Avrupa Bilim ve Teknoloji Dergisi
Sayı 33, S. 354-362, Ocak 2022

Derleme Makalesi

www.ejosat.com ISSN:2148-2683

European Journal of Science and Technology
No. 33, pp. 354-362, January 2022

Review Article

Assessment of Fluoride Intake in Children According to the World Health Organization and European Union Guidelines

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(First received 31 December 2021 and in final form 31 January 2022)

(**DOI:** 10.31590/ejosat.1051641)

ATIF/REFERENCE: Aydenk Köseoğlu, S. Z. (2022). Assessment of Fluoride Intake in Children According to the World Health Organization and European Union Guidelines. *European Journal of Science and Technology*, (33), 354-362.

Abstract

The purpose of this review is to consider the assessment of integrated fluoride exposure and "tolerable daily intake" in children including bottle-fed infants according to the World Health Organisation (WHO) and European Union (EU) guidelines.All people have the right to access drinking-water that is safe for human consumption, and it is the responsibility of the governments to regulate the supply and distribution of drinking-water that is essential to sustain life with respect to international health regulations and human rights. National drinking-water standards must be based on varying environmental, socio-cultural, socio-economic, dietary, and other factors affecting potential exposure. Total daily fluoride intake may vary depending on the different sources of exposure that are for instance, fluoride concentration in the air, drinking water and the amount consumed, levels in food and beverages and using dental preparations. The impact of fluoride is estimated based on the exposure duration and factors such as age i.e., daily mg dose per kg of body weight. Bottle-fed infants are considered as a high exposure group relative to their body weights. Therefore, the risk should be separately assessed for every life stage, especially children under 3 years old, partially breastfed and formula fed infants, certainly pregnant and breastfeeding mothers. In this article, the "Guideline Value" and "Tolerable Daily Intake" for children which do not result in any significant risk to health over a lifetime of consumption will be explained. Additionally, this review will keep light on public health, especially children's health, in evaluating fluoride intake and it can improve national drinking-water quality based on fluoridation and derogation which is in progress to eliminate high values.

Keywords: Child health, infant formula, fluoride exposure, tolerable daily intake

Çocuklarda Florür alımının Dünya Sağlık Örgütü ve Avrupa Birliği Kılavuzlarına Göre Değerlendirilmesi

Öz

Bu derlemenin amacı, Dünya Sağlık Örgütü (WHO) ve Avrupa Birliği (AB) kılavuzlarına göre biberonla beslenen bebekler de dahil olmak üzere çocuklarda entegre florür maruziyeti ve "tolere edilebilir günlük alım" değerlendirmesini ele almaktır.
Tüm insanlar, insan tüketimi için güvenli içme suyuna erişim hakkına sahiptir ve uluslararası sağlık düzenlemeleri ve insan haklarına uygun olarak, yaşamı sürdürmek için gerekli olan içme suyunun temini ve dağıtımını düzenlemek hükümetlerin sorumluluğundadır. Ulusal içme suyu standartları, değişen çevresel, sosyo-kültürel, sosyo-ekonomik, diyet ve potansiyel maruziyeti etkileyen diğer faktörlere dayanmalıdır. Toplam günlük florür alımı, örneğin havadaki florür konsantrasyonu, içme suyu ve tüketilen miktar, yiyecek ve içeceklerdeki seviyeler ve diş preparatlarının kullanımı gibi farklı maruziyet kaynaklarına bağlı olarak değişebilir. Florürün etkisi, maruz kalma süresine ve yaş, yani vücut ağırlığının kg'ı başına günlük mg doz gibi faktörlere dayalı olarak tahmin edilir. Biberonla beslenen bebekler, vücut ağırlıklarına göre yüksek maruziyet grubu olarak kabul edilir. Bu nedenle risk, özellikle 3 yaş altı çocuklar, kısmen anne sütü ve formül mama ile beslenen bebekler, kesinlikle hamile ve emziren anneler olmak üzere her yaşam evresi için ayrı ayrı değerlendirilmelidir. Bu makalede, çocuklar için ömür boyu tüketildiğinde sağlık açısından önemli bir risk oluşturmayan "Kılavuz Değer" ve "Tolere Edilebilir Günlük Alım" açıklanacaktır. Ek olarak, bu derleme, florür alımının değerlendirilmesinde başta çocuk sağlığı olmak üzere halk sağlığına ışık tutacak ve yüksek değerleri ortadan kaldırmak için sürmekte olan floridasyon ve derogasyona dayalı ulusal içme suyu kalitesini iyileştirebilir.

Anahtar Kelimeler: Çocuk sağlığı, bebek maması, florür maruziyeti, tolere edilebilir günlük alım

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1. Introduction

Regardless of their country's level of development and socioeconomic situation, people from all over the world bear the right to access drinking water safe for human consumption. For this reason, it is the responsibility of the governments to regulate the supply and distribution of drinking water that is essential to sustain life concerning international health regulations and human rights [WHO, 2004].

