children in the high-fluoride area were lower than in the low-fluoride area. (Eswar et al. 2011; Yang et al. 2008; Fan et al. 2007; Zhang et al. 1998) The 4 studies that did not find any association between fluoride exposure and IQ, significant or otherwise, are: Broadbent et al. 2015; Kang et al. 2011; He et al. 2010; and Li et al. 2010.

[8] Petitioners are aware of two unpublished fluoride/IQ studies from Mexico, one which reports a significant relationship between prenatal fluoride exposure and reduced IQ (water F = 3.1 mg/L; urine F = 2.0 mg/L) (Rocha Amador et al. 2016), and one which reports no association between childhood IQ and low-level prenatal and postnatal exposures (Thomas 2014). The Thomas study failed to detect an association between IQ and urinary/serum fluoride concentrations in a population with average urinary and serum fluoride levels among pregnant women of 0.89 mg/L and 0.02 mg/L, respectively, and average urinary fluoride concentrations among children of 0.64 mg/L. The Thomas study, however, failed to find a significant correlation between urinary and serum fluoride levels, which raises questions about whether the study's spot-sample testing method reliably reflected the chronic fluoride intake among the cohort.

In addition to the above studies, Petitioners are submitting three post-NRC systematic reviews of the literature, including two that address the human/IQ literature, and one that addresses the animal/cognition literature. (NTP 2016; Choi et al. 2012; Tang et al. 2008).

V. FLUORIDE POSES NEUROTOXIC RISKS AT LEVELS RELEVANT TO U.S. POPULATION

A frequent claim made by those who continue to promote fluoridation is that the doses of fluoride associated with neurotoxicity in humans and animals so vastly exceed the levels which Americans drinking fluoridated water receive as to be entirely irrelevant. In support of this claim, proponents of fluoridation often point to the *highest* levels that have been linked to neurotoxicity, while ignoring the *lowest* levels (and even the *typical* levels) that have been associated with harm.[9] This focus on the *highest* levels that cause harm as the starting point for analysis, rather than the lowest levels, clashes with standard tenets of risk assessment, including EPA's *Guidelines*, where the starting point for risk characterization analysis is to determine the *Lowest* Observable Adverse Effect Level (LOAEL) or No Observable Adverse Effect Level (NOAEL).[10]

A. Fluoride Repeatedly Linked to Reduced IQ at "Safe" Water Fluoride Levels

Contrary to the oft-repeated claim that fluoride neurotoxicity is only found at irrelevantly high doses, the existing studies of fluoride-exposed human populations have consistently found neurotoxic effects at water fluoride levels well below the current MCLG. To help clarify this issue, we examined the IQ studies that were included in the meta-review by Choi, et al. (2012). Proponents of fluoridation have dismissed the relevance of the Choi meta-review on the grounds that the IQ studies it included were in communities with fluoride levels that ranged as high as 11 ppm. As can be seen in the following table, however, the majority of waterborne fluoride studies (i.e., 13 of 18)[11] that Choi reviewed included communities with fluoride levels below the 4 mg/L MCLG. Further, each of the 13 studies that investigated the effect of fluoride levels below 4 mg/L (average F = **2.3 mg/L**) found these communities to have a lower average IQ than the control (average reduction = 6.3 IQ points), with the difference reaching statistical significance in 10 of the 13 studies.[12]

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[9] Another common misconception is that the endemic fluorosis/IQ studies prove the safety of fluoridated water because the control populations in these studies often have 0.7 to 1.0 mg/L fluoride in their water. Using areas with 0.7 to 1.0 mg/L as the *control*, however, says nothing about the safety of these levels since they are not compared against communities with *lower* fluoride levels.

[10] As the *Guidelines* note, "Typically, estimates of the NOAEL/LOAEL are taken from the *lowest* part of the dose-response curve associated with impaired function or adverse effect." (EPA 1998, at 58). Similarly, when the Benchmark Dose (BMD) approach is utilized instead of the NOAEL/LOAEL methods, EPA's point of departure is the low end of the dose-response curve, not the high end.

[11] We excluded any waterborne-fluoride exposure studies that did not report the water fluoride levels in the endemic fluorosis area(s). We excluded Li et al. (2010) because it did not compare a high fluoride community against a low-fluoride community, but simply looked at whether children with dental fluorosis in the high-fluoride community (2.5 mg/L) had lower IQ than children without dental fluorosis in the same community. We treated the Wang et al. 2001 and Yang et al. 1994 papers as a single study because it is apparent from the IQ data in the two papers that they are based on the same underlying IQ study. For the 18 qualifying studies, we reviewed the manuscripts to determine the lowest average fluoride concentration in each of the studies that was associated with reduced IQ. In studies with multiple exposure groups (e.g., Yao et al. 1996; Yao et al. 1997), we selected the lowest exposure group that had a reduction in IQ. For studies that only provide a range of fluoride levels for a given exposure group, we selected the midway point in the range to represent the average fluoride concentration for the group.

[12] As set forth in the accompanying table, one of the two studies that failed to find a statistically significant difference in average IQ (Wang et al. 2001) found an "obvious" increase in the rate of children with IQ scores lower than 80 (36.7% vs. 16.7%).

TABLE 1: Water Fluoride Levels and Associated IQ Changes in Studies Reviewed by Choi, et al.		
Study	Water F Level	IQ Change
Zhang et al. 1998	0.8 mg/L	-2.1[g]
Lin et al. 1991	0.9 mg/L[Ω]	-7.0[a]
Xu et al. 1994	2.0 mg/L[Ω]	-5.6[d]
Yao et al. 1996	2.0 mg/L	-3.6[d]
Yao et al. 1997	2.0 mg/L	-5.1[d]
Pourleslami et al. 2011	2.4 mg/L	-6.4[a]
Xiang et al. 2003	2.5 mg/L	-8.2[d]
Seraj et al. 2006	2.5 mg/L	-11.0[b]
An et al. 1992	2.7 mg/L	-7.9[f]
Hong et al. 2001	2.9 mg/L[Ω]	-7.2[d]
Wang 2001/Yang 1994[¶]	3.0 mg/L	-5.0[h]
Lu et al. 2000	3.2 mg/L	-10.9[e]
Fan et al. 2007	3.2 mg/L	-2.3[g]
Zhao et al. 1996	4.1 mg/L	-7.5[c]
Chen et al. 1991	4.6 mg/L	-3.8[d]
Wang et al. 1996	4.8 mg/L	-5.6[a]
Wang et al. 2006	5.5 mg/L	-4.1[d]
Wang et al. 2007	8.3 mg/L	-6.0[a]

[a] $p<0.05$; [b] $p=0.025$; [c] $p<0.02$; [d] $p<0.01$; [e] $p<0.005$; [f] Statistical significance not reported; [g] Not statistically significant; [h] Not statistically significant when analyzed in terms of average IQ, but "obvious" difference seen when analyzed in terms of percentage with low IQ; [Ω] High-fluoride + low-iodine versus low-fluoride + low-iodine; [¶] These two papers appear to be the same study.

Additional studies finding reduced IQ in communities with less than 4 mg/L have become available in the years since Choi's review, including Sudhir et al. 2009 (**0.7 to 1.2 mg/**L); Zhang S. et al. 2015 (**1.4 mg/L**), Das & Mondal 2016 (**2.1 mg/L**), Choi et al. 2015 (**2.2 mg/L**), Sebastian & Sunitha 2012 (**2.2 mg/L**); Trivedi et al. 2012 (**2.3 mg/L**), Khan et al. 2015 (**2.4 mg/L**); Nagarajappa et al. 2013 (**2.4 to 3.5 mg/L**), Seraj et al. 2012 (**3.1 mg/L**), and Karimzade et al. 2014a,b (**3.94 mg/**L). Another study (Ding et al. 2011), which did not fit within Choi's dichotomous exposure criteria, found reduced IQ in an area with fluoride levels ranging from **0.3 to 3 mg/L**. In total, there are now 23 studies reporting statistically significant reductions in IQ in areas with fluoride levels currently deemed safe by the EPA (less than 4 mg/L).[13]

B. Fluoride Linked to Cognitive Deficits at Levels of Individual Exposure Seen in Western Fluoridated Populations

Although the water fluoride levels associated with IQ reductions are modestly higher than the levels currently used in artificially water fluoridation programs, it is important to distinguish between the *concentration* of fluoride in a community's water supply and the *dose* of fluoride that an individual ingests. For example, in rural China (where most of the IQ studies have been conducted), fluoridated toothpaste is rarely used, with less than 10% of children using any fluoride toothpaste at all.[14] By contrast, in the United States, over 95% of toothpastes are fluoridated and research shows that toothpaste can contribute more fluoride to a child's daily intake than fluoridated water. (CDC 2013c; Zohoori et al. 2013, Zohoori et al. 2012; Levy et al.

[13] The 23 studies include the 10 studies listed in Table 1, the 11 studies listed in the paragraph above, and the studies by Eswar et al. 2011 and Shivaprakash et al. 2011.

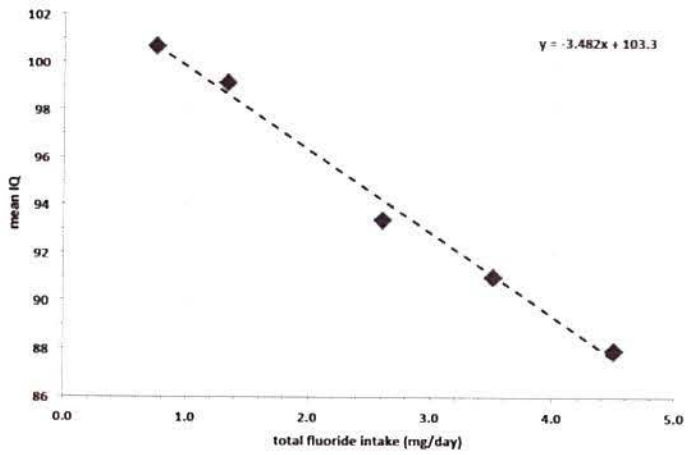
[14] According to a 1996 national oral health survey in China, 75% of 12-year-old children use toothpaste, and of the children who use toothpaste, only 11% use fluoride-containing varieties. (Zhu et al. 2003, at 291, Tbl 1.)

1999). As noted by a review in the *Journal of Public Health Dentistry*, "Virtually all authors have noted that some children could ingest more fluoride from dentrifice alone than is recommended as a total daily fluoride ingestion."[15] (Levy and Guda-Chowdhury 1999, at 216-17). The abundance of fluoridated toothpaste in the U.S., versus its relative scarcity in rural China, will therefore lessen the difference in total daily fluoride intake between these populations. In fact, as set forth below, available evidence suggests that the (i) daily fluoride doses, (ii) urine fluoride levels, (iii) serum fluoride levels, and (iv) dental fluorosis levels associated with IQ reductions in the Chinese studies are seen in children and adults in western countries living in fluoridated areas. Each of these four metrics of fluoride exposure provide a more direct assessment of individual fluoride exposure than water fluoride concentration, and are thus more probative for risk assessment purposes.

(i) Daily Fluoride Intake

The overlap between the daily fluoride intake associated with significant IQ loss in China and the daily doses American children now receive is highlighted by the recent studies from Wang et al. (2012) and Das et al. (2016). In the study by Wang, researchers investigated the impact of total daily intake of fluoride on IQ among the same group of 512 rural Chinese 8-to-13 year old children studied by the Xiang team in 2003. (Xiang et al. 2003a,b). As the following table shows, the Wang study found a clear dose response relationship between daily fluoride dose and reduced IQ.

FIGURE 1: Relationship Between Daily Fluoride Dose and IQ
(SOURCE: Wang et al. 2012, Tbl. 4)



Wang found that a daily intake of just 2.61 mg F/day was associated with a large, statistically significant 7.28-point drop in *average* IQ. Assuming an average weight of 32 kg,[16] a daily intake

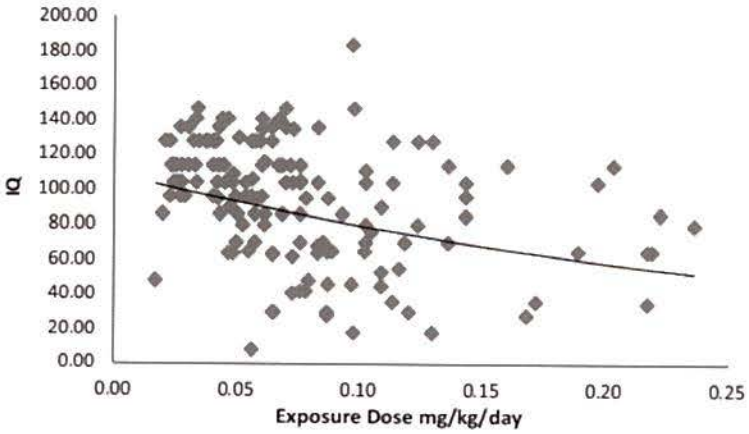
[15] Petitioners recognize that the FDA has jurisdiction over fluoride toothpaste, but any assessment of the safe level of a contaminant in drinking water cannot be conducted in a vacuum, and must consider the additive effect of waterborne exposures with identifiable non-water sources of exposure. When considering the neurologic safety of fluoridated water, therefore, it is critical to consider the aggregate dose of fluoride in fluoridated communities from all sources, including toothpaste. EPA has recognized this principle in its "relative source contribution" analyses, which the EPA OW conducts when calculating the drinking water equivalent level (DWEL) of a reference dose. EPA (2016). TSCA also specifically contemplates consideration of aggregate and sentinel exposures in Section 6 risk evaluations. *See* 15 U.S.C. § 2605(b)(4)(F).

[16] The authors did not provide data on the average weight of the children in the study, and we could not find data on the average weight of rural Chinese children between the ages of 8 and 13. We did, however, find published data on

of 2.61 mg would provide a dosage of approximately **0.08 mg/kg/day**,[17] which is *lower* than the *average* daily intake (**0.087 mg/kg/day**) for non-nursing infants in the United States, as estimated by the NRC, and just two times greater than the *average* daily dose for 8-12 year old American children.[18] (NRC 2006, at 65, Tbl. 2-13). Moreover, recent research has found that 10 to 15% of children under the age of 6 ingest over 0.05 mg/kg/day *from toothpaste alone*, with some children ingesting as much as **0.159 mg/kg/day** from this single source. (Strittholt et al. 2016 at 70 tbl. 2; Zohoori et al. 2012 at 418 tbl 2; Zohoori et al. 2013 at 460 tbl 1; Levy & Guha-Chowdhury 1999 at 217 tbl 3). In one study, published by Proctor & Gamble scientists (Strittholt et al. 2016), 5% of pre-schoolers were found to ingest at least 0.49 mg fluoride per brushing, which, at two brushings per day, will produce a daily dosage of 0.07 mg/kg/day from toothpaste alone for the average-weighing 2-year-old. (CDC 2000a,b). Other studies are consistent with these estimates. (Oliveria et al. 2007; Bentley et al. 1999; Levy 1993; Naccahe et al. 1992). For the many pre-school children ingesting these dosages from toothpaste, the consumption of fluoridated water will readily push them over the daily dosage (0.08 mg/kg/day) associated with sharp reductions in IQ among rural Chinese children.

Finally, as with other forms of fluoride toxicity, the potential for fluoride neurotoxicity is magnified among children with suboptimal nutrient intake. (Sun et al. 2016; Ge et al. 2011; Hong et al. 2008; Ge et al. 2005; Wang et al. 2004; Ekambaram & Paul 2002; Xu et al. 1994; Lin et al. 1991; Ren et al. 1989; Guan et al. 1988). This is highlighted by the recent study by Das and Mondal which assessed the relationship between fluoride intake and IQ among a population with a high prevalence of underweight children suggestive of an area with pervasive malnutrition. In this population, Das and Mondal confirmed a significant correlation between total fluoride intake and reduced IQ ($r = -0.343$, $p < 0.01$), as plotted in the following figure:

FIGURE 2: Relationship Between Total Daily Intake and IQ
(SOURCE: Das & Mondal 2016, Fig. 6)



the weight of rural Chinese children ages 0 to 7, as well as average weight data on U.S. children between the ages of 2 and 20. (Li et al. 2011; CDC 2000a,b) A comparison of these two datasets shows that rural Chinese children weigh approximately 4 kg less than U.S. children (18.7 kg vs. 23 kg) between the ages of 6 and 7. We thus determined the average weight of 8-to-13 year old rural Chinese children by calculating the average weight of 8-to-13 year old U.S. from the CDC growth charts (=36 kg) and subtracting 4 kg (=32 kg).

[17] It bears noting that 0.08 mg/kg/day is EPA's new reference dose for fluoride, which the Agency established to protect solely against severe dental fluorosis (without the protection of a single uncertainty factor to account for potential neurotoxic risks). (EPA 2010)

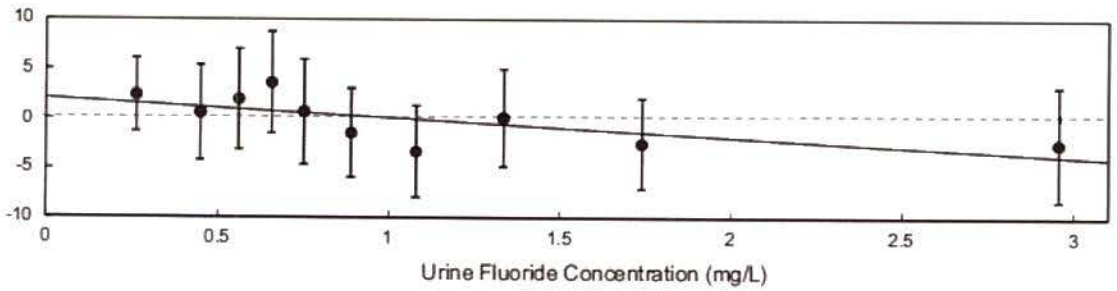
[18] A recent national analysis of urinary fluoride levels in the United Kingdom UK concluded that over 65% of adults living in fluoridated areas consume more than 0.057 mg/kg/day. (Mansfield 2010)

Notably, Das and Mondal found a sharp 15-point drop in IQ among underweight children with *mild* dental fluorosis who were consuming average total daily fluoride exposures of just **0.06 mg/kg/day**. (Das & Mondal 2016, at 218, Tbl. 3). As discussed above, this is a dose that many infants and children in the U.S. are estimated to exceed.

