Comments
on the
Fluoridation of Drinking Water
for Prevention of Dental Caries

Submitted to the
Committee on Health and Social Services
Québec

Regarding
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The author of these comments is a professional in the field of risk analysis, including exposure assessment, toxicity evaluation, and risk assessment. She has recently served on two subcommittees of the National Research Council's Committee on Toxicology that dealt with fluoride exposure and toxicity, including the NRC's Committee on Fluoride in Drinking Water. She has also authored an Environmental Protection Agency report on fluoride toxicity.

These comments are not to be considered a comprehensive review of fluoride exposure or toxicity. Opinions and conclusions expressed herein are those of the author.

Summary. Although fluoridation of drinking water for the purpose of caries prevention is widely practiced in the United States and a few other countries, and is strongly encouraged by some governments and public health agencies, several important concerns have not been adequately addressed:

(1) Available data do not support a role of community water fluoridation in improving dental health.

(2) A variety of adverse health effects are associated with fluoride exposures.

(3) By fluoridation of drinking water, governments and water suppliers are indiscriminately administering a drug to the population, without individual evaluation of need, appropriate dose, efficacy, or side effects.

These concerns are discussed in more detail below. Governments and health agencies that are serious about protecting the health of their populations should call for an immediate end to community water fluoridation.

(1) Available data do not support a role of community water fluoridation in improving dental health.

The U.S. Department of Health and Human Services (HHS) considers community water fluoridation to be important in the prevention of dental caries (Federal Register 2011), as do governments and health agencies in a few other countries. However, the question of whether water fluoridation actually produces a benefit requires further attention.

The University of York has carried out perhaps the most thorough review to date of human studies on effects of fluoridation. Their work (McDonagh et al. 2000) is often cited as showing the safety and efficacy of water fluoridation, but it actually does neither (Wilson and Sheldon 2006; Cheng et al. 2007). The report mentions a surprising lack of high quality studies demonstrating benefits, and also finds little evidence that water fluoridation reduces socioeconomic disparities:

> Given the level of interest surrounding the issue of public water fluoridation, it is surprising to find that little high quality research has been undertaken. (McDonagh et al. 2000)
>
> Water fluoridation aims to reduce social inequalities in dental health, but few relevant studies exist. The quality of research was even lower than that assessing

> overall effects of fluoridation. (Cheng et al. 2007)
>
> Evidence relating to reducing inequalities in dental health was both scanty and unreliable. (Wilson and Sheldon 2006)

The apparent benefit is modest, about a 15% difference in the proportion of caries-free children (McDonagh et al. 2000). The American Dental Association (2005) states that "water fluoridation continues to be effective in reducing dental decay by 20-40%," which would translate to less than 1 decayed, missing, or filled permanent tooth (DMFT) in older children and adolescents (based on U.S. data from CDC 2005).

Neither McDonagh et al. (2000) nor the ADA (2005) mentions that fluoride exposure appears to delay the eruption of permanent teeth, although this has been known since the 1940s (Short 1944; NRC 2006). A delay in tooth eruption alters the curve of caries rates with respect to age and complicates the analysis of age-specific caries rates (Psoter et al. 2005; Alvarez 1995; Alvarez and Navia 1989). Specifically, "the longer the length of exposure to the oral environment the greater is the risk of the tooth becoming carious" (Finn and Caldwell 1963; citing Finn 1952). Komárek et al. (2005) have calculated that the delay in tooth eruption due to fluoride intake may explain the apparent reduction in caries rates observed when comparisons are made at a given age, as is usually done.

Most studies of benefits of fluoride intake or fluoridation have failed to account for a number of important variables, including individual fluoride intakes (as opposed to fluoride concentrations in the local water supplies), sugar intake, socioeconomic variables, and the general decline in caries rates over the last several decades, independent of water fluoridation status. When World Health Organization data on oral health of children in various countries are compared, similar declines in caries over time are seen in all developed countries, regardless of fluoridation status (Cheng et al. 2007; Neurath 2005). The only peer-reviewed paper to be published from California's major oral health survey in the 1990s reported no association between fluoridation status and risk of early childhood caries (Shiboski et al. 2003). Several studies show differences in caries rates with socioeconomic status or dietary factors but not with fluoridation status (e.g., Adair et al. 1999; Hamasha et al. 2006).

In general, the role of diet and nutrition in good dental health seems to be underappreciated. For example, Cote et al. (2004) have documented a much lower rate of caries experience in refugee children from Africa than in U.S. children or refugee children from Eastern Europe, a situation that the authors attribute more to the amount of sugar in the diet than the presence of fluoride in the water. Finn (1952) provides an extensive review of dental caries in "modern primitive peoples," concluding that they "show less dental caries than do most civilized peoples. . . . Evidence indicates, however, that primitive peoples have an increased caries attack rate when brought into contact with modern civilization and a civilized diet."

A number of sources (reviewed by NRC 2006), including the Centers for Disease Control and Prevention (CDC 2001), indicate that any beneficial effect of fluoride on teeth is topical (e.g., from toothpaste), not from ingestion. Featherstone (2000) describes mechanisms by which topical fluoride has an anti-caries effect and states that "[f]luoride incorporated during tooth development [i.e., from ingested fluoride] is insufficient to play a significant role in caries protection." Also:

> The fluoride incorporated developmentally—that is, systemically into the normal tooth mineral—is insufficient to have a measureable effect on acid solubility. (Featherstone 2000)
>
> The prevalence of dental caries in a population is not inversely related to the concentration of fluoride in enamel, and a higher concentration of enamel fluoride is not necessarily more efficacious in preventing dental caries. (CDC 2001)

Fluoride concentrations in drinking water or saliva are too low to be contributing significantly to a topical anti-caries effect, especially since most drinking water is not "swished" around the teeth before being swallowed. CDC (2001) states that "The concentration of fluoride in ductal saliva, as it is secreted from salivary glands, is low—approximately 0.016 parts per million (ppm) in areas where drinking water is fluoridated and 0.006 ppm in nonfluoridated areas. This concentration of fluoride is not likely to affect cariogenic activity."

The single study that has examined caries experience in relation to individual fluoride intakes at various ages during childhood (the Iowa study) has found no association between fluoride intake and caries experience; caries rates (% of children with or without caries) at ages 5 and 9 were similar for all levels of fluoride intake (Warren et al. 2009). The authors state that "the benefits of fluoride are mostly topical" and that their "findings suggest that achieving a caries-free status may have relatively little to do with fluoride *intake*" (emphasis in the original). Most of the children with caries had "relatively few decayed or filled surfaces" (Warren et al. 2009). The authors' main conclusion:

> Given the overlap among caries/fluorosis groups in mean fluoride intake and extreme variability in individual fluoride intakes, firmly recommending an "optimal" fluoride intake is problematic. (Warren et al. 2009).

The national data set collected in the U.S. in 1986-1987 (more than 16,000 children, ages 7-17, with a history of a single continuous residence) shows essentially no difference in caries rates in the permanent teeth of children with different water fluoride levels (Table 1; Fig. 1; data obtained from Heller et al. 1997; similar data can be obtained from Iida and Kumar 2009). Analysis in terms of mean DMFS (decayed, missing, or filled tooth surfaces) for the group (Fig. 2), as opposed to caries prevalence, shows an apparent 18% decrease between the low-fluoride (< 0.3 mg/L) and fluoridated (0.7-1.2 mg/L) groups. In absolute terms, this is a decrease of about one-half (0.55) of one tooth surface per child. One possible explanation is delayed tooth eruption, which was not considered in the study. Note that the mean DMFS for the highest fluoride group is higher than for either of the two intermediate groups, also indicating that DMFS scores are not solely a function of water fluoride concentration. When the data are examined by the distribution of DMFS scores (Fig. 3), no real difference in caries experience with respect to water fluoride concentration is observed.

The available data, responsibly interpreted, indicate little or no beneficial effect of water fluoridation on oral health.

(2) A variety of adverse health effects are associated with fluoride exposures.

For most of the U.S. population, the single largest source of fluoride exposure is municipal tap water, including tap water used directly, beverages and foods prepared with municipal tap water

either at home or in restaurants, and commercial beverages and processed foods prepared with municipal tap water. For a water fluoride level of 1 mg/L (1 ppm), which is the level still used in most fluoridated U.S. cities, estimated average exposures to fluoride from all sources range from about 0.03 mg/kg/day (mg of fluoride per kg of body weight per day) for adults and nursing infants to 0.09 mg/kg/day for non-nursing infants (especially infants fed formula prepared with fluoridated tap water). Note that these are estimated *average* exposures. For individuals with high tap water consumption (discussed by NRC 2006), total fluoride exposures can exceed 0.1 mg/kg/day for some adults and may reach 0.2 mg/kg/day for some infants. In one of the few studies to evaluate individual intake of fluoride from all sources, Warren et al. (2009) report individual fluoride intakes (from all sources) in excess of 0.2 mg/kg/day for some infants.

The NRC (2006) identified several sizeable subgroups of the U.S. population that require special consideration due to above-average fluoride exposures, increased fluoride retention, or greater susceptibility to effects from fluoride exposures. Groups known to be at risk of high fluoride intake include those with high water intake (e.g., outdoor workers, athletes, and individuals with diabetes insipidus or other medical conditions) or exposure to other sources of fluoride intake (NRC 2006). In addition, people with impaired renal function are at higher risk of adverse effects per unit intake of fluoride, due to impaired excretion of fluoride and consequent higher fluoride concentrations in the body. Tap water consumption varies among individuals by more than a factor of 10, depending on age, activity level, and the presence of certain health conditions such as diabetes insipidus (NRC 2006; see also Warren et al. 2009 for an example of estimated fluoride intakes for individual children at different ages). A substantial number of infants have water consumption rates in excess of 0.1 L/kg/day (100 mL per kg body weight per day; NRC 2006; EPA 2004a).

The U.S. Department of Health and Human Services (HHS) recently proposed a new recommendation regarding fluoride concentrations in drinking water (Federal Register 2011), the primary change being from a recommended range of 0.7-1.2 mg/L fluoride in drinking water (0.7-1.2 ppm) based on ambient local temperatures, to a single value of 0.7 mg/L (0.7 ppm), regardless of temperature. At the proposed fluoride concentration of 0.7 mg/L in drinking water, infants consuming at least 0.1 L/kg/day of tap water will have fluoride intakes at and above 0.07 mg/kg/day, and some will exceed 0.15 mg/kg/day (NRC 2006).

The HHS recommendation addresses only dental fluorosis (discussed below), while ignoring a long list of other health concerns for the U.S. population. Dental fluorosis itself has been associated with increased risks of various adverse health effects, including thyroid disease, lowered IQ, and bone fracture (Alarcón-Herrera et al. 2001; Zhao et al. 1996; Li et al. 1995; Lin et al. 1991; Desai et al. 1993; Yang et al. 1994; Jooste et al. 1999; Li et al. 2003; Susheela et al. 2005; Rocha-Amador et al. 2009). To the best of my knowledge, no studies in the U.S. or Canada have looked for associations between dental fluorosis and risk of other adverse effects. However, the failure to look for adverse health effects does not demonstrate the absence of adverse health effects.

The NRC (2006) indicated that the Environmental Protection Agency's (EPA's) present drinking water standards for fluoride (maximum contaminant level goal [MCLG] and maximum contaminant level [MCL], both at 4 mg/L) are not protective of human health, based on preventing severe dental fluorosis, stage II skeletal fluorosis, and increased risk of bone fractures. Given the wide range of water intake within the American population and the presence

of other sources of fluoride intake, one can reasonably expect that a "safe" level of fluoride in drinking water would be at least a factor of 10 below the "unsafe" level of 4 mg/L. EPA's MCLG is defined as a "non-enforceable health goal which is set at a level at which no known or anticipated adverse effect on the health of persons occurs and which allows an adequate margin of safety" (EPA 2009). Dental fluorosis, skeletal fluorosis, and increased risk of bone fracture are all reasonably well known and acknowledged adverse health effects from fluoride exposure. However, EPA is also required to consider the "anticipated" adverse effects (which may occur at lower levels of fluoride exposure than the "known" effects) and allow for an adequate margin of safety. The proposed HHS recommendation for water fluoridation at 0.7 mg/L is not adequate to protect against known or anticipated adverse effects and does not allow an adequate margin of safety to protect young children, people with high water consumption, people with kidney disease (resulting in reduced excretion of fluoride), and other potentially sensitive population subgroups.