Therefore, the first document known as the "International Standards for Drinking-water" dealing specifically with public drinking-water quality was published by the World Health Organization (WHO) in 1958, and WHO continues to develop these recommendations under the name of WHO Guidelines for Drinking-water Quality (GDWQ). Selected chemicals in public drinking water are also addressed [WHO, 2004].

According to the information given in WHO GDWQ (2011) at 4th Edition, few chemicals are responsible for large-scale health effects through drinking-water exposure, including arsenic, fluoride, lead, nitrate, selenium, and uranium, for which the contribution from drinking-water to overall intake is an essential factor in preventing disease [WHO, 2011]. In WHO GDWQ (2009), it is mentioned from a "Guideline Value" (G.V.), which is described as "normally represents the concentration of a constituent that does not result in any significant risk to health over a lifetime of consumption"[WHO, 2009; WHO, 2013]. WHO has established several provisional guideline values is higher than the calculated health-based value based on the practical level of treatment performance or analytical achievability [WHO, 2011]

Health outcome goals based on defined tolerable risk levels are the more common. Therefore, WHO has called for minimum exposure in drinking water to reduce the risk and incidence of diseases in consider health-based targets. It is found out that establishing a health-based target to reduce the overall levels of exposure has been possible [WHO, 2011]. European Union (E.U.) countries are updating their policies based on the Drinking Water Directive of the Council of the European Union, which is to be amended according to the latest Edition of WHO GDWQ. WHO is also changing its regulations provided with health-based targets and risk management strategies [WHO, 2004].

The management strategies of the authorities should rely on the detection and remediation of unsafe conditions since the sensitive nature of the health effects over a lifetime of consumption and the commitment to policies should give priority to chemicals in drinking water such as fluoride that poses a risk and a significant impact on human health [WHO, 2011] The current guideline value for fluoride in drinking-water laid down by WHO is 1.5mg/L [WHO, 2017; WHO, 1984; WHO, 2011, 2013, 2018a].

Many Non-Government Organizations (N.G.O.) and WHO also claim the dangers of high chemical substances in drinking water and express critical reviews and evaluations of the effects of chemical substances found in drinking water on human health [WHO, 2004].

Drinking water is exposed to a few chemical substances from natural soil sources or additives, so which level is beneficial or harmful? What are the risks for human health from exposure to particular chemicals in drinking water?

Although the traced database is extensive, data gaps are observed for fluoride and fluoridation. The literature search shows that the values for surface waters are slightly exceeded, and some excesses have been observed for fluoride in groundwater [WHO, 2013].

2. Discussion

If the level of chemical substances in drinking-water is low, exposure will have a minor impact on human health. On the contrary, when the level of chemical substances in drinking-water is high, exposure will have maximum impact on human health [WHO, 2004].

2.1. Human Exposure to Fluoride

Fluorine (F) is “defined as the first element of the halogen family, which includes chlorine and iodine, and is the most reactive element. “Fluoride” refers to its ionic form (F-) and “fluorides” to fluoride-containing compounds. Fluorine is never found by itself in nature, but fluorides are found everywhere: in soil, air, and water, as well as in plant and animal life [European Commission, 2016]. Fluorine is one of the naturally occurring substance chemicals in drinking-water. Fluoride is not essential for human growth, development and for most organisms in the world [WHO, 2011]. Traces of fluorides are derived from (i) naturally occurring; (environmental occurrence) rocks, soil and the effects of geological setting, (ii) industrial sources; mining (extractive industries) and manufacturing and processing industries, (iii) agricultural activity manures; (geochemistry) fertilizers and (iv) additive; principally from chemical used in the production and distribution of drinking-water [WHO, 2017].

The fluoride in final water is always present as fluoride ions, whether from natural sources or from artificial fluoridation. Fluorosilicic acid, sodium hexafluorosilicate and sodium fluorine are used in municipal water fluoridation schemes [WHO, 2002, 2004].

The additive’s physiochemical properties are [ECHA], n.d.; WHO, 2004, 2011, 1982]

1) Hydrogen fluorine (HF) is a colorless, pungent liquid fluor with a boiling point of 19.5 °C. It is highly soluble in water, in which it forms hydrofluoric acid. (Chemical Abstracts Service (CAS) No. 7664-39-3)

2) Sodium fluorine (NaF) is a colorless fluor solid that is moderately soluble in water. (CAS No. 7681-49-4)

3) Fluorosilicic acid (H2SiF6) which is also known as hexafluorosilicic acid, is a colorless solid that is highly soluble in water. (CAS No. 16961-83-4)

While drinking-water may not contribute to the overall exposure to a specific chemical, in some situations, controlling levels in drinking-water may not have the desired effect on overall exposure. Thus, risk management strategies for drinking-water should be created by taking other potential sources such as food, air and dental preparations, etc. into consideration [WHO, 2017].