(ii) Urine Fluoride Level

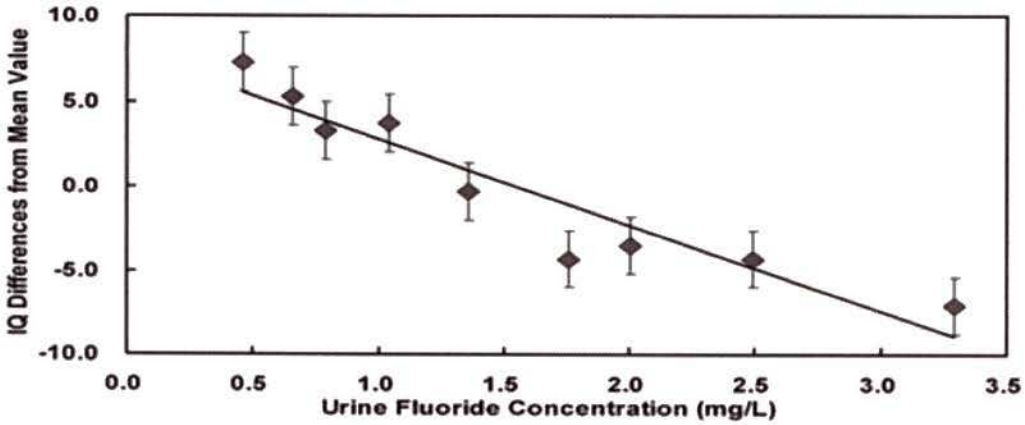
Many of the studies on fluoride and IQ have measured the concentration of fluoride in children's urine as a marker of individual fluoride exposure. As summarized in a 2011 review, these studies have repeatedly found significant, often large reductions in IQ when the average urinary fluoride level exceeds 2.5 mg/L, (Spittle 2011), and multiple regression analyses have repeatedly found that increased urinary fluoride correlates with reduced IQ, (Das et al. 2016; Zhang S. et al. 2015; Wang et al. 2007), even when controlling for other key risk factors. (Rocha Amador et al. 2009). While urinary fluoride levels exceeding 2.5 mg/L present a clear risk for neurotoxicity, recent studies have also found decrements in IQ at urinary fluoride concentrations well below this level. Most notable in this regard is the study by Ding et al., which examined the correlation between urinary fluoride and IQ among children with urinary fluoride levels ranging from just 0.25 mg/L to 3 mg/L. As shown in the following figure, a clear dose response trend was found within this urinary fluoride range (p <0.0001), with the downward trend becoming apparent at roughly 1 mg/L. When adjusted for age, each 1 mg/L increment in urinary fluoride correlated with an average drop of 0.59 IQ points ($p < 0.0001$).

FIGURE 3: Relationship Between Urinary Fluoride and IQ
(SOURCE: Ding et al. 2011, Fig. 2)



The dose-response trend found by Ding is consistent with more recent data published by Zhang et al. 2015, which is displayed in the following figure. As can be seen, the Zhang study found a clear drop in IQ at urinary fluoride levels between 0.5 and 1.5 mg/L.

FIGURE 4: Relationship Between Urinary Fluoride and IQ
(SOURCE: Zhang S. et al. 2015, Fig. 1)



More recently, researchers have investigated the prevalence of cognitive impairment among elderly individuals living in an endemic fluorosis region of China. (Li et al. 2016). The researchers found a very high prevalence of cognitive impairment (81.2%) in the fluorosis region, and, in a case-control analysis, found a significantly elevated urinary fluoride level (2.5 mg/L vs. 1.5 mg/L, $p < 0.05$) in the cognitive impairment group.[19] (Li et al. 2016, at 57, Tbl. 3). The data from this case-control analysis is presented in the following table:

TABLE 2: Urinary Fluoride & Cognitive Impairment in Elderly
(SOURCE: Li et al. 2016, Tbl 3)

Characteristics [a]	Normal group (n=38)	Cognitive impairment group (n=38)	P value
Male/female	26/12	26/12	
Age (years)	64.95±4.60	65.05±4.40	0.920
MMSE score	27.79±0.96	21.50±4.37	0.000
Total daily water fluoride intake(mg[b]	2.23±2.23	3.62±6.71	0.228
Urinary fluoride(mg/L[b]	1.46±1.04	2.47±2.88	0.046
fluorosis score [b]	0.74±0.98	1.29±1.01	0.018
Serum Hcy(μmol/L[b]	19.97±8.88	20.14±9.29	0.934

[a] Values are n/n for gender and mean±SD for other indices.

[b] The original values were log-transformed before comparison. The difference between two groups was tested using Student's t test.

Although there is a paucity of published data on urinary fluoride levels in the United States, a study from England found that the average urinary fluoride level among 88 adults living in a fluoridated area was 1.28 mg/L, with 16% of the tested individuals having over 2 mg/L, and 6%

[19] A clear dose-response relationship between urinary fluoride and cognitive impairment was not detected in the non-case control component of Li et al.'s analysis, although urinary fluoride was found to be elevated in the population with severe cognitive impairment.

of individuals having over 3 mg/L.[20] (Mansfield 1999, at 28, Tbl. 1). These levels overlap those that have been associated in endemic fluorosis areas with both reduced IQ in children and cognitive impairment in the elderly. (Li et al. 2016; Zhang S. et al. 2015; Ding et al. 2011). A more recent study from Canada found that 5 percent of *children* had ≥ 1.3 mg/L fluoride in their urine, which is well within the range of urinary fluoride levels associated with reduced IQ in the Ding and Zhang studies. (Saravanabhavan et al. 2016). A separate Canadian study found that the *average* urinary fluoride concentration in fluoridated areas was 0.76 mg/L, which was almost twice the concentration (0.47 mg/L) found in non-fluoridated areas. (McLaren 2016).

(iii) Serum Fluoride Level

In 2011, Xiang et al. published a paper which assessed the relationship between IQ and serum fluoride levels in the same group of 512 children studied in Wang's daily dose analysis discussed above. As with the daily dose analysis, the authors found a significant dose-response relationship between serum fluoride level and reduced IQ. As shown in the following table, children with just 0.05 to 0.08 mg/L fluoride in their serum had a statistically significant 4.2-point drop in IQ when compared against children with less than 0.05 mg/L.[21]

TABLE 3: Association Between Serum Fluoride and Children's IQ
(SOURCE: Xiang et al. 2011, Tbl 2)

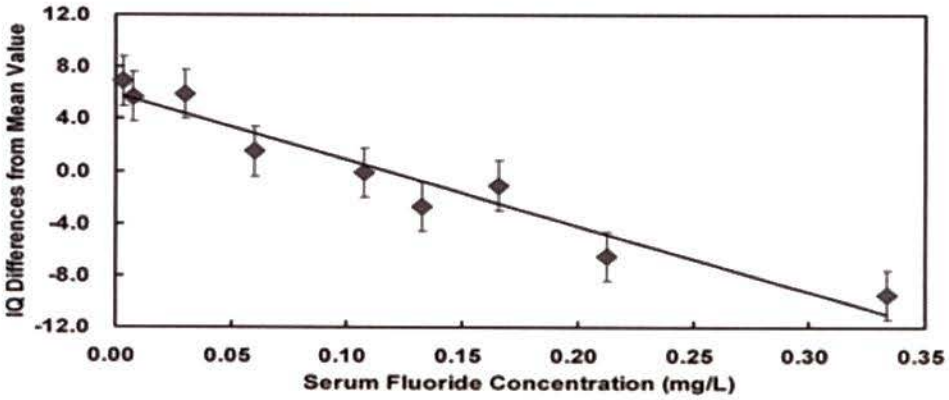
Serum fluoride level quartiles	N	Mean IQ	SD IQ	p[b]	IQ<80 (%)	p[c]	OR (95% CI) for IQ<80
Q1 and Q2 (<0.05 mg/L)	259	100.1	13.4	<0.001	7.0		1
Q3 (0.05–0.08 mg/L)	126	95.9	13.7		15.1	0.004	2.22 (1.42–3.47)
Q4 (>0.08 mg/L)	127	92.1	13.4		17.3		2.48 (1.85–3.32) p trend<0.001[d]

[a]Adjusted for age and gender using Logistic regression analysis. The data from two villages were combined.
[b]NOVA.
[c]Chi-square test.
[d]Tests of linear trend were computed using ordinal scoring.
Abbreviations: CI Confidence Interval, IQ Intelligence Quotient, OR Odds Ratio, SD Standard Deviation.

The Xiang team's findings are consistent with the findings of other recent studies, including Guo Z. et al. (2008), which found impairment in neurobehavioral function among adult industrial workers with average serum fluoride levels of 0.066 mg/L, and Zhang S. et al. (2015), which found significant reductions in IQ among children with just over 0.05 mg/L fluoride in their blood when compared to children with the lowest levels. The Zhang study plotted the serum data in the following figure:

[20] These urinary fluoride levels exceeded those that were found among individuals (n = 165) living in non-fluoridated areas. The average urinary fluoride level in the non-fluoridated areas was 0.96 mg/L; with 8% having more than 2 mg/L; and 4% having more than 3 mg/L. (Mansfield 1999, at 28, Tbl. 1)
[21] As the authors emphasize, their finding of a 4-point IQ drop in children with more than 0.05 mg/L fluoride in their serum does *not* mean that serum levels lower than 0.05 mg/L are safe.

FIGURE 5: Relationship Between Serum Fluoride and IQ
(SOURCE: Zhang S. et al. 2015, Fig. 1)



To put these serum fluoride levels in the context of U.S. exposures, typical serum fluoride levels for adults in the U.S. have been stated to range from about 0.01 to 0.076 mg/L (0.5 to 4 uM/L). (CDC 2014, at 2; *see also* Kissa 1987). In one study of infants, an average concentration of 0.08 mg/L was found among healthy 4-to-6 month old infants, while an average concentration of 0.10 to 0.18 mg/L was found among 4-to-18 month old infants receiving peritoneal dialysis. (Warady et al. 1989). A study by Ekstrand found that infants ingesting 0.25 mg in supplement form have spikes in their blood ranging as high as 0.092 mg/L, and averaging 0.063 mg/L. (Ekstrand 1994, at 159 tbl 3). Ekstrand's study did not measure the impact of ingesting fluoride in the form of infant formula reconstituted with fluoridated water, but the resulting daily peaks in serum fluoride levels may be comparable, since Ekstrand estimates that infants consuming fluoridated formula receive doses (up to five times a day) that are comparable to a supplement (i.e., 20-30 ug/kg of fluoride per formula feeding vs. 32 ug/kg per supplement). (Ekstrand 1994, at 162).

While there has long been a paucity of serum fluoride data available for children in the U.S., a recent NHANES survey found that roughly 1 in 200 American children between the ages of 3 to 19 have serum fluoride levels exceeding 0.04 mg/L. (NHANES 2016). Since there are approximately 70 million American children in this age range, (US Census Bureau 2011), the NHANES data indicates that approximately 350,000 American children have serum fluoride levels in the approximate range associated with overt neurotoxic effects.

(iv) Dental Fluorosis Level

EPA OW's 2010 risk assessment of the non-cancer effects of fluoride rests on the implicit assumption that *severe* dental fluorosis is the most sensitive adverse endpoint of fluoride exposure. This assumption, however, is at odds with a number of studies which have found significant associations between fluoride exposure and cognitive deficits among children with *non-severe* forms of fluorosis. Most notably, the study by Ding et al. (2011) found a dose-dependent relationship between reduced IQ and urinary fluoride concentration in a population where severe dental fluorosis was *completely absent*. The Ding study thus suggests that the doses of fluoride that impair cognitive ability are lower than the doses that cause severe fluorosis. Other recent studies have found impairment in cognitive abilities among children with *mild* fluorosis, *moderate* fluorosis, and *moderate/severe* fluorosis when compared with children with no fluorosis, thus suggesting that the doses of fluoride associated with the milder forms of

fluorosis are sufficient to impair brain development.[22] (Das & Mondal 2016 at tbl 3; Choi et al. 2015; Li et al. 2009; Khan et al. 2015; Shivaprakash et al. 2011; Sudhir et al. 2009 at tbl 3).

Consistent with the above studies of human populations, studies of rodents have repeatedly found significant impairments in learning ability as well as other neurotoxic harms among rats with only mild forms of fluorosis.[23] (Liu et al. 2011; Pereira et al. 2011; Niu et al. 2008; Chioca et al. 2008). As noted by Niu et al., "these findings indicate that fluoride . . . can influence spontaneous behaviors and lower the learning ability of rats before the appearance of dental lesions."[24] (Angmar-Mansson & Whitford 1982).

Taken together, the available human and animal studies suggest that fluoride can impair cognitive abilities prior to the development of severe fluorosis. This has obvious public health relevance in the United States, since recent studies show that the prevalence of dental fluorosis is now at historically unprecedented levels. In CDC's 1999-2004 NHANES survey, for example, 41% of adolescents were diagnosed with dental fluorosis, including 8.6% with mild fluorosis, and 4% with moderate and severe. These rates are considerably higher than what was found in the 1986-87 national survey by the National Institute of Dental Research. (Beltran et al. 2010; Heller et al. 1997). Moreover, the rates appear to have increased yet further since the 1999-2004 NHANES survey. Specifically, the 2011-2012 NHANES survey found dental fluorosis in 58.3% of the surveyed adolescents, including an astonishing 21.2% with moderate fluorosis, and 2% with severe. (NHANES 2014). Since there are an estimated 42 million adolescents currently living in the U.S.,[25] the NHANES data suggests that up to 24 million adolescents now have some form of dental fluorosis, with over 8 million adolescents having moderate fluorosis, and 840,000 having severe fluorosis.

The NHANES surveys do not provide data on the respective rates of fluorosis in fluoridated vs. non-fluoridated communities, but research has repeatedly confirmed that both the prevalence and severity of dental fluorosis are greater in U.S. communities with fluoridated water than in communities without. (Heller et al. 1997; Jackson et al. 1995; Williams & Zwemer 1990). Ending fluoridation will thus reduce the number of children developing dental fluorosis, and the accompanying neurotoxic risks associated with the doses that produce fluorosis.[26]

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[22] Some studies, however, including Ding, have not found a clear relationship between IQ and dental fluorosis status, thus suggesting that a person's susceptibility to fluoride-induced neurotoxicity may be distinct from their susceptibility to dental fluorosis. (Asawa et al. 2014; Li et al. 2010)

[23] Consistent with this, Zhou Z. et al. (2016) recently reported that biochemical changes occur in rats at doses well below those that cause dental fluorosis.

[24] While rodent teeth undergo constant remodeling, thus distinguishing them from human teeth, research has found that rat teeth develop dental fluorosis at the same serum fluoride levels that produce fluorosis in humans. According to Angmar-Mansson & Whitford, "It is well known that, in fluoridated drinking water studies with rats, a water fluoride concentration of 10-25 ppm is necessary to produce minimal disturbances in enamel mineralization. Because of the high water concentrations required, the rat has been regarded as more resistant to this adverse effect of fluoride. However, when the associated plasma levels are considered, the rat and the human appear to develop enamel fluorosis at very nearly the same concentrations." (Angmar-Mansson & Whitford 1982, at 339) Based on this finding, Angmar-Mansson & Whitford concluded that "the rat is a better model for the study of human enamel fluorosis than previously believed." (*Id.* at 334)

[25] This estimate is based on the number of Americans between the ages of 10 and 19. It comes from the Office of Adolescent Health, which is part of the Department of Health & Human Services. (DHHS 2016).

[26] Decreases in dental fluorosis have been documented following temporary suspensions of fluoridation as short as 11 months. (Burt et al. 2000)

VI. NEUROTOXIC RISK OF LOW DOSE FLUORIDE IS FURTHER SUPPORTED BY ANIMAL AND CELL STUDIES

The studies linking fluoride exposure with neurotoxic effects in humans are consistent with research on both experimental animals and cell cultures. Studies on rodents, for example, have found neurotoxic effects, including learning impairments, at water fluoride levels less than 15 mg/L, with 8 studies published since the NRC review reporting neurotoxic effects at water fluoride levels less than 5 mg/L. These are notably low fluoride levels for rodents, since it is generally estimated that rats require approximately 5 times more fluoride in their water to achieve the same level of fluoride in their blood as humans, and over 10% of children living in fluoridated areas receive the same waterborne dosage of fluoride (mg/kg/day) as rats drinking water with up to 9 mg F/L. (NTP 2016, at 56-57)

The following table lists the water fluoride concentrations associated with neurotoxic effects in rodents:

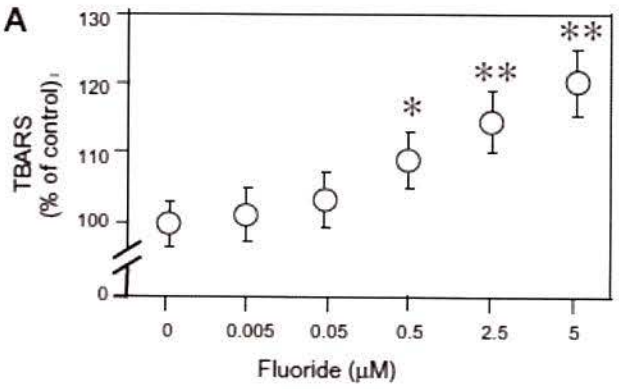
TABLE 4: Water Fluoride Levels Associated With Neurotoxic Effects in Rodents

Study	F Concentration (F-)	Duration of Treatment	Effects
Chouhan (2010)	1 mg/L	4 months	Oxidative stress; alterations in neurotransmitters
Wu (2008)	1 mg/L	Gestation	Behavioral alterations
Gao (2009)	2.3 mg/L	6 months	Enzyme inhibition; impaired cognition; oxidative stress
Liu (2014)	2.3 mg/L	1 month	Impaired learning
Liu (2010)	2.3 mg/L	6 months	Impaired cognition; alterations in neurotransmitters
Sandeep (2013)	2.3 mg/L	3 months	Behavioral alterations; enzyme inhibition
Zhang (2015)	2.3 mg/L	6 months	Oxidative stress; activation of AGE/RAGE system
Zhang Z. (2008)	4.5 mg/L	10 weeks	Impaired learning; pathological changes in synaptic structure
Zhu (2011); Zhang (2011); Zhang J. (2013)	6.8 mg/L	9 months	Trend towards decreased synaptic membrane fluidity & PSD-95 expression level; altered expression of CaMKIIα, c-fos, Bax, and Bcl-2 (statistically significant at 13.6 mg/L)
Bhatnagar (2011)	8 mg/L	1 month	Morphological changes in neurons
Banala (2015)	9 mg/L	Gestation + 30 days postnatal	Impaired learning; loss of motor control; & oxidative stress
Reddy (2014)	9 mg/L	3 months	Alterations in neurotransmitters; altered immunological parameters; oxidative stress
Lou (2014); Lou (2013)	10 mg/L	6 months	Increase in apoptotic neurons; altered expression of Bax and Bcl-2 at protein & mRNA levels; abnormal mitochondrial dynamics
Sun (2008)	10 mg/L	6 months	Impaired learning; increased ChE
Han (2014)	11 mg/L	6 months	Trend towards impaired learning (Fig 2a)
Zhou (2014)	11.3 mg/L	6 months	Altered expression levels of cytokines in hippocampus
Guner (2016)	13.6 mg/L	Gestation + Postnatal	Increased catalase immunoreactivity

Fluoride's ability to cause neurotoxic effects at low levels of exposure is further corroborated by in vitro cell studies conducted subsequent to the NRC review. While most of the in vitro studies

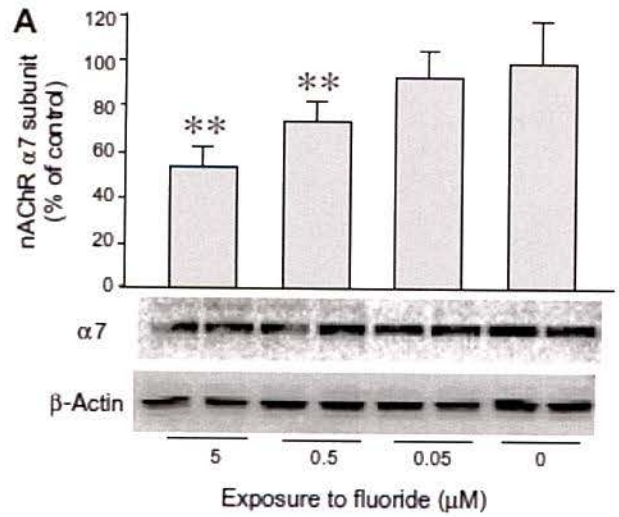
used high levels of fluoride (≥10 mg/L), two of the studies investigated the effects of concentrations that are found in the bloodstream of many Americans.[27] Both of these low-concentration studies detected adverse effects. As displayed in the following figure, Gao et al. (2008) found that just 0.5 uM of fluoride (i.e., 0.009 mg/L) caused lipid peroxidation in SH-SY5Y cells after 48 hours of exposure. Most individuals living in fluoridated areas in the United States have fluoride levels in their blood that exceed this level. (CDC 2014; Kissa 1987).

