

# International Academy of Oral Medicine and Toxicology (IAOMT) Comprehensive Review on Fluoride in Drugs (including "Supplements")

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## Section 1: Chemical Profile and Examples of Products with Added Fluoride

Fluorine (F) is the ninth element on the periodic table and is a member of the halogen family. Fluoride (F-) is a chemical ion of fluorine that contains an extra electron, thereby giving it a negative charge. Fluoride is not essential for human growth and development.<sup>1</sup> In fact, it is not required for any physiological process in the human body; consequently, no one will suffer from a lack fluoride. In 2014, Dr. Philippe Grandjean of the Harvard School of Public Health and Dr. Philipp J. Landrigan of Icahn School of Medicine at Mount Sinai identified fluoride as one of 12 industrial chemicals known to cause developmental neurotoxicity in humans.<sup>2</sup>

Other than its natural existence in minerals, as well as in soil, water, and air, fluoride is also chemically synthesized for use in community water fluoridation, dental products, and other manufactured items, as shown in Table 1.

Table 1: Examples of Products that May Contain Added Fluoride

Artificially fluoridated municipal water	Beverages (made with fluoridated water)
Dental cements with fluoride	Dental fillings with fluoride
Dental gels with fluoride	Dental varnishes with fluoride
Floss with fluoride	Fluoride drugs ("supplements")
Food (that contains or has been exposed to fluoride)	Mouthwash with fluoride
Pesticides with fluoride	Pharmaceutical drugs with perfluorinated compounds
Stain resistant and waterproof items with PFCs	Toothpaste with fluoride

# Section 2: Brief History of Fluoride's Use for Alleged Dental Purposes

Human knowledge of the mineral fluorspar dates back centuries.<sup>3</sup> However, the discovery of how to isolate fluorine from its compounds is an essential date in the history of humankind's use of fluoride: Several scientists were killed in early experiments involving attempts to generate elemental fluorine, but in 1886, Henri Moissan reported the isolation of elemental fluorine, which earned him the Nobel Prize in chemistry in 1906.<sup>4</sup> <sup>5</sup>

This discovery paved the way for human experimentation to begin with chemically synthesized fluorine compounds, which were eventually utilized in a number of industrial activities. Notably, uranium fluoride and thorium fluoride were used during the years of 1942-1945 as part of the Manhattan Project<sup>6</sup> to produce the first atomic bomb. Data from reports about the Manhattan Project, some of which were initially classified and unpublished, include mention of fluoride poisoning and its role in the hazards of the uranium industry. As industry expanded during the 20<sup>th</sup> century, so did the use of fluoride for industrial processes, and cases of fluoride poisoning likewise increased. 8

Fluoride was not widely used for any dental purposes prior to the mid-1940's,<sup>9</sup> although it was studied for dental effects caused by its natural presence in community water supplies at varying levels. Early research in the 1930's by Frederick S. McKay, DDS, correlated high levels of fluoride with increased cases of dental fluorosis (a permanent damage to the enamel of the teeth that can occur in children from overexposure to fluoride) and demonstrated that reducing levels of fluoride resulted in lower rates of dental fluorosis.<sup>10</sup> This work led H. Trendley Dean, DDS, to research fluoride's minimal threshold of toxicity in the water supply.<sup>12</sup> In work published in 1942, Dean suggested that lower levels of fluoride might result in lower rates of dental caries.<sup>13</sup>

While Dean worked to convince others to test his hypothesis about adding fluoride to community water supplies as a means of reducing caries, not everyone supported the idea. In fact, an editorial published in the *Journal of the American Dental Association* (JADA) in 1944 denounced purposeful water fluoridation and warned of its dangers. <sup>14</sup>

A few months after this warning was issued, Grand Rapids, Michigan, became the first city to be artificially fluoridated on January 25, 1945. Dean had succeeded in his efforts to test his hypothesis, and in a landmark study, Grand Rapids was to serve as a test city, and its decay rates were to be compared with those of non-fluoridated Muskegon, Michigan. After only slightly more than five years, Muskegon was dropped as a control city, and the results published about the experiment only reported the decrease in caries in Grand Rapids. <sup>15</sup> Because the results did not include the control variable from the incomplete Muskegon data, many have stated that the initial studies presented in favor of water fluoridation were not even valid.

Concerns were made to the United States Congress in 1952 about potential dangers of water fluoridation, the lack of evidence as to its alleged usefulness in controlling dental caries, and the need for more research to be conducted. Yet, in spite of these concerns and many others, experiments with fluoridated drinking water continued. By 1960, fluoridation of drinking water for alleged dental benefits had spread to over 50 million people in communities throughout the United States.<sup>17</sup>

The use of fluoride in pharmaceutical drugs appears to have begun at about the same time as water fluoridation. Prior to the 1940's, the use of fluoride in American medicine was virtually unknown, with the exception of its rare use as an externally applied antiseptic and antiperiodic. There is a consensus among authors of scientific reviews about fluoride's addition to "supplements" that this pharmaceutical use was introduced no earlier than the mid-1940s and was not widely used until the late 1950s or early 1960s. Quinolones for clinical use were first discovered in 1962, and fluoroquinolones were created in the 1980's. Quinolones for clinical use were

Meanwhile, fluoridated toothpastes were introduced and their increase in the market occurred in the late 1960s and early 1970s.<sup>22</sup> By the 1980s, the vast majority of commercially available toothpastes in industrialized countries contained fluoride.<sup>23</sup>

Other fluoridated materials for dental purposes were likewise promoted for more common commercial use in recent decades. Glass ionomer cement materials, used for dental fillings, were invented in 1969,<sup>24</sup> and fluoride-releasing sealants were introduced in the 1970s.<sup>25</sup> Studies on the use of salt fluoridation for reduction of caries took place from 1965-1985 in Colombia, Hungary, and Switzerland.<sup>26</sup> Similarly, the use of fluoride in milk for caries management first began in Switzerland in 1962.<sup>27</sup>

# Section 3: Overview of U.S. Regulations for Fluoride "Supplements" and Fluorine-containing Drugs

Fluoride is intentionally added to pharmaceutical drugs (drops, tablets, and lozenges often called "supplements" or "vitamins") that are routinely prescribed to children, allegedly to prevent cavities. In 1975, the FDA addressed the use of fluoride supplements by withdrawing the new drug application for Ernziflur fluoride. After the FDA's actions on Ernziflur lozenges were published in the *Federal Register*, an article appeared in *Drug Therapy* stating that the FDA approval was withdrawn "because there is no substantial evidence of drug effectiveness as prescribed, recommended, or suggested in its labeling." The article also stated: "The FDA has therefore advised manufacturers of combination fluoride and vitamin preparations that their continued marketing is in violation of the new drug provisions of the Federal Food, Drug, and Cosmetic Act; they have, therefore, requested that marketing of these products be discontinued." 30 31

In 2016, the FDA sent yet another warning letter out about the same issue of unapproved new drugs in many forms including the fluoride supplements addressed in 1975. A letter, dated January 13, 2016, was sent to Kirkman Laboratories in regard to four different types of pediatric fluoride concoctions labeled as aids in the prevention of dental caries.<sup>32</sup> The FDA warning letter offered the company 15 days to become compliant with law<sup>33</sup> and serves as a yet another example of children hazardously receiving unapproved fluoride preparations, which has now been an issue in the U.S. for over 40 years.