It is vital to examine the levels of water consumption by the related population and fluoride intake from other sources such as toothpaste, air, food, etc. when setting national standards for fluoride or assessing the risks of health consequences of fluoride exposure [WHO, 2011]

It is difficult to reach a maximum guideline value for human health considering a lifetime of consumption. National drinking-water standards must be based on varying environmental, socio-cultural, socio-economic, dietary, and other factors affecting potential exposure [WHO, 2011].

For instance, the regions may vary significantly in total daily fluoride exposure depending on fluoride concentration in drinking-water and the amount consumed, levels in foods and using dental preparations. Moreover, the results of some practices such as tea consumption, cooking and warming with high fluoride coal increases fluoride exposure considerably in some regions [WHO, 2017].

2.1.1. Total Fluoride Exposure

1) Air: In areas where fluoride-containing coal is burned or phosphate fertilizers are produced and used and volcanic areas with high fluoride levels, the fluoride concentration in air is elevated leading to increased exposure by the inhalation route [International Labour Organization, 1984].

2) Dental products: A way of exposure is dental products containing fluoride such as toothpaste (1.0-1.5g/kg) fluoride solutions and gels for topical treatment (0.25-24.0g/kg), tablets (0.25-0.5 or 1.0mg per tablet) which are used by children to reduce dental caries(International Labour Organization, 1984).

3) Foods and beverages (except water); While vegetables and fruits contain small amounts of fluoride (0.1-0.4mg/kg), barley, rice (about 2.0mg/kg), taro, yams and cassava contain relatively high fluoride levels. Generally, meat contains about 0.2-1.0mg/kg fluoride. Fish normally includes fluoride around 2-5mg/kg whereas fish protein concentrates contain up to 370mg/kg of fluoride. Milk typically contains low levels of fluoride, e.g., 0.02mg/L in human breast milk 0.02-0.05mg/L in cow's milk. Tea leaves have been found to contain up to 400mg/kg (dry weight) of fluoride [WHO, 1986].

4) Water: Drinking-water is typically the largest single contributor to daily fluoride intake. For a given individual, fluoride exposure (mg/kg of body weight per day) via drinking-water is determined by the fluoride level in the water and the daily water consumption (litres per day). The levels of daily exposure to fluoride by drinking-water is also depending on the climate [W. SLooff & J.P.M. Ros (eds.), 1988].

2.2. Effects of Fluoride on Humans

There are several epidemiological studies associated with fluoride in drinking-water and cancer prevalence rates. The International Agency for Research on Cancer (IARC) considered and evaluated studies and found out that these studies proved to be inadequate sources of evidence regarding carcinogenicity in humans in 1982 and 1987. Moreover, WHO International Programme on Chemical Safety (IPCS) also concluded that data belonging to carcinogenicity studies in laboratory animals is insufficient and this condition does not support the argument that fluoride causes cancer in humans whereas the data on bone cancer is limited [WHO, 2002, 2004].

WHO conducted an extensive review in 1984 and informed that (i) there were insufficient data to conclude that fluoride produces cancer or birth defects, (ii) the mottling of teeth (i.e. dental fluorosis) is sometimes associated with fluoride levels in drinking-water above mg/L and (iii) crippling skeletal fluorosis can ensue when fluoride levels exceed 10mg/L. As a result of these information, a guideline value of 1.5mg/L was recommended by WHO as a level at which dental fluorosis should be minimal [WHO, 1984, 2018b].

Signs of acute fluoride intoxication can be seen when minimum oral doses of at least 1mg fluoride per kg of body weight is taken [WHO, 2004]

Low concentrations of fluoride protect against dental caries, especially in children whereas high fluoride intakes have serious effects on skeletal tissues. As a result of most epidemiological studies concerning the effects of fluoride on teeth and bone have correlated the effects with the concentration of fluoride in the drinking-water (mg/L) consumed rather than total fluoride exposure [WHO, 2018b, 1982; WHO, 2006].

There is insufficient data concerning determining the minimum nutritional requirement in humans [W. SLooff & J.P.M. Ros (eds.), 1988; WHO, 2004].

According to the conclusions of the European Commission (EC) Scientific Committee on Health and Environmental Risks (SCHER) in 2011; Dental fluorosis risk in children exists with systemic fluoride exposure and the threshold level cannot be determined. Moreover, fluoride intake in drinking-water at the level that is present in the EU did not seem to affect children's neurodevelopment and IQ levels [European Commission, 2011].

Despite this there have been known reports regarding endemic skeletal fluorosis in the EU's general population, there is also sufficient evidence which links fluoride to the prevalence of osteosarcoma. The studies do not indicate any thyroid effects at exposure to fluoride and new evidence has reported its effects on male and female reproductive capacity [European Commission, 2011].