In addition to the "known" adverse health effects of dental fluorosis, skeletal fluorosis, and increased risk of bone fracture, "anticipated" adverse health effects from fluoride exposure or community water fluoridation include (but are not limited to) carcinogenicity, genotoxicity, endocrine effects, increased blood lead levels, and hypersensitivity (reduced tolerance) to fluoride. These effects (described in more detail below) are not as well studied as the dental and skeletal effects, which should indicate that a greater margin of safety is necessary to ensure protection of the population—"in the face of uncertain evidence it is important to act in a manner that protects public health" (Tickner and Coffin 2006). In addition, it should be noted that some of these effects may occur at lower fluoride exposures than those typically associated with dental or skeletal effects, such that protection against the dental or skeletal effects does not necessarily ensure protection against other anticipated adverse health effects. Elimination of community water fluoridation is the best way to reduce fluoride exposures for most individuals to a level at which adverse health effects are unlikely.

A few comments regarding the interpretation of the available fluoride studies may be helpful. As Cheng et al. (2007) have described, a "negative" study may simply mean that the study was not sufficiently sensitive to demonstrate a moderate (as opposed to large) effect. This is often due to use of too small a sample size. In addition, study populations are often grouped by community, water source, or fluoride concentration in the water, rather than by individual intake. Due to the wide variation in drinking water intake, this approach results in study groups with overlapping intakes and makes it difficult to detect dose response relationships that do in fact exist.

The few studies that have looked at age-dependent exposure to fluoride have found increased risks of adverse effects (e.g., Bassin et al. 2006 for osteosarcoma; Danielson et al. 1992 for hip fracture risk); studies that have not looked at age-dependent exposure cannot be assumed to provide evidence of no effect. Similarly, studies that have used a measure of current exposure where a cumulative measure would be more appropriate, or vice versa, cannot be assumed to demonstrate lack of an effect.

Studies of fluoride toxicity in laboratory animals are sometimes dismissed as irrelevant because the exposures or fluoride concentrations used were higher than those expected for humans drinking fluoridated tap water. It is important to know that animals require much higher exposures (5-20 times higher, or more; see NRC 2006; 2009) than humans to achieve the same

effects or similar fluoride concentrations in bone or serum. In other words, humans are considerably more sensitive to fluoride than are most animal species that have been studied.

A number of adverse health effects can be expected to occur in at least some individuals when estimated average intakes of fluoride are around 0.05 mg/kg/day or higher (NRC 2006; 2009). For persons with iodine deficiency, average intakes as low as 0.01-0.03 mg/kg/day could produce effects (NRC 2006). The next few sections briefly summarize some (not all) of the adverse health effects, known and anticipated, that should be considered in any reevaluation of the drinking water standards for fluoride. Most of these effects have been reviewed in detail by the NRC (2006), although the NRC did not specifically evaluate health risks over the whole range of fluoride intakes or attempt to identify a "safe" level of fluoride exposure.

Dental fluorosis

The main reason for the change in fluoridation levels proposed by HHS is the prevention of dental fluorosis, a condition ranging from mild spotting of the teeth to severe pitting and staining. Dental fluorosis is caused by excessive fluoride ingestion during the early years of childhood, before the permanent teeth erupt. The HHS recommendation is intended to limit the risk of dental fluorosis while maintaining caries protection (Federal Register 2011). The most recent data indicate a fluorosis prevalence in the U.S. (all levels of severity) of 40.7% in 1999-2004 vs. 22.6% in 1986-1987 for children ages 12-15 (Beltrán-Aguilar et al. 2010). The proposed change in water fluoridation level will put the U.S. in agreement with Canada, which in 2009 recommended a fluoride concentration of 0.7 mg/L for all parts of the country (Health Canada 2009).

Based on the 1986-1987 data set (as reported by Heller et al. 1997), which included water fluoride concentrations, fluoridating at 0.7 mg/L can be expected to bring the fluorosis prevalence in the U.S. down to about 27%. Elimination of fluoridation entirely, for the whole population, would be expected to bring the fluorosis prevalence down to that of the current low-fluoride population (to around 13% based on Heller et al. 1997; Fig. 4).

The only U.S. study to have looked at dental fluorosis and individual fluoride intake at various ages (the Iowa study) reported that for children with fluoride intakes above 0.06 mg/kg/day during the first 3 years of life, fluorosis rates were as high as 50% (Hong et al. 2006b). As mentioned above, at a fluoride concentration of 0.7 mg/L in drinking water, many infants will have fluoride intakes at and above 0.07 mg/kg/day, and some will exceed 0.15 mg/kg/day (NRC 2006). Thus a large fraction of infants and young children fed formula made with fluoridated tap water can be expected to develop dental fluorosis even at a water fluoride concentration of 0.7 mg/L.

The National Research Council considers severe dental fluorosis to be an adverse health effect and reports the general consensus in the literature that both severe and moderate dental fluorosis should be prevented (NRC 2006). Health Canada (2009) considers moderate dental fluorosis to be an adverse effect. The Iowa study indicates that high fluoride intake during the first 2 years of life is most important with respect to development of dental fluorosis of the permanent maxillary central incisors (the "top front teeth")—the teeth that most affect a person's appearance—although fluoride intake up to at least 4 years old was also important (Hong et al. 2006a). The American Dental Association has issued a brief statement to the effect that parents

should not prepare infant formula with fluoridated water if they are concerned about the possibility of their child developing dental fluorosis (ADA 2007). This is an admission that dental fluorosis is undesirable, and that fluoridated tap water is not "safe" for all individuals. The CDC (2005) reports a higher likelihood of moderate and severe fluorosis for minority and low-income children. While for a variety of reasons it is appropriate for governments and health agencies to encourage breastfeeding of infants, in many family situations breastfeeding is not possible (e.g., in cases of adoption or of ill-health or death of the mother). It is therefore essential that tap water be safe for use in infant formula, without putting infants at increased risk of dental fluorosis.

Skeletal fluorosis

Bone fluoride concentrations in the ranges reported for stage II and III skeletal fluorosis will be reached by long-term fluoride exposures of 0.05 mg/kg/day or higher (estimated from NRC 2006). Bone fluoride concentrations, radiologic changes, and symptoms are not clearly correlated (Franke et al. 1975), and most U.S. studies do not categorize cases by stage. Recent case reports include fluorosis attributed to excessive ingestion of tea or toothpaste (Whyte et al. 2005; Hallanger Johnson et al. 2007; Kurland et al. 2007). Most of the literature addresses high fluoride exposures over a few years; there has been essentially no investigation of effects of low exposures over many years and no effort to identify fluorosis of any stage in the U.S. "Arthritis" (defined as painful inflammation and stiffness of the joints) is the leading cause of disability in the U.S., currently affects at least 46 million adults in the U.S. (including 50% of the population > 65 years old), and is expected to affect 67 million adults in the U.S. by 2030 (CDC 2006). The possibility that a sizeable fraction of "bone and joint pain" or "arthritis" in U.S. adults is attributable to fluoride exposure has not been addressed, although it is plausible, given what is known about fluoride intakes.

Increased risk of bone fractures

The NRC (2006) concluded that lifetime exposure to fluoride at an estimated average daily intake of 0.08 mg/kg/day (average adult fluoride intake with water at 4 mg/L) is likely to result in higher bone fracture rates, and the available information suggests an increased likelihood of bone fracture for daily fluoride intakes of 0.05 mg/kg/day (average adult fluoride intake at 2 mg/L). The Agency for Toxic Substances and Disease Registry (ATSDR) has identified a chronic-duration Minimal Risk Level (MRL) for oral exposure to fluoride of 0.05 mg/kg/day, based on an increased risk of bone fracture (ATSDR 2003). The NRC's findings (NRC 2006) indicate that the ATSDR's MRL is not protective enough. The available studies consider fluoride intake only in terms of the concentration in the local drinking water, and most use fluoridated water (1 mg/L, corresponding to an average daily intake of 0.03 mg/kg/day for adults) as a control. Thus there is probably considerable overlap in exposures between groups, making effects more difficult to distinguish, and the entire dose response range of interest has not been well studied. The findings in humans are consistent with animal studies that have found increased brittleness of bones with increased fluoride exposure (Clark and Mann 1938; Turner et al. 1997; 2001).

Danielson et al. (1992) reported an increased relative risk for hip fracture in a fluoridated area of 1.27 (95% CI 1.08-1.46) for women and 1.41 (95% CI 1.00-1.81) for men. These authors reported a difference between women exposed to fluoride prior to menopause and those exposed afterwards. For women exposed prior to menopause, the fracture risk was considerably higher than for those not exposed to fluoride. Many studies of fracture risk have not looked at age-specific exposure, or have involved women exposed only after menopause, when fluoride uptake into bone is probably substantially lower.

The Iowa study reported effects on bone mineral concentration and bone mineral density with average childhood fluoride intakes of 0.02-0.05 mg/kg/day (Levy et al. 2009). Linear correlation between dental fluorosis and risk of bone fracture has been reported for children and adults (Alarcón-Herrera et al. 2001; Fig. 5). Bone fracture rates in children in the U.S. may be increasing (e.g., Khosla et al. 2003), but fluoride exposure has not been examined as a possible cause or contributor.

Carcinogenicity

Three U.S. courts have found water fluoridation to be injurious to human health, specifically that it may cause or contribute to the cause of cancer and genetic damage (described in detail by Graham and Morin 1999). The NRC's committee on fluoride toxicology unanimously concluded that "Fluoride appears to have the potential to initiate or promote cancers," even though the overall evidence is "mixed" (NRC 2006). Referring to the animal studies, the committee also said that "the nature of uncertainties in the existing data could also be viewed as supporting a greater precaution regarding the potential risk to humans." The committee discussed the limitations of epidemiologic studies, especially ecologic studies (those in which group, rather than individual, measures of exposure and outcome are used), in detecting small increases in risk—in other words, the studies are not sensitive enough to identify small or moderate increases in cancer risk; therefore a "negative" study does not necessarily mean that there is no risk (see also Cheng et al. 2007).

While the NRC did not assign fluoride to a specific category of carcinogenicity (i.e., known, probable, or possible), the committee did not consider either "insufficient information" or "clearly not carcinogenic" to be applicable. The committee report (NRC 2006) includes a discussion of how EPA establishes drinking water standards for known, probable, or possible carcinogens; such a discussion would not have been relevant had the committee not considered fluoride to be carcinogenic. The question becomes one of how strongly carcinogenic fluoride is, and under what circumstances.

The case-control study by Bassin et al. (2006) is the only published study thus far to have looked at age-dependent exposure to fluoride. This study reported a significantly elevated risk of osteosarcoma in boys as a function of estimated age-specific fluoride intake. Osteosarcoma is a bone cancer that commonly results in amputation of an affected limb and may result in death. At the very least, this study indicates that similar studies of pediatric osteosarcoma that have not looked at age-dependent intake cannot be considered to show "no effect." A recent review of osteosarcoma risk factors (Eyre et al. 2009) lists fluoride among "a number of risk factors that emerge with some consistency" and considers fluoride exposure to have a "plausible" role in etiology of osteosarcoma.

While a few other studies (e.g., Gelberg et al. 1995; Kim et al. 2011) have looked at individual fluoride exposure (as opposed to group or ecologic measures of exposure), these have looked at total fluoride exposure until time of diagnosis or treatment. Given that there is a "lag time" of a few years between onset of a cancer and its diagnosis, use of cumulative fluoride exposure until time of diagnosis is potentially misleading, as fluoride exposure during the last several years (during the "lag time") cannot have contributed to the initiation of a cancer but could have a significant effect on the estimate of cumulative fluoride exposure.

The 1990 National Toxicology Program (NTP) study on sodium fluoride officially concluded that "there was *equivocal evidence of carcinogenic activity* of sodium fluoride in male F344/N rats, based on the occurrence of a small number of osteosarcomas in dosed animals" (NTP 1990; italics in the original). According to the published report, a "small number of osteosarcomas occurred in mid- and high-dose male rats. These neoplasms occurred with a significant dose response trend, but at a rate within the upper range of incidences previously seen in control male rats in NTP studies" (NTP 1990). It is important to realize that the historic controls from previous studies had not had the special low-fluoride diet used for this study, and therefore more properly constitute a low- to mid-range exposed group rather than a control group. This and other concerns were described in a memo within the Environmental Protection Agency (Marcus 1990) and reported in the press (Hileman 1990). These concerns and the testimony before the U.S. Senate of the union representing EPA scientists (Hirzy 2000) should be taken seriously.