FIGURE 6: Level of Lipid Oxidation in SH-SY5Y Cells Exposed to Fluoride
(SOURCE: Gao et al. 2008, Fig. 1)



The Gao study also found that 0.5 uM had an effect on the level of a7 nAChR protein in the SH-SY5Y cells, as displayed in the following figure:

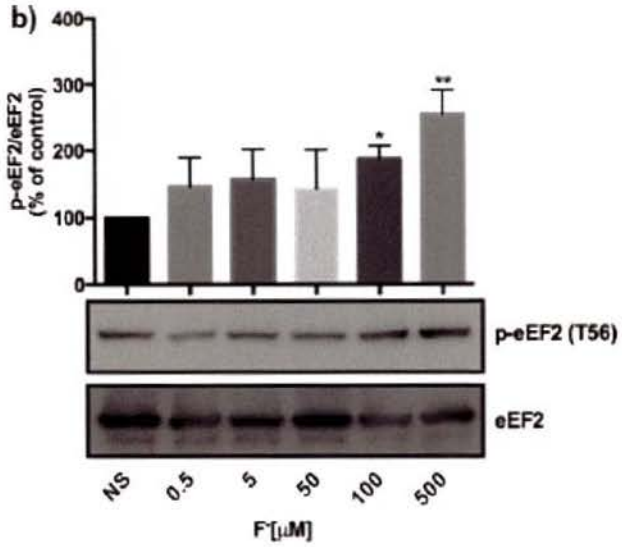
FIGURE 7: Level of a7 nAChR subunit protein in SH-SY5Y Cells Exposed to Fluoride
(SOURCE: Gao et al. 2008 Fig. 3)



[27] Consistent with the findings of these two brain cell studies, the in vitro studies by Gutowska have repeatedly found that concentrations of just 1 to 3 uM (i.e., 0.019 to 0.057 mg/L) are sufficient to affect inflammatory responses. (Gutowska et al. 2015, 2012, 2010). The Gutowska team's findings underscore the biologically active nature of even micromolar concentrations of fluoride, and warrant consideration for their implications to neuroinflammation. (Louveau et al. 2011).

Flores-Mendez et al. (2014) also investigated the effect of 0.5 uM, and, per the following figure, found a suggestive trend towards an increase in eEF2 phosphorylation in cultured Bergmann glia cells (BGC) after 15 minutes of treatment.

FIGURE 8: eEF2 Phosphorylation in BGC Cultures Treated with Fluoride
W(SOURCE: Flores-Mendez et al. 2014., Fig. 4b)



Flores-Mendez also found a suggestive trend towards an increased influx of calcium into the cell after 3 minutes of treatment with 5 uM fluoride (i.e., 0.095 mg/L). (Flores-Mendez et al. 2014, at 130 Fig. 5c) This concentration can be found chronically in the blood of children with kidney disease living in fluoridated areas, (Warady et al. 1989), and is intermittently exceeded by children ingesting fluoride supplements, fluoridated toothpaste, and other dental products.[28]

VII. RECENT EPIDEMIOLOGICAL STUDIES CORROBORATE NEUROTOXIC RISK FROM FLUORIDATED WATER IN WESTERN POPULATIONS

The overlap between the internal doses of fluoride experienced in western populations and the internal doses associated with neurotoxic effects in humans, animals, and cell cultures, is cause for public health concern. Although there has been a notable lack of epidemiological research into fluoride's neurotoxic effects in the U.S., a 2015 study by Malin and Till found a statistically significant correlation between the prevalence of water fluoridation at the state level and Attention-Deficit Hyperactivity Disorder (ADHD). Fluoridation prevalence significantly correlated with ADHD even after controlling for socioeconomic status (SES), and fluoridation "appeared to be the more robust predictor." As Malin and Till note, their findings "are consistent with prior epidemiological studies that have associated high and low fluoride concentration exposure with neurodevelopmental effects in children."

[28] While there is a paucity of research on the serum fluoride levels following use of fluoride tablets and toothpaste, Ekstrand found that, among a group of 5 preschool children, ingestion of 0.5 mg fluoride tablets caused serum fluoride levels to spike to 0.095 mg/L in 30 minutes, while ingestion of 0.6 mg fluoride in toothpaste caused serum fluoride levels to exceed 0.08 mg/L. (Ekstrand et al. 1983, Fig. 1). Since some preschool children swallow considerably more than 0.6 mg fluoride per brushing, the serum fluoride levels will likely be higher than 0.08 mg/L in those children. Levy & Guha-Chowdhury, for example, cite research showing that 10% of preschool children swallow in excess of 0.73 mg of fluoride per brushing. (Levy & Guha-Chowdhury 1999, Tbl. 3).

Another epidemiological study from 2015, by Peckham et al., provides further corroborative evidence that fluoridation can cause neurotoxic effects. Peckham's study examined the relationship between water fluoride levels and hypothyroidism in the United Kingdom, and found that fluoride levels ≥ 0.7 mg/L significantly correlated with higher rates of hypothyroidism. This correlation was strengthened, not weakened, when controlling for the covariates of age, gender, and index of deprivation.

The correlation between fluoridation and hypothyroidism reported by Peckham is (i) plausible and (ii) adds further support for the capacity of fluoridated water to cause neurotoxic effects. First, the correlation is plausible because, as summarized by the NRC, multiple lines of research indicate that fluoride can lower thyroid function, including the fact that fluoride was once used as a drug for this precise purpose, at doses as low as 2 to 5 mg/day. (NRC 2006; Galletti & Joyet 1958). Second, the correlation between fluoridation and hypothyroidism adds further support for fluoridation's neurotoxic potential because, as recognized in EPA's *Guidelines*, "the development of the nervous system is intimately associated with the presence of circulating hormones such as thyroid hormone." (EPA 1998, at 50). Since both clinical and subclinical hypothyroidism during pregnancy have been associated with reduced IQ in offspring, (Korevaar et al. 2016; Murphy et al. 2015; Klein et al. 2001), the relationship between fluoridation and hypothyroidism provides a mechanism by which fluoridation can reduce IQ, even absent a direct neurotoxic effect.

VIII. SUSCEPTIBLE SUBPOPULATIONS ARE AT HEIGHTENED RISK OF FLUORIDE NEUROTOXICITY AND NEED PROTECTION

EPA's *Guidelines* recognize that individual susceptibility to the neurotoxicity of environmental toxicants can vary by a factor of ten or more,[29] and is influenced by factors such as nutritional status, age, genetics, and disease. (EPA 1998, at 63-65, 78). Each of these factors—nutritional status, age, genetics,[30] and disease—are known to influence an individual's susceptibility to chronic fluoride toxicity.[31] Any factor that can predispose an individual to chronic fluoride toxicity should be suspected as a factor that will predispose to fluoride neurotoxicity as well. In fact, recent research in both humans and animals has specifically demonstrated that nutrient deficiencies (i.e., iodine[32] and calcium[33]) amplify fluoride's neurotoxicity.[34] Further, Zhang S. et al. (2015) reported that certain COMT gene polymorphism

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[29] "In general, it is assumed that an uncertainty factor of 10 for intrapopulation variability will be able to accommodate differences in sensitivity among various subpopulations, including children and the elderly. However, in cases where it can be demonstrated that a factor of 10 does not afford adequate protection, another uncertainty factor may be considered in conducting the risk assessment." (EPA 1998, at 65)

[30] Studies have repeatedly confirmed that genetic factors can significantly increase susceptibility to fluoride toxicity, (Everett 2011), including effects on bone (Kobayashi et al. 2014; Yan et al. 2007; Mousny et al. 2006); teeth (Buzalaf et al. 2014; Ba et al. 2011; Huang et al. 2008; Everett et al. 2002); and reproductive hormones (Zhou et al. 2016).

[31] *See, e.g.*, Irigoyen-Camacho ME et al. (2016); Simon et al. (2014); Ravula et al. (2012); Itai et al. (2010); Schiffl (2008); NRC (2006); Teotia et al. (1998); Torra et al. (1998); Warady et al. (1989); and Turner et al. (1995). For additional citations and discussion, see http://www.fluoridealert.org/studies/skeletal_fluorosis03.

[32] *See, e.g.*, Ge et al. (2011); Hong et al. (2008); Ge et al. (2005); Wang et al. (2004); Xu et al. (1994); Lin et al. (1991); Ren et al. (1989); Guan et al. (1988).

[33] Sun et al. (2016); Ekambaram & Paul (2002).

[34] As discussed earlier, the study by Das & Mondal (2016) examined the impact of fluoride on IQ in a population with a high prevalence of underweight children, suggestive of an area with chronic malnutrition. In this population, a daily fluoride dose of just 0.06 mg/kg/day was associated with a sharp 15-point drop in IQ among children with mild fluorosis. (Das & Mondal 2016, at 218, Tbl. 3).

greatly influences the extent of IQ loss resulting from fluoride exposure, which is consistent with research on other neurotoxins, including methyl mercury. (Julvez & Grandjean 2013).

While the full range of individual susceptibility to fluoride neurotoxicity in the U.S. cannot be precisely calculated, some subpopulations can be identified as being at elevated risk, including infants,[35] the elderly,[36] and individuals with (A) deficient nutrient intake (particularly iodine and calcium),[37] (B) certain COMT gene polymorphisms,[38] and (C) kidney disease.[39] Various factors suggest that African Americans may also suffer disproportionate risks as well, including elevated use of infant formula,[40] elevated exposure to lead,[41] depressed calcium and anti-oxidant intake,[42] and significantly higher rates of dental fluorosis, including in its moderate and severe forms.[43]

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[35] Although *breast fed* infants receive the lowest fluoride intake by bodyweight (<0.001 mg/kg/day) of all age-groups (Ekstrand et al. 1981), this situation is flipped on its head when infants are fed *formula reconstituted with fluoridated water*. As noted by the NRC, "On a per-body-weight basis, infants and young children have approximately three to four times greater exposure than do adults." (NRC 2006, at 3). Not only do formula-fed infants receive an unnaturally high dose, they have an impaired ability to excrete the fluoride they ingest, retaining up to 87% of the absorbed dose. Ekstrand et al. (1994). Infants exposed to formula made with fluoridated water are at significantly higher risk for developing dental fluorosis on their permanent front teeth. Hong et al. (2006). In light of the research linking dental fluorosis and modest levels of fluoride exposure with reduced IQ, infants are a susceptible subpopulation of critical concern for fluoride neurotoxicity.

[36] As noted in the *Guidelines*, "[T]he aged population is considered to be at particular risk [of neurotoxicity] because of the limited ability of the nervous system to regenerate or compensate to neurotoxic insult." (EPA 1998, at 65). This is of concern because the brain will be more exposed to fluoride in older age due to the (1) increased level of fluoride circulating in the serum from both age-related decreases in renal function and age-related increases in bone resorption (particularly in post-menopausal women), and (2) increased permeability of the blood-brain barrier. Rosenberg (2014); Ravula et al. (2012); Itai et al. (2010); Torra et al. (1998). This may help explain the very high prevalence of cognitive impairment (82%) found among elderly individuals in an endemic fluorosis area. Li et al. (2016); *see also* Shao et al. (2003).

[37] According to a consensus paper in the *Journal of the National Medical Association*, "Eighty-six percent of African Americans get just more than half of the daily recommended amount of calcium, and only half consume one or more servings of dairy a day. Of particular concern, 83% of African-American children 2-17 years of age are not getting enough calcium." Wooten & Price (2004). Insufficient nutrient intakes in the United States are severe enough in some individuals to qualify as nutrient deficiencies. Recent NHANES data, for example, found that 6% of Americans have a vitamin C deficiency. CDC (2012). Vitamin C deficiency has been found to exacerbate fluoride's toxicity in humans, while vitamin C supplementation has been found to ameliorate fluoride's neurotoxic effects in animals. Nabavi et al. (2013; Basha & Madhusudhan (2010); Pandit et al. (1940). With respect to iodine, NHANES data shows that women of *child bearing* age (20 to 39 years old) have "*median* urine iodine concentrations bordering on insufficiency." Pfeiffer et al. (2013). Children born to women with insufficient iodine levels should be considered a susceptible subpopulation for fluoride neurotoxicity due to fluoride's ability to exacerbate the neurological effects of inadequate iodine.

[38] The study by Zhang S. et al. (2015) suggests that children with the COMT val/val genotype suffered a five-fold larger drop in IQ than children with the COMT val/met and met/met genotypes. As noted by Zhang, "In the subpopulation carrying the COMT reference genotype (Model 3), 1 unit increase in urinary fluoride (1 mg/l) was associated with a decrease of 9.67 points of IQ and was significant after controlling for covariates (P=0.003). Among children carrying variant genotypes, 1 unit increase in [urinary fluoride] resulted in a decrease of 1.85 IQ points, but this was not statistically significant in this stratum."

[39] *See, e.g.*, Schiffl (2008); Ibarra-Santana et al. (2007); Torra et al. (1998); Warady et al. (1989).

[40] In national surveys conducted between 2000 and 2008, "Black infants consistently had the lowest rates of breastfeeding initiation and duration across all study years." CDC (2013b).

[41] It is well established that non-Hispanic black children have higher levels of lead in their blood than non-Hispanic white children. CDC (2013a); Bernard & McGheein (2003). This has relevance to the risks of fluoride exposure, since animal studies have found that fluoride can exacerbate the toxicity of lead, and vice versa. Leite et al. (2011); Sawan et al. (2010); Mahaffey & Stone (1976).

[42] Watters et al. (2007); Wooten & Price (2004). The reduced level of anti-oxidants found in the blood of African American adults, which may relate to low consumption of fresh fruits and vegetables (Zenk et al. 2005), has implications for fluoride toxicity, because oxidative stress is a key mechanism by which fluoride harms cells, (Barbier 2010), including in the brain. (*E.g.*, Banala & Karnati 2015; Zhang K. et al. 2015; Basha et al. 2014; Nabavi et al.

Any risk assessment on the neurotoxicity of fluoride must thus be mindful of the need to protect susceptible subpopulations; anything less would be inconsistent with EPA's *Guidelines*. In fact, even where there is *no* specific information to indicate differential susceptibility to a neurotoxin, EPA's *Guidelines* state that a margin of safety (i.e., "uncertainty factor") should still be incorporated to account for "*potential* differences in susceptibility." (EPA 1998, at 78). In the case of fluoride, there is *uncontroverted* evidence indicating substantial differences in susceptibility, and thus the basis for applying an uncertainty factor is especially strong.

IX. A REFERENCE DOSE PROTECTIVE AGAINST FLUORIDE NEUROTOXICITY IS INCOMPATIBLE WITH WATER FLUORIDATION IF STANDARD RISK ASSESSMENT PROCEDURES ARE APPLIED

As recognized in EPA's *Guidelines*, it is standard risk assessment practice to apply "uncertainty factors" (UF) of 10 when converting a LOAEL, NOAEL, or BMD into a safe "reference dose" (RfD) or "reference concentration" (RfC). (Martin et al. 2013) This is significant because application of even a single UF of 10 to the daily doses/concentrations of fluoride associated with neurotoxic harm in humans and animals produces an RfD or RfC that is less than, and thereby *incompatible with*, the levels of fluoride added to water for fluoridation (0.7 to 1.2 mg/L). This point is illustrated in the following table, which shows what the RfD and RfC would be if *merely* one UF of 10 was applied to the various fluoride exposures that have been associated with neurotoxic harm.

TABLE 5: RfCs/RfDs for Fluoride If Just One Uncertainty Factor of 10 Is Applied

Fluoride Dose/Concentration Producing Harm	Study	Effect	RfD/RfC After Application of one UF	Water Fluoridation Doses/Concentrations
0.06 mg/kg/day (Dose/Humans)	Das (2016)	Reduced IQ	0.006 mg/kg/day	0.03 to 0.09 mg/kg/day (Average Total Daily Dose in F areas) (NRC 2006, Tbl 2-13)
0.08 mg/kg/day (Dose/Humans)	Wang (2012)	Reduced IQ	0.008 mg/kg/day	0.03 to 0.09 mg/kg/day (Average Total Daily Dose in F areas) (NRC 2006, Tbl 2-13)
1 mg/L (Water/Rats)	Chouhan (2010); Wu (2008)	Behavioral alterations; Neurochemical changes	0.1 mg/L	0.7 to 1.2 mg/L (Water F Levels in F areas)
0.7 to 1.2 mg/L (Water/Humans)	Malin (2015); Peckham (2015)	Hypothyroidism; ADHD	0.07 to 0.12 mg/L	0.7 to 1.2 mg/L (Water F Levels in F areas)
0.7 to 1.2 mg/L (Water/Humans)	Sudhir (2009)	Reduced IQ	0.07 to 0.12 mg/L	0.7 to 1.2 mg/L (Water F Levels in F areas)

2013; Nabavi et al. 2012a,b,c; Basha et al. 2011; Inkielewicz-Stepniak & Czarnowski 2011; Nabavi et al. 2011; Bharti & Srivastava 2009; Gao et al. 2009).

[43] Studies dating back to the 1960s have found that African Americans suffer higher rates of dental fluorosis than Caucasians. Martinez-Mier & Soto-Rojas 2010; Beltran-Aguilar et al. (2015, tbl. 23); Kumar (2000); Williams & Zermer (1990); Butler et al. (1985); Russell (1962). Consistent with this, documents obtained through the Freedom of Information Act show a stark racial disparity in adolescent fluorosis rates in CDC's 1999-2004 NHANES survey, with 58% of African American adolescents diagnosed as having the condition, versus 36% of white adolescents. FOIA (2011).

2.3 mg/L (Water/Rats)	Gao (2009); Liu (2014); Liu (2010); Sandeep (2013); Zhang K (2015)	Impaired learning; Behavioral alterations; Neurochemical changes	0.23 mg/L	0.7 to 1.2 mg/L (Water F Levels in F areas)
2.3 mg/L (Water/Humans)	The average water F concentration in the 13 studies reviewed by Choi (2012) which found effects at < 4 mg/L	Reduced IQ	0.23 mg/L	0.7 to 1.2 mg/L (Water F Levels in F areas)
0.05 mg/L (Serum/Humans)	Xiang (2011)	Reduced IQ	0.005 mg/L	0.019 to 0.076 mg/L (Typical range of Serum F in US) (CDC 2014)

The need to apply *at least* one UF to the doses/concentrations associated with fluoride neurotoxicity cannot seriously be disputed. After all, these are doses and concentrations associated with overt neurotoxic harm, and thus the safe reference dose will obviously need to be set at a lower level. Moreover, as discussed above, EPA's *Guidelines* recognize that there is often a large degree of intra-species variability in the way humans respond to neurotoxins and a default factor of 10 is generally considered necessary to protect against this variability.[44]

Although we have only utilized one uncertainty factor in the analysis here, we do *not* mean to imply that only one UF is sufficient for converting these adverse effect levels into RfDs or RfCs. Indeed, it is clearly insufficient to apply only one UF when converting a LOAEL from an animal study into a safe dose for humans. We present the above Table, therefore, for the limited purpose of demonstrating that *even if* EPA were to apply an *insufficiently* protective UF, the resulting RfD or RfC would still be incompatible with water fluoridation; thus highlighting, once again, the overlap between the doses associated with a neurotoxic risk and the doses many Americans now receive.