2.2.1. Dental Effects of Ingested Fluoride

It was established in the 1930's and 1940's that fluoride was naturally present in drinking-water and Trendley Dean at the US Public Health Service (USPHS) worked on its dental effects. It was demonstrated in a study that naturally occurring fluoride in drinking-water caused dental fluorosis and decreased dental caries. Dean's study pointed out that the effect of 1.0mg/L of fluoride causing dental fluorosis was not crucial for public health whereas resistance to dental caries was of high importance leading to the question as to whether raising the level of fluoride in drinking-water artificially would have the same effect[WHO, 2005].

The first intervention study was undertaken under the direction of USPHS in Grand Rapids in 1945. The results after 6 years of fluoridation were published in 1953. Additional studies were started in 1945/6 in New York State, Illinois, and Ontario Canada [National Research Council, 1993]. Further intervention studies were established in the Netherlands (1953), New Zealand (1954), the UK (1955-6), and East Germany (1959) [Lennon et al., 2004]

2.2.2. Studies of Fluoride in Laboratory Animals

There is no storage of fluoride in soft tissue but incorporation into teeth and skeletal tissue can be reversed; cessation of exposure provides mobilization from tissues [WHO, 2002].

An excessive dose of 16mg/L of fluoride given orally to rats produced effects such as inhibition of bone mineralization and formation, delays in fracture healing, reductions of bone volume

and collagen synthesis. An increase in bone fragility was seen at concentrations of 64mg/L [WHO, 2002].

In a study that aimed to evaluate whether fluoride is a carcinogen, mice were given drinking-water containing 70mg/L of fluoride as sodium fluoride for 2 years. As a result of the study, neither an incidence of a tumour nor a significant increase was seen in any exposed group (mice exposed to up to 11.3mg/kg of body weight per day in the diet) [WHO, 2002].

2.3. Intake of Fluoride

2.3.1. Intake of Fluoride Relative to Bodyweight

It is reported in several studies that fluoride intake of 0.46 to 3.6-5.4mg/day takes place daily. This shows that daily fluoride intake may vary depending on different sources of exposure [International Labour Organization, 1984].

The impact of fluoride is estimated best by the dose (i.e., mg fluoride per kg of body weight per day) basis exposure duration and factors such as age. Three factors must be considered in assessing "dietary exposure" to a food additive: (i) the concentration of the food additive in food; (ii) the amount of food consumed; and (iii) the average body weight of the population (kg). As standard terminology, "consumption" is suggested to be used to describe the amount of food intake and "dietary exposure" to describe the amount of food additives consumed with food which includes beverages, drinking water and food supplements. The term "dietary exposure" is used synonymously with the term "dietary intake" in relation to current regulatory frameworks or other relevant issues [WHO & FAO, 2009).

The general equation for dietary exposure is:

Dietary exposure = Σ (concentration of food additive in food x food consumption) / body weight (kg) [FAO & WHO, 2014).

2.3.2. The Level of Fluoride in Food

Some foods contain high amounts of fluoride. These are field-grown vegetables such as (i) curly kale with 40mg/kg, (ii) endive with 0.3-2.8mg/kg fresh weight, (iii) fish with 0.1-30mg/kg, and (iv) dry tea with 3-300mg/kg (average 100mg/kg). Additionally, 2–3 cups of tea contain approximately 0.4-0.8mg of fluoride. In areas where water with a high fluoride content is used to prepare tea, the intake via tea can be several times greater [W. SLooff & J.P.M. Ros (eds.), 1988].

2.3.3. Default Assumptions of Drinking-water

There is variation in both the volume of water consumed daily and the body weight of consumers. The default assumption for consumption by (i) an adult is 2 litres of water per day, whereas the default assumption for body weight is 60 kg, and (ii) for children it is 1 litre of water per day, whereas the default assumption for body weight is 10 kg [WHO, 2008].

Global data on the consumption of drinking-water a show large variation in intake in different parts of the world. "Data from studies carried out in temperate countries including, Canada, the Netherlands, the United Kingdom and the USA indicate that average daily per capita consumption is usually less than 2 litres, but there was considerable variation between individuals, particularly for those who have a high level of physical activity. A significant proportion of water required for hydration will come from food, but this will also vary in different parts of the world. The range of water intake, in food and fluids, required for hydration ranges from 2 to greater than 4 litres depending on climate and physical activity. There is also a sharp rise in fluid intake at temperatures above 25°C, largely to meet the demands of an increased sweat rate" [WHO, 2009].

Bottle-fed infants are considered as high exposure group relative to their body weights since an intake of 0.75 litres of drinking-water is assumed for a bodyweight of 5 kg [WHO, 2008].

The health effects arising through drinking-water or different sources of exposure and period of exposure of the consumer to fluoride is important [WHO, 2011]. Daily intake of fluoride vary widely according to the various sources of exposure. Values ranging from 0.46 to 3.6-5.4mg/day have been reported in several studies [International Labour Organization, 1984].