Meanwhile, fluorine is also *permissibly* added to other pharmaceutical drugs. Some reasons that have been identified for its addition to drugs include claims that it can "increase the drug's selectivity, enable it to dissolve in fats, and decrease the speed at which the drug is metabolized, thus allowing it more time to work."<sup>34</sup> 20-30% of pharmaceutical compounds have been estimated to contain fluorine.<sup>35</sup> Some of the most popular drugs include Prozac, Lipitor, and Ciprobay (ciprofloxacin),<sup>36</sup> as well as the rest of fluoroquinolone family (gemifloxacin [marketed as Factive], levofloxacin [marketed as Levaquin], moxifloxacin [marketed as Avelox], norfloxacin [marketed as Noroxin], and ofloxacin [marketed as Floxin and generic ofloxacin]).<sup>37</sup>

In regard to fluoroquinolones, the FDA issued a new warning about disabling side effects in 2016, years after these drugs were first introduced to the market. In their July 2016 announcement, the FDA stated:

These medicines are associated with disabling and potentially permanent side effects of the tendons, muscles, joints, nerves, and central nervous system that can occur together in the same patient. As a result, we revised the Boxed Warning, FDA's strongest warning, to address these serious safety issues. We also added a new warning and updated other parts of the drug label, including the patient Medication Guide.<sup>38</sup>

Because of these debilitating side effects, the FDA advised that these drugs should only be used when there is no other treatment option available for patients because the risks outweigh the benefits.<sup>39</sup> At the time of this 2016 FDA announcement, it was estimated that over 26 million Americans were taking these drugs annually.<sup>40</sup>

## **Section 4: Health Effects of Fluoride**

In a 2006 report by the National Research Council (NRC) of the National Academy of Sciences in which the health risks of fluoride were evaluated, concerns were raised about potential associations between fluoride and osteosarcoma (a bone cancer), bone fractures, musculoskeletal effects, reproductive and developmental effects, neurotoxicity and neurobehavioral effects, genotoxicity and carcinogenicity, and effects on other organ systems.<sup>41</sup>

Since the NRC report was released in 2006, a number of other relevant research studies have been published. The discussion below includes a synopsis of some of the major research included in the 2006 NRC report, as well as some of the research of interest that has been published since that time.

#### Section 4.1: Skeletal System

Fluoride taken into the human body enters the bloodstream through the digestive tract. 42 Most of the fluoride that is not released through urine is stored in the body. It is generally stated that 99% of this fluoride resides in the bone, 43 where it is incorporated into the crystalline structure and accumulates over time. 44 Thus, it is indisputable that the teeth and bones are tissues of the body that concentrate the fluoride to which we are exposed.

In fact, in its 2006 report, the National Research Council (NRC)'s discussion on the danger of bone fractures from excessive fluoride was substantiated with significant research. Specifically, the report stated: "Overall, there was consensus among the committee that there is scientific evidence that under certain conditions fluoride can weaken bone and increase the risk of fractures." 45

#### Section 4.1.1: Dental Fluorosis

Exposure to excess fluoride in children is known to result in dental fluorosis, a condition in which the teeth enamel becomes irreversibly damaged and the teeth become permanently discolored, displaying a white or brown mottling pattern and forming brittle teeth that break and stain easily. <sup>46</sup> It has been scientifically recognized since the 1940's that overexposure to fluoride causes this condition, which can range from very mild to severe. According to data from the Centers for Disease Control and Prevention (CDC) released in 2010, 23% of Americans aged 6-49 and 41% of children aged 12-15 exhibit fluorosis to some degree. <sup>47</sup> These drastic increases in rates of dental fluorosis were a crucial factor in the Public Health Service's decision to lower its water fluoridation level recommendations in 2015. <sup>48</sup>

<u>Figure 1: Dental Fluorosis Ranging from Very Mild to Severe</u> (Photos from Dr. David Kennedy and are used with permission from victims of dental fluorosis.)



Section 4.1.2: Skeletal Fluorosis and Arthritis

Like dental fluorosis, skeletal fluorosis is an undeniable effect of overexposure to fluoride. Skeletal fluorosis causes denser bones, joint pain, a limited range of joint movement, and in severe cases, a completely rigid spine.<sup>49</sup> Although considered rare in the U.S., the condition does occur,<sup>50</sup> and it has been recently suggested that skeletal fluorosis could be more of a public health issue than previously recognized.<sup>51</sup>

As research published in 2016 noted, there is not yet a scientific consensus as to how much fluoride and/or how long levels of fluoride need to be taken in before skeletal fluorosis occurs.<sup>52</sup> While some authorities have suggested skeletal fluorosis only occurs after 10 years or more of exposure, research has shown that children can develop the disease in as little as six months,<sup>53</sup> and some adults have developed it in as little as two to seven years.<sup>54</sup> Similarly, while some authorities have suggested that 10 mg/day of fluoride is necessary to develop skeletal fluorosis, research has reported that much lower levels of exposure to fluoride (in some cases less than 2ppm) can also cause the disease.<sup>55</sup> Furthermore, research published in 2010 confirmed that skeletal tissue response to fluoride varies by individual.<sup>56</sup>

In patients with skeletal fluorosis, fluoride has also been suspected of causing secondary hyperparathyroidism and/or causing bone damage resembling secondary hyperparathyroidism. The condition, which commonly results from kidney disease, is triggered when the levels of calcium and phosphorous in the blood are too low.<sup>57</sup> A number of studies that have been collected by the Fluoride Action Network (FAN) examine the possibility that fluoride is one contributor to this health effect.<sup>58</sup>

Because arthritic symptoms are associated with skeletal fluorosis, arthritis is another area of concern in relation to fluoride exposures. Notably in this regard, research has linked fluoride to osteoarthritis, both with or without skeletal fluorosis. Additionally, temporomandibular joint disorder (TMJ) has been associated with dental and skeletal fluorosis. How the skeletal fluorosis. How the skeletal fluorosis is another area of concern in relation to fluoride exposures. Notably in this regard, research has linked fluoride to osteoarthritis, both with or without skeletal fluorosis. How the skeletal fluorosis is another area of concern in relation to fluoride exposures.

