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- 1 Commentary
- 2 Fluoride and Fluorine Compounds in Consumer
- **3 Products: Nescience of Cumulative Sources of**

4 Chronic Exposure

5 David Kennedy, John Kall,* Griffin Cole, and Amanda Just

6 International Academy of Oral Medicine and Toxicology (IAOMT), ChampionsGate, FL, USA

7 *Correspondence: Email: jack.kall@iaomt.org; Telephone: +1 (863) 420-6373

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9 Abstract: Exposure to sources of fluoride and other fluorine compounds has significantly increased 10 for consumers since the 1940s when community water fluoridation was first initiated. In 11 subsequent decades, the use of fluoride was also introduced in dental products such as toothpaste, 12 mouthwash, and dental fillings. During this time frame, fluoride and fluorine compounds were 13 simultaneously added to an array of additional consumer products. For example, fluorinated 14 compounds are now used in a substantial quantity of pharmaceutical drugs, and perfluorinated 15 chemicals are used in carpets, cleaners, clothing, cookware, food packaging, paints, paper, and 16 other products. The purpose of this commentary is to identify sources of exposure to fluoride and 17 fluorine compounds, provide a brief synopsis of each product's contribution to overall intake 18 levels, and necessitate risk assessments, recommendations, and regulations that recognize a 19 lifetime of chronic exposure to these cumulative sources.

- Keywords: fluoride, fluorine compounds, perfluorinated chemicals, chronic daily fluoride
 exposure from air, drinking water, foods, dental products, and drugs
- 22

23 1. Introduction

Several scientists were killed in early experiments attempting 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. This discovery paved the way for human experimentation to begin with fluorine compounds, which were eventually utilized in a number of industrial activities.

The use of fluoride in consumer products was insignificant prior to the mid-1940s when it was first studied for dental effects in community water at varying levels. In spite of concerns [1] [2] (pp. 104-107), experiments with fluoridated drinking water continued. By 1960, water fluoridation for alleged dental benefits had spread to over 50 million people in communities throughout the U.S. [3].

32 The use of fluoride and fluorinated compounds in other consumer products began at about the 33 same time as water fluoridation was infiltrating communities across America. The production of 34 perfluorinated carboxylates (PFCAs) and perfluorinated sulfonates (PFSAs) in consumer products 35 began over sixty years ago [4]. Meanwhile, fluoridated toothpastes were likewise introduced, and 36 their increase in the market occurred in the late 1960s and early 1970s [5]. By the 1980s, the vast 37 majority of commercially available toothpastes in industrialized countries contained fluoride [6]. 38 Similarly, quinolones were first discovered in 1962, and fluoroquinolones (certain types of 39 antibiotics) were approved for use in clinical medicine in the 1980's [7, 8].

The growth in number and popularity of products containing fluoride and fluorine compounds has resulted in a lifetime of chronic exposure to consumers. Current intake estimates are generally reported on a product-by-product basis. However, risk assessments, recommended intake levels, and regulations must now recognize the overall exposure levels to fluoride and fluorinated compounds from this gamut of sources in order to adequately protect public health.

45 2: Sources of Exposure to Fluoride and Fluorine Compounds

46 Natural sources of fluoride include volcanic activity, soil, and water from run-off exposed to

47 fluoride-containing rock. Sources of fluoride and fluorine compounds have expanded over the past

48 75 years due to industrial emissions and the development of a wide variety of consumer products.

49 Table 1 provides a list of chemically synthesized sources of fluoride and fluorine compounds.

50 <u>Table 1: Most Prevalent Chemically Synthesized Sources of Fluoride and Fluorine Compounds</u>