Finally, Petitioners recognize that EPA has a preference for utilizing Benchmark Dose (BMD) methodology for risk assessments where there is dose-response data that permits the analysis. In the case of fluoride neurotoxicity, the Xiang dataset is a suitable dataset for conducting a BMD analysis, as it shows a dose-related reduction in IQ spanning five dose groups ranging from 0.75 to 4.5 mg F/day without an apparent NOAEL. (Wang et al. 2012). EPA's *Guidelines* recognize the probative value (and rarity) of a human dataset covering more than three dose groups.[45] Further, the Xiang dataset benefits from the fact that the study controlled for most of the key confounding factors, including lead, arsenic, iodine, parental education, and socioeconomic status. (Xiang et al. 2003a,b; Xiang et al. 2013).

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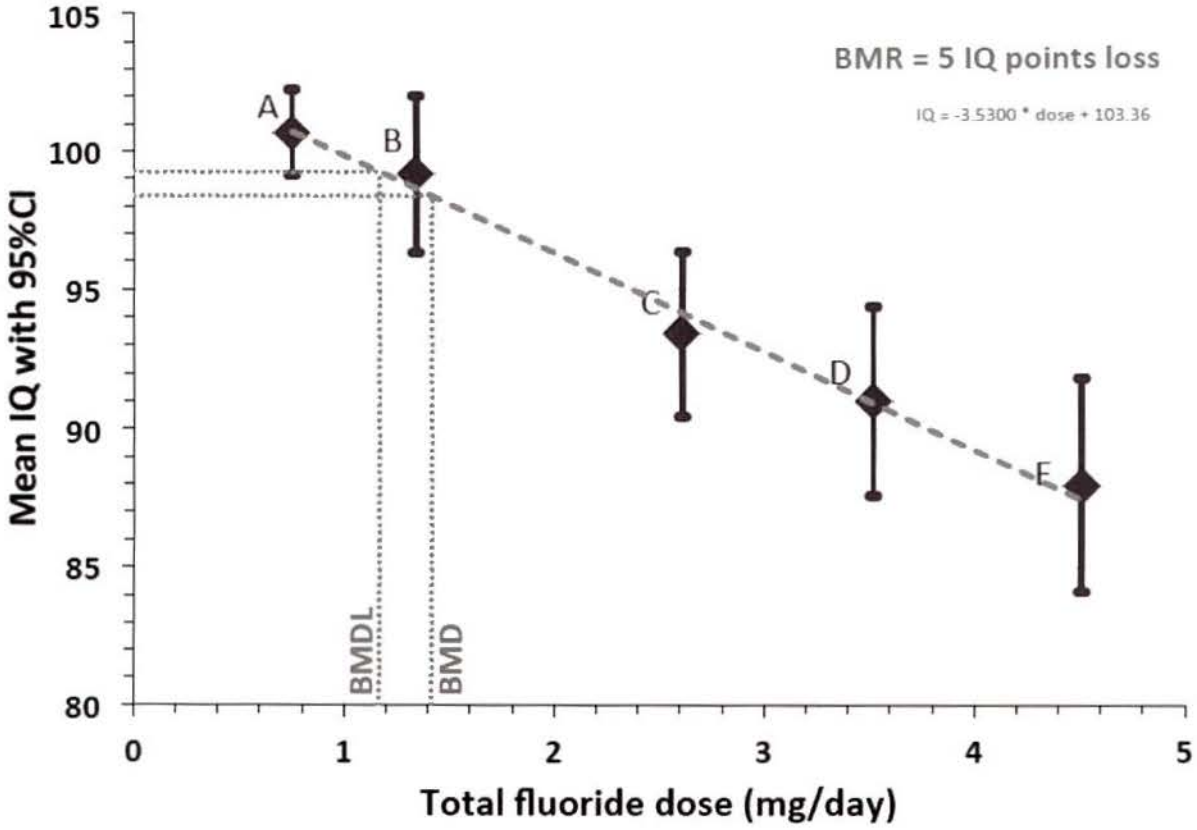
[44] According to the *Guidelines*, "In general, it is assumed that an uncertainty factor of 10 for intrapopulation variability will be able to accommodate differences in sensitivity among various subpopulations, including children and the elderly. However, in cases where it can be demonstrated that a factor of 10 does not afford adequate protection, another uncertainty factor may be considered in conducting the risk assessment." (EPA 1998, at 65). As demonstrated by Martin et al. (2013), the use of a default uncertainty factor of 10 to account for intra-species variability is amply justified by empirical data on differences in human sensitivity related to genetic polymorphisms, gender, disease, old age, and toxicokinetics.

[45] The *Guidelines* note that (1) "Human studies covering a range of exposures are rarely available" and (2) "Evidence for a dose-response relationship is an important criterion in establishing a neurotoxic effect, although this analysis may be limited when based on standard studies using three dose groups or fewer." (EPA 1998, at 50 & 106).

As with the LOAEL analyses discussed above, application of the BMD methodology to the Xiang dataset produces an RfD for fluoride that is incompatible with water fluoridation. Specifically, applying EPA's BMDS software to Xiang's dataset produces a BMD of just **1.4 mg F/day**, if the BenchMark Response (BMR) is set at 5 IQ points, as displayed in the following figure.[46] This result can be interpreted as predicting that children exposed to 1.4 mg fluoride per day will have, on average, 5 less IQ points than children exposed to no fluoride. The RfD would obviously need to be set at a lower level, since such a large loss in IQ is clearly an adverse effect, and because uncertainty factors would need to be added to account for variation in sensitivity within a population as large as the U.S.

FIGURE 9: BMD for Loss of 5 IQ Points from Fluoride
(Linear Model, BMR = 5 IQ Points)



X. THE BROADBENT STUDY DOES *NOT* ESTABLISH THE SAFETY OF FLUORIDATION

Some commentators have incorrectly claimed that the recent study by Broadbent et al. establishes the safety of water fluoridation for neurologic development. The Broadbent study found no difference in the IQs of children and adults who spent their first 3 to 5 years of life in fluoridated (0.7 to 1.0 mg/L) vs. non-fluoridated (0 to 0.3 mg/L) areas of Dunedin, New Zealand. A glaring limitation with the Broadbent study, however, is that a substantial portion of the "non-fluoridated" control population used 0.5 mg/day fluoride tablets and fluoridated toothpaste, resulting in only a marginal difference in average total fluoride exposure between the fluoridated

[46] If the BMR is set at 1 IQ point, the BMD is 0.28 mg/day of fluoride.

and non-fluoridated populations.[47] In fact, in response to criticism on this point, (Osmunson et al. 2016), the authors conceded that the average difference in total daily intake between the children in the fluoridated and non-fluoridated areas would be ≤ 0.3 milligrams per day, while the average intake for all subjects was 0.9 mg/day.[48] (Broadbent et al. 2016). At most, therefore, the Broadbent study established that ≤ 0.3 milligrams of fluoride was not a sufficiently large enough contrast in daily fluoride exposure to produce a demonstrable effect on *average IQ* in the study cohort. This does *not* mean, however, that the fluoride exposures in a fluoridated community are safe, since no truly low exposure comparison group existed in the Broadbent study, and the Broadbent team made no attempt to study vulnerable subsets of the population (e.g., those with suboptimal nutrition, genetic polymorphisms, etc).

The inherent limitation resulting from the Broadbent study's comparison of populations with marginal contrasts in fluoride intake highlights an important strength of the endemic fluorosis/IQ studies from China, India, Iran, and Mexico. Specifically, the endemic fluorosis studies have generally compared communities with clear and stable contrasts in fluoride exposure, thus increasing the power of these studies to detect fluoride's effect on IQ. Moreover, unlike Broadbent's study, many of the endemic fluorosis studies have analyzed the relationship between IQ and individual measures of exposure (e.g., individual urine fluoride levels), thus overcoming the limitation imposed by Broadbent's ecological (group level) estimates of fluoride intake. Although Broadbent and others have criticized the endemic fluorosis studies for failing to control for potential confounders, several of these studies did carefully control for confounders and the association between fluoride and cognitive impairment remained intact. (Choi et al. 2015; Rocha Amador et al. 2009; Xiang et al. 2003a,b; Xiang et al. 2013). Further, while it's undisputed that many of the IQ studies used relatively simple study designs, the consistency of these studies, and their repeated corroboration by research showing that fluoride impairs learning in rodents under carefully controlled laboratory conditions, gives confidence to the conclusion that fluoride is a neurotoxin that impairs cognition.

For the foregoing reasons, the reference dose for protecting against fluoride neurotoxicity cannot reasonably be based on a risk assessment that treats the Broadbent study as establishing 0.7 to 1.0 mg/L as a NOAEL without application of an uncertainty factor(s) to account for intra-human variability and other issues left unanswered by Broadbent's study. Indeed, as spelled out in the *Guidelines*, it is problematic to develop an NOAEL based on a single study of a single neurotoxic endpoint,[49] particularly a study with such limited "dose spacing" between the groups.[50]

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[47] There are several other significant problems with the Broadbent study as well. First, the study did not collect any data on individual water intake or internal biomarkers of fluoride exposure (e.g., urine fluoride, etc). Second, the study used a crude estimate of fluoride toothpaste usage ("always" vs "sometimes" vs "never") that fails to account for the frequency of brushings per day and actual amount of toothpaste used per brushing, thus obscuring the very large variations of daily exposure that occur among children using fluoride toothpaste. Zohoori et al. 2012; Levy & Guha-Chowdhury 1999, tbl 3. Third, it did not control for potential confounders including blood lead and maternal IQ, even though such information was available and there are plausible reasons for the non-fluoridated subjects to have elevated lead exposure from living in a more rural area known for its highly corrosive drinking water. (Osmunson et al. 2016).

[48] A previous study of total fluoride intake among 3-to-4 year olds in fluoridated and non-fluoridated areas of New Zealand found the daily intakes to be 0.68 ± 0.27 and 0.49 ± 0.25 mg F/day, respectively. (Guha-Chowdhury et al. 1996).

[49] According to the *Guidelines*, "Neurotoxic effects (and most kinds of toxicity) can be observed at many different levels, so only a single endpoint needs to be found to demonstrate a hazard, but many endpoints need to be examined to demonstrate no effect. For example, to judge that a hazard for neurotoxicity could exist for a given agent, the minimum evidence sufficient would be data on a single adverse endpoint from a well-conducted study. In

XI. THE BENEFITS OF PREVENTING FLUORIDE NEUROTOXICITY DWARF THE COSTS OF RESTRICTING FLUORIDE CHEMICALS

EPA's authority to act under Section 6 of TSCA is premised on two distinct findings: (1) a *risk* exists and (2) the risk is *unreasonable*. Here, in evaluating the preliminary question of whether a neurotoxic risk exists from use of fluoridation chemicals, the EPA is duty bound to follow its *Guidelines*, as the Agency has stated it "*will* follow" the *Guidelines* when "evaluating data on *potential* neurotoxicity associated with exposure to environmental toxicants." (EPA 1998, at 3). For the reasons set forth above, a good faith application of these *Guidelines* to the current research on fluoride will show that neurotoxicity is a hazard of fluoride exposure, and that the doses associated with this hazard overlap the doses—as reflected by (a) total daily intake, (b) urinary fluoride level, (c) serum fluoride level, and (d) severity of dental fluorosis—that U.S. children are exposed to in areas with fluoridated water. Neurotoxicity must thus be considered a risk from adding fluoridation chemicals to drinking water.

Petitioners now turn, therefore, to the second prong of the inquiry: whether the neurotoxic risk posed by fluoridation chemicals is an unreasonable one. As EPA has stated, the reasonableness inquiry considers the benefits of reducing the risk with the costs of doing so. EPA (1985); 15 U.S.C. § 2605(c)(A). In considering these respective benefits and costs of risk reduction, EPA has stated it will take into account "the extent and magnitude of risk posed; the societal consequences of removing or restricting use of products; availability and potential hazards of substitutes, and impacts on industry, employment, and international trade." EPA (1985); *see also* 15 U.S.C. § 2605(c)(A). We turn now to a consideration of these factors

A. Extent and Magnitude of Neurotoxic Risk from Fluoridation Chemicals

There is little question that neurotoxicity is a serious insult to health. (Grandjean & Landrigan 2014). In a nation besieged by neurological disorders of poorly understood etiology, both in young children and the elderly, minimizing exposures to known neurotoxic substances should be a public health priority. (*Id.*)

The reduction in IQ associated with fluoride exposure has been found to be severe enough in some children to produce mental retardation. (*E.g.*, Lin et al. 1991). But even the loss of a single IQ point is associated with significant economic loss. As calculated by Spadaro et al. (2008), a loss of a single IQ point causes an average drop in lifetime earnings of $18,000 in 2005 U.S. dollars, which, when adjusted for inflation, amounts to $22,250 in current dollars.[51] Since 200 million Americans now live in areas where water is fluoridated,[52] and since virtually all Americans consume processed foods and beverages made with fluoridated water, any reduction in IQ from consumption of fluoride-treated water stands to have very large economic consequences.

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contrast, to judge that an agent is unlikely to pose a hazard for neurotoxicity, the minimum evidence would include data from a host of endpoints that revealed no neurotoxic effects." (EPA 1998, at 55).

[50] According to the *Guidelines*, "the NOAEL is also directly dependent on the dose spacing used in the study." (EPA 1998, at 57)

[51] We adjusted for inflation by using the U.S. Bureau of Labor Statistics' CPI Inflation Calculator at http://data.bls.gov/cgi-bin/cpicalc.pl.

[52] The CDC states that 211,393,167 Americans now drink fluoridated water; the vast majority of this population is consuming artificially fluoridated water, as CDC estimates that only 11,883,007 Americans have "naturally" fluoridated water. See: http://www.cdc.gov/fluoridation/statistics/2014stats.htm

While the precise extent to which fluoridation is reducing IQ in the U.S. cannot yet be calculated, the dose-response data from Wang et al. (2012) indicates that daily consumption of a liter of fluoridated water per day (=0.7 mg F/day) during childhood would cause IQ to drop by an average of 2.5 points when compared to children with no exposure to fluoride, while consumption of half a liter per day (=0.35 mg F/day) would cause IQ to drop by an average of 1.25 IQ points. (Wang's data is consistent with a linear, no threshold, dose-response relationship between fluoride and IQ, and we have applied Wang's data here with that assumption.)

In 2010, there were 74.2 million children under the age of 18 living in the U.S., of which we can estimate roughly 50 million were living in fluoridated areas.[53] US Census Bureau (2011). If we apply Wang's dose-response data and assume that these 50 million children consumed between 0.5 to 1 liters of fluoridated water per day during childhood, fluoridation would have caused a loss of between 62.5 to 125 million IQ points. Based on the earnings data from Spadaro et al. (2008), a loss in the range of 62.5 to 125 million IQ points represents a total loss in lifetime earnings of between $13.9 to 27.8 *trillion* for this generation.

Due to the sheer number of people exposed to fluoridation chemicals, even if only sentinel or susceptible populations in fluoridated areas suffer IQ loss, the economic impacts will still be substantial. For example, even if we conservatively assume that only 1 to 5% of children in a fluoridated area suffer any IQ loss,[54] and even if this IQ loss averaged just 1 IQ point,[55] this would still amount to 500,000 to 2,500,000 lost IQ points, with a total loss in lifetime earnings ranging from $11.1 billion to $55.6 billion for this generation alone.

In short, because of the *massive* extent of exposure to fluoridation chemicals in the U.S., even small effects on IQ will have very substantial economic consequences.

B. Societal Consequences of Restricting Use of Fluoridation Chemicals

If EPA exercised its authority under TSCA to ban the waterborne use of fluoridation chemicals, the one and only potential societal consequence would be an increase in tooth decay. Current research, however, indicates that any increase in dental treatment costs would be small, inconsistent, and far less than the loss in earnings associated with even small drops in IQ.

First, Petitioners wish to call the Agency's attention to the fact that there are no randomized controlled trials on the effectiveness of fluoridation, and few of the available studies adequately account for potential confounders like socioeconomic status, sealants, and dietary habits. (Iheozor-Ejiofor et al. 2015; Cheng et al. 2007). The evidence has thus been characterized by the Cochrane Collaboration as having "high risk of bias" and limited applicability to modern lifestyles. (Iheozor-Ejiofor et al. 2015).

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[53] According to the CDC, 66% of the U.S. population receives fluoridated tap water. See: http://www.cdc.gov/fluoridation/statistics/fsgrowth.htm.

[54] We base the 1 to 5% estimate on the approximate percentage of children with serum fluoride levels in the range (~0.05 mg/L) associated with a 4-point IQ drop (n = ~1%), and the approximate percentage of children with urinary fluoride levels (≥ 1.3 mg/L) associated with clear reductions in IQ (n = 5%). For discussion of this data, see pages 9 to 12 above. Since the serum and urinary fluoride data is for the *general population*, these estimates likely *understate* the percentage of children in *fluoridated* areas with serum and urinary fluoride levels in this range.

[55] This is a substantially lower loss in IQ than would be predicted by existing research. As noted in footnote 54 above, the serum fluoride level (~0.05 mg/L) upon which this estimate is based was associated with a 4-point drop in IQ by Xiang et al. (2011). Further, research on susceptible populations has found dramatic losses in IQ from fluoride exposure, including an average 15-point drop among malnourished children with mild fluorosis. Das & Mondal (2016).

Second, methodological limitations notwithstanding, modern studies of fluoridation and tooth decay have found that the difference in cavity rates between fluoridated and non-fluoridated areas is small, inconsistent, and often non-existent, particularly in the permanent teeth. (Chankanka et al. 2011a,b; Maupome et al. 2007; Warren et al. 2006; Shiboski et al. 2003; Colquhoun 1997; Heller et al. 1997; Diesendorf et al. 1997; Leroux et al. 1996; Brunelle & Carlos 1990; Yiamouyiannis 1990; Hildebolt et al. 1989).

Because of the small and inconsistent differences in cavities now seen between fluoridated and non-fluoridated areas, sensitive measurements of tooth decay must be utilized in order to detect *any* differences in decay.[56] But, even when sensitive measurements are utilized, the differences remain small in absolute terms, inconsistent, and overshadowed by the influence of other factors known to affect decay. (Chankanka et al. 2011a; Warren et al. 2006; Armfield & Spencer 2004). A large-scale study in Australia, for example, found that adolescents who consumed fluoridated water their entire life had just 0.08 less decayed tooth surfaces (1.35 vs. 1.43 DMFS) than adolescents who consumed non-fluoridated water their entire life. (Armfield & Spencer 2004, at 290 tbl.3). Consistent with these findings, studies from Canada, Cuba, Finland, Germany, and the United States did not detect *any* measurable increase in decay following the termination of water fluoridation programs.[57] (Maupome et al. 2001; Burt et al. 2000; Kunzel et al. 2000a,b; Seppa et al. 2000).