## Section 4.1.3: Cancer of the Bone, Osteosarcoma

In 2006, the NRC discussed a potential link between fluoride exposure and osteosarcoma. This type of bone cancer has been recognized as "the sixth most common group of malignant tumors in children and the third most common malignant tumor for adolescents." The NRC stated that while evidence was tentative, fluoride appeared to have the potential to promote cancers. They elucidated that osteosarcoma was of significant concern, especially because of fluoride deposition in bone and the mitogenic effect of fluoride on bone cells. 63

While some studies have failed to find an association between fluoride and osteosarcoma, according to the research completed by Dr. Elise Bassin while at Harvard School of Dental Medicine, exposure to fluoride at recommended levels correlated with a seven-fold increase in osteosarcoma when boys were exposed between the ages of five and seven. Bassin's research, published in 2006, is the only study about osteosarcoma that has taken age-specific risks into account. 155

# Section 4.2: Central Nervous System

The potential for fluorides to impact the brain have been well-established. In their 2006 report, the NRC explained: "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 and the body by direct and indirect means." Both dementia and Alzheimer's disease are also mentioned in the NRC report for consideration as being potentially linked to fluoride. 67

These concerns have been substantiated. Studies about water fluoridation and IQ effects were closely examined in research published in October of 2012 in *Environmental Health Perspectives*. In this meta-review, 12 studies demonstrated that communities with fluoridated water levels below 4 mg/L (average of 2.4 mg/L) had lower IQs than the control groups. Since the publication of the 2012 review, a number of additional studies finding reduced IQs in communities with less than 4 mg/L of fluoride in the water have become available. To be more precise, in a citizen petition to the EPA in 2016, Michael Connett, Esq., Legal Director of FAN, identified 23 studies reporting reduced IQ in areas with fluoride levels currently accepted as safe by the EPA.

Moreover, in 2014, a review was published in *The Lancet* entitled "Neurobehavioral effects of developmental toxicity." In this review, fluoride was listed as one of 12 industrial chemicals known to cause developmental neurotoxicity in human beings. The researchers warned: "Neurodevelopmental disabilities, including autism, attention-deficit hyperactivity disorder, dyslexia, and other cognitive impairments, affect millions of children worldwide, and some diagnoses seem to be increasing in frequency. Industrial chemicals that injure the developing brain are among the known causes for this rise in prevalence." The provided in the state of the provided in the state of the provided in the state of the provided in the provided in

#### Section 4.3: Cardiovascular System

According to statistics published in 2016, heart disease is the leading cause of death for both men and women in the U.S., and it costs the country \$207 billion annually. Thus, recognizing the potential relationship between fluoride and cardiovascular problems is essential not only for safe measures to be established for fluoride but also for preventative measures to be established for heart disease.

An association between fluoride and cardiovascular problems has been suspected for decades. The 2006 NRC report described a study from 1981 by Hanhijärvi and Penttilä that reported elevated serum fluoride in patients with cardiac failure. Fluoride has also been related to arterial calcification, arteriosclerosis, arteriosclerosis, eardiac insufficiency, electrocardiogram abnormalities, hypertension, and myocardial damage. Additionally, researchers of a study from China published in 2015 concluded: The results showed that, NaF [sodium fluoride], in a concentration dependent-manner and even at the low concentration of 2 mg/L, changed the morphology of the cardiomyocytes, reduced cell viability, increased the cardiac arrest rate, and enhanced the levels of apoptosis.

## Section 4.4: Endocrine System

Fluoride's effects on the endocrine system, which consists of glands that regulate hormones, have also been studied. In the 2006 NRC report, it was stated: "In summary, evidence of several types indicates that fluoride affects normal endocrine function or response; the effects of the fluoride-induced changes vary in degree and kind in different individuals." The 2006 NRC report further included a table demonstrating how extremely low doses of fluoride have been found to disrupt thyroid function, especially when there was a deficiency in iodine present. In more recent years, the impact of fluoride on the endocrine system has been re-emphasized. A study published in 2012 included sodium fluoride on a list of endocrine disrupting chemicals (EDCs) with low-dose effects, and the study was cited in a 2013 report from the United Nations Environment Programme and the World Health Organization.

Meanwhile, increased rates of thyroid dysfunction have been associated with fluoride. Research published in 2015 by researchers at the University of Kent in Canterbury, England, noted that higher levels of fluoride in drinking water could predict higher levels of hypothyroidism. They further explained: "In many areas of the world, hypothyroidism is a major health concern and in addition to other factors—such as iodine deficiency—fluoride exposure should be considered as a contributing factor. The findings of the study raise particular concerns about the validity of community fluoridation as a safe public health measure." Other studies have supported the association between fluoride and hypothyroidism, an increase in thyroid stimulating hormone (THS), and iodine deficiency.

According to statistics released by the Centers for Disease Control and Prevention (CDC) in 2014, 29.1 million people or 9.3% of the population have diabetes. 93 Again, the potential role of fluoride in this condition is essential to consider. The 2006 NRC report warned:

The conclusion from the available studies is that sufficient fluoride exposure appears to bring about increases in blood glucose or impaired glucose tolerance in some individuals and to increase the severity of some types of diabetes. In general, impaired glucose metabolism appears to be associated with serum or plasma fluoride concentrations of about 0.1 mg/L or greater in both animals and humans (Rigalli et al. 1990, 1995; Trivedi et al. 1993; de al Sota et al. 1997). 94

Research has also associated diabetes with a reduced capacity to clear fluoride from the body, <sup>95</sup> as well as a syndrome (polydispsia-polyurea) that results in increased intake of fluoride, <sup>96</sup> and research has also linked insulin inhibition and resistance to fluoride. <sup>97</sup>

Also of concern is that fluoride appears to interfere with functions of the pineal gland, which helps control circadian rhythms and hormones, including the regulation of melatonin and reproductive hormones. Jennifer Luke of the Royal Hospital of London has identified high levels of fluoride accumulated in the pineal gland <sup>98</sup> and further demonstrated that these levels could reach up to 21,000 ppm, rendering them higher than the fluoride levels in the bone or teeth. <sup>99</sup> Other studies have linked fluoride to melatonin levels, <sup>100</sup> insomnia, <sup>101</sup> and early puberty in girls, <sup>102</sup> as well as lower fertility rates (including men) and reduced testosterone levels. <sup>103</sup>