Water: fluoridated municipal drinking water [9]	Water: bottled water with fluoride [9]
Water: perfluorinated compounds [10]	Beverages: those made with fluoridated water and/or made with water/ingredients exposed to fluoride-containing pesticides [9]
Food: general [9]	Food: perfluorinated compounds [4]
Pesticides [9]	Soil: phosphate fertilizers and/or airborne emissions from industrial activities [9]
Air: fluoride releases from industry [9]	Dental product: toothpaste [9]
Dental product: prophy paste [11]	Dental product: mouthwash/rinse [9]
Dental product: dental floss [12, 13]	Dental product: fluoridated toothpicks and interdental brushes [14]
Dental product: topical fluoride gel and foam [15]	Dental product: fluoride varnish [15]
Dental material for fillings: all glass ionomer cements [16]	Dental material for fillings: all resin-modified glass ionomer cements [16]
Dental material for fillings: all giomers [16]	Dental material for fillings: all polyacid-modified composites (compomers) [16]
Dental material for fillings: some composites [16]	Dental material for fillings: some dental mercury amalgams [16]
Dental material for orthodontics: glass ionomer cement, resin-modified glass ionomer cement, and polyacid-modified composite resin (compomer) cement [17]	Dental material for pit and fissure sealants: resin-based, glass-ionomer, and giomers [18]
Dental material for tooth sensitivity/caries treatment: silver diamine fluoride [19]	Pharmaceutical/prescription drugs: fluoride tablets, drops, lozenges, and rinses [9]
Pharmaceutical/prescription drugs: fluorinated chemicals [9] such as those used in antibiotics, anti-cancer and anti-inflammatory agents, drugs used to induce general anesthesia, and psychopharmaceuticals [20]	Other consumer products: perfluorinated chemicals (PFCs) used as protective coatings for carpets and clothing, paints, cosmetics, insecticides, non-stick coatings for cookware, and paper coatings for oil and moisture resistance [10]
Household dust: perfluorinated compounds [21, 22]	Occupational sources of exposure [9]
Cigarette smoke [9]	Fluoridated salt and/or milk [5, 23]
Aluminofluoride exposure from ingesting a fluoride source <i>with</i> an aluminum source [9]	Nuclear reactors and nuclear weapons [24]

51 3. Exposure Levels

52 3.1. Fluoride Exposure Limits and Recommendations

53 Due to increased rates of dental fluorosis and increased sources of exposure to fluoride, the 54 Public Health Service (PHS) lowered its recommended drinking water levels of fluoride, set at 0.7 to 55 1.2 milligrams per liter in 1962 [25], to 0.7 milligrams per liter in 2015 [26]. Generally, the "optimal" 56 intake of fluoride has been defined as between 0.05 and 0.07 mg of fluoride per kilogram of body 57 weight [27]. However, in a 2009 longitudinal study, researchers at the University of Iowa noted the 58 lack of scientific evidence for this intake level and concluded: "Given the overlap among 59 caries/fluorosis groups in mean fluoride intake and extreme variability in individual fluoride 60 intakes, firmly recommending an 'optimal' fluoride intake is problematic" [27] (p. 111).

61 Comparing some of the existing guidelines for fluoride intake helps to exemplify the 62 complexity of establishing levels, enforcing levels, utilizing them to protect all individuals, and 63 applying them to everyday life. To illustrate this point, Table 2 provides a comparison of 64 recommendations from the Public Health Service (PHS), recommendations from the Institute of 65 Medicine (IOM), and regulations from the Environmental Protection Agency (EPA).

TYPE OF FLUORIDE LEVEL	SPECIFIC FLUORIDE RECOMMENDATION/ REGULATION		SOURCE OF INFORMATION AND NOTES
Recommendation for Fluoride Concentration in Drinking Water for the Prevention of Dental Caries	0.7 mg per liter		U.S. Public Health Serv (PHS) [28] <i>This is a non-enforceable</i> <i>recommendation.</i>
Dietary Reference Intake: Tolerable Upper Intake Level of Fluoride	Infants 0-6 mo. Infants 6-12 mo. Children 1-3 y Children 4-8 y Males 9->70 y Females 9->70 y [*] (*includes pregnancy and	<u>0.9 mg/d</u> <u>1.3 mg/d</u> <u>2.2 mg/d</u> <u>10 mg/d</u> 10 mg/d	Food and Nutrition Boa Institute of Medicine (IOM), National Academies [29 <i>This is a non-enforceable</i> <i>recommendation</i> .
Dietary Reference Intake: Recommended Dietary Allowances and Adequate Intakes	Infants 0-6 mo. Infants 6-12 mo. Children 1-3 y Children 4-8 y Males 9-13 y Males 14-18 y Males 19->70 y Females 9-13 y Females 14->70 y*	0.5 mg/d 0.7 mg/d 1.0 mg/d 2.0 mg/d 3.0 mg/d 4.0 mg/d 2.0 mg/d	Food and Nutrition Boa Institute of Medicine (IOM), National Academies [30 <i>This is a non-enforceable</i> <i>recommendation.</i>

