REPORT OF THE FORT COLLINS FLUORIDE TECHNICAL STUDY GROUP

April 2003

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- Larimer County Board of Health
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The Fluoride Technical Study Group (FTSG) was charged with compiling a report that assesses risks and benefits of community water fluoridation in order to assist risk managers (The Larimer County Board of Health, the City of Fort Collins Water Board, and the Fort Collins City Council) to decide whether to continue, alter or discontinue the City’s water fluoridation program.

A more complete discussion of the FTSG’s work and a description of the studies and findings are contained in the attached report. This summary begins with five of the most important considerations underlying the report and its findings, and then presents the findings themselves:

These are some of the essential considerations:

1. The FTSG elected to use a tiered approach to reviewing the existing literature on water fluoridation, turning first to already conducted and published scientific literature research reviews and compilations. Only when a gap in the data became evident or when a specific need for more information was needed did the group turn to and evaluate published, peer-reviewed primary studies.

2. The FTSG, for the most part, limited consideration to scientific studies of drinking water fluoridation at or around 1 milligram per liter (mg/L) or 1 part per million (ppm), because it is the target amount of fluoride added to the City of Fort Collins water supply (range of 0.7 – 1.2 mg/L with data indicating stringent control at 1.0 mg/L).

3. The levels of fluoride in untreated water range from 0.15 - 0.25 mg/L fluoride ion. If the City were to end its water fluoridation program, the drinking water in Fort Collins would continue to contain some fluoride.

4. The United States Environmental Protection Agency (EPA), under the Safe Drinking Water Act (42 USC 300), promulgates the National Primary Drinking Water Regulations. These regulations set the maximum contaminant levels (MCLs) for chemicals in finished water supplied by public water systems. The EPA has established an MCL for fluoride of 4.0 mg/L.

5. The FTSG endeavored to create a balanced product for use by decision-makers that took into account the most current and best available analysis of the weight of the scientific evidence on the risks and benefits of community water fluoridation. The group also acknowledged that there are gaps in the knowledge and uncertainties are inherent in the ability to fully understand what may be subtle, yet important health effects that are yet to be detected via a weighted evidence approach. Thus, the report includes stated uncertainties and areas where additional research is needed to better understand the true benefits and risks.

FINDINGS

After considering public concerns and discussion—then focusing—the list of important questions, the FTSG has developed consensus findings in four categories:

The effectiveness of drinking water fluoridation.

1. The risks of drinking water fluoridation and of cumulative exposure to fluoride from all sources, including drinking water (over time) with specific attention to cancer, bone fractures, skeletal fluorosis, dental fluorosis, thyroid function, and immune system effects.
3. The costs and benefits of fluoridating the drinking water supply, and of not fluoridating the drinking water supply, including assessing the distribution costs and benefits (equity), and including the costs and benefits of using alternative methods to deliver fluoride.

4. The potential for increased contaminant levels in the drinking water due to the use of hydrofluorosilicic acid in the fluoridation process.

**Finding #1 – The Effectiveness of Drinking Water Fluoridation in Preventing Caries (Cavities)**

The weight of the evidence suggests that there is caries (cavities) reduction in populations exposed to water fluoridation at or near an optimal level. The primary mode of action of fluoride in preventing caries is its topical action on the surface of the teeth; systemic action from ingestion is now thought to play a minor role. It appears that community water fluoridation is effective in all age groups in preventing dental caries. This benefit amounts to a relative caries reduction of 25% and an absolute prevalence difference of 1.14 surfaces with caries in primary teeth and 0.5 surfaces with caries in permanent teeth in children according to the most recent U.S. surveys of schoolchildren. Among the four studies of caries prevention in adults, the most recent study showed that community water fluoridation reduced surfaces with caries by 0.35 surfaces per year of fluoride exposure. The benefit of drinking water fluoridation decreases as individuals in the population receive fluoride from other sources (e.g., toothpastes, dental care, etc.). Even with the limitations of some of the studies, there appears to be a net benefit in caries reduction from drinking water fluoridation over and above that from toothpaste and other sources of fluoride. Among the 14 recent studies (completed after 1985) reviewed in which water fluoridation was discontinued, nine showed an increase in caries rates. Five communities (all of them in other countries) that suspended water fluoridation did not find that caries rates increased. It is uncertain to what degree changes in oral health behaviors, introduction of new preventive programs and increased delivery of professional treatments in response to cessation of fluoridation can account for these findings. Since these studies were conducted in foreign communities in which there was socialized dental care and school-based oral health programs, their results may not apply to Fort Collins.

**Finding #2 – The Risk of Drinking Water Fluoridation**

**Total Fluoride Exposure**

Total fluoride exposure must be considered when evaluating health effects. The amount of total fluoride ingested will vary between individuals and is not precisely known. The FTSG review of the literature finds that likely total exposure values for children older than six months living in communities with water fluoridated at up to 1.2 mg/L (ppm) do not exceed the upper limit set to be protective of moderate dental fluorosis by the Institute of Medicine. Total dietary exposures of fluoride can exceed this threshold amount (0.7mg/day) in infants fed formula reconstituted with optimally fluoridated water.

**Cancer**

Although a small increase in cancer risk cannot be excluded, there is no consistent evidence from human or animal studies that exposure to optimally fluoridated drinking water and other sources causes any form of cancer in humans, including bone and joint cancer. The agreement between the epidemiological and toxicological literature reduces the uncertainty associated with any one line of evidence finding. Additional research is needed to address the remaining uncertainty whether community water fluoridation may cause cancer in humans following long-term exposures of greater than 40 years.

**Bone Effects**

The FTSG agrees with the conclusion of the Medical Research Council of Great Britain that states, “The possibility of an effect on the risk of hip fracture is the most important in public health terms. The available evidence on this suggests no effect, but cannot rule out the possibility of a small percentage change (either an increase or a decrease) in hip fractures” (Medical Research Council 2002, page 3).
Skeletal Fluorosis
At the concentrations of fluoride provided in Fort Collins water including exposures from all sources over a lifetime, skeletal fluorosis caused by drinking water exposure is not likely to be a health issue. The available data are not consistent with a likelihood of increased human skeletal fluorosis from city water fluoridation.

Additional research is needed to reduce the remaining uncertainty if cumulative exposure to all sources of fluoride (including drinking water fluoride at levels of 1 mg/L) over a lifetime may lead to pre-clinical or milder forms of skeletal fluorosis in some sensitive populations.

Dental Fluorosis
At the concentrations of fluoride provided in Fort Collins water, in combination with other sources of fluoride, as many as one in four children under age 8 may develop very mild to mild dental fluorosis. This degree of fluorosis may or may not be detectable by the layperson. With oral health as the goal, this degree of dental fluorosis is considered an acceptable adverse effect given the benefits of caries prevention. Since about 60% of dental fluorosis can be attributed to other sources of fluoride, particularly toothpaste and other dental products, parental supervision over tooth paste swallowing in their young children and proper prescribed supplementation in infants will likely reduce development of enamel fluorosis more than the removal of added fluoride in drinking water.

Thyroid Effects
In the literature reviewed, doses appropriate for caries reduction were not shown to negatively impact thyroid function. Studies in which humans received doses significantly higher than the optimum fluoride intake for long periods of time showed no negative impact on thyroid function. For those with hypothyroidism, the risks of alteration of thyroid structure or function are very low. The absence of our finding any conclusive evidence that drinking water fluoride exposures causes increased risk to thyroid function does not prove that fluoride can not affect thyroid function. The available data are consistent with a finding of a low likelihood of risk to human thyroid function from water fluoridation.

Immunological Effects
Overall, evidence is lacking that exposure to fluoride through drinking water causes any problems to the human immune system. The absence of our finding any conclusive evidence that drinking water fluoride exposures causes increased risk to human immune system function does not prove that fluoride is harmless to the human immune systems.

Other Health Effects
The potential for other health effects was reviewed by the FTSG. There was not adequate evidence to consider any of these other potential adverse effects a concern with respect to fluoridation of Fort Collins water supplies. The absence of our finding any conclusive evidence that drinking water fluoride exposures causes other potential health effects does not prove that fluoride can not cause other potential health effects.

Finding #3 – Costs and Benefits, Including the Distribution of Costs and Benefits
The research indicates that the public health goal of a reduction in the incidence of caries is better achieved through community water fluoridation than through individual approaches. It requires minimal behavioral changes compared to alternative delivery methods. It is effective in reaching people in all socioeconomic strata.

The FTSG finds that, even in the current situation of widespread use of fluoride toothpaste and lower baseline caries risk, it is likely that community water fluoridation remains effective and cost saving at preventing dental caries. Based on best available evidence, suspending fluoridation of water in Fort
Collins would yield a net increase in costs of preventing and treating caries of approximately $4.25 per person per year (range $3.22 - $10.31). The burden of caries is disproportionately borne by those with lower socio-economic status. There is some evidence that water fluoridation reduces this inequality in oral health.

Not considering the costs of enamel fluorosis or other potential adverse health effects may have led to an over-estimation of the cost-savings of water fluoridation in Fort Collins. The magnitude of the costs of adverse effects is likely to fall well below the estimated net savings.

In summary, this cost analysis assumes that there is a significant benefit from community water fluoridation in preventing caries and that suspending community water fluoridation would result in a relative increase in caries. It also assumes that potential adverse health effects are not significant. The analysis also assumes that the city will continue using current fluoride additives (hydrofluorosilicic acid). Using this set of assumptions, there appears to be a net cost benefit to community water fluoridation. If any of these assumptions are not valid the cost-benefit picture could change significantly.

The FTSG did not review any study or measure that will achieve the same levels of prevention as water fluoridation for the same resources.

**Finding #4 – The Potential for Increased Contaminant Levels Due to the Use of Hydrofluorosilicic Acid**

The FTSG’s review identified three potential concerns associated with hydrofluorosilicic acid (HFS). 1) co-contamination (i.e. arsenic and lead), 2) decreased pH leading to increased lead solubility or exposure, and 3) potential toxicological effects from incomplete dissociation products of HFS. The FTSG used the raw and finished water quality data for the City of Fort Collins to determine whether the addition of HFS was responsible for the potential addition of contaminants such as heavy metals to the city's drinking water. There was no evidence that the addition of HFS increased the concentrations of copper, manganese, zinc, cadmium, nickel, or molybdenum. The concentrations of arsenic and lead were below the detection limit for the Fort Collins Water Quality Control Laboratory in both the source water and the finished water and below the maximum contaminant level (MCL) for these naturally occurring elements. There was no evidence that the introduction of HFS changed the pH of the water appreciably. Concern that HFS incompletely disassociates may be unfounded when the fundamental chemical facts are considered. Therefore, it is unlikely that community water fluoridation poses a health risk from the exposure to any of these chemicals present in the water as it leaves the plant. Further studies related to the health effects of HFS are in progress.
Finding #1 – The Effectiveness of Drinking Water Fluoridation in Preventing Caries

Historical Perspective

In 1901, a Colorado Springs dentist recognized that his patients with teeth with a brown stain or mottled dental enamel also had a very low prevalence of cavities (also called caries) (Centers for Disease Control and Prevention [CDC], 1999b). At this time in history, extensive dental caries were common, so this observation and its subsequent correlation with high amounts of fluoride ion in the water supply (2.0 - 12.0 milligrams per liter, mg/L) proved to be significant. Another dentist, H.T. Dean, DDS., took this information and conducted a survey of dental caries in relation to natural concentrations of fluoride in drinking water of 21 U.S. cities (Committee to Coordinate Environmental Health and Related Programs, USPHS [USPHS], 1991 pp.18-19; CDC, 1999a, p. 934). Dean observed that at a concentration of 1 mg/L, fluoride would significantly reduce caries while causing a low incidence of mottled enamel, now called fluorosis, of the mostly very mild type. Beginning in 1945 and 1946, community trials were conducted over 13-15 years in four pairs of cities in the U.S. and Canada. These studies found a 50-70% reduction of caries in children following addition of fluoride (in the form of sodium fluoride) to community water supplies at 1 mg/L. The incidence of mild fluorosis remained low (CDC, 1999a, p. 936). Some of the early studies were criticized for lacking appropriate controls, not applying randomization, and not controlling for potential examiner bias (Sutton, 1960). However, the large effect sizes in these trials, along with replication of these findings in subsequent studies, led to the acceptance of community water fluoridation as a public health approach to caries prevention.

Since those early times, community water fluoridation and the use of fluoridated water in the production of foods and beverages have become widespread. Beverages and foods prepared with fluoridated water contain fluoride. When these processed products are transported to nonfluoridated communities for sale, people consume them and ingest fluoride (Lewis & Banting, 1994, p. 156). People also travel across “fluoridation boundaries” to work or to attend school. This has been called the “halo” or “diffusion effect” and accounts for some of the narrowing difference in fluoride intake between fluoridated and nonfluoridated communities (CDC, 2001b, p. 9). A “reverse diffusion effect” also occurs, in which products from fluoride-deficient communities are ingested by people living in fluoridated areas. This has the same leveling effect when caries rates between fluoridated and nonfluoridated communities are compared (Ripa, 1993, p. 23).

Another trend that has contributed to a lowering of caries rates in both fluoridated and nonfluoridated communities has been the successive introduction of readily available fluoride products since the 1950s, including topical gels, fluoridated toothpaste, fluoride supplements and mouth rinses (Ripa, 1993, p. 23). With the introduction of fluoridated toothpaste in 1965 (at 1100 mg/L), the use of fluoridated dental products has become widespread. Between 1972 and 1983, fluoridated toothpaste sales in the U.S. market increased from about 70% to more than 95% (Driscoll, et al., 1986, pp. 50-51).

The level of dental decay in a population is typically summarized by measures of its distribution and its severity. Prevalence of caries—the percent of the population with any caries—is the most widely used measure of distribution. Severity of dental decay is measured as the mean number of decayed, missing and filled teeth (abbreviated “dmft” for primary teeth or baby teeth and “DMFT” for permanent teeth) or the mean number of decayed, missing or filled surfaces (abbreviated “dmfs” for primary tooth surfaces and “DMFS” for permanent tooth surfaces).

As a consequence of many factors, including fluoridation of public water supplies, almost universal use of fluoride products, and improved oral health behaviors, there has been a reduction in caries levels in the U.S. and many other established market economies since the 1970s. As shown in Table 1 (Featherstone,
n 1999, p. 32), national surveys of decay in children demonstrated dramatic decreases in both prevalence and severity in the 1970s and 1980s. Recent smaller surveys indicate that the decline in caries may have stalled since then (Featherstone, 1999, p. 31). The current national survey, NHANES IV, began collecting measures of dental caries, sealant use and enamel fluorosis in 1999. This survey will help determine whether or not caries rates in the U.S. have stabilized or continued to fall (http://www.cdc.gov/nchs/nhanes.htm).

| Table 1 |
| Mean DMFS and % Caries Free in Four U.S. Surveys |

<table>
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<tr>
<th>Age Range</th>
<th>NCHS * 1971-74</th>
<th>NIDR 1979-80</th>
<th>NIDR 1986-87</th>
<th>NHANES III %</th>
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<tr>
<td>5-11</td>
<td>DMFS 3.0</td>
<td>2.0</td>
<td>1.2</td>
<td>.9</td>
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<td></td>
<td>% caries free 44%</td>
<td>58%</td>
<td>70%</td>
<td>74%</td>
</tr>
<tr>
<td>12-17</td>
<td>DMFS 10.4</td>
<td>6.8</td>
<td>4.7</td>
<td>4.4</td>
</tr>
<tr>
<td></td>
<td>% caries free 10%</td>
<td>17%</td>
<td>27%</td>
<td>33%</td>
</tr>
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(adapted from Featherstone, 1999, p 32)

* NCHS – National Center for Health Statistics

† NIDR – National Institute for Dental Research

% National Health and Nutrition Examination Survey

The extent of water fluoridation in a region determines the magnitude of the diffusion effect. This was evident in the 1986-87 National Institute of Dental Research (NIDR) survey of school children. The Midwest region had the highest percentage of the population having water fluoridation (72%) and the lowest difference in mean or average caries scores (-5.6%) among the seven U.S. regions, while the Pacific region had the lowest water fluoridation coverage (18%) and the highest difference in mean caries scores (61%) (Ripa, 1993, p. 23). In Region V (Texas, Oklahoma, New Mexico, and Colorado) 57% of persons was living in fluoridated communities and an 8% difference in average caries scores were found. The 1986-87 NIDR survey is the most recent and geographically relevant data the Fluoride Technical Study Group (FTSG) found to estimate caries levels in the Fort Collins area.

Even though overall decay rates on all tooth surfaces have fallen dramatically in children, caries continue to be an important public health problem. However, the distribution of the problem has changed over the past two decades. First, the distribution of decay among children has become skewed, with one quarter of children accounting for 80% of the caries experience in permanent teeth in the U.S. (Kaste, et al., 1996 ). According to the Centers for Disease Control and Prevention:

“Lower-income, Mexican American and African-American children and adults have more untreated decayed teeth than their higher-income or non-Hispanic white counterparts (4,5,8,9). Among low-income children, approximately one-third have untreated caries in primary teeth that could be associated with pain, difficulty in eating, and underweight (9)” (CDC, 2001a, p.2).

Second, the distribution of caries in the mouth has changed. Fluoride and brushing are both less effective in preventing caries on pit-and-fissure surfaces (the chewing surfaces) of teeth, leading to lesser reductions in caries on these surfaces than on the smooth tooth surfaces (U.S. Department of Health and Human Services [USDHHS, ]2000, p. 38). The width of most pits and fissures is smaller than a toothbrush bristle, making cleaning of their deep recesses almost impossible. The debris that accumulates forms a mechanical barrier that is thought to impede the flow of topical fluoride to these recesses. According to national surveys, the majority of all dental caries in school-age children now occurs on pit and fissure surfaces (Kaste et al., 1996 ; USDHHS, p. 166).

Finally, there has been a shift in the burden of caries from children to adults, due to the fact that tooth retention has increased among older adults over the past several decades (CDC, 2001b, p. 11). Gingival tissues tend to recede over time, exposing the tooth root to cariogenic bacteria that can cause root caries.
The latest national survey, the 1988-91 NHANES III, found that only 7% of adults with teeth were caries free. Figure 1 shows the marked increase in caries experience with age.

![Figure 1. Mean caries levels by age, U.S., 1988-91](image)

The first questions that the FTSG addressed were, “What is the effectiveness of community water fluoridation in preventing caries?” and “Is there an effect over and above that of fluoride in toothpaste and other dental products and processed foods and beverages?”

**How Fluoride Works**

The main benefit of fluoride is that it inhibits dental decay. The basic process of decay begins in the bacteria-rich coating of the teeth called plaque (Featherstone, 1999, p. 32). Certain bacteria produce acids when they digest fermentable carbohydrates such as sugars and cooked starch. These acids can dissolve the calcium phosphate mineral of the enamel or dentin resulting in a carious or “white spot” lesion—a process called demineralization. The process of demineralization occurs each time carbohydrates are taken into the mouth. If not halted or reversed, the carious lesion progresses and a cavity is formed. If fluoride is present in the saliva and plaque fluid at the time bacteria is producing acid, it diffuses into the crystal surface with the acid and inhibits demineralization. Fluoride also enhances remineralization if a carious lesion begins to form and the remineralized surface is then more resistant to caries. Fluoride also interferes with the production of acid and adhesion by bacteria—whether this reduces the caries producing potential of bacteria is unclear (CDC, 2001b, p. 3).

Early theories about how fluoride worked held that it needed to be incorporated into developing enamel before the tooth erupted or emerged from the gums (CDC, 2001a, p. 4). Therefore, it needed to be swallowed by infants and children in order to reduce risk of caries. However, according to recent reviews, laboratory and epidemiological research over the past two decades indicates that fluoride’s predominant effect is post-eruptive and topical and therefore of benefit to adults as well as children (CDC, 2001b, p. 4; Featherstone, 1999; Locker, 1999). Most of the benefits of water fluoridation appear to accrue the same way they do for toothpaste and other dental products—through frequent topical exposures.

“When fluoridated water is the main source of drinking water, a low concentration of fluoride is routinely introduced into the mouth. Some of this fluoride is taken up by dental plaque; some is transiently present in saliva, which serves as a reservoir for plaque fluoride; and some is loosely held on the enamel surfaces (76). Frequent consumption of fluoridated drinking water and beverages and food processed in fluoridated areas maintains the concentration of fluoride in the mouth” (CDC, 2001b, p. 9).
That does not mean that ingestion (swallowing) of fluoride does not contribute to caries prevention benefits. An analysis of data from the Netherlands estimated that, for 15 year olds, half of the reduction in caries attributable to fluoride exposure was due to pre-eruptive exposure and half due to post-eruptive exposure, and that the best protection is achieved if fluoridation is available from birth (Groeneveld, 1990; reviewed by Ripa, 1993, p. 26). The relative benefits of pre and post-eruptive fluoride have yet to be resolved.

The fact that water fluoridation’s major benefit is topical, combined with the fact that potential adverse effects can only be caused by systemic absorption, was an important concern to the FTSG. However, evidence suggests that the pre-eruptive benefits of water fluoridation, although smaller, should not be overlooked.

**Evidence of Effectiveness of Community Water Fluoridation**

**The FTSG’s Approach**

The potential effectiveness of exposure to fluoride in preventing and controlling caries can be evaluated from observation (epidemiologic studies) or experiment (randomized trials). With either approach, the researcher compares measures of caries among a group exposed to fluoride versus measures of caries in a concurrent or historical group that was not exposed or was less exposed. Randomized clinical trials (with concurrent controls, double blind design and placebos) are considered the gold standard of evidence for effectiveness of a clinical treatment. Such experiments have shown that fluoride delivered in toothpaste, mouthwash, gels, supplements and varnishes reduce caries (CDC, 2001b, pp. 20-21; USPHS, 1991, p. 27). However, it is not possible to conduct randomized controlled experiments to measure the effectiveness of adding fluoride to community water supplies. Study subjects (members of communities) can neither be randomly allocated to treatment and control groups, and it is difficult to blind examiners to whether or not study subjects are living in a fluoridated community (CDC, 2001b, p. 20). Therefore, evidence of the effectiveness of community water fluoridation must be based on observational studies. Since the researcher does not control the allocation of treatment in an observational study, there is a potential for the validity of such studies to be threatened by a variety of biases. Some study designs are more vulnerable than others. Furthermore, because background caries rates have dropped since the early community trials, and differences between exposed and non-exposed individuals have narrowed, biases introduced by weak study designs could be large enough to mask a true difference in caries measures or demonstrate a difference when one does not exist (Expert Panel for Water Fluoridation Review, City of Calgary, 1998, p. 23). Therefore it is critical that both the quantity of studies and their quality be considered in assessing the weight of evidence regarding the current effectiveness of community water fluoridation. A thorough assessment of the evidence requires a systematic approach to searching for and selecting studies to include and to assess their validity.

The FTSG’s approach was to identify recently published comprehensive summaries of the evidence of water fluoridation effectiveness commissioned by health authorities, to evaluate how each review protected against biases (review quality), to highlight findings of reviews of high quality, and to use all reviews to identify areas of uncertainty. A subset of eight of the fluoride evidence reviews initially selected by the FTSG addressed the issue of the effectiveness of community water fluoridation. Descriptions of the approaches of each of these reviews to collecting and weighing the evidence regarding the benefits of community water fluoridation are found in Appendix 1. The FTSG identified five comprehensive reviews published since 1990 in which the review or research panel made an attempt to identify all relevant research and evaluate the threats to validity of individual studies. Four were commissioned by national health authorities and one by a provincial government. Two of the reviews specifically addressed the question of whether the effectiveness of water fluoridation remains significant in the current context of lower mean caries levels and widespread exposure to other sources of fluoride (National Health Service Centre for Reviews and Dissemination, University of York [NHS], 2000; Locker, 1999).

(76) Reference within a quote is available in the source document.
The FTSG first reviewed the four nationally commissioned studies and their findings. The group then described evidence of the declining magnitude of effectiveness in recent times. Finally, the FTSG examined several recently conducted epidemiological studies in which no caries benefit was found to ascertain why this might be.

**What Recent Comprehensive Reviews Found**

In 1991, the Ad Hoc Subcommittee on Fluoride convened by The U.S. Department of Health and Human Services and the United States Public Health Service (USPHS) published their comprehensive review and evaluation of the public health benefits and risks of fluoride in drinking water (USPHS, 1991). Using the traditional epidemiological criteria for establishing causation, the Subcommittee found:

“The reduction in dental caries among persons exposed to fluorides fulfills all the criteria for a causal relationship: an association was found with a dose-response effect, the findings were replicated under a great variety of circumstances by different investigators, alternative explanations and observer bias have been excluded, the findings are biologically plausible, and the effect, prevention of dental caries, continues to show that the fluoridation of water supplies substantially reduces the scores of dental caries. The decline over time in difference in caries scores between fluoridated and non-fluoridated areas is due in part to the increased availability of fluorides in non-fluoridated areas, as in toothpaste and other vehicles for fluorides” (USPHS, 1991, p. 35).

The Subcommittee did not use explicit criteria for assessing the quality of studies, instead addressing threats to validity by examining and excluding alternative explanations for study results (USPHS, 1991, pp. 26-28).

In 2000, a systematic review of the literature on the effectiveness of fluoridation conducted for the British National Health Services by the Center for Reviews and Dissemination at the University of York published their results. The independent panel of experts established explicit search and selection criteria for inclusion of research on community water fluoridation conducted between 1966 and February 2000 in industrialized countries. The review included only studies presenting both baseline and follow-up data on child caries per tooth (DMFT) in two communities with different levels of fluoride in drinking water. A total of 26 studies on the effect of water fluoridation on caries rates were found that met their minimum design standards, five of them unpublished. Only one examined adults. Based on these 26 studies completed between 1951 and 2000, they found sufficient evidence of moderate quality to conclude “fluoridation of drinking water supplies does reduce caries prevalence” (NHS, 2000, p. 23). This amounted to a (median) 14.6% increase in children without caries (range –5.0% to 64%) or a median 2.25 (range 0.5 to 4.4) fewer teeth per mouth having caries (McDonagh, et al., 2000). The evidence included both studies that compared fluoridated and nonfluoridated communities (30 measures) as well as studies that compared never fluoridated or still fluoridated communities with communities that stopped fluoridating the water supply (22 measures). “The best available evidence from studies following withdrawal of water fluoridation indicates that caries prevalence increases, approaching the level of the low fluoride group” (NHS, 2000, p. xii). The quality of evidence for this finding was rated as “of moderate quality” by the research panel.

The Fluoride Recommendations Work Group was assembled by the U.S. Centers for Disease Control and Prevention (CDC) in the late 1990s to develop recommendations for using fluoride to prevent and control caries. In 2001, they came to the following consensus regarding the current effectiveness of water fluoridation in preventing decay in children:

“Initial studies of community water fluoridation demonstrated that reductions in childhood dental caries attributable to fluoridation were approximately 50-60%. More recent estimates are lower, 18-40%. This decrease in attributable benefit is likely caused by the increasing use of fluoride from other sources, with the widespread use of fluoride toothpaste probably the most important.
The diffusion or “halo” effect of beverages and food processed in fluoridated areas, but consumed in non-fluoridated areas also indirectly spreads benefits of fluoridated water to non-fluoridated communities. This effect lessens the differences in caries experience among communities” (CDC, 2001b, p. 11).

The group noted that quantifying the benefits of water fluoridation in adults is more complicated, but found evidence to support effectiveness in this group as well (CDC, 2001b, p. 11). Using a system developed to assess the quality of evidence regarding clinical preventive services (U.S. Preventive Services Task Force, 1996), the group rated the evidence as II, on a scale from I (randomized controlled trials which are considered the highest quality) to III (the lowest level as in the opinions of experts).

The Task Force on Community Preventive Services, a 15-member independent expert panel supported by the CDC, the U. S. Department of Health and Human Services and other federal and public/private partners, published the results of its systematic review of the evidence of effectiveness of selected population-based interventions to prevent and control dental caries in 2001 (CDC, 2001a, p. 8). Similar to the British National Health Services panel, the group sought to review and evaluate all research on community water fluoridation conducted between 1966 and December 2000 in the U.S. and other industrialized countries. The process yielded 21 studies that met validity criteria. The median decrease in dental caries upon starting or continuing community water fluoridation among the highest quality studies was 29.1% (21 measures, range 110.5% decrease to 66.8% increase). The median increase in caries following cessation of water fluoridation in the three qualifying studies was 17.9% (five measures, range 42.2% decrease to 31.7% increase). Two of the nine studies in the highest quality group showed negative results (did not show an increase in caries after cessation of fluoridation). Reviewers concluded, “These inconsistent estimates of effectiveness appear to have resulted from inadequate control of confounding due to notably lower baseline caries prevalence in fluoridated compared with non-fluoridated areas” (Truman, et al., 2002, p. 27). Based on this review, the Task Force made the following recommendation, “Based on the evidence of effectiveness, the Taskforce strongly recommended community water fluoridation” (CDC, 2001a, p. 7).

**Evidence of the Current Magnitude of Effectiveness**

Over the last 30 years, the overall prevalence of caries has decreased dramatically (Table 1). All the reviews above noted that the declining levels of caries in the U.S. and elsewhere translate into smaller net differences in mean caries levels between fluoridated and nonfluoridated communities. The second component of the effectiveness question the FTSG raised was, “What is the magnitude of caries protection from water fluoridation in the current setting of widespread availability of other sources of fluoride?”

Comparing the summary estimates of effectiveness from a series of sequential comprehensive literature reviews demonstrates the shrinking differences attributable to water fluoridation. In 1982, Murray and Rugg-Gunn (1982) reviewed 95 water fluoridation studies conducted in 20 countries between 1945 and 1978. They found evidence that fluoridation reduced caries by 40-50% for primary teeth and 50-60% for permanent teeth in this period (Murray & Rugg-Gunn, 1982). In 1989, Newbrun (1989) reviewed the world literature from 1976 to 1987. He found 30-60% reductions in primary teeth and 30-40% reductions in permanent teeth in adolescents and adults during this period. Figure 2 shows the decrease in mean caries prevalence from 1979-80 to 1986-87 in eight and fifteen year olds from a national sample of school children conducted by the NIDR. The mean percent reductions in caries rates between continuous residents of fluoridated and nonfluoridated communities is also demonstrated (Brunelle & Carlos, 1990; Brunelle & Carlos, 1982).
Lewis and Banting (1994) began with Newbrun’s review and updated it through 1992. They showed that although the overall mean percent reductions between the years 1977-82 and 1983-91 were similar (27% and 25% respectively), the absolute mean difference between fluoridated and nonfluoridated communities in number of surfaces with caries dropped from 1.61 to 0.73 between these periods (Lewis & Banting). They pointed out the sharp contrast between these results and the original community trials where differences of about ten surfaces (five DMFTs) were seen in adolescents. The authors suggested that since the diffusion of fluoride into nonfluoridated communities is impossible to control for, the effectiveness of water fluoridation could no longer be determined (Lewis & Banting).

Two recent reviews specifically addressed the question of the current magnitude of effectiveness. First, Dr. David Locker of University of Toronto conducted a systematic literature review of the effectiveness of community water fluoridation spanning 1994 through November 1999, for the Public Health Branch, Ontario Ministry of Health & First Nations and Inuit Health Branch, Health Canada. Twenty-nine published studies were found in which optimally fluoridated communities were compared with concurrent or historical controls (Locker, 1999). Twenty-five were weak “before-after” ecological study designs—four were more robust cross-sectional studies. They examined the magnitude of the current caries prevention effect using two of the more robust studies, both cross-sectional; one based on the 1986-87 National Survey of U.S. School Children and the other from Australia. While the U.S. study found water fluoridation reduced caries by 25%, the absolute difference in mean caries prevalence between those living in fluoridated and those living in nonfluoridated communities was 1.14 surfaces in deciduous (baby) teeth and 0.55 surfaces in permanent teeth (Heller, Eklund, & Burt, 1997). In South Australia, the differences were smaller, ranging from 0.12 to 0.3 surfaces in permanent teeth (Slade, Davies, Spencer, & Stewart, 1995). The reviewers concluded that caries reductions are now relatively small in absolute terms, particularly in permanent teeth and that water fluoridation explains only a small part of the variation in caries experience between children. The authors concluded:

“Given the weaknesses in design and the methodological flaws to which many of the studies were subject, the data from these more recent studies must be treated with some caution. While the balance of evidence overall suggests that water fluoridation does reduce caries experience, the magnitude of the effect is subject to a degree of uncertainty but is unlikely to be large in absolute terms” (Locker, 1999, p. 33).
The NHS Center for Reviews and Dissemination (2000) analyzed studies conducted since 1974 to examine the effect of water fluoridation over and above other sources of fluoride. Of the ten studies that met their inclusion criteria, seven examined the discontinuation of fluoridation. Although two of these studies (Kunzel & Fischer, 1997; Maupome, Clark, Levy, & Berkowitz, 2001) found that mean levels of caries did not increase after the fluoridated community stopped fluoridating, the remainder showed that there was a greater increase in caries levels in the fluoridated-ended communities than in the controls. The panel concluded, “a beneficial effect of water fluoridation was still evident despite an assumed exposure to non-water fluoride in the populations studied” (NHS, 2000, p. xii). The quality of evidence for this finding was rated as “of moderate quality” by the research panel.

The Medical Research Council of the British Health Service established a Working Group to consider what further research is needed to improve knowledge about water fluoridation and health, following the release of the NHS review. The Working Group report published in September 2002 specifically recommended more research of the effects of water fluoridation against a background of widespread use of fluoride toothpaste, while controlling for age, social class, ethnic group, sugar consumption and use of other discretionary fluorides.

**Studies of the Effectiveness of Community Water Fluoridation in Adults**

Locker also reviewed recent studies of effectiveness of community water fluoridation in adults (Locker, 1999, p. 31). Four studies published since 1990 met inclusion criteria. All four studies found substantial reductions in coronal and root caries in adults living in fluoridated as compared with nonfluoridated communities. Two of the studies had prospective cohort designs (a design with fewer threats to validity). Grembowski, Fiset and Spadafora (1992) tracked caries rates in 972 Washington state employees and spouses, aged 20 to 34 years, in two fluoridated communities and a nonfluoridated community. After controlling for an extensive array of variables, they found that drinking water fluoridation reduced DMFS by 0.35 surfaces per year of fluoridation exposure (Grembowski, et al.). For 18 months, Hunt, Eldredge and Beck (1989) prospectively followed seniors who were long-term residents of fluoridated and nonfluoridated communities. They found that the risk of developing caries was 20% less on the crowns of teeth and 27% less on root surfaces in those with long-term residence in fluoridated communities (Hunt, et al.).

Considering that the population is aging, that tooth retention has increased in adults in recent decades (CDC, 2001b, p. 11), and that root surface exposure due to gingival recession renders adults particularly susceptible to root caries, the question of the effectiveness of water fluoridation in prevention of caries in adults is particularly important. The small number of studies examining this population, while consistent, cannot provide robust proof of effectiveness. In addition to Locker, the CDC, the U.S. Task Force for Community Preventive Services, and the British Medical Review Council (see below) all identified this as an area where future research should be focused (Locker, 1999; CDC, 2001a; Truman et al., 2002; Medical Research Council [MRC], 2002).

**Fluoridation-Ended Sites in Which No Caries Increases Were Found**

While virtually all studies examining the initiation of fluoridation demonstrate caries reductions compared to nonfluoridated communities, recent studies in which the impact of ending fluoridation has been measured have yielded mixed results. The NHS review and the review by the Task Force of Community Preventive Services both examined this evidence and concluded that mean caries rates generally increase when fluoridation is stopped. The Task Force review estimated the relative increase at 17.9% based on the highest quality studies (CDC, 2001a). However each review included examples of communities in which caries rates did not increase. Studies demonstrating these inconsistent results are frequently cited by opponents of fluoridation. For this reason, and because the impact of stopping fluoridation is of particular interest to the current policy question in Fort Collins, the FTSG chose to examine these studies in detail.
Among the 14 recent studies (completed after 1985) in which water fluoridation was discontinued, nine showed an increase in caries rates. Five found that caries levels had either remained stable or dropped after fluoridation ended. To the extent that these study settings are generalizable to Fort Collins, it is important to determine whether or not their results can be explained. If explanations are wanting, they raise the level of uncertainty of the FTSG’s findings. A brief review of each of these studies follows.

Two ecological time-series studies published in 1997 and 2000 found that caries prevalence among children decreased in four fluoridation-ended sites in former East Germany (Kunzel & Fischer 1997; Kunzel, Fischer, Lorenz, & Bruhmann, 2000). In these four industrial towns, systematic surveys of caries prevalence in children have been conducted every two to four years since fluoridation began (1959-1972). During the first three decades of these surveys, the level of caries prevalence was strictly correlated with the availability of an optimal fluoride concentration in the drinking water. Water fluoridation was followed by a decrease of caries, and interruptions in fluoridation were followed by increasing caries levels. A different trend was noted in the 1990s. Contrary to an expected caries increase there was a consistent statistically significant decrease across virtually all ages (ages 6-15) in surveys of life-long residents conducted three to eight years after cessation of fluoridation. These two studies raise important questions, but both have serious design flaws. First, the authors note that the reunification in Germany in 1990 led to “dramatic social transformation,” including not only cessation of water fluoridation, but also “complete change” in provision of preventive dental care and oral health services. Dental services and school dental services were largely privatized (though coverage remained comprehensive), dentist utilization increased, fissure sealants were introduced, fluoridated salt was introduced, use of fluoridated toothpastes increased from 15% to 88%, use of topical fluorides and antibiotics increased and sugar consumption decreased, all within several years (Kunzel, Fischer, Lorenz, & Bruhmann). Because the design of the 1997 study was ecological, the authors were not able to control for these important intervening factors. In the 2000 study, some of these factors were measured in individual subjects, but there was no concurrent control community, so the net impact could not be estimated. Both studies were also flawed by changes in methods of subject selection before and after cessation of fluoridation, lack of blinding, and measurement issues. The authors conclude:

“The causes for the changed caries trend were seen on the one hand in improvements in attitudes towards oral health behavior and, on the other hand, to the broader availability and application of preventive measures (F-salt, F-toothpastes, fissure sealants etc.). There is, however, still no definitive explanation for the current pattern and further analysis of future caries trends in the formerly fluoridated towns would therefore seem to be necessary” (Kunzel, Fischer, Lorenz, & Bruhmann, 2000, p. 382).

Further corroboration of this apparent phenomenon was noted in a two-community ecological before-after study of caries in 6-15 year olds conducted in Finland (Seppa, Karkkainen, & Hausen, 1998). The city of Kuopio was fluoridated (1.0 mg/L) in 1959 and discontinued the practice in 1992. The comparison town of Jyvaskyla was not fluoridated (0.1 mg/L). The percentage of children using fluoridated toothpaste was 85% in both towns. “In 1995, a decline in caries was seen in the two older age groups in this nonfluoridated town. In spite of discontinued water fluoridation, no indication of increasing trend of caries could be found in Kuopio” (Seppa et al., p. 256). However, once Kuopio stopped fluoridating there was a slower decline in caries so that by three years post-fluoridation the relative advantage of Kuopio over Jyvaskyla in terms of caries rates had disappeared. This was in spite of more frequent use of other fluoride measures, including fluoride tablets in Kuopio (Seppa, p. 261). It is important to note that Finland has comprehensive prevention-oriented dental services for all children and adolescents, and the use of fluoride toothpaste, varnishes and tablets are common.

La Salud, Cuba was fluoridated in 1973. Water fluoridation at 0.8 mg/L ceased in 1990. “Toothbrushes were scarce, F-toothpastes were not available, and the sugar consumption was high” (Kunzel & Fischer, 2000), yet, in 1997 there was a significant decrease in caries levels in the oldest age group (12 and 13 yr.
olds) and levels in the younger ages remained stable. This before-after survey had no control group so no distinction can be made between what was due to secular trends and what was due to cessation of fluoridation. Perhaps most important, a fluoride mouth rinsing program was initiated in the schools of La Salud soon after cessation of water fluoridation (Kunzel & Fischer, 2000).

A study conducted in two communities in British Columbia, a fluoridated-ended and a still fluoridated site, included both a time-series analysis and a prospective cohort analysis of 8-11 and 14-17 year old children at 1½ and 3½ years after the study community stopped fluoridating in 1992 (Maupome, Clark, Levy, & Berkowitz, 2001; Maupome, Shulman, Clark, Levy, & Berkowitz, 2001). The prevalence study found that while caries rates stayed the same in the still fluoridated community, they dropped significantly in the fluoridated-ended community over the three years. However, overall caries prevalence rates in 8 and 11 year olds were still 52% and 35% lower in the still fluoridated community in the final survey. Caries incidence rates (new cases) were also 20% lower in the still fluoridated community. This suggested that confounding by other factors might account for this unexpected drop in caries. After adjusting for socio-economic status, age, frequency of mouth washing and tooth brushing with fluoridated products, exposure to fluoride supplements and overall snacking practices, the researchers noted higher caries scores for at-risk surfaces (erupted and unsealed surfaces) in the fluoridation-ended group. The researchers also tracked progression and reversal of “white spots,” the surface lesions that lead to cavities. Comparing children/adolescents in the two communities, the odds were more than two times greater (odds ratio was 2.42, 95% confidence interval was 1.97-2.98) that an early smooth surface “white spot” would progress to a cavity in the fluoridation-ended community than in the still fluoridated community (Maupome, & Shulman, et al. 2001). The researchers noted that, together with increasing use of sealants in both communities, there appeared to be earlier and more common fillings applied in the fluoridation-ended site, and that this might account for reductions in active caries in both communities. This study demonstrates the complicated shifts in caries and caries treatment experience following cessation of fluoridation in a relatively affluent community with low baseline caries risk. Like the studies above, caries prevalence decreased over time in the fluoridation-ended site, yet in this well designed study, the researchers found that the risk of caries progression was greater once other factors were controlled for.

In spite of their respective design flaws, these five studies raise important issues: First, there are multiple factors that determine caries incidence in a community. In some contexts, community water fluoridation’s contribution to caries prevention and reversal is over-shadowed by other factors such as wide-spread use of fluoridated toothpaste combined with a high standard of living, universal access to dental care, or school-based prevention programs. When fluoridation was stopped in these contexts, mean caries levels did not increase, though individuals who did not receive enough fluoride may have suffered. Second, the act of suspending water fluoridation may provide the impetus to change personal oral health behaviors or to initiate other public oral health programs, as it did in each of these settings. These changes can prevent expected increases in caries. Third, differences in caries rates between exposed and non-exposed individuals have narrowed to the point where biases introduced by weak study designs could be large enough to mask a true difference in caries measures or demonstrate a difference when one doesn’t exist. Fourth, there may be other factors, as yet unidentified, that contributed to caries rates not increasing after stopping water fluoridation in these cities.

Perhaps the most important difference between the settings reviewed and those in Fort Collins (and the U.S. as a whole) is the lack of universal access to dental care and the lack of substantive school-based prevention programs locally (see Finding #3).

**Gaps in Knowledge**

The Task Force for Community Preventive Services summarized the gaps in knowledge regarding community water fluoridation effectiveness in their 2002 review (Truman, et al., 2002, p. 32):
• "What is the effectiveness of laws, policies, and incentives to encourage communities to start or continue water fluoridation?"
• "What is the effectiveness of community water fluoridation in reducing socioeconomic or racial and ethnic disparities in caries burden?"
• "What is the effectiveness of community water fluoridation among adults (aged ≥18 years)?"
• "What, if any, are the effects of the increasing use of bottled water and in-home water filtration?"
• "How effective is community water fluoridation in preventing root-surface caries?"

The Medical Research Council added the need for more studies designed to estimate the impact of community water fluoridation in children ages 3-15 in today’s environment of widespread use of fluoride dentifrices (MRC 2002, p. 18). In reviewing the York Study, the Medical Research Council noted that:

“The York Review concluded that water fluoridation was effective, but the authors were reluctant to estimate the likely impact in today’s environment. Therefore, to inform policy, future research-including economic evaluation-should determine the short-term impacts of water fluoridation on dental caries (i.e. within four years of implementation), though there would be advantages in extending studies to ten years and beyond in order to capture more fully the effects on the permanent dentition” (MRC, 2002, p. 19).

A member of the FTSG raised a concern that exposure to water fluoridation may delay eruption of teeth and this could account for apparent effectiveness of caries prevention in children. The FTSG was not able to find credible evidence to support this concern.

**FINDINGS: The Effectiveness of Drinking Water Fluoridation in Preventing Caries (Cavities)**

The weight of the evidence suggests that there is caries reduction in populations exposed to water fluoridation at or near an optimal level. The primary mode of action of fluoride in preventing caries (cavities) is its topical action on the surface of the teeth; systemic action from ingestion is now thought to play a minor role. This benefit amounts to a relative caries reduction of 25% and an absolute prevalence difference of 1.14 surfaces with caries in primary teeth and 0.5 surfaces with caries in permanent teeth in children according to the most recent U.S. surveys of schoolchildren. Among the four studies of caries prevention in adults, the most recent study showed that community water fluoridation reduced surfaces with caries by 0.35 surfaces per year of fluoride exposure. It appears that community water fluoridation is effective in all age groups in preventing dental caries. The benefit of drinking water fluoridation decreases as individuals in the population receive fluoride from other sources (e.g., toothpastes, dental care, etc.). Even with the limitations of some of the studies, there appears to be a net benefit in caries reduction from drinking water fluoridation over and above that from toothpaste and other sources of fluoride. Among the 14 recent studies (completed after 1985) reviewed in which water fluoridation was discontinued, nine showed an increase in caries rates. Five communities (all of them in other countries) that suspended water fluoridation did not find that caries rates increased. It is uncertain to what degree changes in oral health behaviors, introduction of new preventive programs and increased delivery of professional treatments in response to cessation of fluoridation can account for these findings. Since these studies were conducted in foreign communities in which there was socialized dental care and school-based oral health programs, their results may not apply to Fort Collins.
Reference List


Finding #2 – The Risk of Drinking Water Fluoridation

In this section, the Fluoride Technical Study Group (FTSG) summarizes the evidence from toxicologic and epidemiologic studies that addresses the potential for community water fluoridation to cause adverse health outcomes in the community. The major outcomes considered include cancer, effects on bone, dental enamel fluorosis, effects on the immune system and effects on thyroid function. While the focus of this evaluation is on potential risks from the city's practice of drinking water fluoridation at 1mg/l, the risks from total fluoride dose including other sources is also considered.

Total Exposure to Fluoride

The FTSG evaluated total consumption of fluoride from all sources so that the likelihood of health risks from fluoridation could be evaluated for the appropriate potential total dose, not just the dose from water fluoridation. The sources of fluoride intake for the U.S. population are primarily water, food, and dental products (Tables 4 and 5). Although fluoride exposure is generally greater in areas with fluoridated water than in areas with nonfluoridated or low-fluoridated water, populations in both areas are exposed to fluoride from food sources, drinking water, processed beverages and dental products. According to the US Public Health Service:

"In optimally fluoridated areas, most of the estimated daily intake of fluoride for children and adults is from drinking water, beverages and food. In low-fluoride or non-fluoridated areas, children can receive their highest proportion of daily intake from fluoride supplements and dentifrice[see Table 3]. The daily intake of most adults is about equally divided among food, drinking water, beverages, and mouthrinses [see Table 4 below]." (Committee to Coordinate Environmental Health and Related Programs, USPHS [USPHS], 1991, p. 15).

Dietary sources of fluoride (other than drinking water) are outlined in Table 1.

Table 1

<table>
<thead>
<tr>
<th>Foods (Note A)</th>
<th>Mean (mg/L or Kg)</th>
<th>Standard Deviation</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dairy Products</td>
<td>0.25</td>
<td>0.38</td>
<td>0.02 - 0.82</td>
</tr>
<tr>
<td>Meat Fish &amp; Poultry</td>
<td>0.22</td>
<td>0.15</td>
<td>0.04 - 0.51</td>
</tr>
<tr>
<td>Grain &amp; Cereal Products</td>
<td>0.42</td>
<td>0.40</td>
<td>0.08 - 2.01</td>
</tr>
<tr>
<td>Potatoes</td>
<td>0.49</td>
<td>0.26</td>
<td>0.21 - 0.84</td>
</tr>
<tr>
<td>Leafy Vegetables</td>
<td>0.27</td>
<td>0.25</td>
<td>0.21 - 0.84</td>
</tr>
<tr>
<td>Legumes</td>
<td>0.53</td>
<td>0.05</td>
<td>0.49 - 0.57</td>
</tr>
<tr>
<td>Root Vegetables</td>
<td>0.38</td>
<td>0.11</td>
<td>0.27 - 0.48</td>
</tr>
<tr>
<td>Fruits</td>
<td>0.06</td>
<td>0.03</td>
<td>0.02 - 0.08</td>
</tr>
<tr>
<td>Oils &amp; Fats</td>
<td>0.25</td>
<td>0.15</td>
<td>0.02 - 0.44</td>
</tr>
<tr>
<td>Sugar and Adjuncts</td>
<td>0.28</td>
<td>0.27</td>
<td>0.02 - 0.78</td>
</tr>
<tr>
<td>Nonclassifiable Foods</td>
<td>0.59</td>
<td>0.19</td>
<td>0.29 - 0.87</td>
</tr>
</tbody>
</table>

Note: The foods were ready to eat or prepared for eating. When preparation required the use of water (e.g. preparing juice from concentrate or boiling vegetables), the local water was used which contained 1 mg/L (1 ppm) of fluoride. Nonclassifiable foods included certain soups and puddings, among other items.

Most foods have fluoride concentrations below 0.5 mg/liter or kg (Dabeka & Mckenzie, 1995). Among beverages the highest amounts of fluoride are reported in teas. Due to the ability of tea leaves to
concentrate fluoride, brewed tea contains fluoride ranging from 1 to 6 mg/liter depending on amount, brewing time and fluoride concentration in water (USPHS, 2000, p. 294).

Intake from fluoridated dental products sometimes exceeds that from diet, particularly in young children who swallow toothpaste due to poor control of the swallowing reflex. An average of about 0.3 mg of fluoride is introduced with each brushing in young children (USPHS, 2000, p. 296). In communities with low levels of fluoride in the water supply, oral fluoride supplements are recommended by the American Academy of Pediatrics, American Dental Association, and the American Academy of Family Physicians. Table 2 shows the 1995 recommended supplement endorsed by these associations. No supplement is recommended for children under six months of age.

Table 2
**Recommended Fluoride Supplementation (mg/day) for Children of Different Ages at Different Drinking Water Fluoride Concentrations**

<table>
<thead>
<tr>
<th>Drinking Water Fluoride Concentration</th>
<th>Child Age 0 to 6 Months</th>
<th>Child Age 6 to 36 Months</th>
<th>Child Age 3 to 6 Years</th>
<th>Child Age 6 to 10 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.3 ppm</td>
<td>Not recommended</td>
<td>0.25 mg/day</td>
<td>0.5 mg/day</td>
<td>1.0 mg/day</td>
</tr>
<tr>
<td>0.3-0.6 ppm</td>
<td>Not recommended</td>
<td>Not recommended</td>
<td>0.25 mg/day</td>
<td>0.5 mg/day</td>
</tr>
<tr>
<td>&gt;0.6 ppm</td>
<td>Not recommended</td>
<td>Not recommended</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>

**Reference**

According to the Institute of Medicine:

“Based on the 1986 National Health Interview Survey (NHIS) data, it is estimated that 15 percent of children in the United States up to age 5 years and 8 percent of children 5 to 17 years old use dietary fluoride supplements. Fluoride supplements are rarely prescribed for adults” (Committee on the Scientific Evaluation of Dietary Reference Intakes, Institute of Medicine [IOM], 2000, p. 295).

Tables 3 and 4 illustrate the ranges of fluoride intake (mg/day) for children and adults from all sources in areas with water fluoridated at three different levels, including 1 mg/L fluoride. The ranges presented are estimated total intakes extrapolated from published studies and are not derived from data measured in individuals. The maximum values are derived by summing the highest intakes reported in published literature for each type of ingested fluoride source. The estimates also assume that adults in both optimally fluoridated and non-fluoridated areas use fluoride mouth-rinse twice daily.
### Table 3
*Estimated Daily Fluoride Intake of Child Weighing 20kg (44 lbs)*
(adapted from USPHS, 1991, Table 10, p. 16)

<table>
<thead>
<tr>
<th>Fluoride in Water (mg/L)</th>
<th>Intake from Food in mg/kg/day</th>
<th>Fl Containing Beverages in mg/kg/day</th>
<th>Fluoride Dentifrices in mg/kg/day</th>
<th>F Supplements in mg/kg/day</th>
<th>Estimated Total Intake in mg/kg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.3</td>
<td>0.15-0.3 (0.007-0.015)</td>
<td>0.1-0.3 (0.005-0.015)</td>
<td>0.2-1.2 (0.01-0.06)</td>
<td>0.50 (0.025)</td>
<td>0.95-2.3 (0.047-0.115)</td>
</tr>
<tr>
<td>0.7-1.2</td>
<td>0.4-0.6 [0.02-0.03]</td>
<td>0.3-1.8 [0.015-0.09]</td>
<td>0.2-1.2 [0.01-0.06]</td>
<td>Not recommended</td>
<td>0.9-3.6 [0.045-0.18]</td>
</tr>
<tr>
<td>&gt;2.0</td>
<td>1.0-2.0 [0.05-0.10]</td>
<td>0.6-3.0 [0.03-0.15]</td>
<td>0.2-1.2 [0.01-0.06]</td>
<td>Not recommended</td>
<td>1.8-6.2 [0.09-0.31]</td>
</tr>
</tbody>
</table>

*a Calculations based on child weighing 20 kg (44 lbs)
*b Based on ranges of data extrapolated from various literature sources by PHS.
*c Assumed that dentifrice used twice daily
*d Assumed that dental fluoride supplement taken daily

### Table 4
*Estimated Daily Fluoride Intake of Adult Weighing 50 kg (110 lbs)*
(adapted from USPHS, Table 11, p. 17)

<table>
<thead>
<tr>
<th>Fluoride in Water (mg/L)</th>
<th>Intake from Food in mg/kg/day</th>
<th>Fl Containing Beverages in mg/kg/day</th>
<th>Fluoride Dentifrices in mg/kg/day</th>
<th>F Mouthrinses in mg/kg/day</th>
<th>Estimated Total Intake in mg/kg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.3</td>
<td>0.2-0.8 (0.004-0.016)</td>
<td>0.1-0.7 (0.002-0.014)</td>
<td>0.018-0.145 (0.0004-0.003)</td>
<td>0.56 (.010)</td>
<td>0.88-2.20 (0.016-0.40)</td>
</tr>
<tr>
<td>0.7-1.2</td>
<td>0.4-2.7 [0.008-0.54]</td>
<td>0.6-3.2 [0.012-0.064]</td>
<td>0.018-0.145 [0.0004-0.003]</td>
<td>0.56 [0.01]</td>
<td>.58-6.6 [0.03-0.13]</td>
</tr>
<tr>
<td>&gt;2.0</td>
<td>1.2-3.4 [0.02-0.07]</td>
<td>0.9-3.5 [0.018-0.07]</td>
<td>0.018-0.145 [0.0004-0.003]</td>
<td>Not recommended</td>
<td>2.1-7.05 [0.04-0.14]</td>
</tr>
</tbody>
</table>

*a Calculations based on adult weighing 50 kg (110 lbs)
*b Based on ranges of data extrapolated from various literature sources by PHS.
*c Assumed that dentifrice and mouth-rinse are used twice daily

According to the Institute of Medicine:

“Ten independent U.S. and Canadian studies published from 1958 to 1987 have shown that dietary fluoride intakes by adults range from 1.4 to 3.4 mg/day in areas where the water fluoride concentration was 1.0 mg/liter. In areas where the water fluoride concentration was less than 0.3 mg/liter, the daily intakes ranged from 0.3 to 1.0 mg/liter day” (IOM, 2000, p. 293).
Table 5 shows the *average* total daily intake of fluoride by age.

### Table 5

**Average Intake of Dietary Fluoride by Age**

(Whitford, 1994, p. 6)

<table>
<thead>
<tr>
<th>Age</th>
<th>Mg F/Day</th>
<th>Mg F/Kg/Day</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-6 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast-fed</td>
<td>&lt;0.01</td>
<td>&lt;0.003</td>
<td>Ekstrand et al., 1984</td>
</tr>
<tr>
<td>Formula-fed:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ready-to-feed</td>
<td>&lt;0.4</td>
<td>&lt;0.13</td>
<td>Johnson and Bawden, 1987</td>
</tr>
<tr>
<td>Reconstituted</td>
<td>ca. 1.0</td>
<td>&lt;0.30</td>
<td>McKnight-Hanes et al., 1988</td>
</tr>
<tr>
<td>6 months</td>
<td>0.2-0.5</td>
<td>0.03-0.07</td>
<td>Ophaug et al., 1980a</td>
</tr>
<tr>
<td>2 years</td>
<td>0.3-0.66</td>
<td>0.02-0.05</td>
<td>Ophaug et al., 1980b</td>
</tr>
<tr>
<td>Adult</td>
<td>1.2</td>
<td>0.016-0.022c</td>
<td>Singer et al., 1980</td>
</tr>
<tr>
<td></td>
<td>1.8</td>
<td>0.023-0.033c</td>
<td>Taves, 1983</td>
</tr>
<tr>
<td></td>
<td>2.2</td>
<td>0.029-0.040c</td>
<td>SanFilippo &amp; Battisonte, 1971</td>
</tr>
</tbody>
</table>

* Reconstituted with water fluoridated at 1 ppm.
* Lower value is for nonfluoridated water. Higher value is for optimally fluoridated water.
* Range calculated for persons with body weights of 75 kg and 55 kg whose drinking water is optimally fluoridated.

Dietary reference intakes established by the Institute of Medicine (IOM, 2000) include adequate intake levels set for all children and adults at 0.05 mg/kg/day. For infants newborn to six-months old the recommended amount (based on the amount found in breast milk) is 0.01 mg/day. The upper limit set to protect against moderate dental fluorosis is 0.1 mg/kg/day for all ages. This upper limit of 0.7 mg/day, assuming a seven kg infant weight, can be exceeded in optimally fluoridated water communities when water of 1.0 mg/l of fluoride is used to make reconstituted formula and fed to infants less than six months old. The upper limit set for infants 7 to 12 months is 0.9 mg/day. The Institute of Medicine set the upper limits for children age 1 to 3 at 1.3 mg/day and age four to eight at 2.2 mg/day based on reference weights of 13 kg and 22 kg respectively.

The FTSG noted that for children six months to six years, total fluoride consumption from food and beverages nearly equals the recommended adequate intake levels of 0.05 mg/kg/day. If excess water or beverages are consumed or fluoridated toothpaste is inappropriately eaten, fluoride levels may exceed the 0.1 mg/kg/day upper limit standard and may cause dental fluorosis. Repeated over-ingestion during the formative years of tooth development (three months to six years) may result in varying degrees of dental fluorosis on a dose-dependent scale. After age six to seven, all anterior (front) teeth have completed their enamel formation, and after age eight, all but the wisdom teeth crowns are formed. The risk of moderate dental fluorosis is low because of the low likelihood of exposures at the extremes of the range presented in Table 3. The estimated upper range of the total intakes in Table 3 exceeds the values set by the Institute of Medicine to be protective of moderate dental fluorosis. The upper limit established for children older than 8 years and adults is 10 mg/day. This level is not exceeded at optimal levels of water fluoridation.