## Section 4.5: Renal System

Urine is a major route of excretion for fluoride taken into the body, and the renal system is essential for the regulation of fluoride levels in the body. 104 105 Urinary excretion of fluoride is influenced by urine pH, diet, presence of drugs, and other factors. 106 Researchers of a 2015 article published by the Royal Society of Chemistry explained: "Thus, plasma and the kidney excretion rate constitutes the physiologic balance determined by fluoride intake, uptake to and removal from bone and the capacity of fluoride clearance by the kidney." 107

The 2006 NRC report likewise recognized the role of the kidney in fluoride exposures. They noted that it is not surprising for patients with kidney disease to have increased plasma and bone fluoride concentrations. They further stated that human kidneys "have to concentrate fluoride as much as 50-fold from plasma to urine. Portions of the renal system may therefore be at higher risk of fluoride toxicity than most soft tissues." 109

In light of this information, it makes sense that researchers have indeed linked fluoride exposures to problems with the renal system. More specifically, researchers from Toronto, Canada, demonstrated that dialysis patients with renal osteodystrophy had high levels of fluoride in the bone and concluded that "bone fluoride may diminish bone microhardness by interfering with mineralization." <sup>110</sup>

# Section 4.6: Respiratory System

The effects of fluoride on the respiratory system are most clearly documented in literature about occupational exposures. Strictly from an occupational standpoint, the aluminum industry has been the subject of an array of investigations into fluoride's impact on the respiratory systems of workers. Evidence from a series of studies indicates a correlation between workers at aluminum plants, exposures to fluoride, and respiratory effects, such as emphysema, bronchitis, and diminished lung function.<sup>111</sup>

#### Section 4.7: Digestive System

Upon ingestion, including through fluoridated water, fluoride is absorbed by the gastrointestinal system where it has a half-life of 30 minutes. The amount of fluoride absorbed is dependent upon calcium levels, with higher concentrations of calcium lowering gastrointestinal absorption. Also, according to research published in 2015 by the American Institute of Chemical Engineers, fluoride's interaction in the gastrointestinal system results in formation of hydrofluoric [HF] acid by reacting with hydrochloric [HCL] acid present in the stomach. Being highly corrosive, the HF acid so formed will destroy the stomach and intestinal lining with the loss of microvilli.

Another area of research related to fluoride's impact on the gastrointestinal tract is the accidental ingestion of toothpaste. In 2011, the Poison Control Center received 21,513 calls related to overconsumption of fluoridated toothpaste. The numbers of impacted individuals are likely to be much higher, however. Concerns have been raised that some gastrointestinal symptoms might not be readily considered as related to fluoride ingestion, as researchers explained in 1997:

Parents or caregivers may not notice the symptoms associated with mild fluoride toxicity or may attribute them to colic or gastroenteritis, particularly if they did not see the child ingest fluoride. Similarly, because of the nonspecific nature of mild to moderate symptoms, a physician's differential diagnosis is unlikely to include fluoride toxicity without a history of fluoride ingestion. 117

Other areas of the digestive system are also known to be impacted by fluoride. For example, the 2006 NRC report called for more information about fluoride's effect on the liver: "It is possible that a lifetime ingestion of 5-10 mg/day from drinking water containing fluoride at 4 mg/L might turn out to have long-term effects on the liver, and this should be investigated in future epidemiologic studies." As another example, fluoride toothpaste may cause stomatitis, such as mouth and canker sores in some individuals. 119

#### Section 4.8: Immune System

The immune system is yet another part of the body that can be impacted by fluoride. An essential consideration is that immune cells develop in the bone marrow, so the effect of fluoride on the immune system could be related to fluoride's prevalence in the skeletal system. The 2006 NRC report elaborated on this scenario:

Nevertheless, patients who live in either an artificially fluoridated community or a community where the drinking water naturally contains fluoride at 4 mg/L have all accumulated fluoride in their skeletal systems and potentially have very high fluoride concentrations in their bones. The bone marrow is where immune cells develop and that could affect humoral immunity and the production of antibodies to foreign chemicals. <sup>120</sup>

Allergies and hypersensitivities to fluoride are another risk component related to the immune system. Research published in 1950's, 1960's, and 1970's showed that some people are hypersensitive to fluoride. <sup>121</sup> Interestingly, authors of research published in 1967 pointed out that while some still questioned the fact that fluoride in toothpaste and "vitamins" could cause sensitivities, the case reports presented in their publication established that allergic reactions to fluoride do exist. <sup>122</sup> More recent studies have confirmed this reality. <sup>123</sup>

## Section 4.9: Integumentary System

Fluoride can also impact the integumentary system, which consists of the skin, exocrine glands, hair, and nails. In particular, reactions to fluoride, including fluoride used in toothpaste, have been linked to acne and other dermatological conditions. 124 125 126 Moreover, a potentially life-threatening condition known as fluoroderma is caused by a hypersensitive reaction to fluorine, 127 and this type of skin eruption (a halogenoderma) has been associated with patients using fluoridated dental products. 128 Additionally, hair and nails have been studied as biomarkers of fluoride exposure. 129 Nail clippings are capable of demonstrating chronic fluoride exposures 130 and exposures from toothpaste, 131 and using fluoride concentrations in nails to identify children at risk for dental fluorosis has been examined. 132

## Section 4.10: Fluoride Toxicity

Fluoride toxicity from a dental product in the United States occurred in 1974 when a three-year old Brooklyn boy died due to a fluoride overdose from dental gel. A reporter for the *New York Times* wrote of the incident: "According to a Nassau County toxicologist, Dr. Jesse Bidanset, William ingested 45 cubic centimeters of 2 percent stannous fluoride solution, triple an amount sufficient to have been fatal." <sup>133</sup>

The urgency for fluoride toxicity to be more widely recognized was explored in a 2005 publication entitled "Fluoride poisoning: a puzzle with hidden pieces." Author Phyllis J. Mullenix, PhD, began the article, which was presented in part at the American College of Toxicology Symposium, by warning: "A history of enigmatic descriptions of fluoride poisoning in the medical literature has allowed it to become one of the most misunderstood, misdiagnosed, and misrepresented health problems in the United States today." <sup>134</sup>

#### **Section 5: Exposure Levels**

Due to increased rates of dental fluorosis and increased sources of exposure to fluoride, the Public Health Service (PHS) lowered its recommended levels of fluoride in community drinking water set at 0.7 to 1.2 milligrams per liter in 1962<sup>135</sup> to 0.7 milligrams per liter in 2015.<sup>136</sup> The need to update previously established fluoride levels for all products is extremely urgent, as fluoride exposures have obviously surged for Americans since the 1940's, when community water fluoridation was first introduced.