Third, one of the few *empirical* investigations of *actual* dental costs in fluoridated vs. non-fluoridated areas found little meaningful difference in frequency or costs of treatment. (Maupome et al. 2007). The study examined the frequency and costs (in 1995 U.S. dollars) of restorative dental procedures over a six-year time period in fluoridated and non-fluoridated areas of Oregon and Washington. Consistent with other recent research, the authors noted that the difference in frequency and costs of dental treatment was "generally small," with several of the age groups in the fluoridated areas having a higher frequency of dental treatment procedures than their peers in the non-fluoridated areas. (Maupome et al. 2007, at 228, tbl. 3). In total, the dental treatment costs in the fluoridated areas over the six-year period averaged $355 versus $387 in the non-fluoridated areas.[58] (*Id.* at 228, tbl. 4). When adjusted to 2016 dollars, the average difference in dental costs was thus only $51 over the 6-year period, *or just over $8 per person per year*. With an average life expectancy of 78.8 years,[59] the Maupome study suggests that fluoridation saves an average of $665 in lifetime dental costs in the U.S. This amounts to less than 3 percent of the reduction in lifetime earnings that results from the loss of a single IQ point ($22,250).

Finally, the cost-effectiveness study (Griffin et al. 2001) that advocates of fluoridation generally rely upon, is based on theoretical estimates that have several major, demonstrable problems that inflate the purported savings. (Ko & Thiessen 2015). The Griffin paper provides estimates of the annual savings in dental costs from fluoridation (in 1995 U.S. dollars) based on a review of several studies of caries rates in fluoridated vs. non-fluoridated communities. The paper estimates that fluoridation provides a net savings of anywhere from $0.85 to $33.71 per year.

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[56] As evident by the studies of Yiamouyiannis (1990) and Brunelle and Carlos (1990), the difference in tooth decay between fluoridated and non-fluoridated populations, while detectable when calculated in terms of Decayed, Missing & Filled Surfaces (DMFS), is not large enough to be detectable when calculated in terms of Decayed, Missing and Filled Teeth (DMFT).

[57] A recent Canadian study by McLaren et al. (2016) reported an increase in decay following cessation of fluoridation in Calgary. However, as explained by Connett (2016), the entirety of this purported increase disappears when survey data omitted from the paper is considered.

[58] The average costs estimate is for people who had at least one restorative procedure during this time.

[59] See: http://www.cdc.gov/nchs/fastats/life-expectancy.htm

(Griffin et al. 2001, at 82, tbl. 4). Over the course of the average lifespan, this amounts to a lifetime savings ranging from $67 to $2656 per person when expressed in 1995 U.S. dollars. Adjusting for inflation, this amounts to a lifetime savings of $106 to $4,207 in 2016 dollars, which, even at its zenith, amounts to less than 20% of the costs ($22,500) incurred from loss of a single IQ point

As discussed by Ko and Thiessen (2015), Griffin's cost-savings estimates suffer from several important limitations. First, and foremost, Griffin did not make any attempt to include the costs of treating dental fluorosis in the costs side of the ledger, thereby inflating the net savings. This is a particularly significant omission since Griffin elsewhere estimated, in a separate paper, that fluoridating water causes 2 percent of children to develop aesthetically objectionable fluorosis on their front teeth. (Griffin et al. 2002). With approximately 50 million children now living in fluoridated areas, this amounts to roughly 1 million children developing aesthetically objectionable fluorosis on their front teeth as a direct result of water fluoridation. But even this is an under-estimate, since Griffin based this on the NIDR's 1986-87 national survey, and more recent national surveys show that both the rate and severity of dental fluorosis have increased considerably over the past 20 years. (NHANES 2014; Beltran 2010). In fact, as mentioned earlier, the 2011-2012 NHANES survey found that an astonishing 21% of adolescents now have *moderate* fluorosis, and an additional 2% have severe fluorosis. (NHANES 2014) Since many children who have fluorosis staining on their front teeth will have it cosmetically treated,[60] the aggregate costs of this treatment will be substantial, and any cost-effectiveness evaluations of fluoridation that fail to account for these treatment costs will artificially inflate the cost-savings of fluoridation. Griffin's cost-savings estimates should not, therefore, be taken at face value, but even if they are, they suggest a range of lifetime savings for the current population under 18 (i.e., $5.3 to $210 billion) that is still substantially less than the range of earnings losses associated with fluoridation-related drops in IQ (i.e., $11.1 billion to $27.8 trillion).

C. Availability and Potential Hazards of Substitutes to Fluoridation Chemicals

The addition of fluoridation chemicals to drinking water began in the U.S. prior to the advent of topical fluoride products in an era when public health authorities believed fluoride's predominant benefit to teeth comes from *ingestion*. Things have changed dramatically since that time.

Today, over 95% of toothpastes contain fluoride, as do many other dental products, (CDC 2013c), and dental researchers now universally acknowledge that fluoride's predominant benefit is topical, not systemic. (*E.g.*, Fejerskov 2004; Featherstone 2000). As explained in the *Journal of the American Dental Association*, "fluoride incorporated during tooth development is insufficient to play a significant role in cavity protection." (Featherstone 2000, at 891). The Centers for Disease Control has confirmed the primacy of fluoride's topical mechanisms, declaring that "fluoride's predominant effect is *post*eruptive and *topical*." (CDC 2001, at 4). The NRC has confirmed this as well, stating that "the major anticaries benefit of fluoride is *topical* and *not systemic*." (NRC 2006, at 13).

Since fluoride's primary benefit comes from topical contact with the teeth, there is little benefit from swallowing fluoride, in water or any other product. In fact, a recent study of the relationship between tooth decay and total daily fluoride ingestion failed to find a detectable relationship

[60] Research has found that teeth with dental fluorosis, including in its "mild" forms, is perceived as an objectionable condition that warrants dental treatment. (*E.g.*, Alkhatib et al. 2004; Riordan 1993). Consistent with this, studies have repeatedly found that staining of the front teeth, including the white splotches of fluorosis, can cause children significant anxiety and distress about the appearance of their teeth. (*E.g.*, Tellez et al. 2012; Marshman et al. 2008).

between the two. (Levy et al. 2009). Other recent studies investigating the relationship between tooth decay and individual biomarkers of fluoride intake (e.g., toenail fluoride content and dental fluorosis) have reported similar results. (Charone et al. 2012; Komarek et al. 2005).

The widespread availability of topical fluoride products highlights the lack of necessity of adding fluoridation chemicals to water, particularly since the quality of evidence for fluoride toothpastes has been recognized as vastly superior to the quality of evidence for water fluoridation.[61] (Cheng et al. 2007, at 701). Furthermore, it is well established that western countries that do not fluoridate their water have tooth decay rates that are just as low, and often lower, as western countries that do fluoridate their water.[62] (Cheng et al. 2007; Pizzo et al. 2007; Neurath 2005; Colquhoun 1997; Diesendorf et al. 1997; Bratthall et al. 1996; Diesendorf 1986).

While fluoride toothpastes and other fluoridated dental products carry their own potential hazards *when ingested*, these products—unlike drinking water—are not *designed* to be ingested. Further, unlike the addition of fluoridation chemicals to drinking water, the use of topical fluoride products does not result in the contamination of processed foods and beverages, thus making it easier to regulate the amount of fluoride ingested when topical fluoride products are the vehicle for delivering fluoride to those who want it.

D. Impacts on Industry, Employment & International Trade from Restricting Fluoridation Chemicals

Prohibiting the addition of fluoridation chemicals to drinking water will have little, if any, impact on industry, employment and international trade. The chemicals used for fluoridation are waste by-products of the U.S. phosphate industry and various Chinese fertilizer and chemical companies. The sale of fluoridation chemicals represents a very small portion of the U.S. phosphate industry's overall sales, and thus removing this very limited market will have little impact on the profitability of the phosphate industry. Finally, while ending fluoridation will curb *imports* of fluoridation chemicals from China, it will not impact American exports, because—to the best of Petitioners' knowledge—U.S. companies do not export fluoridation chemicals abroad. Accordingly, ending fluoridation will not have any disadvantageous impact on America's balance of trade.

XII. IT IS IN THE PUBLIC INTEREST FOR EPA TO ACT UNDER TSCA

EPA has recognized that TSCA invests the Agency with the authority to regulate drinking water additives. (EPA/FDA 1979). Although EPA also has certain authorities to regulate fluoride in drinking water under the SDWA, it is in the public interest for EPA to act under TSCA because it allows EPA to enact a far less expensive regulation that targets fluoridation chemicals in a more narrowly crafted manner that is justified on both policy and scientific grounds.

Under SDWA, the EPA can limit the legally permissible levels of chemicals in public drinking water supplies by enacting "Maximum Contaminant Levels" (MCLs). The EPA can effectively ban fluoridation under SDWA, therefore, by enacting an MCL below the so-called "optimal"

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[61] This is evident when comparing the Cochrane Collaboration's systematic review of the effectiveness of fluoride toothpastes with its systematic review of water fluoridation. *Compare* Iheozor-Ejiofor et al. (2015) *with* Marinho et al. (2003).

[62] For additional data demonstrating the lack of difference in tooth decay rates between countries with extensive water (and/or salt) fluoridation and those without, Petitioners refer EPA to the documentation available at: http://fluoridealert.org/studies/caries01/

concentration of fluoride used in fluoridation programs (0.7 mg/L). Since an MCL does not distinguish, however, between fluoride that is *added* to water and fluoride that occurs naturally therein, implementing an MCL below the level used in fluoridation would force communities with elevated levels of naturally occurring fluoride to implement filtration programs. Banning fluoridation *indirectly* by reducing the MCL under SDWA would thus be more expansive in scope, and far more expensive in implementation, than a *direct* ban on fluoridation additives under TSCA.

As with other naturally occurring toxicants, like arsenic, Petitioners recognize that natural fluoride contamination of some rural water supplies is a problem that needs to be addressed. However, there is a distinct policy difference between a risk *imposed* on a population through the *purposeful addition* of a chemical to water, versus a risk that arises from a naturally occurring phenomena beyond human control. The difference between these two scenarios is material under TSCA because it speaks to the ease by which the risk can be eliminated, and thereby the *reasonableness* of continuing to endure the risk. Differential treatment of the two scenarios is thus justified.

Differential treatment is further justified by laboratory and epidemiological research linking artificial fluoridation chemicals (i.e., fluorosilicic acid and sodium fluorosilicate) with pipe corrosion and elevated blood lead levels. (Coplan et al. 2007; Maas et al. 2007; Macek et al. 2006; Masters et al. 2000). This research includes the CDC's own study of the issue, which analyzed the blood lead levels of children from the 1988-1994 National Health and Nutrition Examination Survey. (Macek et al. 2006).

Although the CDC study is sometimes touted as refuting the link between fluoridation and lead hazards, a close look at its data reveals that it is actually *consistent* with the fluorosilicate/lead thesis. As can be seen in Table 4 of the study, fluorosilicic acid was associated with:

- a 20% increased risk (but not statistically significant) for high blood lead levels among children living in houses made prior to 1946;
- a 40% increased risk (but not statistically significant) for high blood lead levels among children living in houses made between 1946 and 1973;
- a 70% increased risk (but not statistically significant) for high blood lead levels among children living in houses made after 1974;
- a 530% increased risk (which *was* statistically significant) for high blood lead levels among children living in houses with unknown ages.

Since three of these four elevated risks were not statistically significant, the CDC dismissed them as essentially random aberrations. However, the consistency in the *direction* of the risk, coupled with the large and significant five-fold increased risk for children in homes of unknown age, raises a serious red flag.

Even the CDC acknowledged that this study does not refute the connection between fluoridation and lead, and that "it is possible that larger samples might have identified additional, significant differences." (Macek et al. 2006, at 133). Indeed, when Coplan et al. re-analyzed CDC's data by placing all children exposed to fluorosilic acid and sodium fluorosilicate in one group ("silicofluorides"), and all other children in another, they found that the children exposed to "silicofluoridated" water had a significantly elevated risk of having high blood lead levels. (Coplan et al. 2007, at 1039-40). According to Coplan's re-analysis, children from the silicofluoridated communities had a 20% greater risk of having blood lead levels in excess of 5

ug/dl. Coplan's team estimated that the risk for exceeding the 10 ug/dl threshold would be even greater. (*Id.* at 1039 tbl.9).

The repeated association between fluoridation chemicals and elevated blood levels provides further reason why it is in public interest for EPA to prioritize a targeted ban on fluoridation additives under TSCA over broad-based regulatory action against all fluoride in drinking water under SDWA.

XIII. CONCLUSION

Petitioners request that EPA exercise its authority under Section 6 of TSCA, 15 U.S.C. § 2605(a)(2), to prohibit the purposeful addition of fluoridation chemicals to U.S. water supplies. As set forth above, Petitioners make this request on the grounds that a large body of animal, cellular, and human research shows that fluoride is neurotoxic at doses within the range now seen in fluoridated communities. When considering the principles set forth in EPA's *Guidelines for Neurotoxicity Risk Assessment*, Petitioners submit that fluoridation is incompatible with a neurologically safe use of fluoride. Petitioners further make this request on the grounds that fluoride's predominant role in caries prevention comes from *topical* contact and thus there is no reasonable justification to expose hundreds of millions of Americans to the neurotoxic risks of *systemic* fluoride via water (and the many processed beverages and foods made therefrom) when topical fluoride products are now widely available for individual use. Most western nations, including the vast majority of western Europe, have already rejected water fluoridation. The EPA is the one federal agency with the authority to make this happen here in the U.S. We urge EPA to act accordingly.

Petitioners are represented by, and this Petition was prepared by:

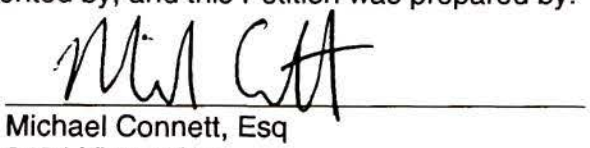

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EXHIBIT 2

cards, letters, and flats; USPS Marketing Mail automation letters and flats; USPS Marketing Mail Carrier Route, High Density, and Saturation letters; Periodicals Outside County barcoded or Carrier Route letters and flats; Periodicals In-County automation or Carrier Route letters and flats; and Bound Printed Matter Presorted, non-DDU barcoded flats. Mailers who present at least 95 percent of their eligible First-Class Mail and USPS Marketing Mail volume as Full-Service in a calendar month would receive electronic address correction notices for their qualifying Basic automation and non-automation First-Class Mail and USPS Marketing Mail pieces, at the address correction fee for pieces eligible for the Full-Service Intelligent Mail option as described in DMM 705.23.0 for future billing cycles. The Basic First-Class Mail and USPS Marketing Mail mailpieces must:

1. Bear a unique IMb printed on the mailpiece;
2. Include a Full-Service or OneCode ACS STID in the IMb;
3. Include the unique IMb in eDoc;
4. Be sent by an eDoc submitter providing accurate Mail Owner identification in eDoc, and;
5. Be sent by an eDoc submitter maintaining 95 percent Full-Service compliance to remain eligible for this service and undergo periodic Postal Service re-evaluation.

* * * * *

4.2.8 Address Correction Service Fee

[Revise 507.4.2.8 by deleting the old language and replacing with new language as follows:]

ACS fees would be assessed as follows:

a. The applicable fee for address correction is charged for each separate notification of address correction or the reason for nondelivery provided, unless an exception applies.

b. Once the ACS fee charges have been invoiced, any unpaid fees for the prior invoice cycle (month) would be assessed an annual administrative fee of 10 percent for the overdue amount.

c. Mailers who present at least 95 percent of their eligible First-Class Mail and USPS Marketing Mail volume as Full-Service in a calendar month would receive electronic address correction notices for their qualifying Basic automation and non-automation First-Class Mail and USPS Marketing Mail mailpieces, as specified in 4.2.2. The electronic address correction notices are charged at the applicable Full-Service address correction fee for all future billing cycles.

* * * * *

600 Basic Mailing Standards for All Mailing Services

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602 Addressing

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5.0 Move Update Standards

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[Revise 602.5.3 by deleting former contents and replacing with new title and contents as follows:]

5.3 Move Update Verification

Mailers who submit any Full-Service volume in a calendar month will be verified pursuant to the Address Quality Census Measurement and Assessment Process beginning in the next calendar month. First-Class Mail and USPS Marketing Mail letter and flat-size mailpieces with addresses that have not been updated in accordance with the Move Update Standard will be subject to the Move Update assessment charge, if submitted via eDoc with unique Basic or Full-Service IMbs. Supporting details are described in Publication 6850, *Publication for Streamlined Mail Acceptance for Letters and Flats,* available at *www.postalpro.usps.com.*

[Revise 602.5.4 as follows:]

5.4 Mailer Certification

The mailer's signature on the postage statement or electronic confirmation during eDoc submission certifies that the Move Update standard has been met for the address records including each address in the corresponding mailing presented to the USPS.

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700 Special Standards

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705 Advanced Preparation and Special Postage Payment Systems

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23.0 Full-Service Automation Option

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23.5 Additional Standards

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23.5.2 Address Correction Notices

* * * * *

[Revise 705.23.5.2a as follows:]

a. Address correction notices would be provided at the applicable Full-Service address correction fee for letters and flats eligible for the Full-Service option, except for USPS Marketing Mail ECR flats, BPM flats dropshipped to DDUs, or BPM carrier route flats. Mailers who present at least 95 percent of their eligible First-Class Mail and USPS Marketing Mail volume as Full-Service in a calendar month would receive electronic address correction notices for their qualifying Basic automation and non-automation First-Class Mail and USPS Marketing mailpieces charged at the applicable Full-Service address correction fee for future billing cycles. The Basic automation and non-automation First-Class Mail and USPS Marketing Mail mailpieces must:

1. Bear a unique IMb printed on the mailpiece.
2. Include a Full-Service or OneCode ACS STID in the IMb.
3. Include the unique IMb in eDoc.
4. Be sent by an eDoc submitter providing accurate Mail Owner identification in eDoc.
5. Be sent by an eDoc submitter maintaining 95 percent Full-Service compliance to remain eligible for this service and undergo periodic USPS re-evaluation.

* * * * *

We will publish an appropriate amendment to 39 CFR part 111 to reflect these changes, if our proposal is adopted.

Stanley F. Mires,

Attorney, Federal Compliance.

[FR Doc. 2017–03723 Filed 2–24–17; 8:45 am]

BILLING CODE 7710–12–P

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Chapter I

[EPA–HQ–OPPT–2016–0763; FRL–9959–74]

Fluoride Chemicals in Drinking Water; TSCA Section 21 Petition; Reasons for Agency Response

AGENCY: Environmental Protection Agency (EPA).

ACTION: Petition; reasons for Agency response.

SUMMARY: This document announces the availability of EPA's response to a petition it received on November 23, 2016, under section 21 of the Toxic Substances Control Act (TSCA). The TSCA section 21 petition was received from the Fluoride Action Network, Food & Water Watch, Organic Consumers Association, the American Academy of Environmental Medicine, the International Academy of Oral Medicine and Toxicology, and other individual petitioners. The TSCA section 21 petition requested that EPA exercise its authority under TSCA section 6 to ''prohibit the purposeful addition of fluoridation chemicals to U.S. water supplies.'' After careful consideration,

EPA has denied the TSCA section 21 petition for the reasons discussed in this document.

DATES: EPA's response to this TSCA section 21 petition was signed February 17, 2017.