Several regulatory bodies have determined thresholds for safe daily intake of fluoride based on potential adverse effects (tooth or bone effects). The Agency for Toxic Substances and Disease Registry (ATSDR) has set a chronic Minimal Risk Level (MRL) for ingestion of fluoride at 0.05 mg/kg/day (ATSDR: [http://www.atsdr.cdc.gov/mrls.html](http://www.atsdr.cdc.gov/mrls.html)). The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse non-cancer health effects over
Fluoride Exposure Uncertainties

The gaps in knowledge regarding total fluoride exposure from all sources are captured in the following summaries:

In the “Tier One” literature, the Medical Research Council of Great Britain noted several uncertainties with regard to total fluoride exposure estimates and the impacts of total exposure uncertainties on health effects assessments cited as follows:

“As previously recounted, developments since 1960 have altered the general pattern of fluoride exposure and may have created a new situation in the population at large, both with respect to total exposure and the main sources of exposure. There are therefore several deficiencies in the existing body of evidence when evaluating effects relating to fluoride exposure, and other questions that need to be addressed: The effects of fluorides are probably related to total exposure, not just fluoride in drinking water. There are very few data relating total fluoride exposure to health effects” (Medical Research Council [MRC], 2002, p. 14).

In general, the absorption of fluoride ion into the body (called “bioavailability”) is high, however it depends to a certain extent on the nature of the vehicle it is ingested with. According to the Institute of Medicine’s Dietary Reference Intake Guide, “If it is ingested with milk, baby formula, or foods, especially those with high concentrations of calcium or certain other divalent or trivalent ions that form insoluble compounds, absorption may be reduced by 10-25%” (IOM, 2000, p.291).

The Medical Research Council of Great Britain recommends the following:

“New studies are required to investigate the bioavailability and absorption of fluoride from naturally fluoridated and artificially fluoridated drinking water, looking also at the impact of water hardness. This is particularly important because if the bioavailability is the same, many of the findings relating to natural fluoride can also be related to artificial fluoridation.

Further attempts should be made to calculate lifetime intakes of fluoride, using both urinary and ingestion data, and to determine the relative contribution of fluoride in artificially fluoridated water to total fluoride uptake. If the bioavailability of artificial and natural fluoride are found to be the same, then studies on people who have lived in naturally high fluoride areas could be informative” (MRC, 2002, p. 15).

Other observations have appeared in the peer-reviewed literature and in the summaries of review panels.

“Investigators seeking to examine possible relations between fluoride intake and biological effects or health outcomes, such as dental fluorosis or the quality of bone or its strength, need to be aware of the complex situation that exists today. It is no longer feasible to estimate with reasonable accuracy the level of fluoride exposure based simply on the concentration of the ion in the drinking water” (Whitford, 1994, pp. 7-8).

“There was considerable concern amongst many Taskforce members that water fluoridation could increase the total intake of fluoride in excess of a safe level for babies and young children. The evidence relating to what constituted a safe or a toxic dose of fluoride was uncertain and confusing.
A majority of Taskforce members were concerned that the margin of safety between a safe and toxic dose may not be sufficiently wide” (The Lord Mayor’s Taskforce on Fluoridation, 1997, p. 89)

**FINDINGS: Total Fluoride Exposure**

Total fluoride exposure must be considered when evaluating health effects. The amount of total fluoride ingested will vary between individuals and is not precisely known. The FTSG review of the literature finds that likely total exposure values for children older than six months living in communities with water fluoridated at up to 1.2 mg/L (ppm) do not exceed the upper limit set to be protective of moderate dental fluorosis by the Institute of Medicine. Total dietary exposures of fluoride can exceed this threshold amount (0.7mg/day) in infants fed formula reconstituted with optimally fluoridated water.

**Review of Potential Adverse Health Effects**

Our review of the literature, consistent with community input, indicates that there are four major potential health concerns associated with long-term exposure to fluoride: cancer, bone fractures, skeletal fluorosis and dental enamel fluorosis, and several other conditions for which a much more limited literature database is available. In this section, we present a summary of the evidence on the likelihood of specific health risks from drinking water fluoridation. We also include more comprehensive documentation of the literature reviewed in Appendix 2 to this report.

As described in more detail in the introduction, the FTSG reviewed the toxicological and epidemiological studies for each of these outcomes as independent lines of evidence. The group considered the weight of evidence findings as stronger when the toxicological and epidemiological studies were in agreement. The weight of evidence conclusions are more uncertain when these two independent lines of evidence disagree with regard to the likelihood of health risks from water fluoridation.

**Cancer**

**Animal Toxicological Studies**

There have been two major, recent animal studies that explored the possibility that long-term exposure to fluoride causes cancer. These studies have been examined by a number of federal agencies and their interpretations and conclusions of these data are provided below. The first animal toxicology study, conducted by the National Toxicology Program (NTP), administered fluoride at concentrations of up to 175 mg/L of drinking water [approximately 79 times the concentration in Fort Collins water]. “Although the results were negative for male and female mice and female rats, there was some evidence of a dose-related increase in the incidence of osteosarcomas in male rats” (National Research Council [NRC], 1993, p. 10).

The Agency for Toxic Substances and Disease Registry of the U.S. Public Health Service (ATSDR) summarized the NTP study as follows:

“Based on the finding of a rare tumor in a tissue known to accumulate fluoride, but not at the usual site for chemically-associated osteosarcomas, a weakly significant dose-related trend, and the lack of supporting data in female rats and mice of either gender, the NTP concluded that there was ‘equivocal evidence of carcinogenic activity of sodium fluoride in male F344/N rats.’ NTP defined equivocal evidence of carcinogenic activity to be a situation where the results show ‘a marginal increase in neoplasms that may be chemically related.’ NTP further concluded that there
was no evidence that fluoride was carcinogenic at doses up to 4.73 mg/kg/day\(^1\) in female N344/N rats, or at doses up to 17.8 and 19.9 mg/kg/day in male and female B6C3F\(_1\) mice, respectively” (Agency for Toxic Substances and Disease Registry [ATSDR], 2001, p. 100).

A second study, sponsored by Proctor and Gamble examined carcinogenic potential of sodium fluoride administered in feed to Sprague-Dawley rats and CD-1 mice. The data from the Procter and Gamble Study were reviewed by the Carcinogenicity Assessment Committee, Center for Drug Evaluation and Research, Food and Drug Administration (CAC/CDER/FDA) who reported that statistical analysis of the incidence of bone tumors found no dose-response relationship and that:

“...the CAC review concluded that there were flaws and uncertainties in the studies that keep them from providing strongly reassuring data. However, the committee concluded that the study results reaffirm the negative finding of the NTP study in female rats, and do not reinforce equivocal findings in male rats” (as cited by ATSDR, 2001, p. 101).

However, these results were not confirmed by:

“...a ...study conducted by Procter & Gamble, in which fluoride was administered in the diet at doses higher than those in the NTP study. The Procter & Gamble study did produce a significant dose-related increase in the incidence of osteomas (benign bone tumors) in male and female mice. However, these lesions were not considered to be neoplastic and, in any event, have no known counterpart in human pathology” (NRC, 1993, p. 10-11).

Subsequently, the data from both of these toxicology studies were reviewed by the National Research Council and a U.S. Public Health Service committee. The National Research Council subcommittee concluded, “the available laboratory data are insufficient to demonstrate carcinogenic effects of fluoride in animals” (NRC, 1993, p. 11).

Similarly, the U.S. Public Health Service committee concluded:

“...When the NTP and the Proctor and Gamble studies are combined, there is a total of eight individual sex/species groups examined. Seven of these groups showed no significant evidence of malignant tumor formation. One of these groups, male rats from the NTP study, showed “equivocal” evidence of carcinogenicity, which is defined by NTP as a marginal increase in neoplasms – i.e. osteosarcomas – that may be chemically related. Taken together, the two animal studies available at this time fail to establish an association between fluoride and cancer” (USPHS, 1991, p. 76).

**Human Epidemiological Studies**

The potential for an association between human cancer and exposure to fluoridated water has also been explored in many epidemiologic studies and summarized in reviews conducted by the Agency for Toxic Substances and Disease Registry, U.S. Public Health Service, the World Health Organization, the National Research Council, National Academy of Science, the U.S. Public Health Service, and the Medical Research Council of Great Britain. Relevant citations from the texts of these reviews follow; a fuller description of each is found in Appendix 2.

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\(^1\) As typically practiced in animal toxicology studies these doses are about 100-400 times the average dose in humans in fluoridated communities. The 4.73 mg/kg/day dose is approximately equivalent to an average adult in Fort Collins drinking about 100 gallons of water per day for a lifetime.
The Agency for Toxic Substances and Disease Registry, U.S. Public Health Service (ATSDR) summarized the epidemiological studies of human cancer as follows:

“Numerous epidemiological studies have examined the issue of a connection between fluoridated water and cancer. The weight of evidence indicates that no such connection exists. However, all of the investigations were ecologic studies, and the sensitivity limit of even the most sensitive analysis in these studies appears to be a 10-20% increase in risk” (ATSDR, 2001, p. 96).

A large epidemiological study conducted by the National Cancer Institute was summarized by ATSDR as follows:

“An epidemiological study (Hoover et al. 1991) examined >2,300,000 cancer deaths and 125,000 cancer cases in U.S. counties exposed to artificially fluoridated drinking water for up to 35 years. Taking into account the results of the NTP study… detailed analyses were conducted of cancers of the joints and bones (especially osteosarcomas), and cancers of the oral cavity and pharynx. The statistical evaluation was based on analysis of time trends in the observed/expected (O/E) ratios relative to duration of fluoridation. While elevated O/E were observed for osteosarcomas in males, the O/E ratio was inversely related to duration of fluoridation. Thorough analyses of incidences of oral cancers and cancers at a variety of other sites were conducted by means of very sensitive statistical tests that were designed to detect changes as small as 10-20%. No consistent correlation between cancer incidence or mortality and duration of fluoridation was found. An addendum to the report noted that the age-adjusted national incidence of osteosarcomas increased by 18% in males for the years 1973-80 and 1981-87; most of the increase was due to a 53% increase in males under 20 years of age, and there was a larger increase in fluoridated than nonfluoridated areas. A similar time-trend analysis to that done in the main report found no correlation between the cancer incidence O/E ratio and duration of fluoridation. Additional analyses also failed to find a relationship between osteosarcoma incidence in males and exposure to water fluoridation” (ATSDR, 2001, p. 98).

The National Research Council (National Academy of Sciences) examined the epidemiologic studies of cancer and exposure to fluoridated drinking water and came to the following conclusion:

“More than 50 epidemiological studies have examined the relation between fluoride concentrations in drinking water and human cancer. Most studies compared geographic or temporal patterns of cancer occurrences with distributions of fluoride in drinking water. These studies provide no credible evidence for an association between fluoride in drinking water and the risk of cancer” (NRC, 1993, p. 10).

The National Research Council Committee concluded that “the weight of the evidence from the epidemiological studies completed to date does not support the hypothesis of an association between fluoride exposure and increased cancer risk in humans” (NRC, 1993, p. 11).

A committee appointed by the U.S. Public Health Service to review the risks and benefits of fluoride summarized their findings regarding potential cancer risk as follows:

“The ad hoc subcommittee of the Committee to Coordinate Environmental Health and Related Programs reviewed the results from numerous epidemiologic studies of the relation between exposure to fluoridated water and cancer that have been conducted during the last 40 years. In addition to the review of these studies, the Subcommittee reviewed the findings of a recent study from the National Cancer Institute (NCI), which updated and expanded an earlier county-specific analysis for cancer mortality in the United States in relation to water fluoridation…. Both this report and reports from previous international expert panels which have reviewed earlier data concluded that there is no credible evidence of any association between the risk of cancer and
Several international bodies have also examined the potential for cancer risk from consumption of fluoridated water. The NHS Center at the University of York in Great Britain review (2000) included 26 studies of the association of water fluoridation and cancer, 21 of these studies were from the lowest level of evidence, level C, with the highest risk of bias, and five from level B. Among the 10 studies that examined the relationship between fluoride exposure and all-cause cancer incidence and mortality, only two studies found a statistically significant association: one found a mixed effect with more cancer in two of eight subgroups, while the other found a significant protective effect (fewer cancers) in persons exposed to drinking water fluoride. The possible relationship between fluoride exposure and cancers of bone is of particular interest because fluoride accumulates in bone. Contained in the four studies meeting the inclusion criteria established by the NHS in which the association between water fluoride exposure and bone related cancer was examined, there were eight analyses. Four analyses found the direction of association to be positive (fewer bone cancers in those exposed to fluoride) and three found the direction to be negative (more cancers in those exposed to fluoride). Similarly, among the 12 analyses of the association between water fluoride exposure and osteosarcoma (a rare tumor derived from bone producing cells called osteoblasts), seven found fewer tumor cases; three found more tumor cases and two found no association. Only one study found a statistically significant association between fluoridation and either bone related cancer or osteosarcoma. This study found an increased prevalence of osteosarcoma in males but not females. This study however, also had the lowest validity score (NHS Centre for Reviews and Dissemination, University of York [NHS], 2000, pp. 54-57). The NHS reviewers concluded:

“There is no clear association between water fluoridation and overall cancer incidence and mortality. This was also true for osteosarcoma and bone/joint cancers. Only two studies considered thyroid cancer and neither found a statistically significant association with water fluoridation. Overall, no clear association between water fluoridation and incidence or mortality of bone cancers, thyroid cancer or all cancers was found” (NHS, 2000, p. xiii).

In the most recent of these reviews, the Medical Research Council of Great Britain examined an earlier analysis by the University of York (the NHS review discussed above) as well as earlier studies and reviews. The Medical Research Council concluded:

“The evidence available does not suggest that fluoridation of water increases the risk for cancer in general or for any particular type of cancer, including osteosarcoma. Neither the York Review nor other reviews have calculated a pooled estimate of effect; therefore it is difficult to estimate the maximum increase in risk, which is compatible with the available data. For osteosarcoma, the three small case-control studies cannot exclude an increase in risk of the order of twofold for exposure to fluoridated water, but an increase as large as this is not compatible with the ecological data, in particular those analyzed by Hoover et al. (1991). In conclusion, although a small increase in cancer risk cannot be excluded, the data do not suggest any increase in risk and in view of the type of data available it does not seem appropriate to estimate the number of cases of cancer that might be caused by fluoridation” (MRC, 2002, p. 30).

Fluoride Carcinogenicity Uncertainties
The previously discussed animal toxicological studies were equivocal. To address the uncertainty that these studies raise, the National Research Council recommended:

“…conducting one or more carefully designed analytical epidemiological (case-control or cohort) studies to more fully evaluate the relation between fluoride exposure and cancer, especially osteosarcomas, at various sites, including bones and joints. In conducting such studies, it is
important that individual exposure to fluoride from all sources be determined as accurately as possible” (NRC, 1993, p. 11).

The NHS, University of York review of human epidemiological studies regarding water fluoridation and osteosarcoma showed that the studies had weak designs and showed mixed results. The National Research Council concluded that current evidence is not sufficient to rule out a small risk of increased cancer:

“The existence of such an extensive epidemiological database on fluoride with no consistent evidence of carcinogenic effects suggests that, if there is any increase in cancer risk due to exposure to fluoride, it is likely to be small. However, most of these studies used geographic and temporal comparisons of cancer rates and hence are of limited sensitivity. Further analytical studies with accurate information on individual fluoride exposures and disease diagnoses are therefore desirable” (NRC, 1993, p. 10).

The Medical Research Council of Great Britain noted:

“The majority of information, therefore, relates to whether exposure to artificially fluoridated water for up to about 30 years may alter cancer rates, with some data for up to 35 years…. In view of this, there is a need to continue to monitor cancer rates in artificially fluoridated populations for at least 70 years after fluoridation was introduced. However, it should also be noted that studies of populations using water with naturally high fluoride levels, to which the people would have been exposed throughout their life, have not given any indication of an increase in cancer risk” (MRC, 2002 pp. 30-31).

**FINDINGS: Cancer**

Although a small increase in cancer risk cannot be excluded, there is no consistent evidence from human or animal studies that exposure to optimally fluoridated drinking water and other sources of fluoride causes any form of cancer in humans, including bone and joint cancer. The agreement between the epidemiological and toxicological literature reduces the uncertainty associated with any one line of evidence finding. Additional research is needed to address the remaining uncertainty whether community water fluoridation may cause cancer in humans following long-term exposures of greater than 40 years.

**Bone Fractures and Osteoporosis**

Two types of studies have been used to examine the possible association between bone fracture and exposure to fluoride. In the first type, clinical trials have been designed to evaluate the efficacy of fluoride in reducing fracture risk in persons with osteoporosis, a condition common in post-menopausal women in which decreased bone density can lead to fractures, especially of the spine, hip and wrist. Because fluoride increases bone density, it has been hypothesized that it might be effective as a treatment for osteoporosis. Fluoride doses in earlier studies (30-80 mg F-ion/day) were typically an order of magnitude higher than the usual exposure from drinking optimally fluoridated water. Lower levels of fluoride (9-23 mg F-ion/day that are about 4 to 10 times the average dose from dietary sources in a fluoridated community) and sustained release preparations have been used more recently. A systematic review and meta-analysis of these clinical trials was published in 2000 by researchers at the University of Ottawa (Haguenauer, Welch, Shea, Tugwell, & Wells, 2001). As summarized by the Agency for Toxic Substance and Disease Research:

“Haguenauer et al. (2000) performed a meta-analysis to examine the effects of fluoride on the treatment and prevention of post-menopausal osteoporosis using the data from the Riggs et al. (1990, 1994), Kleerekoper et al. (1991) and 10 other studies. The meta-analysis showed a significant increase in bone mineral density in the lumbar spine and hip and a decrease in bone
mineral density in the forearm after 2 or 4 years of fluoride treatment. When the data from all studies was used, fluoride treatment for 2 or 4 years did not affect the relative risk of vertebral fractures. However, studies in which the subjects were exposed to low levels of fluoride or a slow-release formulation for 4 years, a significant decrease in vertebral fracture relative risk was seen. An increase in the relative risk of nonvertebral fractures was observed when data from all studies were used; no effect was seen in studies using low levels of fluoride (<30mg/day) or slow-release fluoride” (ATSDR, 2001, p.87).

The second type of study compares fracture rates among persons or populations exposed to fluoridated and to nonfluoridated water supplies. A summary of the evidence from five “Tier One” sources (Agency for Toxic Substances and Disease Registry, NHS University of York, National Research Council, U.S. Public Health Service and the World Health Organization) follows.

The Agency for Toxic Substances and Disease Registry, stated:

“Numerous studies have examined the possible relationship between exposure to fluoride in drinking water and the risk of bone fractures. Many of these studies are ecological studies that examined communities with high level of fluoride in the water or fluoridated water” (ATSDR, 2001, p. 83).

Several prospective and retrospective studies also examined the possible association:

“These studies have found conflicting results, with studies finding a higher or lower incidence of hip fractures or no differences in hip fracture between humans exposed to fluoride in drinking water. Several studies have found decreases in hip fracture incidences in communities with fluoride in the drinking water, suggesting that there may be a beneficial effect” (ATSDR, 2001, p. 83).

The NHS Centre for Reviews at the University of York included 29 epidemiologic studies in a systematic review. Most of these studies were not statistically significant in either direction. “The statistically significant studies were evenly distributed, five indicating an increased risk of fracture and four indicating a decreased risk” (NHS, 2000, p. 53).

The National Research Council reviewed the evidence regarding fluoride exposure and risk of bone fracture:

“Of the six epidemiological studies that used geographic comparisons (where no actual intake data were available), four found a weak association between fluoride in drinking water and a small increase in the risk of hip (or other bone) fracture…and the other showed no difference in fracture risk in women who drank fluoridated or nonfluoridated water” (NRC, 1993, p. 60).

They concluded:

“In view of the conflicting results and limitations of the current data base of fluoride and the risk of hip fractures and other fractures, there is no basis at this time to recommend that EPA lower the current maximum contaminant level (MCL) of fluoride of 4 mg/L” (NRC, 1993, p. 61).

The U.S. Public Health Service reviewed the evidence that fluoride in drinking water was associated with either an increase or a decrease in bone fractures. They concluded:

“Although some epidemiologic studies have suggested that the incidence of certain types of bone fractures may be higher in some communities with either naturally high or adjusted fluoride levels, other studies have not detected increased incidence of bone fractures. However, a variety of potentially confounding factors must be examined to assess whether there is an association between exposure to fluoride and bone fractures” (USPHS, 1991, Executive Summary, p. 5 ).
The World Health Organization (1994) reached a similar conclusion:

“Several recent epidemiological studies of long-term exposure to fluoride in drinking-water at optimal levels for caries prevention have reached conclusions implicating fluoride as the causative factor in the increasing incidence of hip fractures in the elderly, owing to increased brittleness of the cortical bone plates. However, independent reviews of these contemporary studies conclude that they fail to establish an adequate basis for concluding that fluoride levels in drinking water are related to hip fractures and bone health (Gordon et al. 1992). Most of the studies have important limitations that restrict generalization of their results either to the population as a whole or to determining risks for individuals. Therefore no basis exists for altering current public health policy on the use of fluorides for caries prevention” (World Health Organization [WHO], 1994, p. 11).

**Bone Effects Uncertainties**

The uncertainty regarding the risk of bone fracture from community water fluoridation is evidenced by the summary of 29 studies reviewed by the NHS at the University of York that found 14 studies (five statistically significant) with decreased hip fractures among those living in fluoridated communities, 13 studies (four statistically significant) with increased rates of hip fractures, and three additional studies finding no association. Results of studies of other bone fractures sites were also mixed. The reviewers rated all but one of the included bone studies as having “low” validity and one as yielding “moderate” validity (NHS, 2000, p. 48). Studies of this type that compare the incidence of bone fracture across communities are subject to confounding from a number of sources as described above, including calcium levels in the water, total calcium and vitamin D intake, use of exogenous estrogens among women and individual fluoride intake.

The Medical Research Council of Great Britain identified an additional uncertainty:

“A broader consideration of the epidemiological evidence on fluoride and bone health suggests that it is of higher quality than the York Review indicates. At this stage, perhaps the most important gap in knowledge concerns the bioavailability of fluoride from different dietary sources, and in particular the influence, if any, of calcium on uptake of fluoride from drinking water ... If fluoride were shown to be much less completely absorbed from hard than soft water, the absence of an increased risk of fracture in some published studies would be less reassuring” (MRC, 2002, p. 28).

The National Research Council called for more studies of fractures that use information from individuals rather than populations.

“In these studies, it is important that individual information be collected about fluoride intake from drinking water and from all other sources, reproductive history, past and current hormonal status, intake of dietary and supplemental calcium and other cations, bone density and other factors that might influence risk of fracture” (NRC, 1993, p. 61).

Regarding research recommendations on bone effects other than fractures, the Medical Research Council of Great Britain concluded:

“There are also gaps in the evidence base on bone disorders other than fractures, only a few epidemiological studies having attempted to assess risks for any of these diseases directly. However, the gaps could only be regarded as important if there were good reasons to suspect an effect of fluoridation from out knowledge of biochemistry and toxicology” (MRC, 2002, p. 28).
FINDINGS: Bone Effects

The FTSG agrees with the conclusion of The Medical Research Council of Great Britain that states, “The possibility of an effect on the risk of hip fracture is the most important in public health terms. The available evidence on this suggests no effect, but cannot rule out the possibility of a small percentage change (either an increase or a decrease) in hip fractures” (Medical Research Council, 2002, p. 3).

Skeletal Fluorosis

When ingested in large doses for an extended period of time, fluoride results in thickened bones and exostoses (skeletal fluorosis). According to the Agency for Toxic Substances and Disease Registry:

“Signs of skeletal fluorosis range from increased bone density to severe deformity, known as crippling skeletal fluorosis…. Reported cases are found almost exclusively in developing countries, particularly India, and are associated with malnutrition (Pandit et al. 1940). Tea consumption and high water intake due to tropical climate are probably also contributing factors…. It is generally stated that a dose of 20-80 mg/day (equivalent to 10 to 40 ppm in the water) is necessary for the development of crippling skeletal fluorosis (NAS 1971a), but individual variation, variation in nutritional status, and the difficulty of determining water fluoride levels in such situations make it difficult to determine the critical dose.

A study of 116 people who had lived in an area with an average of 8 ppm fluoride in the drinking water for at least 15 years found a 10-15% incidence of fluoride-related bone changes (Leone et al. 1995). Coarsened trabeculation and thickened bone were observed, but no exostoses were evident, and the subjects were asymptomatic” (ATSDR, 2001, p. 82).

Approximately 50% of ingested fluoride is excreted by the kidneys within 24 hours, a small amount is stored in the teeth, and the rest is mainly deposited in the skeleton (The Lord Mayor’s Taskforce on Fluoridation, 1997, p. 51). Over time, excessive levels of fluoride can produce abnormalities in bone, if dose and duration are great enough. As shown in Table 6, these abnormalities become detectable on x-rays, and rarely can result in a clinical syndrome of skeletal fluorosis). Table 6 shows the pre-clinical (asymptomatic) and clinical stages of skeletal fluorosis along with the most common symptoms. The amount of fluoride accumulation in the bone tissue of subjects in each stage is also given. One study found a linear relationship between the concentration of fluoride in bone at autopsy in adult humans and the concentration of fluoride in their drinking water (ranging from 0.1 to 4 ppm). “Average fluoride levels in the iliac crest bone ash in people with drinking water fluoride levels of ≤0.3, 1 and 4 ppm were 700, 2,300, and 6,900 ppm, respectively” (ATSDR, 2001, p. 123, citing Zipkin et al. 1958).
Table 6

Preclinical and Clinical Stages of Human Skeletal Fluorosis and Correlation to Bone Ash Fluoride Concentration
(adapted from Table 23, USPHS 1991, p. 46)

<table>
<thead>
<tr>
<th>Osteosclerotic Phase</th>
<th>Ash Concentration&lt;sup&gt;1&lt;/sup&gt; (mg F/Kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Bone</td>
<td>500-1,000</td>
</tr>
<tr>
<td>Preclinical Phase</td>
<td>3,500-5,000</td>
</tr>
<tr>
<td>Asymptomatic; slight radiographically-detectable increase in bone mass</td>
<td></td>
</tr>
<tr>
<td>Clinical Phase I</td>
<td>6,000-7,000</td>
</tr>
<tr>
<td>Sporadic pain; stiffness of joints; osteosclerosis of pelvis &amp; vertebral column</td>
<td></td>
</tr>
<tr>
<td>Clinical Phase II</td>
<td>7,500-9,000</td>
</tr>
<tr>
<td>Chronic joint pain; arthritic symptoms; slight calcification of ligaments; increased osteosclerosis/cancellous bones; with/without osteoporosis of long bones</td>
<td></td>
</tr>
<tr>
<td>Phase III: Crippling Fluorosis</td>
<td>&gt;8,400</td>
</tr>
<tr>
<td>Limitation of joint movement; calcification of ligaments/neck, vertebral column; crippling deformities; spine &amp; major joints; muscle wasting; neurological defects/compression of spinal cord</td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup> Ash concentration is the amount of fluoride per weight of bone ash, usually measured from a sample of bone from the iliac crest

The concentration of fluoride also increases with age. A study cited by Agency for Toxic Substances and Disease Registry (2001) examined fluoride bone ash concentrations in five people between 64 and 85 who had lived in an area with water containing 1mg/L fluoride for at least 10 years. Their average bone fluoride concentration was 2,250 mg F/Kg (ATSDR, 2001, p. 82). Note that the level of fluoride per weight of bone ash in long-term residents of fluoridated communities is above the level in "normal bone" but below the level at which changes can be identified on x-rays, and well below the levels at which symptoms of skeletal fluorosis begin to appear.

According to a U.S. Public Health Service Committee, “The total quantity of fluoride ingested is the single most important factor in determining the clinical course of skeletal fluorosis (Krishnamachari, 1986); the severity of symptoms correlates directly with the level and duration of exposure (Fischer, et al., 1989)” (USPHS, 1991, p. 45). However there appear to be other important cofactors that render individuals susceptible to this disease since, “crippling skeletal fluorosis continues to be extremely rare in the United States…even though for many generations there have been communities with drinking water fluoride concentrations in excess of those that resulted in this condition in other countries (Singh and Jolly, 1970)” (IOM, 2000, p. 308).

The National Research Council made the following observations concerning skeletal fluorosis in their review:

“Crippling skeletal fluorosis might occur in people who have ingested 10-20 mg of fluoride per day for 10-20 years. During the last 30 years, only five cases have been reported in the United States. The history of fluoride intake for two of the cases was determined with reasonable accuracy (Sauerbrunn et al., 1965; Goldman et al., 1971). The individuals consumed up to 6 L of water per day containing fluoride at 2.4-3.5 mg/L in one case and 4.0-7.8 mg/L in the other. The
daily fluoride intake was estimated at 15-20 mg for 20 years. In general, this intake would be associated with a drinking-water supply containing fluoride at about 10 mg/L\(^2\).

Thus, crippling skeletal fluorosis in the United States has been rare and not a public health problem (Leone et al., 1954; Stevenson and Watson, 1957), even though for many generations there have been communities with drinking water fluoride concentrations in excess of those that have resulted in the condition in other countries (Singh and Jolly, 1970). The puzzling geographic distribution of the disorder usually is ascribed to unidentified dietary factors that render the skeleton more or less susceptible.

The small number of cases of skeletal fluorosis in the United States has ruled out the possibility of systematic epidemiological evaluation. Based on limited data in the literature on skeletal fluorosis, the subcommittee [National Research Council] concludes that skeletal fluorosis is not a public health issue in the United States” (NRC, pp. 59-60).

The Locker review conducted for the Ontario Ministry of Health (1999) reported:

“Most estimates indicate that crippling fluorosis is associated with chronic fluoride exposures of \( \geq 10 \) mg/day for at least ten years. These exposures occur as either endemic (exposure to the naturally fluoridated drinking water) or industrial (e.g. exposure to the cryolite dust) (Fejerskov, 1996; Whitford, 1996). Beside the dose and duration of fluoride exposure, the development of skeletal fluorosis is influenced by various other factors. The most common are age, physical activity, kinetics of bone remodeling, nutritional status and renal insufficiency. Epidemiological studies of bone mineral density have not detected changes consistent with skeletal fluorosis resulting from the consumption of drinking water containing fluoride at the concentrations considered optimal for caries prevention” (Locker, 1999, p. 44).

**Skeletal Fluorosis Uncertainties**

According to the Agency for Toxic Substances and Disease Registry, “The incidence of skeletal fluorosis in the United States is unknown, since it appears that the early signs can only be identified radiologically” (ATSDR, 2001, p. 82).

Three members (GM, EC, RN) of the FTSG were concerned that the studies on skeletal fluorosis estimated the likelihood of occurrence based on a dosage of 10-20 mg of fluoride per day over at least 10-20 years, but there was limited data regarding the likelihood of occurrence based on a cumulative dose over a lifetime of exposure. This was particularly concerning to them given the fact that fluoride accumulates in the bone. Skeletal fluorosis is rarely reported in the United States. Because the symptoms of clinical non-crippling stages of skeletal fluorosis (pain in the bones and joints, muscle weakness, fatigue, calcification of ligaments and bone spurs) two FTSG members (GM, EC) wondered if these symptoms could be misdiagnosed, resulting in under-reporting among susceptible individuals living in communities with optimally fluoridated drinking water (e.g. persons with long-term nutritional deficiencies such as deficiencies of protein, calcium, magnesium, and/or vitamin C and people with chronic kidney failure).

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\(^2\) Approximately 10 times the concentration in Fort Collins water.
**FINDINGS: Skeletal Fluorosis**

At the concentrations of fluoride provided in Fort Collins water including exposures from all sources over a lifetime, skeletal fluorosis caused by drinking water exposure is not likely to be a health issue. The available data are not consistent with a likelihood of increased human skeletal fluorosis from city water fluoridation.

Additional research is needed to reduce the remaining uncertainty if cumulative exposure to all sources of fluoride (including drinking water fluoride at levels of 1 mg/L) over a lifetime may lead to pre-clinical or milder forms of skeletal fluorosis in some sensitive populations.

**Dental Enamel Fluorosis**

A summary of the issue concerning enamel fluorosis and water fluoridation is found in the report from the Centers for Disease Control and Prevention, *Recommendations for using fluoride to prevent and control dental caries in the United States* (2001):

“Fluoride ingested during tooth development can also result in a range of visually detectable changes in enamel opacity (i.e., light refraction at or below the surface) because of hypomineralization. These changes have been broadly termed enamel fluorosis, certain extremes of which are cosmetically objectionable (49). (Many other developmental changes that affect the appearance of enamel are not related to fluoride (50).) Severe forms of this condition can occur only when young children ingest excess fluoride, from any source, during critical periods of tooth development. The occurrence of enamel fluorosis is reported to be most strongly associated with cumulative fluoride intake during enamel development, but the severity of the condition depends on the dose, duration, and timing of fluoride intake. The transition and early maturation stages of enamel development appear to be most susceptible to the effects of fluoride (51); these stages occur at varying times for different tooth types. For central incisors of the upper jaw, for example, the most sensitive period is estimated at age 15-24 months for boys and age 21-30 months for girls (51,52).

Concerns regarding the risk for enamel fluorosis are limited to children aged ≤8 years; enamel is no longer susceptible once its pre-eruptive maturation is complete (11). Fluoride sources for children aged ≤8 years are drinking water, processed beverages and food, toothpaste, dietary supplements that include fluoride (tablets and drops), and other dental products.

The very mild and mild forms of enamel fluorosis appear as chalklike, lacy markings across a tooth’s enamel surface that are not readily apparent to the affected person or casual observer (53). In the moderate form, >50% of the enamel surface is opaque white. The rare, severe form manifests as pitted and brittle enamel. After eruption, teeth with moderate or severe fluorosis might develop areas of brown stain (54). In the severe form, the compromised enamel might break away, resulting in excessive wear of the teeth. Even in its severe form, enamel fluorosis is considered a cosmetic effect, not an adverse functional event. (8, 11, 55, 56)

When enamel fluorosis was first systemically investigated during the 1930s and 1940s, its prevalence was 12%-15% for very mild and mild forms and zero for moderate and severe forms among children who lived in communities with drinking water that naturally contained 0.9-1.2 ppm fluoride (53). Although the prevalence of this condition in the United States has since increased (8, 58, 59), most fluorosis today is of the mildest form, which affects neither cosmetic appearance nor dental function. The increased prevalence in areas both with and without fluoridated community drinking water indicates that, during the first 8 years of life (8), the total intake of fluoride from all sources has increased for some children (Centers for Disease Control and Prevention [CDC], 2001, pp. 6-7).

(8, 11, 49, 50, 51, 52, 53, 54, 55, 56, 58, 59) References within a quote are available in the source document.
The Medical Research Council of Great Britain adds the following terminology, “Dental fluorosis is a form of developmental defect of tooth enamel. Histologically it presents as hypocalcification, while clinically it ranges from barely visible white striations on the teeth through to gross defects and staining of the enamel” (MRC, 2002, p.19).

Prevalence of Enamel Fluorosis in the U.S.

The U.S. Centers for Disease Control and Prevention reviewed the most recent national estimates of the prevalence of fluorosis:

“The 1986-1987 National Survey of Dental Caries in U.S. School Children (the most recent national estimates of enamel fluorosis prevalence) indicated that the prevalence of any enamel fluorosis among children was 22%-23% (range 26% of children aged 9 years to 19% of those aged 17 years (60, 61). Almost all cases reported in the survey were of the very mild or mild form, but some cases of the moderate (1.1%) and severe (0.3%) forms were observed” (CDC, 2001, pp. 8-9).

The estimates cited above were averages across all communities, ranging from very low to very high levels of fluoride. “In communities with drinking water containing 0.7-1.2 ppm fluoride, the prevalence was 1.3% for the moderate form of enamel fluorosis and zero for the severe form; thus, few cases of enamel fluorosis were likely to be of cosmetic consequence (8,61)” (CDC, 2001, p. 12).

According to a recent study, the mean prevalence of dental fluorosis, relative to Dean’s original data, has increased by 39% in optimally fluoridated areas and by 91% in nonfluoridated areas (Pendrys & Stamm, 1990, cited in Lewis & Banting, p. 156).

Figure 1. Taken from Figure 8-1, page 299, of the Committee on the Scientific Evaluation of Dietary Reference Intakes, Food & Nutrition Board, Institute of Medicine (2000)

Relationships among caries experience (solid line), dental fluorosis index (dashed line), and the fluoride concentration of drinking water. A fluorosis index value of 0.6 was judged to represent the threshold for a problem of public health significance. The data are based on the examination of 7,257 12-to 14-year old children (Dean, 1942).

(8, 60, 61) References within a quote are available in the source document.
As demonstrated in the total exposures section earlier in this finding, total exposures have increased and at optimal levels of water fluoridation are higher than shown in Figure 1 above.

The NHS Review at the University of York found that at a fluoride level of 1 ppm an estimated 12.5% of exposed people would have fluorosis that they would find aesthetically concerning” (NHS, 2000, p. xiii). The NHS Review looked at 88 studies of dental fluorosis:

“All of the studies were of evidence level C (lowest quality), except one level B. From these models, the pooled estimate of the prevalence of fluorosis at a water fluoride concentration of 1.0 ppm was 48%...and for fluorosis of aesthetic concern 12.5%” (NHS, 2000, p. 45).

**Contribution of CWF to Enamel Fluorosis**

Only a fraction of current levels of fluorosis in a fluoridated community like Fort Collins can be attributed to drinking optimally fluoridated water. In the context of multiple sources of ingested fluoride, how much does water fluoridation at optimal levels contribute to the overall prevalence of fluorosis? There are two lines of reasoning that have been used to answer this question. The first is to use levels of fluorosis in studies conducted in communities before fluoride was present in the diet, bottled waters, and dental products as an estimate of what water fluoride contributes. The National Research Council follows this line of reasoning with the following:

“In general, the evidence supports the conclusion that fluoridation at the recommended concentrations, in the absence of fluoride from other sources, results in a prevalence of mild-to-very mild (cosmetic) dental fluorosis in about 10% of the population and almost no cases of moderate or severe dental fluorosis. At five or more times the recommended concentration, the proportion of moderate-to-severe dental fluorosis is substantially higher” (NRC, 1993, p. 5).

A second approach is to compare relative levels of fluorosis in communities with and without fluoridated water. Lewis and Banting (1994) and the NHS Center for Reviews and Dissemination at the University of York (2000) conducted reviews and synthesis of the literature regarding fluorosis. Both reviews found that the risk of fluorosis has increased in both optimally fluoridated (1.0 mg/L) and low-fluoride communities (0.4 mg/L), with the absolute difference in prevalence of fluorosis remaining stable at about 15%. Lewis and Banting estimated that the percent of fluorosis attributable to water fluoridation dropped from nearly 100% in the 1940s to 40% in the early 1990s. The remaining 60% was attributed to increased use of fluoride dental products and to the “halo effect” (Lewis & Banting, 1994, p. 156).

**Other Contributing Causes of Enamel Fluorosis**

A large number of studies have reported an association between fluoride supplement use and enamel fluorosis (NRC, 1993 p. 43). In response to accumulated evidence the supplement dosage schedule for children nine and younger was markedly reduced in the U.S. in 1994. Levy and Muchow (1992) and Pendrys and Morse (1990) are among those who documented that improper dosing of supplements is common and that inappropriate use of fluoride supplements in children living in fluoridated communities is an important cause of fluorosis. Swallowing of toothpaste by preschool children and prolonged use of powdered infant formula in fluoridated communities have been identified as risk factors for fluorosis as well (NRC, 1993, pp. 311-312; CDC, 2001, pp. 11-12). Several studies have attempted to estimate the relative impact of specific fluoride sources on the prevalence of enamel fluorosis in the U.S. and Canada (Pendrys, Katz, & Morse, 1994; Osuji, et al., 1988; Pendrys, 2000). Pendrys (2000) reported findings from a study of 663 middle school students:

“In the nonfluoridated study sample, sixty-five percent of the enamel fluorosis cases were attributed to fluoride supplementation under the pre-1994 protocol. An additional 34 percent were explained by the children having brushed more than once per day during the first two years of
life. In the optimally fluoridated study sample, 68 percent of the enamel fluorosis cases were explained by the children using more than a pea-sized amount of toothpaste during the first year of life, 13 percent by having been inappropriately given a fluoride supplement, and 9 percent by the use of infant formula in the form of a powdered concentrate” (Pendrys, 2000, p. 746).

The Institute of Medicine committee report on dietary reference intakes (1997) concluded that intakes of fluoride from water and diet have remained about the same since the 1940s, so that, in optimally fluoridated communities, “…the additional intake by children at risk of enamel fluorosis almost certainly derives from the use of fluoride-containing dental products” (IOM, 2000, p. 312).

Using the National Research Council’s logic in estimating fluorosis rates attributable to community water fluoridation in the absence of other fluoride sources, the 12-15% prevalence of dental fluorosis that existed in optimally fluoridated communities before the introduction of other fluoride sources can be thought to be the amount of current fluorosis due to drinking Fort Collins water. Given that, as many as 160-200 children in Fort Collins may develop enamel fluorosis in their permanent teeth annually that may be statistically attributable to consumption of community fluoridated water, all of it of the very mild or mild form. This estimate theoretically represents the amount and severity of fluorosis that would be averted by suspending water fluoridation. Many more children, not so easily determined, may develop dental fluorosis from incorrectly using fluoridated dental products such as ingesting toothpaste or taking fluoride supplements on a regular basis, between the ages of four months and eight years. Fluorosis attributable to these sources would not be expected to decrease if Fort Collins suspended water fluoridation. Although moderate to severe enamel fluorosis is not caused by community water fluoride at 1 ppm by itself, some reduction in the incidence of moderate to severe fluorosis from exposure to all sources of fluoride would be expected if community water fluoridation were eliminated.

Given the availability and indiscriminate use of fluoridated dental products, children in the vulnerable ages in both fluoridated and nonfluoridated communities may be exposed to excessive amounts of fluoride. The Canadian city of Calgary came to the following conclusion regarding the problem of enamel fluorosis among children:

“The Panel recommends that health authorities pay more attention to identifying uncontrolled sources of fluoride, especially due to children swallowing high fluoride toothpaste. Reducing uncontrolled sources of fluoride would be a more effective means of reducing dental fluorosis than eliminating fluoridation of water” (Expert Panel for Water Fluoridation Review, City of Calgary, 1998, p. 30).

The Center for Disease Control and Prevention recommends that the medical and dental communities and the media educate the public about the potential for increasing the prevalence and severity of enamel fluorosis if children consuming fluoridated water are treated with fluoride supplements or consume excessive amounts of fluoridated toothpaste (CDC, 2001, p. 26).

**Dental Fluorosis Uncertainties**

Uncertainties identified by the FTSG (or specific members):

- The current prevalence of dental fluorosis in fluoridated and nonfluoridated communities in our region is unknown.
- The public’s perceptions regarding the aesthetic acceptability or lack of acceptability of mild to moderate dental fluorosis is unknown.

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3 The average number of children in each age of life between 4 months and 8 years in Fort Collins is about 1350 according to 2000 U.S. Census data. The prevalence of fluorosis measured in the early community fluoridation trials was 12%-15% all the very mild to mild forms. Therefore, \((1350)*(12\%\text{ to }15\%) = 162\text{ to }203\) children per year may develop fluorosis.
• It is not known whether the prevalence of dental fluorosis would decrease or increase if Fort Collins were to suspend water fluoridation.

**FINDINGS: Dental Fluorosis**

At the concentrations of fluoride provided in Fort Collins water, in combination with other sources of fluoride, as many as one in four children under age eight may develop very mild to mild dental fluorosis. This degree of fluorosis may or may not be detectable by the layperson. With oral health as the goal, this degree of dental fluorosis is considered an acceptable adverse effect given the benefits of caries prevention. Since about 60% of dental fluorosis can be attributed to other sources of fluoride (particularly toothpaste and other dental products) parental supervision over tooth paste swallowing in their young children and proper prescribed supplementation in infants will likely reduce development of enamel fluorosis more than the removal of added fluoride in drinking water.

**Thyroid Function**

Questions raised at the public meeting about the potential for thyroid impacts from drinking water fluoridation led the FTSG to inquire about studies of the relationship between fluoride intake and thyroid function. Some at the public meeting pointed out that fluoride had been used to treat hyperthyroidism and questioned whether drinking water fluoridation would exacerbate hypothyroidism.

Staff pursued this question and produced 25 abstracts and some information from the “Tier One” literature for FTSG review and discussion. The literature search included an extensive search of the National Library of Medicine Database as well as Medline and all major biomedical databases available through the Colorado State University Morgan Library and the University of Colorado Health Sciences Center Dennison Library. See reference list in Appendix A.

Of most relevance and therefore having the greatest impact on the FTSG findings are three publications. Eichner, Borner, Henschler, Kohler, and Moll (1981) examined 26 women who received 40 mg of sodium fluoride twice a day (equivalent 36 mg of fluorine) for three to six months as a treatment for osteoporosis. In a second study published separately by two different lead authors, Hasling, Nielsen, Melsen, and Mosekilde (1987) and Mosekilde, Charles, Eriksen, Hasling, and Melsen (1986), described 163 patients treated for eight years (total of 460 patient years) with a combination of sodium fluoride (60 mg/day), calcium phosphate (45 mmol/day) and vitamin D2 (18,000 IU/day). Both cited studies found no change in thyroid function.

**Thyroid Uncertainties**

There were some studies identified in the FTSG’s literature search that suggested a deleterious effect on the thyroid by fluoride. While these studies were considered to be of lower quality or relevance, two members of the FTSG held that there remains uncertainty regarding the effect of fluoride on thyroid structure and function. The Medical Research Council commented:

“The York review listed three studies in which goiter was the outcome of interest. Two of these studies (Gedalia & Brand, 1963; Jooste et al., 1999) found no significant association with water fluoride level. The third (Lin et al., 1991) found a significant positive association between combined high fluoride/low iodine levels and goiter. However, because this study looked at combined fluoride/iodine uptakes, and has not been published in a peer reviewed journal, the findings should be treated cautiously. Further work on this aspect is of low priority” (MRC, 2002, p. 34).
**FINDINGS: Thyroid Effects**

In the literature reviewed, doses appropriate for caries reduction were not shown to negatively impact thyroid function. Studies in which humans received doses significantly higher than the optimum fluoride intake for long periods of time showed no negative impact on thyroid function. For those with hypothyroidism, the risks of alteration of thyroid structure or function are very low. The absence of our finding any conclusive evidence that drinking water fluoride exposures causes increased risk to thyroid function does not prove that fluoride can not affect thyroid function. The available data are consistent with a finding of a low likelihood of risk to human thyroid function from water fluoridation.

**Immune System Effects**

Potential immune system effects are of two types—hypersensitivity (allergic) reactions and immunotoxicity effects (weakening of the immune system). Information on both is limited.

With respect to allergic reactions, the Medical Research Council of Great Britain notes:

“Information regarding the allergic potential of fluoride in drinking water is sparse. A paper by Spittle (1993) concluded that some individuals exhibit an allergic/hypersensitivity reaction to fluoride, but reviews by NRC (1993), NHMRC (1991) and Chalacombe (1996) all concluded that the studies undertaken do not support claims that fluoride is allergenic. They considered the weight of evidence to show that fluoride is unlikely to produce hypersensitivity or other immunological effects” (MRC, 2002, p. 32).

The U.S. Public Health Service (1991) and the National Research Council (1993) both concluded the following:

“The literature pertaining to immunological effects of fluoride is limited. Although direct exposure to high concentrations of sodium fluoride in vitro affects a variety of enzymatic activities, the relevance of the effects in vivo is unclear. Standardized immunotoxicity tests of sodium fluoride at relevant concentrations and routes of administration have not been conducted. The weight of evidence shows that fluoride is unlikely to produce hypersensitivity and other immunological effects” (NRC, 1993, p. 9; USPHS, 1991, p. 70).

**Immunological System Effects Uncertainties**

The Medical Research Council noted the sparse amount of evidence regarding adverse effects to the human immune system. They concluded that, “There is no information on the immunotoxicity of fluoride. Further work in this area would be useful, but in the absence of obvious toxic mechanisms for such an effect is considered to be of low priority” (MRC, 2002, p. 32).

With respect to immunotoxicity effects, one FTSG member submitted a paper entitled *Is the Ingestion of Fluoride an Immunosuppressive Practice?* that cites several *in vitro* observations to suggest that, “the habitual ingestion of small doses of fluoride, even as small as the 1 mg/L contained in fluoridated water, may decrease the function of the immune system” (Sutton, 1991).
**FINDINGS: Immunological Effects**

Overall, evidence is lacking that exposure to fluoride through drinking water causes any problems to the human immune system. The absence of our finding any conclusive evidence that drinking water fluoride exposures causes increased risk to human immune system function does not prove that fluoride is harmless to the human immune systems.

**Other Potential Health Effects**

The potential for associations between a number of other potential adverse health effects and exposure to fluoridated water has been explored in many epidemiologic and toxicological studies and summarized in reviews conducted by the Agency for Toxic Substances and Disease Registry, the World Health Organization, the National Research Council of the National Academy of Science, and the U.S. Public Health Service. The following areas have been studied:

Effects of fluoride on the renal system
- Effects of fluoride on the gastrointestinal system
- Effects of fluoride on hypersensitivity and the immune system (described above)
- Effects of fluoride on reproduction
- Genotoxicity
- Developmental effects including birth defects and Down Syndrome
- Effect of fluoride on all-cause mortality

As in the above sections, relevant citations from the texts of these reviews follow; a fuller description of each is found in Appendix 2 to this document.

The National Research Council of the National Academy of Sciences came to the following conclusion on these issues:

“...The subcommittee concludes that available evidence shows that the threshold dose of fluoride in drinking water for renal toxicity in animals is approximately 50 mg/L. The subcommittee therefore believes that ingestion of fluoride at currently recommended concentrations is not likely to produce kidney toxicity in humans.... The subcommittee concludes that the available data show that the concentrations of fluoride found in drinking water in the United States are not likely to produce adverse effects in the gastrointestinal system.... The weight of evidence shows that fluoride is unlikely to produce hypersensitivity and other immunological effects.... The subcommittee concludes that the fluoride concentrations associated with adverse reproductive effects in animals are far higher than those to which human populations are exposed. Consequently, ingestion of fluoride at current concentrations should have no adverse effects on human reproduction.... The subcommittee concludes that the genotoxicity of fluoride should not be of concern at the concentrations found in the plasma of most people in the United States.... Based on its review of available data on toxicity of fluoride, the subcommittee concludes that EPA’s current MCL of 4 mg/L for fluoride in drinking water is appropriate as an interim standard” (NRC, 1993, pp. 7-11).

The U.S. Public Health Service concluded in 1991:

“...Chronic low-level exposure of healthy individuals does not appear to present problems in other organ systems, such as the gastrointestinal, the genitourinary, and the respiratory systems.... Chronic low level fluoride exposure is not associated with birth defects. Studies also fail to establish an association between fluoride and Down Syndrome. Genotoxicity studies of fluoride, which are highly dependent on the methods used, often show contradictory findings. The most...
common finding is that fluoride has not been shown to be mutagenic in standard tests on bacteria (Ames Test). In some studies with different methodologies, fluoride has been reported to induce mutations and chromosome aberration in cultured rodent and human cells. The genotoxicity of fluoride in humans and animals is unresolved despite numerous studies” (USPHS, 1991, pp. 87 & 89).

**Uncertainties Regarding Other Health Effects**

Several other adverse effects have been proposed as being associated with elevated with fluoride intake. They include:

- Effects on the pineal gland
- Senile dementia
- Age at menarche
- Anemia during pregnancy
- Sudden infant death syndrome
- Primary degenerative dementia
- Reduced intelligence and other central nervous system effects
- The possibility that fluoride added to water could influence toxicity from other substances (i.e., by causing leaching of aluminum from cookware or affecting the uptake or bioavailability of toxic substances such as aluminum and lead in the gut)

The Medical Research Council of Great Britain as well as the Agency for Toxic Substances and Disease Registry found the available information on these effects to be limited and inconclusive. The Medical Research Council noted, “Further targeted research may be warranted, but this is presently of low priority unless and until critical literature reviews are undertaken that demonstrate specific research needs” (MRC, 2002, p. 34).

**Fluoride and Blood Lead Levels**

The concern regarding the possible association between blood lead levels and the use of hydrofluorosilicic acid (HFS) is considered in Finding #4. Two recent ecological studies found a significant association between community average blood lead levels in children residing in areas with water fluoridated using HFS, compared to those residing in communities fluoridated with sodium fluoride, or not fluoridated (Masters & Coplan, 1999; Masters, Coplan, Hone, & Dykes, 2000). According to the U.S. Environmental Protection Agency, there is no reliable evidence to suggest that this fluoridation agent may increase blood lead levels. The Medical Research Council of Great Britain concludes, “This appears to be a controversial area and further studies are awaited” (MRC, 2002, p. 36). The National Toxicity Program recently nominated the use of HFS as a fluoridation agent for a formal review.

**Sensitive Populations**

The Agency for Toxic Substances Disease Registry toxicological profile identified the following populations as potentially exhibiting a different or enhanced response to fluoride exposure.

“Existing data indicate that subsets of the population may be unusually susceptible to the toxic effects of fluoride and its compounds. These populations include the elderly, people with deficiencies of calcium, magnesium, and/or vitamin C, and people with cardiovascular and kidney problems. However, these effects would not be expected at typical exposure levels (at 1 ppm fluoride)” (ATSDR, 2001, p. 143).
### FINDINGS: Other Health Effects

The potential for other health effects was reviewed by the FTSG. There was not adequate evidence to consider any of these other potential adverse effects a concern with respect to fluoridation of Fort Collins water supplies. The absence of our finding any conclusive evidence that drinking water fluoride exposures causes other potential health effects does not prove that fluoride can not cause other potential health effects.
Reference List


Finding #3 – Costs and Benefits, Including the Distribution of Costs and Benefits

Cost-Effectiveness of Community Water Fluoridation

Economic analyses conducted before the mid-1980s found that the value of dental decay averted by community water fluoridation exceeded the cost to fluoridate community water supplies by as much as 8:1 (Davies, 1973; Nelson & Swint, 1976; Niessen & Douglass, 1984; White, Antczak-Bouckoms, & Weinstein, 1989). However, since the 1970s, a number of factors have given rise to questions about the possible reduced effectiveness and cost-effectiveness of community water fluoridation (Lewis & Banting, 1994). First, as noted in Finding #1, the widespread use of discretionary fluorides and the increased levels of fluoride in processed foods and beverages has led to smaller differences in the mean exposure to topical and systemic fluorides between fluoridated and nonfluoridated communities. Second, there has been a related decrease in the overall level of caries in the U.S. and many other developed countries, whether water supplies are fluoridated or not (Committee to Coordinate Environmental Health and Related Programs, USPHS [USPHS], 1991, p. 31). Finally, there has been an increase in the prevalence of dental fluorosis in both fluoridated and nonfluoridated communities (see Finding #2). The general reduction in caries and increase in dental fluorosis raises the question of whether it is still clinically and economically justified to replace existing fluoridation equipment and continue to fluoridate water supplies in Fort Collins.

Literature Review

The Fluoride Technical Study Group (FTSG) conducted a Medline, Internet, and secondary reference search for economic analyses of community water fluoridation published since the dramatic drop in caries prevalence that was documented by national survey data up through the mid-1980s. Criteria for inclusion of articles for review were:

1. the study included an assessment of community water fluoridation,
2. there was a comparison between cost and consequences, and
3. the study was published in English in a peer-reviewed journal between 1989 and 2002.

We defined an ideal economic analysis by the following criteria: the analysis took a societal perspective; it was based on a synthesis of U.S. incidence and effectiveness data from the 1980s or later from several sources; it included costing, which allowed for estimation of resources used; it used a long enough time horizon to capture all the effects of fluoridation; it specified a discount rate\(^1\); and it included multi-way sensitivity analyses\(^2\) to assess uncertainties.

The FTSG identified two U.S.-based cost-effectiveness analyses of community water fluoridation published between 1989 and 2001 (Appendix 3, Table 1). Several cost-effectiveness analyses from other industrialized countries were also identified: two 1990 studies using data from the UK, a 1993 unpublished report from the UK and a report from New Zealand published in 2001 (Appendix 3, Table 2). The two U.S. studies, the report from NZ and a UK study estimated the cost of community water fluoridation per averted single surface restoration; two UK studies used tooth-level caries data. Two additional foreign studies that addressed the effectiveness of community water fluoridation in light of the general reduction in caries prevalence in Ireland and Scotland are included in Appendix 3, Table 2.

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\(^1\) A measure of people’s preference for money and health now rather than in the future.

\(^2\) “A method to determine the robustness of an assessment by examining the extent to which results are affected by changes in methods, values of variables, or assumptions” (Last, 1995).
In general, all cost-effectiveness analyses reviewed were based on evidence that community water fluoridation is effective in preventing or reducing cavities and that there are no treatment costs attributable to any adverse health effects associated with the practice. The analyses assumed that caries would increase if community water fluoridation were ceased.

Analyses that accounted for estimated treatment savings found that for all but the smallest communities, community water fluoridation remained cost-saving under a wide range of reasonable assumptions regarding baseline caries risk and the effectiveness of community water fluoridation (Birch 1990; Griffin, Jones, & Tomar 2001; Wright, Bates, Cutress, & Lee, 2001). The study which best met criteria for validity both in terms of study quality and applicability to our local situation was the 2001 report by Griffin et al. of the Centers for Disease Control and Prevention (CDC). They estimated per capita cost savings each year from community water fluoridation in larger communities from $3.52 to $33.71 in 1995 U.S. dollars, depending on baseline caries risk and estimated effectiveness of water fluoridation (Griffin, Jones & Tomar, 2001).

**Estimation of Local Cost-Effectiveness Ratio**

The cost per unit health benefit produced from water fluoridation can vary by at least a factor of four according to the underlying level of caries risk in the community, and by a factor of ten depending on the size of the community served by the distribution system (Birch, 1990). Therefore, local estimates of these parameters are important. Since there are no local data on baseline caries incidence, the FTSG asked researchers at the CDC to provide the group with regional estimates from the most recent national survey of oral health (the National Institute of Dental Research [NIDR] National Survey of the Oral Health of U.S. School Children, 1986-87), adjusted by estimates of the reduction in caries incidence that might have occurred since then.

The total costs of community water fluoridation are the direct and indirect costs of fluoridating our water minus the estimated treatment savings secondary to the fluoridation program (White et al., 1989). The total direct cost of fluoridating the Fort Collins community water supply has remained fairly constant at less than a dollar per capita per year since current facilities were constructed in 1993 (Kevin Gertig, City of Fort Collins Water Department). The annual operating cost (materials, operating costs and maintenance), estimated to be $57,500 in 2001, has averaged $0.52 per capita and has ranged from $0.41-$0.65 per capita (adjusted to 2000 dollars) since 1995. These costs are similar to published cost estimates from other large facilities (Ringelberg, Allen, & Brown, 1992). Given the estimated capital cost of $500,000 for proposed new equipment with a total useful life of at least 15-20 years, the total annuitized per capita cost is $0.21-$0.28. Assuming stable annual chemical, operating and maintenance costs per capita, a mean population of 120,000 over the next 15 years and a useful life of 15 years, the total cost of continuing fluoridation will be $0.96 per capita per year through 2023. Applying a discount rate of 4% and estimating opportunity cost of the capital investment at 4% compounding interest, the average present value of per capita costs is $0.76 in 2000 dollars.

Drs. Griffin et al. using our projections of local fluoridation costs, calculated mean decay increments from the most recent national survey of school children in Region V (Texas, Oklahoma, New Mexico, and Colorado) and calculated cost-benefit estimates according to the analysis of Griffin et al. 2001. Adjusting for inflation and the 2000 population age distribution of Fort Collins, the estimated net costs per capita per year if community water fluoridation were discontinued were estimated to be $4.25. To account for uncertainties regarding the estimates of local caries rates from regional survey data collected over a decade ago, Griffin conducted a sensitivity analysis using least and most favorable estimates of caries increment and fluoridation effectiveness. Applying these estimates, averted cost savings could be as little as $3.22 per person per year and as high as $10.31 per person per year if Fort Collins suspends water fluoridation. (See Appendix 3, Table 1 for complete report.)