# Section 5.1: Multiple Sources of Fluoride Exposure

Understanding fluoride exposure levels from *all sources* is crucial because recommended intake levels for fluoride should be based upon these common multiple exposures. The concept of evaluating fluoride exposure levels from multiple sources was addressed in the 2006 National Research Council (NRC) report, which acknowledged the difficulties with accounting for all sources and individual variances. Yet, the NRC authors attempted to calculate combined exposures from pesticides/air, food, toothpaste, and drinking water. While these calculations did not include exposures from other dental materials, pharmaceutical drugs, and other consumer products, the NRC still recommended to lower the MCLG for fluoride, which has not yet been accomplished.

The American Dental Association (ADA), which is a trade group and not a government entity, has recommended that collective sources of exposure should be taken into account. In particular, they have recommended that research should "estimate the total fluoride intake from all sources individually and in combination." Furthermore, in an article about the use of fluoride "supplements" (prescription drugs given to patients, usually children, that contain additional fluoride), the ADA mentioned that all sources of fluoride should be evaluated and that "patient exposure to multiple water sources can make proper prescribing complex." <sup>141</sup>

Several studies conducted in the U.S. have offered data about multiple exposures to fluoride, as well as warnings about this current situation. A study published in 2005 by researchers at the University of Illinois at Chicago evaluated fluoride exposures in children from drinking water, beverages, cow's milk, foods, fluoride "supplements," toothpaste swallowing, and soil ingestion. They found that the reasonable maximum exposure estimates exceeded the upper tolerable intake and concluded that "some children may be at risk for fluorosis." It's

Additionally, a study published in 2015 by researchers at the University of Iowa considered exposures from water, toothpaste, fluoride "supplements," and foods. <sup>144</sup> They found considerable individual variation and offered data showing that some children exceeded the optimal range. They specifically stated: "Thus, it's doubtful that parents or clinicians could adequately track children's fluoride intake and compare it [to] the recommended level, rendering the concept of an 'optimal' or target intake relatively moot." <sup>145</sup>

#### Section 5.2: Pharmaceutical Drugs (Including Supplements)

20-30% of pharmaceutical compounds have been estimated to contain fluorine. <sup>146</sup> Fluorine is used in drugs as anesthetics, antibiotics, anti-cancer and anti-inflammatory agents, psychopharmaceuticals, <sup>147</sup> and in many other applications. Some of the most popular fluorine-containing drugs include Prozac and Lipitor, as well as the fluoroquinolone family (ciprofloxacin [marketed as Ciprobay], <sup>148</sup> gemifloxacin [marketed as Factive], levofloxacin [marketed as Levaquin], moxifloxacin [marketed as Avelox], norfloxacin [marketed as Noroxin], and ofloxacin [marketed as Floxin and generic ofloxacin]). <sup>149</sup> The fluorinated compound fenfluramine (fenphen) was also used for many years as an anti-obesity drug, <sup>150</sup> but it was removed from the market in 1997 due to its link with heart valve problems. <sup>151</sup>

Fluoride accumulation in tissue as a result of exposure to these pharmaceuticals is one potential culprit in quinolone chondrotoxicity, <sup>152</sup> and fluoroquinolones have received media attention as a result of their serious health risks. Reported side effects from fluoroquinolones include retinal detachment, kidney failure, depression, psychotic reactions, and tendinitis. <sup>153</sup> In a *New York Times* article published in 2012 about the controversial family of drugs, writer Jane E. Brody revealed that more than 2,000 lawsuits have been filed over the fluoroquinolone Levaquin. <sup>154</sup> In 2016, the FDA acknowledged "disabling and potentially permanent side effects" caused by fluoroquinolones and advised that these drugs only be used when there is no other treatment option available for patients because the risks outweigh the benefits. <sup>155</sup>

Defluorination of any type of fluorinated drug can occur, and this, among other risks, led researchers to conclude in a 2004 review: "No one can responsibly predict what happens in a human body after administration of fluorinated compounds. Large groups of people, including neonates, infants, children, and ill patients serve thus as the subjects of pharmacological and clinical research." <sup>156</sup>

One other major type of prescription drug is essential to consider in regard to overall fluoride exposure levels. Many dentists prescribe fluoride tablets, drops, lozenges, and rinses, which are often referred to as fluoride "supplements" or "vitamins." These products contain 0.25, 0.5, or 1.0 mg fluoride, <sup>157</sup> and they are **not approved** as safe and effective for caries prevention by the FDA. <sup>158</sup>

The dangers of these fluoride "supplements" have been made clear. The author of a 1999 publication warned: "Fluoride supplements, when ingested for a pre-eruptive effect by infants and young children in the United States, therefore, now carry more risk than benefit." Similarly, the 2006 NRC report established that age, risk factors, ingestion of fluoride from other sources, inappropriate use, and other considerations should be taken into account for these products. The NRC report further included statistics that "all children through age 12 who take fluoride supplements (assuming low water fluoride) will reach or exceed 0.05-0.07 mg/kg/day." 161

Yet, these products continue to be prescribed by dentists and regularly used by consumers, especially children, the even as concerns about fluoride "supplements" continue to be repeated. For example, researchers of a Cochrane Collaboration review published in 2011 advised: "No data were available concerning adverse effects related to fluoride supplementation in children aged less than 6 years. The ratio benefit/risk of fluoride supplementation was thus unknown for young children." Moreover, in 2015, scientists conducting an analysis of fluoride in toothpaste and fluoride supplements wrote: "Taking into consideration the toxicity of fluorides, more strict control of fluoride content in pharmaceutical product[s] for oral hygiene is proposed." 164

## Section 5.3: Individualized Responses and Susceptible Subgroups

Setting one universal level of fluoride as a recommended limit is problematic because it does not take individualized responses into account. While age, weight, and gender are *sometimes* considered in recommendations, the current EPA regulations for water prescribe one level that applies to everyone, regardless of infants and children and their known susceptibilities to fluoride exposures. Such a "one dose fits all" level also fails to address allergies to fluoride, <sup>165</sup> genetic factors, <sup>166</sup> <sup>167</sup> <sup>168</sup> nutrient deficiencies, <sup>169</sup> and other personalized factors known to be pertinent to fluoride exposures.