2.4. EU CouncilDirectives and Protocols Concerning Drinking-water

The Drinking Water Directive (80/778/EEC) as amended by Council Directive (98/83/EC) of 3rd November 1998 states that the quality of water intended for human consumption must be free of contamination, wholesome and clean thus, protecting human health from any adverse effects [European Commission, 1998].

The chemical parameter of fluoride in drinking water is mentioned as "1.5 mg/L" at Drinking Water Directive [European Commission, 1998]. At Council Directive 2009/54/EC25 regarding with the exploitation and marketing of natural mineral waters, the indication and criteria of fluoride content laid down as greater than 1 mg/L [European Commission, 2009]. In general, WHO guidelines explain that the opinion of the Scientific Advisory Committee are used as the scientific basis for the quality standards in the drinking water [UNECE), n.d.].

One of the most important concerns in the world is the safety and accessibility of drinking-water. In order to ensure that drinking-water is safe for human consumption, the Drinking Water Directive sets out minimum water quality requirements which identifies chemical parameters that could pose a risk to human health when concentrations exceed certain thresholds [European Commission, 2014].

When translating the Drinking Water Directive into national legislation of Member States of the EU, (i) EU member states may include additional requirements such as regulatory additional substances that are relevant within their territory or setting higher standards, (ii) member states are not allowed to set lower standards since the level of protection of human health should be the same within the EU, and (iii) member states may depart from chemical quality standards specified in the directive (Annex I) for a limited period.

2.5. Guideline Value

A "guideline value" usually indicates significant health risks in a lifetime of consumption. For most kinds of toxicity, it is believed that there is a dose below which no adverse effect will occur. For chemicals that give rise to such toxic effects, WHO derived a "tolerable daily intake" and guideline value in drinking-water.

In additional, acceptable daily intakes (ADIs) are established for food additives and pesticide residues that occur in food for necessary technological purposes or plant protection reasons. The term "tolerable daily intake" is more appropriate than "acceptable

daily intake", as it signifies permissibility rather than acceptability[FAO & WHO, 2014; WHO, 2011].

According to the data collected up to 2015 from 104 countries and territories whose are members of the WHO International Network of Drinking-water Regulators (RegNet), 102 of 104 have set a regulatory guideline value. Eight of them have set a regulatory guideline value greater than WHO Guideline value, 77 of them have set the WHO Guideline value, and 17 of them have set a regulatory guideline value less than the WHO Guideline value [WHO, 2018a].

Setting national standards for fluoride consumption requires serious consideration concerning climate conditions and the amount of drinking-water intake. The importance of this point cannot be stressed enough; as local conditions differ from one another, application of the data that is taken from one part of the world may not apply to another region [WHO, 2002].

National reviews base their assumptions for guideline values depending on various factors such as body weight, drinking-water consumption and allocation factor. High fluoride concentrations in ground water pose drinking-water as an important source of fluoride [WHO, 2013].

The standards are based on [WHO, 2011]:

1) Local circumstances in regions where the intake of contamination in drinking-water is greater than that of other sources such as food, air, etc.

2) Intake of drinking-water according to seasonal differences in different parts of the world.

3) Local adjustments to the daily water consumption value may be needed in setting local standards.

4) Very low rate of ventilation in some houses causing inhalation to become a major means of exposure.

GV is calculated as follows:

GV (guideline value) = TDI x BW x P / C

TDI = Tolerable daily intake, "The TDI is an estimate of the amount of a substance in food and drinking-water, expressed on a body weight basis (milligram or microgram per kilogram of body weight), that can be ingested over a lifetime without appreciable health risk, and with a margin of safety" [WHO, 2011].

BW = Body weight

P = Fraction of the TDI allocated to drinking-water intake

C = Daily drinking-water consumption

2.6. Integrated Exposure to Fluoride from All Major Sources

In order to achieve an integrated fluoride exposure assessment from all sources previously discussed, water, food and toothpaste are aggregated. On that basis, EC Scientific Committee on Health and Environmental Risks (SCHER) has been used [European Commission, 2011].

1) The legally defined concentration for the Republic of Ireland (0.8mg/L) and others as appropriate total exposure levels but for being reference, the dose only applied is 0.8mg/L on the quality of drinking-water intended for human consumption.

2) The European Food Safety Authority (EFSA) database (database is only for adult) compiling the results of water consumption surveys across European countries. The mean consumption of water-based beverages, namely tap water, bottled water, soft drinks and stimulants, i.e., coffee, tea, cocoa, ranges from about 400mL to about 1950mL with a median value of 1321mL/day/person. These figures are consistent with the default value for water consumption (2000mL/day) used by WHO. The value for total consumption of liquids across European countries ranges from about 700mL/day/person at the lowest reported mean to about 3800mL/day/person at the highest reported 97.5th percentile. Total consumption ranged from 3300 to 3800mL/day/person.