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3 Adjusted to the 2000 CPI-dental for U.S. cities.
Griffin writes:

“Community water fluoridation actually saves Fort Collins money. Fort Collins has approximately 100,968 residents who benefit from community water fluoridation. Using data on caries increment from Region V of the National Survey of the Oral Health of U.S. School Children [2] and cost data specific to Ft. Collins, the annual cost savings per person from community water fluoridation equals $4.25 (year 2000 US$). Thus after netting out the amortized capital costs as well as annual operating expenses, the annual cost savings to the Fort Collins community attributable to community water fluoridation would be approximately $429,000 (2000 US$). Because we did not have caries data specific to Ft. Collins we allowed caries increment to vary between the 1986-1987 estimates for the U.S. adjusted for the secular decline in caries (best-case scenario) and the 1986-1987 Region V estimates adjusted for the secular decline in caries (worst-case scenario). Our findings suggest that the annual cost savings to the Ft. Collins community could vary from $325,000 to $1,041,000” (Griffin, personal communication, July 3, 2002).

Approximately half of these costs would be personal out of pocket costs (Centers for Disease Control and Prevention [CDC], 2001b, p. 21). Of the remainder, a portion would be subsidized through local, state and federal taxes funneled through Medicaid, Child Health Plan Plus, and the Health District dental program.

Some local data exist to evaluate the impact of community water fluoridation on costs of publicly subsidized dental care. The Colorado Department of Public Health and Environment (CDPHE) Oral Health recently asked state Medicaid to compare the mean annual cost of all professional dental services for Medicaid eligible children in Larimer County (the large majority of eligibles live in fluoridated Loveland and Fort Collins) with those in nonfluoridated Logan County in 2001 (personal communication, Brunson, June 25, 2002). The goal was to replicate a study from Louisiana published in the Center for Disease Control’s (CDC) Morbidity and Mortality Weekly Report (Water fluoridation and costs of Medicaid treatment for dental decay - Louisiana, 1995-6. CDC, 1999).

The sample was all Medicaid enrolled children in 2001. They found that 1) only 24% of all children eligible for Medicaid at any time during the year received any dental services during the year in either county, and 2) that the average annual cost of dental services per child receiving any dental care was 20% higher in nonfluoridated Logan County ($396 per child) than in mostly fluoridated Larimer County ($329 per child). The weakness in this assessment is that all services were included (not just caries treatment) and all children were included, not just those with lifetime residence. Both of these factors would tend to attenuate the apparent effect of increased caries incidence and treatment. The difference in cost on a per child basis was $67, a cost that is borne by taxpayers.

The assumptions of the Griffin et al. model are as follows:

- Cost savings applies to permanent teeth only.
- All decay is eventually treated.
- Benefits of community water fluoridation are topical and post-eruptive (i.e., start at age six for permanent teeth).
- Benefit is constant, non-cumulative and accrues only to community residents.
- Costs and benefits are discounted at 4%.
- The discounted cost of treating decay in the future is no less than the cost of treating it when it appears.

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4 According to the 2000 Census Fort Collins had 100,968 residents, aged 6 to 64 years. According to Griffin [1] water fluoridation has been shown to be effective in reducing tooth decay in the permanent dentition of individuals, aged 6 to 64 years.
• Simple amalgam fillings will always be used and require replacement with single surface fillings every 12 years until age 65. Potentially costlier treatments (composite fillings, root canals, crowns, bridges) and related treatments (i.e., for periodontal disease related to fillings) are not included.
• Dental fees are the same as the cost of resources to provide the services ($54 for single surface amalgam filling).
• Productivity costs averted were limited to one hour at average hourly wage ($18) for filling a cavity.
• Costs due to adverse effects of community water fluoridation are negligible.
• Fluoride from sources other than toothpaste and community water fluoridation are controlled for.
• The population of 6-64 year olds will remain fixed at 2000 levels.
• Suspending water fluoridation increases caries rates by the percentage equal to the relative difference in mean caries rates between fluoridated and nonfluoridated communities (adjusted for estimated decline in caries since then) according to the 1986-87 NIDR National Survey of the Oral Health of U.S. School Children.

Most of these assumptions would tend to under-estimate the potential costs of suspending fluoridation. For instance, fluoridation is believed to reduce caries in primary (baby) as well as permanent teeth, (and has been found to be effective in reducing root caries, an increasing problem for seniors (CDC, 2001b, p. 11). Weakening of tooth structure from accumulated treated caries, a problem that often leads to more expensive restorations or extractions and loss of function, is not accounted for in this analysis. Because of the “halo effect,” fluoridation of Fort Collins water may also benefit those outside the community who ingest foods and beverages processed with city water. Griffin, Gooch, Lockwood and Tomar (2001) have shown that those living in nonfluoridated communities in regions where water fluoridation is widespread experience substantial caries reductions. Finally, the non-monetized benefits of an averted decayed surface—i.e., the pain and dysfunction that accompanies active untreated decay—might make fluoridation worthwhile even if there were no net savings to the program.

**Uncertainties Regarding Cost-Effectiveness of Water Fluoridation**

Several assumptions used in published cost-effectiveness analyses could, if incorrect, lead to over-estimations of cost-savings. First, costs of potential adverse effects of water fluoridation are assumed to be negligible. The only adverse health effect (presently known) for which there is greater than very low risk is enamel fluorosis. None of the cost-effectiveness analyses reviewed estimated costs of enamel fluorosis. While fluorosis is thought to be caused primarily by the early use or over use of fluoridated toothpaste and the inappropriate use of fluoride supplements, absolute levels of enamel fluorosis, mostly of the very mild-to-mild form, are still higher in communities with fluoridated water. Using McDonagh et al. (2000) estimate of the prevalence of fluorosis of aesthetic concern (12.5%) and Lewis and Banting’s (1994) estimate of attributable fraction (39%) (see Finding #2), nearly 5% (12.5% X 39%) of lifetime residents in a fluoridated community will have enamel fluorosis attributable to water fluoridation that may be of aesthetic concern. Some people (generally those with moderate to severe mottling involving the anterior teeth) choose to modify this condition with elective treatment. The definitive treatment for moderate enamel fluorosis of aesthetic concern and severe fluorosis is application of a porcelain veneer or porcelain to metal crown (median charge $662 and $875 per tooth, respectively). Because the treatment is elective, and the “need” subjective, it would be difficult to estimate the number of people who would choose such treatment or are estimates available of the number who currently receive it. Furthermore, it is uncertain whether or not levels of fluorosis of aesthetic concern decrease when a community stops fluoridating. Even if these treatment costs could be estimated, they do not include intangibles such as reduced self-esteem. Based on these concerns, the FTSG concluded that not considering the costs of enamel fluorosis might lead to over-estimation of the cost-savings of water fluoridation.

As noted in Finding #2, the FTSG did not find conclusive evidence of any other adverse effects of optimally fluoridated water, but identified some gaps in knowledge (see Finding#2). If increased risk of
bone fractures, cancers or other adverse health effects were in fact real, they would have a substantial impact on the cost effectiveness of water fluoridation.

Also, if baseline caries risk in Fort Collins is substantially lower than the conservative estimates used in this analysis (see Appendix 3), and if the diffusion effect of foods and beverages shipped in from fluoridated areas sufficiently buffers the loss of drinking water fluoride, the net expense of suspending fluoridation will be lower (at least from the perspective of the Fort Collins community).

Cost savings were calculated based on the use of hydrofluorosilicic acid (HFS), which is commonly used in community water fluoridation. However, questions have been raised by some members of the public about the safety of using this material, and they have requested that sodium fluoride be used instead. If the calculation were performed incorporating the higher cost of using sodium fluoride, the cost savings would be less.

Finally, using results of the Griffin analysis to estimate the net cost of suspending water fluoridation in the City of Fort Collins also presumes that changes in the behavior of dentists or consumers of dental products will not result and that caries levels will increase. In fact, as discussed in Finding #1, behaviors may change and caries levels may not increase. Some studies have found indications of increased use of preventive dentistry and use of alternative sources of fluoride in fluoridation-ended communities (Maupome, Clark, Levy, & Berkowitz, 2001; Kunzel, Fischer, Lorenz, & Bruhmann, 2000; Kunzel & Fischer, 1997). To the extent that these less cost-effective approaches are being substituted for a more cost-effective approach, caries rates may increase less than the analysis predicts, but net costs are likely to be higher.

**Distributional Effects of Community Water Fluoridation**

Because the Fort Collins Water Utility is operated as an enterprise fund, all costs—both operating and capital costs—are borne by customers of the Water Utility in proportion to the amount of domestic water used. The benefits are distributed to all those who live and drink water in the community, as well as those who ingest foods and beverages produced with community water. Fluoride modalities may be most effective and therefore cost-effective for persons at highest risk for caries. The risk factors for caries include (CDC, 2001b, p. 5):

- lower socio-economic status,
- lower levels of parent education,
- those without access to or who do not seek dental care, and
- individual factors.*

Numerous studies in the U.S. and elsewhere have found that the distribution of caries in a community is skewed, with caries experienced much higher among children and adults in lower socioeconomic strata (SES) than those in higher SES groups (CDC, 2001b, p. 5; CDC, 2001a, p. 2)

“Eighty percent of dental caries identified in permanent teeth of children aged 5-17 years in the United States occur in 25% of children (4,6,7). Lower-income, Mexican American and African-American children and adults have more untreated decayed teeth than their higher-income or non-Hispanic white counterparts (4,5,8,9). Among low-income children, approximately one third have untreated caries in primary teeth that could be associated with pain, difficulty in eating, and underweight (9)” (CDC, 2001a).

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(4, 5, 6, 7, 8, 9) References within a quote are available in the source document.

* Active caries, history of caries in siblings or care-givers, gingival recession, high levels of cariogenic bacteria, impaired ability to maintain oral hygiene, malformed enamel or dentin, decreased salivary flow, radiation treatment, low salivary buffering capacity, space maintainers/oral appliances or dental prostheses and consumption of refined sugars.
The reasons for this discrepancy are probably multifactorial. Many factors can contribute to high rates of caries in low-income populations:

“Low indices of socioeconomic status (SES) have been associated with elevations in caries, although the extent to which this indicator may simply reflect previous correlates is unknown. Low SES is also associated with reduced access to care, reduced oral health aspirations, low self-efficacy, and health behaviors that may enhance caries risk” (National Institute of Health, Office of the Director, Consensus Statement [NIH], 2001, p. 12).

All “Tier One” references that addressed the issue of the impact of community water fluoridation on different socioeconomic groups observed that lower SES groups would be more likely to benefit from community water fluoridation, thereby reducing the disparity in oral health and increasing equity (CDC, 2001b, p. 11; USPHS, p. 28; NHS Centre for Reviews and Dissemination, University of York, 2000, p. 33; Spencer, Slade, & Davies 1996; Locker, 1999, p. 4).

However, the recent systematic review conducted by the University of York for the British National Health Service found the quality and quantity of evidence addressing this issue to be lacking. As reviewed by Medical Research Council of Great Britain:

“The York Review concluded that there appears to be evidence that water fluoridation reduces the inequalities of dental health across the social classes in five and twelve year olds using the dmft/DMFT measure. This effect was not seen in the proportion of caries free children among five-year olds; the data on caries prevalence in children of other ages also did not demonstrate an effect. The review suggested caution in interpreting these results because of the small quality of studies, differences between the studies, and their low quality rating” (Medical Research Council, 2002, p. 21).

Effectiveness and Cost-Effectiveness of Other Fluoride Modalities Relative to Community Water Fluoridation

Laboratory research suggests that maintenance of constant low levels of fluoride in the oral cavity is most effective at reducing caries (World Health Organization [WHO] 1994, p. 1). The WHO Expert Committee on Oral Health Status and Fluoride Use concluded that the goal of a community-based caries prevention program should be to “…implement the most appropriate means of maintaining a constant low level of fluoride in as many mouths as possible” (WHO, 1994 p. 1). One of the key advantages cited by public health authorities for water fluoridation, when compared to other possible strategies for delivering fluoride to the oral cavity, is that it does not require behavioral changes from its recipients, and that those most likely to benefit from it will do so (CDC, 2001b, p. 11). Both the WHO committee and the CDC’s Fluoride Recommendations Work Group found that, provided a community had a piped water supply, community water fluoridation is the most effective method of reaching the whole population.

There are, however, a wide variety of other methods to deliver fluoride to the oral cavity. To the extent that they supply frequent low-level exposures of fluoride to the mouth, they will yield similar caries reductions (see Appendix 3, Table 3). However they differ in their applicability to community-based interventions, in the degree to which they depend on individual behavior changes, in how logistically difficult it is to target them to needy members of the community and in their cost (see Appendix 3, Table 3).

School-based water fluoridation systems and classroom mouth rinse programs are amenable to a community-based approach and have been shown to be effective, but the former are logistically difficult and neither of these approaches benefits adults. Costs of school water fluoridation range from $1 to $14 per student/year (CDC, 2001b, p. 23). The expense of mouth rinse programs comes not from the materials but from the weekly or monthly supervision that is required. Risks of fluorosis in school-based programs
would be expected to be low since children 6 years and older are generally past the age of fluorosis susceptibility (CDC, 2001b, pp. 12 & 16). In several European countries, fluoridated salt (analogous to iodized salt) is widely available as a caries reducing agent (WHO, 1994, pp. 20-21). Because it is not available in the U.S., it is not a feasible option in our community.

Fluoride toothpaste has been shown in high quality studies to be safe, effective and inexpensive in older children and adults at reducing caries, but has been found to be an important cause of enamel fluorosis in young children due to inadvertent swallowing. According to the CDC, “Children who begin using fluoride toothpaste at age <2 years are at higher risk for enamel fluorosis than children who begin later or who do not use fluoride toothpaste at all” (CDC, 2001b, p. 14).

Dietary fluoride supplements (tablets, lozenges, liquids) have been used for caries prevention since the 1940s, but the evidence for their effectiveness is mixed (CDC, 2001b, p. 16; WHO, 1994, p. 23). Supplements are designed to be used in settings of fluoride-deficient drinking water, but studies have found their use in fluoridated communities to be common—7% to 35% in studies reviewed by the Fluoride Recommendations Work Group (CDC, 2001b, p. 16). There is good evidence for the association between use of supplements and the development of enamel fluorosis (see Finding #2). Fluoride supplements are inexpensive but they require a prescription and the dosage schedule is complex, particularly for parents with children of different ages (WHO, 1994, p. 24).

Professionally applied fluoride compounds include gels, foams, and varnishes. They have an effectiveness similar to that of community water fluoridation and the risk for fluorosis is reported to be low (CDC, 2001b, pp. 17-18). They require professional application at six-month intervals and therefore are the least cost-effective method of delivery. Pit and fissure sealants have also been shown to be effective as long as the sealants are maintained (see Appendix 3, Table 4) (NIH, 2001, p. 15). Sealants and fluoride modalities are complementary approaches to caries prevention, since topical fluoride is less effective at preventing caries on the pit and fissure surfaces than on the smooth surfaces of teeth.

There is very little data on the relative cost-effectiveness of these other methods of caries prevention. Recently, the Fluoride Recommendations Work Group compared what is known of the effectiveness and cost-effectiveness of the various methods of fluoride delivery (CDC, 2001b, pp. 21-24). The results are summarized in the second column of Table 3 in Appendix 3. The costs of the fluoride material alone are higher for toothpaste, mouth rinse, supplements and professionally applied compounds than the entire per capita cost of community water fluoridation. To those material costs one must add the costs of promoting the health behavior. Kay and Locker (1998) conducted a systematic review of the effectiveness of health promotion programs aimed at oral health. They reported that there are no established cost-effective methods for reliably bringing about the personal use of fluoride. Oral health promotion delivered at the dentist’s office was most effective, but was most expensive. According to this review, school-based brushing programs and mass media programs have not been shown to be effective (Kay & Locker, 1998). School-based sealant delivery programs, were found to be effective and were “strongly recommended” by the Task Force on Community Preventive Services (CDC, 2001a, p. 9). Under some circumstances, these programs may be cost-saving (Zabos et al., 2002).

Considering the effectiveness and costs of the various modalities discussed above, the CDC expert panel recommended community water fluoridation in all areas of the U.S. and fluoride toothpaste, used as directed, for all persons. Other fluoride modalities were recommended only for certain high-risk individuals and only after consultation with their dentist or health care provider (CDC, 2001b, pp. 26-27). To meet the public health challenge presented by dental caries, the U.S. Department of Health and Human Services outlined the goals for community water fluoridation as part of the Healthy People 2000 and 2010. These national health goals include objectives to increase national baseline fluoridation level to 75% of the U.S. population served by community water systems from the 1989 and 1992 levels of 61 and 62% (CDC, 2002 p.144.) The Centers for Disease Control and Prevention states, “Fluoridation of the
public water supply is the most equitable, cost-effective, and cost-saving method of delivering fluoride to the community” (CDC, 2002, p. 144).

Other effective caries modalities are in current use in other countries to prevent caries. Examples include fluoridated salt (France, Germany, Switzerland, and others), fluoridated milk, and use of xylitol-containing chewing gum (Hayes, 2001). Fluoridated salt and milk are not available in the U.S. Xylitol-containing gum is available in the U.S. and regular use has been shown in one study in Finland to be similar in cost and effectiveness to school-based sealant programs in that country (Alanene, Holsti, & Pienihakkinen, 2000). However, cost-effectiveness data are not available for the U.S., thus its application as a public health strategy is unclear.

**FINDINGS: Costs and Benefits**

The research indicates that the public health goal of a reduction in the incidence of caries is better achieved through community water fluoridation than through individual approaches. It requires minimal behavioral changes compared to alternative delivery methods. It is effective in reaching people in all socioeconomic strata.

The FTSG finds that, even in the current situation of widespread use of fluoride toothpaste and lower baseline caries risk, it is likely that community water fluoridation remains effective and cost saving at preventing dental caries. Based on best available evidence, suspending fluoridation of water in Fort Collins would yield a net increase in costs of preventing and treating caries approximately $4.25 per person per year (range $3.22 - $10.31.) The burden of caries is disproportionately borne by those with lower socio-economic status. There is some evidence that water fluoridation reduces this inequality in oral health.

Not considering the costs of enamel fluorosis or other potential adverse health effects may have led to an over-estimation of the cost-savings of water fluoridation in Fort Collins. The magnitude of the costs of adverse effects is likely to fall well below the estimated net savings.

In summary, this cost analysis assumes that there is a significant benefit from community water fluoridation in preventing caries and potential adverse health effects are not significant. The analysis also assumes that the city will continue using current fluoride additives (hydrofluorosilicic acid). Using this set of assumptions, there appears to be a net cost benefit to community water fluoridation. If any of these assumptions are not valid the cost-benefit picture could change significantly.

The FTSG did not review any study or measure that will achieve the same levels of prevention as water fluoridation for the same resources.
Reference List


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Finding #4 - The Potential for Increased Contaminant Levels Due to the Use of Hydrofluorosilicic Acid

The Fluoride Technical Study Group’s (FTSG) review identified three potential concerns associated with hydrofluorosilicic acid (HFS):
1. co-contamination (i.e. arsenic and lead),
2. decreased pH leading to increased lead solubility or exposure, and
3. potential toxicological effects from incomplete dissociation products of HFS.

Background

The City of Fort Collins has fluoridated its treated water supply since 1967. The form of fluoride added from 1967 to 1992 was called Sodium Silicofluoride, which is a dry product. As the Water Treatment Facility continued to expand, a liquid form of fluoride called Hydrofluorosilicic Acid (HFS) has been utilized since 1993. Liquid forms of fluoride are easier to handle due to the size of larger treatment facilities. The levels of fluoride are monitored carefully at the Water Treatment Facility and throughout the distribution system, and meet or exceed all recommendations set forth by the Colorado Department of Public Health and Environment (CDPHE) and the U.S. Centers for Disease Control and Prevention (CDC).

Fluoride Sources

The City of Fort Collins Utilities currently fluoridates its water with a chemical called Fluorosilicic Acid. The chemical is sometimes called Hydrofluorosilicic Acid (HFS). The term ‘HFS’ will be used in this report. The product is shipped to Fort Collins by truck from any one of several points in the United States. The form used in Fort Collins is typically a 23 - 24% aqueous solution of HFS (H₂SiF₆) and has a formula weight of 144.08. HFS in its full strength, non-diluted form is corrosive and requires special handling considerations. The Fort Collins Utilities complies with all special handling requirements as stated in the Material Safety Data Sheet included in Appendix 4.1.

Fluoride Manufacturing Process

All of the fluoride chemicals used in the United States for water fluoridation (sodium fluoride, sodium fluorosilicate, and HFS) are byproducts of the fertilizer industry. The process diagram of how fluorides are obtained during the manufacture of phosphoric acid is shown in Appendix 4.2, Figures 1 and 2.

Methods of Application

Fort Collins utilizes a liquid feed system to apply the optimum level of fluoride at all times. The equipment consists of the unloading station, bulk tank, day tank, pumping system, and flow measurement system. The system is monitored around the clock, 365 days per year. The amount of fluoride added is determined by measuring the background fluoride concentration in the raw (untreated) water supply. Typical background levels range from <0.15 - 0.25 mg/L of fluoride (Figure 1). Once the background levels are established, the amount of fluoride added is set to maintain the desired optimal range of 0.7 - 1.2 mg/L of fluoride. Fort Collins Utilities ensures that the amount of fluoride added is at the optimum level (1.0 mg/L) as recommended by the CDPHE and the U.S. Environmental Protection Agency (EPA). (See Report Form 1 in Appendix 4.3)
Daily samples of water are measured in the City of Fort Collins Water Treatment Facility Process Laboratory (Figure 2). The analytical methods used are the specific electrode method (Standard Methods for the Examination of Water and Wastewater, 19th edition, 4500-F C). In addition to routine sampling for the raw and finished water, samples are analyzed throughout the city for many different parameters. See the Fort Collins Utilities Drinking Water Consumer Confidence Report, 2001 at http://fcgov.com/water/pdf/wqr2001.pdf and in Appendix 4.4. At all times, on-line monitoring equipment alert operators to any change in feed rates for chemical addition.
Split samples are conducted on a routine basis between Fort Collins Utilities Water Quality Laboratory, the Fort Collins Utilities Process Lab and the CDPHE. The Fort Collins Utilities Water Quality Laboratory is a CDPHE and EPA certified laboratory and all data for quality assurance is reviewed on an annual basis. Results are reported to the CDPHE on a monthly basis (see Report Form 1 in Appendix 4.3).

**Water Quality**

The Fort Collins Water Treatment Facility uses a number of chemicals in the water treatment process to treat the raw untreated water. All of the chemicals used at the facility must meet specific industry accepted quality standards. Two of the standards utilized by Fort Collins Utilities are 1) American Water Works Association (AWWA) and 2) National Sanitation Foundation Standard 60 for Water Treatment (NSF) which can be found at www.nsf.org.

Upon receiving each load of HFS, the Fort Collins Utilities samples the product and runs a specific gravity test to verify the solution strength. Samples are stored for further analytical verification if warranted. As per industry standards, inorganic chemistry analyses are not routinely performed on each shipment. Each shipment requires a certification assuring compliance for each load (see NSF Certification in Appendix 4.4). The FTSG found that the vendor used by the City of Fort Collins meets or exceeds the standards set forth by AWWA and the NSF. In addition to chemical standards, the City of Fort Collins must comply with standards set forth by the EPA. The City of Fort Collins complies with all regulations and in many cases exceeds the minimum requirements (see Appendix 4.5 – Fort Collins Utilities Drinking Water Consumer Confidence Report, 2001 also available at http://fcgov.com/water/pdf/wqr2001.pdf).

**Analytical Information**

The FTSG reviewed data from the City of Fort Collins Water Quality Laboratory with respect to its Annual Water Quality Summary. Summaries for 2001 and 2002 are included in Appendix 4.6 and are available at http://fcgov.com/water/pdf/2001wqt.pdf.

Data is shown for Arsenic and Lead (Figures 3 and 4). Other parameters evaluated were Iron, Copper, Manganese, Zinc, Cadmium, Molybdenum, and Nickel. These can be found in Appendix 4.7 as Figures 3 – 9. These data represent values collected each week for a period from January 1997 - 2001. This data set was chosen for figures that are based on mean values for weekly samples for the time period indicated. Along with other water quality parameters, the FTSG reviewed each inorganic constituent in regards to trends or changes. The FTSG reviewed data for pH in the untreated and finished water and one distribution system site (Poudre Valley Hospital) as well (Figure 5).

The following graphs represent the values for the raw water, finished water, and the Maximum Contaminant Level (MCL) or the Secondary Maximum Contaminant Level (SMCL) for each parameter shown. For a description on MCL and SMCLs, please refer to the Consumer Confidence Report located in Appendix 4.
Fort Collins monitors its treated water regularly for arsenic, lead and other potential contaminants. Figure 3 shows the concentration of Arsenic (As) in both sources of raw, untreated water, the finished drinking water, Poudre Valley Hospital (PVH), and the SMCL is for arsenic. The EPA maximum concentration level for arsenic is 50 \( \mu g/\text{liter} \), but has been reduced to 10 \( \mu g/\text{liter} \) effective in 2006 due to the fact that arsenic is a recognized human carcinogen.

The levels of 2.0 \( \mu g/L \) shown on the chart are the detection limits of the test instruments for arsenic. The concentration of arsenic in the source waters is below the detection limit for arsenic of 2.0 \( \mu g/L \). The concentration in the finished water is also below the detection limit of 2.0 \( \mu g/L \). Because arsenic levels are below the detection limits both before and after the addition of HFS, the actual changes in arsenic concentrations are not measurable.

In response to citizen concerns, Fort Collins Utilities had a single batch of HFS tested on May 17, 2001 using EPA Method 200.7 at the Utility's Pollution Control Laboratory. This laboratory scored 100% accuracy on all analytes of the 2001 EPA required DMR-QA "unknown" performance audit samples. In this sample, the HFS measured contained 29.0 mg/L arsenic. In addition, an analytical result from one former supplier (PENCO, Inc.), measured in 1993, indicated an arsenic concentration of 61 mg/L. The FTSG estimated the effect of the addition of arsenic contained in HSF on the concentration of arsenic in the finished water (Arsenic Concentration in Finished Water in Appendix 4.8). Using these two measures (29.0 mg/L and 61 mg/L) and conservative assumptions regarding the analytical method and the volume dilution, it was estimated that the additional contribution to the arsenic concentration in finished water is approximately between 0.10 \( \mu g/L \) to 0.24 \( \mu g/L \) (or 0.10 ppb to 0.24 ppb).

\[ 50 \mu g/L \text{ is approximately equivalent to 50 part per billion (50 ppb). In other words 50 } \mu g/\text{liter is similar to saying the MCL is fifty “drops” of arsenic in one billion “drops” of water.} \]

\[ 0.10 \text{ or 0.10 ppb is approximately equal to saying “one tenth of a “drop” of arsenic in one billion “drops” of water. The range could be interpreted as saying there is between one tenth to one quarter of a drop of arsenic in one billion drops of treated water”} \]
Lead (Pb) levels for both source waters, Fort Collins Utilities finished drinking water, Poudre Valley Hospital (PVH), and the MCL are shown in Figure 4. The concentration of lead in the source waters is below the detection limit for lead in the department’s laboratory of 1.0 µg/liter. Because lead levels are below the detection limits both before and after the addition of HFS, the actual changes in lead concentrations are not measurable.

Fort Collins Utilities implemented a corrosion control program in 1983 and maintains pH levels in finished water leaving the treatment facility at values of 7.8 to 8.0 (acidic is 6.9 and lower, neutral is 7.0 and alkaline is 7.1 and above). As shown in Figure 5, the addition of HFS at the amount applied is not decreasing pH to an acidic level that could be corrosive to plumbing materials.

Figure 7. pH
UNCERTAINTIES

Safety of Hydrofluorosilicic Acid

Members of the public have raised concerns that HFS has not been adequately tested for safety in experimental animals since virtually all of the initial testing in animals was done with sodium fluoride. The National Toxicology Program (NTP) continuously solicits and accepts nominations for toxicological studies to be undertaken by the program on substances of potential human health concern. Nominations can come from Federal agencies, industry, the public, and other interested parties and undergo several stages of review before selections for testing are made. Possible public health consequences of exposure are the overriding factors considered in selecting substances. Nominations are first reviewed internally and toxicological summaries based on an extensive literature review are prepared. The summary is then distributed to the NTP Interagency Committee for Chemical Evaluation and Coordination (ICCEC). The ICCEC is composed of representatives from the Agency for Toxic Substances and Disease Registry, the Consumer Product Safety Commission, the Department of Defense, the Environmental Protection Agency, the Food and Drug Administration's National Center for Toxicological Research, the Occupational Safety and Health Administration, the National Cancer Institute, the National Institute of Environmental Health Sciences, the National Institute for Occupational Safety and Health, and the National Library of Medicine. Evaluation by the ICCEC is the initial external review step. The ICCEC makes testing recommendations and priorities. These recommendations are presented to the NTP Board of Scientific Counselors (BSC) for review and comment in an open public session. The BSC's recommendations are then submitted to the NTP Executive Committed for review and final approval (Federal Register: March 2, 2000, Volume 65, Number 42, pp. 11329-11331).

HFS was nominated to the NTP by Mr. Coplan (of Masters and Coplan) and other private individuals in 2001 for “chemical characterization, toxicological characterization including chronic toxicity, carcinogenicity, neurotoxicity, and toxicokinetics, [and] mechanistic studies related to cholinesterase inhibition and lead bioavailability.” According to the toxicological summary for nomination, “Sodium hexafluorosilicate and fluorosilicic acid were nominated for toxicological testing based on their widespread use in water fluoridation and concerns that if they are not completely dissociated to silica and fluoride in water that persons drinking fluoridated water may be exposed to compounds that have not been thoroughly tested for toxicity.” On April 17, 2002, the ICCEC recommended, “chemical characterization studies to assess chemical fate under aqueous conditions. Toxicological studies may be considered when results of chemical characterization studies are available for review” (Federal Register: June 12, 2002, Vol. 67, No. 113, pp. 40329 -40333). The nomination is now in the hands of the NTP Board of Scientific Counselors.

The public concern that HFS has not been tested for toxicity can be addressed by a better understanding of the chemical fate of fluorosilicate drinking water additives as presented by a review by Urbansky in 2002. Quickly upon addition to water supplies, HFS reaches an equilibrium where, according to Urbansky (2002, p. 2843), “the hexafluorosilicate molecule is totally decomposed to a silicic acid molecule, four hydrogen cations and six fluoride anions.” Furthermore, the "dissolved silica contribution of the fluoridating agent is trivial compared to the native silica" (Urbansky, 2002, p. 2844). Complicated fractional distribution plots for fluoride species as a function of pH presented by Urbansky (2002) illustrate the proportion of each species at equilibrium. The conclusion drawn by Urbansky from a review of these diagrams are that “The concentration of any fluorosilicate species is extremely small at drinking water pH”(Urbansky, p 2844). For example:

“It is concluded that in any drinking water supply with a pH of 5 or higher, fluoridated with sodium silicofluoride [HFS] to the extent of 16 ppm of F or less, all of the silicofluoride is completely hydrolyzed to silicic acid, fluoride ion, and hydrogen fluoride. There can be no question of toxicity of SiF4 or SiF6-2 under such conditions” (Urbansky, pp. 2844 & 2845).
While Urbansky states (2002, p. 2850) that, "The kinetics of the dissociation and hydrolysis of hexafluorosilicate are poorly understood from a mechanistic or fundamental perspective." the take home message by Urbansky for non-chemists is that, "the rate data suggest that equilibrium should have been achieved by the time the water reaches the consumer's tap if not by the time it leaves the waterworks plant" (Urbansky, 2002, p. 2850). So while further research is being conducted on this subject, Urbansky states on page 2851, "we must try to make the best use of the information available to us and focus on the consistencies as well as what is unequivocally established as chemical fact." The Urbansky review suggests that fears over HFS and the unknown toxicity of any resulting fluoride species as the HFS quickly dissociates to fluoride ion and the other chemical species may be unfounded when the fundamental chemical facts are considered.

On April 25, 2002, the EPA released a request for research on the hexafluorosilicates in a Request For Assistance (RFA).

"The primary objective of this RFA is to investigate the reactions that take place when fluorsilicates are added to drinking water supplies and what concentrations of which fluorsilicate species may monitored in finished drinking water supplies and what techniques may be used for such monitoring" (The RFA is issued under the name of Edward T. Urbansky, U.S. EPA, National Risk Management Research Laboratory Water Supply and Water Resources Division).

**Potential for Increased Absorption of Lead**

Studies published in 1999 and 2000 of 280,000 children in Massachusetts and 151,000 children in New York showed an increase in the prevalence of blood lead concentrations in children's blood in communities in which fluorsilicates [HFS] were used for community water fluoridation (Masters & Coplan, 1999; Masters, Coplan, Hone, & Dykes, 2000). The increases were from 1.9% above 10 ug/dl, to 2.9% above 10 ug/dl. The 1999 study (Masters & Coplan) concluded "the fluoridation agents used in water treatment have a major effect on lead levels in children's blood." They found that lead levels were significantly lower in communities that used sodium fluoride, or did not fluoridate, than those who used silicofluorides (SiF) such as hydrofluorosilicic acid (Masters & Coplan, p. 440).

The study published in 2000 concluded, “For every age/race group, there was a consistently significant association of SiF treated community water and elevated blood lead.” In addition, they found poor black children in old housing to be at a higher risk of elevated blood lead if their community provided silicofluoride-treated water (Masters, Coplan, Hone, et al., 2000).

Because of the ecologic design of the Master’s studies, the possibility that the findings are due to confounding cannot be ruled out. The data show that 49.4% of the homes in communities treated with silicofluorides were built before 1939. Conversely, 23.3% of the homes in the communities not treated with silicofluorides were built before 1939. Similarly, 22.3% of the children in silicofluoride-treated communities were below the poverty level while 8.5% of children in non-silicofluoride treated communities were below the poverty level. The method of analysis in the Masters, Coplan, Hone, et al (2000) paper relied on classifying covariates as above and below the median for each risk factor, potentially resulting in misclassification of exposure to the confounder (e.g. poverty) by inclusion of large numbers of subjects in the category considered exposed to the confounder. In addition, the age of the house in which the child resided and the age of the water distribution system infrastructure would be expected to differ across communities characterized by differences in age of housing. There is therefore a possibility of differences in lead containing piping through the distribution system. There also may be differences in exposure to household sources of lead. For example, the increased tendency of poor or malnourished children to chew on objects such as window-sills, to eat dirt, and to mouth objects...
potentially contaminated with lead flakes from chipped paint. These differences are not accounted for in the analysis and may have been responsible for the differences observed in blood lead concentrations.

A possible mechanism proposed by Masters and Coplan (1999, p. 437) for the putative increase in lead is the lowering of drinking water pH by addition of HFS (a strong acid) in poorly buffered water supplies leading to a pH dependent increase in lead solubility (Stumm & Morgan, 1996). This mechanism is only plausible for poorly buffered water supplies such as those studied by Masters et al. The Fort Collins water supply is maintained at a well buffered pH greater than 7 (neutral to alkaline), as shown in figure 5, and as such lead solubility should not be increased through the addition of small amounts of HFS. To the extent that the mechanism of lead increase is due to HFS induced changes in pH and therefore lead solubility, Fort Collins drinking water lead concentrations are not susceptible to this reported side effect of HFS addition.

No other plausible biological/chemical mechanism for the source of the increases in blood lead has been proposed in the literature. Studies with stronger designs would be needed to fully address any remaining uncertainties.

The Medical Research Council of Great Britain stated the following:

> “Two recent studies (Masters & Coplan, 1999; Masters, et al., 2000) have found an association between ingestion of drinking water treated with silicofluorides and elevated blood lead in children…. However, according to the US EPA there is no substantive evidence to suggest that fluoridation of drinking water with any fluoridating chemical increases the concentration or bioavailability of lead in drinking water via chemical reactions in the plant, the distribution system, the home plumbing system, or the human body itself (Urbansky & Schock, 2000). This appears to be a controversial area and further studies are awaited” (Medical Research Council Working Group, 2002, p. 36).

Peer review of the Masters and Coplan report, coming at the request of US EPA and Urbansky, has confirmed Urbansky and Schock’s critique. The peer review letters are included as Appendix 4.X to this report.

**Lead Levels in Colorado Children**

The issue raised by a pair of papers by Masters and Coplan - that exposure to HSF in drinking water might be a risk factor for elevated lead levels in children - could make information regarding the prevalence of elevated blood lead levels in children in our area relevant to decision makers. The Colorado Board of Health recommends that all low-income children in Colorado should be routinely screened for blood lead levels at 12 months and 24 months of age or between the ages of 36 months and 72 months of age if they have not been previously screened (Colorado Childhood Blood Lead Screening Plan, CDPHE, 2001). Low-income children are identified as children eligible for Medicaid, Child Health Plan Plus, or the Colorado Resident Discount Program, and children residing in certain areas in Denver found to be high risk. A report released in April 2002 by the Colorado Department of Public Health and Environment Lead Poisoning Prevention Program reports that the proportion of children with one or more elevated blood lead levels (≥10 mcg/dl) in the period 1/1996 through 12/2001 was 1.5% (95% C.I., 0.8%-2.1%) in Larimer County, one of the lowest proportions among the ten largest counties in Colorado (see Table 1). Statewide, the proportion of children tested who were found to have elevated blood lead levels was 2.7% (95% C.I., 2.5%-2.9%) during this period. It is important to note that this data represents only a fraction
of children defined as high risk and may not be representative of all low-income high risk children. However, the proportion of all children in our community with elevated lead levels would be expected to be lower than those reported above. Masters and Coplan reported elevated lead levels from a survey of children 0-6 years old in Massachusetts in 1991, based on the fluoridation status of community of residence. Lead levels were elevated in 3.0%, 2.9%, 1.6% and 1.9% of communities fluoridated with silicofluoride compounds (SFC), hydrofluorosilicic acid (HFS), sodium fluoride and no fluoride, respectively.

Mean lead levels have been decreasing since the late 1970s attributed primarily to the phase-out of leaded gasoline. A national sample of children ages 1 to 5 years found a decrease from 2.7 (95% C.I., 2.6-2.9) mcg/dl in 1991-94 to 2.0 (95% C.I., 1.7-2.3) in 1999 (MMWR. 49(50):1133-7, Dec 2000).

In recent years the most common source of lead in children with elevated lead levels is from lead based paint that is poorly maintained in older homes. Low-income children living in older housing have been found to be at much higher risk of elevated blood lead levels than other children (CDC, Blood lead levels in young children—United States and selected states, 1996-1999, MMWR 49(50):1133-7). In Larimer County (see Table 1) there are a relatively low proportion of residences deemed high-risk—defined as “housing unit built before 1950 and occupied by a low income family” (based on 1990 US Census data, see http://www.scorecard.org/).

Table 1
Blood Lead Levels In Colorado Counties, 1996-2001

<table>
<thead>
<tr>
<th>County</th>
<th># ≥10 µg/dl</th>
<th>Total tests</th>
<th>% ≥10 µg/dl</th>
<th>Est. 95% C.I.</th>
<th>% of 6-72 month olds screened</th>
<th>% of housing units with high-risk of lead hazards</th>
<th>% of population on Fl water</th>
<th>% of population on HFS or SFC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adams</td>
<td>20</td>
<td>546</td>
<td>3.7%</td>
<td>2.1%, 5.2%</td>
<td>0.4%</td>
<td>0.7%</td>
<td>15%</td>
<td>11%</td>
</tr>
<tr>
<td>Arapahoe</td>
<td>48</td>
<td>1787</td>
<td>2.7%</td>
<td>1.9%, 3.4%</td>
<td>1.1%</td>
<td>0.3%</td>
<td>64%</td>
<td>64%</td>
</tr>
<tr>
<td>Boulder</td>
<td>17</td>
<td>563</td>
<td>3.0%</td>
<td>1.6%, 4.4%</td>
<td>?</td>
<td>1.4%</td>
<td>92%</td>
<td>90%</td>
</tr>
<tr>
<td>Denver</td>
<td>461</td>
<td>17362</td>
<td>2.7%</td>
<td>2.4%, 2.9%</td>
<td>7.8%</td>
<td>5.7%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>ElPaso</td>
<td>26</td>
<td>1849</td>
<td>1.4%</td>
<td>0.9%, 1.9%</td>
<td>1.3%</td>
<td>1.2%</td>
<td>8%</td>
<td>3%</td>
</tr>
<tr>
<td>Jefferson</td>
<td>20</td>
<td>798</td>
<td>2.5%</td>
<td>1.4%, 3.6%</td>
<td>0.7%</td>
<td>0.4%</td>
<td>44%</td>
<td>43%</td>
</tr>
<tr>
<td><strong>Larimer</strong></td>
<td><strong>20</strong></td>
<td><strong>1376</strong></td>
<td><strong>1.5%</strong></td>
<td><strong>0.8%, 2.1%</strong></td>
<td><strong>3.4%</strong></td>
<td><strong>1.7%</strong></td>
<td><strong>95%</strong></td>
<td><strong>94%</strong></td>
</tr>
<tr>
<td>Mesa</td>
<td>14</td>
<td>471</td>
<td>3.0%</td>
<td>1.4%, 4.5%</td>
<td>2.6%</td>
<td>2.7%</td>
<td>98%</td>
<td>98%</td>
</tr>
<tr>
<td>Pueblo</td>
<td>34</td>
<td>972</td>
<td>3.5%</td>
<td>2.3%, 4.7%</td>
<td>1.8%</td>
<td>6.4%</td>
<td>89%</td>
<td>87%</td>
</tr>
<tr>
<td>Weld</td>
<td>74</td>
<td>2518</td>
<td>2.9%</td>
<td>2.3%, 3.6%</td>
<td>2.4%</td>
<td>3.8%</td>
<td>76%</td>
<td>74%</td>
</tr>
</tbody>
</table>

\(^{a}\) Childhood Lead Poisoning in Colorado, Colorado Department of Public Health And Environment, April 2002 (http://www.cdphe.state.co.us/dc/\//Lead/survbullet2.PDF)

\(^{d}\) 95% confidence intervals were calculated using a normal approximation to the binomial distribution assuming a random sample of \(n = \text{total tests}\)

\(^{c}\) Environmental Defense Fund, Scorecard, Colorado Counties (http://www.scorecard.org/), based on 1990 Census data.


HFS: hydrofluorosilicic acid; SFC: silicofluoride compounds.

The data for statewide blood levels exceeding 10 µg/dl are important to the considerations by the FTSG and decision makers for several reasons:

\(^{3}\) In the 3\(^{rd}\) quarter of 2001 in Larimer County, approximately 3,725 of 18,527 6-72 month olds met the definition of high-risk based on Medicaid or CHP enrollment (20%). Of these about 1,850 would have been eligible for a lead test in 2001 (became either 12 or 24 months of age). However only 622 children were screened (34%).
1. They provide information about childhood blood levels and community water fluoridation and other conditions that may affect blood lead that are relevant to our local conditions. Local conditions include age of housing, use of lead piping in distribution and household water systems, use of lead paint, and socio-economic and demographic factors.

2. The data from CDPHE can be screened on an ecologic basis, similar to the approach taken by Masters and Coplan (1999, 2000) in their analyses of blood lead in Massachusetts, New York and elsewhere. Masters and Coplan conducted their analyses at the community level (not on individuals). In Colorado, the analysis is done at the county level with the available data.

From a qualitative basis, there is a lack of association between community water fluoridation with HFS and the percent of children with blood lead > 10 µg/dl. The highest prevalence of elevated blood lead is seen in Adams County (3.7%) where 11% of the population receive HFS fluoridated water. Larimer County and El Paso County have the lowest prevalence of elevated blood lead (1.4% and 1.5%, respectively). El Paso County (containing Colorado Springs) has high naturally occurring concentrations of fluoride in their water supply and most communities within the county (including Colorado Springs) do not use community fluoridation. Larimer County, similar in many aspects to El Paso County (e.g. the percent of housing with high risk lead hazards is 1.7% and 1.2%, respectively) also has a very low prevalence of elevated blood lead, and provides 94% of its population with water fluoridated with HFS.

Qualitatively, there is a lack of relationship between community fluoridation with HFS and blood lead in the data for these two counties. The lack of relationship between HFS and blood lead in these two counties would not be expected to occur if the hypothesized association as postulated by Masters and Coplan was causal.

From a quantitative perspective, the data in Table 1 can be subjected to regression analyses to determine whether there is evidence of a statistical association between child blood lead and use of HFS at the county level. The results of our analyses are provided in Appendix 4. The r-squared value provides a measure of the variation in the dependent variable (prevalence of elevated blood lead) explained by the independent variable (% HFS treated water or % of housing units with high-risk lead hazards). The county analysis for percent of population supplied by HFS shows no relationship (r-squared = 1.9%, p > 0.7). The analysis for % of housing units with high-risk lead hazards also shows very little correlation (r-squared = 8.8%, p > 0.4). When both variables are placed in the model, the r-squared is 8.9%, p > 0.7. The partial correlation coefficient was calculated to estimate the degree of correlation between elevated blood lead and the % of population supplied by HFS, controlling for % of housing units with high-risk lead hazards. This analysis shows no significant correlation (r-squared =0.12%, p >0.9) between elevated childhood blood lead and percent of the population receiving HFS treated water in Colorado counties. These data have been adjusted for potential confounding by the percent of housing with high-risk lead housing in each county. There were no data available to evaluate other potential confounders such as age and race.
FINDINGS: The Potential for Increased Contaminate Levels Due to the Use of Hydrofluorosilicic Acid

The FTSG’s review identified three potential concerns associated with hydrofluorosilicic acid (HFS): 1.) co-contamination (i.e. arsenic and lead), 2.) decreased pH leading to increased lead solubility or exposure, and 3.) potential toxicological effects from incomplete dissociation products of HFS. The FTSG used the raw and finished water quality data for the City of Fort Collins to determine whether the addition of HFS was responsible for the potential addition of contaminants such as heavy metals to the city's drinking water. There were no evidence that the addition of HFS increased the concentrations of copper, manganese, zinc, cadmium, nickel, or molybdenum. The concentrations of arsenic and lead were below the detection limit for the Fort Collins Water Quality Control Laboratory in both the source water and the finished water and below the maximum contaminant level (MCL) for these naturally occurring elements. There was no evidence that the introduction of HFS changed the pH of the water appreciably. Concern that HFS incompletely disassociates may be unfounded when the fundamental chemical facts are considered. Therefore, it is unlikely that community water fluoridation poses a health risk from the exposure to any of these chemicals present in the water as it leaves the plant. Further studies related to the health effects of HFS are in progress.
Reference List


APPENDIX A-1
Fort Collins Fluoride Technical Study Group Reference List

“TIER ONE”
Reviews by widely recognized national and international public health agencies


**Other Literature Reviewed***

* In some cases only abstracts were reviewed


in their drinking water. *Caries Research, 29*(2), 137-142.


Jacobsen, S. J., O'Fallon, W. M., & Melton, L. J. (1993). Hip fracture incidence before and after the fluoridation of


The Lord Mayor’s Taskforce on Fluoridation. (1997). The Lord Mayor’s Taskforce on Fluoridation - Final Report to Brisbane City Council. Brisbane, Australia.


**Materials Submitted by Members of the Public**

These were reviewed by at least 3 members of the FTSG. Some submissions (including published and peer-reviewed journal articles) are included above. This list represents a best-possible representation of submitted materials. In some cases proper referencing information was lacking and this list does not conform to the APA Publication Manual guidelines.

A concise critical bibliography of fluoride. (February 13, 2002). Compiled by Eric Levine.


Assorted anti-fluoride information. No publication source/author.


Biologic Effects of Atmospheric Pollutants - Fluorides

Brunson, Diane. (May 10, 2001). *Commentary to the residents of Colorado.*


Cities rejecting fluoridation of water since 1990.

Citizens for Safe Drinking Water. Fluoridation on-point – congressional investigation and recent events.


Citizens for Safe Drinking Water. Three reasons why those who supported the use of fluoride say no to fluoridation today.


DAMS, Inc. Fluoride is an unapproved drug. International DAMS Newsletter.


Fluoridation negatives published in The Lancet. True Health, date, volume and number unknown.


Fluoridation: The Great Dilemma – Miscellaneous Information


Fluoride of drinking water bibliography, no author, no date.


Glasser, George. Citizen writer uncovers overlooked, vital facts about fluoride toxicity. True Health.


Hip fracture rates are much higher in people residing in fluoridated communities. (Miscellaneous information).

Hirzy, William J. (April 6, 2000). Letter to San Diego City Council (Including 20 letters from other countries regarding fluoridation of drinking water.

Hirzy, William J. (June 29, 2000). Statement for National Treasury Employees Union Chapter 280 Before Subcommittee on Wildlife, Fisheries, and Drinking Water United States Senate.

Hirzy, William J. (May 1, 1999). Why EPA’s headquarters union of scientists opposes fluoridation. The National Treasury Employees Union.


Insight Magazine. (Dec 2002) Reinforcements arrive in campaign against fluoride.


Pit and Fissure Tooth Decay and Fluoridation – Miscellaneous Information

Prystupa, Jeff (editor). Fluoride: A matter of choice? No date or publication information.

Publications of interest on community water fluoridation bibliography. No author, no date.

Reeves, Thomas G. (2001). Arsenic MCL. A Report From a National Fluoridation Engineer at the National Center for Chronic Disease Prevention and Health Promotion.

Reeves, Thomas G. (March 2001). The fluoride ion. A report From a National Fluoridation Engineer at the National Center for Chronic Disease Prevention and Health Promotion.


Responding to questions about community water fluoridation and fluoride products. No author or publication information available.

Satcher, David. (September 8, 2000). Address at the National Fluoridation Summit.


SENES Oak Ridge Inc. Center for Risk Analysis Review of California Oral Health Needs Assessment


Wade, Roger, Director of Public Health, Natick Board of Health. (August 13, 2002). Natick Study Results.

Yiamouyiannis, John. Fluoride the aging factor: How to recognize and avoid the devastating effects of fluoride, pp. 42-43, 118-131, 204

**APPENDIX A-2**

**Fluoride Mass Balance Calculations**

**City of Fort Collins Water Treatment Facility**

**Background**

The amount (pounds/day) of fluorosilicic acid (HFS) added at the Water Treatment Facility is continuously measured and controlled by the HFS chemical feed system in order to ensure the proper dosing of fluoride to the finished water. The concentration (mg/L) of fluoride ion in the raw and finished water is measured by the Water Treatment Facility Process Control Lab in order to verify the dosing of fluoride to the finished water. The question being addressed here is:

Does the concentration of fluoride ion measured by the Process Control Lab agree with the quantity of HFS that is dosed to the finished water?

This question is answered using process data for the month of February 2003. Note that the Process Control Lab uses an ion-selective electrode to determine the concentration of fluoride ions (F⁻) in water samples (Standard Method 4500-F⁻ C).

**Fluorosilicic Acid (HFS) Properties**

- Commercial Purity = 24.4% (the commercial product is 24.4% H₂SiF₆ and 75.6% water)
- Fluoride Ion Purity = 79.2% (pure H₂SiF₆ is 79.2% F⁻ by weight)

**Water Treatment Facility Process Data for February 2003**

- Total finished water produced during the month = 434.6 million gallons (MG)
- Total HFS added during the month = 15,381 pounds
- Measured fluoride ion in raw water = 0.20 mg/L (monthly avg., measured by Process Control Lab)
- Measured fluoride ion in the finished water = 1.00 mg/L (monthly avg. at Sample Station 2, measured by Process Control Lab)

Concentration of added fluoride ions determined from known quantity of added HFS

\[
\text{Mass of F}^{-} \text{ added} = (\text{pounds of HFS added}) \times (\text{Commercial Purity}) \times (\text{Fluoride Ion Purity})
\]

\[
= (15,381 \text{ pounds}) \times (0.244) \times (0.792)
\]

\[
= 2,972 \text{ pounds of fluoride added during the month of Feb. 2003}
\]

\[
\text{Concentration of added F}^{-} \text{ in the finished water (mg/L)}
\]

\[
= \left( \frac{\text{pounds of added F}^{-}}{\text{Volume of Finished Water, MG}} \right) \times \left( \frac{1 \text{ mg/L}}{8.34 \text{ lb/MG}} \right)
\]

\[
= \frac{2,972 \text{ lb}}{(434.6 \text{ MG}) \times (8.34 \text{ lb L/MG mg})}
\]

\[
= 0.82 \text{ mg/L}
\]
Compare concentration of fluoride ion measured by the Process Control Lab to the concentration determined using the known quantity of HFS dosed to the finished water

\[
\begin{align*}
\text{Concentration determined by Process Control Lab} & = 0.80 \text{ mg/L} \\
\text{Concentration determined from known quantity of added HFS} & = 0.82 \text{ mg/L}
\end{align*}
\]

The two values differ by less than 3 percent, which is a very acceptable margin of error. These values show that the fluoride ion concentration detected by the lab agrees with the quantity of HFS that is dosed to the finished water. The data further indicate that the hydrolysis of HFS to form fluoride ions is essentially 100% complete before water leaves the Water Treatment Facility.
APPENDIX 1
Effectiveness of Community Water Fluoridation
Methodological Approaches of “Tier One” and Other Reviews

A vast literature has accumulated on the effectiveness of fluoride in decreasing tooth decay since the 1940s. Conducting a systematic analysis of the evidence of effectiveness was beyond the scope of the FTSG. Instead the committee sought recent comprehensive reviews conducted by expert panels in which precautions were taken to limit review biases. The following questions guided the Fluoride Technical Study Group’s (FTSG) appraisal of the reviews included (based on Andrew Oxman’s work in Sackett, et. al, 1991, p. 380):

1. Were the questions and methods clearly stated?
2. Were the search methods used to locate relevant studies comprehensive?
3. Were explicit methods used to determine which studies to include in the review?
4. Was the methodologic quality of the primary studies assessed?
5. Were the selection and assessment of the primary studies reproducible and free from bias?
6. Were differences in individual study results adequately explained?
7. Were the results of the primary studies combined appropriately?
8. Were the reviewer’s conclusions supported by the data cited?

The following list identifies the reviews considered by the FTSG, and describes the approach each reviewing body used to find, select and rate the quality and quantity of evidence of effectiveness. Among these, there were two formal systematic reviews—the 2002 review by the Task Force on Community Preventive Services and the 2000 review by the NHS Center for Reviews and Dissemination at the University of York.

“Tier One” Reviews


Sponsoring entity: Centers for Disease Control and Prevention
Researchers affiliation: Fluoride Recommendations Work Group, CDC

Methods: Explicit search and selection criteria were not established. Relied on judgment of expert panel members. “Evidence was drawn from the most relevant English-language, peer-reviewed scientific publications regarding the current effectiveness of fluoride modalities” (CDC 2001a, p. 19). Members collectively agreed on the quality of evidence. The criteria were adapted from the U.S. Preventative Services Task Force.

Conclusion: “Despite the strengths of early studies of the efficacy of naturally occurring fluoride in community drinking water, the limitations of these studies make summarizing the quality of evidence on community water fluoridation as Grade I [randomized controlled trials] inappropriate. The quality of evidence from studies on the effectiveness of adjusting fluoride concentration in community water to optimal levels is Grade II-1 [included controlled clinical trials without randomization]. Research limitations are counterbalanced by broadly similar results from numerous well-conducted field studies by other investigators that included thousands of persons throughout the world” (Centers for Disease Control and Prevention [CDC], 2001a, p. 20).


Sponsoring entity: US Department of Health and Human Services, with support from the CDC and other federal agencies, public and private partners.

Researcher affiliations: The Task Force is an independent, non-federal expert committee and consists of 15 members, including a chair, appointed by the Director of the CDC. The Task Force’s membership is multi-disciplinary, and includes perspectives representative of state and local health departments,
managed care, academia, behavioral and social sciences, communications sciences, mental health, epidemiology, quantitative policy analysis, decision and cost-effectiveness analysis, information systems, primary care, and management and policy. The purpose of the Task Force is to “review and assess the quality of available evidence on the effectiveness and cost-effectiveness of essential community preventive health services, and develop recommendations.”

(http://www.thecommunityguide.org/home_f.html)

Methods: The Task Force uses an explicit systematic approach to reviewing the evidence on a preventive intervention: Search strategy included multiple electronic database searches, bibliography/reference searches, and consultation with experts.

Inclusion criteria: From 1966 to 12/2000, human, community water fluoridation, published in English, Established Market Economies, two groups with differing exposures to fluoride, tooth-level caries or other caries measures reported.

Quality: Assessed by 2 reviewers.

Suitability of study design: A: prospective before and after measures of tooth level caries and concurrent comparison group, B: studies not in A with post-exposure measures of tooth-level caries and concurrent comparison group, C: other comparison designs and measures. Included only first 2.

Threats to validity: Considered potential selection, confounding and measurement biases; rated good, fair and limited; included only the first two.

Overall: number of studies, suitability of study designs, the quality of execution, the consistency of results and the effect size. 4000 citations reviewed (oral health promotion); 21 met inclusion criteria and minimum quality standards (9 A, 7 B, 5 C).

Conclusion: “Starting or continuing community water fluoridation effectively prevents dental caries in communities at varying levels of baseline caries prevalence (centers 2001b, p. 8): Estimated: % reduction in tooth level caries: 29.1% median decrease (7 A studies); 50.7% median decrease (7 B studies); 17.9% median increase (3 A studies), 59.5% increase (1 B study).


Sponsoring entity: The review was requested and commissioned by the U.S. Assistant Secretary of Health, DHHS.

Researcher affiliations: The study was conducted by the USPHS Committee to Coordinate Environmental Health and Related Programs (CCEHRP). The CCEHRP is comprised of all USPHS agencies with responsibilities for health programs. These agencies include: the Agency for Toxic Substances and Disease Registry; the Alcohol, Drug Abuse and Mental Health Administration; the Centers for Disease Control and Prevention; the Food and Drug Administration; the Health Resources and Services Administration; the Indian Health Service; and the National Institutes of Health. The report was prepared by a specially created sub-committee of the CCEHRP, the Ad Hoc Subcommittee on Fluoride.

Methods: “The Subcommittee performed an extensive examination of the worldwide biomedical literature on fluorides and health. To ensure public input, an announcement was published in the Federal Register on March 1, 1990, soliciting peer reviewed published articles on fluorides.” (USPHS, 1991, p. iv) The Subcommittee addressed the relationship between fluorides and caries with respect to the epidemiological criteria for causality: “detecting an association, seeking a dose-response relationship, replicating the findings under a variety of circumstances and by different investigators, excluding alternative explanations and observer bias, finding biological plausibility for the relationship, and observing the disappearance of the effect when the cause is removed.” (USPHS, p. 18). Previously published comprehensive reviews were updated through 1990. The Subcommittee did not use explicit criterion for assessing the quality of studies, instead addressing threats to validity by examining and excluding alternative explanations for individual study results (for assessment of alternative explanations for studies examining caries reductions, see USPHS, 1991, pp. 26-28).

Conclusion: “The reduction in dental caries among persons exposed to fluorides fulfills all the criteria for a causal relationship: an association was found with a dose-response effect, the findings were
replicated under a great variety of circumstances by different investigators, alternative explanations and observer bias have been excluded, the findings are biologically plausible, and the effect, prevention of dental caries, continues to show that the fluoridation of water supplies substantially reduces the scores of dental caries. The decline over time in difference in caries scores between fluoridated and non-fluoridated areas is due in part to the increased availability of fluorides in non-fluoridated areas, as in toothpaste and other vehicles for fluorides” (USPHS, 1991, p. 35).