The NRC recognized such individualized responses to fluoride numerous times in their 2006 publication, <sup>170</sup> and other research has affirmed this reality. For example, urine pH, diet, presence of drugs, and other factors have been identified as relative to the amount of fluoride excreted in the urine. <sup>171</sup> As another example, fluoride exposures of non-nursing infants were estimated to be 2.8-3.4 times that of adults. <sup>172</sup> The NRC further established that certain subgroups have water intakes that greatly vary from any type of assumed average levels:

These subgroups include people with high activity levels (e.g., athletes, workers with physically demanding duties, military personnel); people living in very hot or dry climates, especially outdoor workers; pregnant or lactating women; and people with health conditions that affect water intake. Such health conditions include diabetes mellitus, especially if untreated or poorly controlled; disorders of water and sodium metabolism, such as diabetes insipidus; renal problems resulting in reduced clearance of fluoride; and short-term conditions requiring rapid rehydration, such as gastrointestinal upsets or food poisoning. <sup>173</sup>

Considering that the rate of diabetes is on the rise in the U.S., with over 9% (29 million) Americans impacted, <sup>174</sup> this particular subgroup is especially essential to factor into account. Furthermore, when added to the other subgroups mentioned in the NRC report above (including infants and children), it is apparent that hundreds of millions of Americans are at risk from the current levels of fluoride added to community drinking water.

The American Dental Association (ADA), a trade-based group that promotes water fluoridation, <sup>175</sup> has also recognized the issue of individual variance in fluoride intake. They have recommended for research to be conducted to "[i]dentify biomarkers (that is, distinct biological indicators) as an alternative to direct fluoride intake measurement to allow the clinician to estimate a person's fluoride intake and the amount of fluoride in the body."<sup>176</sup>

Additional comments from the ADA provide even more insight into individualized responses related to fluoride intake. The ADA has recommended to "[c]onduct metabolic studies of fluoride to determine the influence of environmental, physiological and pathological conditions on the pharmacokinetics, balance and effects of fluoride." Perhaps most notably, the ADA has also acknowledged the susceptible subgroup of infants. In regard to infant exposure from fluoridated water used in baby formula, the ADA recommends following the American Academy of Pediatrics guideline that breastfeeding should be exclusively practiced until the child is six months old and continued until 12 months, unless contraindicated. 178

While suggesting to exclusively breastfeed infants is certainly protective of their fluoride exposures, it is simply not practical for many American women today. The authors of a study published in 2008 in *Pediatrics* reported that only 50% of women continued to breast feed at six months and only 24% of women continued to breast feed at 12 months.<sup>179</sup>

What these statistics mean is that, due to infant formula mixed with fluoridated water, millions of infants most certainly exceed the optimal intake levels of fluoride based on their low weight, small size, and developing body. Hardy Limeback, PhD, DDS, a member of a 2006 National Research Council (NRC) panel on fluoride toxicity, and former President of the Canadian Association of Dental Research, has elaborated: "Newborn babies have undeveloped brains, and exposure to fluoride, a suspected neurotoxin, should be avoided." <sup>180</sup>

# Section 5.4: Interactions of Fluoride with Other Chemicals

The concept of multiple chemicals interacting within the human body to produce ill-health should now be an essential understanding required for practicing modern-day medicine. Researchers Jack Schubert, E. Joan Riley, and Sylvanus A. Tyler addressed this highly relevant aspect of toxic substances in a scientific article published in 1978. Considering the prevalence of chemical exposures, they noted: "Hence, it is necessary to know the possible adverse effects of two or more agents in order to evaluate potential occupational and environmental hazards and to set permissible levels." <sup>181</sup>

The need to study the health outcomes caused by exposures to a variety of chemicals has also been reported by researchers affiliated with a database which tracks associations between approximately 180 human diseases or conditions and chemical contaminants. Supported by the Collaborative on Health and the Environment, the researchers for this project, Sarah Janssen, MD, PhD, MPH, Gina Solomon, MD, MPH, and Ted Schettler, MD, MPH, clarified:

More than 80,000 chemicals have been developed, distributed, and discarded into the environment over the past 50 years. The majority of them have not been tested for potential toxic effects in humans or animals. Some of these chemicals are commonly found in air, water, food, homes, work places, and communities. Whereas the toxicity of one chemical may be incompletely understood, an understanding of the effect from exposures to mixtures of chemicals is even less complete. <sup>182</sup>

Clearly, the interaction of fluoride with other chemicals is crucial to understanding exposure levels and their impacts. While countless interactions have yet to be examined, several hazardous combinations have been established.

Aluminofluoride exposure occurs from ingesting a fluoride source *with* an aluminum source.<sup>183</sup> This synergistic exposure to fluoride and aluminum can occur through water, tea, food residue, infant formulas, aluminum-containing antacids or medications, deodorants, cosmetics, and glassware.<sup>184</sup> Authors of a research report published in 1999 described the hazardous synergy between these two chemicals: "In view of the ubiquity of phosphate in cell metabolism and together with the dramatic increase in the amount of reactive aluminum now found in ecosystems, aluminofluoride complexes represent a strong potential danger for living organisms including humans."<sup>185</sup>

Furthermore, fluoride, in its form of hydrofluosilicic acid (which is added to many water supplies to fluoridate the water), attracts manganese and lead (both of which can be present in certain types of plumbing pipes). Likely because of the affinity for lead, fluoride has been linked to higher blood lead levels in children, <sup>186</sup> especially in minority groups. <sup>187</sup> Lead is known to lower IQs in children, <sup>188</sup> and lead has even been linked to violent behavior. <sup>189</sup> <sup>190</sup> Other research supports the potential association of fluoride with violence. <sup>191</sup>

#### Section 6: Lack of Efficacy, Lack of Evidence, and Lack of Ethics

# Section 6.1: Lack of Efficacy

The fluoride in toothpastes and other consumer products is added because it allegedly reduces dental caries. The suggested benefits of this form of fluoride are related to its activity on teeth of inhibiting bacterial respiration of Streptococcus mutans, the bacterium that turns sugar and starches into a sticky acid that dissolves enamel. <sup>192</sup> In particular, the interaction of fluoride with the mineral component of teeth produces a fluorohydroxyapatite (FHAP or FAP), and the result of this action is said to be enhanced remineralization and reduced demineralization of the teeth. While there is scientific support for this mechanism of fluoride, it has also been established that fluoride primarily works to reduce tooth decay *topically* (i.e. scrubbing it directly onto to teeth with a toothbrush), as opposed to *systemically* (i.e. drinking or ingesting fluoride through water or other means). <sup>193</sup>

Although the *topical* benefits of fluoride have been distinctly expressed in scientific literature, research has likewise questioned these benefits. For example, researchers from the University of Massachusetts Lowell explained several controversies associated with topical uses of fluoride in an article published in the *Journal of Evidence-Based Dental Practice* in 2006. After citing a 1989 study from the National Institute of Dental Research that found minimal differences in children receiving fluoride and those not receiving fluoride, the authors referenced other studies demonstrating that cavity rates in industrialized countries have decreased