FOR FURTHER INFORMATION CONTACT:

For technical information contact: Darlene Leonard, National Program Chemicals Division (7404T), Office of Pollution Prevention and Toxics, Environmental Protection Agency, 1200 Pennsylvania Ave. NW., Washington, DC 20460–0001; telephone number: (202) 566–0516; fax number: (202) 566–0470; email address: *leonard.darlene@epa.gov.*

For general information contact: The TSCA-Hotline, ABVI-Goodwill, 422 South Clinton Ave., Rochester, NY 14620; telephone number: (202) 554–1404; email address: *TSCA-Hotline@epa.gov.*

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this action apply to me?

This action is directed to the public in general. This action may, however, be of interest to individuals or organizations interested in drinking water and drinking water additives, including fluoride. Since other entities may also be interested, the Agency has not attempted to describe all the specific entities that may be affected by this action.

B. How can I access information about this petition?

The docket for this TSCA section 21 petition, identified by docket identification (ID) number EPA–HQ–OPPT–2016–0763, is available online at *http://www.regulations.gov* or in person at the Office of Pollution Prevention and Toxics Docket (OPPT Docket), Environmental Protection Agency Docket Center (EPA/DC), EPA West Bldg., Rm. 3334, 1301 Constitution Ave. NW., Washington, DC. Six binders containing copies of references were submitted along with the petition (Ref. 1). Those binders are not available electronically in the docket but may be reviewed in the Public Reading Room. The Public Reading Room is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Public Reading Room is (202) 566–1744, and the telephone number for the OPPT Docket is (202) 566–0280. Please review the visitor instructions and additional information about the docket available at *http://www.epa.gov/dockets.*

II. TSCA Section 21

A. What is a TSCA section 21 petition?

Under TSCA section 21 (15 U.S.C. 2620), any person can petition EPA to initiate a rulemaking proceeding for the issuance, amendment, or repeal of a rule under TSCA sections 4, 6, or 8 or an order under TSCA sections 4, 5(e), or 5(f). A TSCA section 21 petition must set forth the facts that are claimed to establish the necessity for the action requested. EPA is required to grant or deny the petition within 90 days of its filing. If EPA grants the petition, the Agency must promptly commence an appropriate proceeding that is ''in accordance'' with the underlying TSCA authority. If EPA denies the petition, the Agency must publish its reasons for the denial in the **Federal Register**. 15 U.S.C. 2620(b)(3). A petitioner may commence a civil action in a U.S. district court to compel initiation of the requested rulemaking proceeding within 60 days of either a denial or the expiration of the 90-day period. 15 U.S.C. 2620(b)(4).

B. What criteria apply to a decision on a TSCA section 21 petition?

TSCA section 21(b)(1) requires that the petition ''set forth the facts which it is claimed establish that it is necessary'' to issue the rule or order requested. 15 U.S.C. 2620(b)(1). Thus, TSCA section 21 implicitly incorporates the statutory standards that apply to the requested action. In addition, TSCA section 21 establishes standards a court must use to decide whether to order EPA to initiate rulemaking in the event of a lawsuit filed by the petitioner after denial of a TSCA section 21 petition. 15 U.S.C. 2620(b)(4)(B). Accordingly, EPA has relied on the standards in TSCA section 21 (and those in the provisions under which action has been requested) to evaluate this TSCA section 21 petition.

III. TSCA Section 6

Of particular relevance to this TSCA section 21 petition are the legal standards regarding TSCA section 6(a) rules. These standards were significantly altered in 2016 by the ''Frank R. Lautenberg Chemical Safety for the 21st Century Act,'' Public Law 114–182 (2016), which amended TSCA. One of the key features of the new law is the requirement that EPA now systematically prioritize and assess existing chemicals, and manage identified risks. Through a combination of new authorities, a risk-based safety standard, mandatory deadlines for action, and minimum throughput requirements, TSCA effectively creates a ''pipeline'' by which EPA will conduct review and management of existing chemicals. This new pipeline—from prioritization to risk evaluation to risk management (when warranted)—is intended to drive forward steady progress on the backlog of existing chemical substances left largely unaddressed by the original law. (Ref. 2).

In the initial phase of the review pipeline, EPA is to screen a chemical substance for its priority status, propose a designation as either high or low priority, and then issue a final priority designation within one year of starting the screening process. 15 U.S.C. 2605(b)(1)(C). If the substance is high priority, EPA must initiate a risk evaluation for that substance. 15 U.S.C. 2605(b)(4)(C). EPA must define the scope of the risk evaluation within six months of starting, 15 U.S.C. 2605(b)(4)(D), and complete the risk evaluation within 3 to 3.5 years. 15 U.S.C. 2605(b)(4)(G). If EPA concludes that a chemical substance presents an unreasonable risk, EPA must propose a risk management rule under TSCA section 6(a) within one year and finalize that rule after another year, with limited provision for extension. 15 U.S.C. 2605(c). As EPA completes risk evaluations, EPA is to designate replacement high-priority substances, on a continuing basis. 15 U.S.C. 2605(b)(2)(C) and (b)(3)(C).

In general, to promulgate a rule under TSCA section 6(a), EPA must first determine ''in accordance with section 6(b)(4)(A) that the manufacture, processing, distribution in commerce, use, or disposal of a chemical substance or mixture . . . presents an unreasonable risk.'' 15 U.S.C. 2605(a). TSCA section (b)(4)(A) is part of the risk evaluation process whereby EPA must determine ''whether a chemical substance presents an unreasonable risk of injury to health or the environment,'' and thus, whether a rule under TSCA section 6(a) is necessary. 15 U.S.C. 2605(b)(4)(A). In particular, EPA must conduct this evaluation ''without consideration of costs or other non-risk factors, including an unreasonable risk to a potentially exposed or susceptible subpopulation identified as relevant to the risk evaluation by the Administrator, under the conditions of use.'' Id. Unless EPA establishes an exemption under TSCA section 6(g) (whereby certain unreasonable risks may be allowed to persist for a limited period) or EPA is addressing a persistent, bioaccumulative, and toxic substance as set forth in TSCA section 6(h), the standard for an adequate rule under TSCA section 6(a) is that it regulates ''so that the chemical

substance or mixture no longer presents'' unreasonable risks under the conditions of use. 15 U.S.C. 2605(a).

Prior to the 2016 amendment of TSCA, EPA completed risk assessments that were limited to selected uses of chemical substances. The amended TSCA authorizes EPA to issue TSCA section 6 rules that are not comprehensive of the conditions of use, so long as they are consistent with the scope of such pre-amendment risk assessments. 15 U.S.C. 2625(l)(4). But EPA has interpreted the amended TSCA as requiring that forthcoming risk evaluations encompass all manufacture, processing, distribution in commerce, use, and disposal activities that the Administrator determines are intended, known or reasonably foreseen. (Ref. 2, p. 7565). EPA interprets the scope of post-risk-evaluation rulemaking under TSCA section 6(a) in a parallel fashion: While risk management rules for a certain subset of the conditions of use may be promulgated ahead of rulemaking for the remaining conditions of use, rules covering the complete set of conditions of use must be promulgated by the deadlines specified in TSCA section 6(c). 15 U.S.C. 2605(c). While EPA has authority under TSCA section 6(a) to establish requirements that apply only to ''a particular use,'' the restriction of just one particular use would not constitute an adequate risk management rule unless that particular use were the only reason that the chemical substance presented an unreasonable risk.

TSCA section 21(b)(4)(B) provides the standard for judicial review should EPA deny a request for rulemaking under TSCA section 6(a): ''If the petitioner demonstrates to the satisfaction of the court by a preponderance of the evidence that . . . the chemical substance or mixture to be subject to such rule . . . 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,'' the court shall order the EPA Administrator to initiate the requested action. 15 U.S.C. 2620(b)(4)(B). EPA notes that bills preceding the final amendment to TSCA retained language in section 21 that resembled the pre-amendment criteria for rulemaking under section 6. Compare 15 U.S.C. 2620(b)(4)(B)(ii) (2015) (amended 2016), 15 U.S.C. 2605(a) (2015) (amended 2016), S. Rep. 114–67 at 135 (Ref. 3), and H.R. Rep. No. 114–176 at 81 (Ref. 4). But the effect of the revision in the final bill is to align the standard for judicial review of a TSCA section 21 petition with the standard for EPA's preparation of risk evaluation under TSCA section 6(b)(4)(A). Consistent with these revisions, EPA concludes that Congress intended for a petition to set forth facts that would enable EPA to complete a risk evaluation under TSCA section 6(b).

In light of this, EPA interprets TSCA section 21 as requiring the petition to present a scientific basis for action that is reasonably comparable, in its quality and scope, to a risk evaluation under TSCA section 6(b). This requirement includes addressing the full set of conditions of use for a chemical substance and thereby describing an adequate rule under TSCA section 6(a)—one that would reduce the risks of the chemical substance ''so that the chemical substance or mixture no longer presents'' unreasonable risks under all conditions of use. 15 U.S.C. 2605(a). Specifically, EPA interprets section 21(a)—which authorizes petitions ''to initiate a proceeding for the issuance . . . of a rule under . . . section 6''—as authorizing petitions for rules that *would comply with the requirements of* sections 6(a) and 6(c).

EPA recognizes that information on a single condition of use could, in certain instances, suffice to demonstrate that a chemical substance, as a whole, presents an unreasonable risk. Nonetheless, EPA concludes that such information does not fulfill a petitioner's burden to justify ''a rule under [TSCA section 6],'' under TSCA section 21, since the information would merely justify a subset of an adequate rule. To issue an adequate rule under section 6, EPA would need to conduct a catch-up risk evaluation addressing all the conditions of use not addressed by the petition, and either determine that those conditions do not contribute to the unreasonable risk or enlarge the scope of the rule to address those further conditions of use. See 15 U.S.C. 2605(a). To issue this rule within the time required by section 6(c), EPA would have to proceed without the benefit of the combined 4 to 4.5-year period that TSCA section 6(b) would ordinarily afford EPA (*i.e.,* time to prioritize a chemical substance, conduct a careful review of all of its conditions of use, and receive the benefit of concurrent public comment). Additionally, before even initiating the prioritization process for a chemical substance, EPA would generally screen the chemical substance to determine whether the available hazard and exposure-related information are sufficient to allow EPA to complete both the prioritization and the risk evaluation processes. (Ref. 5).

EPA's interpretation is most consonant with the review pipeline established in TSCA section 6. In particular, the prioritization process established in section 6(b) recognizes that a number of chemical substances may present an unreasonable risk of injury to health or the environment and charges EPA with prioritizing those that should be addressed first. EPA is required to have 10 chemical substances undergoing risk evaluation as of December 19, 2016, and must have a steady state of at least 20 high-priority substances undergoing risk evaluation by December 2019 (and as many as 10 substances nominated for risk evaluation by manufacturers). 15 U.S.C. 2605(b)(2)(A), (B), 2605(b)(4)(E)(i). EPA is obligated to complete rulemakings to address any unreasonable risks identified in these risk evaluations within prescribed timeframes. 15 U.S.C. 2605(c)(1). These required activities will place considerable demands on EPA resources. Indeed, Congress carefully tailored the mandatory throughput requirements of TSCA section 6, based on its recognition of the limitations of EPA's capacity and resources, notwithstanding the sizeable number of chemical substances that will ultimately require review. Under this scheme, EPA does not believe that Congress intended to empower petitioners to promote chemicals of particular concern to them above other chemicals that may well present greater overall risk, and force completion of expedited risk evaluations and rulemakings on those chemicals, based on risks arising from individual uses.

EPA recognizes that some members of the public may have safety concerns that are limited to a single condition of use for a chemical substance. But EPA's interpretation of TSCA section 21 does not deprive such persons of a meaningful opportunity to request that the Administrator proceed on their concerns. For example, such persons may submit a petition under the Administrative Procedure Act, requesting EPA to commence a ''risk-based screening'' of the chemical substance under TSCA section 6(b)(1)(A), motivated by their concern about a single condition of use.

IV. Summary of the TSCA Section 21 Petition

A. What action was requested?

On November 23, 2016, a TSCA section 21 petition was submitted by the Fluoride Action Network, Food & Water Watch, Organic Consumers Association, the American Academy of Environmental Medicine, the

International Academy of Oral Medicine and Toxicology, Moms Against Fluoridation, and the following individuals signing on behalf of themselves and their children: Audrey Adams of Renton, Washington, Jacqueline Denton of Asheville, North Carolina, Valerie Green of Silver Spring, Maryland, Kristin Lavelle of Berkeley, California, and Brenda Staudenmaier of Green Bay, Wisconsin (Ref. 1). The general object of the petition is to urge EPA ''to protect the public and susceptible subpopulations from the neurotoxic risks of fluoride by banning the addition of fluoridation chemicals to water'' (Ref. 1). The specific action sought is a rule, under TSCA section 6(a)(2), to ''prohibit the purposeful addition of fluoridation chemicals to U.S. water supplies.'' However, such a restriction on the allowable use of fluoridation chemicals would actually be based on a rule under TSCA section 6(a)(5), not a rule under TSCA section 6(a)(2). In light of the discrepancy between the description of the rule sought and the cited authority, EPA interprets the petition as requesting *both* a TSCA section 6(a)(5) rule whereby the purposeful addition of any fluoridation chemical to a drinking water supply would be prohibited *and* a TSCA section 6(a)(2) rule whereby the manufacture, processing, or distribution in commerce of any fluoridation chemical for such use would be prohibited.

B. What support does the petition offer?

The petition is focused on the potential for fluoride to have neurotoxic effects on humans; it cites numerous studies bearing on this issue. The petition contends that the purposeful fluoridation of drinking water presents an unreasonable risk to human health from neurotoxicity, and that a ban on this use of fluoridation chemicals is necessary to curtail this unreasonable risk. The following is a summary of the primary support given in the petition for this view:

1. *Fluoride neurotoxicity at levels relevant to U.S. population.* The petition claims that fluoride poses neurotoxic risks to the U.S. population. The petition claims that the cited studies of fluoride-exposed human populations have consistently found neurotoxic effects (lower-than-average IQs) at water fluoride levels below the current Maximum Contaminant Level Goal of 4 mg/L set by EPA's Office of Water. The petition argues that the difference between the fluoride levels in the United States and the greater levels in rural China (where most of the cited IQ studies were conducted) is ''lessen[ed]'' by the abundance of fluoridated toothpaste in the U.S.

2. *Recent epidemiological studies corroborate neurotoxic risk in Western populations.* The petition cites two studies from Western populations to attempt to corroborate the assertion that exposure to fluoride in drinking water presents unreasonable risks for neurotoxicity (Refs. 6 and 7).

3. *Neurotoxic risks supported by animal and cell studies.* The petition argues that studies on both experimental animals and cell cultures are consistent with cited human research linking fluoride exposure with neurotoxic effects in humans.

4. *Susceptible subpopulations are at heightened risk.* The petition argues that certain subpopulations (*e.g.,* infants, the elderly, and persons with nutritional deficiencies, kidney disease or certain genetic predispositions) are more susceptible to fluoride neurotoxicity.

5. *RfD/RfC derivation and uncertainty factor application.* The petition argues that EPA's 1998 *Guidelines for Neurotoxicity Risk Assessment* support the need to apply a 10-fold uncertainty factor in deriving an oral Reference Dose (RfD) or inhalation Reference Concentration (RfC).

6. *Benefits to public health.* The petition bases, in part, its claim of unreasonable risk on the assertion that the fluoridation of drinking water confers little benefit to public health, relative to the alleged neurotoxic risks. The petition argues that since fluoride's primary benefit comes from topical contact with the teeth, there is little benefit from swallowing fluoride, in water or any other product. The petition argues that there is therefore ''little justification'' in exposing the public to ''*any* risk'' of fluoride neurotoxicity.

7. *Extent and magnitude of risk from fluoridation chemicals.* The petition bases, in part, its claim of unreasonable risk on estimates of the extent and magnitude of risk posed to portions of the U.S. population living in areas where artificial fluoridation occurs.

8. *Consequences of eliminating use of fluoridation chemicals.* The petition argues that the risks of fluoride exposure from fluoridated drinking water are unreasonable, in part, because they could be easily and cheaply eliminated, and because alternative products containing topical fluoride are widely available.

9. *Link to elevated blood lead levels.* The petition argues that artificial fluoridation chemicals are linked with pipe corrosion and elevated blood lead levels. The petition interprets data in several studies as demonstrating an association between fluoridation chemicals and elevated blood lead levels.

In addition to supplying the petition, on January 30, 2017, the petitioners also delivered an in-person oral presentation of their views (Ref. 8). At their oral presentation, petitioners reiterated the information already supplied in writing, and requested that EPA also consider an additional study that was not part of the petition (Ref. 9). EPA has discretion (but not an obligation) to consider extra-petition materials when evaluating a petition submitted under TSCA section 21. In cases where the petitioners themselves attempt to enlarge the scope of materials under review while EPA's petition review is pending, EPA exercises its discretion to consider or not consider the additional material based on whether the material was submitted early enough in EPA's petition review process to allow adequate evaluation of the study prior to the petition deadline, the relation of the late materials to materials already submitted. Given the particularly late submittal of the additional study, EPA conducted an abbreviated review of the study and found that the health concerns covered were substantially the same as those covered in other studies submitted with the petition. Based on this abbreviated review, EPA does not believe that the new study provided any new scientific grounds for granting the petition.

V. Disposition of TSCA Section 21 Petition

A. What was EPA's response?

After careful consideration, EPA denied the TSCA section 21 petition, primarily because EPA concluded that the petition has not set forth a scientifically defensible basis to conclude that any persons have suffered neurotoxic harm as a result of exposure to fluoride in the U.S. through the purposeful addition of fluoridation chemicals to drinking water or otherwise from fluoride exposure in the U.S. In judging the sufficiency of the petition, EPA considered whether the petition set forth facts that would enable EPA to complete a risk evaluation under TSCA section 6(b).

EPA also denied the petition on the independent grounds that the petition neither justified the regulation of fluoridation chemicals as a category, nor identified an adequate section 6 rule as the action sought. Rather than comprehensively addressing the conditions of use that apply to a particular chemical substance, the petition requests EPA to take action on a single condition of use (water

fluoridation) that cuts across a category of chemical substances (fluoridation chemicals). A copy of the Agency's response, which consists of a letter to the petitioners, is available in the docket for this TSCA section 21 petition.

B. What were EPA's reasons for this response?

To take the actions under TSCA section 6 requested by the petitioners, EPA would need to make a determination of whether a chemical substance or substances present an unreasonable risk to human health or the environment. This section describes why the petitioners have not provided adequate and sufficient scientific information to make such a determination.

1. *Fluoride neurotoxicity at levels relevant to U.S. population.* The petition ignores a number of basic data quality issues associated with the human studies it relies upon. Many of the human studies cited in the petition are cross-sectional in design, and are affected by antecedent-consequent bias. The antecedent-consequent bias means it cannot be determined whether the exposure came before or after the health effects, since both are evaluated at the same time. Cross-sectional studies are most useful for developing hypotheses about possible causal relationships between an exposure and a health effect, but are rarely suitable for the development of a dose-response relationship for risk assessment. These studies are most useful in supporting more robust epidemiological studies in which defined exposures can be linked quantitatively to an adverse outcome.