The Expert Committee on Oral Health Status and Fluoride Use met for seven days in 1993 and adopted a consensus statement. Only a brief statement was made regarding the effectiveness of community water fluoridation. Approach to assessment of evidence of effectiveness was not stated in report. References cited included only reviews, including The USPHS, 1.5, and a comprehensive monograph published in 1991 (Murray, Rugg-Gunn, & Jenkins, 1991).


Sponsoring entity: National Health Service Research and Development Division, United Kingdom
Researcher affiliations: NHS Center for Reviews and Dissemination, University of York
Methods: Used an explicit systematic approach to reviewing the evidence. Search strategy included electronic and hand database searches, bibliography searches, World Wide Web and invitations to public and experts to submit references.
Inclusion criteria: Up to February of 2000, human, any language, community water fluoridation, two groups with differing exposures to fluoride, prospective with at least 2 points in time, percent caries free or tooth-level caries measures reported.
Quality: Assessed by two reviewers.
Selection of study population: A: prospective before and at least two years after measures of tooth level caries and concurrent comparison group, B: prospective studies not in A with post-exposure measures of tooth-level caries and concurrent comparison group, C: other comparison designs and measures. Included only first two.
Threats to validity: Considered potential selection, confounding and measurement biases; rated highest, moderate and lowest quality; included only the first two.
Overall: 3200 citations reviewed; 26 published and 5 unpublished studies met inclusion criteria. All but three were “before-after” study designs—the remaining three were follow-up studies. Summary measure using meta-regression was estimated: absolute reduction in tooth level caries: 2.25 teeth (inter-quartile range 1.28-3.63).
Conclusion: “The best available evidence suggests that fluoridation of drinking water supplies does reduce caries prevalence, both as measured by the proportion of children who are caries free and by the mean change in dmft/DMFT score. The studies were of moderate quality but of limited quantity. The degree to which caries is reduced, however, is not clear from the data available” (NHS Center for Reviews and Dissemination, 2000, p. xii).

Note – Other “Tier One” Reviews were not included because they were published prior to 1990 or did not address the effectiveness of community water fluoridation
Other Reviews


Sponsoring entity: City of Brisbane, Australia
Researchers affiliation: Panel of members from professional and community bodies, council members and citizens
Methods: Search included electronic database literature searches (Medline, Biological Abstracts), Internet searches, solicitations of references from public and experts, and invited presentations by two noted opponents to water fluoridation. Sufficient detail to replicate search strategy was not provided in report. Study inclusion criteria and approaches to weighing the quality of individual studies was not addressed in the main report. A commissioned paper on dental costs and benefits was not available for FTSG review.

Conclusion of review: “Task Force members were satisfied that the weight of evidence from the large number of studies in many different countries pointed overwhelmingly to a protective effect form water fluoridation. As outlined earlier, however, there were sharp differences of opinion about the extent of the benefits” (The Lord Mayor’s Taskforce on Fluoridation, 1997, 39).


Sponsoring entity: City of Calgary, Calgary Regional Health Authority
Researchers affiliation: University of Calgary
Methods: Search strategy was not detailed in report, but included literature searches by panel members, solicitations of references from public and experts, and invited presentations by two experts, one supporting and another opposing water fluoridation. Focus was on primary studies and review literature since 1989. Quality of evidence standards were established using model of the Canadian Task Force on the Periodic Health Examination but the results of applying these standards to individual studies was not reported. In the report, the evidence of effectiveness was discussed in the context of the pro-con expert presentation. Conclusion: Consensus on effectiveness among panel members could not be reached—four of five members of the panel produced a majority report: “The relative health benefits are now less than they were forty years ago, because of other sources of fluoride in the diet, better oral hygiene and better dental procedures, as well as a general improvements in overall health. However, these other improvements have not reduced the benefits of water fluoridation to the point where it is no longer needed” (Expert Panel for Water Fluoridation Review, 1998, p. 30). The lone dissenter, a bio-statistician, concluded that the “relative importance of beneficial effect of water fluoridation has decreased and may no longer be necessary” (Expert Panel for Water Fluoridation Review, 1998, p. 28).


Sponsoring entity: Public Health Branch, Ontario Ministry of Health & First Nations and Inuit Health Branch, Health Canada
Researchers affiliation: Community Dental Health Services Research Unit, University of Toronto

Quality: Assessed by one reviewer. Suitability of study design was the main criterion used to assess quality.
Treats to validity: Considered potential selection, confounding and measurement biases qualitatively; no rating of quality was attempted.
Overall: Unknown number of citations reviewed; 29 published studies met inclusion criteria. All but four were “before-after” study designs—four were cross-sectional studies. In addition to weak study designs, a variety of methodological flaws were identified which could either increase or decrease the effect size. The magnitude of the caries prevention effect was examined using two of the more robust studies conducted in the later 1990s. The reviewer concluded that caries reductions in the 1990s are relatively small in absolute terms, particularly in permanent teeth and that water fluoridation explains only a small part of the variation in caries experience between children.

Conclusion of review: “Given the weaknesses in design and the methodological flaws to which many of the studies were subject, the data from these more recent studies must be treated with some caution. While the balance of evidence overall suggests that water fluoridation does reduce caries experience, the magnitude of the effect is subject to a degree of uncertainty but is unlikely to be large in absolute terms.” And, “The few studies that have assessed rates of dental decay in communities where fluoridation has been discontinued do not suggest that dental decay increases to any significant degree” (Locker, 1999, p. 33).


Sponsoring entity: Town of Natick, Massachusetts

Researchers affiliation: None. Members of committee were “qualified, scientifically trained and experienced people” formed by town board.

Methods: Search methods: Committee identified proponents (the Board of Health) and opponents (two citizens of Natick) and asked each to supply a limited number of documents containing study reports as well as letters of endorsement for their perspective. “The committee was not constrained to limit its search to the above materials” but search and inclusion criteria were not defined. The report did not identify any attempts to rate the quality of evidence of effectiveness. Examples of reviewer bias were evident in the final report. (e.g. a report by J. Yiamouyiannis claiming no difference in dental caries prevalence in 1986-87 between U.S. children in fluoridated and non-fluoridated communities that was fully discredited by the National Institutes of Health was referenced, but none of the several well-designed analytic studies showing significant differences in caries rates from the same dataset were referenced).

Conclusion of Review: “Recent studies of the incidence of cavities in children show little to no difference between fluoridated and non-fluoridated communities.”
Table 1:
Scoring the Reviews

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<td>Were the reviewer’s conclusions supported by the data cited?</td>
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APPENDIX 2
Risks According to “Tier One” Reviews

Introduction
All major “Tier One” and two documents used by the Fort Collins technical study group were scanned for relevant passages, and an effort was made to group these by the potential health outcome so that for each outcome, some of the most thorough completed reviews of the literature were available in one location. In order to keep this appendix to a reasonable size and scope, not all passages from each reference were included. Priority was given to passages that summarized studies that examined the exposure of humans to naturally or adjusted fluoridated water. Because “the dose makes the poison” some studies of human populations exposed to higher doses of fluoride (>1 ppm F) where ill effects were not detected were included. With the exception of some animal cancer data, animal toxicology studies are not included in this appendix. Additionally, some material was judged repetitive of material that was already cited and not included; only summary findings were included of some of the non-tier works where reviews of the literature were less than thorough. Readers are encouraged to check the complete documents for additional information.

Passages from the Agency for Toxic Substances and Disease Registry are from the 2001 Draft for Public Comment, 2001 References cited can be located within the cited document.
Topic: CANCER

Major “Tier One” Reviews (United States, World Health Organization, & York)

Medical Research Council. Medical Research Council working group report: water fluoridation and health. (September 2002).

Pages 29-32: The possibility that fluoridation might increase the risk of developing cancer was raised by a series of reports of experiments in mice (Taylor, 1954; Taylor & Taylor 1965) and by a report in 1975 purporting to show a higher overall cancer mortality rate among the 10 largest US cities that practiced water fluoridation than amongst the 10 largest cities that did not (Burk & Yiamouyiannis, 1975). Neither the results of these early experiments nor the report of Burk & Yiamouyiannis have been accepted by subsequent expert reviews (e.g. IARC 1982; Knox, 1985), but the important public health implications of the question have stimulated many further investigations.

The early studies looked at the possible association of fluoride with cancers of all types. Particular attention has been given to bone cancer, especially osteosarcoma, because ingested fluoride is concentrated in the bones. Some attention has also been given to cancers of the stomach, kidney and thyroid, because fluoride is usually absorbed in the stomach and can be concentrated in the kidneys and thyroid.

Current evidence. The York systematic review identified 26 studies that met the defined inclusion criteria, although two of these were not included in the main analysis (NHS CRD 2000). Other reviews have evaluated studies using different criteria, and have generally included more studies in their evaluations. This overview is based on material presented in the York review and other significant reviews (Knox, 1985; DHHS, 1991; Cook-Mozaffari, 1996; NHMRC, 1999)

Human data: ecological studies. The majority of data on the association of fluoridation with cancer rates come from ecological studies. Several studies have analyzed data sets from ten fluoridated and ten non-fluoridated cities in the USA (Yiamouyiannis & Burk, 1977; NHMRC, 1999; NHS CRD 2000). With the exception of the analysis by Yiamouyiannis & Burk, which did not adjust appropriately for sex, age, and ethnic group, none of these analyses has suggested that overall cancer mortality rates were positively associated with fluoridation. Similar analyses in other areas in the US, and in the UK and elsewhere, have not shown any differences in total cancer rates between fluoridated and non-fluoridated populations, or between populations with water supplies naturally high or low in fluoride. Some ecological studies have looked specifically at bone cancer or at osteosarcoma, and have not observed any associations with water fluoridation (Hoover et al., 1991; Freni et al. 1992).

The largest ecological study was that of Hoover et al. (1991), which included 125,000 incident cancers and 2.3 million cancer deaths, with follow-up for up to 35 years of fluoridation. This study met the inclusion criteria of the York Review but was not included in the main analysis because it grouped non-fluoridated areas together with areas fluoridated within the most recent five years. In our opinion, this aspect of the analysis by Hoover et al. is appropriate, because it is very unlikely that cancer incidence or mortality would increase enough within five years of fluoridation to affect results. We also consider that the results of this study are very important for the evaluation of the effects of fluoridation, because the large number of cancers studied produces high power to detect small effects. Hoover et al. singled out osteosarcomas for detailed analysis and found no relationship with fluoridation. The only cancer site for which there was suggestive evidence of a relationship between incidence rates and duration of fluoridation was renal cancer, but in contrast the mortality data for renal cancer yielded some evidence for an adverse relationship with duration of fluoridation. Overall, Hoover et al. identified no trends in cancer incidence or mortality that could be ascribed to the consumption of fluoridated drinking water.

Human data: analytical studies with data for individuals. There are few studies of this type. Three small case control studies of osteosarcoma have been reviewed by NHMRC (1999); two studies estimated individual exposure to fluoridated water from place of residence (McGuire et al., 1995; Moss et al., 1995), the third also included reported use of fluoride tablets and fluoridated toothpaste (Gelberg et al., 1995). None found an increase in cancer risk to be associated with increased exposure to fluoride. Further data are expected from an extension of the preliminary report of the McGuire et al. (1995) study (Lennon, personal communication).

Data from animal experiments. In 1987, IARC concluded that the few data available were insufficient to allow an evaluation of the carcinogenicity of fluoride to animals. Subsequently, however, concern was raised by the publication of the results from a study of lifetime administration of sodium fluoride to rodents (Bucher et al., 1991). The authors interpreted their results as equivocal evidence of carcinogenicity, based on the findings of 1 osteosarcoma in 50 male rats.
at a dose of 45 ppm and 3 osteosarcomas among 80 rats at a dose of 79 ppm; no associations between fluoride and osteosarcoma were observed among female rats or among mice.

**Evaluation of existing data.** Overall, the current evidence does not support the hypothesis that exposure to artificially fluoridated water causes an increase in the risk for cancer in humans. It is too early to see whether there might be an effect after very long exposure (see section below), but the results available rule out more than a very small effect of artificial fluoridation on cancer risk for up to about 35 years of exposure. Furthermore, studies of cancer rates in relation to variations in naturally occurring fluoride levels provide information on lifetime exposure and the absence of any detectable adverse effects of fluoride in these studies provides a high level of reassurance concerning safety. (Knox, 1985).

**Risk estimate.** The evidence available does not suggest that fluoridation of water increases the risk for cancer in general or for any particular type of cancer, including osteosarcoma. Neither the York Review nor other reviews have calculated a pooled estimate of effect, therefore it is difficult to estimate the maximum increase in risk which is compatible with the available data. For osteosarcoma, the three small case-control studies cannot exclude an increase in risk of the order of twofold exposure to fluoridated water, but an increase as large as this is not compatible with the ecological data, in particular those analyzed by Hoover et al. (1991). In conclusion, although a small increase in cancer risk cannot be excluded, the data do not suggest any increase in risk and in view of the type of data available it does not seem appropriate to estimate the number of cases of cancer that might be caused by fluoridation.

**Exposure considerations:****

**Duration of exposure.** Artificial fluoridation was introduced to selected areas in the 1940s and 1950s. Most of the studies conducted so far have used data on cancers diagnosed up until the 1970s and 1980s. The majority of the information, therefore, relates to whether exposure to artificially fluoridated water for up to about 30 years may alter cancer rates, with some data for up to 35 years. There are examples of other agents that do not substantially increase cancer risk until about 25 years after first exposure, and most cancers occur in old age as a result of the accumulation of a lifetime of exposure to genotoxic and/or growth promoting agents. In view of this, there is a need to continue to monitor cancer rates in artificially fluoridated populations for at least 70 years after fluoridation was introduced. However, it should also be noted that studies of populations using water with naturally high fluoride levels, to which the people would have been exposed throughout their life, have not given any indication of an increase in cancer risk.

**Accurate estimation of total exposure to fluoride.** The majority of previous studies have used place or residence as an index of exposure to fluoridated water. However, total exposure to fluoride will depend on the volume of water consumed and on other sources of fluoride such as food, drink and toothpaste. Assessment of all sources would in theory allow estimation of cancer risk in relation to total fluoride intake, and assessment of the component due to fluoridated water. In practice, however, it may be very difficult to obtain sufficiently accurate measures of intakes from all sources. The use of biomarkers such as toenails could be further investigated (see Feskanich et al., 1998 and Section 3).

**Plausibility of effect.** Very high levels of fluoride have long been known to be toxic, but the features and consequences characteristic of fluorosis is humans and other animals have not included the occurrence of cancer. Most agents that cause cancer directly do so because they are genotoxic, although some (non-genotoxic) agents can cause or promote cancer by other mechanisms, for example by stimulating cell division.

For fluoride, in vitro genotoxicity data are mostly for doses much higher than those to which humans are exposed. Even at these high doses, genotoxic effects are not always observed (NRC, 1993), and fluoride is consistently negative in the Ames test (DHHS, 1991). Some in vivo studies have shown that fluoride can in some circumstances induce mutations and chromosome aberrations in rodent and human cells. Overall, the evidence available has not established that fluoride is genotoxic in humans, and most of the studies suggest that it is not, but the possibility of some genotoxic effect cannot be excluded (DHHS, 1991, NRC, 1993).

Fluoride can have a mitogenic effect on osteoblasts (Bucher et al., 1991); this could provide a mechanism by which fluoride could increase the risk for osteosarcoma.

**Gaps in the evidence.** As noted above, there is no evidence yet on the possible effects of exposure to artificially fluoridated water for more than 40 years, and there are very few data relating individual exposure to fluoride from water and other sources with cancer risk.
Feasibility of research. Ecological analyzes are feasible and should continue for the purpose of looking for possible effects of lifetime exposure to artificially fluoridated water.

More detailed information could be collected on a case-control basis, and might include estimates of total water consumption, other important dietary sources such as tea, and use of toothpaste, plus biomarkers such as toenails (Feskanich et al., 1998). Methodological studies would be needed to develop appropriate methods and to validate their accuracy.

Osteosarcoma is of interest but difficult to study because it is rare, and is not categorized separately in routine statistics. In England and Wales, there were 372 incident cases of bone cancer in 1994, and 204 deaths. Assuming that 34% of bone cancers are osteosarcomas (Hoover et al., 1991, cited in Cook-Mozaffari, 1996), this gives about 125 cases per year.

Research recommendations.

1. An updated analysis of ecological data in the UK on fluoridation and cancer rates is required. It would be relatively straightforward to analyze recent cancer incidence and mortality data from ONS in relation to residence in fluoridated areas. Comparisons could be made between similar cities, and data on potentially confounding variables might also be incorporated. The long period since fluoridation began would give a new analysis the possibility to detect any effect on cancer rates after long exposure.

2. The aetiology of osteosarcoma is poorly understood. If new case control studies of osteosarcoma are undertaken, exposure to fluoride should be included along with the other possible risk factors investigated.


Page 96: Numerous epidemiological studies have examined the issue of a connection between fluoridated water and cancer. The weight of evidence indicates that no such connection exists. However, all of the investigations were ecologic studies, and the sensitivity limit of even the most sensitive analysis in these studies appears to be a 10-20% increase. Since any carcinogenic effect of fluoride at the levels found in water supplies would probably be below this level of sensitivity, a National Toxicology Program (NTP) cancer bioassay was conducted to assess the effect of fluoride on cancer incidence in animals (Bucher et al., 1991; NTP, 1990). The NTP study found equivocal evidence of a fluoride related increase in osteo-sarcomas in male rats, and no evidence of any fluoride-related neoplasm in female rats or male and or female mice. A study sponsored by Proctor & Gamble (Maurer et al., 1990) found no evidence of fluoride carcinogenicity in either male or female rats. Both studies contain limitations that preclude strong conclusions. The NTP study is presently carrying out additional experiments on the relationship, if any, between fluoride and cancer. The International Agency for Research on Cancer (IARC) reviewed the literature on carcinogenicity in 1982. It concluded that there is no evidence from epidemiological studies of an association between fluoride ingestion and human cancer mortality, and the available data are inadequate for an evaluation of the carcinogenicity of sodium fluoride in experimental animals (IARC). Several major cancer bioassays have been conducted since the IARC review.

Page 97: Data suggesting that increased fluoride exposure from drinking water supplies is associated with an increase in cancer incidence come from the study published by Yiamouyiannis and Burk (1977) comparing cancer incidence rates in 10 US cities with artificial fluoridation and 10 cities without fluoridation. The authors of the study interpret the data as showing that cancer mortality was higher in the cities with artificially fluoridated water. Data from this study has been re-analyzed several times in an attempt to further explore the hypothesis that fluoridation of water supplies causes cancer (Chivers, 1982, 1983; Doll & Kinlen, 1977; Hoover et al., 1976; Kinlen & Doll, 1981; Oldham & Newell, 1977; Taves, 1977). None of these re-analyses provided evidence of a positive association between fluoridation of water supplies and cancer of any of the sites considered. The re-analyses attributed the positive association between fluoride exposure and cancer reported by Yiamouyiannis and Burk (1977) to dissimilarities in age, race, sex, and demographic factors for the populations studied. Other studies of large populations, both in the US and Great Britain have identified no relationship between artificially or naturally occurring fluoride in drinking water and an increase in cancer incidence (Griffith, 1985; Hoover et al., 1991; Kinlen, 1975).

Page 98: An epidemiological study (Hoover et al., 1991) examined >2,300,000 cancer deaths and 125,000 cancer cases in US counties exposed to artificially fluoridated drinking water for up to 35 years. Taking into account the results of the NTP study, detailed analyses were conducted of cancers of the joints and bones (especially osteosarcomas), and cancers of the oral cavity and pharynx. The statistical evaluation was based on analysis of time
trends in the observed/expected (O/E) ratios relative to duration of fluoridation. While elevated O/Es were observed for osteosarcomas in males, the O/E ratio was inversely related to duration of fluoridation. Thorough analyses of incidences of oral cancers and cancers at a variety of other sites were conducted by means of very sensitive statistical tests that were designed to detect changes as small as 10-20%. No consistent correlation between cancer incidence or mortality and duration of fluoridation was found. An addendum to the report noted that the age-adjusted national incidence of osteosarcoma increased by 18% in males for the years 1973-80 and 1981-87; most of the increase was due to a 53% increase in males under 20 years of age, and there was a larger increase in fluoridated than nonfluoridated areas. A similar time-trend analysis to that done in the main report found no correlation between the cancer incidence O/E ratio and duration of fluoridation. Additional analyses also failed to find a relationship between osteosarcoma incidence in males and exposure to water fluoridation.

Pages 98-100: Based on the finding of a rare tumor in a tissue known to accumulate fluoride, but not at the usual site for chemically-associated osteosarcomas, a weakly significant dose-related trend, and the lack of supporting data in female rats and mice of either gender, the NTP concluded that there was “equivocal evidence of carcinogenic activity of sodium fluoride in male F344/N rats.” NTP defined equivocal evidence of carcinogenic activity to be a situation where the results show “a marginal increase in neoplasms that may be chemically related.” NTP further concluded that there was no evidence that fluoride was carcinogenic at doses up to 4.73 mg/kg/day in female N344/N rats, or at doses up to 17.8 and 19.9 mg/kg/day in male and female B6C3F1 mice, respectively.

Page 100-101: A study sponsored by Proctor and Gamble examined carcinogenic potential of sodium fluoride administered in feed to Sprague-Dawley rats (Maurer et al., 1990). Statistical analysis of the incidence of bone tumors found no dose-response relationship (CDER, 1991). The Carcinogenicity Assessment Committee, Center for Drug Evaluation and Research, Food and Drug Administration (CAC/CDER/FDA) review concluded that there were “flaws and uncertainties in the studies that keep them from providing strongly reassuring data.” However, the committee concluded that the study results reaffirm the negative finding of the NTP study in female rats, and do not reinforce equivocal findings in male rats.


Page xiii: There were 26 studies of the association of water fluoridation and cancer included. Eighteen of these studies were from the lowest level of evidence (level C) with the highest risk of bias.

There was no clear association between water fluoridation and overall cancer incidence and mortality. This was also true for osteosarcoma and bone/joint cancers. Only two studies considered thyroid cancer and neither found a statistically significant association with water fluoridation.

Overall, no clear association between water fluoridation and incidence or mortality on bone cancers, thyroid cancer or all cancers was found.

Page 58: The evidence of the effect of water fluoridation on cancer was of the highest quality available under objective 4 (3.8 out of 8 compared to a mean of 2.7 for other possible negative effects) but was still only low to moderate. Twenty-one of the 26 studies presented are from the lowest level of evidence (level C) with the highest risk of bias. While prospective study designs may be more difficult to conduct in cancer studies due to long incubation periods and rarity of some cancers, they are possible. Blinding of outcome assessment to exposure is certainly possible in such studies, for example outcomes assessed using published sources could blind investigators to fluoride levels in the study areas.

There is no clear picture of association between water fluoridation and overall cancer incidence and mortality. Whilst there were 11 analyses that found the direction of association of water fluoridation and cancer to be positive (fewer cancers), a further nine analyses found a negative direction of association (more cancers), and two studies found no effect. Only two studies found statistical significance, both suggesting an association in different directions. One of these studies contained 8 analyses of which only 2 found a statistically significant adverse effect of water fluoridation.

While a broad number of cancers were represented in the include studies, osteosarcoma, bone/ joint and thyroid cancers were of particular concern due to fluoride uptake by bone and thyroid. Again, no clear association between water fluoridation and increased incidence or mortality was apparent. Of eight analyses from the six studies of
osteosarcoma and water fluoridation reporting variance data, none found statistically significant differences. Thyroid cancer was also considered but only two studies examined this and neither found a statistically significant association with water fluoride level.

The findings of cancer studies were mixed, with small variations on either side of no effect. Individual cancers examined were bone cancers and thyroid cancer, where once again no clear pattern of association was seen. Overall, from the research evidence presented no association was detected between water fluoridation and mortality from any cancer, or from bone or thyroid cancers specifically.


Page 12: Claims of osteosarcoma induced by fluoride are based on equivocal evidence from studies of rats, which received extremely high amounts of fluoride. The correlation between osteosarcoma and fluoride thus remains unproven. Examination of the medical records of human osteosarcoma, a rare condition, has failed to identify any relationship between osteosarcoma and fluoride history, and other extensive evaluations of available information have failed to find any potential association between fluoride-induced osteosarcoma and fluoride intake in humans.


Page 10-11: More than 50 epidemiological studies have examined the relation between fluoride concentrations in drinking water and human cancer. Most studies compared geographic or temporal patterns of cancer occurrences with distributions of fluoride in drinking water. These studies provide no credible evidence for an association between fluoride in drinking water and the risk of cancer. The existence of such an extensive epidemiological database on fluoride with no consistent evidence of carcinogenic effects suggests that, if there is any increase in cancer risk due to exposure to fluoride, it is likely to be small. However, most of these studies used geographic and temporal comparisons of cancer rates and hence are of limited sensitivity. Further analytical studies with accurate information on individual fluoride exposures and disease diagnoses are therefore desirable.

The subcommittee also reviewed the literature on the potential carcinogenic effects of fluoride in animals. Although the results of earlier animal studies were largely negative, the studies were not conducted using current bioassay techniques and are thus of limited value. The sub-committee placed greater weight on two recent studies. The first, conducted by the National Toxicology Program (NTP), administered fluoride at concentrations of up to 175mg/L of drinking water. Although the results were negative for male and female mice and female rats, there was some evidence of a dose-related increase in the incidence of osteosarcomas in male rats. However, these results were not confirmed by a second study conducted by Procter & Gamble, in which fluoride was administered in the diet at doses higher than those in the NTP study. The Procter & Gamble study did produce a significant dose-related increase in the incidence of osteomas (benign bone tumors) in male and female mice. However, these lesions were not considered to be neoplastic and, in any event, have no known counterpart in human pathology.

The subcommittee concludes that the available laboratory data are insufficient to demonstrate carcinogenic effects of fluoride in animals. The subcommittee also concludes that the weight of the evidence from the epidemiological studies completed to date does not support the hypothesis of an association between fluoride exposure and increased cancer risk in humans.

The relevant scientific literature has been exhaustively reviewed by several independent expert panels of epidemiologists. The two most comprehensive evaluations were conducted by the British Working Party on the Fluoridation of Water and Cancer under the chairmanship of E.G. Knox (Knox, 1985) and by an international panel of epidemiologists convened by the Monographs Programme of the International Agency for Research on Cancer in Lyon, France (IARC, 1982). The expert panel reviews generally agree that available data provide no credible evidence for an association between either naturally occurring fluoride or added fluoride in drinking water and risk of human cancer. The Knox Report concluded that there is “no reliable evidence of any hazard to man in respect to cancer.” The IARC group (1982) came to a similar conclusion, namely, that “Variations geographically and in time in the fluoride content of water supplies provide no evidence of an association between fluoride ingestion and mortality from cancer in humans.”

**Page 3-4 of executive summary:** Epidemiologic studies – the subcommittee reviewed the results from numerous epidemiologic studies of the relation between exposure to fluoridated water and cancer that have been conducted during the last 40 years. In addition to the review of these studies, the subcommittee reviewed the findings of a recent study from the National Cancer Institute (NCI), which updated and expanded an earlier county-specific analysis for cancer mortality in the U.S. in relation to water fluoridation. This study evaluated the cancer mortality data and examined patterns of cancer incidence from 1973 through 1987 in the Surveillance, Epidemiology and End Results (SEER) program cancer registries. The SEER registries were used to obtain data on incidence for all types of cancer, with special emphasis on trends in osteosarcomas.

The NCI study identified no trends in cancer risk that could be attributed to the introduction of fluoride into drinking water. There were no substantial differences in cancer mortality rates among persons who lived in counties that had initiated water fluoridation and those in persons who lived in counties without water fluoridation. Similarly, there was no apparent relation between introduction and duration of fluoridation and the incidence of cancer, including bone and joint cancer and the subset of osteosarcomas.

The NCI also conducted a more detailed evaluation of osteosarcomas using nationwide age-adjusted incidence from the entire SEER database for the years 1973-1987. During this time, the annual incidence of osteosarcoma among males <20 years of age increased from 3.6 cases/10^6 population to 5.5 cases/10^6 population. The incidence among females decreased slightly during the same period (from 3.8 cases/10^6 population to 3.7 cases/10^6 population). Although the increase in rates of osteosarcoma for males during this period was greater in fluoridated than non-fluoridated areas, extensive analyses revealed that these patterns were unrelated to either the introduction or duration of fluoridation. Consequently, the NCI report concluded that, while the explanation for the increase in rates of osteosarcoma among young males is unknown, it is not due to exposure to water fluoridation. Both this report and reports from previous international expert panels which have reviewed earlier data concluded that there is no credible evidence of any association between the risk of cancer and exposure to either natural or adjusted fluoride in drinking water.

**Page 4 of executive summary:** Animal Studies: The NTP study found that rates of osteosarcomas rose as the dose of sodium fluoride exposure for male rats increased, but not for female rats or for mice of either gender. These findings were interpreted as “equivocal evidence” of carcinogenicity for male rats but no evidence of carcinogenicity for the other gender/species tested. In another recent carcinogenicity study conducted by Maurer, Cheng, Boysen, and Anderson and sponsored by Proctor and Gamble (P&G), no evidence was found for an association between the development of malignant tumors and exposure to sodium fluoride in rodents of either gender. Taken together, the NTP and P & G studies fail to establish an association between fluoride and cancer.

**Page 76 of full report:** The mouse data from the P & G study can be compared and contrasted with the NTP mouse study data. The NTP study conducted in B6C3F1 mice at lower doses of fluoride administered in the drinking water showed no evidence of carcinogenicity. The P & G study conducted in CD1 mice at higher doses of fluoride administered via the diet showed osteomas, but was confounded by the type C retrovirus in mice. The NTP mice had few histopathologic effects on bone but definite discoloration of teeth compared with the P & G mice; the latter showed histopathologic bone and teeth effects associated with chronic fluoride toxicity. This difference is consistent with the lower levels of bone fluoride detected in the NTP study, although many different bones were evaluated. No malignant bone tumors associated with fluoride exposure were seen in mice in either study.

In the P & G rat study, 2 osteosarcomas occurred in the 4 mg/kg-BW females and 1 osteosarcoma in the 25 mg/kg-BW males. The incidence in either sex was not statistically significant. One osteosarcoma was identified by P & G in the pre-maxilla of a low-dose female rat (Maurer, 1990). The osteosarcoma in the high-dose male was identified as such by pathologists at the Armed Forces Institute of Pathology (AFIP) and this diagnosis is the subject of divided expert opinion (FDA, 1990). No agreement has been reached regarding this discrepancy; however CAC and this subcommittee opted to use the “worst case scenario” in interpreting the data and therefore considers the results to encompass two osteosarcomas in 4-mg/kg-BW female rats, one osteosarcoma in a 25 mg/kg-BW male rat, and one fibroblastic sarcoma in the 175 ppm sodium fluoride male rat. In the NTP study researchers found 3 osteosarcomas in the 175ppm sodium fluoride male rats (8.6 mg/kg BW sodium fluoride) and one osteosarcoma in the 100ppm male rats (5.2 mg/kg BW sodium fluoride).
When the NTP and the P&G studies are combined, there is a total of 8 individual sex/species groups examined. Seven of these groups showed no significant evidence of malignant tumor formation. One of these groups, male rats from the NTP study, showed “equivocal” evidence of carcinogenicity, which is defined by NTP as a marginal increase in neoplasms – i.e. osteosarcomas – that may be chemically related. Taken together, the two animal studies available at this time fail to establish and association between fluoride and cancer.


Page 85: Cancer mortality rates in areas with different amounts of fluoride naturally present in the drinking water have been compared in a considerable number of epidemiological studies. These studies have been carefully reviewed and evaluated by IARC (1982) with the following conclusions: “When proper account was taken of the differences among population units in demographic composition, and in some cases also in their degree of industrialization and other social factors, none of the studies provided any evidence that an increased level of fluoride in water was associated with an increase in cancer mortality.” Thus “variations geographically and in time in the fluoride content of water supplies provide no evidence of an association between fluoride ingestion and mortality from cancer in humans.”

Other Reviews
(examples of municipal or territorial reviews of the water fluoride issue)


Page 15: There is no epidemiological evidence linking fluoride with increased rates of cancer. The International Agency for Research on Cancer (1982) compiled demographic data comparing cancer rates in regions with naturally or artificially fluoridated water to those in regions with low fluoride levels. The IARC found no correlation of cancer rates with fluoride exposure. Similar investigations performed by the EPA (USEPA, Fed Register, 1985b) and the National Research Council (1977) likewise found no correlation of fluoride levels with cancer.

The National Cancer Institute (NCI) evaluated the relationship between fluoridation and cancer mortality in the US during a 36-year period and a 15-year period. There were 2.2 million cancer death records and 125,000 cancer case records in counties using fluoridated water but there was no correlation between cancer cases and fluoridated drinking water. These statistics speak volumes: considering that the exposure to so many carcinogenic substances are so easily correlated with the epidemiology of cancer, and indeed exposure to non-carcinogenic substances can be correlated to cancer, it is remarkable that to date no epidemiological correlation of fluoride exposure to cancer incidence has been demonstrated.


Page 6, summary: The few studies published during the review period do not challenge earlier research showing there is no reason to believe that exposure to fluoridated water increases the risk of cancer in bones or other body tissues. While an ecological study did suggest an association with uterine cancer, the limitations of this kind of study in terms of linking exposures and outcomes in individuals, mean that it does not contradict the evidence derived from more systematic and scientifically credible case-control studies.

Page 52: Numerous studies have been undertaken to determine if water fluoridation is linked to increases in the risk of cancer. Many studies claiming that such a risk exists have been re-analyzed and found to provide no evidence of a link. Moreover, many used the correlational ecologic design, which has significant limitations in terms of establishing cause and effect relationships.

A recently published ecological study (Tohyama, 1996) did find a significant correlation between fluoride concentration in drinking water and uterine cancer mortality in 20 municipalities in Okinawa, Japan. This association remained
significant after adjusting for a number of confounders such as population ratio, income gap, still birth rate and divorce rate. However, the study did not control for more relevant confounders such as smoking and sexual activity.

A 1990 animal study showing a possible link between fluoride and osteosarcoma stimulated a number of more rigorous studies using case-control designs, which were published between 1994 and 1999. Three case-control studies from the US found no association between exposure to fluoridated drinking water and osteosarcoma (Moss et al., 1995; McGuire et al., 1995; Gelberg et al., 1995). For example, a multi-center study involving 147 patients and 248 controls found no differences between the proportions exposed to optimally fluoridated water or average yearly exposure (McGuire et al., 1995). The study by Gelberg et al. (1995) found no association between fluoride exposure and osteosarcoma in a study of 130 cases aged 24 years or less and 130 age and sex matched controls. The finding of no association held whether fluoride exposure was based on data provided by patients or their parents. The study also suggested that there might be a protective effect for males.

Studies of other cancer sites, one an ecologic study from South Africa (Borner & Aggett, 1994) and a case-control study of bladder, colon, and rectal cancer in Ontario (Marrett & King, 1995) showed no association between water fluoridation and increased risk of cancer. Two recent reviews of the literature also concluded that there is no evidence that fluoride in the water supply is linked with an elevated risk of cancer at any body site (Cook-Mozaffari, 1996; Cantor, 1997).


Summary majority opinion, page 30: From the perspective of epidemiology and toxicology, the available scientific literature has not substantiated the claims that water fluoridation was a factor in other adverse health effects. The results found in the literature have not eliminated the need for further research.


Cancer (Pages 50-51): There were upwards of 50 published reports of studies looking at the association between water fluoridation and cancer. The majority of these studies reported no significant association between fluoride and cancer rates thus providing no evidence that fluoridation was a cause of cancer. One study from the US reported a statistically significant positive association in 1977. However, in this type of study it was impossible to rule out confounding as a possible explanation for any association seen. Furthermore, the study has been heavily criticized in the literature for the way in which the analysis was performed, and re-analyses of the same data have consistently shown no association.

Using the classification above, all of this evidence would be classed as level 1 or possibly level 2 and, in the absence of any stronger data there was, therefore, no scientific evidence on which to base an evaluation of causality. There have also been several studies looking at the specific association between fluoride and the risk of osteosarcoma. Again the majority of these were conducted at the population level and found no association between water fluoride levels and either osteosarcoma or bone cancer rates generally. Three further studies considered individuals with and without bone cancer, and could, therefore, be considered to provide stronger evidence for an evaluation of causality. Of these, the two largest and most recent studies found no consistent association between osteosarcoma and fluoride. The earliest study was very small and reported a significant protective effect associated with fluoride.

In summary, the majority of the data would be classed as level 1 and there was none of level 3 which would be required to provide any reliable evidence of causality. Therefore, there was, therefore, no scientific evidence to support claims that water fluoridation causes osteosarcoma.


Page 4, finding: Animal bioassays suggest that fluoride is a carcinogen, especially for tissues such as bone (osteosarcoma) and liver. The potential for carcinogenicity is supported by fluoride’s genotoxicity and pharmacokinetic properties. Human epidemiology studies to date have been inconclusive, but no appropriate major study has been conducted.

Page 36-37: The animal study conducted by the National Toxicology Program (NTP) provides evidence that fluoride causes osteosarcoma, a malignant bone tumor. Although the NTP concluded that its study gave “equivocal” results with respect to cancer, the background memos and documents suggest that the results are actually stronger
than suggested by the report. Similarly, the P & G study likely gave stronger evidence of carcinogenicity, notably bone cancer, than suggested in the summary statements.

That fluoride is associated with bone cancer is reasonable from the point of view of what is known about the effects of fluoride: fluoride causes the division of immature bone cells (proliferation of osteoblasts) and fluoride accumulates in the bone and thus can cause damage there. Fluorine has been shown to be genotoxic in numerous test systems, which is another property that is associated with carcinogens. In other words, the biochemistry, pharmacokinetics, and other toxicology studies support the view that fluoride may be a bone carcinogen.

Epidemiology studies examining cancer in general and bone cancer in particular have been inconsistent. Studies using ecologic designs (the studies are based on cancer incidence or mortality for given geographic areas, not for individuals) have given conflicting results for cancer in general, for all bone cancer, and for osteosarcoma. The larger case-control studies do not show an association of fluoride or water fluoridation with bone cancer although at least one small study has shown an association. Most of these studies are handicapped by completely inadequate measures of exposure, which would mask any effects that may be there because of non-differential misclassification of exposure. Given the widespread deliberate exposure of humans to water fluoridation and the suggestive animal data regarding cancer, especially osteosarcoma, it is incomprehensible why a large case-control epidemiology study with good measures of fluoride exposure has not been initiated.
Appendix 2 - Risks According to “Tier One” Reviews

Topic: BONE FRACTURES AND OTHER BONE EFFECTS
(not including bone cancer or skeletal fluorosis)

Major “Tier One” Reviews (United States, World Health Organization, & York)

Medical Research Council. Medical Research Council working group report: water fluoridation and health. (September 2002).

Pages 27-29: The York Review included 29 studies on the relation of fluoride in water to bone health. These covered fractures at various anatomical sites, slipped epiphysis and otosclerosis. Eighteen of the investigations provided data on hip fracture. The validity of the studies was generally assessed as low (mean score 3.4 out of 8; see Appendix D of the York Review for details of the assessment criteria) and all but one were classed to the lowest of the three levels of evidence that had been specified at the start of the review.

A total of 55 estimates for the risk of fracture associated with fluoride concentration of 1ppm in water were obtained from 20 studies. The relative risks ranged either side of the null value with a polled estimate from a univariate meta-regression of 1.00 (95% CI 0.94-1.06). However, the authors warn that these figures should be interpreted with caution since multivariate analysis revealed significant heterogeneity between the studies.

Two studies of otosclerosis both suggested a beneficial effect of fluoridation, and in a single investigation of slipped epiphysis, fluoride in water was associated with an increased risk in boys and a reduced risk in girls, neither of which was statistically significant.

Potential risk/population effect. Of the potential effects on bone that have been investigated, hip fracture is the most important in public health terms.

In the York Review, the upper 95% confidence limit for the relative risk of all fractures at a water fluoride concentration of approximately 1ppm was 1.06. Because of the heterogeneity between studies, this figure is subject to some uncertainty. Furthermore, although it was derived largely from studies of hip fracture, some of the data on which it was based related to fracture at other sites. Taking account of these limitations, a reasonable upper bound (i.e., worst case estimate) for the relative risk of hip fracture from a water fluoride concentration of 1ppm would be 1.2 (although it is most likely that there is no impact on risk, and there could even be a protective effect).

A relative risk of 1.2 for hip fracture would imply an increase in the lifetime risk of a woman from 14% to approximately 17%, i.e., an excess risk over a lifetime of about 3%. In men, who have a lower incidence of hip fracture, the excess lifetime risk would be less than 1%. The crude annual incidence of hip fracture in the US is approximately 1 per 1000 per year.

The epidemiological data currently available do not allow a useful estimate of the potential impact of fluoridation on bone disorders other than fracture, although the few studies that have been carried out to date do not suggest a problem.

Plausibility of effect. An effect of fluoridation on the risk of fracture, adverse or beneficial, is plausible. Fluoridation of water can increase normal dietary intake of the mineral by some 50%, and about half of the fluoride ingested is taken up by bone. Within the bone, fluoride ions can replace hydroxyl ions in the hydroxyapatite lattice with possible implications for its mechanical properties. In addition, elevation of the fluoride concentration in plasma directly increases osteoblastic differentiation and activity.

In theory, a number of other bone disorders could also be affected by these mechanisms. For example, alterations in the hydroxyapatite lattice might influence the development of otosclerosis.

Exposure issues. Many of the epidemiological studies on fluoride and bone health have only assessed risk in relations to current or recent exposure to fluoridated water. However, given the possible mechanisms for an effect on bone, a more relevant metric is likely to be some index of cumulative exposure. This was explored in a recent MRC case-control study of hip fracture, which found no elevation of risk with exposures to high fluoride concentrations over a lifetime (Hillier, 2000). A possible limitation of that study, however, was that the exposure to fluoride was almost all from natural sources in water that also contained high concentrations of calcium. It has been proposed that calcium might reduce the bioavailability of fluoride from the gastrointestinal tract, perhaps through ion-pairing, although the importance of any such effect is uncertain.

Studies of exposure to fluoride in water (especially long-term exposure) are limited by unavoidable inaccuracies in the assessment of individual differences in water intake and of fluoride intake from other dietary sources. In practice, however, these are unlikely seriously to bias estimates of average risks from fluoridation. In particular, confounding by
other sources of fluoride in the diet would only have a major impact if total fluoride intake had an important effect on risk (positive or negative), and at the same time, intake from sources other than water differed substantially between fluoridated and non-fluoridated populations.

**Gaps in the evidence.** The York Review suggests that the evidence base on fluoride and bone health is weak, but this conclusion may be misleading because the criteria by which studies were classified were not entirely appropriate. As outlined above, any effect of fluoride on bone is likely to derive from cumulative exposures, possibly over a lifetime. However, a prime requirement for classification as high level evidence in the review was that studies should have started within three years of the initiation or discontinuation of fluoridation. Any such studies would not be informative about the long-term risk of bone disorders.

A further limitation of the review was that, in grading the validity of studies, it assigned each study a score of zero or one in relation to a pre-defined checklist of features. This is standard practice in systematic reviews, the aim being to make the assessment as objective as possible. However, it has the drawback that the full implications of any weaknesses in the design or execution of individual studies, and the direction of any resultant biases, are not considered.

A broader consideration of the epidemiological evidence on fluoride and bone health suggests that it is of higher quality than the York Review indicates. At this stage, perhaps the most important gap is knowledge concerns the bioavailability of fluoride from different dietary sources, and in particular the influence, if any, of calcium on uptake of fluoride from drinking water. If fluoride were shown to be much less completely absorbed from hard than soft water, the absence of an increased risk of fracture in some published studies would be less reassuring.

There are also gaps in the evidence base on bone disorders other than fractures, only a few epidemiological studies having attempted to assess risks for any of these diseases directly. However, the gaps could only be regarded as important if there were good reasons to suspect an effect of fluoridation from our knowledge of biochemistry and toxicology.

**Feasibility of research.** A study to assess the bioavailability of fluoride from soft as compared with hard water should not be difficult or expensive. If such a study cast serious doubt on the relevance of negative findings from investigations of fracture in relation to water naturally high in fluoride, useful information might be obtained from a well designed case-control study of hip fracture in a population that included people with long-term exposure to artificially fluoridated soft water and others exposed only to low levels of fluoride in water.

In the absence of differential bioavailability, understanding of the risks of fracture from fluoridation will only be advanced materially by further case-control or cohort studies if they are not only designed to minimize the effects of bias and confounding, but also extremely large. Such an effort could only be justified if the upper bounds on risk derived from current evidence were deemed too high for comfort (or the lower bounds were judged to include a potentially important beneficial effect), and if a new study would have sufficient statistical power to achieve the required reduction in uncertainty.

Studies on bone disorders other than fracture could be feasible, particularly if the diseased are relatively common, such as Paget’s disease.

**Research recommendations.** The main priority is for research to establish whether the bioavailability of fluoride differs when it is encountered in artificially fluoridated soft water as compared with hard water that is naturally high in fluoride. If important difference were demonstrated, there would then be a need for a case control study to investigate the relation of hip fractures to long-term consumption of artificially fluoridated water.

Studies of other bone diseases would be feasible, but in the absence of clear a priori toxicological concern, are of lower priority.
possible association. These studies have found conflicting results, with studies finding a higher or lower incidence of hip fractures or no differences in hip fracture between humans exposed to fluoride in drinking water. Several studies have found decreases in hip fracture incidences in communities with fluoride in the drinking water, suggesting that there may be a beneficial effect. Simonen and Laittenen (1985) examined male & female residents older than 50 years of age living in two cities in Finland with either trace amounts of fluoride in the water or with 1ppm fluoride in the water. The occurrence of femoral neck fractures was lower in men 50-80 years old and women >70 years old living in the area with fluoridated water, as compared to the low fluoride community. No difference in femoral neck fracture was observed in women 50-69 years of age. Madans et al. (1983) examined the association between fluoride in drinking water and risk of hip fractures using hip fracture data for the National Health Interview Surveys of 1973-77 and CDC data on the percent of a population in each US county served with water having natural or adjusted fluoride content of at least 0.7 ppm in 1963. Female residents over 45 years of age living in areas with lower fluoride levels in the drinking water had 9% more hip fractures than women living in high fluoride areas; however, the difference was not statistically significant. In a prospective study of older women, Phipps et al. (2000) examined the possible relationship between living in an area with fluoridated water and the risk of fractures. Higher bone mineral density of the lumbar spine and femoral neck and trochanter and lower bone mineral density of the radius were observed in women continuously living in an area with fluoridated water, as compared to residents in a non-fluoridated water area. Fewer spine, hip, and humerus fractures were also observed in this group. However, a higher incidence of wrist fractures was also observed in this group. Cauley et al. (1995) examined a subset of this population, and found no effect on age-adjusted axial and appendicular bone mineral density and no effect of the risk of vertebral or non-vertebral fractures.

Page 84: In contrast to the results of these studies, other studies have found an increase in the incidence of hip fractures in communities with fluoride in the drinking water. Sowers et al. (1986) examined female residents living in three communities in northwest Iowa with either high fluoride (4 mg/L)-low calcium (14-19 mg/L), low fluoride (1 mg/L)-high calcium (336-390 mg/L), or low fluoride (1 mg/L)-low calcium (62-71 mg/L) levels in the drinking water. The subjects had lived in the communities for at least 5 years and did not have wrist or forearm fractures in the previous 2 years. Among women 55-80 years old living in the high fluoride community, bone mass of the radius was significantly lower and a higher incidence of hip fractures was observed, as compared to the other groups. No effect was seen in younger women (20-35 years old). A geographical correlational study of 541,985 white women hospitalized for hip fractures found a weak association (regression coefficient = 0.001, p=0.1) between hip fracture incidence and fluoridation of water (Jacobsen et al., 1990). The association was strengthened (regression coefficient = 0.003, p=0.0009) after correcting by county for other factors found to correlate with hip fracture incidence (latitude, hours of sunlight, water hardness, income levels, and percentage of land in farms).

Page 85: A study in England and Wales also found increased rates of hip fractures in men and women over age 45 as water fluoride levels increased up to 0.93 ppm (Cooper et al., 1991). Hip fracture rates in 39 counties (standardized by age and sex) were compared with water fluoride levels in those counties. In the original analysis (Cooper et al., 1990), no significant correlation was found. However, when the authors reanalyzed the data using a weighted least-squares technique to account for the differences in the precision of the county specific rates, a significant positive correlation between water fluoride levels and hip fracture rates was found (r=0.41, p=0.009). The correlation existed for both women (4=0.39, p=0.014) and men (r=0.42, p=0.0007) (Cooper et al., 1991). Kurttio et al. (1999) studied over 144,000 residents living in rural areas of Finland from 1967-80. When all age groups were considered together, no relationship between fluoride levels in drinking water and the risk of hip fractures was found. However, among women aged 50-64 years with higher fluoride levels, an increase in the risk of hip fractures was found. No consistent relationships were found in men or older women. The study authors suggested that the other risk factors for hip fracture may be more important than fluoride exposure in determining the risk of hip fracture in older women. An ecologic cohort study compared the hip fracture rate for men and women in a Utah community that had water fluoridated to 1 ppm with the rate in two communities with water containing <0.3 ppm fluoride (Danielson et al, 1992). Fluoridation began in the fluoridated community in 1966. The age-adjusted rate was significantly elevated in both women (relative risk 1.27, 95% CI 1.08-1.46) and men (relative risk 1.41, 95% CI 1.00-1.81). In men, the rates in the fluoridated and nonfluoridated communities were similar until age 70. From age 75 on, the difference between the rates in the fluoridated and nonfluoridated areas increased with age. The difference between the hip fracture rates in the fluoridated and non-fluoridated areas increased for women in the 70 and 75-year age groups. However, the fracture rates in women at ages ≥80 years old were similar in the fluoridated and nonfluoridated towns. The study authors attributed this to the fact that women older than 80 years of age would have already gone through menopause by the beginning of fluoridation, and so would have had less bone remodeling and less incorporation of fluoride into the bone. The study authors also suggested that the reason that they found an effect when other investigators have not was the low levels of exposure to risk factors for osteoporosis (smoking and
alcohol) in the Utah populations. This was a well-conducted study that suggests that communities with fluoridated water have an elevated risk of hip fracture. However, several possible confounding factors were not examined. Calcium levels in the water, total calcium and vitamin D intake, and individual fluoride intake were not determined. Estrogen use was not evaluated, but was assumed to be similar since the communities were similar distances from larger medical centers. In addition, estrogen levels would not cause the effect in men.

Pages 85-86: Other studies have not found a relationship between fluoride in drinking water and hip fracture prevalence. No significant differences in the incidence or type of upper femoral fracture were observed when groups of subjects living in communities with low fluoride (0.3 ppm), fluoridated (1.0-1.2 ppm), or high fluoride (>1.5 ppm) drinking water (Amala et al., 1986). An increase in the fluoride content of bone and an increase in the volumetric density of the osteoid were observed in the residents in the high fluoride area. Kroger et al. (1994) found no effect on self-reported fractures among a group of older Finnish residents (mean age approximately 53 years) living in an area with fluoridated water (1.0-1.2 mg/L), as compared to residents living in an area with low fluoride levels in the drinking water (<0.3 ppm). Increases in spine and femoral neck bone mineral density were observed in the fluoridated water group.

Page 87: Haguenauer et al. (2000) performed a meta-analysis to examine the effects of fluoride on the treatment and prevention of post-menopausal osteoporosis using the data from Riggs et al. (1990, 1994), Kleerekoper et al. (1991) and 10 other studies. The meta-analysis showed a significant increase in bone mineral density in the lumbar spine and hip and a decrease in bone mineral density in the forearm after 2 or 4 years of fluoride treatment. When the data from all the studies was used, fluoride treatment for 2 or 4 years did not affect the relative risk of vertebral fractures. However, in studies in which the subjects were exposed to low levels of fluoride or a slow-release formulation for 4 years, a significant decrease in vertebral fracture risk was seen. An increase in the relative risk of non-vertebral fracture was observed when the data from all sources were used; no effect was seen in studies using low levels of fluoride (<30 mg/day) or slow-release fluoride.

Results of animal studies are included on page 87-88 (not included here)


Discussion page 53. There were 29 studies included on bone fracture and bone development problems. Other than fluorosis, bone effects (not including cancers) were the most studied potential adverse effect. These bone studies also had a low validity (3.4 out of 8) with all but one study being evidence level C. These studies included both retrospective and prospective cohort designs, some of which included appropriate analyses controlling for potential confounding factors. Observer bias could potentially play a role in bone fracture, depending on how the study is conducted.

The graph of estimates of association for all bone fracture studies shows that the individual estimates of effect lie very close to a relative risk of 1.0. Most of the confidence intervals cross 1.0 (statistically non-significant). The only confidence intervals that do not include 1.0 (statistically significant) are evenly distributed, five indicating an increased risk of fracture and four indicating a decreased risk. The meta-regression showed that the pooled estimate of the association of bone fracture with water fluoridation was 1.00 (0.94, 1.06), however due to the significant heterogeneity between the studies this value should be interpreted with extreme caution. The meta-regression showed that the only variable (out of 30 total) associated with the summary measure at the 5% significance level was duration. Factors, which would be expected to show an association with fracture incidence, such as fracture site, age, and sex, were not associated with water fluoride level at the 5% significance level in either the univariate or multivariate models. This adds support to the result suggested by the pooled estimate of no association between water fluoridation and fracture incidence.

The evidence on bone fracture can be classified into hip fracture and other sites as there were a greater number of studies on hip fracture than any other site. Using a qualitative method of analysis, there is no clear association of hip fracture with water fluoridation. Of 18 studies, three showed a statistically significant benefit, and two showed statistically significant harm, and three showed no effect of water fluoridation on hip fracture. One study found no cases of hip fracture in the low fluoride group, indicating harm from water fluoridation. The evidence on other fractures is similar; of 30 study comparisons one found statistically significant benefit, one found statistically significant harm and three found no effect. The evidence on other bone outcomes was extremely limited. A negative association was suggested in the risk of slipped epiphysis in boys, but this finding was not statistically significant.

Page 300: Several reports published 30 to 40 years ago suggested that the long-term ingestion of fluoride at levels slightly above optimum for caries prevention improved the quality of the human skeleton (Bernstein et al., 1966; Leone et al., 1955, 1960). A recent Finnish study concluded that, compared with the low-fluoride control group, vertebral bone mineral density (BMD) was increased slightly while femoral neck BMD was not affected among peri-menopausal women who had used fluoridated water (1.0 to 1.2 mg/liter) for 10 years of more (Kroger, 1994). There was no difference between the groups in the prevalence of self-reported bone fractures. Richards et al. (1994) reported that the normal, age-related increase in bone fluoride concentrations (range 463-4,000 mg/kg) had no effect on the compressive strength or ash density of vertebra in Danish men and women whose ages ranged from 20 to 91 years. Sowers et al. (1986, 1991), however, reported a marginal increase in bone fractures (self-reported) and lower bone densities among women whose drinking water contained 4 mg/liter of fluoride.


Page 11: Several recent epidemiological studies of long-term exposure to fluoride in drinking water at optimal levels for caries prevention have reached conclusions implicating fluoride as the causative factor in the increasing incidence of hip fractures in the elderly, owing to increased brittleness of the cortical bone plates. However, independent reviews of these contemporary studies conclude that they fail to establish an adequate basis for concluding that fluoride levels in drinking water are related to hip fractures and bone health (Gordon et al., 1992). Most of the studies have important limitations that restrict generalization of their results either to the population as a whole or to determining risks for individuals. Therefore no basis exists for altering current public health policy on the use of fluorides for caries prevention.


Pages 6-7: The effect of fluoride on bone strength, hip fractures, and skeletal fluorosis in humans has been addressed in 2 types of studies. The first type involves clinical trials of the effectiveness of high concentrations of fluoride supplements in strengthening bones and preventing further fractures in patients with osteoporosis; this treatment has been used primarily in Europe for almost 30 years. When conducted using proper control groups, these studies showed little or no benefit even at dosage of 20-32 mg per day, well over 10 times the exposure from fluoridated drinking water. If anything, the treated groups experienced a greater number of new fractures, including painful stress fractures in bones other than the vertebrae.

The second type of human study involves epidemiological investigations. These studies compared the rate of bone fracture in populations of the elderly that differed in their exposure to natural or added fluoride in drinking water. Geographic and time-trend analyses were made; time-trend analysis is considered the stronger methodology because there is less opportunity for confounding by other risk factors. Of the 6 epidemiological studies that used geographic comparisons (where no actual intake data were available), 4 found a weak association between fluoride in drinking water and risk of hip fracture. Two additional studies examined time trends in bone fracture before and after water fluoridation: one found no association and the other a negative association. Only two additional studies collected information on individual exposure: one (essentially a geographic comparison) found an increased risk of hip fracture at water fluoride concentrations of 4 mg/L, and the other observed no differences in risk.

Studies with several species of experimental animals have yielded various outcomes. Most of the studies indicated little or no negative effect on bone strength, even with very high fluoride intake and very high concentrations of fluoride in bone. The subcommittee identified many potential problems in the experimental design of the animal studies, including the lack of suitable control groups with reasonably low fluoride exposures. However, the subcommittee concluded that the weight of evidence indicates that bone strength is not adversely affected in animals that are fed a nutritionally adequate diet unless there is long-term ingestion of fluoride at concentrations of at least 50 mg/L of drinking water or 50 mg/kg in diet.

In view of the conflicting results and limitations of the current database of fluoride and the risk of hip fractures, the subcommittee concludes that there is no basis at this time to recommend that EPA lower the current standard for fluoride in drinking water for this end point.
Page 5 of executive summary: Although some epidemiologic studies have suggested that the incidence of certain types of bone fractures may be higher in some communities with either naturally high or adjusted fluoride levels, other studies have not detected increased incidence of bone fractures. However, a variety of potentially confounding factors must be examined to assess whether there is an association between exposure to fluoride and bone fractures.

Osteogenic Effects and Bone fractures, page 48: The issue of the role of fluoride in the etiology of bone fractures initially appeared as a consequence of the findings of clinical trials using fluoride as a treatment for osteoporosis. However, several community studies have further investigated this relationship. In one study, 39 countries with varying levels of calcium and concentrations of fluoride ranging from 0.005 mg/L in Sandwell to 0.93 mg/L in Birmingham, UK were compared. No significant correlations were found between the level of water fluoridation or calcium and the prevalence of hip fractures. (Cooper, 1990).

Another geographical correlational study of hip fracture in the US observed a small but positive correlation between the incidence of hip fracture and diet, calcium content, and fluoride levels (Jacobsen et al., 1990). In the most comprehensive study to date, Sowers and coworkers (in press) studied women in three demographically similar rural communities. The communities were identified on the basis of both fluoride and calcium levels in the drinking water supplies. One community (high fluoride, low calcium) had natural levels of fluoride of 4 mg/L and calcium levels of 15 mg/L; the second community had fluoride levels of 1 mg/L and calcium levels of 67 mg/L. There were no significant differences in the five-year risk of fractures occurring at the wrist, spine, or hip in the high calcium versus the control community, there was a two-fold increased risk of fractures of all sites in among women 55-80 years of age in the higher fluoride community when compared with the control community. Possible confounding factors such as hormone use, body size and weight, age, and dietary intake of calcium were examined and were not found to be exerting any differential effects in the study communities.

Currently, the body of data on the role of fluoride in the etiology of fractures is not resolved.