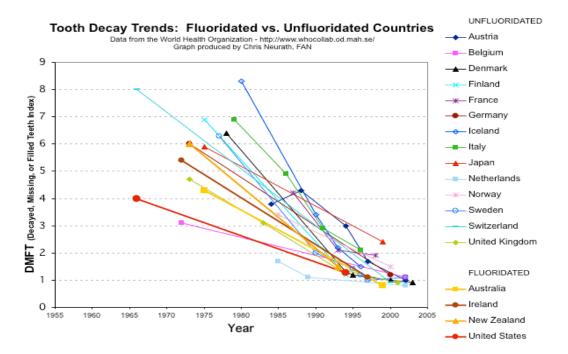
without fluoride use.<sup>194</sup> The authors further referenced studies indicating that fluoride does not aid in preventing pit and fissure decay (which is the most prevalent form of tooth decay in the U.S.) or in preventing baby bottle tooth decay (which is prevalent in poor communities).<sup>195</sup>

As another example, early research used to support water fluoridation as a means of reducing dental caries was later re-examined, and the potential of misleading data was identified. Initially, the reduction of decayed and filled deciduous teeth (DFT) collected in research was interpreted as proof for the efficacy of water fluoridation. However, subsequent research by Dr. John A. Yiamouyiannis suggested that water fluoridation could have contributed to the delayed eruption of teeth. Such delayed eruption would result in less teeth and therefore, the absence of decay, meaning that the lower rates of DFT were actually caused by the lack of teeth as opposed to the alleged effects of fluoride on dental caries.

Other examples in the scientific literature have questioned fluoride's use in preventing tooth decay. A 2014 review affirmed that fluoride's anti-caries effect is reliant upon calcium and magnesium in the tooth enamel but also that the remineralization process in tooth enamel is not dependent on fluoride. Research published in 2010 identified that the concept of "fluoride strengthening teeth" could no longer be deemed as clinically significant to any decrease in caries linked to fluoride use. Rurthermore, research has suggested that *systemic* fluoride exposure has minimal (if any) effect on the teeth, 199 200 and researchers have also offered data that dental fluorosis (the first sign of fluoride toxicity 201) is higher in U.S. communities with fluoridated water as opposed to those without it. 202

Still other reports show that as countries were developing, decay rates in the general population rose to a peak of four to eight decayed, missing, or filled teeth (in the 1960's) and then showed a dramatic decrease (to today's levels), regardless of fluoride use. It has been hypothesized that increased oral hygiene, access to preventative services, and more awareness of the detrimental effects of sugar are responsible for the visible decrease of tooth decay. Whatever the reasons might be, it should be noted that this trend of decreased tooth decay occurred with and without the systemic application of fluoridated water, <sup>203</sup> so it would appear that factors other than fluoride caused this change. Figure 2 below exhibits the tooth decay trends by fluoridated and non-fluoridated countries from 1955-2005.

Figure 2: Tooth Decay Trends in Fluoridated and Unfluoridated Countries, 1955-2005



Several other considerations are relevant in any decision about using fluoride to prevent caries. First, it should also be noted that fluoride is not an essential component for human growth and development. Second, fluoride has been recognized as one of 12 industrial chemicals "known to cause developmental neurotoxicity in human beings." And finally, the American Dental Association (ADA) called for more research in 2013 in regard to the mechanism of fluoride action and effects:

Research is needed regarding various topical fluorides to determine their mechanism of action and caries-preventive effects when in use at the current level of background fluoride exposure (that is, fluoridated water and fluoride toothpaste) in the United States. Studies regarding strategies for using fluoride to induce arrest or reversal of caries progression, as well as topical fluoride's specific effect on erupting teeth, also are needed.<sup>206</sup>

## Section 6.2: Lack of Evidence

References to the unpredictability of levels at which fluoride's effects on the human system occur have been made throughout this document. However, it is important to reiterate the lack of evidence associated with fluoride usage, and thus, Table 3 provides an abbreviated list of stringent warnings from governmental, scientific, and other pertinent authorities about the dangers and uncertainties related to fluoridated dental products used at home.

Table 3: Selected Quotes about Fluoride Warnings Categorized by Product/Process and Source

PRODUCT/	QUOTE/S	SOURCE OF INFORMATION
PROCESS	QUOTE/S	SOURCE OF INFORMATION
REFERENCED		
Fluoride "supplements" (tablets)	"Evident disagreements among the results show that there's a limited effectiveness on fluoride tablets."	Tomasin L, Pusinanti L, Zerman N. The role of fluoride tablets in the prophylaxis of dental caries. A literature review. <i>Annali di Stomatologia</i> . 2015 Jan;6(1):1.
Pharmaceuticals, fluorine in medicine	"No one can responsibly predict what happens in a human body after administration of fluorinated compounds."	Strunecká A, Patočka J, Connett P. Fluorine in medicine. <i>Journal of Applied Biomedicine</i> . 2004; 2:141-50.
Fluoride intake in children	"The 'optimal' intake of fluoride has been widely accepted for decades as between 0.05 and 0.07 mg fluoride per kilogram of body weight but is based on limited scientific evidence."  "These findings suggest that achieving a caries-free status may have relatively little to do with fluoride intake, while fluorosis is clearly more dependent on fluoride intake."	Warren JJ, Levy SM, Broffitt B, Cavanaugh JE, Kanellis MJ, Weber-Gasparoni K. Considerations on optimal fluoride intake using dental fluorosis and dental caries outcomes—a longitudinal study. <i>Journal of Public Health Dentistry</i> . 2009 Mar 1;69(2):111-5.

Review of safety	"If we were to consider only fluoride's	Prystupa J. Fluorine—a current
standards for	affinity for calcium, we would	literature review. An NRC and
exposure to	understand fluoride's far-reaching	ATSDR based review of safety
fluorine and	ability to cause damage to cells, organs,	standards for exposure to
fluorides	glands, and tissues."	fluorine and fluorides.
		Toxicology Mechanisms and
		Methods. 2011 Feb 1;21(2):103-
		70.