The petition also does not properly account for the relatively poor quality of the exposure and effects data in the cited human studies (*e.g.,* it appears to give all studies equivalent weight, regardless of their quality). When an association is suggested between an exposure and a disease outcome, the studies need to be assessed to determine whether the effect is truly because of exposure or if alternate explanations are possible. The way to do that is to adjust for potential confounders, such as diet, behavior, and socioeconomic status, in order to appropriately assess the real relationship between the exposures to a specific substance and health effects. In other words, when these confounding factors are potentially present, but not recognized or controlled for, it is not possible to attribute effects to the contaminant of concern (fluoride) as opposed to other factors or exposures. The evidence presented did not enable EPA to determine whether various confounding factors (*e.g.,* nutritional deficiencies) were indeed placing particular subpopulations at a ''heightened risk of fluoride neurotoxicity,'' as alleged, because the evidence did not adequately account for the possibility that the *confounding factors themselves,* rather than concurrent fluoride exposure, were partly or wholly responsible for the health effects observed. Specific confounding factors or variables were noted by the National Research Council (NRC) (Ref. 10). They may include climate, drinking water intake, excessive dietary fluoride, low calcium intake, drinking water sources with fluctuating fluoride levels, and industrial pollution such as use of coal for domestic heating. These factors have the potential to confound efforts to identify a causal relationship between drinking water fluoride exposure and particular health effects, either by introducing additional, unaccounted for sources of fluoride exposure, by being associated with the pertinent health endpoint through some mechanism other than fluoride toxicity, or by directly affecting the health endpoint.

The petition relies heavily on two meta-analyses which include human cross-sectional (Ref. 11) and case control (Ref. 19) studies. All of the studies listed in Table 1 of the petition were examined in detail by the 2012 Choi et al. study (Ref. 11) as part of their systematic review and meta-analysis to investigate the possibility that fluoride exposure delays neurodevelopment in children. The Choi *et al.* analysis analyzes studies in which IQ was measured using various IQ tests, compares children of various fluoride exposure ranges without accounting for differences in susceptibility to fluoride by age, and used different exposure measures which only delineated between high and low exposure groups. A variety of measures of fluoride exposure were present across studies included in the Choi et al. study, including levels of fluoride in drinking water, observed dental fluorosis, coal burning in houses (*i.e.,* air fluoride levels), and urine fluoride. Despite this disparate collection of types of measurements, all exposure measures were treated equally in the analysis (Ref. 11, Table 1). The authors of the analysis identified a variety of data quality issues associated with this collection of studies. For example, they recognized that several of the populations studied had fluoride exposures from sources other than drinking water (*e.g.,* coal burning; Refs. 13–15); they therefore controlled for this confounding factor by excluding such studies from their analysis. Co-exposures to other potentially neurotoxic chemicals (*e.g.,* iodine) (Refs. 16–18) and arsenic (Refs. 19–22) were also recognized and accounted for in the Choi et al. analysis to understand confounding by these factors. Yet the petitioners include such studies in making their assertion that fluoride is neurotoxic, but have not indicated any attempts to control for the confounding factors. Choi et al. also noted that basic information such as the study subjects' sex and parental education was missing in 80 percent of the studies and household income was missing in 93 percent of studies; they stated that they could not therefore control for these co-variables in their analysis. Consideration of these confounding factors and their impact on the applicability of these studies in a risk assessment context is evident in the authors' discussion. The authors caution readers that ''our review cannot be used to derive an exposure limit, because the actual exposures of the individual children are not known'' and they are measured in their conclusions (*i.e.,* ''our results support the possibility of adverse effects of fluoride exposures on children's neurodevelopment'') (Ref. 11). The authors indicate that ''further research should formally evaluate dose-response relationships based on individual-level measures of exposure over time, including more precise prenatal exposure assessment and more extensive standardized measures of neurobehavioral performance, in addition to improving assessment and control of potential confounders'' (Ref. 11). EPA agrees with the conclusions by Choi et al. (Ref. 11) that the studies included in Table 1 of the petition are unsuitable for evaluating levels of fluoride associated with neurotoxic effects and for deriving dose-response relationships necessary for risk assessment.

The petition also cites an article by Grandjean and Landrigan (Ref. 23), for the proposition that fluoride is ''known'' to cause developmental neurotoxicity in humans. Grandjean and Landrigan refer only to the study of Choi et al. (2012), of which Grandjean is a co-author, in discussing fluoride. EPA's observations about the limitations of Choi et al. (2012) thus apply with equal force to the cited statement from Grandjean and Landrigan. Grandjean and Landrigan summarize that Choi et al. (2012) ''*suggests* an average IQ decrement of about seven points in children exposed to raised fluoride concentrations.'' (Ref. 23). But Grandjean and Landrigan do not opine on whether fluoride exposures, arising from the purposeful addition of fluoridation chemicals to

U.S. water supplies, are in fact causing developmental neurotoxic effects to persons in the U.S. The petition itself concedes that the actual existence of such effects is unestablished, in urging EPA to conduct ''a diligent risk assessment, per EPA's *Guidelines,* to ensure that the general public, and sensitive subpopulations, are not ingesting neurotoxic levels'' (Ref 1, p. 3).

The other meta-analysis cited in the petition (Ref. 12) showed that, based on 16 case-control studies in China, children living in an area with endemic fluorosis are more likely to have low IQ compared to children living in an area with slight fluorosis or no fluorosis. While this analysis may suggest an association between fluorosis and lowered IQ (both of which are possible effects of fluoride exposure at certain levels) any fluoride concentration-to-IQ effect relationship (*i.e.,* dose-response relationship) is only inferred because actual fluoride exposures were not measured. Further, the two effects (fluorosis and lower IQ) both occur at fluoride exposures well above those found in fluoridated U.S. drinking water, such that any inference would only apply at fluoride concentrations not relevant to exposures in the U.S. The studies in the Tang et al. review (Ref. 12) correlate one effect (fluorosis) to another effect (neurotoxicity), but do not establish a dose-response relationship between fluoride exposure and neurotoxicity. This lack of a dose-dependent increase in effect with increasing exposure is a critical limitation of these data. Establishing a dose-response relationship between exposure to a toxicant and an effect ''is the most fundamental and pervasive concept in toxicology. Indeed, an understanding of this relationship is essential for the study of toxic materials'' (Ref. 12). Likewise, the IQ changes noted in Table 1 (Ref. 1) do not increase with increasing water fluoride concentration (*e.g.,* dose) (Ref. 1).

The petition suggested that a dose-response relationship between urinary fluoride and IQ is seen in several studies (Refs. 24–26) shown in Figures 1–5 of the petition (Ref. 1). Assuming, as the petitioners claim, that all children were malnourished in the Das and Mondal (Ref. 26) study, it is not possible to determine whether effects on IQ were due to fluoride or to malnutrition (*i.e.,* nutritional status may be an uncontrolled confounding factor). The study authors caution that ''it is difficult to determine with any degree of accuracy whether the difference of children's IQ scores solely depends on the exposure dose because many social and natural factors like economic condition, culture and geological environments are also responsible'' (Ref. 26). Hence, extrapolating relationships from this study population to other populations is not scientifically defensible.

Choi et al. (2015) (Ref. 27) report that moderate and severe dental fluorosis was significantly associated with lower cognitive functions. However, associations between drinking water and urine fluoride and the same cognitive functions were not found to be significantly associated. They reached this conclusion from a study of 51 children in China and a comparison group of eight with dental fluorosis (Table 4 in Choi et al., 2015). The authors discuss potential problems associated with using these biomarkers of exposure to fluoride. For example, water samples may be imprecise because internal dose of fluoride depends on total water intake, and urine samples may be affected by the amount of water the subject drank prior to sampling. With regard to fluorosis, the degree of dental fluorosis is dependent not only on the total fluoride dose but also on the timing and duration of fluoride exposure. A person's individual response to fluoride exposure depends on factors such as body weight, activity level, nutritional factors, and the rate of skeletal growth and remodeling. These variables, along with inter-individual variability in response to similar doses of fluoride, indicate that enamel fluorosis cannot be used as a biological marker of the level of fluoride exposure for an individual (Ref. 28). Hence, the petitioner's use of fluorosis levels as a surrogate for evidence of neurotoxic harm to the U.S. population is inappropriate evidence to support an assertion of unreasonable risk to humans from fluoridation of drinking water.

The petition also cites four studies (Refs. 24, 29–31) that rely on human urine or serum fluoride concentrations as biomarkers of exposure but does not discuss the limitations associated with the biomarkers used in the studies. In their report, *Human Biomonitoring for Environmental Chemicals,* NRC defines properties of biomarkers and created a framework for grouping biomarkers of exposure (Ref. 32). Figure 3–1 in the NRC report illustrates the relationship between external dose (*e.g.,* water), internal dose (*e.g.,* fluoride concentration) and biological effects, and indicates that internal dose is measured through biomonitoring (*e.g.,* fluoride concentrations measured in urine or serum). NRC grouped the quality of biomarkers based on the robustness of these relationships. NRC designated biomarkers for substances that have been observed in bodily fluids, but that lack established relationships between external dose (*e.g.,* water), internal dose (*e.g.,* urine or serum) and biological effects (*e.g.,* neurotoxicity) as ''Group I'' biomarkers. Although many human studies have been collated and reviewed in the petition, for the reasons outlined previously—particularly study design and confounding factors—relationships between urine and serum fluoride (internal doses), water fluoride concentration (external dose), and neurotoxic effects in humans have not been established. Further, serum and urine biomarkers for fluoride reflect only recent exposures, not long-term exposures, and may be different from the exposures during the specific time when developmental effects can occur. A lack of established sampling protocols and analytical methods are also hallmarks of ''Group I'' biomarkers. The main studies cited in the petition which attempt to relate urine or serum levels to possible neurotoxic effects suffer from either lack of good sampling protocols or absence of documenting the sampling protocols. Important issues such as the timing and methods of sample collection were also often not reported in the studies. Using the NRC Framework, urine and serum fluoride levels would be at best ''Group I'' biomarkers for fluoride-related neurotoxicity. The NRC Framework states ''[b]iomarkers in this category may be considered useless'' for risk assessment purposes (Ref. 32, p. 78).

2. *Recent epidemiological studies corroborate neurotoxic risk in Western populations.* The petition cites two studies from Western populations to attempt to corroborate the assertion that exposure to fluoridated water presents unreasonable risks for neurotoxicity. Two population-level studies were cited which link fluoridated water to attention-deficit/hyperactivity disorder (ADHD) prevalence in the U.S. (Ref. 6) and drinking water exposures and hypothyroidism prevalence in England (Ref. 7). These studies use cross-sectional population-level data to examine the association between ADHD and hypothyroidism and fluoridated water levels. The studies make reasonable use the population-level data available, but causal inference cannot be made from these studies (Ref. 3).

As stated in the conclusion of Malin and Till, an association has been reported, but ''[p]opulation studies designed to examine possible mechanisms, patterns and levels of exposure, covariates and moderators of

this relationship are warranted'' (Ref. 6, p. 8). In epidemiology, studies using cross-sectional data are most often used to generate hypotheses that need to be further studied to determine whether a ''true'' association is present. Ideally, the study designs and methods are improved by each study that is undertaken, such as, among other things, identifying additional potential confounders, considering timing issues or resolving ambiguity in collection of samples and disease outcome, improving upon the exposure analysis, and evaluating the magnitude and consistency of the results, so that the evaluation can adequately assess the association (Ref. 34). For example, the authors assert that there are design issues with their study, especially related to the exposure categories, and they suggest how to address these issues in future studies. Although it is possible that there may be biological plausibility for the hypothesis that water fluoridation may be associated with ADHD, this single epidemiological study is not sufficient to ''corroborate'' neurotoxic health effects, as stated in the petition. More study would be needed to develop a body of information adequate to make a scientifically defensible unreasonable risk determination under TSCA.

The Peckham et al. study (Ref. 7) suffers from similar issues noted in Malin and Till (Ref. 6). Adjustment for some confounders was considered, including sex and age, but other potential confounders (such as iodine intake) were not assessed. Fluoride from other sources and other factors associated with hypothyroidism were not assessed in this study. Exposure misclassification, in which populations are placed in the wrong exposure categories based on the water fluoridation status, is very possible in either of the studies presented and is a limitation of the study designs.

3. *Neurotoxic risks supported by animal and cell studies.* The National Toxicology Program (NTP) conducted a systematic review of animal and cell studies on the effects of fluoride on learning and memory available up to January 2016 (Ref. 35). Almost all (159 out of 171) of the animal and cell culture studies cited in the petition in Appendix D–E were included in the NTP systematic review. From among 4,656 studies identified in the NTP database search, 4,552 were excluded during title and abstract screening, 104 were reviewed at the full-text level and 68 studies were considered relevant and were included in the analysis. NTP assessed each study for bias, meaning a systematic error in the study that can over or underestimate the true effect and further excluded any studies with a high risk of bias. Of the 68 studies, including studies provided by the Fluoride Action Network, 19 were considered to pose a very serious overall risk of bias, primarily based on concern for at least three of the following factors: Lack of randomization, lack of blinding at outcome assessment in conjunction with not using automated tools to collect information, lack of reporting on what was administered to animals (source, purity, chemical form of fluoride), lack of control for litter effects, lack of expected response in control animals, and lack of reporting of key study information such as the number or sex of animals treated. Of the studies cited in Table 4 in the petition, two were excluded from the NTP analysis because of serious concerns for study bias (Refs. 36 and 37). Based on its review of animal and cell studies, NTP concluded that ''[t]he evidence is strongest (moderate level-of-evidence) in animals exposed as adults tested in the Morris water maze and weaker (low level-of-evidence) in animals exposed during development'' and ''[v]ery few studies assessed learning and memory effects at exposure levels near 0.7 parts per million, the recommended level for community water fluoridation in the United States.'' The animal studies cited in the petition (Ref. 1, p. 14, Table 4) reflect these high drinking water exposures ranging from 2.3 mg/L to 13.6 mg/L, equivalent to 3–20 times the levels to which drinking water is fluoridated in the U.S. Overall, NTP concluded that, ''[r]esults show low-to-moderate level-of-evidence in developmental and adult exposure studies for a pattern of findings suggestive of an effect on learning and memory'' (Ref. 35, p. 52). Based on this review of available evidence, and the identified limitations in the database, NTP is currently pursuing experimental studies in rats to address key data gaps, starting with pilot studies that address limitations of the current literature with respect to study design (*e.g.,* randomization, blinding, control for litter effects), and assessment of motor and sensory function to assess the degree to which impairment of movement may impact performance in learning and memory tests. If justified, follow-up studies would address potential developmental effects using lower dose levels more applicable to human intakes.

Two studies included in Table 4 (Ref. 1) were not included in the NTP review, but do not show neurotoxicity effects at doses relevant to U.S. populations. One study aimed to establish vitamin A as a marker for fluoride neurotoxicity (Ref. 38), but changes in vitamin A were measured only at an excessive fluoride dose of 20 mg/L. The other study dosed rats with fluoride in drinking water (Ref. 39) and showed effects on behavior and brain neurotransmitters at a dose of 5 mg/L, a level well above the 0.7 parts per million level recommended for community water fluoridation in the United States. Other studies in Table 4, which, according to the title of the table, are indicative of ''Water Fluoride Levels Associated with Neurotoxic Effects in Rodents,'' erroneously report effect levels not supported by the studies themselves. In Wu et al. (Ref. 36), which NTP excluded based on high bias, no adverse effects were seen at a dose of 1 mg/kg-day as claimed in the petition. In fact, the behavioral effects occurred only at doses of 5 and 25 mg/L. In Chouhan et al. (Ref. 40), which NTP excluded in the initial screen for relevancy, no significant neurotoxicity was seen at 1 mg/L fluoride, in contrast to what the petition claims. In addition, the petition's statement that ''rats require 5 times more fluoride in their water to achieve the same level of fluoride in their blood as humans'' (Ref. 1) as a rationale for why higher exposure levels in animals are relevant to lower levels in humans is not supported by the NTP review in the petition. The NTP review indicates that ''assuming approximate equivalence [of drinking water concentrations in rodents and humans] is not unreasonable'' (Ref. 35, p. 58). These several erroneously reported studies do not change EPA's agreement with the conclusions of the NTP report that their ''[r]esults show low-to-moderate level-of-evidence in developmental and adult exposure studies for a pattern of findings suggestive of an effect on learning and memory'' (Ref. 35, p. 52).

In cell studies cited in the petition, two studies demonstrated effects following exposure of artificial brain cells to fluoride at concentrations in the range purported to be in the bloodstream of humans. However, relevance of cell assays to humans is limited because the concentrations of fluoride experienced by cells by themselves in culture are not directly comparable to an animal or human exposure due to lack of metabolism, interactions between cells, and the ability to measure chronic (long-term) effects (Ref. 41). Extrapolation from concentrations in cell cultures to human exposures is not straightforward. Pharmacokinetic modeling is necessary to convert the concentrations to a

human equivalent dose relevant to risk assessment (Ref. 42), but the petition did not address whether data are available or lacking to complete such an analysis.

4. *Susceptible subpopulations are at heightened risk.* The data and information provided in the petition do not support the claims that ''nutritional status, age, genetics and disease are known to influence an individual's susceptibility to chronic fluoride toxicity.'' The only reference the petition presents that specifically addresses the claim that nutrient deficiencies (*i.e.,* deficiencies in iodine and calcium) can ''amplify fluoride's neurotoxicity'' is the study by Das and Mondal (Ref. 26). However, the study did not measure any nutrients in their test subjects. Rather, they measured Body Mass Index (BMI), acknowledging that ''BMI is the most commonly used measure for monitoring the prevalence of overweight and obesity at population level'' and ''it is only a proxy measure of the underlying problem of excess body fat or underweight cases.'' Not only is the BMI an indirect proxy for the iodine and calcium deficiencies supposed in the petition, the BMI results presented in this study are themselves equivocal, as they show that BMIs ranged from underweight to overweight to obesity depending on the sex and age of the study subjects. Furthermore, the petition concedes that the Das and Mondal study data are only ''suggestive'' of an area with chronic malnutrition. A few human studies cited provide only suggestive evidence that low levels of iodine may increase the effects of high levels of fluoride in children, but these studies suffer from study design and confounding issues already described previously. Other cited studies describe the effects of iodine or calcium on rats or rat brain cells in addition to irrelevantly high fluoride levels. The petition also claims that a certain ''COMT gene polymorphism greatly influences the extent of IQ loss resulting from fluoride exposure,'' citing a study by Zhang et al. (Ref. 29) as support. The COMT gene encodes for the enzyme, catechol-O-methyltransferase, which is responsible for control of dopamine levels in the brain. Zhang et al. concludes that, ''[t]he present study has several limitations. First, the cross-sectional observational design does not allow us to determine temporal or causal associations between fluoride and cognition. Second, the study has a relatively small sample size, which limits the power to assess effects of gene-environmental interactions on children's IQ'' (Ref. 29). Zhang et al. continues ''[d]espite the study limitations, this is the first gene-environment study investigating the potential impact of COMT single-nucleotide polymorphism (SNP) on the relationship between children's cognitive performance and exposure to elemental fluoride'' (Ref. 29). Several studies are cited in the petition to support the assertion that infants, the elderly and individuals with deficient nutritional intake and kidney disease are more susceptible to fluoride neurotoxicity. However, the level of supporting evidence from these studies (*i.e.,* to specify the potentially greater susceptibility of any particular subpopulation) is insufficient to overcome the petition's broader failure to set forth sufficient facts to establish that fluoridation chemicals present an unreasonable risk to the general population, to allow EPA to reach a risk evaluation.