Page 87: There is some suggestion from epidemiological studies that the incidence of certain bone fractures may be greater in some communities with either naturally high or adjusted fluoride levels. However, there are a number of confounding factors that need resolution to determine whether or not an association exists. Additionally, other studies do not show an increase in the incidence of bone fractures; one study provided evidence of a lower incidence of bone fractures in an optimally fluoridated community as compared to a similar community with trace levels of fluoride in the water. Therefore, further research is required.

Other Reviews
(examples of municipal or territorial reviews of the water fluoride issue)


Page 14: In clinical trials, high doses of sodium fluoride such as 75 mg/day produced bone that was less mechanically strong than regular bone, but a lower dose (25 mg/twice daily with a slow release of F) produced fewer new vertebrate fractures and higher bone mass with minimal effects (Cerklewski, 1997). Fluoride’s role in bone development is well documented (Cerklewski, 1997), and a report that lifetime of fluoride exposure was associated with increased hip fracture has not been supported by others.


Page 5, summary: Studies of the association between water fluoridation and bone fracture are largely ecological in design. Of 11 studies published prior to 1994, two showed a protective effect, five showed no association and four suggested an increase in hip fracture rates. In the latter, the strength of the association was weak, with relative risks
ranging from 1.1 to 1.4. Of four studies published between 1994 and 1999, one showed a non-significant protective effect, two showed no association and one suggested an increased risk (RR= 1.3-1.4). The public health significance of small increases in hip fracture rates in elderly populations means that more studies with better research designs are needed.

**Pages 45-51:** The conclusions reached by each of these studies are limited since they used an ecologic measure of fluoride exposure. The associations found in studies using aggregate level data may differ from the associations measured with individual level data are collected [sic]. Even when the residential history is determined for each subject, the measurement of the fluoride exposure may be biased since the fluoridation of the public water supplies does not necessarily mean that all residents are equally exposed and individual variations in water intake can be such that residents of different communities have similar fluoride intakes. In addition, ecological studies do not allow for the control of potential confounders and effect modifiers. In the studies with a hybrid design this has been overcome to some degree by collecting data on variables known to be confounders [sic] on the individual level. Therefore, the association observed in an ecological study is always tenuous. Nevertheless, consistency of evidence across studies should enhance the overall credibility of risks or benefits suggested by ecological data. Since the results of the ecological studies on water fluoridation and hip fracture have been far from consistent, the possibility of a cause-effect relationship cannot be established. Consequently, the studies conducted to date do not provide systematic and compelling evidence of an adverse effect on bone.

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**Report of the expert panel for water fluoridation review. (March 1998). City of Calgary, and Calgary Regional Health Authority: Appointed by the Standing Committee on Operations and Environment.**

**Summary majority opinion, page 30:** The scientific literature on fluoride and bone fractures, especially hip fractures in the elderly, did not provide evidence that would lead to substantial changes in water fluoridation policy. Questions about exercise and activity, calcium and vitamin D intake, overall health status, other sources of fluoride, use of other medication, and general standards of osteoporosis medical practice in the studied communities have to be addressed before the results of the inconclusive epidemiological studies can be confirmed.

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**The Lord Mayor’s taskforce on fluoridation – final report. (1997). Brisbane, Australia: Brisbane City Council.**

**Osteoporosis and Hip Fracture (Page 50):** A series of studies, mostly conducted in the USA, the UK and Canada, have addressed the question of whether fluoride affects the risk of fracture of the hip. In summary, of 17 ecological studies (i.e. studies of groups or populations), six reported no association with hip fracture, two a significant decrease in risk and nine an increased risk of fracture, although this was not statistically significant in three studies. None of the studies provided strong evidence of an association, at the levels of fluoride used for artificial fluoridation, that cannot be explained by chance, bias or confounding. In summary, there was no evidence that could be classed as level 3 and used reliably to evaluate causality.

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**Natick Fluoridation Study Committee. (1997). Should Natick fluoridate?: A report to the town and Board of Selectmen. (On-line).**

**Page 3, findings:** Water fluoridation shows a positive correlation with increased hip fracture rates in persons 65 years of age and older, based on two recent epidemiology studies.

**Page 34:** In a national study of ecological design Jacobsen et al. (1992) examined the association between water fluoridation and the incidence of hip fractures. For the period 1984-87, a total of 218,951 eligible hip fracture cases were studied. Raheb (1995) characterized the results of Jacobsen’s study as “a small, statistically significant positive association was found between fluoridation and fracture incidence rates.” However, a careful review of the data of Jacobsen and his coworkers show an 8% increase in women (+/- 2%) and a 17% increase for men (+/- 4%). A more recent study on a smaller population (which was restricted to Mormon communities in Utah to correct for confounding factors such as smoking and or use of alcohol) showed an increased incidence of hip fractures of 27% in women and 41% in men, albeit with a larger 95% confidence interval (Danielson, 1992). While four other studies indicate either no effect or a negative effect of fluoridation, these studies involved a total of only 6,874 subjects as opposed to positive correlation in the case of 781,575 subjects.
Page 34, summary: Well-controlled studies have not demonstrated a beneficial effect of the use of high doses of fluoride in reducing osteoporosis and related bone fractures. However, there has been a positive relationship between water fluoridation and increase hip fractures in persons 65 years of age and older.
Appendix 2 - Risks According to “Tier One” Reviews

Topic: SKELETAL FLUOROSIS

Major “Tier One” Reviews (United States, World Health Organization, & York)


Pages 81-83: Fluoride results in thickened bones and extoses (skeletal fluorosis) when ingested in large doses for an extended period of time. Reported cases are found almost exclusively in developing countries, particularly India, and are associated with malnutrition (Pandit et al., 1940). Tea consumption and high water intake due to tropical climate are probably also contributing factors. It is generally stated that a dose of 20-80 mg/day (equivalent to 10 to 40 ppm in the water) is necessary for the development of crippling skeletal fluorosis (NAS, 1971a), but individual variation, variation in nutritional status, and the difficulty of determining water fluoride levels in such situations make it difficult to determine the critical dose. Pandit et al. (1940) found severe skeletal fluorosis in people who had consumed 13-24 mg/day for >15 years.

The incidence of skeletal fluorosis in the US is unknown, since it appears that the early signs can only be identified radiologically. A study of 116 people who had lived in an area with an average of 8ppm fluoride in the drinking water for at least 15 years found a 10-15% incidence of fluoride-related bone changes (Leone et al., 1955). Coarsened trabeculation and thickened bones were observed, but no extoses were evident, and the subjects were asymptomatic.

A limited number of cases of crippling skeletal fluorosis due to oral exposure have been reported in the United States. Where the doses are known, they are generally in the 15-20 mg/fluoride/day for over 20 years; two of the cases were associated with renal disease, which would reduce fluoride excretion. Two of the cases were associated with drinking large quantities of water with >3.5 ppm fluoride.

Fluoride is found in all bone, with the concentration depending on total fluoride exposure. The amount varies among different bones. Levels of fluoride in human bone are generally determined by biopsy of the iliac crest bone, and are generally reported as ppm bone ash. Average bone contains 500-1,000 ppm fluoride. (Boivin, 1988; Franke, 1975). Bone from people with pre-clinical skeletal fluorosis, which is asymptomatic and characterized by slight radiologically detectable increases in bone mass, contains 3,500-5,500 ppm fluoride. Sporadic pain, joint stiffness, and osteosclerosis of the pelvis are observed at 6,000-7,000ppm, while chronic joint pain, increased osteosclerosis, and slight calcification of ligaments occur at 7,500-9,000ppm. Crippling fluorosis is observed at fluoride bone concentrations >10,000 ppm (Franke, 1975). The fluoride concentrations in bone increases with age (Zipkin, 1958). In a group of five people ages 64-85 that had lived for at least 10 years in an area with water containing 1 ppm fluoride, the average fluoride concentration of the iliac crest bone was 2,250 ppm of bone ash.


Pages 307-308: Three recent reviews of the literature attempted to identify adverse functional effects of fluoride ingestion in adults (Kaminisky et al., 1990; NRC, 1993; USPHS, 1991). Fluoride exposures included those associated with drinking water containing as much as 8 mg/liter of fluoride and the use of dental products. These reviews indicate that the primary functional adverse effect associated with excess fluoride intake is skeletal fluorosis.

In the asymptomatic, pre-clinical stage of skeletal fluorosis, patients have slight increases in bone mass that are detectable radiographically, bone ash fluoride concentrations that range from 3,500 to 5,500 mg/kg, and bone concentrations that are 2 to 5 times higher than those of life-long residents of optimally fluoridated communities (Eble et al., 1992). Stage 1 skeletal fluorosis is characterized by occasional stiffness or pain in joints and some osteosclerosis of the pelvis and vertebra. Bone ash fluoride concentrations usually range from 6,000 to 7,000 mg/kg. In stages 2 and 3, bone ash concentrations exceed 7,500 to 8,000 mg/kg (Hodge and Smith, 1977). The clinical signs in stages 2 and 3, which may be crippling, may include dose-related calcification of ligaments, osteosclerosis, extoses, possibly osteoporosis of long bones, muscle wasting, and neurological defects due to hypercalcification of vertebra (Krishnamachari, 1986).

The development of skeletal fluorosis and its severity is directly related to the level and duration of exposure. Most epidemiological research has indicated that an intake of at least 10 mg/day for 10 or more years is needed to produce clinical signs of the milder forms of the condition. Hodge (1979) reported that evidence of crippling fluorosis “was not seen in communities in the United States where water supplies contained up to 20 ppm.” In such communities...
daily fluoride intakes of 20 mg would not be uncommon. In a recent case report, severe joint pain and stiffness in a 64-year-old man were attributed to a fluoride intake of approximately 50 mg/day for 6 years. The well water ingested had a fluoride concentration of 25 mg/liter and a low calcium concentration (Boyle and Chagnon, 1995). Stevenson and Watson (1957) surveyed 170,000 radiographs of patients from Texas and Oklahoma whose drinking water fluoride concentrations ranged from 4 to 8 mg/liter. They identified 23 cases of osteosclerosis but no evidence of skeletal fluorosis.

Crippling skeletal fluorosis continues to be extremely rare in the United States (only 5 cases have been confirmed during the last 35 years), even though for many generations there have been communities with drinking water fluoride concentrations in excess of those that have resulted in the condition in other countries (Singh & Jolly, 1970). This puzzling geographic distribution has usually been attributed to unidentified metabolic or dietary factors that rendered the skeleton more or less susceptible.

Identification of a NOAEL and Critical Endpoint (Page 310): Epidemiological studies reported no detectable radiographic changes in bone density in persons in the United States exposed to drinking water containing less than 4 mg/liter of fluoride (McCauley & McClure, 1954; Schlesinger et al., 1956; Sowers et al., 1986; Stevenson & Watson, 1957). Leone (1955) compared bone x-rays of long-term residents of Bartlett & Cameron, Texas, which had water supplies with fluoride concentrations of 8.0 and 0.4 mg/liter, respectively. In this study, osteosclerosis was detected radiographically in 10-15% of individuals exposed to water containing 8.0 mg/liter of fluoride for an average of 37 years. However, no clinical symptoms of skeletal fluorosis were reported. Another report dealing with a variety of other medical conditions among residents of Bartlett and Cameron revealed no significant differences except for a slightly higher rate of cardiovascular abnormalities in Cameron residents (Leone et al., 1954). Therefore, based on the available data addressing the association between fluoride intake and skeletal fluorosis in North America, a NOAEL of 10 mg/day of fluoride was identified. This level of intake for some individuals would occur in areas where the drinking water has a fluoride concentration of 5 mg/liter and the diet is the main source of fluoride.

Uncertainty Assessment. Based on the fact that the NOAEL derives from human studies and the lack of evidence for symptomatic skeletal fluorosis observed at this level of fluoride intake, a UF of 1 was selected.

Derivation of the UL (Pages 310-311): The risk of developing early signs of skeletal fluorosis is associated with a fluoride intake greater than 10 mg/day for 10 or more years. Therefore a UL of 10 mg/day was established for children older than 8 years and for adults. Data from studies of fluoride exposure from dietary sources or work environments (Hodge & Smith, 1977) indicate the a UL of 10 mg/day for 10 or more years carries only a small risk for an individual to develop pre-clinical or stage 1 skeletal fluorosis.

Special considerations Page 311): Reports of relatively marked osteofluorotic signs and symptoms have been associated with concentrations of fluoride in drinking water of approximately 3 mg/liter in tropical climates. This adverse effect has been attributed to poor nutrition, hard manual labor, and high levels of water intake (Krishnamachari, 1986; Singh and Jolly, 1970; WHO, 1984). Therefore, an increased risk of skeletal fluorosis from excess fluoride intake may exist for malnourished individuals living in hot climates or tropical areas.
cases of greater fluoride exposure, even if that exposure was difficult to define precisely. Fluoride retention in bone appeared to be higher in people who have ingested 10-20 mg of fluoride per day for 10-20 years. During the last 30 years, only five cases have been reported in the United States. The history of fluoride intake for two of the cases was determined with reasonable accuracy (Sauerbrunn et al., 1965; Goldman et al., 1971). The individuals consumed up to 6 L of water per day containing fluoride at 2.4-3.5 mg/L in one case and 4.0-7.8 mg/L in the other. The daily fluoride intake was estimated at 15-20 mg for 20 years. In general, this intake would be associated with a drinking-water supply containing fluoride at about 10 mg/L.

Thus crippling skeletal fluorosis in the United States has been rare and not a public health problem (Leone et al., 1954; Stevenson & Watson, 1957), even though for many generations there have been communities with drinking water fluoride concentrations in excess of those that have resulted in the condition in other countries (Singh & Jolly, 1970). The puzzling geographic distribution of the disorder usually is ascribed to unidentified dietary factors that render the skeleton more or less susceptible.

The small number of cases of skeletal fluorosis in the United States has ruled out the possibility of systematic epidemiological evaluation. Based on limited data in the literature on skeletal fluorosis, the subcommittee concludes that skeletal fluorosis is not a public health issue in the United States.


Page 5, executive summary: Fluoride has a complex dose-related action on bone. Although crippling skeletal fluorosis is more common in parts of the world with high natural fluoride (>10 ppm) levels in drinking water, its occurrence is affected by a variety of factors, including nutritional deficiencies, impaired renal function, and age at exposure. Human crippling skeletal fluorosis is endemic in several countries of the world, but is extremely rare in the United States.

Pages 45-47: The preclinical & three clinical stages of skeletal fluorosis (Smith & Hodge) are described in table 23, along with reported correlations of accumulated fluoride in bone ash to the osteosclerotic phase (Franke et al; Schlegal 1974). The earliest bone changes associated with skeletal fluorosis are radiographic enlargements of the trabeculae in the lumbar spine. These preclinical findings have been associated with bone ash fluoride concentrations of 3,500 to 4,500 ppm. Singh & Jolly (1970) reported that osteosclerosis in the pelvis and vertebral column, coarse trabeculae, and diffuse increased bone density of clinical phase I are seen in industrial cases but rarely are reported in areas where fluorosis is endemic. Most of the latter cases show the more severe changes of phases II or the crippling fluorosis of phase III. Bone changes observed in human skeletal fluorosis are structural and functional, with a combination of: 1) osteosclerosis, the predominant lesion in fluorosis patients who have an adequate dietary intake of calcium; 2) osetomalacia, which predominates in patients who have marginal or suboptimal dietary intake of calcium; 3) osteoporosis and exostosis formation of varying degrees; and 4) secondary hypoparathyroidism in a proportion of patients (Krishnamachari, 1986).

Boivin and coworkers (1988) reported measuring bone fluoride content from iliac crest bone to determine the degree of fluoride retained in bone and, over time, the amount of fluoride eliminated. Subjects with skeletal fluorosis primarily of industrial etiology, had bone fluoride values over 0.50 percent of bone ash by weight, and the values were always statistically higher than the highest control value, 0.10% (p< 0.001). Fluoride retention in bone appeared to be higher in cases of greater fluoride exposure, even if that exposure was difficult to define precisely.

The total quantity of fluoride ingested is the single most important factor in determining the clinical course of skeletal fluorosis (Krishnamachari, 1986); the severity of symptoms correlates directly with the level and duration of exposure (Fisher et al., 1989). As most commonly reported for a person to develop crippling skeletal fluorosis, he or she must ingest 20 to 80 mg/day of fluoride (the equivalent to 10 ppm fluoridated water for 10 to 20 years (Hodge & Smith, 1965; Hodge, 1979; WHO, 1984; National Academy of Science (1980). For endemic, tropical areas, the level of clinical effect for skeletal fluorosis is less certain (NAS, 1980); Singh & Jolly (1970) stated that it may not be
possible to determine the average minimal dose of fluoride needed to produce skeletal fluorosis, because of individual variations and the crude level of water analysis in many of the endemic areas.

For almost 40 years, investigators in the US have searched for evidence of skeletal fluorosis. Radiographic changes in bone indicative of skeletal fluorosis, changes in bone mass, and effects on skeletal maturation were not observed at water fluoride concentrations of 1.2 mg/L for 10 years and from 3.3 – 6.2 mg/L for a lifetime (Hodge & Smith, 1981; Sowers et al., 1986; Schlesinger et al., 1956; McCauley & McClure, 1954). In a survey of 170,000 radiographs of patients living in Texas and Oklahoma with water fluoride levels between 4 - 8 mg/L, Stevenson & Watson (1957) found 23 cases of radiographic osteosclerosis, but no evidence of skeletal fluorosis.

Skeletal fluorosis is highly variable in its clinical severity among individuals living in the same environment and exposed to the same risk of fluoride ingestions (Krishnamachari, 1986). In the past 30 years, only five cases of crippling skeletal fluorosis have been reported in the literature in the US (Sauerbrunn et al., 1965; Goldman et al., 1971; Fisher et al., 1981 & 1989; Bruns & Tytle, 1988). Yet, over several generations many individuals in the US have consumed water containing high natural levels of fluoride, without demonstrating signs or symptoms of skeletal fluorosis. The unequal worldwide distribution of this disorder generally has been ascribed to unidentified dietary factors that render the skeleton more or less susceptible. Whitford (1989) suggests that differences among populations with respect to fluoride metabolism and fluoride balance are responsible. Acid-base status and the concomitant changes in urinary pH (Whitford & Reynolds, 1979) are the most important contributors to population variation.

In the 5 cases of crippling skeletal fluorosis in the US, retrospectively assessed, exposure to natural levels of fluoride in drinking water ranged from 3.9-8.0 mg/L. All possible confounding factors were not addressed. Two of these cases were associated with daily consumption of up to 6 liters of water containing fluoride levels of 2.4-3.5 ppm in one case and 4.0-7.8 ppm in the other (Sauerbrunn et al., 1965; Goldman et al., 1971). Large quantities of tea, itself high in fluoride, were consumed daily as well. The total fluoride intake was estimated to be 15-20 mg/day for 20 years.

Severe crippling fluorosis is not seen in all residents of endemic areas; age of exposure as well as dose and duration of fluoride intake are critical in predicting the clinical signs and symptoms of skeletal fluorosis. Other factors reported to influence the incidence of skeletal fluorosis include: nutritional and calcium deficiencies; renal insufficiency (Singh & Jolly, 1970); the level of bone turnover (Boivin et al., 1988); and diets containing high levels of fluoride (Sauerbrunn et al., 1965; Goldman et al., 1971). Also, in certain occupational settings, the duration and exposure from the inhalation of products of manufacturing, e.g. aluminum, steel, iron, pesticides, fertilizers, and smelting of precious metals (Hodge & Smith, 1972). Other factors influencing skeletal fluorosis include soil type or areas of volcanic rock, geophasia, syndromes of polydipsia, excessive water consumption (Fisher et al., 1989), and the type of physical activity (Singh & Jolly 1970). Finally, the following factors have been associated with increased incidence of skeletal fluorosis: pre-existing inflammation; increased serum haptoglobin levels; cortisol levels (Susheela et al., 1988); the use of fluoride in the treatment of inflammatory conditions (Bruns & Tytles, 1988).


Pages 77-78: On the basis of an extensive epidemiological survey, Singh & Jolly (1970) stated that crippling fluorosis was the result of continuous daily intake of 20-80 mg fluoride for 10-20 years. On the basis of more recent balance studies on patients with endemic fluorosis, which showed an average daily fluoride intake of 9.88 mg, Jolly (1976) suggested that a daily intake exceeding 8 mg in adults would be harmful. In tropical areas with endemic fluorosis, high fluoride levels in the drinking water seem to constitute an important factor in a multi-factorial causation (Reddy, 1979). Thus, poor nutrition, including calcium deficiency, and hard manual labor seem to play an additional role. In addition, protein deficiency may increase individual susceptibility to fluorosis (Siddiqui, 1955; Singh et al., 1961a).

In non-tropical countries, no cases of skeletal fluorosis with clinical signs and symptoms have been detected in relation to drinking water containing fluoride levels of less than 4 mg/liter (Victoria Committee, 1980). In Bartlett, Texas, with a (previous) water-fluoride level of 8-mg/ liter, radiological evidence of fluorosis in the form of osteosclerosis was recorded in 10-15% of the people (Leone et al., 1955). X-ray changes were also noted in a few people living in Oklahoma and Texas where the drinking water contained a fluoride level of 4-8 mg/liter (Stevenson & Watson, 1957). In other studies, no signs or symptoms of osteofluorosis were detected in areas with fluoride levels of up to 6 mg/liter in water supplies (McClure, 1946; Eley et al., 1957; Knishikov, 1958).
Other Reviews
(examples of municipal or territorial reviews of the water fluoride issue)


Pages 44-45: The intake of fluoride at high levels for protracted periods results in a systemic osteosclerosis known as skeletal fluorosis or osteofluorosis. This condition is characterized by 1: a thickened cortical and cancellous bone with signs of hypomineralization and mineralization defects; 2. spur bony formations at tendon insertions; and 3. ossification of interosseous membranes and ligaments. These changes are more pronounced in the central skeleton and to a lesser degree in the skull and the peripheral bones (Fejerskov, 1996). Clinically they range from asymptomatic radiographic bone mass increase to crippling skeletal fluorosis involving spine and joint deformities and dysfunctions, muscle wasting and neurological problems due to spinal cord compression (Whitford, 1996; Kleerekoper, 1996).

Most estimates indicate that crippling fluorosis is associated with chronic fluoride exposures of ≥ 10 mg/day for at least 10 years. These exposures occur as either endemic (exposure to the naturally fluoridated drinking water) or industrial (e.g. exposure to the cryolite dust) (Fejerskov, 1996; Whitford, 1996). Besides the dos and duration of fluoride exposure, the development of skeletal fluorosis is influenced by various other factors. The most common are age, physical activity, kinetics of bone remodeling, nutritional status and renal insufficiency (Kleerekoper, 1996). Epidemiological studies of bone mineral density have not detected changes consistent with skeletal fluorosis resulting from the consumption of drinking water containing fluoride at the concentrations considered optimal for caries prevention.


Page 9: When fluoride accumulates in the skeleton to high levels (usually above 5000 ppm in bone ash) a clinical problem of skeletal fluorosis can be documented. At very high levels (usually well above 5000 ppm) of fluoride accumulation, patients may have a crippling osteo-arthritis-like syndrome that is attributed to the fluoride stimulation of mineral deposition around the joints and probable multiple micro-fractures in bones adjacent to the joints due to fluoride inhibition of normal mineralization. There is a concern that this level of fluorosis might occur in subjects with a high lifetime intake of fluoride. As we age, our ability to remove fluoride from our body (excretion in the urine) declines, so a theoretical risk in the aged population occurs in areas where water fluoridation is present. Early studies of fluoride content in bone autopsy specimens from communities with higher levels of water fluoride than used in Calgary (greater than 1.5 ppm) have shown some individuals had bone levels in the range, which has been associated with skeletal fluorosis (over 5000 ppm in bone ash) (Amala et al., 1985). I know of no reported cases of skeletal fluorosis that can be related solely to the consumption of artificially fluoridated water at 1 mg/L or less.


Page 51: Approximately 50% of ingested fluoride is excreted by the kidneys within 24 hours, a small amount is stored in the teeth, and rest is mainly deposited in the skeleton. Exposure to high levels of fluoride can lead to skeletal fluorosis. This condition produces pain, stiffness and immobility in joints and can lead to more serious neurological disorders. There have been no reports of skeletal fluorosis attributable to water fluoridation in Australia and overseas, most reports have been linked to sustained high levels of exposure in areas where water fluoride levels are naturally very high or in workers who are occupationally exposed to fluoride. However, no systemic research on skeletal fluorosis has been carried out in Australia, and NHMRC have acknowledged that it would not be surprising if there were undetected cases. The review concluded that it was possible that certain individuals, for instance patients under going dialysis for renal disease, might have a slightly increased risk of skeletal fluorosis.


Pages 32-33: Osteofluorosis is a complicated disease with a number of stages. The first two stages are pre-clinical, that is, the patient feels no symptoms but changes have taken place in the body. In the first pre-clinical stage,
biochemical changes occur in the blood and bone composition; in the second stage histological changes can be observed in bone biopsies. Some experts call these changes harmful because they are precursors of more serious conditions. Other experts say they are harmless (Hileman, 1988). Most admit that the effects of long-term ingestion of fluoridated water on bone are poorly understood (Hileman, 1988).

The clinical stages of osteofluorosis includes pain in the bones and joints, muscle weakness, fatigue, calcification of ligaments and bone spurs. Most experts in skeletal fluorosis agree that ingestion of 10-20 mg/day for 10-20 years or more can cause crippling skeletal fluorosis and doses as low as 2 – 5 mg/day over the same time period can cause the pre-clinical stages. (Hileman, 1988). Moreover, the total quantity of fluoride ingested is the single most important factor in determining the clinical course of osteofluorosis (Ad hoc committee, 1991). The severity of the symptoms correlates directly with the level and duration of exposure. For almost 40 years, investigators in the US Public Health Service reports that:

“Radiographic changes in bone indicative of skeletal fluorosis, changes in bone mass, and effects on skeletal maturation were not observed at water fluoride concentrations of 1.2 mg/L for 10 years and from 3.3 – 6.2 mg/L for a lifetime (Hodge & Smith, 1981; Sowers et al, 1986; Schlesinger et al., 1956; McCauley & McClure, 1954). In a survey of 170,000 radiographs of patients living in Texas and Oklahoma with water fluoride levels between 4 - 8 mg/L, Stevenson & Watson (1957) found 23 cases of radiographic osteosclerosis, but no evidence of skeletal fluorosis.”

Nevertheless, large numbers of people in Japan, China, India, the Middle East and Africa have been diagnosed with skeletal fluorosis (Hileman, 1988). In India, Tanzania and South Africa, crippling forms of skeletal fluorosis have been reported in pediatric age groups as well (Ad hoc committee, 1991).
Appendix 2 - Risks According to “Tier One” Reviews

Topic: ENAMEL (DENTAL) FLUOROSIS

Medical Research Council. Medical Research Council working group report: water fluoridation and health. (September 2002).

Pages 19-20: Dental fluorosis is a form of developmental defect of tooth enamel. Histologically it presents a hypocalcification, while clinically it ranges from barely visible white striations on the teeth through to gross defects and staining of the enamel. There are about 90 different causes of enamel defects of which three or four causes are common. Differential diagnosis is not straightforward, and therefore in epidemiological studies, inter- and intra-examiner variability remains a problem. Minor forms of dental fluorosis are not aesthetically troublesome and may even enhance the appearance of dental enamel (Hawley et al., 1996).

The York Review identified 88 studies (mainly cross-sectional) investigating dental fluorosis, from 30 countries, which suggested a prevalence (all levels of severity) of 48% in fluoridated areas and 15% in non-fluoridated areas. Limiting consideration to aesthetically important levels of severity, the York Review reported the prevalence of fluorosis to be 12.5% in fluoridated areas and 6.3% in non-fluoridated areas. For any given fluoride concentration in water the prevalence of aesthetically important dental fluorosis was higher in naturally fluoridated areas than in artificially fluoridated areas. A sensitivity analysis excluding data points above 1.5ppm fluoride found prevalences for all levels of severity of 46% and 18% and for aesthetically important dental fluorosis of 10% and 6% in fluoridated and non-fluoridated areas respectively. The York Review suggested that there was a dose-response relationship and that most studies failed to take full account of confounding factors. However, the York Review included studies in countries with hotter climates than the UK: in hot climates, water intake is typically higher than in the US and the risk of fluorosis correspondingly greater for any given water fluoride concentration (Murray, 1986).

Relevant studies. In the US, the prevalence of aesthetically important dental fluorosis is probably lower than that reported in the York Review. For example, a study by Tabari et al., (2000) found prevalence of fluorosis (in upper permanent incisor teeth) to be 3% in fluoridated Newcastle and 0.5% in non-fluoridated Northumberland. An EU BIOMED funded study (O’Mullane et al., 1999) reported the prevalence of aesthetically important fluorosis (based on photographic diagnosis) in seven European countries, including the US. Results are reported in Table 3. Only in Cork was the drinking water artificially fluoridated.

Table 3.
Prevalence of aesthetically important fluorosis in seven European Countries

<table>
<thead>
<tr>
<th>Number of children photographed</th>
<th>Prevalence of aesthetically important fluorosis (TF/3)a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cork (Ireland) Fluoridated</td>
<td>325</td>
</tr>
<tr>
<td>Knowsley (UK)</td>
<td>314</td>
</tr>
<tr>
<td>Haarlem (Netherlands)</td>
<td>303</td>
</tr>
<tr>
<td>Athens (Greece)</td>
<td>283</td>
</tr>
<tr>
<td>Almada (Portugal)</td>
<td>210</td>
</tr>
<tr>
<td>Reykjavik (Iceland)</td>
<td>296</td>
</tr>
<tr>
<td>Oulu (Finland)</td>
<td>315</td>
</tr>
</tbody>
</table>

a The “TF” index of dental fluorosis is named after Thylstrup and Fejerskov who developed it (Thylstrup & Fejerskov, 1978)
Source: EY BIUMED study, report to EU dated July 1999 (O’Mullane et al., 1999)

The British Society for Paediatric Dentistry has published guidelines that indicate that discretionary fluorides are an important aetiological factor for dental fluorosis, and recommends that children at low risk of caries should use a small pea sized amount of lower fluoride toothpaste under parental supervision. Fluoride tablets and drops should not be prescribed routinely (Holt, et al., 1996). A National survey for 1½ and 4½ year olds and a recent study in the North East of England both indicated that these recommendations were being heeded by significant numbers of parents (Hinds & Gregory, 1995; Tabari et al., 2000). The latter study found that the use of low fluoride toothpaste in infancy was related to a lower prevalence of dental fluorosis in upper permanent incisor teeth.
A higher incidence of dental fluorosis has been reported in children in the USA compared with the US. However, studies have suggested that 7 to 30% of children living in fluoridated US communities may also be receiving fluoride supplements inappropriately prescribed by their physician or paediatrician (US Department of Health and Human Services, 2001), which could contribute to the higher prevalence values reported in the international data. In addition, low fluoride toothpastes have not been marketed in the USA.

**Research recommendations.** There are discrepancies between the dental fluorosis data reported by the York Review and recent data from the US and Europe (detailed above). The public’s awareness and understanding of fluorosis is, in general, low. Any future research should aim to provide further understanding of these two aspects. Further methodological work is needed to validate the Thystrup-Fejerskow (TF) index of dental fluorosis using histological appearance as the validating criterion.

Specific recommendations are as follows:

- Cross-sectional studies to determine the current prevalence of dental fluorosis in fluoridated and non-fluoridated communities. Photographic techniques are recommended, with careful attention to examiner training, calibration and blinding. Due regard should be given to potential confounding factors and/or effect modifiers such as social class, ethnic group and the use of discretionary fluorides.

- Further studies should determine the public’s perception of dental fluorosis with particular attention to the distinction between acceptable and aesthetically unacceptable fluorosis.

- Any prospective epidemiological studies of fluoridation and dental caries should incorporate dental fluorosis as one of the outcome measure.


Pages 6-7, 11-12: Concerns regarding the risk for enamel fluorosis are limited to children aged < 8 years; enamel is no longer susceptible once its pre-eruptive maturation is complete (IOM, 1997). Fluoride sources for children aged ≤ 8 years are drinking water, processed beverages and food, toothpaste, dietary supplements that include fluoride (tablets and drops), and other dental products.

The very mild and mild forms of enamel fluorosis appear as chalklike, lacy markings across a tooth’s enamel surface that are not readily apparent to the affected person or casual observer (Dean, 1942). In the moderate form, >50% of the enamel surface is opaque white. The rare, severe form manifests as pitted and brittle enamel. After eruption, teeth with moderate or severe fluorosis might break away, resulting in excessive wear of the teeth. Even in its severe form, enamel fluorosis is considered a cosmetic effect, not an adverse functional event (USPHS, 1991; IOM, 1997; Kaminsky et al., 1990; Clark et al., 1993).

When enamel fluorosis was first systemically investigated during the 1930s and 1940s, its prevalence was 12%-15% for very mild and mild forms and zero for moderate and severe forms among children who lived in communities with drinking water that naturally contained 0.9-1.2 ppm fluoride (Dean, 1942). Although the prevalence of this condition in the United States has since increased (USPHS, 1991; Clark, 1994; Szupnar & Burt, 1987), most fluorosis today is of the mildest form, which affects neither cosmetic appearance nor dental function. The increased prevalence in areas both with and without fluoridated community drinking water indicates that, during the first 8 years of life, the total intake of fluoride from all sources has increased for some children. (USPHS, 1991). The 1986-87 National Survey of Dental Caries in U.S. School Children (the most recent national estimates of enamel fluorosis prevalence) indicated that the prevalence of any enamel fluorosis among children was 22%-23% (range: 26% of children aged 9 years to 19% of those aged 17 years) (Brunelle, 1987; Heller et al., 1997). Almost all cases reported in the survey were of the very mild or mild form, but some cases of the moderate (1.1%) and severe (0.3%) forms were observed. Cases of moderate and severe forms occurred even among children living in areas with low fluoride concentrations in the drinking water (Heller et al., 1997). Although this level of enamel fluorosis is not his is not considered a public health problem (Hutton et al., 1951) prudent public health practice should seek to minimize this condition, especially moderate to severe forms. Research into the causes of enamel fluorosis has focused on identifying appropriate risk factors (Pendrys et al., 1994; Osuji et al., 1988; Pendrys et al., 1989; Pendrys, 1995).

Enamel fluorosis occurs among some persons in all communities, even in communities with a low natural concentration of fluoride. During 1930-60, US studies documented that, in areas with a natural or adjusted concentration of fluoride approximately 1.0 ppm in the community drinking water, the permanent teeth of 7%-16% of children with a lifetime residence in those areas exhibited very mild or mild forms of enamel fluorosis (Dean,
1942; Ast et al., 1956; Russell, 1962). Before 1945, when naturally fluoridated drinking water was virtually the only source of fluoride, the moderate and severe forms of this condition were not observed unless the natural fluoride concentration was ≥2 ppm (Dean, 1942). The likelihood of a child developing the mild forms of enamel fluorosis might be higher in a fluoridated area than in a non-fluoridated area, but prevalence might not change in every community (Lewis & Banting, 1994; Kumar & Swango, 1999). The most recent national study of this condition indicated that its prevalence had increased in both fluoridated and non-fluoridated areas since the 1940s, with the relative increase higher in non-fluoridated areas. In communities with drinking water containing 0.7-1.2 ppm fluoride, the prevalence was 1.3% for the moderate form of enamel fluorosis and zero for the severe form; thus few cases of enamel fluorosis were likely to be of cosmetic consequence (USPHS, 1991; Heller et al., 1997). Because combined fluoride intake from drinking water and processed beverages and food by children in fluoridated areas has reportedly remained stable since the 1940s, the increase in fluoride intake resulting in increased enamel fluorosis almost certainly stems from the use of fluoride-containing dental products by children aged <6 years (IOM, 1997).

Two studies reported that extended consumption of infant formula beyond age 10-12 months was a risk factor for enamel fluorosis, especially when formula concentrate was mixed with fluoridated water (Pendrys et al., 1994; Osuji et al, 1988). These studies examined children who used pre-1979 formula (with higher fluoride concentrations). Whether fluoride intake from formula that exceeds the recommended amount during only the first 10-12 months of life contributes to the prevalence or severity of enamel fluorosis is unknown.

Fluoride concentrations in drinking water should be maintained at optimal levels, both to achieve effective caries prevention and because changes in fluoride concentration as low as 0.2 ppm can result in a measurable change in the prevalence and severity of enamel fluorosis (Evans & Stamm, 1991; Szupnar & Burt, 1988).


Pages 80-81: There is some evidence that levels of fluorosis have increased due to the multiple, widespread sources of fluoride in food processed with fluoridated water and dentifrices containing fluoride, in addition to the water of fluoridated communities. Comparison of fluorosis levels in 21 cities with fluoride ranging (0.4 to 2.7 ppm that were surveyed by Dean in the 1940s, and studies of dental fluorosis in 21 cities that were conducted in the 1980s found that both the prevalence and the severity of dental fluorosis were correlated with the level of fluoride in the drinking water (DHHS, 1991). During this 40 year period, the prevalence of fluorosis in areas with <0.4 ppm fluoride increased from <1 to about 6%; nearly all of the increase was the in the very mild and mild categories. Both the prevalence and severity of fluorosis increased in communities with 0.7-1.2 ppm fluoride, with prevalence increasing from about 13 to about 22%. Most of the increase was in the very mild and mild categories, which increased from 12.3 to 17.7%, and from 1.4 to 4.4% of the population respectively. The combined prevalence of the severe and moderate categories increased from 0.0 to 0.9%. While there were some differences between the studies in the 1940s and those in the 1980s, such as the subject population and examination conditions, they do not effect overall trends. Although total fluoride intake was not measured, these studies indicate that intake has increased since the 1940s, because fluorosis levels increased for all water fluoride levels.

Fluorosis levels in 1985 in communities with fluoride levels at about 1,2,3 and 4 ppm were compared with levels of fluorosis in the same communities in 1980 (Heifetz et al., 1988). Both examinations included 8-10 year old and 13-15 year old children. The 13-15 year old children in the follow-up study had also participated in the initial study. While there were no marked changes in fluorosis levels in 8-10 year old children, both the prevalence and severity increased in the 13-15 year old children. Increases in the 1ppm communities were mostly in the category of barely visible white spots. However, the percentages of labial surfaces of incisors and canines from children in the 2 ppm group that had brown mottling increased from 0 to 7.6%. Less marked increase in mottled and pitted teeth were seen in the higher dosage groups. The increased levels of fluorosis were attributed to increased fluoride exposure from multiple sources.

While drinking water fluoride levels ranging from 0.7-3.0 ppm can reduce the incidence of dental caries, susceptibility to caries can increase at higher fluoride levels. Adolescents consuming water containing 5 ppm fluoride since birth were evaluated for fluorosis and prevalence of caries. The prevalence of dental fluorosis was 100%, with the 182 subjects showing effects ranging from mild to severe (Mann et al., 1987).
Page xiii, executive summary: Dental fluorosis was the most widely and frequently studied of all negative effects. The fluorosis studies were largely cross-sectional designs, with only 4 before-after designs. Although 88 studies of fluorosis were included, they were of low-quality. The mean validity score for fluorosis was only 2.8 out of 8. All but one of the studies were of evidence level C. Observer bias may be of particular importance in studies assessing fluorosis. Efforts to control for the effects of potential confounding factors, or reducing potential for observer bias was uncommon.

As there may be some debate about the significance of a fluorosis score at the lowest level of each index being used to define a person as ‘fluorosed’, a second method of determining the proportion ‘fluorosed’ was selected. This method describes the number of children having dental fluorosis that may cause ‘aesthetic concern.’

With both methods of identifying the prevalence of fluorosis, a significant dose-response relationship was identified through a regression analysis. The prevalence of fluorosis at a water fluoride level of 1.0 ppm was estimated to be 48% (95% CI 40-57) and for fluorosis of aesthetic concern it was predicted to be 12.5% (95%CI 7.0-21.5). A very rough estimate of the number of people who would have to be exposed to water fluoride levels of 1.0 ppm for one additional person to develop fluorosis of any level is 6 (95% CI 4-21), when compared with a theoretical low fluoride level of 0.4 ppm. Of these approximately one quarter will have fluorosis of aesthetic concern, but the precision of these rough estimates is low. These estimates only apply to the comparison of 1.0 ppm to 0.4 ppm, and would be different if other levels were compared.

Discussion, page 45: Fluorosis was the most widely and frequently studied of all the possible adverse effects considered. The fluorosis studies used were cross-sectional designs, with a few before-after designs (again using different groups of people at each time point). The mean validity score was only 2.8 out of 8 and all but one of the studies was evidence level C. Observer bias may be of particular importance in studies assessing fluorosis. Efforts to control for potential confounding factors, or reducing potential observer bias were infrequently undertaken. Seventy-two of 88 studies did not use any form of blinding by the assessor, and 50 of 88 did not control for confounding factors, other than by simple stratification by age or sex.

The primary fluorosis analysis was based on prevalence of ‘fluorosed’ people, including any degree of fluorosis. A conservative approach for defining fluorosis was used in this analysis, in that the ‘questionable’ category in Dean’s index was counted as fluorosis. Because there is evidence that very mild forms of fluorosis are not concerning to people (indeed some even preferred photographs of mildly fluorosed teeth) a secondary analysis assessed the prevalence of fluorosis of ‘aesthetic concern’.

With both methods of measuring the prevalence of fluorosis, a significant dose-response relationship was identified through the univariate regression analysis. The prevalence of fluorosis at a water fluoride level of 1.0 ppm was estimated to be 48% (95% CI 40-57) for any fluorosis and 12.5% (95% CI 7.0-21.5) for fluorosis of aesthetic concern. The numbers of additional people who would have to be exposed to water fluoride levels of 1.0 or 1.2 ppm for one additional person to develop fluorosis of any level were quite low, 5 or 6 when comparing to a theoretical low fluoride level of 0.4 ppm. For fluorosis of esthetic concern to occur in one additional person, however, the number was 22 at 1 ppm, but the 95% CI included infinity.

The multivariate analysis of fluoride took into account variables potentially contributing to the heterogeneity between studies. This analysis found a statistically significantly higher risk in children with permanent teeth, compared with primary teeth or both types. The multivariate analysis of fluorosis of aesthetic concern confirmed these findings. A sensitivity analysis limiting the range of water fluoride levels entered into the model did not alter the findings in any meaningful way.

The estimated NNT for one extra child to be caries-free was seven (95% CI 5-10), while the NNH for fluorosis is six (95% CI 4-21), with approximately a quarter of these being of aesthetic concern. These estimates are based on comparisons of specific levels of water fluoridation (e.g. <0.7 ppm vs. 0.7 – 1.2 ppm for caries, and 0.4 ppm vs. 1.0 ppm for fluorosis). The numbers would change if different levels of fluoridation were compared.
Enamel fluorosis is a dose-response effect caused by fluoride ingestion during the pre-eruptive development of the teeth. After the enamel has completed its pre-eruptive maturation, it is no longer susceptible. Inasmuch as enamel fluorosis is regarded as a cosmetic effect, it is the anterior teeth that are of most concern. The pre-eruptive maturation of the crowns of the anterior permanent teeth is finished and the risk of fluorosis is over by 8 years of age (Fejerskov et al., 1977). Therefore, fluoride intake up to the age of 8 years is of most interest. Several reports suggest that enamel in the transitional or early maturation stage of development is most susceptible to fluorosis, which for the anterior teeth, occurs during the second and third years of life (Evans, 1989; Evans and Darvell, 1995; Pendrys and Katz, 1989; Pendrys and Stamm, 1990). Some evidence indicates that the risk of mild enamel fluorosis in the primary teeth is somewhat increased as a result of the relatively high fluoride intake associated with feeding some infant formulas reconstituted with fluoridated water (Larsen et al., 1988).

Fluorosed enamel has a high protein content. This results in increased porosity, which, in the moderate and severe forms, may eventually become stained and pitted (Fejerskov et al., 1977; Kaminsky et al., 1990). Clinically, the milder forms of enamel fluorosis are characterized by opaque striations that run horizontally across the surfaces of the teeth. The striations may become confluent giving rise to white opaque patches, often most apparent on the incisal edges of anterior teeth of cusp tips of posterior teeth (“snow-capping”). Mild fluorosis has no effect on tooth function and may render the enamel more resistant to caries. It is not readily apparent to the affected individual or casual observer and often requires a trained specialist to detect. In contrast, the moderate and severe forms of enamel fluorosis are generally characterized by esthetically objectionable changes in tooth color and surface irregularities. Most investigators regard even the more advanced forms of enamel fluorosis as a cosmetic effect rather than a functional adverse effect (Clark et al., 1993; Kaminsky et al., 1990).

Dental fluorosis has a strong dose-response relationship with fluoride intake. Dean (1942) established that the milder forms of enamel fluorosis affected the permanent teeth of 10-12% of permanent residents in communities where the drinking water has a fluoride concentration close to 1.0 mg/liter. The fluoride intake of children with developing teeth in these communities averaged 0.05 mg/kg/day and ranged from 0.02 to 0.10 mg/kg/day. In areas where the water contained low concentrations of fluoride (0.3 mg/L), fewer than 1% of the permanent residents had enamel fluorosis. Mild enamel fluorosis affected about 50% of residents where the water contained 2.0 mg/l of fluoride. At this concentration, a few cases (<5%) of moderate fluorosis were recorded (Dean, 1942). Fluoride intake by most children in these communities would have ranged from approximately 0.08 to 0.12 mg/kg/day. An average, chronic daily fluoride intake of 0.10 mg/kg appears to be the threshold beyond which moderate enamel fluorosis appears in some children. Where the water concentration was 4.0 mg/L, nearly 90% of the residents had enamel fluorosis, and about ½ of the cases were classified as moderate or severe.

Because cosmetic effect of the milder forms of enamel fluorosis are not readily apparent, moderate enamel fluorosis was selected as the critical adverse effect for susceptible age groups (infants, toddlers, and children from birth through the age of 8 years). Thus a fluoride intake of 1.0 mg/kg/day was identified as a LOEL for moderate enamel fluorosis in children from birth through the age of 8 years, at which age the risk of developing fluorosis of the anterior teeth is over. Based on a LOAEL of 1.0 mg/kg/day for moderate enamel fluorosis and an uncertainty factor of 1, a Tolerable Upper Intake Level (UL) of 1.0 mg/kg/day was established for infants, toddlers and children through 8 years of age. The extensive epidemiological research conducted in the US during the 1930s and 1940s (Dean, 1942) established, with a high degree of certainty, that a chronic fluoride intake of less than 0.10 mg/kg./day by children at risk of enamel fluorosis was associated with a low prevalence (for example, approximately 10%) of the milder forms of the condition. Based on a UL of 0.10 mg/kg/day of fluoride and a reference weight for infants ages 0-6 months of 7 kg, the UL is 0.7 mg/day. For children ages 7-12 months with a reference weight of 9 kg, the UL is 0.9 mg/day. Based on a UL of 0.10 mg/kg/day of fluoride and a reference weight for children ages 1-3 years of 13 kg, the UL is 1.3 mg/day for children ages 1-3 years. For children ages 4-8 years with a reference weight of 22 kg, the UL is 2.2 mg/day.

Prior to the 1960s, the diet, including water, was the only significant source of fluoride. Since then, fluoride ingestion resulting from the use of dental products and fluoride supplements has increased the risk of enamel fluorosis in children. The results of several studies (Kumar et al., 1989; Leverett, 1986; Pendrys & Stamm, 1990; Williams & Zwemer, 1990) have indicated that mild enamel fluorosis in communities with optimally fluoridated water (1.0 mg/L) is now more than twice and prevalent as in the 1930s and 1940s; that is, the prevalence has increased from

an average of about 10% to an average approaching 25%. In communities where the water has a low fluoride concentration (0.3 mg/L or less), the prevalence has increased from <1% to slightly more than 10%. These findings reflect levels of fluoride ingestion by some children with developing teeth that are higher than heretofore.

Moreover a recent national survey (Wagener et al., 1995) found that dietary fluoride supplements were used by 15% of children under 2 years of age, 16% by those 2-4 years of age, and 8% by those 5-17 years of age. In their study of infants born in Iowa City, a university community with a high socioeconomic status, Levy et al. (1995) reported that from 19-25% of infants between the ages of 6 weeks and 9 months were given fluoride supplements. Pendrys & Morse (1990) and Levy & Muchow (1992) are among those who have found that supplements are often prescribed at the wrong dosage and in areas where they are not recommended because the water is already fluoridated at recommended levels. Recommendations have been made to reduce fluoride from non-dietary sources (NRC, 1993; USPHS, 1991; Workshop Reports, 1992).


Pages 14-15: Studies in the United States of America during the late 1930s and early 1940s in communities with varying levels of naturally occurring fluoride in the drinking-water found that, at 1 mg of fluoride per liter, the reduction in the prevalence of dental caries was approximately 50%. This reduction was associated with very mild forms of fluorosis in a small percentage of the population – about 10% (Dean, 1942). At the time this low level of fluorosis was deemed not to represent a public health problem; if it was even noticed, it was considered acceptable and far preferable to the severe dental caries it largely replaced. It is worth noting that this compromise – that is the priority accorded to caries over fluorosis – is found with a number of fluoride procedures.

In the past 30 years our understanding of the method of action of fluoride in the prevention of dental caries has changed; it is now accepted that it is mainly post-eruptive. Achieving the best possible caries prevention usually requires the use of population-based programmes such as adding fluoride to drinking-water or salt or the widespread use of fluoride toothpastes. The question therefore arises whether the maximum caries preventive effect can be achieved without the appearance of some degree of very mild fluorosis in the target population. In communities served with optimally fluoridated water supplies a small proportion of the population will continue to be affected by very mild fluorosis, evident as diffuse white lines and patches, which is not aesthetically damaging and which usually cannot be seen by the untrained eye. In communities where additional sources of fluorides are available, such as fluoridated toothpaste, which can be swallowed by young children, the prevalence of unaesthetic forms of fluorosis will increase. For example, in many parts of the United States of America much of the noticeable rise in the prevalence of very mild fluorosis can be accounted for by physicians prescribing fluoride supplements for children resident in fluoridated communities, a clearly inappropriate procedure. Over the past 20 years different indices have been developed for recording the first, barely perceptible diffuse white lines in enamel that are associated with fluoride ingestion, and it is now feasible to measure these changes reliably in epidemiological studies. Dental fluorosis is being regularly monitored in many communities.
mild, 4% mild, 0.8% moderate, and 0.1% severe). In another city with water fluoride concentration in the range of 1.8 –
2.2 mg/L, dental fluorosis prevalence was 53% (23% very mild, 17% mild, 8% moderate, and 5% severe). The data
from the PHS report also showed that the greatest relative increase in fluorosis prevalence since the early studies was in
communities with very low water fluoride concentrations, demonstrating the influence of sources of fluoride other than
water. Those sources make it difficult to estimate fluoride exposure; they represent a source of possible error in
estimating fluoride intake in studies of the relation between fluoride exposure and dental fluorosis. Moreover there is
disagreement on whether dental fluorosis (even moderate-to-severe dental fluorosis, in which substantial root enamel is
affected and dental treatment might be required) is a cosmetic problem or an adverse health effect.

In general, the evidence supports the conclusion that fluoridation at the recommended concentrations, in the absence
of fluoride from other sources, results in a prevalence of mild-to-very mild (cosmetic) dental fluorosis in about 10%
of the population and almost no cases of moderate or severe dental fluorosis. At five or more times the
recommended concentration, the proportion of moderate-to-severe dental fluorosis is substantially higher.

Committee to Coordinate Environmental Health and Related Programs, USPHS. (1991). Review of
fluoride: Benefits and risks: Report of the subcommittee on fluoride of the EHPC. Public Health
Service: Department of Health and Human Services.

Page 5, executive summary: Although the precise mechanism that causes dental fluorosis is unknown, the
likelihood of dental fluorosis is related directly to the level of fluoride exposure during tooth development. The
clinical spectrum of dental fluorosis varies from symmetrical whitish areas on teeth (very mild) to secondary,
etrinsic, brownish discoloration and varying degrees of pitting of the enamel (severe dental fluorosis). Among
children, the prevalence of moderate and severe forms of dental fluorosis is estimated to be 1.3% nationally.
Although fluorosis has historically been considered to be a cosmetic problem, these forms of dental fluorosis do not
produce adverse dental health effects, such as tooth loss or impaired tooth function.

In the 1940s and 1950s, the major sources of fluoride were from drinking water and food. Since then, additional
sources of fluoride have become available, including processed beverages and food, dental products containing
fluoride (e.g. toothpastes and mouth rinses), and fluoride dietary supplements. Inappropriate use of these products
can substantially increase total fluoride intake.

In the 1940s, approximately 10% of the population had fluorosis when the concentration of fluoride found naturally
in the drinking water was about 1 ppm. Since the 1950s, in non-fluoridated areas, the total prevalence of dental
fluorosis has clearly increased. During the same period, in areas where water fluoride concentrations have remained
in the optimal range (about 1 ppm fluoride), the total prevalence of dental fluorosis may have increased. Increases in
the prevalence of dental fluorosis suggest that total fluoride exposure is increasing. Because dental fluorosis does not
compromise oral health or tooth function, an increase in dental fluorosis does not represent a public health concern;
however, it indicates that total fluoride exposure may be higher than that necessary to prevent tooth decay. In
general, prudent public health practice dictates using no more than the amount necessary to achieve a desired effect.

Summary page 62 of full report: Human dental fluorosis is associated with high tissue fluoride concentration
during tooth formation. The greater the fluoride exposure during tooth development, the greater the likelihood of
dental fluorosis. The actual concentration of fluoride that correlated with an observed clinical presentation, in a
given individual, is difficult to quantify. The prevalence and severity of fluorosis depend on: 1) the amount,
concentration, and duration of exposure to fluoride; 2) the stage of tooth development; 3) individual variations in
susceptibility; and 4) certain environmental variables.

Overall, dental fluorosis remains more prevalent in fluoridated than non-fluoridated areas. Dental fluorosis appears
to have increased in both non-fluoridated and fluoridated communities, but has increased much more in non-
fluoridated or low fluoride areas. Apparently, in non-fluoridated areas over the period 1939 to about 1980, increases
in very mild and mild forms of dental fluorosis have occurred. Total prevalence and intensity of dental fluorosis may
have increased in optimally fluoridated areas over this same time period. Virtually all of the increase observed in
optimally fluoridated areas since Dean’s time has occurred in the very mild and mild categories. If moderate dental
fluorosis has increased, the increase is minimal and has been most pronounced between the water fluoride ranges of
1.8-2.2 mg/L. During this period of time the prevalence of severe forms of dental fluorosis continues to be very low
in optimally fluoridated areas.

In comparison of cross-sectional studies from 1980 and 1985 in the same midwestern communities, investigators
reported an increased prevalence of dental fluorosis by tooth surface (rather than by individual), which may be due
in part to increased fluoride ingestion among children. Apparently, the increased ingestion began in the early 1970s,
and since then the total fluoride intake has changed very little. Evidence from 1980 and 1985 surveys identified increases in percentages of tooth surfaces with dental fluorosis at optimum, 2X, 3X, and 4X optimal levels of water fluoride in children 13-15 years of age and at optimal levels in children 8–10 years. There may have been a slight increase in moderate to severe forms of dental fluorosis in some children 13-15 years old in communities fluoridated at the 2X, 3X, and 4X optimal levels. The study was geographically restricted to four areas of Illinois, so the general applicability of the study is unknown.

Factors found to be associated with an increase in the reported prevalence of dental fluorosis include the daily – and possibly inappropriate – use of dietary fluoride supplements, the use of fluoride containing toothpaste before a child is 24 months of age, and the use by children beyond 13 months of age of powdered and concentrated forms of infant formula reconstituted with fluoridated water. Because of changes in manufacturing practices of infant foods since 1978, the risks associated with these products may no longer be operative.

In most studies in which the risk of developing dental fluorosis has been assessed, investigators have focused almost exclusively on a single risk factor, that is on a single source of fluoride and have not controlled for multiple sources. The effect on dental fluorosis of multiple risk factors or of the simultaneous use of multiple fluoride modalities, remains largely unknown.


Pages 81-83: Dental fluorosis is a disturbance affecting the enamel during formation, hence all damage occurs before the eruption of the teeth. The level of fluoride induced changes that would be considered aesthetically objectionable is debatable.

The minimal daily fluoride intake in human infants that may cause very mild or mild fluorosis in human beings has been estimated to be about 0.1 mg per kg body weight (Forsman, 1977). This figure was derived from examination of 1094 children from areas with water-fluoride concentrations of 0.2-2.75 mg/liter. It is in agreement with the reported 0.1-0.3 mg per kg body weight necessary to initiate fluorosis in cows.

The results published by Dean and co-workers have been confirmed by many studies in various temperate parts of the world, as reviewed by Myers (1978), i.e. fluorosis is of a very mild of mild character in areas with drinking-water naturally containing fluoride levels of up to 1.5-2.0 mg/liter, severe fluorotic defects with disfiguring appearance are to be found at higher fluoride levels.

It is sometimes difficult or almost impossible to discriminate between fluorosis and other enamel disturbances (Jackson, 1961; Forrest & James, 1965; Goward, 1976; Mervi 1977; Small & Murray, 1978; Murray & Shaw 1979). Opacities similar to fluorotic opacities are also seen in low fluoride areas and many etiological factors other than fluoride have been implicated (Small & Murray, 1978).

Small & Murray (1978) concluded: Although a high concentration of fluoride in drinking water is one factor, it is extremely difficult to decide just how many cases of “enamel fluorosis occur in endemic areas and how many defects are due to other etiological factors.”

Localized enamel defects are reported to be more frequent in low-fluoride areas than in areas with optimal water fluoridation (Zimmerman, 1954; Ast et al., 1956; Forrest, 1956; Forrest & James, 1965; Al-Alousi et al., 1975; Forsman 1977). One of the explanations offered is that part of the difference may be due to the greater amount of caries-induced inflammation in temporary teeth in low-fluoride areas, as such conditions have been found to disturb the mineralization of underlying permanent teeth. It has also been suggested that a certain amount of fluoride is necessary for the proper organization and crystallization of enamel. As a consequence of higher water consumption, the frequency and severity of dental fluorosis increases with increasing mean maximum temperature (Galaghan et al., 1957; Richards et al., 1967; Gobovich & Ovurutskiy, 1969).

As the community index of fluorosis increases, caries prevalence decreases until the destructive forms of fluorosis, scores of 4 and 5 on Dean’s index, become prevalent. Under the latter conditions, an increase in caries may occur, associated with loss of integrity of enamel and exposure of underlying dentine. However, under these situations, the lesions usually progress slowly and frequently become arrested (Barmes, 1983).
Other Reviews
(examples of municipal or territorial reviews of the water fluoride issue)


Pages 35-43: Recent reviews have suggested that the prevalence and severity of dental fluorosis has increased in both fluoridated and non-fluoridated communities with the later exhibiting the largest increase of all (Lewis and Banting, 1994; Clark 1994). A review by Clark (1994) of North American studies published prior to 1994 indicated that prevalence ranged from 35-60% in fluoridated communities and from 20-45% in non-fluoridated communities. These increases have been attributed to the consumption of fluoride from sources other than community water supplies (Lewis and Banting, 1994). Although they are largely confined to the so-called “very mild” and “mild” categories of dental fluorosis the increases are cause for concern. The rationale underlying this concern is that fluorosis at this level is discernible by children aged 10 years and over and can lead to embarrassment, self-consciousness and a decrease in satisfaction with the appearance of the teeth (Spencer et al., 1996). This work confirms and expands previous surveys which have shown that lay people can detect fluorosis and both professionals and lay people view the more severe forms as having negative consequences for children (Riordan, 1993; Clark, 1993; Hawley et al., 1996).