In humans, osteosarcomas tend to occur most commonly in young people (pediatric cases) or the very old (adult or geriatric cases), with a higher incidence in males than in females (Bassin et al. 2006). Sergi and Zwerschke (2008) indicate that 60-75% of cases are in patients between 15 and 25 years old. In the NTP 2-year study, fluoride exposure was begun when the animals were 6 weeks old, as is typical for NTP and similar studies (Hattis et al. 2004). Puberty in the rat typically occurs at about 32 days of age in females and 42 days in males (e.g., Gray et al., 2004; Evans 1986). Thus, the age of 6 weeks in the NTP study probably corresponds to pubertal or post-pubertal animals. The cases of osteosarcoma in the rats were reported in the late stages of the test, and probably corresponded to geriatric osteosarcomas in humans. In Bassin's study, the age range for which the fluoride-osteosarcoma association was most apparent was for exposures at ages 4-12 years, with a peak for exposures at age 6-8 years (Bassin et al. 2006). Very likely, the fluoride exposures in most of the animal studies have started after the age corresponding to the apparent most susceptible age in humans, and thus these animal studies may have completely missed the most important exposure period with respect to initiation of the majority of human osteosarcomas. Therefore, this animal study cannot be interpreted as showing no evidence of causation for pediatric osteosarcoma, although, properly interpreted, it does show evidence for causation of geriatric osteosarcoma.

Genotoxicity

Genotoxicity, or the ability to damage the genetic material (genes and chromosomes) of cells, is considered indicative of potential carcinogenicity. A number of mammalian *in vitro* systems have shown dose-dependent cytogenetic or cell transformational effects from fluoride exposure (reviewed by NRC 2009). Several reports suggest an indirect or promotional mechanism, e.g., inhibition of DNA synthesis or repair enzymes, rather than a direct mutagenic effect (Lasne et al.

1988; Aardema et al. 1989; Aardema and Tsutsui 1995; Meng and Zhang 1997). Human cells seem to be much more susceptible to chromosome damage from fluoride than are rodent cells (Kishi and Ishida 1993).

A recent paper by Zhang et al. (2009) describes a new testing system for potential carcinogens, based on induction of a DNA-damage response gene in a human cell line. Sodium fluoride tests positive in this system, as do a number of other known carcinogens, representing a variety of genotoxic and nongenotoxic carcinogenic mechanisms. Known noncarcinogens—chemicals not associated with carcinogenicity—did not test positive. The system described by Zhang et al. (2009) is considerably more sensitive than the older systems for most chemicals examined; a positive effect was seen at a fluoride concentration of about 0.5 mg/L, or a factor of 10 lower than in other systems.

A fluoride concentration of 0.5 mg/L in urine will routinely be exceeded by many people consuming fluoridated water (NRC 2006); for people with substantial fluoride intake, serum fluoride concentrations may also reach or exceed 0.5 mg/L. Acute fluoride exposures (e.g., accidental poisoning, fluoride overfeeds in drinking water systems) have resulted in fluoride concentrations in urine well in excess of 5 mg/L in a number of cases (e.g., Penman et al. 1997; Björnhagen et al. 2003; Vohra et al. 2008). Urine fluoride concentrations can also exceed 5 mg/L if chronic fluoride intake is above about 5-6 mg/day (0.07-0.09 mg/kg/day for an adult; based on NRC 2006). Thus, kidney and bladder cells are probably exposed to fluoride concentrations in the ranges at which genotoxic effects have been reported *in vitro*, especially when the more sensitive system of Zhang et al. (2009) is considered. Based on the results of Zhang et al. (2009), most tissues of the body are potentially at risk if serum fluoride concentrations reach or exceed 0.5 mg/L. In addition, cells in the vicinity of resorption sites in fluoride-containing bone are potentially exposed to very high fluoride concentrations in extracellular fluid (NRC 2006) and thus are also at risk for genotoxic effects.

Endocrine effects

The NRC (2006) concluded that fluoride is an endocrine disruptor. Endocrine effects include altered thyroid function or increased goiter prevalence (at fluoride intakes of 0.05-0.1 mg/kg/day, or 0.01-0.03 mg/kg/day with iodine deficiency), impaired glucose tolerance (at fluoride intakes above 0.07 mg/kg/day), a decrease in age at menarche in girls in fluoridated towns, and disruptions in calcium metabolism (calcitonin and parathyroid function, at fluoride intakes of 0.06-0.15 mg/kg/day or higher). ATSDR's toxicological profile for fluoride (ATSDR 2003) refers to an animal study of thyroid function that would give a lower MRL (value not given) than the MRL derived for bone fracture risk (0.05 mg/kg/day).

Thyroid dysfunction and Type II diabetes presently pose substantial health concerns in the U.S. (NRC 2006). Of particular concern is an inverse correlation between subclinical maternal hypothyroidism and the IQ of the offspring. In addition, maternal subclinical hypothyroidism has been proposed as a cause of or contributor to development of autism in the child (Román 2007; Sullivan 2009). Steingraber (2007) has described the decrease in age at puberty of U.S. girls and the associated increased risk of breast cancer. Calcium deficiency induced or exacerbated by fluoride exposure may contribute to other health effects (NRC 2006).

Increased blood lead levels

An increased likelihood of elevated blood lead levels is associated with use of silicofluorides (usually H_2SiF_6 or Na_2SiF_6) as the fluoridating agent (NRC 2006; Coplan et al. 2007). Approximately 90% of people on fluoridated water are on systems using silicofluorides (NRC 2006). The chemistry and toxicology of these agents, especially at low pH (e.g., use of fluoridated water in beverages such as tea, soft drinks, or reconstituted fruit juices), have not been adequately studied (NRC 2006). Associations between silicofluoride use and biological effects in humans have been reported, in particular, elevated levels of blood lead in children and inhibition of acetylcholinesterase activity (reviewed by Coplan et al. 2007). A recent study in rats found significantly higher concentrations of lead in both blood and calcified tissues of animals exposed to both silicofluorides and lead (Sawan et al. 2010).

In addition to biological effects of silicofluorides, the interaction of silicofluorides (as the fluoridating agent) and disinfection agents (specifically, chloramines) also increases the leaching of lead from plumbing fixtures into drinking water (Maas et al. 2005; 2007). For example, the interaction of silicofluorides and chloramines is the probable explanation for the high lead levels in drinking water and children's blood in Washington, D.C. a few years ago (Maas et al. 2005; 2007; Leonnig 2010). EPA considers lead to be a probable human carcinogen and to have no practical threshold with respect to neurotoxicity (EPA 2004b)—in other words, there is considered to be no safe level of lead exposure, and the MCLG for lead is zero (EPA 2009).

Neurotoxicity

Grandjean and Landrigan (2006) list fluoride as an "emerging neurotoxic substance" that needs further in-depth studies. The major concern is neurotoxic effects during human development. The NRC (2006) concluded that "it is apparent that fluorides have the ability to interfere with the functions of the brain and the body by direct and indirect means." A number of studies indicate an association of fluoride exposure with lower IQ in children and with other measures of neuropsychological development (reviewed by NRC 2006; Connett et al. 2010; Choi et al. 2012; see also Zhao et al. 1996; Lu et al. 2000; Xiang et al. 2003; Rocha-Amador et al. 2007; 2009; Saxena et al. 2012; Seraj et al. 2012).

Additional adverse health effects

Fluoride intake is likely to affect the male reproductive-hormone environment, beginning at intakes of around 0.05 mg/kg/day (reviewed by NRC 2009). A "safe" intake with respect to male reproductive effects is probably somewhere below 0.03 mg/kg/day.

The NRC has reviewed the possible association between exposure to fluoridated water (approximately 0.02 mg/kg/day for adults) and increased risk of Down syndrome (trisomy 21) in children of young mothers, discussed a possible mechanism, and recommended further study (NRC 2006). Fetuses with Down syndrome are less likely to survive to birth, due both to higher natural fetal loss and to a high rate of pregnancy termination (Buckley and Buckley 2008; Forrester and Merz 1999; Siffel et al. 2004; Biggio et al. 2004).

Hypersensitivity or reduced tolerance to fluoride has been reported for exposure to fluoridated water (approximately 0.02 mg/kg/day for adults) or use of fluoride tablets (approximately 1 mg/day). Symptoms include skin irritation, gastrointestinal pain and symptoms (nausea, vomiting, diarrhea, constipation), urticaria, pruritus, stomatitis, chronic fatigue, joint pains, polydipsia, headaches, and other complaints (Waldbott 1956; 1958; Feltman and Kosel 1961; Grimbergen 1974; Petraborg 1977; Spittle 2008; reviewed by NRC 2006). Patients were often unaware that their drinking water contained fluoride. Symptoms improved with avoidance of fluoridated water and recurred with consumption of fluoridated water or with experimental challenge with sodium fluoride. Double-blind tests of patients have confirmed hypersensitivity to fluoride (Grimbergen 1974; Waldbott 1956; 1958). Many of the observed symptoms represent true allergic phenomena, while others (e.g., gastrointestinal symptoms) could be due to a lower level of tolerance for fluoride (intoxication at lower exposure; Waldbott 1956; 1958).

(3) By fluoridation of drinking water, governments and water suppliers are indiscriminately administering a drug to the population, without individual evaluation of need, appropriate dose, efficacy, or side effects.

The U.S. Food and Drug Administration (FDA) considers fluoride in toothpaste to be a non-prescription drug (e.g., FDA undated-a; undated-b) and fluoride "supplements" (usually tablets or lozenges) to be prescription drugs (e.g., Medline Plus 2008). Most prescription fluoride supplements are considered unapproved drugs (for example, see DailyMed 2011a,b,c), meaning that they "may not meet modern standards of safety, effectiveness, quality, and labeling" (FDA 2011). The goal of community water fluoridation is to provide a dental health benefit to individuals and to the population generally (Federal Register 2010), and EPA's recent reference (Federal Register 2010) to a "treated population" acknowledges this use of drinking water systems to deliver a drug to entire populations. This in effect puts local governments and water treatment personnel in charge of administering a chemical (i.e., a drug) to the population in an effort to improve individual and population health (Cross and Carton 2003; Cheng et al. 2007). Many people consume more fluoride from tap water than from either non-prescription (toothpaste) or prescription (tablets or lozenges) fluoride sources, without any monitoring for either efficacy or side effects, without the "drug information" or warning labels generally provided for drugs, and without any semblance of informed consent.

In addition, most fluoridation operations use fluorosilicates (usually H_2SiF_6 or Na_2SiF_6) rather than sodium fluoride (NaF). The chemistry and toxicology of these compounds have not been adequately studied, although important differences in biological effects between silicofluorides and simple fluorides (e.g., NaF) have been reported (Coplan et al. 2007; NRC 2006; Masters et al. 2000; Masters and Coplan 1999). The NRC (2006) discussed the increased toxicity of aluminofluorides and beryllofluorides vs. fluoride alone, as well as the different mechanisms of action of the different chemical combinations. It is irresponsible to recommend addition of fluoride, or a particular concentration of fluoride to be added, without a comprehensive review of the substances (H_2SiF_6 or Na_2SiF_6,) that are actually added. In addition, fluoridation chemicals often contain impurities such as lead and arsenic, for which EPA has set MCLGs of zero (EPA 2006), such that a water supplier is actually adding contaminants for which the ideal maximum amount in drinking water is zero.

In summary, it is irresponsible to promote or encourage uncontrolled exposure of any population to a drug that, at best, is not appropriate for many individuals (e.g., those who do not want it, those whose water consumption is high, formula-fed infants, people with impaired renal function) and for which the risks are inadequately characterized and inadequately disclosed to the public. Elimination of community water fluoridation at the earliest possible date would be in the best interest of public health.

Table 1. Caries prevalence and fluorosis prevalence with water fluoride concentration.[a]

Water fluoride concentration	Children with no caries	Mean DMFS score[b]	Children with fluorosis[c]	Mean severity of fluorosis[d]
mg/L	%		%	
< 0.3	53.2	3.08	13.5	0.30
0.3 - < 0.7	57.1	2.71	21.7	0.43
0.7 - 1.2	55.2	2.53	29.9	0.58
> 1.2	52.5	2.80	41.4	0.80

[a] Data for permanent teeth of children ages 5-17 (caries experience and DMFS score) or 7-17 (dental fluorosis), with a history of a single residence, from Tables 2 and 5 of Heller et al. (1997).
[b] Decayed, missing, or filled tooth surfaces (permanent teeth).
[c] Includes very mild, mild, moderate, and severe fluorosis, but not "questionable."
[d] Dean's Community Fluorosis Index.