5. *RfD/RfC derivation and uncertainty factor application.* An oral Reference Dose or inhalation Reference Concentration is a daily exposure to the human population, including sensitive subgroups, that is likely to be without an appreciable risk of deleterious effects during a lifetime (Ref. 43). The petition cites EPA's 1998 guidance document, *Guidelines for Neurotoxicity Risk Assessment* (Ref. 44), purporting that it demonstrates the necessity of applying an uncertainty factor of at least 10. It appears that the petition has selected the eight studies presented in Table 5 (Ref. 1, p. 19) as candidates for deriving a Reference Dose (RfD) or Reference Concentration (RfC). The petition asserts that these dose or concentration values are relevant oral reference values for neurotoxic effects. However, the petition fails to recognize that the question of applying an uncertainty factor does not even arise until one has first appropriately performed a hazard characterization for all health endpoints of concern (Ref. 30, Section 3.1). As outlined in EPA's document, *A Review of the Reference Dose and Reference Concentration Processes* (Ref. 43), the first step in deriving an RfD or RfC is to evaluate the available database. The petition does not set forth the strengths and limitations of each of the studies in the overall database of available studies nor any criteria or rationale for selecting the eight particular studies from which to derive an RfD or RfC. Without setting forth the strengths and limitations associated with each study and the weight of evidence provided by the available database, a necessary step in any assessment, it is not possible to determine whether uncertainty factors are necessary.

Following hazard characterization and identification of suitable studies for an RfD or RfC, uncertainty factors are generally applied to a lower limit dose or concentration on the continuum of observed effects (dose-response curve) in an individual study (*e.g.,* NOAEL, LOAEL, Benchmark Dose, etc.). The selection of uncertainty factors and their magnitude should be based on the quality of the data, extent of the database and sound scientific judgment and consider the impact of having adverse effects from an inadequate exposure as well as an excess exposure. Uncertainty factor values may be considered appropriate to account for uncertainties associated with extrapolating from (1) a dose producing effects in animals to a dose producing no effects, (2) subchronic to chronic exposure in animals, (3) animal toxicological data to humans (interspecies), (4) sensitivities among the members of the human population (intraspecies), and (5) deficiencies in the database for duration or key effects (Ref. 43). Conflicting statements in the petition indicate that there is both a robust and certain dose-response relationship between fluoride exposure and IQ including for sensitive subpopulations. However, the petition does not clearly identify which sources/types of uncertainty in the data exist, nor which of the aforementioned uncertainty factors should be applied based on the review of the selected studies.

6. *Benefits to public health.* The petition asserts that the fluoridation of drinking water confers little benefit to public health, claiming that the primary benefit of fluoride comes from topical fluoride contact with the teeth and that there is thus little benefit from ingesting fluoride in water or any other product. The petition claims there are no randomized controlled trials on the effectiveness of fluoridation, and that few studies adequately account for potential confounding factors. In addition, the petition states that modern studies of fluoridation and tooth decay have found small, inconsistent and often non-existent differences in cavity rates between fluoridated and non-fluoridated areas. Further, the petition questions the cost-effectiveness of fluoridation relative to costs associated with what have been asserted to be fluoridation-related drops in IQ. The petition argues, then, that there is ''little justification'' in exposing the public to ''*any* risk'' of fluoride neurotoxicity (Ref. 1).

EPA does not believe that the petition has presented a well-founded basis to doubt the health benefits of fluoridating drinking water. The petition's argument about fluoridation benefits (*i.e.,* that the risks of neurotoxic health effects from fluoridation are unreasonable in part because they outweigh the expected health benefits arising from exposure to fluoride) depends on first setting forth sufficient facts to establish the purported neurotoxic risks, to which the countervailing health benefits from fluoridation could be compared. But as noted earlier, EPA and other authoritative bodies have previously reviewed many of the studies cited as evidence of neurotoxic effects of fluoride in humans and found significant limitations in using them to draw conclusions on whether neurotoxicity is associated with fluoridation of drinking water. Irrespective of the conclusions one draws about the health benefits of drinking water fluoridation, the petition did not set forth sufficient facts to justify its primary claims about purported neurotoxic effect from drinking fluoridated water.

The petition cites several studies as evidence that water fluoridation does not have any demonstrable benefit to the prevention of tooth decay (Refs. 45–49). However, EPA has found substantial concerns with the designs of each of these studies including small sample size and uncontrolled confounders, such as recall bias and socioeconomic status. Additionally, in Bratthall et al. (Ref. 45), for example, the appropriate interpretation of the responses of the 55 dental care professionals surveyed, based on the data provided in the paper, is that in places where water is fluoridated, the fluoridation is the primary reason for the reduction in dental caries. Diesendorf (Ref. 49) cites only anecdotal evidence and Cheng et al. (Ref. 46) is commentary only, with no supporting data.

EPA is mindful of the public health significance of reducing the incidence of dental caries in the U.S. population. Dental caries is one of the most common childhood diseases and continues to be problematic in all age groups. Historically, the addition of fluoride to drinking water has been credited with significant reductions of dental caries in the U.S. population. In 2000, the then-Surgeon General noted that ''community water fluoridation remains one of the great achievements of public health in the twentieth century—an inexpensive means of improving oral health that benefits all residents of a community, young and old, rich and poor alike.'' The U.S. Surgeon General went on to note, ''it [is] abundantly clear that there are profound and consequential disparities in the oral health of our citizens. Indeed, what amounts to a silent epidemic of dental and oral diseases is affecting some population groups.'' (Ref. 50).

At that time, among 5- to 17-year-olds, dental caries was more than five times as common as a reported history of asthma and seven times as common as hay fever. Prevalence increases with age. The majority (51.6 percent) of children aged 5 to 9 years had at least one carious lesion or filling in the coronal portion of either a primary or a permanent tooth. This proportion increased to 77.9 percent for 17-year-olds and 84.7 percent for adults 18 or older. Additionally, 49.7 percent of people 75 years or older had root caries affecting at least one tooth (Ref. 50).

More recently, from the National Health and Nutrition Examination Survey (NHANES) for 2011–2012, approximately 23% of children aged 2–5 years had dental caries in primary teeth. Untreated tooth decay in primary teeth among children aged 2–8 was twice as high for Hispanic and non-Hispanic black children compared with non-Hispanic white children. Among those aged 6–11, 27% of Hispanic children had any dental caries in permanent teeth compared with nearly 18% of non-Hispanic white and Asian children. About three in five adolescents aged 12–19 years had experienced dental caries in permanent teeth, and 15% had untreated tooth decay (Refs. 51).

Further, in 2011–2012, 17.5 percent of Americans ages 5–19 years were reported to have untreated dental caries, while 27.4 percent of those aged 20–44 years had untreated caries (Ref. 52). For those living below the poverty line, 24.6 percent of those aged 5–19 years and 40.2 percent of those aged 20–44 years had untreated dental caries (Ref. 52). Untreated tooth decay can lead to abscess (a severe infection) under the gums which can spread to other parts of the body and have serious, and in rare cases fatal, results (Ref. 53). Untreated decay can cause pain, school absences, difficulty concentrating, and poor appearance, all contributing to decreased quality of life and ability to succeed (Ref. 54).

These data continue to suggest dental caries remains a public health problem affecting many people. Fluoride has been proven to protect teeth from decay by helping to rebuild and strengthen the tooth's surface or enamel. According to the Centers for Disease Control and Prevention and the American Dental Association, water fluoridation prevents tooth decay by providing frequent and consistent contact with low levels of fluoride (Refs. 55 and 56). Thus, the health benefits of fluoride include having fewer cavities, less severe cavities, less need for fillings and removing teeth, and less pain and suffering due to tooth decay (Ref. 55).

Fluoride protects teeth in two ways—systemically and topically (Ref. 57). Topical fluorides include toothpastes, some mouth rinse products and professionally applied products to treat tooth surfaces. Topical fluorides strengthen teeth already in the mouth by becoming incorporated into the enamel tooth surfaces, making them more resistant to decay. Systemic fluorides are those ingested into the body. Fluoridated water and fluoride present in the diet are sources of systemic fluoride. As teeth are developing (pre-eruptive), regular ingestion of fluoride protects the tooth surface by depositing fluorides throughout the entire tooth surface (Ref. 56). Systemic fluorides also provide topical protection as ingested fluoride is present in saliva which continually bathes the teeth (Ref. 56). Water fluoridation provides both systemic and topical exposure which together provide for maximum reduction in dental decay (Ref. 56).

The Surgeon General, the Public Health Service and the Centers for Disease Control and Prevention reaffirmed in 2015 the importance of community water fluoridation for the prevention of dental caries and its demonstrated effectiveness (Refs. 54 and 58). In the Public Health Service's 2015 *Recommendation for Fluoride Concentration in Drinking Water,* they note ''there are no randomized, double-blind, controlled trials of water fluoridation because its community-wide nature does not permit randomization of individuals to study and control groups or blinding of participants. However, community trials have been conducted, and these studies were included in systematic reviews of the effectiveness of community water fluoridation. As noted, these reviews of the scientific evidence related to fluoride have concluded that community water fluoridation is effective in decreasing dental caries prevalence and severity'' (Ref. 59).

7. *Extent and magnitude of risk from fluoridation chemicals.* The petition argues that the purported risks of drinking water fluoridation are unreasonable in part because they are borne by a large population. The petition (in its discussion of the extent and magnitude of risk posed) cites the total U.S. population and estimates the

number of U.S. children under the age of 18 years who live in areas where artificial fluoridation occurs. That estimate is then multiplied by an estimate of the average decrease in lifetime earnings associated with IQ point loss to calculate the overall potential IQ point loss and associated decrease in lifetime earnings for the segment of the U.S. population under the age of 18 years potentially exposed to artificially fluoridated water. The petition concludes, based on the potential extent and magnitude of exposure to fluoridation chemicals, that fluoridation would have caused ''a loss of between 62.5 to 125 million IQ points'' (Ref. 1, p. 24).

The petition has not set forth a scientifically defensible basis to conclude that any persons have suffered neurotoxic harm as a result of exposure to fluoride in the U.S. through the purposeful addition of fluoridation chemicals to drinking water or otherwise from fluoride exposure in the U.S. Still less has the petition set forth a scientifically defensible basis to estimate an aggregate loss of IQ points in the U.S., attributable to this use of fluoridation chemicals. As noted previously, EPA has determined the petition did not establish that fluoridation chemicals present an unreasonable risk of injury to health or the environment, arising from these chemical substances' use to fluoridate drinking water. The fact that a purported risk relates to a large population is not a basis to relax otherwise applicable scientific standards in evaluating the evidence of that purported risk. EPA and other authoritative bodies have previously reviewed many of the studies cited as evidence of neurotoxic effects of fluoride in humans and found significant limitations in using them to draw conclusions on whether neurotoxicity is associated with fluoridation of drinking water. In contrast, the benefits of community water fluoridation have been demonstrated to reduce dental caries, which is one of the most common childhood diseases and continues to be problematic in all age groups. Left untreated, decay can cause pain, school absences, difficulty concentrating, and poor appearance, all contributing to decreased quality of life and ability to succeed (Ref. 54).

8. *Consequences of eliminating use of fluoridation chemicals.* Apparently citing to a repealed provision of TSCA (15 U.S.C. 2605(c)[1](A) (2015)) and guidance issued with respect to that statutory provision, the petition argues that the following factors are germane to determining whether the alleged neurotoxic risks presented by fluoridation chemicals are unreasonable: ''the societal consequences of removing or restricting use of products; availability and potential hazards of substitutes, and impacts on industry, employment, and international trade.'' Along these lines, the petition includes claims such as the following: That any risks of fluoridation chemicals could be easily reduced by discontinuing purposeful fluoridation practices; that alternative topical fluoride products have widespread availability; and that the impacts on the requested rule on industry, employment, and international trade would be little, if any. In short, the petition urges EPA to conclude that the risks of fluoridation chemicals are unreasonable, in part because if EPA found that the risks were unreasonable, the cost and non-risk factors that EPA would need to address in ensuing risk management rulemaking could be readily addressed. But this sort of ends-driven reasoning is forbidden by the texts of section 6(b)(4)(A) and 21(b)(4)(B)(ii) of the amended TSCA, which exclude ''costs or other non-risk factors'' from the unreasonable risk determination. It is also plainly inconsistent with Congress' intent, in amending TSCA, to ''de-couple'' the unreasonable risk decision from the broader set of issues (*e.g.,* chemical alternatives and regulatory cost-effectiveness) that may factor into how best to manage unreasonable risks, once particular risks have been determined to be unreasonable. See S. Rep. 114–67 at 17 (Ref. 3); H.R. Rep. 114–176 at 23 (Ref. 4); and 162 Cong. Rec. S3516 (Ref. 60).

9. *Link to elevated blood lead levels.* To support the contention that TSCA (and not the Safe Drinking Water Act [SDWA]) is the appropriate regulatory authority, the petition asserts an association between fluoridation chemicals and elevated blood lead levels and claims that there is laboratory and epidemiological research linking artificial fluoridation chemicals with pipe corrosion. The petition then argues that issuing a rule under TSCA section 6 rather than SDWA would allow EPA to specifically target and prohibit the addition of fluoridation chemicals to drinking water. The petition argues that SDWA would not allow EPA to distinguish between intentionally-added, artificial and naturally-occurring fluoride. It is in the public interest, says the petition, to opt for the regulatory option that is less expensive and can be more narrowly tailored.

Regarding the claims about the relative extent of legal authorities under TSCA and SDWA, EPA notes that the petition has not set forth any specific legal basis for its views on the purported limitations of SDWA. For this reason, and because the petition has not set forth facts sufficient to show that the fluoridation of drinking water presents an unreasonable risk under TSCA, the Agency need not resolve such legal questions in order to adjudicate this petition.

EPA has further observations about the petition's claims that drinking water fluoridation is linked to lead hazards. The Centers for Disease Control and Prevention (CDC) studied the relationship between fluoridation additives and blood lead levels in children in the United States (Ref. 61). More than 9,000 children between the ages of 1–16 years were included in the study's nationally representative sample. The petition argues that the study, and Table 4 in particular, shows that fluorosilicic acid was associated with increased risk of high blood lead levels. In fact, Macek et al. concluded that their detailed analyses did not support concerns that silicofluorides in community water systems cause high lead concentrations in children. The petition also points to another study (Ref. 62) which re-analyzed CDC's data and concluded that children exposed to ''silicofluoridated'' water had an elevated risk of having high blood lead levels. Coplan et al. (Ref. 62) criticized the Macek et al. approach as flawed and reevaluated the NHANES data comparing systems that used silicofluorides to all systems (*e.g.,* a combination of fluoridated, nonfluoridated and naturally fluoridated) and found a small difference between the number of children in each group with blood lead levels >5 µg/dL; the results were not evaluated to see if the difference was statistically significant. A number of other chemical characteristics are known to increase lead release into water sources such as pH, natural organic matter, water hardness, oxidant levels, and type of piping, age of housing; the Coplan et al. study did not evaluate these factors.

In any event, the Agency is not persuaded that the examination of the relationship between fluoridation chemicals, pipe corrosion, and elevated blood lead levels nor their bearing on the comparative efficacy of TSCA or SDWA is germane to the disposition of the petition. Under TSCA, where the EPA Administrator determines ''that the manufacture, processing, distribution in commerce, use, or disposal of a chemical substance or mixture . . . presents an unreasonable risk of injury

to health or the environment, the Administrator shall by rule [regulate a] . . . substance or mixture to the extent necessary so that the chemical substance or mixture no longer presents such risk'' 15 U.S.C. 2605(a). As previously discussed, the petition does not demonstrate that purposeful addition of fluoridation chemicals to U.S. water supplies presents such unreasonable risk.

10. *Regulation of fluoridation chemicals as a category.* EPA has broad discretion to determine whether to regulate by category under TSCA section 26(c) rather than by individual chemical substances. In a prior evaluation of a section 21 petition seeking the regulation of a category of chemical substances, EPA explained that it does so in light of Congress' purpose in establishing the category authority: To ''facilitate the efficient and effective administration'' of TSCA. See 72 FR 72886 (Ref. 63) (citing Senate Report No. 94–698 at 31). It is of course self-evident that various chemical substances constituting ''fluoridation chemicals'' would have in common their use to fluoridate drinking water. But as discussed in Unit III., the inquiry does not end there. If EPA were to grant the petitioner's request, the Agency would become obligated to address all conditions of use of the category. If certain chemical substances comprising the category present conditions of use that other members do not, and any of those conditions of use would be significant to whether the category as a whole presents an unreasonable risk to human health or the environment, then the overall approach of regulating by category is less suited to the efficient and effective administration of TSCA. But the petition does not set forth facts that would enable the Agency to reasonably evaluate whether a category approach on fluoridation chemicals would be consistent with the efficient and effective administration of TSCA. Nor does the petition set forth the specific chemical substances that should comprise the category of fluoridation chemicals.

11. *Specification of an adequate rule under TSCA section 6(a).* As discussed earlier, the petition does not set forth facts that satisfactorily demonstrate to the Agency that fluoridation chemicals present an unreasonable risk to human health, specifically arising from these chemical substances' use to fluoridate drinking water. But even if the petition had done so, it would still be inadequate as a basis to compel the commencement of section 6(a) rulemaking proceeding under TSCA section 21. This is because the petition does not address whether fluoridation chemicals would still present an unreasonable risk, even after implementing the requested relief, arising from other conditions of use. As discussed earlier in Unit III., EPA interprets TSCA section 21 as requiring a petition to address the full set of conditions of use for a chemical substance and thereby describe an adequate rule under TSCA section 6(a), as opposed to a rule that would merely address a particular subset of uses of special interest. The petition at issue pays little or no attention to the other conditions of use of the various fluoridation chemicals (*i.e.,* uses other than the eponymous use to treat drinking water) and makes no claim for any of these chemical substances that the risks to be addressed by curtailing drinking water fluoridation would be the only unreasonable risks or even the most significant unreasonable risks. This problem is compounded by the petition's lack of specificity as to which chemical substances are being construed as ''fluoridation chemicals.''

EPA acknowledges that its interpretation of the requirements of TSCA section 21, for petitions seeking action under TSCA section 6, was not available to petitioners at the time they prepared this petition. EPA has issued general guidance for preparing citizen's petitions, 50 FR 56825 (1985), but that guidance does not account for the 2016 amendments to TSCA. Particularly relevant under these circumstances, the Agency wishes to emphasize that its denial does not preclude petitioners from obtaining further substantive administrative consideration, under TSCA section 21, of a substantively revised petition under TSCA section 21 that clearly identifies the chemical substances at issue, discusses the full conditions of use for those substances, and sets forth facts that would enable EPA to complete a risk evaluation under TSCA section 6(b) for those substances.

VI. References

As indicated under **ADDRESSES**, a docket has been established for this document under docket ID number EPA–HQ–OPPT–2016–0763. The following is a listing of documents that are specifically referenced in this notice. The docket itself includes both these referenced documents and further documents considered by EPA. The docket also includes supporting documents provided by the petitioner and cited in the petition, which are not available in the electronic version of the docket. For assistance in locating these printed documents, please consult the technical person listed under **FOR FURTHER INFORMATION CONTACT**.

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2. EPA. Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act; Notice. **Federal Register** (82 FR 7562, January 19, 2017).
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List of Subjects

Environmental protection, Fluoridation chemicals, Drinking water, Toxic Substances Control Act (TSCA).

Dated: February 17, 2017.

Wendy Cleland-Hamnett,

Acting Assistant Administrator, Office of Chemical Safety and Pollution Prevention.

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