The most recent estimates of the prevalence of fluorosis in both fluoridated and non-fluoridated communities are found in table 9-11. These studies suffer from the same design and methodological limitations as the studies of the effectiveness of water fluoridation discussed earlier.

North American studies, which confined their estimates to children who were life-long residents of fluoridated and non-fluoridated communities respectively, reported prevalence rates of 20-75% for the former and 12-45% for the latter.

Two U.S. studies using repeated cross-sectional designs were undertaken by the same investigators and provide the best recent estimates of trends in fluorosis. Jackson et al. (1999) studied 7-14 year old children who were life-long residents of a fluoridated and a non-fluoridated city. In the fluoridated city the proportion of children who had a TSIF score of 1 or more increased from 45% in 1992 to 65% in 1994 (NS). In the non-fluoridated city there was a significant increase from 18 to 33%. Kumar and Swango (1999) also compared 7 to 14 year old children who were life-long residents of a fluoridated community, Newburgh, and a non-fluoridated community, Kingston. Dean’s CFI indicated a significant increase in both communities between 1986 and 1995; from 7.9 to 18.6% in the former and from 7.4 to 11.7% in the latter. The difference in rates between the studies is probably due to the fact that Dean’s CFI has a “questionable” category, which is categorized as “normal” for the purpose of calculating prevalence estimates.

The conventional way of estimating the contribution of water fluoridation to dental fluorosis is by the use of relative risks and attributable risk percents (Lewis and Banting, 1994). Relative risks in North American and European studies varied from 1.5 to 2.7, except for one Norwegian study that had a relative risk of 5.4. Attributable risks percents measure the proportion of the fluorosis in those exposed to water fluoridation, which can be attributed to that exposure rather than other sources of fluoride. In North American studies this varied from 40-63% and in the European studies from 33-82%. These studies suggest approximately half of the fluorosis affecting contemporary child populations is the result of water fluoridation and half is the result of exposure to other, discretionary sources of fluoride. However, in some jurisdictions the halo effect could potentially affect these crude estimates (Lewis and Banting, 1994).

Two Canadian studies are worth highlighting here. Clark et al. (1994) used the TSIF to compare life-long residents of a fluoridated and non-fluoridated community in British Columbia. Among samples of children aged 6-14 years, the prevalence of fluorosis (TSIF ≥1) was 75% in the former and 45% in the latter (RR =1.7; AR% = 41%). Brothwell and Limeback (1999) examined grade 2 students living in a non-fluoridated rural area in Ontario, approximately 10% of whom lived in homes where the water was naturally fluoridated to 0.70 mg/L or more. There was no significant differences in the prevalence of fluorosis among students from fluoridated and non-fluoridated homes when judged by a TSIF score of 1 (31% vs. 25%). However, there was a significant difference among the proportions with TSIF scores of 2 or more (18.8% vs. 4.8% respectively; RR =3.9; AR% =77%). This latter study suggests that water fluoridation may play a more prominent role in moderate to severe fluorosis than in fluorosis overall.
The risks associated with discretionary use of fluorides in both fluoridated and non-fluoridated communities have been addressed in a number of recent studies. In addition two reviews (Warren & Levy, 1999 and Ismail and Bandecker, 1999) have been published.

The main risk factors to emerge from the case-control and cross-sectional studies were the use of infant formula, use of fluoride supplements and brushing with fluoridated toothpaste early in life. The two reviews confirm the etiological role of fluoridated toothpaste and fluoride supplements with respect to fluorosis.

**Page 43, summary:** Current studies support the view that dental fluorosis has increased in both fluoridated and non-fluoridated communities, North American studies suggest rates of 20-75% in the former and 12-45% in the latter. Although largely confined to the ‘very mild’ and ‘mild’ categories of the condition, they are of concern insofar as they are discernible to the lay population and may impact on those so affected. Although about half the fluorosis in contemporary child populations living in fluoridated communities can be attributed to fluoride from discretionary sources, efforts to reduce exposure to these sources may not be successful.

**Page 16:** Fluorosis is a side-effect of excessive fluoride ingested during the process of tooth formation. It cannot occur after the teeth have fully developed. Excessive fluoride leads to improper crystallization of enamel with a less tightly formed crystalline lattice. This can lead to a varying degree of enamel surface porosity. In mild cases it causes various degrees of mottling which are often not visible to untrained eyes. In severe cases it leads to pitting of the enamel surface and enamel fragility. It is known that an intake of even a trace amount of fluoride can lead to a mild fluorosis in some individuals. Since normal human diet always contains small amounts of naturally occurring fluoride, there will always be some dental fluorosis in a population.

In North America the vast majority of dental fluorosis is of very mild to mild types. The moderate and severe types which over the years become discolored as result of taking up stain from foods, beverages and tobacco smoke are not common.

The prevalence of dental fluorosis has increased during the last several decades in both fluoridated and non-fluoridated communities. In fact this increase has been more marked in some non-fluoridated areas and has been attributed to the inappropriate use of fluoride supplements (drops, tablets, dental products) as well as the consumption of beverages and foods prepared with fluoridated waters (Pendrys et al., 1990).

Pendrys and Stamm (1990) and Lewis and Banting (1994) have reviewed the literature on enamel fluorosis. Both studies concluded that there is a strong association between mild to moderate fluorosis and the use of fluoride supplements in early childhood. Whereas during the past several decades, there has been a 33% increase in the prevalence of enamel fluorosis in fluoridated communities, the non-fluoridated communities have experienced a 1000% increase during the same period. Obviously the fluorosis prevalence in the fluoridated communities has also been affected by the inappropriate use of fluoridated dentifrices.

In a more recent publication Pendrys (1995) reported the results of his well-designed retrospective case-control study of middle-school-aged children who grew up in “optimally” fluoridated communities. He calculated that about 15% of fluorosis in these communities can be attributed to inappropriate use of supplements (drops and tablets) and about 71% to the inappropriate use of fluoridated dentifrices during the children’s first 8 years of life.

It should not come as a surprise that there is a greater prevalence of dental fluorosis in some non-fluoridated communities since fluoride drops and tablets are more frequently used in those communities. When these children use (and swallow) excessive amounts of fluoridated toothpaste and consume beverages and food prepared with fluoridated water, their total fluoride ingestion becomes greater than that of children in fluoridated communities (Pendrys et al., 1990).

Given the availability and indiscriminate use of fluoridated dental products, it is clear that, at the present time young children can be exposed to excessive amounts of fluoride, which is unnecessary for maintaining their dental health.

**Page 30, summary – majority opinion:** Dental fluorosis occurs when total fluoride is too high during the formation of enamel on children’s teeth. Because the total intake of fluoride from all sources is increasing, more fluorosis is being observed although much of it is of the mild forms, which are only apparent to the trained eye or upon very close inspection. The Panel recommends that health authorities pay more attention to identifying uncontrolled
sources of fluoride, especially due to children swallowing high fluoride toothpaste. Reducing uncontrolled sources of fluoride would be a more effective means of reducing dental fluorosis than eliminating fluoridation of water.


Page 51-52: Dental fluorosis is a specific disturbance of tooth formation caused by excessive intake of fluoride during the formative period of the dentition. The manifestations depend on the peak concentrations achieved in the blood following exposure to fluoride (usually by ingestion), the duration of exposure and the age of the subject. Clinically, dental fluorosis is characterized by lusterless, opaque white patches in the enamel, which may become striated, mottled and/or pitted in more severe forms. The opaque areas may become stained yellow to dark brown. The severity of fluorosis is graded from very mild to severe.

The critical period for developing fluorosis is during the maturation period of tooth enamel, which for the cosmetically important maxillary (upper) anterior teeth is the second and third year of life. Fluorosis is considered probable following intakes of 0.1 mg F/kg body weight during infancy (Forsman, 1977). More recent reports have suggested a lower threshold: 0.03-0.10 F/kg/mg body weight has been suggested as borderline, at least for European children (Fejerskov et al., 1987; Baelum et al., 1987).

In communities receiving artificially fluoridated water prior to the widespread use of fluoride toothpaste, most fluorosis was of the questionable or very mild variety. No treatment was considered necessary for either questionable or very mild fluorosis, as patients were usually unaware of both from a cosmetic standpoint. Mild and moderate fluorosis were more common in situations where toothpaste was swallowed, tablets ingested, or water levels contained high naturally occurring levels of fluoride.


Pages 30-31, summary and conclusions: Excessive fluoride intake by children causes a toxic dental condition known as dental fluorosis which is marked by visible mottling/discholoring of tooth enamel, pitting of the enamel and disturbed tooth shape. Dental fluorosis occurs during early childhood while the baby and permanent teeth and tooth enamel are still being mineralized and before they erupt in the mouth. The severity of the dental fluorosis is directly proportional to the fluoride ingested in excess of 0.03 mg to 0.07 mg fluoride/kg of body weight/day. The ultimate result is the increased porosity of the teeth and, in extreme cases, loss of afflicted teeth. The prevalence of dental fluorosis is increasing in communities that are “optimally fluoridated” and in those with fluoride deficient doing (sic) water because of the ubiquity of products containing fluoride. However the prevalence and severity of dental fluorosis is greater in “optimally fluoridated” communities than those with fluoride-deficient water. Parents are being advised to protect against excessive fluoride intake by infants and children by carefully regulating their total intake of fluoride. It is anticipated that fluoridation of the Natick water supply to 1 ppm of 1 mg/L will result in dental fluorosis to some degree in at least one child out of every ten. However, if care is not exercised in preventing excessive fluoride intake, 2–3 children out of every ten may develop dental fluorosis. Corrective procedures, when required, can be performed by dental clinicians. However, the cost of teeth rehabilitation will be borne, most likely, by the individuals/parent since dental fluorosis is considered to be a cosmetic defect and therefore is not covered by most insurance plans.

Page 3, findings: Ten to thirty percent (10-30%) of Natick’s children will have very mild to mild dental fluorosis if Natick fluoridates its water (up from probably 6% now). Approximately 1% of Natick’s children will have moderate or severe dental fluorosis. Dental fluorosis can cause great concern for the affected family and may result in additional dental bills. It should not be dismissed as a “cosmetic” effect.
Medical Research Council. Medical Research Council working group report: water fluoridation and health. (September 2002).

**Immunological effects.** Information regarding the allergenic potential of fluoride in drinking water is sparse. A paper by Spittle (1993) concluded that some individuals exhibit an allergic/hypersensitivity reaction to fluoride, but reviews by NRC (1993), NHMRC (1991), and Chalacombe (1996) all concluded that the studies undertaken do not support claims that fluoride is allergenic. They considered the weight of evidence to show that fluoride is unlikely to produce hypersensitivity or other immunological effects. There is no information on the immunotoxicity of fluoride. Further work in this area would be useful, but in the absence of obvious toxic mechanisms for such an effect is considered to be of low priority.

**Effects on reproduction.** Adverse effects of fluoride intake on reproductive performance, such as reduced lactation, have been demonstrated in many species. However, these studies have used dietary concentrations much higher than those in the fluoridated drinking water of humans (NRC, 1993).

Fluoride has also been implicated in a number of adverse outcomes relating to fertility and pregnancy, but there is insufficient evidence to establish a link between decreased fertility and fluoride exposure (NHMRC, 1999). The York Review found no evidence or reproductive toxicity in humans (NHS CRD, 2000).

A recent multigenerational study of sodium fluoride in rats, at fluoride levels in drinking water of up to 250ppm, found no impacts on reproduction, and mating fertility and survival indices were not affected (Collins et al., 2001). Parallel studies using the same exposure regimen revealed no evidence for effects on testis structure, spermatogenesis or endocrine function in male rats (Sprando et al., 1997, 1998), nor on numbers of corpora lutea, implants and viable fetuses in females (Collins et al., 2000).

The plausibility of fluoride affecting the reproductive capacity of humans at the intakes experiences from fluoridated drinking water is low.

**Birth defects.** Fluoride crosses the placenta and is incorporated in the tissues of the developing conceptus. Studies in areas of India and Africa that have high levels of naturally fluoridated water have not shown an increase in birth defects (DHSS, 1991). Erickson et al. (1976) found an association between drinking fluoridated water and congenital malformations in one set of data, but not in another. A study in Atlanta, Georgia, using the birth defects registry, found no association between birth defects and fluoridation of community water supplies (DHSS, 1991).

In 1957, an investigator linked an excess of Down’s syndrome to fluoridation. However, later studies by other investigators provided strong evidence against this suggestion (DHSS, 1991; NHS CRD, 2000). The York Review (NHS CRD, 2000) reported six studies that examined whether there is an association between Down’s syndrome and drinking water fluoride level. All of the studies were of poor quality according to the review criteria. Four of the studies (Berry, 1958, Erickson et al., 1976; 1980; Needleman, 1974) showed no significant association. Two studies (Rapaport, 1957; 1963) found a significant (p<0.05 positive association, i.e., increased Down’s syndrome incidence with increased water fluoride level. However, it was noted that these two positive studies have methodological limitations; for example they did not control appropriately for the possible confounding effects of maternal age. Other confounding factors not controlled for in most of the studies were incidence of termination of pregnancy in which the child is diagnosed with Down’s syndrome, and exposure of the mother to other sources of fluoride. Thus the evidence for an association between water fluoride level and the incidence of Down’s syndrome is inconclusive, a conclusion reiterated by Whiting et al. (2001).

If fluoride reaches the developing fetus and is incorporated into its tissues, it could plausibly be teratogenic. The DHSS (1991) review concluded that experimental animal data do not provide any additional evidence for an association between fluoride in drinking water and birth defects; the other major reviews (NHMRC 1991, 1999; NRC, 1993)
provide no comment on this issue. A recent multigenerational developmental toxicity study on rats given up to 250ppm fluoride in drinking water (Collins et al., 2000) showed no effects on fetal morphological development, although ossification of the hyoid bone in F2 fetuses was significantly reduced at the 250ppm top dose level.

Human and experimental animal data suggest that drinking even high levels of fluoride in water does not cause birth defects, though there may be adverse consequences for bone ossification at very high exposure levels. Further work on this aspect is not considered to be of high priority.

**Renal effects.** The kidney is a potential site of acute fluoride toxicity because of its exposure to relatively high fluoride concentrations (NRC, 1993). It has been established from human studies that the kidney removes fluoride from the blood more efficiently than it removes other halides. In addition, renal insufficiency or diabetes mellitus. However, several large community-based epidemiological studies found no increased renal disease associated with long term exposure to drinking water with fluoride concentration of up to 8mg/l (DHSS, 1991; NRC, 1993).

It is plausible that the kidney could be a target for fluoride toxicity, and there is limited evidence for kidney effects in experimental toxicity studies in animals. Further investigation is therefore warranted to determine the level of toxicity, if any, following low level intakes in humans. However, in view of the negative results in the epidemiological studies mentioned above, this is not considered to be of high priority.

**Gastrointestinal tract.** With the exception of monofluorophosphate, high concentrations of fluoride releasing compounds form hydrogen fluoride on mixing with hydrochloric acid in the stomach. Hydrogen fluoride can be irritating to the gastric mucosa, resulting in dose-dependent adverse effects. The data for human effects at low exposure are limited, but the indication is that gastrointestinal effects are not a problem at optimal drinking water fluoride concentrations (DHSS, 1991; NRC, 1993).

A study of Sushella et al. (1993) assessed that prevalence and severity of gastrointestinal disturbances (and other non-skeletal manifestations) in an area of endemic skeletal and dental fluorosis in India. The highest prevalence (52.4% of non-ulcer dyspeptic symptoms was found among 288 individuals (69 families) living in a village where the (Natural) mean fluoride concentration in the 36 separate water sources was 3.2ppm (range 0.25 to 8.0ppm). Eleven of these water sources were defined by the authors as “safe” (i.e., with fluoride levels of 1.0ppm or less). The authors noted that in patients who reverted to “safe” water, dyspeptic symptoms and complaints disappeared within 2-3 weeks. Other research of Sushella et al., (1992) revealed that the long-term ingestion of fluoride by ten patients on sodium fluoride therapy (30mg per day) for otosclerosis was associated with non-ulcer dyspeptic symptoms in eight of the patients (Sushella et al., 1992).

The effects of fluoride on the gastric mucosa have been described in detail by Whitford (1996). Gastric irritation, by release of hydrogen fluoride in the stomach at high doses of fluoride intake, is plausible. However, it is unlikely that sufficient hydrogen fluoride will be released from the low concentrations of fluoride in drinking water in the UK to cause irritation in healthy individuals. It is possible that individuals who have an existing stomach disorder may be susceptible to irritation following ingestion of fluoridated water, but there is no published evidence for this. This issue is considered to be of low priority for further research.

**Intelligence.** Two Chinese studies have found a positive association between high levels of fluoride in drinking water and reduced children’s intelligence/IQ. Confounding factors were dismissed, but their possible influence on the results of the study was not adequately explained by the authors. At lower fluoride concentrations (e.g., 0.91ppm), which are ore comparable to the levels in fluoridated water in the US, a reduction in children’s IQ was not observed (Lu et al., 2000, Zhao et al., 1996). There is a possible link here with lead toxicity and the impact of fluoride on lead bioavailability.

Further investigation of this aspect is considered to be of low priority.

**Thyroid (goiter).** The York Review listed three studies in which goiter was the outcome of interest. Two of these studies (Gedalia & Brand, 1963; Jooste et al., 1999) found no significant association with water fluoride level. The third (Lin et al., 1991) found a significant positive association between combined high fluoride/low iodine levels and goiter. However, because this study looked at combined fluoride/iodine uptakes, and has not been published in a peer reviewed journal, the findings should be treated cautiously. Further work on this aspect is of low priority.
Miscellaneous effects. Several other health outcomes have been postulated as being connected with elevated fluoride intake:

- Effects on the pineal gland
- Senile dementia
- Age at menarche
- Anaemia during pregnancy
- Sudden Infant Death syndrome
- Primary degenerative dementia

Available information on these outcomes is limited and inconclusive. Further targeted research may be warranted, but this is presently of low priority unless and until critical literature reviews are undertaken that demonstrate specific research needs.

Indirect effects of adding fluoride to water. In addition to any direct impact on health resulting from increased uptake of fluoride by the body it is possible that fluoridation of water supplies could influence health through other mechanisms. In particular it is necessary to give consideration to the possibility of:

- Toxicity from other substances added to water as part of the fluoridation process;
- An effect of higher fluoride in water on dietary exposure to toxic metals (e.g., through leaching of copper from pipework and dissolution of aluminium from cooking pans); or
- An effect of fluoride in drinking water on the uptake/bioavailability or toxicity of metals in the gut.

The importance of these theoretical hazards will depend on the intrinsic toxicity of the substances concerned and the impact, if any, of fluoridation on the dose of the toxins.

In addition, it is possible for the presence of other substances in water and food to affect the absorption of fluoride and therefore reduce the effectiveness of intended caries-preventive dose.

Substances added during the fluoridation process. The UK Water (Fluoridation) Act 1985 allows hexafluorosilicic acid (H$_2$SiF$_6$) and disodium hexafluorosilicate (Na$_2$SiF$_6$) to be used to increase the fluoride content of water. The published Code of Practice on Technical Aspects of Fluoridation of Water Supplies (DOE, 1987) gives specifications for these substances and states that “the product… must not contain any mineral or organic substances capable of impairing the health of those drinking water correctly treated with the product.” For H$_2$SiF$_6$, limits are given for a number of possible impurities, including for iron, heavy metals, sulphate, phosphate, and chloride. The specification of Na$_2$SiF$_6$ powder required a minimum of 98% m/m of the pure chemical, and gives maximum limits for impurities, including heavy metals (as lead) and iron. No other substances are allowed to be used in the fluoridation process, other than an anti-caking agent (the identity of which must be disclosed) in the case of Na$_2$SiF$_6$. Synthetic detergents are not permitted.

Thus there is no likelihood, in normal operation, for any fluoridation plants to introduce other compounds into the drinking water supply (other than approved anti-caking agents and any impurities present in the fluoridation chemicals).

It has been suggested that arsenic is introduced into drinking water through the fluoridation process because this element is present as an impurity in fluoride compounds. However, because of the dilution factor, the contribution of arsenic from this source would be extremely small, and in any case there is a standard for the total arsenic level in drinking water.

Dietary exposure to metals. Enhanced leaching of metals from water pipes and cooking utensils can occur if the fluoridation process significantly alters the pH of the water. This can happen in abnormal (accidental) circumstances. For example, incidents in Westby, Wisconsin and New Haven, Connecticut USA, resulted in peak fluoride levels of 150ppm and 51ppm respectively, reduced the pH value of the water and caused copper to be leached from plumbing.

Studies on the leaching of aluminium from cooking utensils at standard fluoride concentration in the region of 1ppm have indicated a small (5%) increase in leaching compared to non-fluoridated water (moody et al., 1990). These studies indicate that aluminium leaching resulting from water fluoridation is not a significant cause for concern.

Effects on bioavailability or toxicity of toxic metals.

Aluminium. Aluminium and fluoride are mutually antagonistic in competing for absorption in the gut. Therefore, the more fluoride in the diet, the less aluminium is absorbed. At the same time, ingestion of
aluminium counteracts dental fluorosis, reducing fluoride stores in teeth and bones. This effect has been demonstrated in experimental animals and humans (Foster, 1993; quoting Navia 1970). Thus fluoride will reduce rather than increase any toxic potential from aluminium in food or water.

Aluminium has been implicated as having an etiological role in Alzheimer’s disease. It follows that if absorption of aluminium is reduced by ingestion of fluoride, this condition should be less common in communities with fluoridated drinking water (Foster, 1993; Kraus & Forbes, 1992). A study conducted in South Carolina (Still & Kelly, 1980) did indeed find a significantly lower rate of admission of Alzheimer’s disease patients to mental hospitals from the county with the highest level of fluoride in the drinking water than from the two counties in the same state with the lowest levels, though it had significant methodological shortcomings. A later study by Forbes (1997) found an increased incidence of Alzheimer’s disease with higher water fluoride levels. In considering this information it must be cautioned that the possible link between aluminium uptake and Alzheimer’s disease is by no means established.

An experimental study (Valner et al., 1998) found that chronic administration of aluminium fluoride or sodium fluoride in the drinking water of rats resulted in distinct morphological alterations in the brain, including effects on neurones and the cerebrovasculature. The authors concluded that further studies of aluminium fluoride and sodium fluoride are needed to establish the relative importance of a variety of potential mechanisms contributing to the observed effects as well as to determine the potential involvement of these agents in neurodegenerative diseases.

**Lead.** It is generally considered that lead passes across the intestinal mucosa by both active and transport. It appears that lead is actively transported by mucosal protein carriers that mediate calcium transport and that calcium can displace lead, although the interactions between lead and calcium metabolism are complex and not well understood. Experimental evidence suggests that dietary calcium deficiency is associated with an increase in the body burden of lead and the susceptibility to lead toxicity during chronic lead ingestion, and that stimulation of the parathyroid and vitamin D endocrine system is associated with an increase in lead and calcium absorption when significant quantities of lead are not consumed (IEH, 1998). The first of these findings implies that if fluoride reduces calcium uptake, then an increase in lead absorption could result. This is plausible because of the strong affinity between calcium and fluoride, but probably occurs only at high calcium concentrations.

Two recent studies (Masters & Coplan, 1999; Masters, et al., 2000) have found an association between ingestion of drinking water treated with silicofluorides and elevated blood lead in children. The authors’ conclude that silicofluoride agents maintain lead in suspension and/or enhance lead uptake from the gastrointestinal tract, and postulate that fluoridated drinking water indirectly increases lead toxicity, including fetal and early childhood developmental deficits, and IQ learning deficits. They also make a link between the use of silicofluorides in water treatment systems and increased violent crime. However, according to the US EPA there is no substantive evidence to suggest that fluoridation of drinking water with any fluoridating chemical increases the concentration or bioavailability of lead in drinking water via chemical reactions in the plant, the distribution system, the home plumbing system, or the human body itself (Urbansky & Schock, 2000). This appears to be a controversial area and further studies are awaited.

**Conclusions.** Further research on the possible effects of fluoride on immunological function, reproduction, birth defects, intelligence, the kidney, gastrointestinal tract and thyroid, and other suggested impacts, is considered to be of low priority.

Substances added to drinking water during the fluoridation process (including impurities of the added substances) are unlikely to add any significant toxic potential to the water. Fluoride in water at normal levels can increase slightly the amount of leaching of aluminium from cooking utensils. High concentrations of fluoride can also result in leaching of copper from pipework. These effects are considered to be of minimal health significance in normal circumstances.

Fluoride appears to reduce the bioavailability of dietary aluminium. The situation with regard to lead is somewhat less clear-cut and may be influenced by calcium status.

Complexities associated with speciation, ionic interactions, etc., yield uncertainties in a number of aspects. It is recommended that this area be kept under review.
Background information on oral exposure (Page 59): Much of the research on fluoride exposure in humans focused on the ingestion of fluoride through supplemented public drinking water supplies. Additional information comes from studies of areas with high natural fluoride levels. Drinking water levels of other minerals may differ between artificially fluoridated areas and areas with naturally fluoridated high fluoride levels. Much of the data regarding toxic effects of oral exposure to fluoride were obtained from studies using sodium fluoride. Fluoride is often added to water in the form of hydrofluosilic acid, so exposure to this chemical is included in some epidemiological studies. For all forms of fluoride discussed, doses are reported as amount of the fluoride ion.

For the most part, summaries of animal studies cited in this document are not cited here, the intended focus was studies of humans exposed fluoridated water.

All cause mortality (Page 61): A comparison of death rates between US cities with fluoridated water and those with non-fluoridated water found no association between fluoride and increased death rate (Erickson, 1978). It is difficult to draw definitive conclusions from this study because it is limited by dissimilarities between the populations, which led to a need for multiple adjustments.

Respiratory effects (Page 62): No studies were located regarding respiratory effects in humans after oral exposure to fluoride, hydrogen fluoride or fluoride.

Cardiovascular effects (Page 76): In two epidemiological studies, fluoride in the drinking water did not increase the mortality rates from cardiovascular effects. One of these studies was a report of 428,960 people in 18 areas of “high” natural fluoride (0.4->3.5 ppm) in England and Wales and 368,580 people in control areas (<0.2 ppm fluoride). The water supply for 52% of the “high” fluoride population had average levels of ≥1 ppm (Heasmann & Martin, 1962). Results indicated that there were no significant differences between areas with different fluoride levels in mortality due to coronary disease, angina, and other heart disease, as evidence by standard mortality ratios (SMRs). The second study (Hagan et al., 1954) examined 32 pairs of cities in the United States that contained 892,625 people in the high fluoride areas and 1,297,500 people in the control cities. A positive relationship between fluoride and increased death rate (Erickson, 1978). It is often added to water in the form of hydrofluosilic acid, so exposure to this chemical is included in some epidemiological studies. For all forms of fluoride discussed, doses are reported as amount of the fluoride ion.

A comparison of Bartlett & Cameron, two Texas towns with water supplies containing 8 and 0.4 ppm fluoride, respectively, found a significantly higher rate of cardiovascular system abnormalities in the town with the lower fluoride level (Leone et al., 1954). The authors attributed the finding of a significant result to the number of statistical tests that were conducted in the study. However, it is interesting to note that a study of 300 North Dakota residents who drank water containing 4-5.8 ppm and 715 people who drank water containing 0.15-0.3 ppm found a lower incidence of calcifications of the aorta in the high-fluoride group (Bernstein et al., 1966). Significant differences were found in the 45-54 year old males (p<0.05), as well as in males aged 55-64 and 65+ years (p=0.01). This effect was not due solely to differences in age distribution, because the incidence in the 55-64 year old – high fluoride group was lower than the incidence in the 45-54 year old, low-fluoride group. A crude analysis also found no association with milk and cheese consumption. Additional studies have suggested a role for fluoride in reducing cardiovascular disease. In a study of four towns in Finland, Luoma (1980) found that incidence of cardiovascular disease correlated negatively with water fluoride concentration. Taves (1978) likewise found that standard mortality ratios decreased to a greater extent in fluoridated cities from 1950-70 as compared to non-fluoridated control cities. Both studies, however, relied on population-summary information for disease rates. A mechanism for this potential reduction in cardiovascular disease could be the ability of fluoride to inhibit the calcification of soft tissue such as the aorta, as demonstrated in in vitro studies (Taves and Neumann, 1964; Zipkin et al., 1970).

Gastrointestinal effects (Page 78): While high levels of fluoride clearly can cause gastrointestinal irritation, it is unclear whether there are any GI effects of chronic exposure to fluoride in drinking water. GI tract disorders were not evaluated in the Bartlett-Cameron study of the effect of water containing 8 ppm fluoride (Leone et al., 1954).
The sole evidence of an effect comes from a study of 20 nonucler dyspepsia patients at an outpatient clinic in India and 10 volunteers with out GI problems from the surgical clinic (Susheela et al., 1992). While none of the drinking water supplies of the controls had fluoride levels >1 ppm, the water supplies of 55% of the dyspepsia patients were at this level. In addition, all of dyspepsia patients and 30% of the controls had serum fluoride levels >0.02 ppm (mean of the dyspepsia group, 0.1 ppm); all of the dyspepsia patients and none of the controls had urine fluoride levels >0.1 ppm (mean 1.34 ppm). The study was compromised by small treatment size, undetermined total fluoride doses, undetermined nutritional status of the subjects, and a lack of statistical comparisons. In addition, the appropriateness of the control population was not clear.

**Hematological effects (Page 79):** The incidence of abnormal white blood cell counts was significantly higher in Bartlett Texas (8 ppm natural fluoride), than in Cameron, Texas (0.4 ppm fluoride). However, the study authors did not consider this finding as necessarily and effect of fluoride (Leone et al., 1954). No other significant hematological effects were observed.

**Hepatic effects (Page 88):** No studies were located regarding hepatic effects in humans after oral exposure to fluorine, hydrogen fluoride, or fluoride.

**Renal effects (Page 89):** One study was located in which ingestion of fluoride appeared to be linked with renal insufficiency (Lantz et al., 1987). A 32 year old man ingested 2-4 liters of Vichy water (a highly gaseous mineral water containing sodium, bicarbonate and approximately 8.5 mg/L of fluoride) every day for about 21 years. This exposure ended 4 years before his hospital admission. The patient also had osteosclerosis and a moderate increase in blood and urinary levels of fluoride. No teeth mottling was observed. The authors could not find factors, other than fluoride, related to his interstitial nephritis. No effect on the incidence of urinary tract calculi or the incidence of albuminuria was found in the Bartlett-Cameron study of people drinking water containing 8 ppm fluoride (Leone et al., 1954).

**Endocrine effects (Page 89):** Significant increases in serum thyroxine levels were observed in residents of North Gujarat, India with high levels of fluoride in the drinking water range of 1.0-6.53 mg/l, mean of 2.7 mg/L (Michael et al., 1996). No significant changes in serum triiodothyronine or thyroid stimulating hormone levels were found. Increases in serum epinephrine and norepinephrine levels were also observed. It is unclear if nutritional deficiencies played a contributing role to the observed endocrine effects.

**Page 90:** It is possible that the decreased level of bone resorption in the presence of fluoride, and the associated lowered serum calcium levels, would lead to secondary hyperparathyroidism in an attempt to maintain normocalcemia. To address this issue, rats were dosed with 3.3 mg/F/kg in drinking water for 46 weeks (Rosenquist et al., 1983). There were no changes in serum calcium or parathyroid hormone levels, and no increase in parathyroid activity.

**Immunological and lymphoreticular effects (Page 90):** A request to the American Academy of Allergy was made by the USPHS for an evaluation of suspected allergic reactions to fluoride used in the fluoridation of community water supplies (Austen et al., 1971). The response to this request included a review of clinical reports and an opinion as to whether these reports constituted valid evidence of a hypersensitivity reaction to fluoride exposure of types I, II, III, or IV (Austen et al., 1971), which are, respectively, anaphylactic or reagenic, cytotoxic, toxic complex, and delayed-type reactivity. The Academy reviewed the wide variety of symptoms presented (vomiting, abdominal pain, headaches, scotomata [blind or partially blind areas in the visual field], personality change, muscular weakness, painful numbness in extremities, joint pain, migraine headaches, dryness in the mouth, oral ulcers, convulsions, mental deterioration, colitis, pelvic hemorrhages, uticaria, nasal congestion, skin rashes, epigastric distress, and hematemesis) and concluded that none of these symptoms were likely to be immunologically mediated reactions of types I-IV. No studies were located that investigated alterations in immune response following fluoride exposure in humans.

**Neurologic effects (Page 91):** As discussed in developmental effects section, decreases in intelligence were reported in children living in areas of China with low levels of fluoride in the drinking water, as compared to matched groups of children living in areas with low levels of fluoride in the drinking water (Li et al., 1995a, Lu et al., 2000), but these studies are weak inasmuch as they do not address important confounding factors.

**Reproductive effects (Page 92):** There are limited data on the potential of fluoride to induce reproductive effects in humans following oral exposure. A meta-analysis found a statistically significant association between decreasing total fertility rate and increasing fluoride levels in municipal drinking water (Freni, 1994). Annual country birth data (obtained from the National Center for Health Statistics) for over 525,000 women aged 10-49 years living in areas with high fluoride levels in community drinking water were compared to a control population approximately 985,000.
specific rates were not determined and tea was not taken into account as a source of fluoride (Berry, 1958). The mean drinking water fluoride levels were 3.9 ppm (approximately 0.11 mg fluoride/kg/day), 4.5 ppm (0.13 mg fluoride/kg/day), and 0.5 ppm (0.014 mg fluoride/kg/day) in the patients with skeletal fluorosis, related men, and a control group of 26 men living in areas with low endemic fluoride levels. No correlations between serum testosterone and urinary fluoride levels or serum testosterone and serum fluoride levels were found. One limitation of this study is that the control men were younger (28.7 years) than the men with skeletal fluorosis (39.6 years) and the related men (38.7 years). In addition, the groups are small and potentially confounding factors are not well addressed.

Page 92: Studies that reported an increased incidence of Down’s syndrome in areas of high fluoridation have not been replicated by several other investigations (Berry, 1958; Erickson et al., 1976; Needleman et al., 1974). No correlation was found between fluoridation and Down’s syndrome incidence (corrected for maternal age) in a study of over 234,000 children in fluoridated areas and over 1,000,000 children in low-fluoride areas (Erickson et al., 1976). Ascertainment was based on birth certificates and hospital records, but was probably incomplete. Ascertainment was nearly complete in a study of over 80,000 children in fluoride areas and over 1,700,00 children (sic) in low-fluoride areas, but no age-specific rates were reported (Needleman et al., 1974). Similarly, a study of the incidence of Down’s syndrome in England did not find an association with the level of fluoride in water, but age-specific rates were not determined and tea was not taken into account as a source of fluoride (Berry, 1958).

Developmental effects (Page 94-95): Fluoride crosses the placenta in limited amounts and is found in fetal and placental tissue (Gedalia et al., 1961; Theuer et al, 1971). The available human data suggest that fluoride has the potential to be developmentally toxic at doses associated with moderate to severe fluorosis. The human and animal data suggest that the developing fetus is not a sensitive target of fluoride toxicity.

Analysis of birth certificates and hospital records for over 200,000 babies born in an area with fluoridated water and over 1,000,000 babies born in a low fluoride area found no difference in the incidence of birth defects attributable to fluoride (Erickson et al., 1976). Exposure to high levels of fluoride has been described together with an increased incidence of spina bifida (Gupta et al., 1995). The occurrence of spina bifida was examined in a group of 50 children aged 5-12 years living in an area of India with high levels of fluoride in the drinking water (4.5 – 8.5 ppm) and manifesting either clinical (bone and joint pain stiffness, and rigidity), dental, or skeletal fluorosis. An age- and weight-matched group of children living in areas with lower fluoride levels (≤1.5 ppm) served as a control group. Spina bifida was found in 22 (44%) of the children in the high fluoride area and in six (12%) children in the control group. This study did not examine the possible role of potentially important nutrients such as folic acid, however, and had other study design flaws.

A study by Li et al. (1995a) examined intelligence in children living in areas with high fluoride levels due to soot from coal burning. A group of 907 children aged 8-13 years were divided into four groups depending on the existence and severity of dental fluorosis; 20-24 children in each age group for each area were examined for intelligence. A significant decrease in IQ was measured in children living in the medium- (mean IQ of 79.7) and severe- (mean of 80.3) fluorosis areas, as compared to the children living in the non- (mean of 89.9) or slight- (mean of 89.7) fluorosis areas. More children with IQs of <70 and 70-79 and fewer children with IQs of 90-109 and 110-119 were found in the medium- and severe-fluorosis areas than in the non- or slight-fluorosis areas. No information on exposure levels were provided; the mean urinary fluoride levels were 1.02, 1.81, 2.01 and 2.69 mg/L in the non-, slight-, medium-, and severe-fluorosis areas, respectively. Numerous potentially confounding variables were not mentioned in this study, however, which raised questions regarding the validity of the study’s findings. A study by Lu et al. (2000) also examined exposure to high fluoride levels in the drinking water (3.15 mg/L) were examined for intelligence. The test results were compared to a group of 58 children with similar social, education, and economic backgrounds who lived in an area with low fluoride levels in water (0.37 mg/L). A significant decrease in IQ was observed in the high fluoride area (mean IQ of 92.27) as compared to the control group (103.05). Additionally, there was a significantly higher number of children from the high exposure area with IQ scores of <70 (retarded) and 70-
79 (borderline retarded) than in the control group. A significant inverse relationship between urinary fluoride levels and IQ was also found. Nevertheless, because this study relied on small groups and presented scant discussion of numerous potential confounders, the strength of its conclusions are questionable.


Various outcomes addressed include: Alzheimer’s disease, impaired mental functioning, primary degenerative dementia, anemia during pregnancy, age at menarche, congenital malformations, Downs’ syndrome, infant mortality, sudden infant death syndrome, all cause mortality, IQ, mental retardation, goiter.

Page xiii, xiv: A total of 33 studies of the association of water fluoridation with other possible negative effects were included in the review. Interpreting the results of studies of other possible negative effects is very difficult because of the small numbers of studies that met inclusion criteria on each specific outcome and poor study quality. A major weakness of these studies generally was failure to control for any confounding factors.

Page 63: Interpreting the results of other possible negative effects is very difficult because of the small number of studies that met inclusion criteria on each specific outcome, the study designs used and the low study quality.

The quality of the research on these topics was generally low, evidence level C (mean of 2.7 out of 8 on validity assessment). Given that all studies are from the lowest level of evidence with the highest risk of bias, the conclusions should be treated with caution.

A major weakness of these studies generally was the lack of control for any possible confounding factors, many of which were highlighted by the study authors. If the populations being studied differed in respect to other factors that are associated with the outcome under investigation then the outcome may differ between these populations leading to an apparent association with water fluoride level. What is clear is that any further research in these areas needs to be of a much higher quality and should address and use appropriate methods to control for confounding factors.

Overall the studies examining other possible negative effects provide insufficient evidence on any particular outcome to permit confident conclusions. Further research in these areas needs to be of a much higher quality and should address and use appropriate methods to control for confounding factors.


Effects of Fluoride on the Renal System (Page 7-8): Renal excretion is the major route of elimination for inorganic fluoride from the body. As a result, kidney cells are exposed to relatively high fluoride concentrations, making the kidney a potential site for acute fluoride toxicity. Animal studies have shown that very high water fluoride concentrations of 100-380mg/L can lead to necrosis of proximal and renal tubules, interstitial nephritis, and dilation of renal tubules. However, human epidemiological studies have found no increase in renal disease in populations with long-term exposure to fluoride at concentrations of up to 8mg/L of drinking water.

The subcommittee concludes that available evidence shows that the threshold dose of fluoride in drinking water for renal toxicity in animals is approximately 50 mg/L. The subcommittee therefore believes that ingestion of fluoride at currently recommended concentrations is not likely to produce kidney toxicity in humans.

Effects of Fluoride on the Gastrointestinal System (Page 8): In the acid environment of the stomach, fluoride and hydrogen ions can combine to form hydrogen fluoride, which, at sufficiently high concentrations, can be irritating to the mucous membranes of the stomach lining. Experimental studies with several animal species have shown dose-dependent adverse effects, such as chronic gastritis and other lesions of the stomach, at fluoride concentrations of 190 mg/L and higher. Reports of gastrointestinal effects in humans often involve workers exposed to unknown concentrations of fluoride in the workplace, so that the contribution of fluoride exposure to the risk of adverse health effects is unknown. The subcommittee noted that these workers could also be exposed to other toxic substances present in the work environment. There have been few studies of the gastrointestinal effects of fluoride at low concentrations.
The subcommittee concludes that the available data show that the concentrations of fluoride found in drinking water in the United States are not likely to produce adverse effects in the gastrointestinal system.

**Effects of Fluoride on Hypersensitivity and the Immune System (Pages 8-9):** Few animal and human data on sodium fluoride-related hypersensitivity reactions are found in the literature. In animal studies, excessively high doses, inappropriate routes of administration of fluoride, or both were used. Thus, the predictive value of those data, in relation to human exposures at accepted exposure levels, is questionable. Reports of hypersensitivity reactions in humans resulting from exposure to sodium fluoride are mostly anecdotal.

The literature pertaining to immunological effects of fluoride is limited. Although direct exposure to high concentrations of sodium fluoride in vitro affects a variety of enzymatic activities, the relevance of the effects in vivo is unclear. Standardized immunotoxicity tests of sodium fluoride at relevant concentrations and routes of administration have not been conducted. The weight of evidence shows that fluoride is unlikely to produce hypersensitivity and other immunological effects.

**Effects of Fluoride on Reproduction (Page 9):** There have been reports of adverse effects on reproductive outcomes associated with high levels of fluoride intake in many animal species. In most of the studies, however, the fluoride concentrations associated with adverse effects were far higher than those encountered in drinking water. The apparent threshold concentration for inducing reproductive effect was 100 mg/L in mice, rats, foxes and cattle; 100-200 mg/L in minks, owls, and kestrels; and over 500 mg/L in hens.

Based on these findings, the subcommittee concludes that the fluoride concentrations associated with adverse reproductive effects in animals are far higher than those to which human populations are exposed. Consequently, ingestion of fluoride at current concentrations should have no adverse effects on human reproduction.

**Genotoxicity (Pages 9-10):** Fluoride has been tested extensively for its genotoxicity. It does not damage DNA or induce mutations in microbial systems, but it has produced mutations and chromosomal damage in several in vitro tests with mammalian cells. Sodium fluoride, in particular, inhibits protein and DNA synthesis and has been reported to cause chromosomal aberrations in human cells. The lowest effective dose in these cell-culture studies was a fluoride concentration of approximately 10 µg/mL, whereas the normal concentration in human plasma is 0.02-0.06 µg/mL, even in areas where drinking water is fluoridated, which means that there is a large margin of safety.

Sodium fluoride and other fluoride salts also have been tested for genotoxicity in the fruit fly *Drosophila*, as well as in mice and rats. The subcommittee’s review of the results of these in vivo studies was inconclusive, however, because of differences in protocols and insufficient detail to support a thorough analysis. There are no published studies on the genetic or cytogenetic effects of fluoride in humans.

The subcommittee concludes that the genotoxicity of fluoride should not be of concern at the concentrations found in the plasma of most people in the United States.
Studies investigating the effects of fluoride on the gastrointestinal system (Page 66): All the soluble, fluoride releasing compounds except monofluorophosphate form hydrogen fluoride when mixed with hydrochloric acid in the stomach. At optimal levels of fluoride in the water, however, gastrointestinal effects are not a problem. There are no reports of gastrointestinal problems in populations with non-occupational fluoride exposure.

Studies investigating the effects of fluoride on the reproductive system (Page 67): It is not yet clear whether fluoride is essential for reproductive performance. Several species are sensitive to fluoride levels higher than those normally encountered, such that their fertility and reproductive performance is impaired. The association of adverse reproductive effects of fluoride exposure in humans has not been adequately evaluated.

Teratologic and developmental effects (Page 69): Fluoride crosses the placenta and is incorporated in tissues of the developing conspectus. Limited animal data report defects of the teeth in offspring of mothers exposed to high dose levels of fluoride. In humans, studies in areas of India and Africa with high levels of naturally fluoridated water showed no increase in birth defects but signs of skeletal fluorosis became evident during childhood. No association was observed between birth defects and fluoridation of community water supplies based on the birth defect registry of the greater metropolitan area of Atlanta, Georgia. About 30 years ago, an investigator linked an excess of Down syndrome, a genetic disorder, to fluoridation, but the results of three later studies conducted by other investigators with a fuller ascertainment of cases did not confirm that finding.

Studies investigating the hypersensitivity and immunologic effects of fluoride (Pages 69-70): The literature contains minimal animal and human data on sodium fluoride-related hypersensitivity reactions. In animal studies, investigators often used excessively high doses, inappropriate routes of administration, or both (Lewis & Wilson, 1985; Jain & Susheela, 1987). Consequently, the predictive value of these data, as they relate to human exposures at accepted exposure levels, is questionable. Reports of human hypersensitivity reactions resulting from exposure to sodium fluoride are scattered and largely anecdotal (Razak & Latifah, 1988; Modly & Burnett, 1987; Richmond, 1985; Arnold et al., 1960). The most common responses observed included dermatitis, urticaria, inflammation of the oral mucosa, and gastrointestinal disturbances. Hypersensitivity reaction associated with dental preparations were mild to moderate with a fuller ascertainment of cases did not confirm that finding.

Waldbott (1962) reported that the ingestion of 1 mg/L fluoride in water produced numerous symptoms, which included gastrointestinal distress and joint pains. These symptoms were also reported in a few patients when a daily dose of 20 mg or more was administered to patients as treatment for bone conditions (Shambaugh & Sundar, 1969; Rich et al., 1964). These symptoms are not believed to be caused by chronic intake of fluoride at any dose level, let alone at the low fluoride exposure levels cited by Waldbott. These findings have been dismissed for the following reasons: 1) insufficient clinical and laboratory evidence of allergy or intolerance to fluorides used in the fluoridation of community water, and 2) no evidence of immunologically mediated reactions in a review of the reported allergic reactions (Austen et al., 1971). Waldbott (1978) proposed that a specific skin manifestation called Chizzola maculae could be caused by airborne fluorides. Waldbott and Steinegger (1973) claimed that this skin lesion was caused by drinking fluoridated water, but could not offer evidence to support this hypothesis. Additional claims (Waldbott & Ceciliioni, 1969) attributed the development of these discrete skin lesions to fluoride exposure in 10 of 32 persons living near fertilizer plants in Ontario, Canada, and Iowa, and near an iron foundry in Michigan. The evidence for Chizzola maculae as a result of exposure to fluoride has been reviewed extensively by several investigators (Hodge & Smith, 1977), who concluded that the evidence was circumstantial and unsupported by field surveys.

The literature pertaining to immunologic and immunomodulation effects of fluoride is limited. Although direct exposure to high concentrations of sodium fluoride in vitro affects a variety of enzymatic activities (Okada & Brown, 1988; Salesse & Garnier, 1984; Takanaka & O’Brien, 1985; Alm, 1983; Mizuguchi et al., 1989; Mircevova et al., 1984; Carr et al., 1985; O’Shea et al., 1987), the in vivo relevance of these observations is unclear. Standardized immunotoxicity testing of sodium fluoride at relevant concentrations and routes of administration has not been conducted.

Genotoxicity (Page 71): Genotoxicity studies of fluoride, which are highly dependent on the methods used, often show contradictory findings. The most consistent finding is that fluoride has not been shown to be mutagenic in standard tests in bacteria (Ames test). In some studies with varying methodologies, fluoride has been reported to induce mutations and chromosome aberrations in cultured rodent and human cells. The genotoxicity of fluoride in humans and animals is unresolved despite numerous studies.
longer at birth, and prematurity was much less frequent, compared with control groups (Glenn et al., 1982).

1962; Luoma et al., 1973; Taves, 1978). Considering reports indicating that fluoride may reduce soft tissue above 35 years of age. No influence of fluoride on the incidence of Down’s syndrome was seen. 

found to range from 1.32 to 1.46. The material was divided into groups according to the maternal age below or in Sweden during 1968-77 to mean water fluoride content of the areas where the mothers were living. Virtually all about a half of the real number of children born with Down’s syndrome. Berglund et al. (1980) related the incidence on the basis of birth certificates. However, the considerable material gathered in this way may only have covered (1980) did not find any difference in the incidence of Down’s syndrome between fluoridated and low-fluoride areas, but age-specific rates were not given. Erickson et al. (1976) and Erickson syndromes among Massachusetts residents during the period 1950-66. The number found was 1.5 per 1000 births in both low-fluoride areas and 0.70 – 0.80 in high-fluoride areas. His study comprised cases of Down’s syndrome registered in specialist institutions in four American states and on birth and death certificates in a fifth state. Information was gathered for the years 1950-56. Many cases may not have been detected, because they were cared for at home.

Berry (1962) examined Down’s syndrome in certain English cities and did not find any differences between areas with low (< 0.2 mg/liter) and high (0.8 - 2.6 mg/liter) fluoride levels in the drinking-water. The rates were 1.58 and 1.42 cases per 1000 births, respectively. The English custom of tea-drinking was not taken into account, and the data were not presented in age-specific groups. Needleman et al., (1974) recorded all children born alive with Down’s syndrome among Massachusetts residents during the period 1950-66. The number found was 1.5 per 1000 births in both low-fluoride and fluoridated areas, but age-specific rates were not given. Erickson et al. (1976) and Erickson (1980) did not find any difference in the incidence of Down’s syndrome between fluoridated and low-fluoride areas, on the basis of birth certificates. However, the considerable material gathered in this way may only have covered about a half of the real number of children born with Down’s syndrome. Berglund et al. (1980) related the incidence in Sweden during 1968-77 to mean water fluoride content of the areas where the mothers were living. Virtually all cases of Down’s syndrome were probably recognized and the incidence rates per 1000 births during the period were found to range from 1.32 to 1.46. The material was divided into groups according to the maternal age below or above 35 years of age. No influence of fluoride on the incidence of Down’s syndrome was seen.

Effects on Mortality Patterns (Pages 86-87): A report stated that the mortality rate from heart diseases had nearly doubled from 1950 to 1970 following the introduction in 1949 of fluoridation of the drinking-water in Antigo, Wisconsin, a little town with only 9000 inhabitants (Jansen & Thomsen, 1974). The report did not adjust for the fact that the number of people ages 75 years or more had also doubled in this period. Subsequently, epidemiologists from the American National Heart and Lung Institute did not find any correlation between deaths due to heart diseases and water fluoridation in Antigo (US NIH, 1972).

Several epidemiological studies, some of them very large, have not revealed any indications that fluoride in drinking-water increases the mortality rate from heart diseases (Hagan et al, 1954; Schlesinger et al, 1956; Heasman & Martin, 1962; Luoma et al., 1973; Bierenbaum & Fleischman, 1974; Erickson, 1978; Rogot et al., 1978; Taves, 1978). In fact, some of these studies point to the beneficial effects of fluoride in heart diseases (Heasman & Martin, 1962; Luoma et al., 1973; Taves, 1978). Considering reports indicating that fluoride may reduce soft tissue
calcification such as atherosclerosis (Leon et al., 1954, 1955; Heasman & Martin, 1962; Taves & Neuman, 1966; Bernstein et al., 1966; Zipkin et al., 1970), it seems of value to encourage further research on the relationship between fluoride and cardiovascular diseases.

**Allergy, Hypersensitivity, and Dermatological Reactions (Pages 87-88):** In 1971, the American Academy of Allergy examined the literature on alleged allergic reactions to fluoride: (Feltman, 1956; Feltman & Kosel, 1961; Burgstahler, 1965; Waldbott, 1965; Shea et al., 1967). The conclusions of the Executive Committee were (Austen et al., 1971): “The review of the reported allergic reactions showed no evidence that immunologically mediated reaction of the types I-IV had been presented. Secondly, the review of the cases reported demonstrated that there was insufficient clinical and laboratory evidence to state that true syndromes of fluoride allergy or intolerance exists.” As a result of this review, the members of the Executive Committee of the American Academy of Allergy adopted unanimously the following statement: “There is no evidence of allergy or intolerance to fluorides as used in the fluoridation of community water supplies.”

Since 1971, only in a few reports in the allergy literature have allergic reactions been suspected to be connected with fluoride exposure. Petraborg (1974) described seven patients with various symptoms appearing a week after the introduction of water fluoridation. Grimbergen (1974) using a double blind provocation test reported on a patient showing allergic reactions to fluoridated water. Waldbott (1978) reviewed previous reports.

However, no animal or laboratory studies have indicated the existence of fluoride allergy or fluoride intolerance, and no plausible mechanism for such allergic reactions has been suggested. Thus, the allergenic effects of fluoride remain unproven.

**Other Reviews**
(examples of municipal or territorial reviews of the water fluoride issue)


**Mutagenicity (Page 15):** There have been several reports of mutagenicity of HF or NaF on plants, Drosophila (Fruit fly), and mammals; and several reports of the lack of mutagenicity in similar organisms have likewise been published (studies cited in U.S. Environmental Protection Agency, 1988). The International Agency for Research on Cancer (1982) describes the lack of mutagenic effects on the bacterium Salmonella typhymurium (the Ames Test, which is a standard screen for mutagenic materials) and the yeast Saccharomyces cerevisae.

Many other studies typically employ in vitro tissue culture into which fluoride is introduced in the culture medium. For instance, a series of studies by Tsutsui and coworkers (1984a; 1984b; 1984c) found evidence for DNA damage in cultured human or Syrian hamster cells including both chromosome aberrations and unscheduled DNA synthesis. Tsutsui et al. (1984c) point out that genotoxicity has been demonstrated in many vitro studies but in a few in vivo studies, and that concentrations employed in such studies are often as high as 10,000 times that of typical environmental exposure. Fluoride ion at these levels inhibits many enzymes, and in such in vitro studies it may interfere with enzymes involved in DNA repair or replication rather than by direct interaction with the DNA itself.

**Brain Effects (Pages 15 – 16):** Varner et al. (1993) published a study of male rats treated with A1F3 – a complex of aluminum and fluoride – at 0.5, 5.0 and 50 ppm in their drinking water. They found significant effects in the lowest concentration rather than at the higher two concentrations. They subsequently refined the study (Varner et al., 1998) with equivalent levels of NaF to deliver the same F as in the A1F3 complex. In these experiments the A1F3-exposed rats showed higher mortality and brain tissue anomalies relative to the NaF or control group rats. To our knowledge, the work described in these papers has been cited almost exclusively on the anti-fluoridation websites, in the journal Fluoride, and in the publications of Varner and coauthors. Since other workers in the field have not responded by either citing or commenting on the work to either support or refute their findings, the work of Varner and colleagues lacks peer response from the scientific community. At present there is insufficient independent information to either confirm or deny these findings.

**Other Adverse Health Effects (Page 16):** In contrast to the above dearth of scientific acknowledgement of the Varner publications, we were able to find many independent studies conducted both before and after the initiation of supplemental fluoridation in which there were no changes in death rates from cancer, heart disease, intracranial lesions, nephritis, cirrhosis, or from all causes (several of these are cited in Richmond, 1985). The issue of adverse
health effects has been reviewed in a *Scientific American* article by Doyle (1996). Several investigations address whether fluoride might adversely affect health in medically compromised mammals or interact with conditions such as renal insufficiency or diabetes. For instance Dunipace and coworkers (1996) found that diabetic rats retained more fluoride than their non-diabetic counterparts; however, they discovered no adverse effects on the physiological, biochemical, or genetic variables monitored.

There is no credible evidence for acute or chronic hypersensitivity (allergic response) among the billions of consumers of fluoride-rich beverage, tea, which provides 1 – 4 mg fluoride per cup (Richmond, 1985). The treatment of several hundred multiple myeloma patients with daily doses of 50 – 100 mg fluoride for up to 70 months resulted in no significant effect on the progress of the disease; nor were there side effects from the fluoride exposure that were different from side effects observed from the placebo controls (Harley and Schilling, 1972; Kyle et al., 1975).

These and many other instances of a lack of even a correlation between fluoride exposure and adverse health or physiological effects is further emphasized when one considers the general good health and longevity of millions of residents in the United States who live for several generations in areas with natural fluoridation of drinking water at 2 to 10 mg/L (Dean, 1936; Dean, 1938; Shaw, 1954; Richmond, 1985; Public Health Service, 1991; see also, National Academy Press, 1999 and papers cited therein; also on the Internet at http://www.nap.edu/books/0309063507/html/288.html).

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**Child Development (Page 53):** Early studies of child development in fluoridated and non-fluoridated communities focused on physical health. No differences were documented with respect to body processes, blood chemistry, vision, hearing or any other general health parameter.

More recent studies have focused on intellectual development. Two conducted in China claimed to have found differences in IQ between children exposed to differing levels of fluoride. Although both fell outside the inclusion criteria they were reviewed to illustrate the flaws in this research. The first (Zhao et al., 1996) compared the IQ of children in one village where the water supply contained 4 ppm fluoride and one village where the concentration of fluoride was 0.9ppm. The mean IQ of random samples of children was 105 in the former and 98 in the latter, a statistically significant difference. In both villages, children of parents with a higher education had a higher IQ. However, analysis of mean IQ scores adjusting for the confounding effect of parental education was not undertaken. Nor was the effect of other potential confounders taken into account. The second study compared the IQ scores of children from four areas with differing levels of dental fluorosis. The source of fluoride was not water but soot due to coal burning. The Dental Fluorosis Index scores varied from 0.4 to 3.0. The latter is seen in areas fluoridated to approximately 8ppm. Significant differences were observed in the IQ scores of children living in non-fluorosis and severe fluorosis areas (90 vs. 80, respectively). It is not clear if the children examined in each area were randomly sampled. Nor was any attempt made to control for potential confounders or the effects of other pollutants present in soot from coal.

**Immune Function (Page 53):** No studies of the effect of water fluoridation on immune function were published between 1994 and 1999. However, a review paper (Challacombe, 1996) examined studies of fluoride and immune response published prior to 1992 and found no support for the suggestions that fluoride affects immunity.

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**Page 30, summary majority opinion:** From the perspective of epidemiology and toxicology, the available scientific literature has not substantiated the claims that water fluoridation was a factor in other adverse health effects. The results found in the literature have not eliminated the need for further research. Carefully designed studies, which take into account total fluoride intake and all other relevant factors, are required. There is no need for or value in further studies which attempt to relate water fluoridation per se to adverse health effects.
Although there is considerable literature on the effects of fluoride, many of these studies were related to high dose toxicity or to the effects of high therapeutic doses. Studies at these high levels were not considered relevant by the Panel.

Renal and Gastrointestinal Effects (Page 52): The kidney is a site for potential toxicity because this organ is exposed to relatively high concentrations of fluoride as approximately 50% of ingested fluoride is cleared from the body by the kidneys. The study found no evidence to suggest that water fluoridation was associated with an increased risk of renal disease.

Water used by kidney dialysis patients for haemodialysis after purification by reverse osmosis, has been reported to contain significantly higher levels of fluoride than commercially prepared peritoneal dialysis fluid (Bello et al., 1990). The authors suggested that the common usage of reverse osmosis to purify water for dialysis meant that in areas with fluoridated water, dialysis patients might, inadvertently, be exposed to too much fluoride. In the US, an outbreak of acute illness occurred in 12 of 15 patients treated in one dialysis room, compared with no cases in 17 patients treated in the second room at the same unit. The cases had unusually high serum fluoride levels and the cause of this was traced to a temporary deionization system (Arnow et al., 1994).

Allergy (Page 52): Cases of asthma have been reported in adults exposed to fluoride in an occupational setting (Kongerud et al., 1994), and in children living near an aluminum smelter and exposed to air containing fluoride. However, there appeared to be no confirmed cases of allergic reactions following water fluoridation.

