Impact of Fluoridation of the Municipal Drinking Water Supply: Review of the Literature

Prepared for:

Escambia County Utilities Authority

Prepared by:

The Center for Environmental Diagnostics and Bioremediation
University of West Florida

Joe Eugene Lepo and Richard A. Snyder

May 2000

This report is available on-line at:

http://www.uwf.edu/rsnyder/fluoride/fluorid.html

The Center for Environmental Diagnostics and Bioremediation
The University of West Florida
11000 University Parkway
Pensacola, Florida 32514

Joe Eugene Lepo, Ph.D.
(850) 474-6098
jlepo@uwf.edu

Richard A. Snyder, Ph.D.
(850) 474-2806
rsnyder@uwf.edu
http://www.uwf.edu/rsnyder/

TABLE OF CONTENTS

I. PREFACE

The Escambia County Utilities Authority (ECUA) has approved addition of fluoride to the municipal drinking water system. Hydrofluosilicic acid will be added to deliver fluoride at a target concentrations of 0.8 mg/L. Citizens have raised questions and concerns about the safety and public health risks of this action. There is a tremendous body of literature that addresses the pros and cons of drinking-water fluoridation. This review of the literature for the ECUA is written to assist understanding of the potential environmental and human health impacts of fluoridation of water.

This review specifically excludes publications that were not scientifically valid. Popular press and Internet sources often contain misleading information from interpretations of research findings based on a lack of understanding of the scientific context and the limitations thereof. In some cases, information based on faulty interpretations has self perpetuated and become accepted by repetition rather than critical review. In still other instances, data are presented in misleading ways or extrapolated beyond their scientific context. Rarely, there are found cases of outright falsehoods, whether intentional or not. The process of science also requires independent confirmation of findings (reproducibility) to ensure their validity. Thus a single paper, even though it has been peer reviewed and has become part of the literature, does not necessarily represent the truth. As examples of how information was critically examined and in some cases excluded from this review, we offer the following:

1) **Purposefully misleading.** The often-cited reviews by Albert Schatz typically describe him as the one who “discovered streptomycin” (Schatz, 1976) without even mentioning Selman Waksman, who won the Nobel Prize in Medicine and Physiology (1952) for that discovery. If indeed Schatz had contributed to this discovery, ethical practice would dictate that he acknowledge that he was perhaps a student of Waksman. In any case, several anti-fluoridation publications in print and on the Internet have Schatz listed as the actual Nobel Laureate for that work, and he was not. This puffing of the credentials of the authors — especially when there is no basis in fact — undermines one’s faith in the particular publication.

   The listing of multiple honorary degrees or academic degrees of dubious origin in a biographical section for an author is not accepted in scientific papers. Nor is it acceptable to take a political stance within a scientific discussion. Such practices detract from the objective presentation of factual information concerning fluoridation. Publications promoting a political agenda have an inherent bias. The peer-review system is the place to screen bias and facilitate the presentation of objective factual information.

2) **Poling practices.** Another “red flag” is the practice of listing 50 or 100 “prominent” scientists who are opposed to fluoridation. The search for truth in science does not progress via a voting or poling mechanism. (As an aside,

the pro-fluoridation side would win on this basis by an overwhelming landslide in that a pro-fluoridation list would include many more prominent scientists of "high status," e.g., Linus Pauling; two Nobel Prizes, Chemistry, Peace; numerous Surgeons General; the vast majority of prominent medical and dental scientists and practitioners).

3) **Review process and editorial quality of source.** There are some periodicals that pose as peer-reviewed scientific journals but are not. One such is the journal "Fluoride." This quarterly publication, which is also available also on the Internet, appears biased toward anti-fluoridation opinion and presents experimental work of questionable quality. Whereas their instructions to authors (found at http://www.fluoride-journal.com/papers.htm) suggest a review process, an examination of a few dozen articles reveals that the same authors appear repeatedly (and tend to cite each other) and the experimental work is poorly described and executed. There may be quality science aired in this journal, but ALL articles we examined have an anti-fluoride theme, and many contained significant technical or scientific errors.

   For example one study (Chlubek et al., 1998) attempted to assess the fluoride levels of maternal plasma, and the marginal- and central-placentas of 30 pregnant women, ages ranging from 19 to 40 years old, living in an area with relatively low water and air fluoride (fluorine) content. They concluded that the placenta could accumulate fluoride in healthy women who are exposed in pregnancy to relatively low fluoride concentrations in water and in the air. However, an examination of their data show that in Table 1 and Table 2, they shift units between "μM/L" (a meaningless unit: it should be either μmol/L or μM) and μg fluoride/g of tissue ash (a unit that is not comparable to exposure data in their publication) makes their findings meaningless, and makes one wonder whether these workers are competent in elementary chemistry. Moreover, their study included no controls that are critical to interpreting the results as they intended.

