July 16, 2025

Docket No. FDA-2025-N-1557: Use of Orally Ingestible Unapproved Prescription Drug Products Containing Fluoride in the Pediatric Population; Public Meeting; Establishment of a Public Docket; Request for Comments

On behalf of the Big Cities Health Coalition (BCHC), I write to provide comment in response to the request by the Food and Drug Administration (FDA) [Docket No. FDA-2025-N-1557] for information on the clinical use and safety concerns associated with the use of orally ingestible prescription drug products containing fluoride in the pediatric population. BCHC is comprised of health officials leading 35 of the nation's largest metropolitan health departments, who together serve more than 61 million — or about one in five — Americans. Our members work every day to keep America's communities safe and healthy.

As requested, comments include evidence supporting the current clinical use of fluoride, factors considered when prescribing fluoride supplements, safety issues, and the convergence of evidence related to the use of fluoride supplements and the health of the pediatric population in the United States.

Fluoride Remains Necessary for the Pediatric Population

Tooth decay remains an endemic disease. Dental caries is the most common chronic disease of children, with over a third of children in the United States suffering from this condition before age 5 years. Tooth decay results in children missing school, having toothaches, developing facial abscesses, and the need for expensive treatment that in very young or medically compromised children can involve sedation and/or general anesthesia.

In the 1930s, researchers conducting epidemiological studies identified populations consuming water with different amounts of naturally occurring fluoride due to the types of rock and aquifer that contacted the water. Multiple studies concluded that consuming small amounts of fluoridated water resulted in a reduction in tooth decay (30-50% depending on the study). A child's exposure to fluoride comes from a variety of sources, including food, beverages, and dental preventive products. The total daily fluoride intake varies based on differing exposures and for infants may range from 0.05 to 0.025 mg F/kg body weight.[1] Studies have suggested that a total daily fluoride intake of 0.05 to 0.07 mg F/kg body weight is protective against developing tooth decay without safety issues or the development of dental fluorosis.[2]

Children consuming fluoridated water have the benefit of frequent, low-dose fluoride exposures that act both systemically and topically to provide optimal caries prevention with maximum safety. Children consuming water deficient in fluoride results in a daily total fluoride intake that is suboptimal and does not aid in the prevention of dental caries.

Pediatric and oral health care providers consider these risk factors, along with others such as diet, tooth defects, history of dental caries, and medications being taken by the child, to determine if the child could benefit from fluoride supplements. Consideration of recommending fluoride supplements involves assessing alternatives such as purchasing fluoridated water, and the likelihood of compliance if fluoride supplements are prescribed.

Recommendations for fluoride dietary supplementation began in the 1940s based on dietary intake studies, natural fluoride consumption levels, and associations of optimal amounts related to tooth decay and dental fluorosis. The dosage and use of fluoride supplements have evolved based on access to fluoridated drinking water, child development, dental development, and the individual child's need for caries prevention measures based on their risk for developing the disease in the future.[3]

Fluoride is known to have a preventive effect on tooth decay, and the mechanisms for this are well-studied and understood. Tooth minerals are composed of the chemical known as carbonate-substituted hydroxyapatite. The outer layer of the tooth crown is made of enamel and is almost 100% mineral by weight. It is the hardest substance in the human body. When exposed to acids, such as those produced by the oral biofilm when it metabolizes carbohydrates, the tooth minerals dissolve, causing dental caries. The incorporation of fluoride into the tooth's mineral makes it less soluble in acid. The reason for this decreased acid solubility is that incorporating fluoride into tooth mineral during development and mineralization of the dentition results in tighter packing of the mineral ions making the ions more adherent and thus more resistant to being pulled apart by acids.[4] Exposure of developing teeth to fluorides from dietary fluoride supplements or drinking water is sufficient to provide this protective health benefit that results in a substantial decrease in tooth decay for the population.