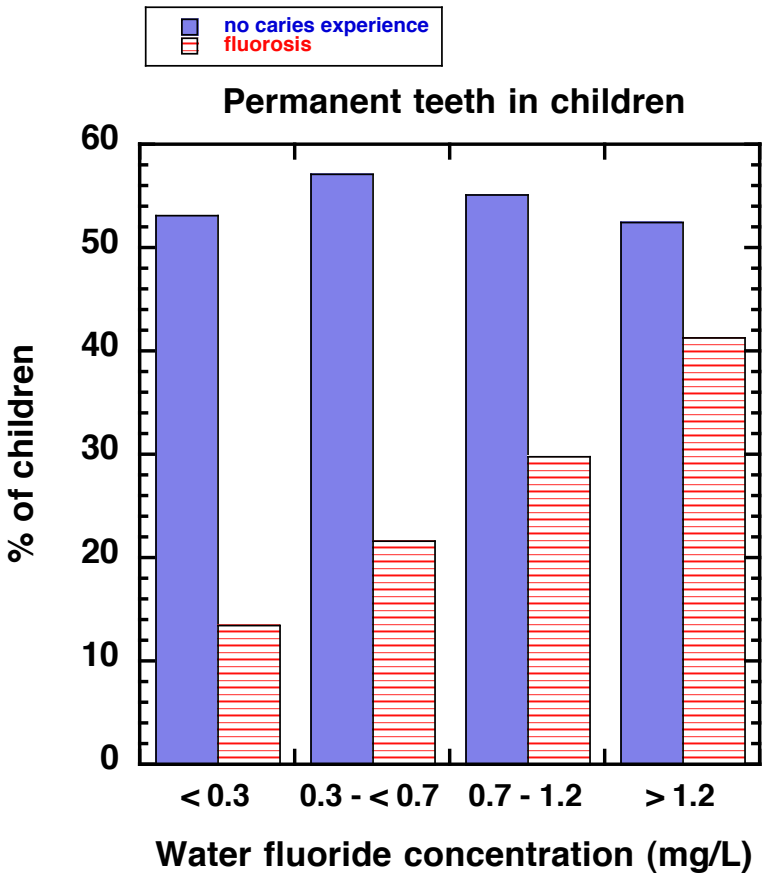

Fig. 1. Percent of children with no caries experience in the permanent teeth (DMFS = 0) and with fluorosis, with respect to water fluoride concentration. Data are shown as % of total children having no caries experience (blue) or having fluorosis (very mild, mild, moderate, or severe, but not questionable; red). Numerical values are provided in Table 1 of these comments and were obtained from Tables 2 and 5 of Heller et al. (1997).

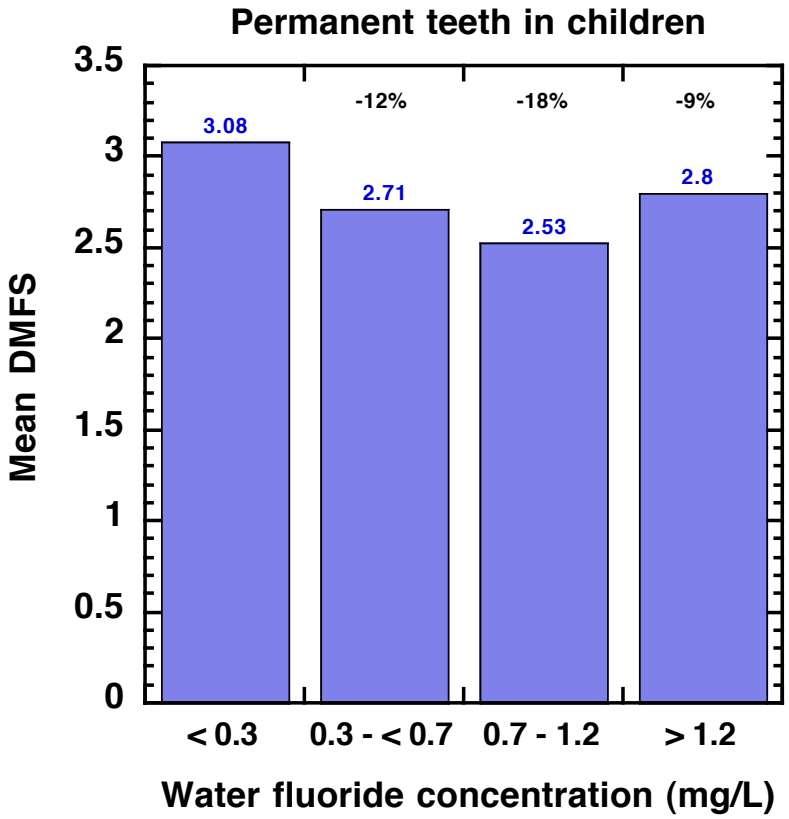

Fig. 2. Mean DMFS score (decayed, missing, or filled permanent tooth surfaces in permanent teeth), with respect to water fluoride concentration. Numerical values are provided in Table 1 of these comments and were obtained from Table 2 of Heller et al. (1997). The percent difference with respect to the lowest fluoride group is also provided.

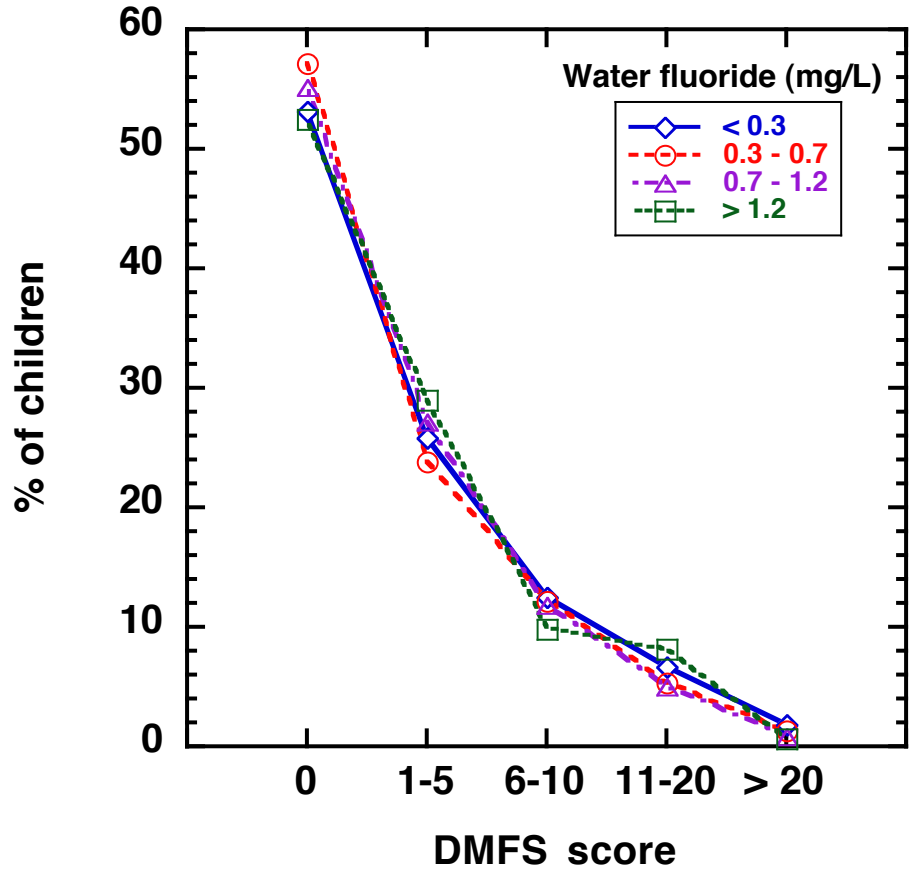

Fig. 3. Percent of children by DMFS score, with respect to water fluoride concentration. Data are shown as % of total children in a given group according to the number of decayed, missing, or filled tooth surfaces in the permanent teeth (DMFS). Data were obtained from Table 2 of Heller et al. (1997).

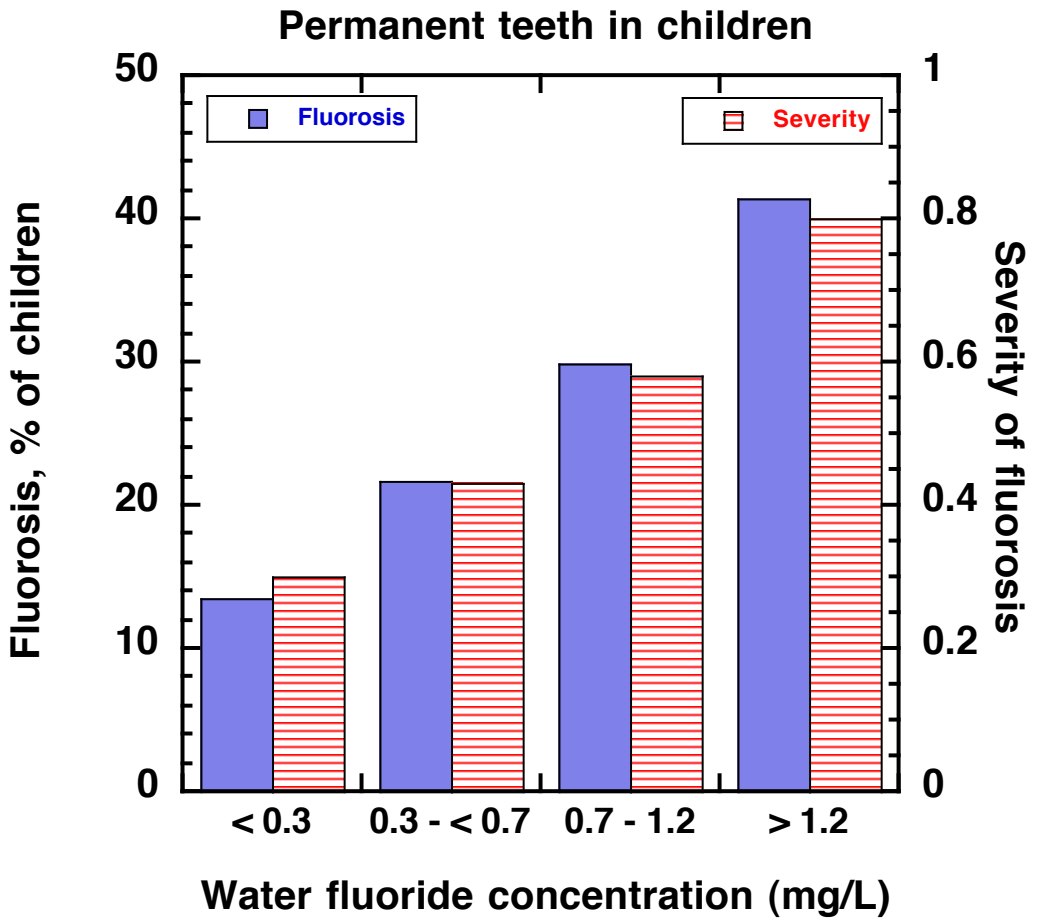

Fig. 4. Fluorosis prevalence and severity with water fluoride concentration for children ages 7-17 with a history of a single continuous residence. Data are shown as (left) % of total children having fluorosis (very mild, mild, moderate, or severe, but not questionable) or (right) severity of fluorosis by Dean's Community Fluorosis Index. Numerical values are provided in Table 1 of these comments and were obtained from Table 5 of Heller et al. (1997).