(*includes pregnancy and lactation)

66 Table 2: Comparison of PHS Recommendations, IOM Recommendations, and EPA Regulations for Fluoride 6

Maximum Contaminant Level (MCL) of Fluoride from Public Water Systems	4.0 mg per liter	U.S. Environmental Protection Agency (EPA) [31] <i>This is an enforceable</i> <i>regulation.</i>
Maximum Contaminant Level Goal (MCLG) of Fluoride from Public Water Systems	4.0 mg per liter	U.S. Environmental Protection Agency (EPA) [31] This is a non-enforceable regulation.
Secondary Standard of Maximum Contaminant Levels (SMCL) of Fluoride from Public Water Systems	2.0 mg per liter	U.S. Environmental Protection Agency (EPA) [31] This is a non-enforceable regulation.

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69 3.2: Water and Food

Fluoridated water is generally considered the main source of fluoride exposure for Americans. The U.S. Public Health Service (PHS) has estimated that the average dietary intake of fluoride for adults living in areas with 1.0 mg/L fluoride in the water as between 1.4 to 3.4 mg/day (0.02-0.048 mg/kg/day) and for children in fluoridated areas as between 0.03 to 0.06 mg/kg/day [24]. Additionally, the Centers for Disease Control and Prevention (CDC) has shared research reporting that water and processed beverages can comprise 75% of a person's fluoride intake [11, 32].

A 2006 report on fluoride from the National Research Council (NRC) came to similar conclusions. The authors estimated how much of overall fluoride exposure is attributable to water when compared to pesticides/air, background food, and toothpaste, and they wrote: "Assuming that all drinking-water sources (tap and non-tap) contain the same fluoride concentration and using the EPA default drinking-water intake rates, the drinking-water contribution is 67-92% at 1 mg/L, 80-96% at 2 mg/L, and 89-98% at 4 mg/L" [9] (p. 55). The levels of NRC's estimated fluoridated water intake rates were higher for athletes, workers, and individuals with diabetes [9].

It is also important to consider that the fluoride added to water is not only taken in through drinking tap water. The water is also used for growing crops, tending to livestock (and domestic pets), food preparation, and bathing. It is also used to create processed foods and cereals and beverages. Disturbingly high levels of fluoride have been recorded in infant formula and commercial beverages, such as juice and soft drinks [9]. Significant levels of fluoride have also been recorded in alcoholic beverages, especially wine and beer [33, 34].

In exposure estimates provided in the 2006 NRC report, fluoride in food consistently ranked as the second largest source behind water [9]. Increased levels of fluoride in food can occur due to food preparation and the use of pesticides and fertilizers [9]. Significant fluoride levels have been recorded in grapes and grape products [9]. Fluoride levels have also been reported in cow's milk due to livestock raised on fluoride-containing water, feed, and soil [35], as well as processed meat, likely due to mechanical deboning, which leaves skin and bone particles in the meat [9].

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96 3.3. Fertilizers, Pesticides, and Other Industrial Releases

Fluoride is an ingredient in phosphate fertilizers and certain types of pesticides, and these sources constitute a portion of overall fluoride intake. The levels vary based upon the exact product and the individual's exposure, but in the 2006 NRC report, an examination of dietary fluoride exposure levels from two pesticides found: "Under the assumptions for estimating the exposure, the contribution from pesticides plus fluoride in the air is within 4% to 10% for all population subgroups at 1 mg/L in tap water, 3-7% at 2 mg/L in tap water, and 1-5% at 4 mg/L in tap water" [9] (p. 47).