#### Section 6.3: Lack of Ethics

Another major concern about fluoride exposure from drinking water and food is related to the production of the fluorides used in community water supplies. According to the Centers for Disease Control and Prevention (CDC), three types of fluoride are generally used for community water fluoridation:

- Fluorosilicic acid: a water-based solution used by most water systems in the United States. Fluorosilicic acid is also referred to as hydrofluorosilicate, FSA, or HFS.
- Sodium fluorosilicate: a dry additive, dissolved into a solution before being added to water.
- Sodium fluoride: a dry additive, typically used in small water systems, dissolved into a solution before being added to water.<sup>207</sup>

Controversy has arisen over the industrial ties to these ingredients. The CDC has explained that phosphorite rock is heated with sulfuric acid to create 95% of the fluorosilicic acid used in water fluoridation. The CDC has further explained: "Because the supply of fluoride products is related to phosphate fertilizer production, fluoride product production can also fluctuate depending on factors such as unfavorable foreign exchange rates and export sales of fertilizer." A government document from Australia has more openly stated that hydrofluosilicic acid, sodium silicofluoride and sodium fluoride are *all* "commonly sourced from phosphate fertilizer manufacturers." Safety advocates for fluoride exposures have questioned if such industrial ties are ethical and if the industrial connection to these chemicals might result in a cover-up of the health effects caused by fluoride exposure.

Furthermore, it is easily recognizable that the dental industry has a major conflict of interest with fluoride because profits are made by corporations that produce fluoride-containing dental products. Additionally, procedures involving fluoride administered by the dentist and dental staff can also earn profits for dental offices, <sup>211</sup> <sup>212</sup> and ethical questions have been raised about pushing these fluoride procedures on patients. <sup>213</sup>

A specific ethical issue that arises with such industry involvement is that profit-driven groups seem to define the evolving requirements of what constitutes the "best" evidence-based research, and in the meantime, unbiased science becomes difficult to fund, produce, publish, and publicize. This is because funding a large-scale study can be very expensive, but industrial-based entities can easily afford to support their own researchers. They can also afford to spend time examining different ways of reporting the data (such as leaving out certain statistics to obtain a more favorable result), and they can further afford to publicize any aspect of the research that supports their activities. Unfortunately, history has shown that corporate entities can even afford to harass independent scientists as a means of ending their work if that work shows harm generated by industrial pollutants and contaminants.

Indeed, this scenario of unbalanced science has been recognized in fluoride research. Authors of a review published in *the Scientific World Journal* in 2014 elaborated: "Although artificial fluoridation of water supplies has been a controversial public health strategy since its introduction, researchers—whom include internationally respected scientists and academics—have consistently found it difficult to publish critical articles of community water fluoridation in scholarly dental and public health journals." <sup>214</sup>

In relation to the ethics of medical and dental practices, a cornerstone of public health policy known as the precautionary principle must be considered as well. The basic premise of this policy is built upon the centuries-old medical oath to "first, do no harm." Yet, the modern application of the precautionary principle is actually supported by an international agreement.

In January 1998, at an international conference involving scientists, lawyers, policy makers, and environmentalists from the U.S., Canada and Europe, a formalized statement was signed and became known as the "Wingspread Statement on the Precautionary Principle." In it, the following advice is given: "When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically. In this context the proponent of an activity, rather than the public, should bear the burden of proof."<sup>216</sup>

Not surprisingly, the need for the appropriate application of the precautionary principle has been associated with fluoride usage. Authors of a 2006 article entitled "What Does the Precautionary Principle Mean for Evidence-Based Dentistry?" suggested the need to account for cumulative exposures from all fluoride sources and population variability, while also stating that consumers can reach "optimal" fluoridation levels without ever drinking fluoridated water. Additionally, researchers of a review published in 2014 addressed the obligation for the precautionary principle to be applied to fluoride usage, and they took this concept one step further when they suggested that our modern-day understanding of dental caries "diminishes any major future role for fluoride in caries prevention." <sup>218</sup>

## **Section 7: Conclusion**

The sources of human exposure to fluoride have drastically increased since community water fluoridation began in the U.S. in the 1940's. In addition to water, these sources now include food, air, soil, pesticides, fertilizers, dental products used at home and in the dental office (some of which are implanted in the human body), pharmaceutical drugs, cookware, clothing, carpeting, and an array of other consumer items used on a regular basis. Official regulations and recommendations on fluoride use, many of which are not enforced, have been based on limited research and have only been updated after evidence of harm has been produced and reported.

Exposure to fluoride is suspected of impacting every part of the human body, including the cardiovascular, central nervous, digestive, endocrine, immune, integumentary, renal, respiratory, and skeletal systems. Susceptible subpopulations, such as infants, children, and individuals with diabetes or renal problems, are known to be more severely impacted by intake of fluoride. Accurate fluoride exposure levels to consumers are unavailable; however, estimated exposure levels suggest that millions of people are at risk of experiencing the harmful effects of fluoride and even toxicity, the first visible sign of which is dental fluorosis. A lack of efficacy, lack of evidence, and lack of ethics are apparent in the current status quo of fluoride usage.

Informed consumer consent is needed for all uses of fluoride, and this pertains to water fluoridation, as well as all dental-based products, whether administered at home or in the dental office. Providing education about fluoride risks and fluoride toxicity to medical and dental professionals, medical and dental students, consumers, and policy makers is crucial to improving the future of public health.

There are fluoride-free strategies in which to prevent dental caries. Given the current levels of exposure, policies should reduce and work toward eliminating avoidable sources of fluoride, including water fluoridation, fluoride-containing dental materials, and other fluoridated products, as means to promote dental and overall health.

This document consists of excerpts taken from the document entitled "International Academy of Oral Medicine and Toxicology (IAOMT) Position Paper against Fluoride Use in Water, Dental Materials, and Other Products for Dental and Medical Practitioners, Dental and Medical Students, Consumers, and Policy Makers."

Click here to access the full document.

#### **Endnotes:**

Enunotes

Dental Journal 1996;41(5):335-42, at 335 ("Around the same time (late 1940s), fluoride supplements seem to have been marketed in the US. Fluoride supplements were being distributed regularly in US non-fluoridated areas in the early 1960s."), attached as Exhibit 9; Szpunar SM, Burt BA. Evaluation of appropriate use of dietary fluoride supplements in the US. Community Dentistry & Oral Epidemiology 1992;20(3):148-54, at 148 ("There is no firm documentation on when [fluoride supplements] first came onto the market, but it seems to have been in the mid-to-late 1940s."), attached as Exhibit 10.

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<sup>18</sup> See Merck Index 1940, attached as Exhibit 5; see also Compilation of News Articles from 1920s/1930s discussing sodium fluoride's role as insecticide, attached as Exhibit 6. The rarity of using sodium fluoride as an antiseptic and antiperiodic is illustrated by the fact that the 1938 and 1940 editions of the United States Pharmacopeia do not include sodium fluoride as a substance with known therapeutic use. See Exhibits 7 and 8.

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