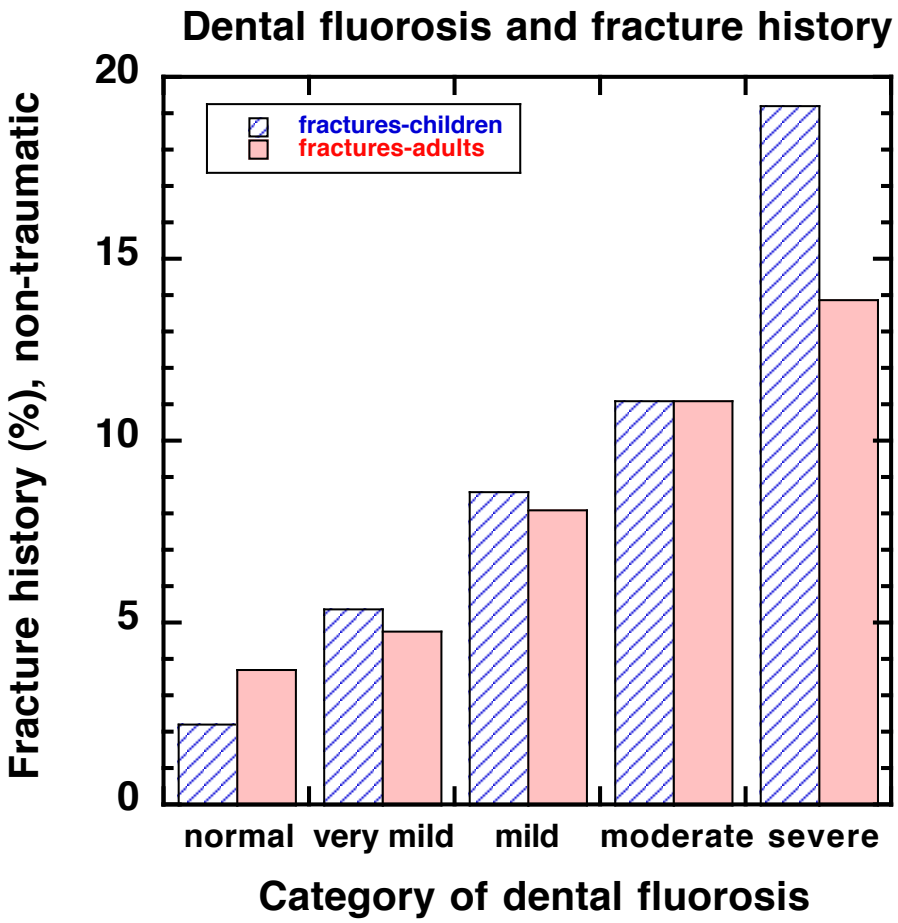

Fig. 5. Fracture history with category of dental fluorosis for children (ages 6-12) and adults (ages 13-60). Numerical values were obtained from information in Tables 5 and 6 of Alarcón-Herrera et al. (2001).

References

Aardema, M.J., Gibson, D.P., and LeBoeuf, R.A. 1989. Sodium fluoride-induced chromosome aberrations in different stages of the cell cycle: A proposed mechanism. Mutation Research 223:191-203.

Aardema, M.J., and Tsutsui, T. 1995. Sodium fluoride-induced chromosome aberrations in different cell cycle stages. Mutation Research 331:171-172.

ADA (American Dental Association). 2005. Fluoridation facts. Chicago, IL: American Dental Association. [Available: http://www.ada.org/sections/professionalResources/pdfs/fluoridation_facts.pdf]

ADA (American Dental Association). 2007. Infants, formula and fluoride. JADA 138:132. [Available: http://www.ada.org/sections/scienceAndResearch/pdfs/patient_70.pdf]

Adair, S.M., C.M. Hanes, C.M. Russell, and G.M. Whitford. 1999. Dental caries and fluorosis among children in a rural Georgia area. Pediatr. Dent. 21(2):81-85.

Alarcón-Herrera, M.T., Martín-Domínguez, I.R., Trejo-Vázquez, R., and Rodriguez-Dozal, S. 2001. Well water fluoride, dental fluorosis, and bone fractures in the Guadiana Valley of Mexico. Fluoride 34:139-149.

Alvarez, J.O. 1995. Nutrition, tooth development, and dental caries. Am. J. Clin. Nutr. 61S:410S-416S.

Alvarez, J.O., and Navia, J.M. 1989. Nutritional status, tooth eruption, and dental caries: a review. Am. J. Clin. Nutr. 49:417-426.

ATSDR (Agency for Toxic Substances and Disease Registry). 2003. Toxicological Profile for Fluorides, Hydrogen Fluoride, and Fluorine. U.S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, Atlanta, GA, September 2003.

Bassin, E.B., Wypij, D., Davis, R.B., and Mittleman, M.A. 2006. Age-specific fluoride exposure in drinking water and osteosarcoma (United States). Cancer Causes Control. 17(4):421-428.

Beltrán-Aguilar, E.D., Barker, L., and Dye, B.A. 2010. Prevalence and severity of dental fluorosis in the United States, 1999–2004. NCHS data brief, no 53. Hyattsville, MD: National Center for Health Statistics.

Biggio, J.R. Jr., Morris, T.C., Owen, J., and Stringer, J.S.A. 2004. An outcomes analysis of five prenatal screening strategies for trisomy 21 in women younger than 35 years. Am. J. Obstet. Gynecol. 190:721-729.

Björnhagen, V., Höjer, J., Karlson-Stiber, C., Seldén, A.I., and Sundbom, M. 2003. Hydrofluoric acid-induced burns and life-threatening systemic poisoning: Favorable outcome after hemodialysis. Clinical Toxicology 41(6):855-860.

Buckley, F., Buckley, S. 2008. Wrongful deaths and rightful lives—screening for Down syndrome. Down Syndrome Res Practice 12:79-86.

CDC (Centers for Disease Control and Prevention). 2001. Recommendations for Using

Fluoride to Prevent and Control Dental Caries in the United States. Morbidity and Mortality Weekly Report 50(RR-14). Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention.

CDC (Centers for Disease Control and Prevention). 2005. Surveillance for Dental Caries, Dental Sealants, Tooth Retention, Edentulism, and Enamel Fluorosis—United States, 1988-1994 and 1999-2002. Morbidity and Mortality Weekly Report 54(SS3):1-43. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention.

CDC (Centers for Disease Control and Prevention). 2006. Prevalence of Doctor-Diagnosed Arthritis and Arthritis-Attributable Activity Limitation—United States, 2003-2005. Morbidity and Mortality Weekly Report 55(40):1089-1092. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention.

Cheng, K.K., Chalmers, I., and Sheldon, T.A. 2007. Adding fluoride to water supplies. BMJ 335:699-702.

Choi, A.L., Sun, G., Zhang, Y., and Grandjean, P. 2012. Developmental fluoride neurotoxicity: A systematic review and meta-analysis. Environ. Health Perspect. 120:1362-2368.

Clark, J.D., and Mann, E.H. 1938. A study of the occurrence of fluorine in the drinking water of New Mexico and the menace of fluorine to health. The University of New Mexico Bulletin, Chemistry Series 2(5):3-23.

Connett, P., J. Beck, and H.S. Micklem. 2010. *The Case Against Fluoride*. White River Junction, VT: Chelsea Green Publishing.

Coplan, M.J., Patch, S.C., Masters, R.D., and Bachman, M.S. 2007. Confirmation of and explanations for elevated blood lead and other disorders in children exposed to water disinfection and fluoridation chemicals. NeuroToxicology 28:1032-1042.

Cote, S., P. Geltman, M. Nunn, K. Lituri, M. Henshaw, and R.I. Garcia. 2004. Dental caries of refugee children compared with US children. Pediatrics 114:e733–e740. [Available at www.pediatrics.org/cgi/doi/10.1542/peds.2004-049]

Cross, D.W., and R.J. Carton. 2003. Fluoridation: A violation of medical ethics and human rights. Int. J. Occup. Environ. Health 9(1):24-29.

DailyMed (2011a). Fluoride (sodium fluoride) tablet, chewable. Available at http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=58b3e7ff-c032-4e42-823a-8ed7b93d606f (revised May 2011).

DailyMed (2011b). Fluoride drops (sodium fluoride) liquid. Available at http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=2e05a9bf-f8e7-41b1-b382-2dc9d8dafee4 (revised May 2011).

DailyMed (2011c). Epiflur TM (sodium fluoride) tablet. Available at http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=97a2ab7a-5a2c-4c35-9bb4-f3cd37dcd180 (revised September 2009).

Danielson, C., Lyon, J.L., Egger, M., and Goodenough, G.K. 1992. Hip fractures and fluoridation in Utah's elderly population. JAMA 268:746-748.

Desai, V.K., Solanki, D.M., and Bansal, R.K. 1993. Epidemiological study on goitre in endemic

fluorosis district of Gujarat. Fluoride 26:187-190.

EPA (Environmental Protection Agency). 2004a. Estimated Per Capita Water Ingestion and Body Weight in the United States—An Update: Based on Data Collected by the United States Department of Agriculture's 1994-96 and 1998 Continuing Survey of Food Intakes by Individuals. EPA-822-R-00-001. Office of Water, U.S. Environmental Protection Agency. October 2004.

EPA (Environmental Protection Agency). 2004b. Lead and compounds (inorganic) (CASRN 7439-92-1). Integrated Risk Information System, U.S. Environmental Protection Agency [online]. [Available: http://www.epa.gov/ncea/iris/subst/0277.htm]

EPA (Environmental Protection Agency). 2009. 2009 Edition of the Drinking Water Standards and Health Advisories. Washington, DC: U.S. Environmental Protection Agency, Office of Water, EPA 822-R-09-011. [Available: http://water.epa.gov/action/advisories/drinking/drinking_index.cfm]

Evans, A.M. 1986. Age at puberty and first litter size in early and late paired rats. Biology of Reproduction 34:322-326.

Eyre, R., R.G. Feltbower, E. Mubwandarikwa, T.O.B. Eden, and R.J.Q. McNally. 2009. Epidemiology of bone tumours in children and young adults. Pediatr. Blood Cancer 53:941-952.

FDA (U.S. Food and Drug Administration). Undated-a. Medicines in My Home. Information for students on the safe use of over-the-counter medicines. [Available: http://www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingOver-the-CounterMedicines/UCM093965.pdf or http://www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingOver-the-CounterMedicines/UCM094872.pdf]

FDA (U.S. Food and Drug Administration). Undated-b. Medicines in My Home. Information for adults on using over-the-counter medicines safely. [Available: http://www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingOver-the-CounterMedicines/UCM094872.pdf]

FDA (U.S. Food and Drug Administration). 2011. Unapproved Drugs: Drugs marketed in the United States that do not have required FDA approval. Available at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/SelectedEnforcementActionsonUnapprovedDrugs/default.htm (updated August 5, 2011).

Featherstone, J.D.B. 2000. The science and practice of caries prevention. JADA 131:887-899.

Federal Register. 2010. National Primary Drinking Water Regulations; Announcement of the Results of EPA's Review of Existing Drinking Water Standards and Request for Public Comment and/or Information on Related Issues. Federal Register 75(59):15500-15572, March 29, 2010.

Federal Register. 2011. Proposed HHS Recommendation for Fluoride Concentration in Drinking Water for Prevention of Dental Caries. Federal Register 76(9):2383-2388, January 13, 2011.

Feltman, R., and Kosel, G. 1961. Prenatal and postnatal ingestion of fluorides—Fourteen years

of investigation. Final report. J. Dent. Med. 16:190-198.

Finn, S.B. 1952. Prevalence of dental caries. In: A Survey of the Literature of Dental Caries. Washington, DC: National Academy of Sciences, Publication 225, pp. 117-173.

Finn, S.B., and R.C. Caldwell. 1963. Dental caries in twins. I. A comparison of the caries experience of monozygotic twins, dizygotic twins and unrelated children. Archives of Oral Biology 8:571-585.

Forrester, M.B., and Merz, R.D. 1999. Prenatal diagnosis and elective termination of Down syndrome in a racially mixed population in Hawaii, 1987-1996. Prenat. Diagn. 19:136-141.

Franke, J., Rath, F., Runge, H., Fengler, F., Auermann, E., and Lenart, G.L. 1975. Industrial fluorosis. Fluoride 8:61-85.

Gelberg, K.H., Fitzgerald, E.F., Hwang, S., and Dubrow, R. 1995. Fluoride exposure and childhood osteosarcoma: A case-control study. American Journal of Public Health 85(12):1678-1683.

Graham, J.R., and Morin, P.J. 1999. Highlights in North American litigation during the twentieth century on artificial fluoridation of public water supplies. J. Land Use & Environmental Law 14(2):195-242.

Grandjean, P., and Landrigan, P.J. 2006. Developmental neurotoxicity of industrial chemicals. Lancet 368:2167-2178.

Gray, L.E., Jr., Wilson, V., Noriega, N., Lambright, C., Furr, J., Stoker, T.E., Laws, S.C., Goldman, J., Cooper, R.L., and Foster, P.M.D. 2004. Use of the laboratory rat as a model in endocrine disruptor screening and testing. ILAR Journal 45(4):425-437.

Grimbergen, G.W. 1974. A double blind test for determination of intolerance to fluoridated water. Preliminary Report. Fluoride 7:146-152.

Hallanger Johnson, J.E., Kearns, A.E., Doran, P.M., Khoo, T.K., and Wermers, R.A. 2007. Fluoride-related bone disease associated with habitual tea consumption. Mayo Clin Proc 82:719-724.

Hamasha, A.A., J.J. Warren, S.M. Levy, B. Broffitt, and M.J. Kanellis. 2006. Oral health behaviors of children in low and high socioeconomic status families. Pediatr. Dent. 28(4):310-315.

Hattis, D., Goble, R., Russ, A., Chu, M., and Ericson, J. 2004. Age-related differences in susceptibility to carcinogenesis: A quantitative analysis of empirical animal bioassay data. Environmental Health Perspectives 112:1152–1158.