103 Additionally, the environment is contaminated by fluoride releases from industrial sources, and 104 these releases likewise impact water, soil, air, food, and human beings in the vicinity. Industrial 105 releases of fluoride can result from coal combustion by electrical utilities and other industries [9]. 106 Releases can also occur from refineries and metal ore smelters [36], aluminum production plants, 107 phosphate fertilizer plants, chemical production facilities, steel mills, magnesium plants, and brick 108 and structural clay manufacturers [9], as well as copper and nickel producers, phosphate ore 109 processors, glass manufacturers, and ceramic manufacturers [37]. Concerns about fluoride exposure 110 from these industrial activities, especially when combined with other sources of exposure, led 111 researchers to state in 2014 that "industrial safety measures need to be tightened in order to reduce 112 unethical discharge of fluoride compounds into the environment" [38] (p. 1).

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114 3.4. Dental Products for Use at Home

115 Fluoride from dental products used at home likewise contribute to overall exposure levels. 116 These levels are highly significant and occur at rates which vary by person due to the frequency and 117 amount of use, as well as individual response. They also vary not only by the type product used, but 118 also by the specific brand of the product used. To add to the complexity, these products contain 119 different types of fluoride, and the average consumer is unaware of what the type and 120 concentrations listed on the labels mean. Additionally, most of the studies that have been done on 121 these products involve children, and even the CDC has explained that research involving adult 122 exposure to fluoridated toothpaste, mouth rinse, and other products is lacking [11] (p.14).

Fluoride added to toothpaste can be in the form of sodium fluoride (NaF), sodium monofluorophosphate (Na₂FPO₃), stannous fluoride (tin fluoride, SnF₂), or a variety of amines [39]. Toothpaste used at home generally contains between 850 to 1,500 ppm fluoride [40], while prophy paste used in the office during a dental cleaning generally contains 4,000 to 20,000 ppm fluoride [11]. Brushing with fluoridated toothpaste is known to raise fluoride concentration in saliva by 100 to 1,000 times, with effects lasting one to two hours [11, 41].

The United States Food and Drug Administration (FDA) requires specific wording for the labeling on toothpaste, including strict warnings for children [40]. Yet, in spite of these labels and directions for use, research suggests that toothpaste significantly contributes to daily fluoride intake in children [35]. In February 2019, the CDC released a report with statistics from a study showing that ">38% of children aged 3–6 years reportedly used a half or full load of toothpaste, exceeding current recommendation for no more than a pea-sized amount (0.25 g) and potentially exceeding recommended daily fluoride ingestion" [42] (p. 88).

Some research has even shown that swallowing toothpaste can result in higher levels of fluoride intake in children than water. Authors of a study published in 2013 reported that children's ingestion of toothpaste accounted for 74% of total fluoride intake in fluoridated areas and 87% in non-fluoridated areas [43] (p. 461). In light of the significant fluoride exposure levels in children from toothpaste and other sources, researchers at the University of Illinois at Chicago have questioned the continued need for fluoridation in the U.S. municipal water supply [35].

Mouth rinses (and mouthwash) also contribute to overall fluoride exposure levels. Mouth rinses can contain sodium fluoride (NaF), phosphate fluoride (APF), stannous fluoride (SnF2), sodium monofluorophosphate (SMFP), amine fluoride (AmF), or ammonium fluoride (NH4F) [44]. A 0.05% sodium fluoride solution of mouth rinse contains 225 ppm of fluoride [45]. Like toothpaste,

146 accidental swallowing of this dental product can raise fluoride intake levels even higher.