The observation of a reduction in tooth decay in populations consuming naturally occurring fluoridated water led to extensive research using animal models (predominantly rodents) that confirmed that fluoride in the drinking water reduced the occurrence of dental caries. Over the ensuing decades, additional clinical studies in humans and animals showed that fluoride supplements decreased the incidence of dental caries in permanent teeth, with little evidence supporting a reduction in caries in primary teeth.[5] The use of fluoride supplements in a special health care needs population (age 6-12 years) showed a 30% reduction in tooth decay over a two-year period.[6]

Impact of Fluoride Supplements or Optimally Fluoridated Water

Immune System Safety

A recent review on fluoride consumption and the potential for immune damage lists a variety of possible mechanisms that could involve the bone marrow, thymus, spleen, immune cells, and cytokines.[12] The studies reviewed are animal studies using models from rodents to fish and assessed high concentrations of fluoride (e.g. 100 ppm F) and did not study low concentrations equivalent to fluoride supplements or water fluoridation.[12,13]

Neurobehavioral Safety

Neurobehavioral effects of fluoride have been studied extensively over the past decade using a variety of models. Numerous human studies addressing this issue, including multiple systematic reviews, are available. One of the more recent reviews was developed as part of the National Toxicology Program to help inform on the state of science related to fluoride and neurodevelopment.[14,15] This study reviewed 74 studies and concluded there was no association between fluoride exposure below 1.5 ppm F in drinking water (more than twice the currently recommended community water recommendation in the United States) and outcomes such as IQ related to neurodevelopment of children. Other systematic reviews on this topic support no association between IQ and fluoride exposure, while others show negative associations at fluoride levels higher than 1.5.[16,17]

Studies in Australia and New Zealand (many fluoride/neurodevelopment studies were conducted in China and Middle East countries) show no effect on community water fluoridation and IQ.[17,18] A long-term study evaluating IQ and fluoride supplement use prior to age 5 years showed no change in IQ throughout childhood and up to age 38 years.[18]

The evidence from animal studies is inconclusive while human studies strongly support that there are not negative cognitive or neurobehavioral outcomes from children consuming fluoride supplements or community water fluoridation.[19]

Other Ogans and Fluoride Effects

A recent and extensive systematic review on fluoride toxicity that included 89 human studies, 199 animal studies, and 10 major reviews found there is limited evidence to evaluate the association of thyroid hormone disruption, sex hormone disruption, kidney dysfunction, and fluoride exposures relevant to current North American drinking water levels.[20]

Systematic reviews report that the evidence available for thyroid disease risk as associated with fluoride exposure is too limited to draw conclusions although there appear to be trends towards thyroid function changes at excessively high fluoride exposures.[20,21]

Potential Impact of Removing Fluoride Supplements from the Market

The use of fluoride supplements has declined over recent decades due to the widespread access to community water fluoridation (CWF) across the United States (over 70% of the US population). This trend is now changing as states are removing the autonomy for municipalities to choose CWF. The result of de-fluoridating will be an increase in dental caries, days children miss school, increased health care costs, increased emergency room visits, increased oral health disparities, and an overall decrease in health and quality of life for the children of the US.

These outcomes are based on communities and populations that have removed fluoride from the drinking water and monitored the populations' oral health and oral health care needs.[22,23]

Fluoride is the most effective therapeutic measure ever applied to the management of rampant and costly human disease – dental caries. While topical fluoride applications are beneficial, there are downsides, including cost and compliance. There are no chemotherapeutic substitutes that work as well as the combination of systemic and topical fluorides.

In closing, it is important to remember that fluoride supplements have been used since the late 1940s and have been proven to be an effective tool for helping control the highly prevalent global disease, dental caries. Concerns over the safety related to fluorides have been discussed and investigated since the element was first discovered and isolated in the late 1800s. The convergence of evidence, assessing a variety of experimental models, indicates that systemic fluoride consumption at the concentrations used for community water fluoridation and fluoride supplements are safe for children. Given the consequences of unchecked tooth decay for a child and the discomfort and expense of treatment, the FDA is urged to recognize and recommend the continued availability and use of systemic fluorides in this, our most deserving population.

We at BCHC greatly appreciate the opportunity to provide input on such a critical matter to the public's health. Please do not hesitate to contact me (juliano@bigcitieshealth.org) if we can be of further assistance.

Sincerely,

Chrissie Juliano, MPP
Executive Director

Citations

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