Health Canada. 2009. Fluoride in Drinking Water. Document for public comment. September 2009.

Heller, K.E., Eklund, S.A., and Burt, B.A. 1997. Dental caries and dental fluorosis at varying water fluoride concentrations. J. Public Health Dentistry 57(3):136-143.

Hileman, B. 1990. Fluoride bioassay study under scrutiny. Chemical & Engineering News 68(38):29-30 (September 17, 1990).

Hirzy, J.W. 2000. Statement of Dr. J. William Hirzy, National Treasury Employees Union Chapter 280, before the Subcommittee on Wildlife, Fisheries and Drinking Water, United States Senate, June 29, 2000. [Available http://www.nteu280.org/Issues/Fluoride/629FINAL.htm or http://www.fluoridealert.org/HirzyTestimony.pdf]

Hong, L., Levy, S.M., Broffitt, B., Warren, J.J., Kanellis, M.J., Wefel, J.S., and Dawson, D.V. 2006a. Timing of fluoride intake in relation to development of fluorosis on maxillary central incisors. Community Dent. Oral Epidemiol. 34:299-209.

Hong, L., Levy, S.M., Warren, J.J., Broffitt, B., and Cavanaugh, J. 2006b. Fluoride intake levels in relation to fluorosis development in permanent maxillary central incisors and first molars. Caries Research 40:494-500.

Iida, H., and Kumar, J.V. 2009. The association between enamel fluorosis and dental caries in U.S. schoolchildren. JADA 140:855-862.

Jooste, P.L., Weight, M.J., Kriek, J.A., and Louw, A.J. 1999. Endemic goitre in the absence of iodine deficiency in schoolchildren of the Northern Cape Province of South Africa. Eur. J. Clin. Nutr. 53:8-12.

Khosla, S., Melton, L.J. III, Dekutoski, M.B., Achenbach, S.J., Oberg, A.L., Riggs, B.L. 2003. Incidence of childhood distal forearm fractures over 30 years. JAMA 290:1479-1485.

Kim, F.M., Hayes, C., Williams, P.L., Whitford, G.M., Joshipura, K.J., Hoover, R.N., Douglass, C.W., and the National Osteosarcoma Etiology Group. 2011. An assessment of bone fluoride and osteosarcoma. J. Dent. Res. 90(10):1171-1176.

Kishi, K., and Ishida, T. 1993. Clastogenic activity of sodium fluoride in great ape cells. Mutation Research 301:183-188.

Komárek, A., Lesaffre, E., Härkänen, T., Declerck, D., and Virtanen, J.I. 2005. A Bayesian analysis of multivariate doubly-interval-censored dental data. Biostatistics 6(1):145-155.

Kurland, E.S., Schulman, R.C., Zerwekh, J.E., Reinus, W.R., Dempster, D.W., and Whyte, M.P. 2007. Recovery from skeletal fluorosis (an enigmatic, American case). J Bone Mineral Res. 22:163-170.

Lasne, C., Lu, Y.-P., and Chouroulinkov, I. 1988. Transforming activities of sodium fluoride in cultured Syrian hamster embryo and BALB/3T3 cells. Cell Biology and Toxicology 4(3):311-324.

Leonnig, C.D. 2010. CDC misled District residents about lead levels in water, House probe finds. The Washington Post, May 20, 2010 [Available: http://www.washingtonpost.com/wp-dyn/content/article/2010/05/19/AR2010051902599_pf.html]

Levy, S.M., Eichenberger-Gilmore, J., Warren, J.J., Letuchy, E., Broffitt, B., Marshall, T.A., Burns, T., Willing, M., Janz, K., and Torner, J.C. 2009. Associations of fluoride intake with children's bone measures at age 11. Community Dent. Oral Epidemiol. 37:416-426.

Li, X.S., Zhi, J.L., and Gao, R.O. 1995. Effect of fluoride exposure on intelligence in children. Fluoride 28:189-192.

Li, Y., Jing, X., Chen, D., Lin, L., and Wang, Z. 2003. Effects of endemic fluoride poisoning on the intellectual development of children in Baotou. Chinese Journal of Public Health

Management 19(4):337-338. English translation (2008) Fluoride 41(2):161-164.

Lin, F.F., Aihaiti, Zhao, H.X., Lin, J., Jiang, J.Y., Maimaiti, and Aiken. 1991. The relationship of a low-iodine and high-fluoride environment to subclinical cretinism in Xinjiang. IDD Newsletter 7:24-25.

Lu, Y., Sun, Z.R., Wu, L.N., Wang, X., Lu, W., and Liu, S.S. 2000. Effect of high-fluoride water on intelligence in children. Fluoride 33(2):74-78.

Maas, R.P., Patch, S.C., and Smith, A.M. 2005. Effects of Fluorides and Chloramines on Lead Leaching from Leaded-Brass Surfaces. Technical Report 05-142. Environmental Quality Institute, University of North Carolina, Asheville, NC. June 2005.

Maas, R.P., Patch, S.C., Christian, A.-M., and Coplan, M.J. 2007. NeuroToxicology 28:1023-1031.

Marcus, W.L. 1990. Fluoride Conference to review the NTP Draft Fluoride Report. Memorandum to A.B. Hais, Acting Director, Criteria & Standards Division, Office of Drinking Water, Environmental Protection Agency.

Masters, R.D., and Coplan, M. 1999. Water treatment with silicofluorides and lead toxicity. Int. J. Environ. Sci. 56:435-449.

Masters, R.D., Coplan, M.J., Hone, B.T., and Dykes, J.E. 2000. Association of silicofluoride treated water with elevated blood lead. Neurotoxicology 21(6):1091-1100.

McDonagh, M., Whiting, P., Bradley, M., Cooper, J., Sutton, A., Chestnutt, I., Misso, K., Wilson, P., Treasure, E., and Kleijnen, J. 2000. A Systematic Review of Public Water Fluoridation. NHS Centre for Reviews and Dissemination, University of York, York, UK.

Medline Plus. 2008. Fluoride. U.S. National Library of Medicine and National Institutes of Health. [Available: http://www.nlm.nih.gov/medlineplus/druginfo/meds/a682727.html]

Meng, Z., and Zhang, B. 1997. Chromosomal aberrations and micronuclei in lymphocytes of workers at a phosphate fertilizer factory. Mutation Research 393:283-288.

Neurath, C. 2005. Tooth decay trends for 12 year olds in nonfluoridated and fluoridated countries. Fluoride 38:324-325.

NRC (National Research Council). 2006. Fluoride in Drinking Water: A Scientific Review of EPA's Standards. [Available: http://www.nap.edu/catalog/11571.html]

NRC (National Research Council). 2009. Emergency and Continuous Exposure Guidance Levels for Selected Submarine Contaminants: Volume 3. [Available: http://www.nap.edu/catalog.php?record_id=12741]

NTP (National Toxicology Program). 1990. Toxicology and carcinogenesis studies of sodium fluoride (CAS No. 7681-49-4) in F344/N rats and B6C3F$_1$ mice (drinking water studies). National Toxicology Program Technical Report Series No. 393.

Penman, A.D., Brackin, B.T., and Embrey, R. 1997. Outbreak of acute fluoride poisoning caused by a fluoride overfeed, Mississippi, 1993. Public Health Reports 112:403-409.

Petraborg, H.T. 1977. Hydrofluorosis in the fluoridated Milwaukee area. Fluoride 10:165-169.

Psoter, W.J., Reid, B.C., and Katz, R.V. 2005. Malnutrition and dental caries: A review of the literature. Caries Res. 39:441-447.

Rocha-Amador, D., Navarro, M.E., Carrizales, L., Morales, R., and Calderón, J. 2007. Decreased intelligence in children and exposure to fluoride and arsenic in drinking water. Cad. Saúde Pública (Rio de Janeiro) 23 Sup 4:S579-S587.

Rocha-Amador, D., Navarro, M., Trejo-Acevedo, A., Carrizales, L., Pérez-Maldonado, I., Díaz-Barriga, F., and Calderón, J. 2009. Use of the Rey-Osterrieth Complex Figure Test for neurotoxicity evaluation of mixtures in children. NeuroToxicology 30:1149-1154.

Román, G.C. 2007. Autism: Transient in utero hypothyroxinemia related to maternal flavonoid ingestion during pregnancy and to other environmental antithyroid agents. J. Neurological Sciences 262:15-26.

Sawan, R.M.M., Leite, G.A.S., Saraiva, M.C.P., Barbosa, F. Jr., Tanus-Santos, J.E., and Gerlach, R.F. 2010. Fluoride increases lead concentrations in whole blood and in calcified tissues from lead-exposed rats. Toxicology 271(1-2):21-26.

Saxena, S., Sahay, A., and Goel, P. 2012. Effect of fluoride exposure on the intelligence of school children in Madhya Pradesh, India. J. Neurosci. Rural Pract. 3(2):144-149.

Seraj, B., Shahrabi, M., Shadfar, M., Ahmadi, R., Fallahzadeh, M., Eslamlu, H.F., and Kharazifard, M.J. 2012. Effect of high water fluoride concentration on the intellectual development of children in Makoo/Iran. J. Dentistry (Tehran) 9(3):221-229.

Sergi, C., and Zwerschke, W. 2008. Osteogenic sarcoma (osteosarcoma) in the elderly: Tumor delineation and predisposing conditions. Experimental Gerontology 43:1039-1043.

Shiboski, C.H., Gansky, S.A., Ramos-Gomez, F., Ngo, L., Isman, R., Pollick, H.F. 2003. The association of early childhood caries and race/ethnicity among California preschool children. J. Public Health Dentistry 63:38-46.

Short, E.M. 1944. Domestic water and dental caries: VI. The relation of fluoride domestic waters to permanent tooth eruption. J. Dent. Res. 23:247-255.

Siffel, C., Correa, A., Cragan, J., Alverson, C.J. 2004. Prenatal diagnosis, pregnancy terminations and prevalence of Down syndrome in Atlanta. Birth Defects Res. A Clin. Mol. Teratol. 70:565-571.

Spittle, B. 2008. Dyspepsia associated with fluoridated water. Fluoride 41(1):89-92.

Steingraber, S. 2007. The Falling Age of Puberty in U.S. Girls: What We Know, What We Need to Know. San Francisco: The Breast Cancer Fund.

Sullivan, K.M. 2009. Iodine deficiency as a cause of autism. J. Neurological Sciences 276:202.

Susheela, A.K., Bhatnagar, M., Vig, K., and Mondal, N.K. 2005. Excess fluoride ingestion and thyroid hormone derangements in children living in Delhi, India. Fluoride 38:98-108.

Tickner, J., and Coffin, M. 2006. What does the precautionary principle mean for evidence-based dentistry? Journal of Evidence-Based Dental Practice 6(1):6-15.

Turner, C.H., Garetto, L.P., Dunipace, A.J., Zhang, W., Wilson, M.E., Grynpas, M.D., Chachra, D., McClintock, R., Peacock, M., and Stookey, G.K. 1997. Fluoride treatment increased serum

IGF-1, bone turnover, and bone mass, but not bone strength, in rabbits. Calcif. Tissue Int. 61:77-83.

Turner, C.H., Hinckley, W.R., Wilson, M.E., Zhang, W., and Dunipace, A.J. 2001. Combined effects of diets with reduced calcium and phosphate and increased fluoride intake on vertebral bone strength and histology in rats. Calcif. Tissue Int. 69:51-57.

Vohra, R., Velez, L.I., Rivera, W., Benitez, F.L., and Delaney, K.A. 2008. Recurrent life-threatening ventricular dysrhythmias associated with acute hydrofluoric acid ingestion: Observations in one case and implications for mechanism of toxicity. Clinical Toxicology 46:79-84.

Waldbott, G.L. 1956. Incipient chronic fluoride intoxication from drinking water. II. Distinction between allergic reactions and drug intolerance. Int. Arch. Allergy 9:241-249.

Waldbott, G.L. 1958. Allergic reactions from fluorides. Int. Arch. Allergy 12:347-355.

Warren, J.J., Levy, S.M., Broffitt, B., Cavanaugh, J.E., Kanellis, M.J., and Weber-Gasparoni, K. 2009. Considerations on optimal fluoride intake using dental fluorosis and dental caries outcomes—A longitudinal study. J. Public Health Dentistry 69:111-115.

Whyte, M.P., Essmyer, K., Gannon, F.H., and Reinus, W.R. 2005. Skeletal fluorosis and instant tea. Am. J. Med. 118:78-82.