147 Fluoridated dental floss is yet another product that contributes to overall fluoride exposure. 148 Flosses that have added fluoride have been reported to contain 0.15mgF/m and release fluoride into 149 the tooth enamel [46] at levels greater than mouth rinse [47]. Elevated fluoride in saliva has been 150 documented for at least 30 minutes after flossing [13], but like other over-the-counter dental 151 products, a variety of factors influence the fluoride release. In work published in 2008, researchers 152 from the University of Gothenburg in Sweden noted that saliva (flow rate and volume), intra- and 153 inter-individual circumstances, and variation between products impact fluoride releases from dental 154 floss, fluoridated toothpicks, and interdental brushes [14]. Additionally, dental floss can contain 155 fluoride in the form of perfluorinated compounds, and authors of a 2012 Springer publication 156 identified 5.81 ng/g liquid as the maximum concentration of perfluorinated carboxylic acid (PFCA) 157 in dental floss and plaque removers [48] (p. 35).

Many consumers utilize toothpaste, mouthwash, and floss in combination on a daily basis, and thus, these multiple routes of fluoride exposure are especially relevant when considering an individual's overall intake levels of fluoride. In addition to these over-the-counter dental products, some of the materials used at the dental office result in even higher fluoride exposure levels for millions of consumers.

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164 *3.5. Dental Products for Use at the Dental Office*

165 There is a major void in the scientific literature that attempts to quantify fluoride releases from 166 procedures and products administered at the dental office as part of estimates of overall fluoride 167 intake. Part of this is likely due to the fact that researchers evaluating exposure levels from sources in 168 the dental office have demonstrated that establishing any type of average release rate for these 169 products is virtually impossible.

A prime example of this scenario is the use of dental "restorative" materials, which are used to fill cavities. Many of the options for filling materials contain fluoride, including *all* glass ionomer cements, *all* resin-modified glass ionomer cements, *all* giomers, *all* polyacid-modified composites (compomers), *certain types of* composites, and *certain types of* dental mercury amalgams [16]. Fluoride-containing glass ionomer cements, resin-modified glass ionomer cements, and polyacid-modified composite resin (compomer) cements are also used in orthodontic band cements [17]

177 Glass ionomers and resin-modified glass ionomers release an "initial burst" of fluoride and then 178 give off lower levels of fluoride long-term [16]. The long-term emission also occurs with giomers and 179 compomers, as well as fluoride-containing composites and amalgams [16]. However, composite and 180 amalgam filling materials are known to release much lower levels of fluoride than the glass 181 ionomer-based materials [49] (p. 334). To put these releases in perspective, a Swedish study 182 demonstrated the fluoride concentration released from glass ionomer cements was approximately 183 2-3 ppm after 15 minutes, 3-5 ppm after 45 minutes, and 15-21 ppm within twenty-four hours, with a 184 total of 2-12 mg of fluoride per ml of glass-ionomer cement released during the first 100 days [50].

185 To complicate matters, these dental materials are designed to "recharge" their fluoride releasing 186 capacity, thereby boosting the amounts of fluoride released. This increase in fluoride release is 187 initiated because the materials are constructed to serve as a fluoride reservoir that can be refilled. 188 Thus, by utilizing another fluoride-containing product, such as a gel, varnish, or mouthwash, more 189 fluoride can be retained by the material and thereafter released over time. Glass ionomers and 190 compomers are most recognized for their recharging effects, but a number of variables influence this 191 mechanism, such as the composition of the material and the age of the material [49] (p. 334), in 192 addition to the frequency of recharging and the type of agent used for recharging [51, 52].

In spite of the many factors that influence fluoride release rates in dental devices, attempts have been made to establish fluoride release profiles for these products. Researchers from Belgium aptly summarized the result of such an attempt when they wrote in 2001: "However, it was impossible to correlate the fluoride release of materials by their type (conventional or resin-modified glass-ionomers, polyacid-modified resin composite and resin composite) except if we compared the products from the same manufacturer" [53] (p. 26). Gels and foams can also be used at the dentist office and sometimes even at home. According to the ADA, some of the most routinely used fluoride gels contain acidulated phosphate fluoride (APF), which consists of 1.23% or 12,300 parts per million (ppm) fluoride ion, and 2% sodium fluoride (NaF), which consists of 0.90% or 9,050 ppm fluoride ion [56]. Brushing and flossing before applying gel can result in higher levels of fluoride retained in the enamel [57]. The ADA has noted that there are few clinical studies on the effectiveness of fluoride foams [56].