Based on reported consumption of water-based beverages, several scenarios have been developed in Table I. Scenario 1 corresponds to the median of mean consumption for all water-based beverages across European countries (1321 mL) with the mean occurrence level of fluoride (0.1mg/L). Scenarios 2 and 3 correspond to the highest consumption for high consumers of one of the relevant categories (3773 mL) with the mandatory water fluoridation in Ireland (0.8mg/L) (scenario 2) and the WHO guideline value for fluoride in drinking-water (1.5mg/L) (scenario 3). Scenario 4 is a worst-case scenario based on the highest 97.5th percentile for consumption of tap water (2950 mL in Austria) with the upper range for fluoride concentration (3.0mg/L in Finland).

*Table I. Adult and children (above 15 years of age) systemic exposure to fluoride from water-based beverages**

Scenario	Consumption (mL/day)	Concentration of F (mg/L)	Exposure (mg/day)
1	1,321	0.1	0.13
2	3,773	0.8	3.02
3	3,773	1.5	5.66
4	2,800	3.0	8.40

*Bottled mineral water was not included in these scenarios.

2.6.1. Exposure of Adult and Children above 15 Years of Age

Systemic exposure to fluoride from water-based beverages and aggregated daily systemic exposure to fluoride (mg/day) for adults and children (above 15 years of age) basis mandatory water fluoridation in Ireland (0.8mg/L) is shown in Table II [European Commission, 2011].

Table II. The aggregated daily systemic exposure to fluoride (mg/day) for adults and children older than 15 years of age.

Drinking-water 0.8 mg F/L	***F intake from water (mg/day)***	***Aggregated F intake (mg/day): water and food (1)***	***Aggregated F intake (mg/day): water, food, toothpaste 0.075 mg F/d***	***Aggregated F intake (mg/day): water, food, toothpaste 0.225 mg F/d***
Scenario 2* Consumption 3,773 mL/day	3.02	3.39	3.47	3.62

*Fluoride levels estimated in water and water-based beverages from the scenario 2 in Table I.

(1) The fluoride intake from food and supplemented food with dietary additives is 0.37mg/day (0.12mg/day food and 0.25mg/day fluoride supplemented food; EFSA 2005 [European Union, 2005] , EFSA 2008 [Aguilar et al., 2008a, 2008b] , and accounts for less than 1-6% of the total fluoride intake.

The upper tolerable intake limit (UL) for fluoride (7mg/day) for adults and children above 15 years of age is only exceeded in areas with high levels of natural fluoride in water, whereas the UL would not be exceeded for adults and children above 15 years of age living in an area with fluoridated drinking-water [European Commission, 2011].

2.6.2. Exposure of Children between 12 to 15 Years of Age

Systemic exposure to fluoride from water-based beverages and aggregated daily systemic exposure to fluoride (mg/day) for children between 12 to 15 years of age basis mandatory water fluoridation in Ireland (0.8mg/L) is shown in Table III [European Commission, 2011].

The consumption data of drinking-water and other water-based products used by EFSA 2005 for children between 12 to 15 years of age is under 600mL/day.

Table III. *Aggregated total daily systemic exposure to fluoride (mg/day) for children between 12 to 15 years of age.*

Drinking-water 0.8 mg F/L	***F intake from water (mg/day)***	***Aggregated F intake (mg/day): water and food (1)***	***Aggregated F intake (mg/day): water, food, 0.15% toothpaste***	
			Low application 0.075 mg F/day	***High application 0.225 mg F/day***
Consumption 0.5 L	0.40	0.83	0.90	1.00
Consumption 1.0 L	0.80	1.23	1.30	1.45
Consumption 1.5 L	1.20	1.63	1.70	1.85

Aggregated fluoride intake from water and food (0.43mg F/day)

The estimated UL for children between 8 to 14 years of age is 5mg/day extrapolated from the UL for adults for whom the critical endpoint is an increased risk of bone fracture [European Union, 2005; WHO: Fawell J, Bailey K,Chilton J,Dahi E,Fewtrell L, 2006].

2.6.3. Exposure of Children between 6 to 12 Years of Age

Systemic exposure to fluoride from water-based beverages and aggregated daily systemic exposure to fluoride (mg/day) for children between 6 to 12 years of age basis mandatory water fluoridation in Ireland (0.8mg/L) is shown in Table IV [European Commission, 2011].

The consumption data of drinking-water and other water-based products used by EFSA (2005) for children under 12 years of age is under 500mL/day.

Table IV. Total daily systemic exposure to fluoride (mg/day) for children between 6 to 12 years of age.

Drinking-water 0.8 mg F/L	***F intake from water (mg/day)***	***Aggregated F intake (mg/day): water and food (1)***	***Aggregated F intake (mg/day): water, food, 0.05% toothpaste***		***Aggregated F intake (mg/day): water, food, 0.15% toothpaste 0.225 mg F/day***
			0.025 mg F/day	***0.075 mg F/day***	
Consup. 0.5 L	0.40	0.70	0.73	0.78	0.93
Consump 1.0 L	0.80	1.10	1.13	1.18	1.33
Consump. 1.5 L	1.20	1.50	1.53	1.58	1.73

Aggregated fluoride intake from water and food (0.30mg F/day).