Wilson, P.M., and Sheldon, T.A. 2006. Muddy waters: evidence-based policy making, uncertainty and the "York review" on water fluoridation. Evidence & Policy 2(3):321-331.

Xiang, Q., Liang, Y., Chen, L., Wang, C., Chen, B., Chen, X., and Zhou, M. 2003. Effect of fluoride in drinking water on children's intelligence. Fluoride 36(2):84-94.

Yang, Y., Wang, X., and Guo, X. 1994. Effects of high iodine and high fluorine on children's intelligence and the metabolism of iodine and fluorine [in Chinese]. Zhonghua Liu Xing Bing Xue Za Zhi 15:296-298.

Zhang, R., Niu, Y., Du, H., Cao, X., Shi, D., Hao, Q., and Zhou, Y. 2009. A stable and sensitive testing system for potential carcinogens based on DNA damage-induced gene expression in human HepG2 cell. Toxicology in Vitro 23:158-165.

Zhao, L.B., Liang, G.H., Zhang, D.N., and Wu, X.R. 1996. Effect of a high fluoride water supply on children's intelligence. Fluoride 29:190-192.

KATHLEEN M. THIESSEN, Ph.D.
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Education

Ph.D. 1986 Genetics, University of Tennessee-Oak Ridge, Graduate School of Biomedical Sciences, Oak Ridge, TN
B.A. 1981 Biology and Chemistry (*Summa cum laude*), Covenant College, GA

Capabilities

Health Effects Assessment
Dose and Risk Assessment
Analysis of Environmental Transport and Exposure Pathways
Uncertainty and Sensitivity Analysis
Technical Writing/Editing, Technical and Public Presentations

Experience Summary

Dr. Thiessen is experienced in the evaluation of exposures, doses, and risks to human health from trace levels of contaminants in the environment and in the use of uncertainty analysis for environmental and health risk assessment. She currently leads the Urban Environments Working Group of the International Atomic Energy Agency's MODARIA (Modelling and Data for Radiological Impact Assessments) program. Prior to the MODARIA program, she led the Urban Remediation and Urban Areas Working Groups within the IAEA's EMRAS (Environmental Modelling for Radiation Safety) and EMRAS II programs and the Dose Reconstruction Working Group of the IAEA's BIOMASS (Biosphere Modelling and Assessment Methods) program. She served as a member of the Coordinating Committee for the EMRAS, EMRAS II, and BIOMASS programs, and currently serves in that role for the MODARIA program. She also serves on a committee for the revision of the International Atomic Energy Agency's Safety Report Series No. 19, "Generic Models for Use in Assessing the Impact of Discharges of Radioactive Substances to the Environment." Dr. Thiessen recently participated in two symposia on reconstruction of internal doses from Fukushima releases organized by Japan's National Institute of Radiological Sciences, and she serves as a consultant on environmental modeling issues to the Korea Atomic Energy Research Institute. Dr. Thiessen has served on two National Research Council subcommittees, one dealing with guidance levels for air contaminants in submarines and one charged with the review of fluoride exposure and toxicology. Dr. Thiessen has drafted several reports on the health effects of specific environmental contaminants for the U.S. Environmental Protection Agency. Dr. Thiessen has also co-authored several papers on contaminant interception and retention by vegetation and assisted with a review paper on this topic prepared for the International Atomic Energy Agency. She contributed to the development of a risk-based screening approach to prioritize further investigation of contaminants and exposure situations in various assessment contexts. For the State of Tennessee, Dr. Thiessen led an analysis of human exposures, doses, and health risks to off-site individuals associated with historic releases of radionuclides to the Clinch River from DOE's Oak Ridge facilities. She also led in the application of risk-based screening techniques for the reconstruction of doses and health risks associated with releases of chemicals and radionuclides from the Oak Ridge

facilities. She served as a consultant to the National Council on Radiation Protection and Measurements for the preparation of "A Guide for Uncertainty Analysis in Dose and Risk Assessments Related to Environmental Contamination" (NCRP Commentary No. 14, 1996). Dr. Thiessen has contributed to a number of open literature publications in the use of international data sets to test and improve the accuracy of mathematical models used to assess the environmental fate and consequences of releases of radioactivity.

Experience

1992-present Senior Scientist and Director, *SENES* Oak Ridge, Inc., Center for Risk Analysis, Oak Ridge, TN.

- Review of data on contaminant exposure and toxicology.
- Analysis of environmental transport and exposure pathways.
- Screening techniques for environmental assessment.
- Dose reconstruction.
- Uncertainty analysis for environmental assessment.
- International model validation using Chernobyl data sets.
- Working Group Leader for International Atomic Energy Agency research programs.
- Project coordination.
- Technical review.

1991-1992 Consultant and Technical Writer. Environmental Sciences Division, Oak Ridge National Laboratory, Oak Ridge, TN.

1987-1992 Lecturer in Genetics. University of Tennessee, Oak Ridge Graduate School of Biomedical Sciences.

1986-1989 Oak Ridge National Laboratory, Health and Safety Research Division, Chemical Hazard Evaluation Program.

- Assessment of health effects from chemicals.
- Risk assessment.
- Technical review.

Professional Affiliations

International Union of Radioecologists

Publications and Technical Reports

Yankovich, T., Beresford, N.A., Fesenko, S., Fesenko, J., Phaneuf, M., Dagher, E., Outola, I., Andersson, P., Thiessen, K., Ryan, J., Wood, M.D., Bollhöfer, A., Barnett, C.L., and Copplestone, D. Establishing a database of radionuclide transfer parameters for freshwater wildlife. *Journal of Environmental Radioactivity.* In press.

IAEA (International Atomic Energy Agency). 2012. Environmental Modelling of Remediation of Urban Contaminated Areas. Report of the Urban Remediation Working Group of the EMRAS (Environmental Modelling for Radiation Safety) programme.

Thiessen, K.M., Andersson, K.G., Berkovskyy, V., Charnock, T.W., Chouhan, S.L., de With, G., Ďúran, J., Fuka, V., Helebrant, J., Hůlka, J., Hwang, W.T., Kuča, P., Mancini, F., Navarro, E.,

Periáñez, R., Prouza, Z., Sdouz, G., Tomás, J., Trifunović, D., Urso, L., and Walter H. 2011. Assessing emergency situations and their aftermath in urban areas: The EMRAS II Urban Areas Working Group. *Radioprotection* 46(6):S601-S607.

NRC (National Research Council). 2009. Emergency and Continuous Exposure Guidance Levels for Selected Submarine Contaminants: Volume 3. Washington, DC: National Academies Press.

Thiessen, K.M., Andersson, K.G., Charnock, T.W., and Gallay, F. 2009. Modelling remediation options for urban contamination situations. *Journal of Environmental Radioactivity* 100:564-573.

Thiessen, K.M., Andersson, K.G., Batandjieva, B., Cheng, J.-J., Hwang, W.T., Kaiser, J.C., Kamboj, S., Steiner, M., Tomás, J., Trifunovic, D., and Yu, C. 2009. Modelling the long-term consequences of a hypothetical dispersal of radioactivity in an urban area including remediation alternatives. *Journal of Environmental Radioactivity* 100:445-455.

Thiessen, K.M., Arkhipov, A., Batandjieva, B., Charnock, T.W., Gaschak, S., Golikov, V., Hwang, W.T., Tomás, J., and Zlobenko, B. 2009. Modelling of a large-scale urban contamination situation and remediation alternatives. *Journal of Environmental Radioactivity* 100:413-421.

Thiessen, K.M., Batandjieva, B., Andersson, K.G., Arkhipov, A., Charnock, T.W., Gallay, F., Gaschak, S., Golikov, V., Hwang, W.T., Kaiser, J.C., Kamboj, S., Steiner, M., Tomás, J., Trifunovic, D., Yu, C., Zelmer, R., and Zlobenko, B. 2008. Improvement of modelling capabilities for assessing urban contamination: The EMRAS Urban Remediation Working Group. *Applied Radiation and Isotopes* 66:1741-1744.

Thiessen, K.M., Batandjieva, B., Andersson, K.G., Arkhipov, A., Charnock, T.W., Gallay, F., Gaschak, S., Golikov, V., Hwang, W.T., Kaiser, J.C., Kamboj, S., Steiner, M., Tomás, J., Trifunovic, D., Yu, C., Zelmer, R., and Zlobenko, B. 2007. Improvement of modeling capabilities for assessing urban contamination: The EMRAS Urban Remediation Working Group. In: Proceedings from the International Conference on Environmental Radioactivity: From Measurements and Assessments to Regulation, Vienna, April 23-27, 2007, pp. 133-134 (IAEA-CN-145/070).

Köteles, G.J., Kanyár, B., and Thiessen, K.M. 2007. Radiation Biology and Radiation Protection. In: *Radiochemistry and Nuclear Chemistry* (S. Nagy, ed.). In: *Encyclopedia of Life Support Systems (EOLSS)*. Developed under the auspices of the UNESCO, Eolss Publishers, Oxford, UK [http://www.eolss.net].

NRC (National Research Council). 2006. *Fluoride in Drinking Water: A Scientific Review of EPA's Standards*. Washington, DC: The National Academies Press.

Thiessen, K.M., Napier, B.A., Filistovic, V., Homma, T., Kanyár, B., Krajewski, P., Kryshev, A.I., Nedveckaite, T., Nényei, A., Sazykina, T.G., Tveten, U., Sjöblom, K.-L., and Robinson, C. 2005. Model testing using data on ^{131}I released from Hanford. *Journal of Environmental Radioactivity* 84(2):211-224.

Thiessen, K.M., Sazykina, T.G., Apostoaei, A.I., Balonov, M.I., Crawford, J., Domel, R., Fesenko, S.V., Filistovic, V., Galeriu, D., Homma, T., Kanyár, B., Krajewski, P., Kryshev, A.I., Kryshev, I.I., Nedveckaite, T., Ould-Dada, Z., Sanzharova, N.I., Robinson, C., and Sjöblom, K.-

L. 2005. Model testing using data on ^{137}Cs from Chernobyl fallout in the Iput River catchment area of Russia. *Journal of Environmental Radioactivity* 84(2):225-244.

Nedveckaite, T., Filistovic, V., Mastauskas, A., and Thiessen, K. 2004. Thyroid dosimetry in the western trace of the Chernobyl accident plume. *Radiation Protection Dosimetry* 108(2):133-141.

IAEA (International Atomic Energy Agency). 2003. Testing of environmental transfer models using data from the atmospheric release of Iodine-131 from the Hanford site, USA, in 1963. Report of the Dose Reconstruction Working Group of the Biosphere Modelling and Assessment (BIOMASS) Programme, Theme 2. Biosphere Modelling and Assessment Methods (BIOMASS) programme. International Atomic Energy Agency, Vienna, IAEA-BIOMASS-2.

IAEA (International Atomic Energy Agency). 2003. Testing of environmental transfer models using Chernobyl fallout data from the Iput River catchment area, Bryansk Region, Russian Federation. Report of the Dose Reconstruction Working Group of BIOMASS Theme 2. Biosphere Modelling and Assessment Methods (BIOMASS) programme. International Atomic Energy Agency, Vienna, IAEA-BIOMASS-4.

Reed, E.W., Thiessen, K.M., Hoffman, F.O., and Apostoaei, A.I. 2003. Comparison of doses and risks obtained from dose reconstructions for historical operations of federal facilities that supported the development, production, or testing of nuclear weapons. *Health Physics* 84(6):687-697.

Thiessen, K.M. 2002. Data sets available for testing environmental transport models. *Atmospheric Environment* 36:3057.

Thiessen, K.M., Napier, B.A., Filistovic, V., Homma, T., Kanyár, B., Krajewski, P., Kryshev, A.I., Nedveckaite, T., Nényei, A., Sazykina, T.G., Tveten, U., Sjöblom, K.-L., and Robinson, C. 2002. Model Testing Using Data from Accidental Releases of ^{131}I and ^{137}Cs. 1: Model Testing Using Data on ^{131}I Released from Hanford. In: Proceedings from the International Conference on Radioactivity in the Environment, Monaco, Sept. 1-5, 2002, pp. 313-316.

Thiessen, K.M., Sazykina, T.G., Apostoaei, A.I., Balonov, M.I., Crawford, J., Domel, R., Fesenko, S.V., Filistovic, V., Galeriu, D., Homma, T., Kanyár, B., Krajewski, P., Kryshev, A.I., Kryshev, I.I., Nedveckaite, T., Ould-Dada, Z., Sanzharova, N.I., Robinson, C., and Sjöblom, K.-L. 2002. Model Testing Using Data from Accidental Releases of ^{131}I and ^{137}Cs. 2: Model Testing Using Data on ^{137}Cs from Chernobyl Fallout in the Iput River Catchment Area of Russia. In: Proceedings from the International Conference on Radioactivity in the Environment, Monaco, Sept. 1-5, 2002, pp. 317-320.