Consumption of tea, which contains high levels of fluoride, was not commonly associated with allergic reaction. Nevertheless, a small proportion of the public were convinced that they have suffered an allergic reaction caused by fluoride in the water.

Sudden Infant Death Syndrome (SIDS) (Page 53): A number of studies have examined whether water fluoridation might be linked with a higher level of SIDS. Although a comparison of SIDS rates in the Australian capitals (Walker, 1992) claimed that Hobart with the longest history of fluoridation had the highest rates, followed by Canberra, while the rates were lowest in Melbourne which was non-fluoridated, there are likely to be many other differences between these cities that could explain the variation in SIDS rates. In conclusion, the study found no scientific evidence to suggest that fluoridation might increase the risk of SIDS.

Reproductive Effects and Fertility (Page 53): A single study has attempted to relate fertility to exposure to fluoride in humans (Freni et al., 1994). A few occupational studies have suggested that workers in certain industries, who are exposed to fluorides amongst other potentially hazardous compounds, experienced a range of adverse health effects including reduced testosterone levels in men and menstrual irregularities and spontaneous abortion in women. In all of these studies it was impossible to ascribe an effect to fluoride with any certainty because of the parallel exposure to a range of other compounds. In conclusion, the review found no reliable evidence to support an association between exposure to fluoridated water and any adverse reproductive effects.

Genetic Defects (Page 53): A number of small studies have suggested an association between fluoride and congenital malformation or Down syndrome. Earlier studies had suggested a link but have since been shown to be flawed, and more recent studies have not supported this hypothesis (IARC, 1982; NHMRC, 1985; PHC, 1993). The review concluded that there was no strong scientific evidence to support such an association.

Thyroid and Brain Function (Page 54): In a study of 26 adolescents aged 13-15 consuming water containing fluoride at 3 ppm, a level higher than in fluoridated water, there was no effect on thyroid function (Baum et al., 1981). Other studies have considered thyroid function in patients treated with high doses of fluoride. In one study of patients treated for osteoporosis with 60 mg of Sodium Fluoride per day, some patients experienced joint pain and gastrointestinal effects but no changes in renal, bone marrow or thyroid function (Hasling et al., 1987). Exposure to fluoride in patients treated for osteoporosis would be considerably greater than that associated with consumption of fluoridated water.

Studies in animals have reported both the presence and absence of adverse effects of high levels of fluoride on thyroid function. A review of fluorine and thyroid function concluded that the published data did not support the view that fluoridated water had an adverse effect on the thyroid (Burgi et al., 1984). Another concern expressed is that fluoridated water may be associated with Alzheimer’s disease because of contamination with aluminum.
However, on the basis of current evidence, aluminum exposure has not been clearly established as a causal factor in the development of Alzheimer’s disease. There is an alleged link between fluoride intake and both brain function impairment and a protective effect. The scientific findings, however, are not consistent.

**Other Conditions (Page 54):** There is an alleged link between fluoridated water consumption and a number of other adverse health effects including ageing, immune system damage, and magnesium/calcium deficiency. However, the review could find no reliable scientific evidence of an increased risk of these conditions.

**Cardiovascular Disease (Page 54):** A number of studies have shown conflicting results in relation to a possible beneficial link between fluoride and the incidence of cardiovascular disease. Some studies have shown an apparent decrease in the prevalence of cardiovascular disease in areas with higher fluoride levels, while others have shown no link. There is insufficient evidence to establish a causal link.

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**Natick Fluoridation Study Committee.** (1997). Should Natick fluoridate?: A report to the town and Board of Selectmen. (On-line).

**Page 3, findings**

- Fluoride adversely effects the central nervous system, causing behavioral changes and cognitive deficits. These effects are observed at fluoride doses that some people in the US actually receive.
- There is good evidence that fluoride is a developmental neurotoxicant, meaning that fluoride affects the nervous system of the developing fetus at doses that are not toxic to the mother. The developmental neurotoxicity would be manifest as lower IQ and behavioral changes.
- Some adults are hypersensitive to even small quantities of fluoride, including that contained in fluoridated water. At least one such person is a Natick resident.
- The impact of fluoride on human reproduction at the levels received from environmental exposures is a serious concern. A recent epidemiology study shows a correlation between decreasing annual fertility rate in humans and increasing levels of fluoride in drinking water.
- Fluoride inhibits or otherwise alters the actions of a long list of enzymes important to metabolism, growth, and cell regulation.
- Sodium fluorosilicate and fluorosilicic acid, the two chemicals Natick intends to use to fluoridate the water supply, have been associated with increased concentrations of lead in tap water and increased blood lead levels in children, based on case reports and a new, as-yet-unpublished study.
APPENDIX 3:
Cost-Effectiveness Studies

Table 1: Cost-Effectiveness Studies, U.S.
<table>
<thead>
<tr>
<th>Author, Pub Date, Author Affiliation</th>
<th>Analytic Method (Comparators), Perspective of Analysis, Reported or Calculated Summary Measure</th>
<th>Study Type, Population Description</th>
<th>Base Year, Discount Rates, Costs included, Caries Baseline Incidence, Measure of Effectiveness &amp; Sources</th>
<th>Summary Measure, Adjusted Value</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burt, BA, ed., 1989</td>
<td>Cost-effectiveness ratio, average (vrs. no fluoridation). Local Government/Water District perspective. Timeframe: lifetime. Cost of fluoridation per decayed surface saved</td>
<td>Economic modeling using consensus estimates of U.S. cost, prevalence and effectiveness data. Children and adults to age 44.</td>
<td>1988 US$. CWF costs discounted at 4%. Direct costs of fluoridation were independently estimated by 5 working groups based on data from a published review (Garcia, 1989); they included operating costs, replacement costs after 15 year depreciation, and labor costs for 3 community sizes: &lt;10,000 ($0.60-$5.41), 10,000-200,000 ($1.18-$7.5), and &gt;200,000($1.12-$2.1); they did not include overhead or political costs. Effectiveness estimates were based on published studies of CWF which included contemporary controls in Western Established Economies between 1983 and 1989: the estimated range of caries reduction over a lifetime (“against a background of nearly universal fluoride use”): 20-40%. Children: 30-39% primary dentition; 11-38% mixed dentition; 13-35% permanent dentition. Adults (“very little data”): age 20-44, coronal caries 20-30%, root caries 20-40%. Net annual caries increment (estimated only by Group 4)=0.22 DF/yr. Costs of disease were considered only by Group 4—included only initial 2-surface amalgam restoration ($44). Estimated Cost of Disease Averted: $4.36/person/year. Costs of adverse effects of water fluoridation were assumed to be negligible.</td>
<td>Cost of fluoridation per decayed surface saved ranged from $2.60 [$3.98 2001 Denver$] in large and medium sized cities to $8 to $12 for small cities and effectiveness estimates on the low end of the range. It was noted that this cost is well below the cost of a surface restoration, making water fluoridation cost-saving.</td>
<td>Weaknesses: Did not explicitly state all assumptions or findings, in particular, the baseline caries rate chosen was not reported. The development of CE ratios did not include cost savings derived from caries reductions (except “preliminary work” by Group 4); no sensitivity analyses were performed. Available data for fluoridation costs and caries incidence was from pre-90s surveys. Oxford EBM level 4.</td>
</tr>
</tbody>
</table>
Table 1: Cost-Effectiveness Studies, U.S. (Page 2 of 2)

| Griffin, SO, 2001, CDC | Cost-effectiveness ratio, average (vrs. no fluoridation). Societal perspective. Timeframe: lifetime. Net cost of fluoridation per permanent decayed surface saved | Economic modeling using parameter estimates from published studies and U.S. epidemiologic surveys. 1995 U.S. population, ages 6 to 64. | 1995 US$. All costs and benefits were discounted at 4%. Direct costs of fluoridation were taken from a 1992 report of 44 communities (Ringelberg, 1992); they included operating costs, replacement costs, maintenance and labor costs. Ranged from $3.17/person per year (4% discount) for communities <5000 to $0.50 for communities >20,000. Did not include overhead or political costs. Effectiveness estimates were based on a review of published studies from 1979-1989 and from the National Survey of Oral Health, 1987. Best-case 29%, base-case 25% and worse-case 12% reductions in caries were estimated for both adults and children. Annual caries increment in non-fluoridated communities was estimated by three methods to yield best-case (studies published from 1978-88), base-case (1987 National Survey of Oral Health, cross-sectional) and worse-case (NHANES I & II, 1971-74 and 1989-94, longitudinal cohort) estimates for three ages ranges: 0.49-1.4 surfaces/yr in children 6-17; 0.49-0.83 in 18-44 year olds and 0.0-1.24 in 45-65 year olds: average 0.33-1.16 surfaces/yr. Base-case net annual caries increment (increment*effectiveness)=0.76*25%=.19 DF/yr. Costs of disease ($100.62/surface) included initial amalgam restorations ($54), costs to replace restorations (every 12 years) and productivity costs ($18/restoration). Estimated Cost of Disease Averted: $2.99-$56.01/person/year (base-case $19.12). Costs of adverse effects of water fluoridation were assumed to be negligible. |
| Cost of fluoridation per decayed surface saved baseline was $2.63 [$3.13*] (range $1.37-$13.64) in cities >20,000. Negative net cost per decayed surface saved in large communities (>20,000) ranged from $3.52 [$4.19*] (worst case) to $33.71 [$40.10*] (best case). Water fluoridation was cost-saving under all scenarios. Break-even analyses showed CWF was cost saving for all effectiveness levels above 1% (assuming baseline caries increment of .76 surfaces/yr.), and all increments above .02 surfaces/yr. (assuming baseline effectiveness of 25%). |
| Strengths: Takes a societal perspective. Includes productivity losses (-). Attempted to estimate lifetime costs of decayed surface (-). Sensitivity analysis varied discount rate, effectiveness and caries increments—demonstrating robustness of results even considering the decline in caries incidence. Weaknesses: Available data for caries incidence was from pre-90s surveys (-). Limited costs of decayed surface to single-surface restorations & replacements (+). Did not account for benefit of deciduous caries prevention. |

*Adjusted to 2001 Denver $ by CPI-U
Table 2: Cost-Effectiveness Studies, Other Countries
<table>
<thead>
<tr>
<th>Author, Pub Date, Author Affiliation</th>
<th>Analytic Method (Comparators), Perspective of analysis, Reported or Calculated Summary Measure</th>
<th>Study Type, Population Description</th>
<th>Base Year, Discount Rates, Costs included, Caries Baseline Incidence, Measure of Effectiveness &amp; Sources</th>
<th>Summary Measure, Adjusted Value</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wright, C et al. 2001 Wellington School of Medicine, Envir. Sci. and Research Inst., New Zealand</td>
<td>Cost-effectiveness ratio, average (vrs. no fluoridation), Societal perspective, New Zealand communities. Timeframe 30 years. Net annual per person cost per permanent decayed surface saved</td>
<td>Economic modeling using parameter estimates from New Zealand data and a U.S. published study. 2000 New Zealand population, ages 4 to 34.</td>
<td>1999 NZ $ (1NZ $=$.66US). All costs and benefits were discounted at 5%. Direct costs of fluoridation were obtained from equipment manufacturers and operators in NZ; they included operating costs, replacement costs at 15 years, maintenance and labor costs. Did not include overhead or political costs. Costs of disease included initial amalgam restorations for both deciduous and permanent teeth (based on reimbursements rates for children-$24; on dentist labor costs for adults-$66) and the costs to replace restorations in permanent teeth (every 8 years up to age 45). Costs of adverse effects of water fluoridation were assumed to be negligible. Did not include productivity costs. Effectiveness estimates were based on 1996 records of publicly funded dental care for NZ children ages 4-13 years and from a 1992 U.S. study of 20-34 y/o adults for those ages &gt;13 (.base-case .33 surface reductions in caries/year). Net annual caries increment averaged 0.24 DMT/yr in 4-13 year olds and 0.29 DMT/yr. (95% CI .19-.39 surfaces) in 14-34 year olds.</td>
<td>Community Water Fluoridation was cost saving for communities above 1000 people under all scenarios.</td>
<td>Strengths: Recent effectiveness and baseline caries data. Included cost savings (but not non-monitized benefits) from preventing decay in deciduous teeth. Sensitivity analysis varied discount rate, number of injection sites, effectiveness and caries increments—demonstrating robustness of results even considering the decline in caries incidence. Weaknesses: Available data for caries incidence in children did not include decayed but untreated surfaces. Assumed no benefits after age 45 and no decay after age 34.</td>
</tr>
<tr>
<td>Akehurst and Sanderson 1993 Centre for Health Economics, University of York</td>
<td></td>
<td></td>
<td>&quot;In terms of cost, effect and the certainty of that effect the most cost-effective policy is fluoridation of water supplies&quot;</td>
<td></td>
<td>Unpublished; no abstract available, report on order</td>
</tr>
</tbody>
</table>
| **Birch, S., 1990**  
**McMaster University, Ontario, Canada** | **Cost-effectiveness analysis; England and Wales, 1985, Time horizon: 14 years.** | **Economic modeling using data from England calculated for three hypothetical population sizes. Ages 4 to 14, primary and permanent dentition.** | **British pounds, unspecified year. All costs and benefits were discounted at 5% and 10%. Direct costs of fluoridation were attributed to a personal communication.**  
**Caries incidence and effectiveness data taken from several epidemiological studies conducted in Great Britain in the 1980s. Net annual caries increment averaged 1.82 dmftDMFT/yr in high caries areas and 0.47 dmftDMFT/yr in low caries areas.**  
**Costs of disease were not considered.** | **“Cost-per unit benefit varies by a factor of four according to the existing level of caries prevalence”.**  
**A simple model is used to show how cost-effectiveness varies by underlying caries risk and community size.** |
| **O’Mullane, DM, 1990:**  
**University Dental School, Wilton, Cork, Ireland** | **Not an economic analysis. Effectiveness (vrs. no fluoridation). Net annual caries increment calculable from data presented.** | **Nation-wide estimates of program cost, prevalence and effectiveness data. Children 8 to age 15.** | **1987 UK Pounds. No discounting. Average direct costs included operating costs, capital costs and labor costs; they did not include overhead or political costs. 33 pence=$0.81/capita in 1995 U.S. dollars.**  
**Effectiveness estimates were based on national surveys in 1961-64 and 1984: ages 8-12: 40%; ages 12-15: 25% permanent dentition.**  
**Annual caries increment in non-fluoridated communities was estimated from table 2: ages 8-12: 1.05 surfaces/yr. ages 12-15: 1.4 surfaces/yr.**  
**Net annual caries increment averaged 0.39 DMFS/yr.**  
**Costs of disease not reported.** | **Authors stated that this cost makes water fluoridation cost-effective.**  
**Weaknesses: Not an economic analysis (cost of treatment averted was not considered). Demonstrated that benefits of fluoridation persisted in spite of a downward secular trend in caries prevalence in both communities.** |
<table>
<thead>
<tr>
<th>Author, Pub Date, Author Affiliation</th>
<th>Analytic Method (Comparators), Perspective of analysis, Reported or Calculated Summary Measure</th>
<th>Study Type, Population Description</th>
<th>Base Year, Discount Rates, Costs included, Caries Baseline Incidence, Measure of Effectiveness &amp; Sources</th>
<th>Summary Measure, Adjusted Value</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Attwood and Blinkhorn, 1989: Royal Hospital for Sick Children, Scotland</td>
<td>Cost Analysis (fluoridated vrs recently non-fluoridated community); Government dental services perspective; Difference in mean cost of restoring carious teeth</td>
<td>Epidemiologic study; Comparison of DMFT scores and treatment costs for 5 &amp; 10 year olds life-time residents in 2 areas: a non-fluoridated community and a community that stopped fluoridating in 1983.</td>
<td>1980 and 1986, no discounting; included cost of restorations and total dental treatment costs. Baseline caries prevalence (non-fluoridated): 1980: 4.38 in 5 y/os, 3.82 in 10 y/os. 1986: 3.35 in 5 y/os, 2.22 in 10 y/os.</td>
<td>1) Mean DMFT/ dmft and treatment costs for caries were lower in all age groups in the fluoride site in both 1980 and 3 years after suspending CWF in 1986, compared to the non-CWF site. 2) Caries prevalence fell by 13% and 16% in the 5 and 10y/o groups, respectively, in the non-CWF site from 1980-86. 3) There was no drop in DMFT (+4%) and an increase in restoration costs (+115%) in 10 year olds in the site suspending CWF from 1980 to 1986, compared to a fall in prevalence (-16%) and no change in costs (+9%) in 10 y/o in the non-CWF site.</td>
<td>Not an economic analysis (cost of fluoridation was not considered). Demonstrated that benefits of fluoridation persisted, though attenuated, 3 years after suspension of CWF in children, even in the context of a downward secular trend in caries prevalence in both communities.</td>
</tr>
</tbody>
</table>
Table 3: Other Delivery Strategies for Fluoride

<table>
<thead>
<tr>
<th>Delivery Strategy</th>
<th>Cost-Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water fluoridation</td>
<td>High</td>
</tr>
<tr>
<td>Dental varnish</td>
<td>Moderate</td>
</tr>
<tr>
<td>FLOSS (fluoride mouth rinse, oral suppository, and toothbrushing)</td>
<td>Low</td>
</tr>
</tbody>
</table>

Appendix 3 – Cost-Effective Studies 167
<table>
<thead>
<tr>
<th>Fluoride Modality</th>
<th>Material Cost of Fluoride/Person/Year (2001 $)</th>
<th>Total Cost of a Community Based Program / Person / Year (2001 $)</th>
<th>Annual Cost Per Single Surface Cavity Averted</th>
<th>Efficacy in Reducing Caries</th>
<th>Applicability as a Public Health Intervention</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community Water Fluoridation</td>
<td>$.47</td>
<td>$0.76</td>
<td>-$4.42 ($3.35 to 10.72)</td>
<td>Up to 60% reduction in caries in early studies; more recent estimates 18-40%. Many studies; moderate to low quality.</td>
<td>High</td>
<td>Cost-saving; most effective method of reaching whole population; requires no active participation by individuals; benefits all ages. Water fluoridation was “strongly recommended” by the Task Force on Community Preventive Services (Centers for Disease Control and Prevention 2001a, p. 8)</td>
</tr>
<tr>
<td>School water Fluoridation</td>
<td>Similar to comm. water fluoridation</td>
<td>$6 ($1-$14)*</td>
<td>No reports located</td>
<td>Up to 40% reduction in caries; more recent estimates lower.</td>
<td>Moderate</td>
<td>Practical and logistical difficulties; no benefit to adults.</td>
</tr>
<tr>
<td>Fluoridated salt</td>
<td>Similar to community water fluoridation</td>
<td>Similar to community water fluoridation</td>
<td>No reports located</td>
<td>Similar to community water fluoridation</td>
<td>Low in US; but well accepted in France, Germany, Switzerland, and others</td>
<td>Has advantage that it does not require a community water supply and is simpler for individuals to accept or reject. Difficulties arise when there are multiple sources of drinking water with varying levels of Fl.—not feasible in the U.S.</td>
</tr>
<tr>
<td>Fluoride Delivery Strategy</td>
<td>Cost ($)</td>
<td>Source</td>
<td>Notes</td>
<td>Effectiveness</td>
<td>Risk-Benefit Analysis</td>
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</tr>
<tr>
<td>Toothpaste</td>
<td>$7-$13*</td>
<td>NA</td>
<td>No reports located</td>
<td>15-30% over 2-3 years; similar to CWF (25%) over lifetime*; many high quality studies*</td>
<td>Safe and effective in older children and adults; additive effectiveness with CWF. Use of toothpaste in young children is associated with enamel fluorosis—therefore requires parental supervision in children &lt;6.</td>
<td></td>
</tr>
<tr>
<td>Dietary fluoride supplements</td>
<td>$3.50*</td>
<td>NA</td>
<td>No reports located</td>
<td>Mixed results*; 4 studies showed caries reductions of 39-80% in younger children but low study quality*. Higher risk-benefit ratio in younger children.</td>
<td>Requires prescription &amp; complex dosing schedule in childhood—inappropriate dosing is reported to be common, making use in young children an important cause of fluorosis in the US*. Requires a high-level of parental motivation*. Not studied in adults*.</td>
<td></td>
</tr>
<tr>
<td>Fluoride mouth rinse</td>
<td>$1.50*</td>
<td>NA</td>
<td>No reports located</td>
<td>Consistently 20%+ in early studies*; estimated 31% in one review*. Good quality studies.</td>
<td>Low (Minimal effect in a large US demonstration project, 1976-81).</td>
<td></td>
</tr>
<tr>
<td>Professionally applied fluoride compounds (gel, varnish)</td>
<td>$72*</td>
<td>NA</td>
<td>No reports located</td>
<td>26% reduction in caries in non-fluoridated areas*.</td>
<td>Requires professional application, at least 6 mo. intervals; indicated for high-risk caries patients. Risk for fluorosis is low*.</td>
<td></td>
</tr>
<tr>
<td>Slow-release fluoride (in dental materials)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Not effective*</td>
<td>Low</td>
<td></td>
</tr>
</tbody>
</table>

*Adapted from Centers for Disease Control and Prevention 2001b.

Adapted from World Health Organization 1994.
Table 4: Other Strategies for Primary Prevention of Dental Caries
### Table 4: Other Strategies for Primary Prevention of Dental Caries

<table>
<thead>
<tr>
<th>Modality</th>
<th>Material Cost/ Person/ Year (2001 $)</th>
<th>Total Cost of a Community Based Program/ Person/ Year (2001 $)</th>
<th>Annual Cost Per Single Surface Cavity Averted</th>
<th>Efficacy in Reducing Caries</th>
<th>Applicability as a Public Health Intervention</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental sealants</td>
<td></td>
<td></td>
<td></td>
<td>Median percent decrease in occlusal caries in posterior teeth 60%, (range 5%-93%), good study quality.¹</td>
<td>Moderate; school-based sealant delivery programs</td>
<td>School-based sealant delivery programs, but not community-wide sealant promotion programs, were found to be effective and were “strongly recommended” by the Task Force on Community Preventive Services (Centers for Disease Control and Prevention 2001a, p.9)</td>
</tr>
<tr>
<td>Products containing noncariogenic sweeteners¹</td>
<td></td>
<td></td>
<td></td>
<td>“…have been delivered to teeth as constituents of chewing gum, hard candy, and dentifrices. Evidence for both sorbitol and xylitol is positive”¹</td>
<td>Low to Moderate</td>
<td></td>
</tr>
</tbody>
</table>

¹Adapted from Centers for Disease Control and Prevention 2001a, pp.9-10.

²Adapted from National Institute of Health, Office of the Director 2001, p 15.
Economic Analysis of Community Water Fluoridation in Fort Collins, Colorado

[The following is an economic analysis of community water fluoridation in Fort Collins based on the model of Griffin, et. al, provided to the Fort Collins Fluoridation Technical Study Group by Susan Griffin, PhD, Centers for Disease Control and Prevention on July 3, 2001. The analysis was based on estimates of the “net present value” average per person costs of community water fluoridation in Fort Collins provided to Dr. Griffin by FTSG members Kevin Gertig and Bruce Cooper.]

Community water fluoridation actually saves Fort Collins money. Fort Collins has approximately 100,968 residents, who benefit from community water fluoridation.¹ Using data on caries increment from region V of the National Survey of the Oral Health of U.S. School Children [2] and cost data specific to Ft. Collins, the annual cost savings per person from community water fluoridation equals $4.25 (year 2000 US$). Thus after netting out the amortized capital costs as well as annual operating expenses, the annual cost savings to the Fort Collins community attributable to community water fluoridation would be approximately $429,000 (2000 US$). Because we did not have caries data specific to Ft. Collins we allowed caries increment to vary between the 1986-1987 estimates for the US adjusted for the secular decline in caries (best-case scenario) and the 1986-1987 Region V estimates adjusted for the secular decline in caries (worst-case scenario). Our findings suggest that the annual cost savings to the Ft. Collins community could vary from $325,000 to $1,041,000.

Estimated Annual Per Person Cost Savings² Attributable to Fluoridation of Fort Collins Water System

Baseline Analysis: Under the assumptions below, the annual cost savings per person from community water fluoridation would equal $3.40 (1995 US$). This value translates to $4.25 in year 2000 US dollars³.

The following values are in 1995 US$:

1. The average per person cost of fluoridation in Ft. Collins equals $0.71.
2. We used data from Region V of the 1986-1987 Survey of Oral Health in U.S. School Children. Mean DMFS among 12-year-olds in nonfluoridated areas of Region V⁴ equals 2.71 surfaces. We assumed that permanent teeth begin to erupt at age 6 and thus the annual caries increment, nonfluoridated, would equal 0.4517 (or 2.71/6) surfaces.
3. Mean DMFS among 12-year-olds in fluoridated areas of Region V equals 2.49 surfaces. Thus, annual caries increment, fluoridated equals 0.415 (or 2.49/6) surfaces.
4. Annual averted caries attributable to fluoridation equals 0.0367 (or 0.4517-0.415) surfaces. Because there were no data on caries increment among adults and the annual caries increment among children in Region V was lower than published estimates of caries increment among adults [2], to be conservative, we assumed that individuals, aged 18 to 64 would receive the same benefit from fluoridation as would children.
5. Assuming the weighted per person discounted lifetime cost of a carious surface across the life span equals $112.00, the annual cost of averted disease equals $4.11 (or 0.0367*$112.00).
6. Annual cost savings per person from community water fluoridation equals $3.40 (or $4.11 - $0.71).

¹ According to the 2000 Census Ft. Collins had 100,968 residents, aged 6 to 64 years. According to Griffin [1] water fluoridation has been shown to be effective in reducing tooth decay in the permanent dentition of individuals, aged 6 to 64 years.
² Analysis limited to individuals, aged 6 to 64 years.
⁴ This data comes from the 1986-1987 Survey of Oral Health in U.S. School Children. The sample age ranged from 5 to 17. The mean age of the sample was 12 years. Region V includes Texas, Oklahoma, New Mexico, and Colorado.
Sensitivity Analysis: Because we did not have data specific to Ft. Collins and because the caries data was collected in 1986-1987 we calculated the cost savings under a best-case scenario and worst-case scenario.

1. Under the best-case scenario we assumed that the annual averted caries in Ft. Collins attributable to fluoridation equaled that of the US in 1986-1987, adjusted for the secular decline in caries\(^5\), or 0.08 DMFS\(^6\). The resulting annual cost savings per person would equal $8.25 (or 0.08*$112 - $0.71). Converted to year 2000 dollars, this value would equal $10.31 per person or approximately $1,041,000 for the community (year 2000 US$).

2. Under the worst-case scenario we assumed that the annual averted caries in Ft. Collins attributable to fluoridation equaled that of region V but factored in a secular decline in caries of 20%. Thus the annual averted decay would equal 0.0294 surfaces (or 0.80 * 0.0367). The resulting annual cost savings per person would equal $2.58 (or 0.0294*$112 - $0.71). Converted to year 2000 dollars, this value would equal $3.22 per person or approximately $325,000 for the community (year 2000 US$).


\(^6\) Brunelle, et al. found that the mean DMFS among US schoolchildren, ages 5 to 17 (mean age equal 12) equaled 3.39 in nonfluoridated communities and 2.79 in fluoridated communities. Thus the annual increment would equal (3.39-2.79)/6 = 0.1. Adjusting for the secular decline in caries this value would equal 0.08.
Reference List


Material Safety Data Sheet

This Information is provided for your protection by:

**LCI LTD**
The Fluoride Specialists
904-241-1200

For 24 Hour Emergency Assistance Call:

**CHEMTREC**
800-424-9300

NFPA Ratings (Scale 0-4)
Health=3; Fire=0; Reactivity=1

Fluorosilicic Acid

Section I  Product Name and Description
Section II  Personal Protection Information
Section III Health Information
Section IV  Emergency and First Aid Procedures
Section V  Ingredients
Section VI  Physical Data
Section VII Reactivity
Section VIII Fire and Explosion Hazards
Section IX  Storage and Special Precautions
Section X  Transportation Requirements
Section XI  Emergency Action - Spill or Leak
# Fluorosilicic Acid

## Product Data Sheet

### Chemical Analysis

<table>
<thead>
<tr>
<th>Assay ($H_2SiF_6$)</th>
<th>23.00 % min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluorine (F)</td>
<td>18.22 % min</td>
</tr>
<tr>
<td>Heavy Metals as Lead (Pb)</td>
<td>0.02 % max</td>
</tr>
<tr>
<td>Hydrofluoric Acid (HF)</td>
<td>Less than 1.00 %</td>
</tr>
</tbody>
</table>

### Physical Properties

**Description**

Water white to straw yellow solution, meeting both the AWWA Standard B703-00 and the ANSI/NSF-60 Standard for Fluorosilicic Acid.

**Straw Yellow shall be determined as material with a maximum of 100 units (APHA) in accordance with method 2120B, visual comparison method.**

**Specific Gravity**

1.234 ($H_2O = 1$) for 25% @ 60° F

222.5° F

**Boiling Point for 25%**

4° F (-15.5° C)

**Freezing Point for 25%**

144.08

**Molecular Weight**

10.29 lbs / gal

**Weight per Gallon for 25%**

6.5 cps

**Viscosity for 23%**

100 tons net weight (approximate)

20 - 25 tons net weight (approximate)

### Containers

- Bulk Rail Cars
- Bulk Tank Trucks

### Freight Description

**DOT Shipping Classification**

Class 8 (Corrosive)

**DOT Shipping Name**

Fluorosilicic Acid

**Packing Group:** II

**DOT/UN number:** 1778

**Placard:** Corrosive

---

The information presented herein is based on data considered to be accurate and that reflects the requirements of the OSHA Hazard Communication Standards in effect as of the date of preparation of this Product Specification Sheet. However, no warranty or representation, express or implied, is made as to the accuracy or completeness of the foregoing data and safety information. In addition, no responsibility can be assumed by vendor for any damage or injury resulting from abnormal use, from any failure to adhere to recommended practices or from any hazards inherent in the nature of the product.

LCI LTD  P.O.Box 49000  Jacksonville Beach, Florida 32240-9000  Phone 904-241-1200  Fax 904-241-1229
Section I

PRODUCT NAME AND DESCRIPTION

DOT Chemical Name: Fluorsilicic Acid
Synonyms: Hydrofluorsilicic Acid, Fluosilicic Acid, Hexafluosilicic Acid
Chemical Family: Inorganic Acid
CAS Number: 16961-83-4
Formula: $\text{H}_2\text{SiF}_6$
NIOSH Registry Number: V-V 8286000

Note: N/A indicates Not Applicable where shown.

Section II

PERSONAL PROTECTION INFORMATION

Respiratory Protection: A NIOSH approved cartridge respirator with full-face shield. Chemical cartridge should provide protection against acid fumes. (Hydrogen Fluoride). For concentrations greater than 20ppm, a NIOSH approved self-contained breathing apparatus with full-face shield should be used.

Eye and Face Protection: Use tight-fitting chemical splash goggles and a full-face shield, 8 inch minimum. Contact lenses should not be worn.

Hand, Arm and Body Protection: Prevent contact with skin by use of acid-proof clothing, gloves and shoes. Use a NIOSH approved acid proof suit and boots where liquid or high vapor concentration is possible.

Other Protective Clothing and Equipment: Eye wash and emergency shower facilities should be available in handling area.

Engineering Controls: General or local exhaust systems sufficient to maintain vapors below 2.5mg/m$^3$ (as F).

Section III

HEALTH INFORMATION

OSHA Permissible Exposure Limit (PEL): 2.5mg/m$^3$ (as F)
ACGIH Threshold Limit Value (TLV): 2.5mg/m$^3$ (as F)
Section IV

EMERGENCY AND FIRST AID PROCEDURES

Inhalation: Remove exposed person to an uncontaminated area immediately. If breathing has stopped, start artificial respiration at once. Oxygen should be provided for an exposed person having difficulty breathing (but only by an authorized person) until exposed person is able to breathe easily by themselves. Exposed person should be examined by a physician.

Eye Contact: Flush eyes for at least 15 minutes with large amounts of water. Eyelids should be held apart during the flushing to insure contact of water with all accessible tissue of the eyes and lids. Medical attention should be given as soon as possible.

Skin Contact: Exposed person should be removed to an uncontaminated area and subjected immediately to a drenching shower of water for a minimum of 15 to 20 minutes. Remove all contaminated clothing while under shower. Medical attention should be given as soon as possible for all burns, regardless of how minor they seem.

Ingestion: If conscious, give the exposed person large quantities of water immediately to dilute the acid. Do NOT induce vomiting. Milk may be given for its soothing effect. A physician should be contacted immediately.

Note to Physician: Beware of late onset of pulmonary edema for up to 48 hours. Treat severe burns similar to Hydrofluoric Acid exposure.

Section V

INGREDIENTS

<table>
<thead>
<tr>
<th>Composition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>H$_5$SiF$_6$</td>
<td>25.0 ± 2%</td>
</tr>
<tr>
<td>H$_2$O</td>
<td>75.0 ± 2%</td>
</tr>
</tbody>
</table>
Section VI

PHYSICAL DATA

Boiling Point: 222°F (105°C)
Specific Gravity (H2O = 1): 1.234 @ 25%
Percent Volatile by Volume: N/A
Solubility in Water: Complete
Physical State: Fuming Liquid
Bulk Density: 10.29 lbs/gal @ 25%
Appearance and Odor: Water white to straw yellow, burning liquid, with pungent odor.

Freezing Point: 4°F (-15.5°C)
Vapor Pressure (mm Hg): 24 @ 77°F
Vapor Density (Air = 1): N/A
Evaporation Rate: N/A
Molecular Weight: 144.08
pH (1% Solution): 1.2

Section VII

REACTIVITY

Stability: Stable.
Hazardous Polymerization: Will not occur.
Conditions and Materials to Avoid: Metal, glass, stoneware, alkali and strong concentrated acids.
Hazardous Decomposition Products: When heated to decomposition (222°F), it emits highly toxic and corrosive fumes of Hydrogen Fluoride, Silica Tetrafluoride and Hydrogen Gas.

Section VIII

FIRE AND EXPLOSION HAZARDS

Flash Point and Method Used: N/A
Flammable Limits - % Volume in Air: Lower N/A Upper N/A
Extinguishing Media: Use agent which is appropriate for surrounding fire.
Special Fire Fighting Procedures and Precautions: Wear NIOSH approved self-contained acid suits.
Auto Ignition Temperature: N/A
Unusual Fire and Explosion Hazards: Reacts with many metals to produce flammable and explosive hydrogen gas. Keep container cool with water, using fog nozzles, as decomposition will occur above 222°F and produce toxic and corrosive fumes of fluorides.

Section IX

STORAGE AND SPECIAL PRECAUTIONS

Handling and Storing Precautions: Store in containers in cool, dry, well ventilated area away from sources of heat or ignition. Do NOT store in glass or stoneware. Use non-sparking tools. Keep separate from alkali metals, oxidizing agents, combustible solids and organic peroxides.

Ventilation: Provide adequate general and/or local exhaust to maintain vapors below 2.5mg/m³ (as F).

Other Precautions: Do not inhale fumes and prevent skin contact. If pungent, irritating odor can be detected, workers are being over-exposed. Eye wash and safety shower should be available in all acid handling areas.
Section X

TRANSPORTATION REQUIREMENTS

DOT Proper Shipping Name: Fluorsilicic Acid
DOT Hazard Class: 8 (Corrosive)
Identification Number: UN 1778
EPA Hazardous Substance: No
RCRA Status of Unused Material if Discarded: Not listed.
Hazardous Waste Number: Not listed.
Waste Disposal Method: Disposer must comply with federal, state, and local disposal or discharge laws.
Additional Comments: For international transportation, Fluorsilicic Acid is regulated by the International Maritime Organization (IMO) and the International Air Transport Association (IATA) for vessel and air movement as a Class 8. Packaging, marking, labeling and shipping paper descriptions must precisely reflect the regulation for export movement.

Section XI

EMERGENCY ACTION - SPILL OR LEAK

Emergency Action: Keep unnecessary people away. Stay upwind, keep out of low areas. Isolate hazard area and deny entry. We recommend that the user establish a spill prevention, control and containment plan. This plan should include procedures for proper storage as well as containment and clean-up of spills and leaks. The procedures should conform to safe practices and provide for proper recovery and disposal in accordance with federal, state and local regulation. Contact Chemtrec at 1-800-424-9300 for 24-hour emergency assistance.

Small Spills: Any personnel in area should wear a NIOSH approved air supplied acid suit. Diak area to contain material. Do not allow solution to enter sewers or surface water. Neutralize the spill with water and lime (hydrated lime). Take up with sand or non-combustible absorbent material and place in containers for later disposal. Provide ventilation and be wary of hydrogen generation upon reaction with some metals. Contact Chemtrec at 1-800-424-9300 for 24-hour emergency assistance.

Large Spills: Contact Chemtrec at 1-800-424-9300 for 24-hour emergency assistance. Any personnel in area should wear a NIOSH approved air supplied acid suit. Diak area ahead of spill to contain material. Do not allow solution to enter sewers or surface water. Neutralize the spill with water and lime (hydrated lime). Provide ventilation and be wary of hydrogen generation upon reaction with some metals. Notify the National Response Center, if required.

DISCLAIMER

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Revised March 1999 by Gustavo R. NAVAR
Process Engineer
4.2 Fluoride Manufacturing Process, Figures 1 and 2

Basic Process Chemistry

The basic chemistry of the wet process is as follows:

1. Phosphate rock is converted by reaction of concentrated sulfuric acid into phosphoric acid and the insoluble salt calcium sulfate (Figure 1 PM).
2. The insoluble calcium sulfate is then separated from the phosphoric acid. Most of this process is by filtration (Figure 1 RM).

![Diagram of a plant for the production of phosphoric acid]

3. Fluorine is present as Calcium Fluoride in most phosphate rocks in the order of 2 - 4% by weight. The element is liberated during the acid process; initially as Hydrogen Fluoride, but in the presence of silica this reacts to form Fluorosilicic Acid (Figure 1.)
4. Once the Fluorosilicic Acid is manufactured, the manufacturer analyzes it to meet specifications by the American Water Works Association and the National Sanitation Foundation.
5. The acid is then shipped to facilities around the country for use in fluoridation of water supplies.
6. The City of Fort Collins receives the product 6 - 8 times per year depending on the water demand. Chemical assay faxes are compared to the sample taken at the point of delivery. If approved, the product is fed to the finished water as described under the methods section.

Figure 1. Source: LCI, Inc. 2002
Figure 2. Fluorosilicic acid recovery from vapors produced in vacuum concentration of a wet-process phosphoric acid chemical plant.

Source LCI, Inc 2002
### FORT COLLINS WTP

**FLUORIDATION SELF - MONITORING FORM**

<table>
<thead>
<tr>
<th>Day</th>
<th>Fluoride Level, mg/L</th>
<th>Chemical Usage Indicate type at right</th>
<th>Water Produced: Millions Gal/Day</th>
<th>Off-Line</th>
<th>Fluoridation Readings.</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mo</td>
<td>Yr</td>
</tr>
<tr>
<td>1</td>
<td>0.99</td>
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<td>1095.68</td>
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</tbody>
</table>

**TOTAL**: 31.08

**AVG**: 1.00

**Count**: 31

**High**: 1.10

**Low**: 0.88

---

**Chemical Usage Measurement:**

- Pounds
- Gallons
- Pounds

**Monthly Sample of Background FI Level:**

- 0.18 mg/L

**Fluoridation Used:**

- NaF
- Na2SF6
- H2SiF6

**Testing Method:**

- ISE Electrode
- SPADNS Colorimetric

**Comments:**

- Your dosage = your optimum - your background fluoride level

---

**Submitted By:**

Fluoridation, Co Dept of Public Hlth
4300 Cherry Creek Dr South
Denver, CO 80246-1530.
### 4.4 NSF Certification

**FARMLAND HYDRO, L.P.**

**ADDRESS REPLY TO:**

Green Bay Plant  
Postal: P.O. Box 960  
Barrow, Florida 33831  
Street: 4350 County Road 645 West  
Barrow, Florida 33830

**CERTIFICATE OF ANALYSIS**

<table>
<thead>
<tr>
<th>SAMPLE</th>
<th>FLUOROSILICIC ACID</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAMPLE RECEIVED</td>
<td>04/19/2001</td>
</tr>
<tr>
<td>SAMPLE REPORTED</td>
<td>04/20/2001</td>
</tr>
<tr>
<td>SAMPLE NO.</td>
<td>GATX 42914</td>
</tr>
<tr>
<td>LAB NO.</td>
<td>FSA 01-0419</td>
</tr>
</tbody>
</table>

**ANALYSIS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>% H₂SiF₆</td>
<td>23.58</td>
</tr>
<tr>
<td>% HF</td>
<td>0.59</td>
</tr>
<tr>
<td>% P₂O₅</td>
<td>0.02</td>
</tr>
<tr>
<td>% Heavy Metals (as Pb)</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Sp.Gr. @ 60 °F</td>
<td>1.229</td>
</tr>
<tr>
<td>Visible Suspended Matter</td>
<td>None</td>
</tr>
<tr>
<td>Color</td>
<td>10</td>
</tr>
</tbody>
</table>

(APHAL platinum-cobalt units)

The above analysis represents FLUOROSILICIC ACID shipped to:

Consignee: LCI  
Quantity: 1 RAILCAR

[Signature]

Robert L. Ganus  
Laboratory Supervisor / Chief Chemist

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Certified to ANSI/NSF-60  
Max. Use: 6 mg/L
PRODUCT COMPLIANCE CERTIFICATION

We certify that the Fluorosilicic Acid supplied will meet the specifications of AWWA Standard B703-00 and further that it has been certified by NSF to meet ANSI/NSF Standard 60 for the treatment of potable water and has been produced within the continental limits of the United States.

Betty Kendall-Jones
Vice President, Bids & Contracts
4.5 Fort Collins Utilities Drinking Water Consumer Confidence Report, 2001

Fluoridation

A task force is reviewing the practice of providing drinking water with a trace amount of fluoride. A report is due for review by the Colorado Board of Health and the City Council by fall 2000. Those interested can provide comments to the Community Development Director, City of Fort Collins, 200 West LaPorte Avenue, Fort Collins, CO 80521, Attention: Community Development Director. Comments can be submitted by phone, e-mail, or fax.

You’re invited

Consumers are invited to attend meetings of the Fort Collins Utilities Board of Directors. Board meetings are scheduled for the last Thursday of each month at 7:00 p.m. at the Utilities Service Center, 700 West Oak Avenue, Fort Collins, Colorado. For more information, call 473-6969 or visit the Fort Collins Utilities Web site at http://www.fcmgov.org.

Fort Collins Water Surpasses State, Federal Standards

Fort Collins Utilities is pleased to present the 2001 Water Quality Report. It details where our water comes from, what we provide customers with, and other relevant information.

Partnership for Safe Water

In support of our efforts to provide the highest quality drinking water, Fort Collins Utilities is a member of the Partnership for Safe Water. The Partnership is a national non-profit organization that benefits water suppliers that serve 1.7 million people. Our Water Treatment Facility has passed the rigorous “Blue Ribbon” program for drinking water quality.

Where Does Our Water Come From?

The Fort Collins Utilities Water Treatment Facility gets its water from Horsetooth Reservoir and the Cache la Poudre River as sources of water. The Silted Canyon Silver Plume are sources of water. Horsetooth Reservoir is a major source of water.

The water begins in rain and snow high in the Rocky Mountains. Horsetooth Reservoir is an important water resource in the Colorado-Big Thompson Water Project. The Cache la Poudre River originates in Rocky Mountain National Park. As much water is used over the course of the year as through the ground, it is used to supply drinking water needs and for irrigation purposes.

Horsetooth Reservoir

The Horsetooth Reservoir is a major source of water. For more information, visit www.horsetoothreservoir.com.

Fort Collins Water Treatment Process


Protecting Our Watershed

A watershed is the land area that drains into a particular stream, lake, or river. The quality of the water source and the resources in the watershed is affected by the activities on both the land and in the water. Water quality protection involves taking action to minimize the negative effects of those activities.

For more information, contact the Big Thompson Watershed Foundation at 970-482-5930 or visit www.btwfoundation.org.

Fort Collins Utilities Drinking Water Sources

188 Report of the Fort Collins Fluoride Technical Study Group – April 2003
## Water Quality Test Results

During 2001, the Fort Collins Utilities Water Quality Lab conducted nearly 51,000 tests to check for the presence of microorganisms, inorganic elements, and organic substances. The charts below list the test results for the various parameters monitored. The charts are based on data from 1998 forward. This information is available from the Colorado Water Quality Laboratory at Fort Collins Utilities and the technical center of the Colorado Water Quality Program.

### Vulnerable Populations

Some people may be more vulnerable to contaminants in drinking water than the general population. Immuno-compromised persons, such as patients with cancer undergoing chemotherapy, persons who have undergone organ transplants, and persons with HIV infection or other immune deficiencies are at increased risk from conditions related to drinking water. This group should consult their doctor about drinking water recommendations.

### Cryptosporidium & Giardia

Cryptosporidium and Giardia are two microscopic organisms that commonly occur in surface water. The organisms come from animal wastes in the watershed and when irrigated can cause frogs, snails and diatoms. They are removed by a self-cleaning water treatment process. In 2001, Fort Collins Utilities monitored the treated water and the results are shown in the chart below.

### Mecolocallaneous

The chart above shows the effectiveness of the filtration process.

### Information from the EPA

According to the U.S. Environmental Protection Agency (EPA), drinking water, including bottled water, may reasonably be expected to contain at least small amounts of some contaminants. The presence of these contaminants does not necessarily indicate that the water poses a health risk. More information about contaminants and potential health effects can be obtained by calling EPA Safe Drinking Water Hotline at (800) 426-4791. You may also visit www.epa.gov/owq/ctsewater on the Web.

### Unidentified Contaminants

In 2001, Fort Collins Utilities drinking water was tested for the following: arsenic, selenium, ammonia, mercury, lead, chromium, fluoride, manganese, nickel, cadmium, and iron. None of these contaminants were found.

### Preventing Drinking Water Contamination

Have you heard of the term “microbe”? Microbes are bacteria, viruses, fungi, and other microorganisms that are commonly found in water and soil. Fort Collins Utilities has a comprehensive program to prevent these problems and ensure clean drinking water. The utility site is located at 22400 W. 72nd St. At the intersection of 72nd and Wadsworth Bypass, or if you need further assistance, call us at 970-219-6798 or visit our website at www.fcgov.com/water/contaminants.php.

### Appendix 4 – The Potential for Increased Contaminant Levels Due to the Use of Hydrofluorosilic Acid

In Appendix 4, the potential for increased contaminant levels due to the use of Hydrofluorosilic Acid (HFA) is discussed. HFA is a chemical compound that is used to treat drinking water to reduce the concentration of certain contaminants. The use of HFA has been controversial due to concerns about its potential health effects.

### Table: Statistical Contaminants

<table>
<thead>
<tr>
<th>Contaminant</th>
<th>MCL</th>
<th>MOQL</th>
<th>Highest Range</th>
<th>Meet the Standard?</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>alpha-amatoxins</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>Yes</td>
<td>Decrease of interest</td>
</tr>
<tr>
<td>furan</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>Yes</td>
<td>Decrease of interest</td>
</tr>
<tr>
<td>total volatile</td>
<td>24</td>
<td>24</td>
<td>24</td>
<td>Yes</td>
<td>Decrease of interest</td>
</tr>
</tbody>
</table>

### Table: Volatile Organic Contaminants

<table>
<thead>
<tr>
<th>Contaminant</th>
<th>MCL</th>
<th>MOQL</th>
<th>Highest</th>
<th>Range</th>
<th>Meet the Standard?</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>total volatile</td>
<td>24</td>
<td>24</td>
<td>24</td>
<td>Yes</td>
<td>Decrease of drinking water contamination</td>
<td></td>
</tr>
</tbody>
</table>

### Table: Unidentified Contaminants

<table>
<thead>
<tr>
<th>Contaminant</th>
<th>Average Range</th>
<th>Meet the Standard?</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>unknown</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

### Table: Micrococcoid Contaminants

<table>
<thead>
<tr>
<th>Contaminant</th>
<th>MCL</th>
<th>MOQL</th>
<th>Highest</th>
<th>Range</th>
<th>Meet the Standard?</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>total volatile</td>
<td>24</td>
<td>24</td>
<td>24</td>
<td>Yes</td>
<td>Decrease of drinking water contamination</td>
<td></td>
</tr>
</tbody>
</table>

### Table: Information from the EPA

According to the U.S. Environmental Protection Agency (EPA), drinking water, including bottled water, may reasonably be expected to contain at least small amounts of some contaminants. The presence of these contaminants does not necessarily indicate that the water poses a health risk. More information about contaminants and potential health effects can be obtained by calling EPA Safe Drinking Water Hotline at (800) 426-4791. You may also visit www.epa.gov/owq/ctsewater on the Web.

### Table: Cryptosporidium & Giardia

- Cryptosporidium in water is common in surface water and can cause gastrointestinal problems.
- Giardia in water is common in surface water and can cause gastrointestinal problems.

### Table: Unidentified Contaminants

- Unidentified contaminants in water can cause gastrointestinal problems.

### Table: Micrococcoid Contaminants

- Micrococcoid in water is common in surface water and can cause gastrointestinal problems.

### Table: Information from the EPA

- Information from the EPA about contaminants and potential health effects can be obtained by calling EPA Safe Drinking Water Hotline at (800) 426-4791.
- More information is available at www.epa.gov/owq/ctsewater on the Web.
The City of Fort Collins is very proud of the high quality of the water delivered to our customers. The U.S. Environmental Protection Agency regulates many chemicals, which have the potential to occur in Drinking Water. The following table lists those chemicals analyzed by the City Water Quality Laboratory that our customers have indicated they are interested in.

For more information about City of Fort Collins drinking water contact the Water Quality Lab at 221-6691.

<table>
<thead>
<tr>
<th>Constituent</th>
<th>Units</th>
<th>City of Fort Collins</th>
<th>City of Fort Collins</th>
<th>EPA Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Entry to Distribution</td>
<td>Distribution System Average</td>
<td>Contaminant Limit</td>
</tr>
<tr>
<td>Antimony</td>
<td>ug/L</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>6</td>
</tr>
<tr>
<td>Arsenic</td>
<td>ug/L</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>50</td>
</tr>
<tr>
<td>Barium</td>
<td>ug/L</td>
<td>27</td>
<td>23</td>
<td>2000</td>
</tr>
<tr>
<td>Beryllium</td>
<td>ug/L</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>4</td>
</tr>
<tr>
<td>Cadmium</td>
<td>ug/L</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>5</td>
</tr>
<tr>
<td>Chromium</td>
<td>ug/L</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>100</td>
</tr>
<tr>
<td>Copper</td>
<td>ug/L</td>
<td>1.7</td>
<td>7.2</td>
<td>[1300]$^4$</td>
</tr>
<tr>
<td>Fluoride</td>
<td>mg/L</td>
<td>0.92</td>
<td>0.92</td>
<td>4</td>
</tr>
<tr>
<td>Lead</td>
<td>ug/L</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>[15]</td>
</tr>
<tr>
<td>Mercury</td>
<td>ug/L</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>2</td>
</tr>
<tr>
<td>Nitrate as Nitrogen</td>
<td>mg/L</td>
<td>0.11</td>
<td>Not tested</td>
<td>10</td>
</tr>
<tr>
<td>Nitrite as Nitrogen</td>
<td>mg/L</td>
<td>&lt;0.03</td>
<td>Not tested</td>
<td>1</td>
</tr>
<tr>
<td>Selenium</td>
<td>ug/L</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>50</td>
</tr>
<tr>
<td>Thallium</td>
<td>ug/L</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>2</td>
</tr>
<tr>
<td>Total coliforms</td>
<td>cfu/100mL</td>
<td>0</td>
<td>0</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Total Trihalomethane</td>
<td>ug/L</td>
<td>15.3</td>
<td>23.6</td>
<td>80</td>
</tr>
</tbody>
</table>

Secondary Standards - Not standards are enforceable prior to the publication of this report. All standards other than those noted above have not been met.

<table>
<thead>
<tr>
<th>Constituent</th>
<th>Units</th>
<th>City of Fort Collins</th>
<th>City of Fort Collins</th>
<th>EPA Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aluminum</td>
<td>ug/L</td>
<td>62.9</td>
<td>51.7</td>
<td>50</td>
</tr>
<tr>
<td>Chloride</td>
<td>mg/L</td>
<td>2.1</td>
<td>Not tested</td>
<td>250</td>
</tr>
<tr>
<td>Copper</td>
<td>ug/L</td>
<td>7.1</td>
<td>7.2</td>
<td>1000</td>
</tr>
<tr>
<td>Iron</td>
<td>ug/L</td>
<td>18.8</td>
<td>19.6</td>
<td>300</td>
</tr>
<tr>
<td>Manganese</td>
<td>ug/L</td>
<td>2.5</td>
<td>2.5</td>
<td>50</td>
</tr>
<tr>
<td>pH</td>
<td>Units</td>
<td>7.86</td>
<td>7.94</td>
<td>6.5 - 8.5</td>
</tr>
<tr>
<td>Silver</td>
<td>ug/L</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>100</td>
</tr>
<tr>
<td>Sulfate</td>
<td>mg/L</td>
<td>13.8</td>
<td>Not tested</td>
<td>250</td>
</tr>
<tr>
<td>Turbidity</td>
<td>NTU</td>
<td>0.10</td>
<td>0.14</td>
<td>1</td>
</tr>
<tr>
<td>Zinc</td>
<td>ug/L</td>
<td>&lt;100</td>
<td>&lt;100</td>
<td>5000</td>
</tr>
</tbody>
</table>

Chemicals and tests not regulated by EPA - These are tests that provide information on the treatment process and an indication of potential interest such as water hardness.