The UL for children between 4 to 8 years of age is 2.5mg/day based on a prevalence of less than 5% of moderate dental fluorosis as the critical endpoint and was used as the reference value for the children between 6 to12 years of age [European Union, 2005].

2.6.4. Exposure of Children between 1 to 6 Years of Age

Systemic exposure to fluoride from water-based beverages and aggregated daily systemic exposure to fluoride (mg/day) for children between 1 to 6 years of age basis mandatory water fluoridation in Ireland (0.8mg/L) is shown in Table V

Table V: Estimate of total daily systemic exposure to fluoride for children between 1 to 6 years of age

Drinking-water 0.8 mg F/L	***F intake from water (mg/day)***	***Aggregated F intake (mg/day): water and food (1)***	***Aggregated F intake (mg/day): water, food, 0.05% toothpaste***		***Aggregated F intake (mg/day): water, food, 0.15% toothpaste 0.90 mg F/day***
			0.10 mg F/day	***0.30 mg F/day***	
Consump. 0.5 L	0.40	0.70	0.80	1.00	**1.60**
Consump. 1.0 L	0.80	1.10	1.20	1.40	**2.00**
Consump. 1.5 L	1.20	**1.50**	**1.60**	**1.80**	**2.40**

(1) Aggregated fluoride intake from water and food (0.30mg F /day).

The estimated UL for children under 3 years of age is 1.5mg/day based on a prevalence of less than 5% of moderate dental fluorosis as the critical endpoint and was used for children between 1 to 6 years of age [European Union, 2005].

2.6.5. Exposure of Infants up to 12 Months

In the early months of their lives, many infants are fully or partially breastfed. While fully breastfed, infants have a low level of fluoride intake, partially breastfed and formula-fed infants receive different levels of fluoride intake. This is mainly because of the fluoride content of the water that is used to prepare infant formulas.

Up to 6 months of age, there are three choices for infant's main food source which are given breast milk or formula or breast

milk together with formula. Due to the low amount of fluoride in breast milk (~6µg/L), breastfed infants are less exposed to fluoride (less than 0.001mg/kg/day) [European Commission, 2011].

The fluoride concentration in the water used in the preparation of formula-fed infant's food is their main source of exposure. An infant who receives a formula prepared with water containing 0.8mg F/L alone digests 0.137mg F/kg/day compared to 0.001mg F/kg/day for an exclusively breastfed infant. The extent to which fluoride intake should generally be in infants between 6 and 12 months of age has not been addressed, as such calculations are not concrete, given that infants are fed different feeding patterns in EU Member States. Therefore, tolerable upper intake levels of fluoride in infants have not been established [European Union, 2005]. In infants younger than 6 months, UK DoH [UK DoH, 1991] states that 0.22mg F/kg BW/day is safe, while US IOM [IOM, 1997] states 0.1mg/kg BW/day UL for fluoride [European Commission, 2011].

2.7. Determination of a National Standard

When developing a national drinking-water standard, a variety of environmental, social, cultural, economic, dietary and other conditions must be taken into consideration. All of these conditions have a major effect on the potential exposure from fluoride in drinking-water compared to other sources such as food, consumer products and air [WHO, 2011].

The guideline value of 1.5mg/L has been recommended for fluoride in drinking-water based on the fact that the volume of water consumed, and intake of other sources should be considered when setting national standards [WHO, 2009; WHO,1984].

For instance, in a country with a warm climate year-round and where piped water is the preferred source of drinking-water, the authorities may select a health-based target for fluoride that is lower than that of WHO guideline value, because water consumption is expected to be higher [WHO, 2017; Fawell J, Bailey K,Chilton J,Dahi E,Fewtrell L, 2006].

On the contrary, the effects of a decision to remove fluoride from public drinking-water are more complex. In countries where public dental awareness is high, fluoride can be received widely through alternative means and the decision to remove fluoride from drinking-water would have no consequences. However, in countries where public dental awareness is lower adding fluoride to water at concentrations around 0.5-1.0mg/L would be an important public health objective [WHO, 2005].

In conclusion, the authorities have to pay attention to (i) the existing natural concentrations of fluoride, (ii) climate conditions, (iii) volume of water intake, (iv) risk of dental caries, (v) public dental awareness level, (vi) availability of alternative ways to receive fluoride for the whole population, and (vii) the appropriate daily intake of fluoride from water and other sources and the need to ensure an appropriate minimum intake to prevent adverse health effects considered.

3. Conclusions and Recommendations

The variations in exposure of fluoride from different sources (e.g., water, food) in different parts of the countries in different parts of the world have to be considered but public drinking-water is the major source of fluoride exposure. Fluoride exposure levels differ according to different volumes of water consumed by different populations which are urban and vulnerable subpopulations as an example. Children from lower socio-economic groups are affected mostly by natural or artificial fluoridation of drinking-water [European Commission, 2011].