Apostoaei, A.I., Nair, S.K., Thomas, B.A., Lewis, C.J., Hoffman, F.O., and Thiessen, K.M. 2000. External exposure to radionuclides accumulated in the shoreline sediments with an application to the lower Clinch River. *Health Physics* 78(6):700-710.

IAEA (International Atomic Energy Agency). 2001. Generic models for use in assessing the impact of discharges of radioactive substances to the environment. International Atomic Energy Agency, Vienna, Safety Report 19.

Apostoaei, A.I., Blaylock, B.G., Caldwell, B., Flack, S., Gouge, J.H., Hoffman, F.O., Lewis, C.J., Nair, S.K., Reed, E.W., Thiessen, K.M., Thomas, B.A., and Widner, T.E. 1999. Radionuclides Released to the Clinch River from White Oak Creek on the Oak Ridge

Reservation—An Assessment of Historical Quantities Released, Off-site Radiation Doses, and Health Risks. Reports of the Oak Ridge Dose Reconstruction, Vols. 4 and 4A. The Report of Project Task 4. Tennessee Department of Health, Oak Ridge Health Studies, Oak Ridge Dose Reconstruction.

Thiessen, K.M., Thorne, M.C., Maul, P.R., Pröhl, G., and Wheater, H.S. 1999. Modelling radionuclide distribution and transport in the environment. *Environmental Pollution* 100:151-177.

Kryshev, I.I., Sazykina, T.G., Hoffman, F.O., Thiessen, K.M., Blaylock, B.G., Feng, Y., Galeriu, D., Heling, R., Kryshev, A.I., Kononovich, A.L., and Watkins, B. 1999. Assessment of the consequences of the radioactive contamination of aquatic media and biota for the Chernobyl NPP cooling pond: Model testing using Chernobyl data. *Journal of Environmental Radioactivity* 42:143-156.

Konoplev, A.V., Bulgakov, A.A., Hoffman, F.O., Kanyár, B., Lyashenko, G., Nair, S.K., Popov, A., Raskob, W., Thiessen, K.M., Watkins, B., and Zheleznyak, M. 1999. Validation of models of radionuclide wash-off from contaminated watersheds using Chernobyl data. *Journal of Environmental Radioactivity* 42:131-141.

Garger, E.K., Hoffman, F.O., Thiessen, K.M., Galeriu, D., Kryshev, A.I., Lev, T., Miller, C.W., Nair, S.K., Talerko, N., and Watkins, B. 1999. Test of existing mathematical models for atmospheric resuspension of radionuclides. *Journal of Environmental Radioactivity* 42:157-175.

Thiessen, K.M., Gouge, J.H., Hoffman, F.O., Apostoaei, A.I., Thomas, B.A., Lewis, C.J., Blaylock, B.G., Caldwell, B., Widner, T.E., Flack, S., Nair, S.K., and Reed, E.W. 1998. Radionuclides Released to the Clinch River from White Oak Creek on the Oak Ridge Reservation – An Assessment of Historical Quantities Released, Off-Site Radiation Doses, and Health Risks. Oak Ridge Health Studies, Oak Ridge Dose Reconstruction.

Hoffman, F.O., Hammonds, J.S., Apostoaei, A.I., Blaylock, B.G., Thomas, B.A., Thiessen, K.M. 1998. Estimation of Health Risks Based on Revised Estimates of HEDR Doses for Maximum Representative Individuals Consuming Fish and Waterfowl from the Columbia River: An Evaluation of HEDR Reports on the Columbia River Pathways. Report prepared for the National Opinion Research Center. ATSDR, Atlanta, GA.

Hammonds, J.S., Hoffman, F.O., Apostoaei, A.I., Thiessen, K.M., Lewis, C.J., Blaylock, B.G., Caldwell, B., Flack, S., Nair, S.K., Reed, E.W., Thomas, B.A., and Widner, T.E. 1997. Radionuclides released from White Oak Creek on the Oak Ridge Reservation to the Clinch River: A reconstruction of historical quantities released, off-site doses, and health risks. Oak Ridge Health Studies, Oak Ridge Dose Reconstruction. Draft Report, November 1997.

Thiessen, K.M., Hoffman, F.O., Rantavaara, A., and Hossain, S. 1997. Environmental models undergo international test: The science and art of exposure assessment modeling were tested using real-world data from the Chernobyl accident. *Environmental Science & Technology* 31(8):358A-363A.

Garger, E.K., Hoffman, F.O., and Thiessen, K.M. 1997. Uncertainty of the long-term resuspension factor. *Atmospheric Environment* 31(11):1647-1656.

Nair, S.K., Miller, C.W., Thiessen, K.M., Garger, E.K., and Hoffman, F.O. 1997. Modeling the resuspension of radionuclides in Ukrainian regions impacted by Chernobyl fallout. *Health Physics* 72(1):77-85.

Hoffman, F.O., and Thiessen, K.M. 1996. The use of Chernobyl data to test model predictions for interindividual variability of ^{137}Cs concentrations in humans. *Reliability Engineering and System Safety* 54:197-202.

Hoffman, F.O., Simon, S.L., and Thiessen, K.M. 1996. The Role of Uncertainty Analysis in Dose Reconstruction and Risk Assessment. 31st Annual Meeting of the NCRP, pp. 107-134.

Nair, S.K., Hoffman, F.O., Thiessen, K.M., and Konoplev, A. 1996. Modeling the wash-off of ^{90}Sr and ^{137}Cs from an experimental plot established in the vicinity of the Chernobyl reactor. *Health Physics* 71(6):896-909.

IAEA (International Atomic Energy Agency). 1996. Validation of models using Chernobyl fallout data from southern Finland--Scenario S. Second Report of the VAMP Multiple Pathways Assessment Working Group. IAEA-TECDOC-904.

IAEA (International Atomic Energy Agency). 1996. Modelling of radionuclide interception and loss processes in vegetation and of transfer in semi-natural ecosystems. Second Report of the VAMP Terrestrial Working Group. IAEA-TECDOC-857.

NCRP (National Council on Radiation Protection and Measurements). 1996. A Guide for Uncertainty Analysis in Dose and Risk Assessments Related to Environmental Contamination. (Consultant to Scientific Committee 64-17.) NCRP Commentary No. 14.

Hoffman, F.O., Thiessen, K.M., and Watkins, B. 1996. Opportunities for the testing of environmental transport models using data obtained following the Chernobyl accident. *Health Physics* 70 (1):5-7.

Thiessen, K.M., Hammonds, J.S., Lewis, C.J., Hoffman, F.O., and White, E.I. 1996. Screening Method for the Oak Ridge Dose Reconstruction. A Task 7 Report. ChemRisk, State of Tennessee. April 1996.

BIOMOVS II. 1996. Wash-off of Sr-90 and Cs-137 from Two Experimental Plots: Model Testing Using Chernobyl Data. Stockholm, Swedish Radiation Protection Institute, BIOMOVS II Technical Report No. 9.

BIOMOVS II. 1996. Assessment of the Consequences of the Radioactive Contamination of Aquatic Media and Biota: Model Testing Using Chernobyl Data. Stockholm, Swedish Radiation Protection Institute, BIOMOVS II Technical Report No. 10.

BIOMOVS II. 1996. Atmospheric Resuspension of Radionuclides: Model Testing Using Chernobyl Data. Stockholm, Swedish Radiation Protection Institute, BIOMOVS II Technical Report No. 11.

Thiessen, K.M., Hoffman, F.O., Hammonds, J.S., and White, E.I. 1995. A Review of the Preliminary Screening Analysis Carried Out during the Oak Ridge Dose Reconstruction Feasibility Study. ChemRisk, State of Tennessee, August, 1995.

Hoffman, F.O., and Thiessen, K.M. 1995. Use of Chernobyl data to test predictions and uncertainty estimates from exposure assessment models. In: Proceedings of a Symposium on

Environmental Impact of Radioactive Releases. International Atomic Energy Agency, Vienna, Austria, 8-12 May 1995. IAEA-SM-339/20:325-336.

IAEA (International Atomic Energy Agency). 1995. Validation of models using Chernobyl fallout data from the Central Bohemia region of the Czech Republic--Scenario CB. First Report of the VAMP Multiple Pathways Assessment Working Group. IAEA-TECDOC-795.

Hoffman, F.O., Thiessen, K.M., and Rael, R.M. 1995. Comparison of interception and initial retention of wet-deposited contaminants on leaves of different vegetation types. *Atmos. Envir.* 29:1771-1775.

USEPA (US Environmental Protection Agency). 1994. Summary Review of Health Effects Associated with Mercuric Chloride: Health Issue Assessment. Research Triangle Park, NC: Office of Health and Environmental Assessment, Report No. EPA/600/R-92/199.

Hoffman, F.O., Blaylock, B.G., Frank, M.L., and Thiessen, K.M. 1993. A risk-based screening approach for prioritizing contaminants and exposure pathways at Superfund sites. *Environ. Monitoring and Assessment* 28:221-237.

Hoffman, F.O., Thiessen, K.M., Frank, M.L., and Blaylock, B.G. 1992. Quantification of the interception and initial retention of radioactive contaminants deposited on pasture grass by simulated rain. *Atmospheric Environment* 26A:3313-3321.

Hoffman, F.O., Thiessen, K.M., Frank, M.L., and Blaylock, B.G. 1992. Determining the collection efficiency of gummed paper for the deposition of radioactive contaminants in simulated rain. *Health Physics* 62:439-442.

USEPA (US Environmental Protection Agency). 1988. Summary Review of Health Effects Associated with Hydrogen Fluoride and Related Compounds: Health Issue Assessment. Research Triangle Park, NC: Office of Health and Environmental Assessment, Report No. EPA/600/8-89/002F.

USEPA (US Environmental Protection Agency). 1988. Evaluation of the Potential Carcinogenicity of Propargyl Bromide (106-96-7) In Support of Reportable Quantity Adjustments Pursuant to CERCLA Section 102. Washington, DC: Office of Health Effects Assessment [draft].

USEPA (US Environmental Protection Agency). 1988. Evaluation of the Potential Carcinogenicity of Ethanol, 1,2-Dichloro-, Acetate (10140-887-1) In Support of Reportable Quantity Adjustments Pursuant to CERCLA Section 102. Washington, DC: Office of Health Effects Assessment [draft].

USEPA (US Environmental Protection Agency). 1988. Evaluation of Cancer Risk Assessment for Coke Oven Emissions (EPA-600/6-82-003F, EPA-450/3-85-028a). Washington, DC: Office of Policy, Planning and Evaluation [draft].

Thiessen, K.M., and Lalley, P.A. 1987. Gene assignments and syntenic groups in the sacred baboon (*Papio hamadryas*). *Cytogenet. Cell Genet*. 44:82-88.

Créau-Goldberg, N., Cochet, C., Turleau, C., de Grouchy, J., Thiessen, K.M., and Lalley, P.A. 1987. Primate genetic maps. Baboon, *Papio papio*, *hamadryas*, *cynocephalus*. In: S.J. O'Brien, ed., Genetic Maps 1987. Cold Spring Harbor Laboratory, Cold Spring Harbor, New York (1987). 511.

Thiessen, K.M., and Lalley, P.A. 1986. New gene assignments and syntenic groups in the baboon (*Papio papio*). *Cytogenet. Cell Genet*. 42:19-23.

Moore, K.L., and Lalley, P.A. 1985. New gene assignments and linkage groups in baboon (*Papio*) species [abstract]. Eighth International Workshop on Human Gene Mapping. *Cytogenet. Cell Genet.* 40:702.

Roderick, T.H., Lalley, P.A., Davisson, M.T., O'Brien, S.J., Womack, J.E., Créau-Goldberg, N., Echard, G., and Moore, K.L. 1984. Report of the committee on comparative mapping. Seventh International Workshop on Human Gene Mapping. *Cytogenet. Cell Genet*. 37:312-339.

Moore, K.L., and Lalley, P.A. 1984. Comparative mapping in man and baboon (*Papio papio*) involving genes assigned to human chromosomes 4, 6, 14, 15, and 20 [abstract]. Seventh International Workshop on Human Gene Mapping. *Cytogenet. Cell Genet*. 37:542-543.

Moore, K.L., and Lane, E.T. 1981. An investigation of mathematical models for the addition reaction of chlorine to oleic acid [abstract]. *J. Tenn. Acad. Sci.* 56:54.