<table>
<thead>
<tr>
<th>Constituent</th>
<th>Units</th>
<th>City of Fort Collins</th>
<th>City of Fort Collins</th>
<th>EPA Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkalinity</td>
<td>mg/L</td>
<td>37.4</td>
<td>37.7</td>
<td>No Limit</td>
</tr>
<tr>
<td>Ammonia as N</td>
<td>mg/L</td>
<td>&lt;0.01</td>
<td>Not tested</td>
<td>=</td>
</tr>
<tr>
<td>Calcium</td>
<td>mg/L</td>
<td>18.2</td>
<td>18.1</td>
<td>=</td>
</tr>
<tr>
<td>Free Chlorine Residual</td>
<td>mg/L</td>
<td>0.57</td>
<td>0.35</td>
<td>=</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------------</td>
<td>------</td>
<td>------</td>
<td>------</td>
<td>-----</td>
</tr>
<tr>
<td>Hardness as Calcium</td>
<td>mg/L</td>
<td>52.3</td>
<td>51.9</td>
<td>*</td>
</tr>
<tr>
<td>carbonate</td>
<td>grains/gal</td>
<td>3.0</td>
<td>3.0</td>
<td>*</td>
</tr>
<tr>
<td>Magnesium</td>
<td>mg/L</td>
<td>1.8</td>
<td>Not tested</td>
<td>*</td>
</tr>
<tr>
<td>Nickel</td>
<td>ug/L</td>
<td>&lt;3.0</td>
<td>&lt;3.0</td>
<td>*</td>
</tr>
<tr>
<td>Potassium</td>
<td>mg/L</td>
<td>0.7</td>
<td>Not tested</td>
<td>*</td>
</tr>
<tr>
<td>Sodium</td>
<td>mg/L</td>
<td>2.9</td>
<td>3.1</td>
<td>*</td>
</tr>
</tbody>
</table>

Notes:
1 - Units mg/L = milligrams per liter or parts per million
    ug/L = microgram per liter or part per billion
    cfu = colony forming units
    NTU = Nephelometric units
2 - "2001 Average Entry to Distribution" - These are yearly average values for the water leaving the Water Treatment plant as it enters the network of supply pipes that deliver water to our customers.
3 - "2001 Distribution System Average" - These values are yearly averages of test results from five sites around the city. Values do not change significantly through the year.
4 - For Primary standards the maximum contaminant level is the maximum safe level of a chemical that is legally allowed in the water supply.
5 - For Secondary standards the maximum contaminant level is the recommended limit of a chemical that should occur in the water.
6 - Action Limit - Copper and Lead do not have a maximum contaminant level, they have an Action Limit. If the 90th percentile of samples collected for lead and copper exceeds the action limit the water supplier must take action to reduce the level of lead and copper occurring in the distribution system.
<table>
<thead>
<tr>
<th>Parameter</th>
<th>MCL</th>
<th>Poudre River</th>
<th>Horsetooth Reservoir</th>
<th>SS#2</th>
<th>Overland Foods</th>
<th>Service Center</th>
<th>Poudre Valley Hospital</th>
<th>1 Drake</th>
<th>PRPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free Chlorine Residual, mg/L</td>
<td>4</td>
<td>0.52</td>
<td>0.36</td>
<td>0.32</td>
<td>0.30</td>
<td>0.46</td>
<td>0.46</td>
<td>0.27</td>
<td></td>
</tr>
<tr>
<td>Temperature, C</td>
<td></td>
<td>8.9</td>
<td>10.1</td>
<td>9.1</td>
<td>12.4</td>
<td>13.4</td>
<td>12.7</td>
<td>10.0</td>
<td>15.4</td>
</tr>
<tr>
<td>Total coliforms /100mL</td>
<td>&lt;1</td>
<td>119</td>
<td>229</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fecal coliforms /100mL</td>
<td>&lt;1</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fecal strep /100mL</td>
<td>-</td>
<td>128</td>
<td>11</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Heterotrophic plate count /1mL</td>
<td>500</td>
<td>342</td>
<td>128</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>5</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Alkalinity, mg/L as CaCO3</td>
<td>-</td>
<td>25.6</td>
<td>29.2</td>
<td>36.8</td>
<td>37.1</td>
<td>37.2</td>
<td>37.2</td>
<td>36.9</td>
<td>37.9</td>
</tr>
<tr>
<td>Ammonia, mg/L as N</td>
<td>-</td>
<td>0.02</td>
<td>0.03</td>
<td>&lt;0.01</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Calcium, mg/L as CaCO3</td>
<td>-</td>
<td>18.0</td>
<td>24.2</td>
<td>43.0</td>
<td>42.4</td>
<td>43.5</td>
<td>42.5</td>
<td>41.8</td>
<td>39.9</td>
</tr>
<tr>
<td>Chlorate, mg/L</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Chloride, mg/L</td>
<td>-</td>
<td>1.4</td>
<td>0.8</td>
<td>2.1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Chlordt, mg/L</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>0.17</td>
<td>0.17</td>
<td>0.16</td>
<td>0.17</td>
<td>0.17</td>
<td>0.20</td>
</tr>
<tr>
<td>Color, APHA units</td>
<td>(15)</td>
<td>12</td>
<td>35</td>
<td>&lt;2.5</td>
<td>&lt;2.5</td>
<td>&lt;2.5</td>
<td>&lt;2.5</td>
<td>&lt;2.5</td>
<td>&lt;2.5</td>
</tr>
<tr>
<td>Conductance, umhos/cm</td>
<td>-</td>
<td>64</td>
<td>74</td>
<td>119</td>
<td>120</td>
<td>119</td>
<td>119</td>
<td>119</td>
<td>117</td>
</tr>
<tr>
<td>Fluoride, mg/L</td>
<td>(2)</td>
<td>0.15</td>
<td>0.14</td>
<td>0.94</td>
<td>0.94</td>
<td>0.94</td>
<td>0.94</td>
<td>0.94</td>
<td>0.92</td>
</tr>
<tr>
<td>Hardness, mg/L as CaCO3</td>
<td>-</td>
<td>25.2</td>
<td>31.3</td>
<td>49.4</td>
<td>49.2</td>
<td>49.7</td>
<td>49.2</td>
<td>48.7</td>
<td>47.6</td>
</tr>
<tr>
<td>Langler Saturation Index</td>
<td>-</td>
<td>-2.28</td>
<td>-2.04</td>
<td>-1.4</td>
<td>-1.32</td>
<td>-1.24</td>
<td>-1.27</td>
<td>-1.32</td>
<td>-1.12</td>
</tr>
<tr>
<td>Nitrate, mg/L as N</td>
<td>10</td>
<td>0.10</td>
<td>0.10</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Nitrile, mg/L as N</td>
<td>-</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>pH</td>
<td>6.5-8.5</td>
<td>7.6</td>
<td>7.5</td>
<td>7.9</td>
<td>7.9</td>
<td>8.0</td>
<td>7.9</td>
<td>8.1</td>
<td></td>
</tr>
<tr>
<td>Silica, mg/L</td>
<td>-</td>
<td>7.5</td>
<td>4.3</td>
<td>6.8</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sulfate, mg/L</td>
<td>(250)</td>
<td>4.1</td>
<td>4.9</td>
<td>13.1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total Dissolved Solids, mg/L</td>
<td>(500)</td>
<td>45</td>
<td>55</td>
<td>73</td>
<td>72</td>
<td>73</td>
<td>72</td>
<td>69</td>
<td>71</td>
</tr>
<tr>
<td>Total Kjeldahl Nitrogen, mg/L as N</td>
<td>-</td>
<td>0.11</td>
<td>0.24</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total Phosphorus, mg/L</td>
<td>-</td>
<td>0.01</td>
<td>0.02</td>
<td>0.01</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Turbidity, NTU</td>
<td>1</td>
<td>0.5</td>
<td>9.0</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>Aluminum, ug/L</td>
<td>(50-200)</td>
<td>48</td>
<td>416</td>
<td>41</td>
<td>50</td>
<td>43</td>
<td>46</td>
<td>47</td>
<td>44</td>
</tr>
<tr>
<td>Antimony, ug/L</td>
<td>6</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
</tr>
<tr>
<td>Arsenic, ug/L</td>
<td>10</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
</tr>
<tr>
<td>Barium, ug/L</td>
<td>2000</td>
<td>21.2</td>
<td>31.8</td>
<td>21</td>
<td>22.9</td>
<td>23.0</td>
<td>19.6</td>
<td>33.9</td>
<td>24.8</td>
</tr>
<tr>
<td>Beryllium, ug/L</td>
<td>4</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Cadmium, ug/L</td>
<td>5</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Chromium, ug/L</td>
<td>100</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Copper, ug/L</td>
<td>(1300)/1000</td>
<td>1.2</td>
<td>4.7</td>
<td>1.6</td>
<td>6.2</td>
<td>8.9</td>
<td>7.0</td>
<td>4.7</td>
<td>8.2</td>
</tr>
<tr>
<td>Iron, ug/L</td>
<td>(300)</td>
<td>120</td>
<td>442</td>
<td>19</td>
<td>16</td>
<td>19</td>
<td>18</td>
<td>15</td>
<td>27</td>
</tr>
<tr>
<td>Lead, ug/L</td>
<td>[15]</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>Magnesium, mg/L</td>
<td>-</td>
<td>1.6</td>
<td>1.7</td>
<td>1.7</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Manganese, ug/L</td>
<td>(50)</td>
<td>5.4</td>
<td>22.1</td>
<td>0.8</td>
<td>0.7</td>
<td>0.9</td>
<td>1.0</td>
<td>0.8</td>
<td>1.0</td>
</tr>
<tr>
<td>Mercury, ug/L</td>
<td>2</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>Nickel, ug/L</td>
<td>100</td>
<td>&lt;3.0</td>
<td>&lt;3.0</td>
<td>&lt;3.0</td>
<td>&lt;3.0</td>
<td>&lt;3.0</td>
<td>&lt;3.0</td>
<td>&lt;3.0</td>
<td>&lt;3.0</td>
</tr>
<tr>
<td>Selenium, ug/L</td>
<td>50</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
</tr>
<tr>
<td>Silver, ug/L</td>
<td>(100)</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Sodium, mg/L</td>
<td>(20)</td>
<td>2.8</td>
<td>2.8</td>
<td>2.9</td>
<td>2.9</td>
<td>2.9</td>
<td>3.0</td>
<td>3.2</td>
<td>3.8</td>
</tr>
<tr>
<td>Thallium, ug/L</td>
<td>2</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>Zinc, ug/L</td>
<td>(5000)</td>
<td>&lt;100</td>
<td>&lt;100</td>
<td>&lt;100</td>
<td>&lt;100</td>
<td>&lt;100</td>
<td>&lt;100</td>
<td>&lt;100</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Total Organic Carbon, mg/L</td>
<td>-</td>
<td>2.5</td>
<td>3.0</td>
<td>1.4</td>
<td>1.3</td>
<td>1.2</td>
<td>1.1</td>
<td>1.3</td>
<td>1.4</td>
</tr>
<tr>
<td>Total Trihalomethane, ug/L</td>
<td>80</td>
<td>&lt;0.4</td>
<td>&lt;0.4</td>
<td>16.9</td>
<td>25.6</td>
<td>28.1</td>
<td>26.4</td>
<td>22.1</td>
<td>28.1</td>
</tr>
</tbody>
</table>

**Notes:**
- mg/L = milligram per liter or part per million
- ug/L = microgram per liter or part per billion
- Overland Foods, N. Hwy 287, Laporte CO
- Poudre River = Cache La Poudre River Raw Water at Plant
- Horsetooth Reservoir = Horsetooth Reservoir Raw Water at Plant
- SS#2 = Sample Station 2, Official dist. System entry point
- PRPA = Platte River Power Authority Office
- MCL = Maximum Contaminant Level () = Secondary level (esthetic) [ ] = 90th %tile action level <= less than
Iron (Fe\textsuperscript{2+}) levels for both source waters, FCU finished drinking water, Poudre Valley Hospital (PVH), and the Secondary Maximum Contaminate Level (SMCL).

Copper (Cu\textsuperscript{2+}) levels for both source waters, FCU finished drinking water, Poudre Valley Hospital (PVH), and the Secondary Maximum Contaminate Level (SMCL) are shown in Figure 4. Slight increases in Cu levels after the water leaves the WTF are typical. Cu will tend to be elevated due to the copper service lines in place throughout the system.
Figure 5

Manganese (Mn$^{++}$) levels for both source waters, FCU finished drinking water, Poudre Valley Hospital, and the Secondary Maximum Contaminate Level (SMCL).

Figure 6

Zinc (Zn) levels for both source waters, FCU finished drinking water, Poudre Valley Hospital, and the Secondary Maximum Contaminate Level (SMCL).
Cadmium (Cd) levels for both source waters, FCU finished drinking water, Poudre Valley Hospital (PVH), and the Maximum Contaminant Level (MCL).

Molybdenum (Mb) and Nickel (Ni) levels for both source waters, FCU finished drinking water, and Poudre Valley Hospital are shown in Figure 8. There are no SMCL or MCL levels for Mb or Ni.
4.8 Arsenic Concentration in Finished Water
Contributed by Fluorosilicic Acid ($H_2SiF_6$) Feed at the FCWTF

- **HFS = Fluorosilicic Acid**
  - **Commercial Purity = 24.4 %**
  - **Specific Gravity = 1.234 @ 25%**

- **Amount of Arsenic in HFS: Range of 29 mg/L to 61 mg/L**
  The Fort Collins Water Pollution Control Lab analyzed a sample of the HFS used by the Water Treatment Facility. They measured an arsenic concentration of 29 mg/L in the sample. However, analytical results provided by PENCCO, Inc. (HFS supplier) indicated an arsenic concentration in the HFS of 61 mg/L.

- **Dilution Factor: Range of 250,000 to 300,000**
  The arsenic present in the HFS will be diluted when it is fed to the finished water. There are several different ways to arrive at the dilution factor (and arrive at the same results). Here we will use actual plant data. HFS is fed at a certain gallons per minute (gpm) rate such that about 0.75 to 0.90 mg/L of fluoride is added to the finished water. When HFS is fed to the finished water, the arsenic in the HFS is diluted by a factor equal to the ratio of the total flow of finished water to the HFS feed rate:

  \[
  \text{Dilution Factor} = \frac{\text{Finished Water flow in gpm}}{\text{HFS feed in gpm}}
  \]

  The following table lists Dilution Factors calculated from actual plant data.

<table>
<thead>
<tr>
<th>Date</th>
<th>HFS Feed (gpm)</th>
<th>Total Finished Water (million gallons/day)</th>
<th>Total Finished Water (gpm)</th>
<th>Dilution Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-20-02</td>
<td>.046</td>
<td>19.80</td>
<td>13,750</td>
<td>298,900</td>
</tr>
<tr>
<td>6-20-02</td>
<td>.091</td>
<td>35.06</td>
<td>24,347</td>
<td>267,500</td>
</tr>
<tr>
<td>7-20-02</td>
<td>.152</td>
<td>58.88</td>
<td>40,889</td>
<td>269,000</td>
</tr>
<tr>
<td>8-20-02</td>
<td>.100</td>
<td>38.00</td>
<td>26,389</td>
<td>263,900</td>
</tr>
<tr>
<td>10-20-02</td>
<td>.060</td>
<td>24.88</td>
<td>17,278</td>
<td>288,000</td>
</tr>
<tr>
<td>12-20-02</td>
<td>.043</td>
<td>18.26</td>
<td>12,681</td>
<td>294,900</td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td></td>
<td></td>
<td>280,400</td>
</tr>
</tbody>
</table>

The above data points are fairly representative of normal conditions at the FCWTF. The average dilution factor from the data listed above is 280,400. The normal range is likely 250,000 to 300,000. Note that the lower the dilution factor, the higher the arsenic concentration contributed by HFS feed.

- **Arsenic Concentration Contributed by HFS Feed**
  \[
  \text{Arsenic Contribution from HFS} = \frac{\text{Amount of Arsenic in HFS}}{\text{Dilution Factor}}
  \]

  The range of arsenic concentrations in the HFS and the range of dilution factors presented above will be used to calculate a range of arsenic concentrations contributed by HFS feed.

  Low Value:
  \[
  \text{Arsenic Contribution from HFS} = \frac{29 \text{ mg/L}}{300,000} = 0.000097 \text{ mg/L} = 0.10 \text{ ug/L}
  \]
High Value (most conservative):

\[
\text{Arsenic Contribution from HFS} = \frac{(\text{Amount of Arsenic in HFS})}{(\text{Dilution Factor})} \\
= \frac{61 \text{ mg/L}}{250,000} \\
= 0.00024 \text{ mg/L} \\
= 0.24 \text{ ug/L}
\]

The calculated range of arsenic concentrations in the finished water contributed by HFS feed is 0.10 to 0.24 ug/L. The analytical detection limit for arsenic is 2 ug/L, so the amount added by the HFS would not be detected.
4.9 Peer Reviews of the Masters and Coplan Report

The University of Kansas

Department of Civil and Environmental Engineering

January 15, 2000

Mr. Walter J. O’Brien
Black & Veatch
P.O. Box 8405
Kansas City, MO 64114

Dear Walt,

I apologize for taking so long to respond to your inquiry concerning the validity of the paper by Masters and Coplan on silicofluoride use and lead toxicity. My desk was buried in an "avalanche" last month, and I am just now digging out a bit before classes start again next week.

My initial reaction upon reading the paper was that it was scientifically weak, as indicated in the statement by CDC, which I assume you and your clients found at least somewhat reassuring. However, before providing a more detailed response, I wanted to examine at least some of the supporting information cited in the paper.

I do not have access to the data base used by the authors, and I have neither the time nor the inclination to attempt to reproduce the results of their statistical analyses. I decided to begin by assuming that the authors had begun with a reasonably large and valid data base, that they had correctly applied the various statistical tools cited in their paper, and that they had indeed found a positive correlation between silicofluoride usage in drinking water treatment and lead levels in children's blood. I then posed the question: Assuming that the reported correlation (association) is genuine (i.e., that objective individuals skilled in statistics could obtain the same result), does this correlation reveal a causal relationship, as the authors believe, or is it simply an artifact?

To answer this question, I followed two lines of reasoning. First, I considered whether more plausible explanations for such a correlation had been adequately ruled out. Second, I considered whether there was any plausible mechanism whereby silicofluoride usage could increase the solubility of lead in drinking water or its "uptake" by children. It is important to note that it is impossible to prove that silicofluoride has no effect whatsoever on blood lead levels, since one cannot "prove a negative," i.e., it would require that an infinite number of possible effects all be proven to be infinitesimal. Thus, one must examine the available evidence and exercise reason and judgement.
It is well known that leaded gasoline, where used, accounts for the great majority of the lead found in the blood of children. As one example, a recently published assessment (Environmental Science & Technology, Vol. 33, No. 22, p. 3942, 1999) of 19 lead studies on six continents found a median correlation coefficient of 0.94 for the correlation between the use of lead in gasoline and blood lead levels in the population. This study also found that, as the lead levels in gasoline were reduced to zero, the blood lead levels in the population converged at about 3 µg/dL (micrograms per deciliter), well below the CDC recommended maximum of 10 µg/dL.

Given the overwhelming influence of the use of leaded gasoline on blood lead levels, it is pointless to examine another cause of elevated blood lead levels without controlling for the effect of leaded gasoline. Since the authors evidently ignored this factor, their results are essentially meaningless. Even a small difference in exposure to lead from gasoline in the various subsets of the populations studied could account for the observed differences in blood levels. Of course, this does not prove that the observed correlation is an artifact; but until the effects of leaded gasoline are accounted for, differences in the use of leaded gasoline must be considered as the most likely cause of the observed differences in blood lead levels.

Even if the observed differences in blood lead levels are in fact due to differences in the use of leaded gasoline, one might still question why such differences would be correlated with the use of silicofluorides. The authors do not provide sufficient information to answer this question, and the explanations they offer certainly appear invalid, as discussed below. However, there is one very plausible explanation — both fluoridation and the use of silicofluorides (rather than sodium fluoride) are associated with water system size, which in turn is associated with lead pollution from the use of leaded gasoline, as well as with crime, racial differences in blood lead levels, etc.

The authors claim to have controlled for the effect of population density, but it is not clear whether their efforts to do so were effective or if "population density" differences adequately accounted for differences in lead pollution associated with the use of leaded gasoline. Fluoride is used far more frequently in larger communities than in smaller communities. This is supported by the authors' own findings: 1) that the 213 communities out of a total of 350 for which good data sets were available included all but one "fluoridated town" and virtually all communities having a population over 3,000; and 2) that "all large cities in Georgia use silicofluorides." The authors compared 30 communities using fluoride with 30 that do not; but, while the total population was the same for each group, it is not clear that the size distribution of the towns was the same, that outliers were considered, or that both groups of communities experienced equal levels of lead pollution associated with the use of leaded gasoline.

Lead pollution associated with the use of leaded gasoline also appears to have been ignored in comparing communities using sodium fluoride with those using silicofluorides. The use of sodium fluoride tends to be favored in smaller and more rural water systems (because its
solubility is relatively independent of temperature, such that a feed solution of constant concentration can be prepared in a dissolution tank), whereas silicofluorides tend to be favored in larger systems due to their lower cost. Thus, one would expect to find a correlation between the use of silicofluorides and proximity to higher concentrations of lead from gasoline, as well as with crime, racial differences in blood lead levels, etc.

It is unfortunate that the authors did not consider and examine possible artifacts associated with the use of leaded gasoline before jumping to conclusions, accepting their hypothesis (which may reflect an anti-fluoridation bias in their research), and alarming the public. It is because scientists, being human, are prone to jump to conclusions that responsible scientists make a habit of submitting their work for peer review by recognized experts. However, the peer review process is not perfect and the quality of peer review varies greatly among journals. I am not familiar with the quality of the peer review process associated with the journal in which this article was published; but it appears to have been deficient.

Even if leaded gasoline use had been (or were to be) ruled out as a cause of the observed correlation, a thorough investigator would still want to know whether there was a plausible explanation for the correlation, and would make at least some attempt to confirm this explanation, before jumping to the conclusion that the relationship was causal. The authors did attempt to find plausible explanations for the correlation they observed. Unfortunately, they evidently lacked sufficient expertise in chemistry to realize that their explanations, some of which appear to be derived from the propaganda of fluoridation opponents, are not plausible. Their explanations, and the reasons they are not plausible, are as follows:

1) The authors contend that silicofluorides do not completely dissociate under the conditions of drinking water treatment, "leaving toxic silicofluorides in the water stream." This is based on a gross misinterpretation of work cited by the authors. For example, Rees and Hudleston (cited in reference 15) did indeed find that there was an observable delay in the reaction of Na₂SiF₆ with base, caused by the slow decomposition of the SiF₆⁻² to SiF₄ and F⁻. However, they found the first-order rate constant for this reaction to be 0.0163 sec⁻¹, such that the reaction is 99.994% complete in 10 minutes, long before water treated with silicofluorides would reach a consumer. This reaction was of interest to Rees and Hudleston not because of any concerns associated with fluoridation but because it was a mono-molecular reaction that was slow enough to be observed and that could be studied colorimetrically at a time (ca. 1936) when few good instruments were available. The hydration of carbon dioxide can be observed in similar fashion, but the authors expressed no concern that hydration of carbon dioxide or other "slow" reactions associated with drinking water treatment might influence lead solubility.

Rees and Hudleston also demonstrated that SiF₆⁻² decomposes to SiF₄ and quantified the equilibrium relationship between these two species. Their data show that, for a dilute solution containing 1 mg/L of fluoride, the ratio of SiF₄ to SiF₆⁻² at 20 °C at
equilibrium would be 361:1; but they also state, in the first paragraph of their paper, that the hydrolysis of SiF₄ to silicate and fluoride ion is relatively rapid compared to the decomposition of SiF₆⁻² to SiF₄. Thus, the work cited indicates that silicofluorides dissociate almost completely and very rapidly relative to the time scale associated with drinking water treatment.

Another aspect of this "mechanism" the authors failed to consider is that an average surface water contains about 20 mg/L of silica and a few tenths of a mg/L of fluoride. Some water sources, especially certain ground waters, contain much higher levels of silica. Since complex formation is an equilibrium reaction, any "silicofluoride complexes" found in water will be found at virtually identical levels regardless of whether the water is unfluoridated or treated with a small amount of either sodium fluoride or a silicofluoride.

2) The authors speculate that chemical reactions associated with silicofluorides will produce acid after the water leaves the treatment plant, thereby lowering the pH of the water and increasing lead solubility. They fail to consider several important points. First, the reactions they refer to are essentially complete long before the water leaves the plant, as discussed above. Second, such reactions are in fact taken into account by water treatment plant operators as they adjust the pH of the treated water prior to distribution, although such reactions are typically negligible in relation to others affecting pH. Third, well treated waters are buffered against significant changes in pH, such that the reactions cited by the authors would have only a negligible effect on pH. Fourth, water utilities monitor the levels of lead (and other chemicals) in drinking water and are required by law to keep lead levels relatively low; and they adjust the pH and alkalinity of the treated water both to maintain low lead levels and to minimize corrosion of their distribution systems. Fluoridation does not inadvertently lower the pH of treated drinking water.

3) The authors speculate that traces of "undissociated fluorinated silica residues may complex dissolved lead and facilitate its transport from the gastrointestinal tract to the blood stream." Although it is true that fluoride forms complexes with lead and that silicates may also form complexes with lead (although no evidence of this is presented by the authors), there are once again several important points the authors have failed to consider. First, as noted above, silica is naturally present in water at levels typically much higher than those associated with water fluoridation, so use of silicofluorides would have no significant effect on silica levels or on lead-silica complexes.

Second, much of the lead present in drinking water is already present in complexed form. Lead forms complexes with hydroxide, carbonate, sulfate, and other ions, and with naturally occurring organic matter; and fluoride and silica must compete with these other substances (referred to as ligands) for the available lead ions. The authors present no
evidence that fluoride or silica compete effectively with other ligands present in drinking water.

Third, at the pH value of stomach contents, about 1.8, both fluoride and silica will be present almost entirely in undissociated form, i.e., as hydrofluoric acid and silicic acid, neither of which forms complexes with lead.

I conclude that the correlation found by the authors is simply an artifact, most likely associated with the use of leaded gasoline, and does not reflect a causal relationship. I believe that a more careful examination of the data will bear this out. I also find the authors' arguments as to why the use of silicofluorides might cause an increase in blood lead levels to be invalid. They have identified no plausible mechanism that could account for a causal relationship between use of silicofluorides and blood lead levels. Accordingly, I strongly recommend that this work be entirely disregarded by anyone making a decision regarding water fluoridation or the use of a particular chemical for treating drinking water.

Please feel free to contact me again if you have any questions regarding these comments.

Best regards,

[Signature]

Stephen J. Randtke
Professor
Dear Dr. Urbansky:

I have examined the paper from International Journal of Environmental Studies, "Water Treatment with Silicofluorides and Lead Toxicity," paying particular attention to the use of equilibrium and kinetic data.

My notes are being sent as an attachment in Microsoft Word 4, so as to make the chemical and mathematical equations more intelligible.

I hope this will be helpful to you.

James N. Butler
Gordon McKay Professor of Applied Chemistry, Emeritus
Harvard University

The questions for consideration mostly derive from p. 437 parag 2 and the footnotes thereto.

"Use of silicofluorides is suspect for several reasons (Footnote 14: According to the to Merck index 10th ed 1983) H₂SiF₆ 1-2% solution used for sterilizing equipment in brewing and bottling, etc. Caution: severe corrosive effect on skin, mucous membranes. Na₂SiF₆ used for insect and rodent poisons, mothproofing of woolens." These comments reflect the toxicity of concentrated silicofluoride (10,000 ppm) which is not comparable with that of typical municipal waters (1 ppm)


As the calculations show, the ratio of silicofluoride to silicic acid at equilibrium is of the order of 10⁻²⁰ to 10⁻²⁸. That is certainly "complete". How fast this reaction occurs may be known, but it is not mentioned in any of the references I have at hand (most of my books and files are still packed away).

"Consequently there is a strong likelihood that additional F⁻ and H₂O⁺ will be liberated into the water after it has left the water treatment facilities, with attendant chemical reactions that increase acidity (lower pH) beyond the expectations established by current practice. Acid water in turn can extract lead from pipes, solder, and fixtures made of lead-bearing alloys, and increase the bioavailability of lead from water (Footnote 16: Reference is to Consumer Reports, 1993)"

In the notes below, the acidity released by dissociation of 1 ppm fluoride from silicofluoride is estimated to be of the order of 3x10⁻⁵ mole/L, and hence would neutralize only about 3% of the alkalinity of typical municipal water. Consumer Reports is not exactly a reliable source of scientific data.

"In addition, traces of undissociated fluorinated silica residues may complex dissolved lead and facilitate its transport from the gastrointestinal tract to the blood stream (footnote 17 - Reference to Waldcott et al "Fluoridation: the Great Dilemma"(1997))"

I have seen no data on the complexation of silicofluoride with any metals. My guess is that such complexes would be weak.
Equilibrium Calculations

The reaction under consideration is

\[ \text{H}_2\text{SiF}_6 + 6 \text{ H}_2\text{O} = \text{Si(OH)}_4 + 6 \text{ F}^- + 6 \text{ H}^+ \]

or if the salt Na\(_2\)SiF\(_6\) is used,

\[ \text{SiF}_6^{2-} + 4 \text{ H}_2\text{O} = \text{Si(OH)}_4 + 6 \text{ F}^- + 4 \text{ H}^+ \]

Typical concentrations (p.439) are 0.8 to 1.2 ppm (mg F per L). This fluoride concentration is 5.23x10\(^{-5}\) mole/L. The corresponding concentration of SiF\(_6^{2-}\) to give this fluoride concentration when fully dissociated is \((1/6)*(5.23x10^{-5}) = 0.87x10^{-5}\) mole/L. The acidity released in that reaction is \((4/6)*(5.23x10^{-5}) = 3.48 x10^{-5}\). This is only about 3% of the typical alkalinity of municipal water (100 ppm CaCO\(_3\) or 10\(^{-3}\) mole/L), and hence the effect on pH of acid produced by SiF\(_6^{2-}\) dissociation is quite small.

Hence the arguments regarding corrosion etc would apply only if the water had extremely low alkalinity (<10 ppm CaCO\(_3\)).

Is SiF\(_6\) only partially dissociated? The equilibrium constant for the reaction

\[ \text{SiF}_6^{2-} = \text{Si(OH)}_4 + 4 \text{ H}^+ + 6 \text{ F}^- \]

\[ \log K = 30.10 \text{ at 25 deg, } I = 0 \]

can be found in Smith and Martell, Stability Constants, Vol. 6, p 455. The references for this system are 788B, 808, 848C, and 848G. The actual references can be found at the back of that volume, and I presume can be obtained by interlibrary loan or some other mechanism - but I have only a copy of page 455 here.

The equilibrium expression is

\[ [\text{SiF}_6^{2-}] = 10^{30.10} \times [\text{Si(OH)}_4][\text{H}^+]^4[\text{F}^-]^6 \]

At pH = 8 and [F\(^-\)] = 5.23x10\(^{-5}\), the degree of dissociation is

\[ [\text{SiF}_6^{2-}]/[\text{Si(OH)}_4] = 2.58x10^{-28}. \]

At pH = 6, this ratio is 2.58x10\(^{-20}\). If the equilibrium constants for the intermediate steps (SiF\(_6^{2-}\) to SiF\(_5^-\) etc) were known, a more complete equilibrium model could be made.

Even so, at equilibrium and at the normal pH of municipal water, [SiF\(_6^{2-}\)] appears to be fully dissociated.

Additional work to be done:

Look up the references in Footnote 15 and see if there is any information on kinetics of the SiF\(_6^{2-}\) dissociation reaction. In addition, look up the references cited in Smith and Martell
and see if there is any information on kinetics. Finally, search the last 20 years of Chemical Abstracts for new information on equilibrium and kinetics of this system.

You will have to ask someone in your office to do this library work, since I am at the moment far away from the Harvard Libraries.


(18) US Department of Health & Human Services, Centers for Disease Control and Prevention, Division of Oral Health G.; (Thomas Reeves); “WATER FLUORIDATION a manual for water plant operators”; Atlanta, GA; June 1994


(20) Sargent JD, et al; “Childhood Lead Poisoning in Massachusetts Communities: Its Association with Sociodemographic and housing Characteristics”; Am J. Pub Health; V 84 (4), pp 528-534; 1995


(22) Sargent JD, and Dalton, MA; “Rethinking the Threshold for an Abnormal Capillary Blood Lead Screening Test”; Arch Pediatr Adolesc Med V 150 (10) pp 1084-1088; 1996

(23) Masters RD and Coplan MI; “Water Treatment with Silicofluorides and Lead Toxicity”; Intern. J. Environ Studies; Vol. 56, pp 435-499; 1999

(24) McClure FJ; “Availability of Fluorine in Sodium Fluoride vs. Sodium Fluosilicate”; Public Health Reports vol 65 No 37; September 15, 1950. pp 1175-1186

(25) Kick CH et al; “Fluorine in Animal Nutrition”; Bulletin 558, Ohio Agricultural Experiment Station; Wooster, Ohio; November 1935; pp1-77

Re: Water treatment with Silicofluorides and lead toxicity and other documents
Reviewed by Eugenio Beltrán, DMD, MPH, MS, DrPH

This reviewer is not knowledgeable in the areas of toxicity or behavioral aspects of crime/drug use so my comments on those areas will be included only as needed to evaluate the epidemiological aspects and scientific rigor of these documents.

I have received the following documents for review:
"Water treatment with silicofluorides and lead toxicity" 15 pp
"Silicofluorides, lead toxicity and behavior" 2pp + 2 figures
"Drug usage and silicofluoride treated water, crime in 24 cities"
"EPA grant award lead, water fluoridation, and toxicity" press release from Dartmouth College
"Chemical in fluoridated water may cause violent behavior, cocaine use, scholar says" press release from The Chronicle of Higher Education.

With the exception of the first document, obviously a pre-publication manuscript, I have not done a detailed analysis of each document. I prefer to provide an overall evaluation of the scientific plausibility and rigor used by the authors. However, a full evaluation of the manuscript "Water treatment with silicofluorides and lead toxicity" (hereinafter labeled as "manuscript") is included with this document.

First, I would like to conclude that the authors have little experience in the biological science writing. It is true that the manuscript includes the different sections any research report should have, but important pieces of information in their text, tables and figure are not included. The uninform ed reader, therefore, gets the impression that whatever is said in the text is fully backed by hard data. Furthermore, the few acknowledgments of potential biases and limitations of their conclusions are included as endnotes (following the format of Science). Tables are not well designed, the titles are not clear, they are not self-supported, and even though statistical figures are included there is no enough information to match the statistic with the actual result in the table. Clearly, the manuscript —and the other two documents— will not pass a peer review process by a scientist, at least those in the statistical and epidemiological area. Furthermore, a major support for the hypothesis linking silicofluorides and lead absorption comes from the same authors, reference No. 7 in the manuscript, a book, not a peer reviewed article.

Second, the authors, through the entire documents —including the two press releases— showed a preconceived bias that fluoride, and especially silicofluorides, are the cause of high lead levels in the individual and ergo, use of cocaine and tendency to violent behavior. It is difficult to understand how any unbiased reviewer of their data can conclude that the culprit of having higher plasmatic lead levels (measured by capillary blood samples) is silicofluorides and not other environmental sources. As Table 3 shows: the main factor was living in houses built before 1940.
September 14, 2000

Dr. Edward T. Urbansky  
U.S. Environmental Protection Agency  
National Risk Management Research Laboratory (MS-681)  
26 West Martin Luther King Drive  
Cincinnati, OH 45268

Dear Ed:

I have reviewed the paper “Water Treatment with Silicofluorides and Lead Toxicity” by Masters and Coplan along with the supporting material in the form of a letter from Coplan to you. This paper states that Pb in blood goes from a level of 2.02 µg/dL to 2.66 – 2.78 µg/dL in the paired communities, attributable to the use of fluorosilicate to fluoridate the water. In this case we are comparing unfluoridated to fluoridated water. I am not a trained statistician, but I have a hard time believing that this correlation is meaningful. However, for the sake of argument we can assume that it is meaningful, and we can go through the details of the known chemistry to see if the indicated level of fluoride is sufficient to interact with the lead.

The paper and the supplemental material provided by Coplan indicate a poor understanding of chemical equilibrium and kinetics by the authors. The chemistry of the SiF$_6^{2-}$ species is quite well understood despite the assertions of ambiguity by the authors (work of Busey, Schwarz, and Mesmer included). This anion completely hydrolyzes to F$^-$ anion on the time scale of delivery of water to a household (assumed to be > 1 hr). Definitive work indicates the species equilibrate on the time scale of a titration. At the pH of drinking water, the only silicon containing species indicated are Si(OH)$_4$ and SiF$_6^{2-}$. The concentration of fluoride ion in drinking water is adjusted to be about 1 ppm (2 × 10$^{-5}$ M). At this fluoride concentration there will be no SiF$_6^{2-}$ ion present in water. In order for the fluoride to make the lead more readily absorbed by the body, it has to react with Pb(II), the oxidation state of lead expected to be present in water and in the body. Table I of the paper shows a very small change in the concentration of Pb in water with fluoridation of the water (21 to 30 ppb, ≈ 1 × 10$^{-7}$ M). The species of lead in water have been discussed by Baes and Mesmer in their book (included). The equilibrium constants for complexation of Pb(II) by Cl$^-$, F$^-$, HCO$_3^-$, and the other potential complexing agents in water or blood are documented in Special Publication No 17 (The Chemical Society). We can look at the known equilibrium constants for complexation, and then calculate the fraction of Pb(II) that could possibly be complexed with F$^-$. The log of the first equilibrium constant for complexation of Pb(II) by fluoride varies with the medium (going down with increasing ionic strength) and it is approximately 0.5. To make the analysis easier we will assume log K is 1. PbF$_2$ and the mixed solid Pb(F)(Cl) are fairly insoluble with log solubility product constants of -7.4 and -8.6 respectively. Since the concentration of F$^-$ is a great deal larger than the Pb(II) concentration in water, we can calculate the fraction complexed by a single fluoride ion from the simple relationships

\[
Pb_T = Pb(II) + PbF^-
\]
\[
Pb(\text{II}) + F^- \leftrightarrow PbF^+ \quad K = 10
\]

The fraction of the lead complexed by F\(^-\), \(f\), is the ratio \([PbF^+] / Pb\(_7\) and it can be shown to be given by

\[
f = K [F^-] / (1 + K [F^-])
\]

From the anticipated value of \(K\) and the fluoride concentration, the computed fraction complexed in the drinking water is <0.02%. The concentration of fluoride in the blood is much less than that in the water. Furthermore the concentration of Cl\(^-\) in the blood is substantial and the complexation constant for chloride is about the same as for fluoride. From a consideration of the known chemical equilibrium, there is no evidence to support the assertion that the presence of F\(^-\) (or SiF\(_6^2\)\(^-\)) has any influence on the level of Pb in blood (or drinking water).

Please feel free to send this review to the authors of the paper.

Sincerely yours,

\[\underline{\text{Gilbert M. Brown}}\]
July 13, 2000

Dr. Edward T. Urbansky
Water Supply and Water Resources Division
Treatment Technology Evaluation Branch
United States Environmental Protection Agency
National Risk Management Research Laboratory
Cincinnati, Ohio 45268

Dear Dr. Urbansky:

I have received and read the copy of the manuscript "Water Treatment with Silicofluorides and Lead Toxicity" by Roger D. Masters and Myron J. Coplan which you sent this week. If the conclusion drawn in this manuscript, that there is a significant correlation between the use of certain fluoridating agents in water and the incidence of violent crime, is valid, we truly have a major health problem in this nation. Consequently, I have given considerable thought to the methodology used in gathering and analyzing the data.

I do not choose to comment on the statistical analysis. Although I have limited experience with statistics, this is clearly a matter for an expert in data analysis and epidemiology. You probably have already showed the manuscript to such a person. Instead, my comments will be directed toward the chemical analyses concerning the acidity of water leaving the water treatment facilities, the effect of this acidity on increasing the lead content of the water, and the determination of levels of lead in the blood of the children who were examined.

The main problem that I see with this manuscript is that there has been only one set of data obtained, the levels of lead in the blood of children, and the links between these measurements and the fluoridation of water at chemical treatment plants are inferred from other data not determined in this study. My overall recommendation would be to verify claims made in the manuscript by additional measurements. The following experiments might be appropriate:

1. Determine that the high lead levels actually come from the drinking water. This could be done by measuring the lead levels and acidity of tap water in the homes of the children in whom blood levels were measured.
2. If the lead levels in tap water are high, determine if the lead comes from plumbing in the homes of the children. This could be done simply by asking about the plumbing.
3. In the likely case that the lead comes from the action of acidic water on lead pipes in the homes, determine the source of the acid. Is it naturally in the water or does it come from the added fluorides? I don’t know about Georgia, but water in metropolitan Boston comes from a series of reservoirs that have dissolved carbon dioxide and possibly acid from acid rain. Thus, it
would be acidic if not neutralized. It would be desirable to know the acidity of water coming into the treatment plants and the acidity of water leaving them after various treatments including fluoridation. (Is this data already available?) The amounts of fluoridating agents is probably quite small. Nevertheless, their effects on acidity should be measured. A comparison between the acidity of water treated with fluosilicic acid, which should add the most acid, and sodium fluoride, which should add none, would be instructive. If acidity of water leaving the treatment plants is not available, such measurements should be made. A waiting period of 20 minutes would ensure that all fluosilicic acid of sodium silicofluoride was hydrolyzed, if the fluoride is added as the last process before the water is sent out of the plants. It is important to compare these acidity values with those of water entering and leaving the treatment plants which do not fluoridate the water. It also is important to know if there are any other differences in water treatments that might affect the acidity of the water.

There may be valid alternatives to the specific experiments and data gathering described above, but the main issue is the approach. What the authors need to do is pin down unequivocally exactly what is responsible for the increased lead in the children's blood. The present methodology leaves too many questions unanswered.

I hope that this review may be of some help to you.

Sincerely yours,

William A. Remers
Professor Emeritus
July 31, 2000

Dr. Edward T. Urbansky
Research Chemist
Water Supply and Water Resources Division
Treatment Technology Evaluation Branch
United States Environmental Protection Agency
National Risk Management Research Laboratory
Cincinnati, Ohio 45268


Dear Dr. Urbansky:

Thank you for allowing me the opportunity to review and comment on the above referenced manuscript. As you requested, I have focused my comments on potential interactions between lead and fluorosilicates in drinking water that could enhance the bioavailability of lead. In my opinion the manuscript does not present appropriate data to support the conclusions put forth by the authors.

The premise of this article by Masters and Coplan appears to be captured in these statements in the Introduction. “...there is a strong likelihood that additional F- and H3O+ will be liberated into the water after it has left the water treatment facilities, with attendant chemical reactions that increase water acidity (lower pH) beyond the expectations established by current practice. Acid water in turn can extract lead from pipes, solder and fixtures made of lead-bearing alloys, and increase the bioavailability of lead from water at the tap. In addition, traces of undissociated fluorinated silica residues may complex dissolved lead and facilitate its transport from the gastrointestinal tract to the blood stream.”

**Increase in water acidity.** It is well accepted that different water treatment methods can influence the pH of water in the distribution system. However, the authors do not
provide any comparative pH measurements for tap water in the communities in their study to support their contention that the pH of tap water in the communities using fluorosilicates is lower than in communities that do not use this method of fluoridation.

**Acid water can extract lead.** It is also accepted that lower pH can mobilize available lead from household plumbing. Other characteristics of the source water and treatment methods that could also influence pH of the finished water are not presented for the communities examined in this study. In the absence of pH measurements and other water supply/treatment characteristics it is not possible to make any conclusions about the effects of fluorosilicates on the pH of tap water in the subject communities.

**Increased bioavailability.** The authors do not specify how the bioavailability of lead from water at the tap will be increased. Lower pH may increase the concentration of lead in the water. This does not necessarily mean that the lead will become more readily absorbed through the gastrointestinal tract. The gastrointestinal tract is a well-buffered system. Small changes in the pH of water (although sufficient to increase solubility of lead) are very unlikely to alter the pH in the various regions of the GI tract. Consider the fact that the normal pH in the lumen of the stomach is about 2. Even “acidic” tap water with a pH in the range of 6 will be inconsequential in the environs of the stomach.

GI tract absorption of lead occurs primarily in the duodenum of the small intestine. The pH of the small intestine is somewhat alkaline. Fluoride is primarily absorbed in the stomach. As mentioned previously, the pH of the stomach is extremely acidic. Although the exact mechanisms of absorption are not known, it is thought that the absorption of lead may involve active transport and/or diffusion through the intestinal epithelial cells or between the cells. Uptake by diffusion is basically the same for small water soluble ions. Lead, fluoride and essential water-soluble ions diffuse into cells along concentration gradients. This mechanism of uptake is relatively non-specific.

Active transport is more selective and frequently involves specific binding proteins. Lead is a divalent cation and may be transported by the same mechanisms that import physiologically necessary divalent cations such as calcium and iron. Fluoride is a monovalent anion and does not share the same active transport mechanisms as the divalent cations calcium, iron and (presumably) lead.

**Facilitated transport of lead from the gastrointestinal tract to the blood stream.** The authors postulate that “traces of undissociated fluorinated silica residues may complex dissolved lead and facilitate its transport from the gastrointestinal tract to the blood stream.” It is difficult to imagine a mechanism by which this would occur unless a lipid soluble complex is formed. A lead-fluorinated silica complex would be much heavier, less mobile and less amenable to diffusion than water soluble lead ions. It also seems unlikely that such a complex would be recognized and bound by a Ca+2 or Fe+2 transport protein.

**Other comments.** The data presented in this study may be useful for generating hypotheses for further investigation, but cannot be used to support statements about
causal associations. In epidemiology terms, the authors of this study have committed an “ecological fallacy” by using aggregate level data to make conclusions about individual risk. Conclusions regarding individual risk (e.g. blood lead levels, violent behavior) on the basis of group risk must be made carefully because data on individual behaviors and exposures that may influence the same risk are not known. The community level data presented in this manuscript cannot be used to make correlations between exposure to lead in tap water and blood lead levels in individuals.

Specifically, the statement that “water treatment with silicofluorides apparently functions to increase the cellular uptake of lead” is not supported by the aggregate level data presented in this manuscript. No individual level exposure data are available. The apparent statistical associations based on manipulation of group level data cannot be used to make inferences about causation, especially not at the cellular level!

Again, I appreciate the opportunity to comment on this interesting manuscript. Please let me know if you would like additional comments or clarification.

Sincerely,

Deborah L. Gray, Ph.D., DABT
Clinical Associate Professor
Phone: (614) 293-6138
FAX: (614) 293-3333
e-mail: gray.49@osu.edu
The following is my detailed review of "Water treatment with silicofluorides and lead toxicity"

This is a very poor conceived and developed piece of research. There are no clear objectives. The review of the literature is highly selective and one of the key documents to support the author’s point of view is authored by one of the authors.

In this research, the authors are trying to associate—at the aggregate level—the mean lead blood levels in 0-5 year-old children with the use water fluoridated with three different chemicals. This is a ecological study with 227 units of observation that correspond to 227 towns in Massachusetts aggregated into four groups according to their water fluoridation status: 1) fluoridation with fluorosilicic acid, 2) fluoridated with sodium silicofluoride, 3) fluoridated with sodium fluoride, and 4) non-fluoridates. The authors combined data from different sources to build up a data set that includes, among other variables, chemical used in water fluoridation, sociodemographic data, lead concentration in capillary blood, among others. Capillary lead levels were obtained from a previous research not available for this review, and the authors did not include, in their manuscript, enough information to make an assessment on the quality of these data. Statistical analysis was done using ANOVA and multivariate models using the data set with not always 227 data points but with no acknowledgment that with such very few observations, spurious results are possible. Finally, for the most important analysis, i.e., lead concentration, the values for the four group of communities are too close to each other.

With all these limitations, the authors venture to speculate that presence of fluoride in the water will produce a liberation of lead from pipes and other metallic elements in the water system, be ingested by 0-5 year-old children, and exposed them to detrimental levels of lead. Furthermore, the authors venture to speculate that this can be associated, always at the ecological level, to higher levels of a wide array of social problems, including crime and other “behavioral dysfunctions.”

First, it is difficult to accept/reject hypotheses with results from ecological studies. Even in those well planned ecological studies, it is impossible to assess if the association observed is part of the variable under study or an effect of a third variable not accounted for. This is even more important when sociodemographic variables are used. The very low coefficient of determination acknowledged by the authors \(R^2 = 0.02\) when community lead levels and levels of lead in water using the “90th percentile first draw” are correlated at the ecological level, should cautioned the authors on the possibility of an spurious effect. Any untrained reader should be aware of these limitations, but the authors chose to ignore them.

Second, even though the authors acknowledge that the levels of lead found in their study may came from different sources and be affected by many other variables not accounted for in their analysis, they chose to label fluoride in water as a “risk factor”. This seems to be a preconceived idea by the authors, diminishing even more the quality of their interpretation.
Third, the only type of statistical analysis the authors have used to prove the link between silicofluorides in the water and the entire array of behavior and social possible consequences is the "ecological" technique. Ecological studies use aggregate values and are mainly used to generate hypothesis, not prove them. Applying multivariate techniques, such as regression analysis or ANOVA and controlling for confounding in ecological studies, is dangerous for various reasons: 1) aggregate values are means, medians, or any other measure of central tendency that, because of their aggregate nature diminish artificially, the variability of the sample. This provide artificial greater statistical power (need for smaller sample to reject the null hypothesis). 2) the number of observations (as noted in all tables in the degrees of freedom of the denominators) is limited (200+) to control effectively for confounding. A model with limited number of observations and large number of variables (mostly third variables) can produce spurious results. Finally, nobody will use results from ecological studies to prove cause-effect as the authors infer from their data.

Fourth, many years ago, I reviewed the results from another ecological study that tried to prove a relationship between water fluoridation and hip fractures. A very ill-conceived piece of research that even though got published, it received very low attention in the scientific and lay media. One thing that this paper had, however, was scientific plausibility --a criteria (but not the only one) to build support for a cause-effect relationship. In this case, the authors have stretched plausibility almost to the limit: silicofluorides in the water, lower the water pH, this acidity release lead from water pipes, this lead is absorbed by children, accumulated in their blood, get into their brains, and after a serious of molecular effects on the calcium-dopamine-serotonin path, determines cocaine use and criminal behavior. This "chain" of events seems more suitable for a sci-fi book, movie or conspiracy theory. First, public water pH is kept very much within a narrow margin; even if enough silicofluoride stays chemically stable to later dissociate and produce H$_2$O$^+$ of H$^+$ to determine how much is dissociated and how much change in the water pH from the distribution lines seems to be a necessary first step to produce any hypothesis relating silicofluorides and blood lead concentrations. Second, why assuming that the major source of lead comes from lead in the water when, in fact, the data presented by the authors shows the opposite. Third, the inference that lead is the direct cause of cocaine use and violent behavior is a quantum leap. Drug use (not abuse, by the way) and crime are essentially social-economical problems. How do the authors respond to the decline in crime in many U.S. cities such as New York (a silicofluoride city) in the last two years?

I do not question the direct effects of lead on the individual—for which we have public health answers— but to say that “silicofluoride ultimately is responsible for more aggressive behavior among people who drink water” and “the government may share in the responsibility for violence in society” demonstrate total disrespect for science, government—the work field of one of the authors—, and ultimately to the 100 million plus Americans who agree on the benefits of fluoridation and extensively support their use.
Other problems:

1) The main reference for the effect of "undissociated fluoridated silica residues" and their effect on facilitating the transport of lead into the blood stream is Waldcott's Fluoridation the Great Dilemma, a book with questionable scientific support (Waldcott was a strong opponent to water fluoridation).

2) Capillary blood samples are, indeed, subject to contamination and not reliable. The authors acknowledge few venous blood samples but use them, anyway, in their analysis.

3) The numbers varied: 227 then 213, then two groups of 30 each and later the groups are reduced to 25 each.

4) In the process of selecting 30-30 communities the authors used the expression "matching" The question is matching on what? If they matched to gain statistical power and control for some variables, it seems appropriate to indicate which variables they matched for. Also, if the selection was matched "just in the number" then the reader should know how these two groups of 30 communities were selected.

5) Results from Table 2 should be in results not in the discussion. By the way, there is a group of n=1 in Table 2 --and the one with highest "mean" score. There is no comment if these results, as well as those in table 1 are after controlling for other variables or are just cross tabulations. This is very important because no "regression" analysis results are included in the paper after indicating that controlling for third variables was done.

6) On format: the manuscript is not clear, some sections do not follow a logical pattern. Tables are not self-supported and do not include the appropriate information.
To: Roger Masters  
From: Adrian J. Bailey, James D. Sargent  
Subj: Letter to EPA  
Date: February 9, 1999

Thank you for sharing with us the review of your work prepared by the EPA, and a draft of a response from you to the EPA. We certainly appreciate your thoughtfulness concerning the ecological design we, and others use in public health research.

However, we do not feel threatened by the comments in the review. Thus, we do not feel an apology is necessary from Dr. Urbansky. Further, we feel it appropriate to answer any such criticisms of our design as may arise directly through communications to us, preferably through the journal in which it was published. Some of the criticisms were addressed in a subsequent letter to the editor of that journal.

Finally, we find it curious that your response emphasizes Dr. Urbansky's criticism of our study, which takes up only a very small portion of his overall review of your work. We feel his other criticisms are much stronger and should be thoroughly addressed. We have stated before that, although we have shared the data on state blood lead levels with you at your request, we do not agree with the conclusions you draw from your analysis and prefer not to be associated with this publication in any way. We appreciate your mentioning that we are not responsible for your findings in point 1 of your response.

Sincerely

Adrian Bailey

James Sargent

CC: Dr. Edward Urbansky  
    Robert Thurnau  
    Stan Laskowski
Edward T. Urbansky, Ph.D.
National Risk Management
EPA
Cincinnati, OH 45268

8/17/00

Dear Dr. Urbansky,

I would like to comment on the paper "Water Treatment With...... by Masters and Coplan.

First, I would like to address my comments to whether fluorides would affect the uptake of Pb. A review of the literature would highlight 3 possible mechanisms by which Pb is taken up by cells: calcium channels (neural cells), anion transport (erythrocytes) and nontransferrin iron transporters (possibly intestine). Each mechanism is under the regulation by both intrinsic and extrinsic factors. For example, calcium channels undergo activation, anion transporters require monovalent anions and nontransferrin iron transporters need an acidic extracellular environment. There is no mechanistic explanation in the literature that discusses interactions between fluorides and uptake of Pb. Nonetheless, a study has not, too my knowledge, been published that argues against an interaction.

Alternatively, the effects described in the paper could be due to the presence of competing metals in the water (hardness). Increased levels of calcium and iron in water could affect the absorption of Pb in the intestine.

I also talked to Dr. J. Chisolm about the paper. You may be familiar with his historical work on treating lead toxicity in children. I thought that he would have been aware of possible contributions of fluoride to lead toxicity when fluoride was first introduced to the water system. He has been in the field since the early fifty's. However, he was not. Furthermore, he was not impressed with the very small changes in blood lead that were reported in the paper.

I hope my comments are helpful. Please contact me if you would like additional dialog.

Sincerely yours,

Joseph Bressler, Ph.D.
Hello,

Please let me know when you receive this message.

Thanks.

Stanley Manahan

Review of paper by Masters and Copland

As I understand the basic premise of this paper, it is that addition of fluoride to water as silicofluorides results in chemical conditions that increase lead levels and availability in water, either by lowering pH or by keeping the lead in suspension through interaction with products of silicofluoride hydrolysis. It is an interesting premise and one that presumably should be pursued with additional investigations. However, the underlying chemistry has not been addressed experimentally, which would have to be done in order to provide any meaningful rationale for limiting the use of silicofluorides for water fluoridation. It is inferred, for example, that use of silicofluorides lowers the pH of water significantly, thus increasing the solubility of lead. This appears to be rather unlikely at the levels of silicofluorides used, and it is acknowledged that base is added to water treated with silicofluorides to neutralize any small quantities of acid that they might add. Furthermore, I did not see any references to work suggesting that silicofluorides or their hydrolysis products serve to keep lead suspended in water.

In summary, this paper raises an interesting possibility, but certainly does not prove anything. Any future work in this area should be done with a strong aquatic chemistry input. The chemical studies required should be relatively simple and straightforward.
August 31, 2000

Dr. Edward T. Urbansky
National Risk Management Research Laboratory
United States Environmental Protection Agency
Cincinnati, OH 45268

Dear Dr. Urbansky:

The papers you sent me show a possible correlation between fluorosilicates and lead levels in drinking water. It is clear that the chemistry involved is NOT understood. The equilibrium constants for the hydrolysis of fluorosilicates are controversial/contradicting, and, most certainly, how unhydrolyzed fluorosilicates immobilize lead remains a total mystery.

Tetrafluorides of Si and Ge are hydrolyzed readily by an excess of water to the hydrous oxides. However, I have not been able to find quantitative kinetics measurements. The main product from SiF₄ and H₂O in the gas phase is F₅SiO-SiF₅. In excess of aqueous HF, the hexafluoro ions (MF₆⁻, M = Si, Ge, Sn, and Pb) are formed. SnF₆²⁻ and PbF₆²⁻ are found with trivalent cations as in SmSnF₆ and TIPbF₆. (G. Graudejus and B. G. Muller, Z. anorg. Allg. Chem. 1996, 622, 1601) The formation of these soluble forms of Sn and Pb fluorides, however, requires very harsh conditions when made from the metal:

\[ 2\text{Sn} + 7\text{(NH}_4\text{)}\text{HF}_2 \xrightarrow{300^\circ\text{C}} 2\text{(NH}_4\text{)}_3\text{SnF}_7 + 4\text{H}_2 + \text{NH}_3 \]

Furthermore, lead fluorides are prepared by high-pressure fluorination. Thus, the formation of soluble lead fluorides from unhydrolyzed fluorosilicates can be excluded.

My recommendation is to assess the products from SiF₆²⁻ under conditions that simulate that of water-treatment, and measure the equilibrium constants via reliable methods. Considering, the high availability of Si- and F-NMR, one could easily measure even micromolar concentrations with a micro-probe.

I hope some of the comments are helpful. With my best regards,

Sincerely Yours,

Mahdi Abu-Omar
Date: October 8, 1998

Manuscript Title: Water treatment with silicofluorides and lead toxicity

Author(s): Masters RD, Coplan M.

Reviewer: Scott L. Tomar, DMD, DrPH
Epidemiologist
Division of Oral Health, NCCDPHP, CDC

General Comments:

This paper presents results from an ecological study of community lead levels, drug use among arrested individuals, and the use of a variety of chemicals for fluoridation of community water supplies. The authors conclude that fluosilicic acid and sodium silicofluoride may be responsible for lower pH levels of drinking water, leaching lead from plumbing systems, and increasing lead uptake by children.

This manuscript is poorly written and provides insufficient detail on study methods to allow a full evaluation. Based on the information presented, this study uses a flawed analytic approach, which undermines the validity of its conclusions. Primarily, the authors rely on an ecological study design to draw conclusions at the level of the individual. The sparse individual-level data presented in this paper in fact contradicts the ability to make such a leap. For example, individual children’s blood lead levels showed virtually no association with “90th percentile first draw” lead levels in public water supplies ($r^2 = 0.02$). Much of the authors’ contentions regarding the relation between fluoridation chemicals (or lead, for that matter) and crime rates is weakly supported, and is likely to be highly confounded by complex social factors including, for example, unemployment rates, occupational chemical exposures, and socioeconomic factors not captured in this simplistic analysis. This reminds me of another flawed ecological study that attempted to identify water fluoridation as an etiologic agent for AIDS.

Specific Comments

Page 1 last para. It is unlikely that the author’s prior ecological studies were really able to “control for” socioeconomic and demographic variables to the extent that he contends. Counties differ in many ways not captured by the few aggregate variables he includes in his analysis.

Page 2 para 2. No reference is provided to support the statement that “additional F- and H3O+ will be liberated into the water after it has left the water treatment facilities, with attendant chemical reactions that increase acidity (lower pH) beyond expectations established by current practice.” In fact, the investigators provide no data on water pH in this paper to support their
hypothesized principle mechanism of leaching of lead into community water supplies.

Page 2 methods. The small sample size of children tested for blood lead level in each community (median = 8 per community; some had as few as 2 children) and the lack of detail on the sampling design in this study raise serious doubts about the representativeness of this sample at the community level.

Page 2 methods. It is unclear what the authors mean by “community average levels of capillary blood were used for statewide multivariate statistical analysis.” Although the authors mention multivariate analysis, the type of multivariate analysis is not specified nor are results from such an analysis discussed in this paper.

Page 3, Public Water Supplies. The authors note that measures of lead in local water systems “vary considerably over time as well as between one household and another in the same neighborhood.” This variance among households may be due to differences plumbing or other factors, and again argues against the use of community-level data to investigate individual-level exposure or disease. In fact, the authors’ own ecological analysis found that the proportion of homes built before 1940 was the strongest correlate of children’s capillary blood lead levels (Table 3). Perhaps much of the inter-household variation in lead levels was related to the age of the plumbing; older houses are more likely to have lead pipes and lead-containing solder. In addition, 76% (44 / 58) of communities with silicofluoride in their water had a high percentage (>29.5%) of their houses built before 1940, compared to 40% (62 / 154) of the non-fluoridated communities (based on data in Table 3). This large difference in the age of the housing stock among communities categorized by fluoridation agent does not appear to be adequately controlled for in the type of crude analysis presented in this study. This residual confounding could easily account for the slightly higher mean blood lead levels in silicofluoride communities than in non-fluoridated communities.

It is unclear what the authors mean when they state that statistical analysis is less reliable than assumed when using lead levels as a continuous variable. The statistical analysis may be reliable if the data meet the assumptions for that analytic method (e.g., Normal distribution, homoscedasticity). It is unknown whether the authors have sufficient expertise in statistics to make that assessment. “Dividing the sample by quartile to compute analyses of variance,” as the investigators report, would not necessarily alleviate problems with data reliability. There is no detail on how the investigators addressed the issue of intra- or inter-household differences in lead levels.

Page 4, Statistical Analysis. It is not clear how the investigators’ choice of measures of lead exposure would overcome “sampling error in each community’s average level of blood lead,” which reportedly was “a matter of concern.” There would still be large sampling error (i.e. large variance) for estimated any community-level estimates of the proportion of children exceeding the threshold of 10 μg / dl. This is likely related to the very small sample sizes at the community level.
Page 4 bottom of page. No detail is provided on how the sample of 30 communities using fluosilicic acid and 30 “matched” non-fluoridated communities were chosen. Purposive selection could easily introduce selection bias, threatening external validity of the study’s findings.

Page 5, Results. Community water lead levels showed nearly no association ($r^2 = 0.02$) with children’s blood lead levels. This strongly argues against the use of community-level measures in this type of analysis.
4.10 Lead Data Regression Analysis

Regression values from Table 1 – Childhood Lead Poisoning in Colorado, April, 2003

Where
perc10 = %>10 ug/dl
perhous = % housing units with high-risk of lead hazards
perpop = % of population on HFS

Regression Analysis

The regression equation is

\[ \text{perc10} = 2.50 + 0.00286 \text{perpop} \]

\[ S = 0.7853 \quad R-Sq = 1.9\% \]

Analysis of Variance for percent of population on HFS

<table>
<thead>
<tr>
<th>Source</th>
<th>DF</th>
<th>SS</th>
<th>MS</th>
<th>F</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>Regression</td>
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<td>0.0949</td>
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<td>0.705</td>
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<tr>
<td>Total</td>
<td>9</td>
<td>5.0290</td>
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<td></td>
</tr>
</tbody>
</table>

The regression equation is

\[ \text{perc10} = 2.44 + 0.101 \text{perhous} \]

\[ S = 0.7571 \quad R-Sq = 8.8\% \]

Analysis of Variance for percent of housing units with high-risk lead hazards

<table>
<thead>
<tr>
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<tr>
<td>Total</td>
<td>9</td>
<td>5.0290</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

The regression equation is

\[ \text{perc10} = 2.48 + 0.109 \text{perhous} - 0.00083 \text{perpop} \]

\[ S = 0.8089 \quad R-Sq = 8.9\% \]

Analysis of Variance for both factors

<table>
<thead>
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<tr>
<td>Regression</td>
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<td>Residual Error</td>
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<tr>
<td>Total</td>
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<td>5.0290</td>
<td></td>
<td></td>
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</tbody>
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<table>
<thead>
<tr>
<th>Source</th>
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<th>Seq SS</th>
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<tbody>
<tr>
<td>perhous</td>
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</tr>
<tr>
<td>perpop</td>
<td>1</td>
<td>0.0055</td>
</tr>
</tbody>
</table>

The adjusted partial correlation:

0.03\% (p-value = 0.9295) of the variance in blood lead levels >10 is explained by the variation in the percent of the population on HFS (adjusted for % housing units with high-risk of lead hazards)

The CORR Procedure

1 Partial Variables: perh
2 Variables: perpop perc
Pearson Partial Correlation Coefficients, N = 10
Prob > |r| under H0: Partial Rho=0

<table>
<thead>
<tr>
<th></th>
<th>perpop</th>
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<tr>
<td>perpop</td>
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<tr>
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<td>1.00000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.9295</td>
</tr>
</tbody>
</table>

if $r = -0.035$ then $r^2 = 0.0012$ or $0.12\%$