The authorities have to evaluate the proportion of the tolerable daily intake of fluoride into drinking-water which may vary depending on the national drinking-water standards so calculating the exposure proportion will be necessary to take account of a variety of local circumstances and conditions (including environmental, social, cultural, economic, dietary and other conditions) affecting potential exposure [WHO, 2011]. It may be appropriate to allocate a major proportion of "tolerable daily intake" to drinking-water to derive a guideline value more suited to the local conditions in areas where the intake of a particular contaminant in drinking-water is known to be greater than other sources. (e.g., air and food).

The risk should be separately assessed for every life stage, especially children under 3 years of age, partially breastfed and formula-fed infants (due to a higher intake of drinking-water in this group in relation to body weight compared to adults) and considered integrated fluoride exposure from all sources that are water, food, and toothpaste mainly. Besides, partially breastfed and formula-fed infants can be exposed to a high proportion of fluoride. For this reason, pregnant and breastfeeding mothers have to meet their water requirements from bottled water that does not contain fluoride. Additionally, the use of water in the preparation of baby formula from bottled water that does not include fluoride is important in order not to reach the upper tolerable intake limit.

When examined the guidelines values for fluoride identified by WHO which to be used to assist evaluation of the risks, the estimated upper tolerable intake limit for children under 3 years of age is 1.5mg/day and when this children group consumed 0.5 litres or more, 1.5 litres from public drinking-water which effected naturally or artificially fluoridation of 0.8mg/L and 1.6mg/L together with food and toothpaste, total fluoride intake exceed to upper tolerable intake limit. Meantime, the group of partially breastfed and formula-fed infants might be the prime affected population so authorities must be promoted to use only bottled drinking-water unaffected from fluoride for pregnant, infant and children under 3 years of age and supplied bottled drinking-water for lower socio-economic groups.

In order to protect health, local and national authority can set regulations related with the reasonable minimum requirements of fluoride in drinking-water basis evidence including changes in sensitive life stages provided by scientific consensus.

In many countries' authorities promote private companies to use fluoride in their product (i.e., fluoridated dental and salt products) and give freedom to people to choose alternative ways but there will be significant variation in individual exposure.

The authorities have to determine the appropriate action in order to modify standards, remove parameters or add new parameters for the safety of public drinking-water according to national standards (quality regulations) to be subjected to periodic review but no changes should be made without proper justification through risk assessment for protection of public health. The volume of drinking-water consumed and intake from other sources should also be considered when setting national standards.

National authorities have to discuss the risks assessment for fluoride they face in conducting on artificial or natural fluoridation or derogation of fluoride in public drinking-water and

how the WHO can help in dealing with them. Of course, the various risks will need to be balanced during evaluating the significance to public health, individuals, and environmental pollution.

This review showing that authorities have to (i) simplifying existing regulations and standards, (ii) enhance transparency on fluoridation and derogation policy in public drinking-water for monitoring the impact of them, (iii) clarifying the rules on the use of remedy measures for derogation of public drinking-water, (iv) improve consumer health protection, (v) cooperate more closely with other nations and international organizations for fluoridation and derogation, (vi) reviewing how they could be harmonized at the EU level, or incorporated under the WHO umbrella, and (vii) develop a data flow and sharing information.

The U.S. Department of Health and Human Services (HHS) and the U.S. Environmental Protection Agency (EPA) announced "New Scientific Assessments and Actions on Fluoride" dated 01.07.2011 and proposed a recommendation of 0.7mg of fluoride per litres of water. This updated recommendation is based on recent EPA and HHS scientific assessments to balance the benefits of preventing tooth decay while limiting any unwanted health effects. These scientific assessments will also guide EPA in making a determination of whether to lower the maximum amount of fluoride allowed in drinking-water, which is set to prevent adverse health effects [E.P.A. United States, 2011].

The adverse effects on health caused by fluoride in drinking-water after long periods of exposure is not definite because of the lack of sufficient information to calculate health risks. Researchers have to work together with authorities to present data to be used by doctors and nutritionists but "the country-by-country data does not include information on countries that artificially fluoridate their public water supplies" [WHO: Fawell J, Bailey K,Chilton J,Dahi E,Fewtrell L, 2006] or countries hesitate to share this information with transparency mentality in a public area so this review will enable both authorities to contribute to the public health in countries and researchers to determine the next steps based on evidence related to fluoride in drinking-water.

For protecting public health, the scientific consensus authorities can set a national regulation related to the minimum requirements of fluoride in drinking-water.

This review, in which fluorine intake is evaluated, can shed light on public health, especially pediatric health in evaluating fluoride intake and it can improve national drinking-water quality based on fluoridation and derogation which is in progress to eliminate high values.

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