Silver diamine fluoride is also used in dental procedures, and the brand used in the U.S. contains 5.0-5.9% fluoride [58]. This is a relatively new procedure that was FDA approved in 2014 for treating tooth sensitivity but not dental caries, which is an off-label use [58]. Concerns have been raised about risks of silver diamine fluoride, which can permanently stain teeth black [58, 59].

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216 3.6. Pharmaceutical Drugs (Including Supplements)

20-30% of pharmaceutical compounds have been estimated to contain fluorine [60]. Fluorine is 218 used in drugs such as general anesthetics, antibiotics, anti-cancer and anti-inflammatory agents, 219 psychopharmaceuticals [20], and other applications. Some of the most popular fluorine-containing 220 drugs include Prozac and Lipitor [61], as well as the fluoroquinolone family (ciprofloxacin 221 [marketed as Cipro], gemifloxacin [marketed as Factive], levofloxacin [marketed as Levaquin], 222 moxifloxacin [marketed as Avelox], and ofloxacin [62].

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 (with acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis, and uncomplicated urinary tract infections) because the risks outweigh the benefits [63]. The fluorinated compound fenfluramine (fen-phen) was also used for many years as an anti-obesity drug, but it was removed from the market in 1997 due to its link to heart valve problems [64].

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" [20] (p. 148).

Meanwhile, certain drugs have been recognized for their capacity to generate high levels of fluoride exposure. For example, fluoridated anesthesia is known to increase plasma fluoride levels. In particular, the anesthesia sevoflurane can result in 20 times the total daily dietary fluoride intake than that obtained from sources of food and water combined [65].

Another prescription drug is likewise essential to consider regarding 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 [11], and they are not approved as safe and effective for caries prevention by the FDA [66].

242 Potential dangers of these fluoride "supplements" have been addressed. The 2006 NRC report 243 included statistics that "all children through age 12 who take fluoride supplements (assuming low 244 water fluoride) will reach or exceed 0.05-0.07 mg/kg/day" [9] (p. 68). Also, researchers of a Cochrane 245 Collaboration review published in 2011 advised: "No data were available concerning adverse effects 246 related to fluoride supplementation in children aged less than 6 years. The ratio benefit/risk of 247 fluoride supplementation was thus unknown for young children" [67] (p. 25). Moreover, in 2015, 248 scientists conducting an analysis of fluoride in toothpaste and fluoride supplements wrote: "Taking 249 into consideration the toxicity of fluorides, more strict control of fluoride content in pharmaceutical 250 product[s] for oral hygiene is proposed" [39] (p. 2264).

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252 3.7. Perfluorinated Compounds

253 In 2015, over 200 scientists from 38 countries signed on to the "Madrid Statement," a 254 research-based call for action by governments, scientists, and manufacturers to address the 255 signatories' concerns about "production and release into the environment of an increasing number 256 of poly- and perfluoroalkyl substances (PFASs)" [22] (p.A107). Products made with PFSAs, also 257 known as perfluorinated chemicals (PFCs), include protective coatings for carpets and clothing 258 (such as stain-resistant or water-proof fabric), paints, cosmetics, insecticides, non-stick coatings for 259 cookware, and food packaging coatings for oil and moisture resistance [10], as well as leather, paper, 260 and cardboard [4], and a wide variety of other consumer items.

261 In research published in 2012, dietary intake was identified as the major source of exposure to 262 perfluorinated compounds (PFCs) [10], and additional scientific investigation has supported this 263 claim. In an article published in 2008, researchers stated that in North America and Europe, 264 contaminated food (including drinking water) is the most essential exposure route of 265 perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) [4]. The researchers also 266 concluded that children have increased uptake doses due to their smaller body weight, and they 267 provided the following statistics for average consumers: "We find that North American and 268 European consumers are likely to experience ubiquitous and long-term uptake doses of PFOS and 269 PFOA in the range of 3 to 220 ng per kg body weight per day (ng/kg(bw)/day) and 1 to 130 270 ng/kg(bw)/day, respectively" [4] (p. 251).

The author of research published in 2012 explored some of the other common sources of PFCs. The data showed that commercial carpet-care liquids, household carpet and fabric-care liquids and foams, and treated floor waxes and stone/wood sealants had higher concentrations of PFCs when compared to other PFC-containing products [48] (p. 35). The author also specified that the exact compositions of PFCs in consumer products are often kept confidential and that knowledge about these compositions is "very limited" [48] (p. 25).

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278 3.8. Cumulative Sources of Exposure

279 Recommended intake levels, regulations, and risk assessments for fluoride in water and food 280 should be based upon exposure levels from all sources. The concept of evaluating fluoride exposure 281 levels from multiple sources was addressed in the 2006 NRC report on fluoride, which 282 acknowledged the difficulties with accounting for all sources and individual variances [9].

Yet, the NRC authors attempted to calculate combined exposure levels from pesticides/air, food, toothpaste, and drinking water [9] (pp.52-56). While these extensive calculations did not include exposure levels from other dental materials, pharmaceutical drugs, and other consumer products, the NRC still recommended to lower the MCLG for fluoride [9], which has not yet been accomplished.

The ADA has also recommended that collective sources of exposure be taken into account. In particular, they have stated that research should "estimate the total fluoride intake from all sources individually and in combination" [68] (p. 85). Furthermore, in an article about fluoride including discussion about "supplements," the ADA mentioned that all sources of fluoride should be evaluated and that "patient exposure to multiple water sources can make proper prescribing complex" [69].

A study published in 2005 by researchers at the University of Illinois at Chicago evaluated fluoride exposure levels in children from drinking water, beverages, cow's milk, foods, fluoride "supplements," toothpaste swallowing, and soil ingestion [35]. They found that the reasonable maximum exposure estimates exceeded the upper tolerable intake and concluded that some children were at risk for fluorosis [35].

299 Canadian researchers reported comparable conclusions in a study published in 2018. The 300 authors emphasized the need to consider multiple sources of fluoride and wrote that "community 301 water fluoridation contributes to increased fluoride intake among children, which leads to reaching,

302 and in some cases even exceeding, the suggested optimal absorbed dose" [70] (p.1358).

Additionally, a study published in 2015 by researchers at the University of Iowa considered exposure levels from water, toothpaste, fluoride "supplements," and foods [27]. 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 with the recommended level, rendering the concept of an 'optimal' or target intake relatively moot" [27] (p. 114).

309

310 <u>4. Conclusion</u>

The sources of human exposure to fluoride and fluorine compounds have drastically increased since community water fluoridation began in the U.S. in the 1940s. In addition to water, these sources now include food, pesticides, fertilizers, dental products used at home and in the dental office (some of which are implanted in the human body and continually release fluoride), pharmaceutical drugs, carpeting, clothing, cookware, and an array of other consumer items used on a routine basis.

Unfortunately, all of these applications were introduced before the health risks of fluoride and fluorine compounds, safety levels for their use, and appropriate guidelines were adequately researched and established. Combining the estimated intake levels of various products establishes that millions of people are at risk of greatly exceeding the levels of fluoride and fluorine compounds associated with systemic injuries and toxicity, the first visible sign of which is dental fluorosis. Susceptible subpopulations, such as infants, children, and individuals with diabetes or renal problems, are known to be more severely impacted by higher intake levels of fluoride.

Risk assessments, recommendations, and regulations that recognize exposure to fluoride and fluorine compounds from multiple sources are crucial. Moreover, when the long-term, chronic exposure to these multiple sources is conscientiously taken into account, the required action is indisputable: Given the current levels of exposure, policies should be implemented that reduce and work toward eliminating avoidable sources of fluoride, including water fluoridation, fluoride-containing dental materials, and other products containing fluoride and fluorine compounds, as means to promote the health and safety of the public.

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