In the process of preparing this report, we have examined a great deal of the non-scientific literature (almost exclusively anti-fluoridation), and have critically examined it based on scientific evidence and context. Where this material could be traced back to objective scientific research, it has been included. The reader should be aware that much of the readily available information on fluoridation does not withstand critical scrutiny and has not been included in this report.

II. ENVIRONMENTAL IMPACTS

A. Fluorine Geochemistry

To understand the environmental impact of modifying fluorine processes in the environment, it is pertinent to first understand the natural cycling of fluorine. The following discussion reviews what is known about this element, its pathways in the environment, and the behavior of its various forms. While this discussion may seem unrelated to fluoridating a municipal water supply, understanding the chemistry and reactivity of fluorine under natural conditions will provide insight into the behavior of this compound in the water supply and potential reactions with pipes and additives. It also addresses the fate of the element once returned to the environment via wastewater treatment plant effluent.

Fluorine (F) is a halogen, atomic weight 18.998, atomic number 9, valence 1. It is a diatomic gas in its elemental state (F_2). Fluorine is the most electronegative element known, and in the gaseous form, F_2, is a very powerful oxidizer. Because of the strong oxidizing power of F_2, fluorine exists naturally as fluoride ion (F^-). This ionic form is the most common and environmentally reactive form. The natural abundance of fluorine ranges from 0.06 to 0.09% by weight in the earth's crust. Although fluorine is an essential element for mammals, it is toxic to both animals and plants at high concentrations (see toxicity discussions in later sections). It is the goal of fluoridation of water supplies to add fluorine in its ionic (fluoride) form. Various compounds are used to achieve this end; all dissociate into their respective ionic forms and reach equilibrium with the chemistry of the receiving water.

In the environment, fluoride flows from the continental drainages to the oceans at an estimated rate of 3.7 million metric tons a year. Mining removes 2 million tons per year, and 0.022 million tons are released to the atmosphere (as HF, SiF_4 and metal fluorides) by combustion of fossil fuels and industrial emissions. Windblown dust and volcanic gases are also sources to the atmosphere (Gaciri and Davies, 1993). Fluorine precipitates in marine sediments, which can then be exposed over geologic time to return fluorine to continental landmasses. Atmospheric fluorine is returned to the earth mostly by precipitation.

B. Fluoride Complexes

Fluoride complexes readily with Al^{+3}, Be^{+2}, and Fe^{+3}, with aluminum fluoride complexes common below pH 7.0. These complexes are usually limited by the aluminum concentrations that tend to be much lower than the fluoride concentrations in natural waters. This results in a greater proportion of the Al^{+3} being complexed than the F^-. Common fluoride minerals (listed in **Table 1** of **APPENDIX C**) have low aqueous solubility. Fluorite (CaF) is the most common fluoride mineral, and its low dissolution tends to control dissolved fluoride ion concentrations in surface waters. Fluorite forms

when dissolved Ca ion is available, but the reaction is fairly slow (Flühler et al., 1982). Fluoride ions do not react with quartz, although hydrofluoric acid and fluorosilicic acid are both well known for their ability to dissolve glass. Cryolite (AlF_6Na_3) precipitates in solutions containing moderate amounts of Na^+ and Al^{+3}, although the concentrations of aluminum are rarely high enough for this reaction to occur naturally. Fluoroapatites of a marine sediment origin are a common source of phosphate for fertilizer (Laghzizil et al., 2000), and the removal of the fluoride from this mineral provides the fluorosilicic acid that is used in municipal fluoridation of drinking water.

C. Fluoride in Soils

In the soils, 90% of the fluoride tends to be insoluble or tightly bound to particles. Under acidic conditions, more fluoride may leech from soils than added by rainfall, with the mobilization likely due to the formation of aluminum complexes (Skjelkvaale, 1994), adsorption onto goethite (FeOOH), and other soil minerals. Thus, although acidic pH increases sorption of fluoride to mineral constituents of soils, these complexes may also enhance fluoride mobility.

Surface soils tend to be depleted relative to deeper layers suggesting leeching by rainfall, which tends to be naturally acidic (average pH 5.3). Where acidic rainfall from atmospheric nitrous and sulfur oxides occurs, fluoride mobility is enhanced. Clay soils retain fluoride better than sandy soils, and calcium in the soil tends to increase retention. Fluoride is adsorbed onto clays (gibbsite, kaolinite, halloysite) in ion-exchange reactions where the fluoride ion competes with hydroxyl ions (OH^-), but the primary exchange reaction appears to be with amorphous aluminum hydroxides ($Al(OH)_3$) at low fluoride levels. High levels of fluoride will result in exchange of F^- for OH^- in clay minerals themselves (Bower and Hatcher, 1967; Flühler et al., 1982). Agricultural use of phosphate fertilizer from fluoroapatite sources (marine deposits) results in enrichment of fluoride to soils as an "impurity." In areas impacted by air pollution containing fluoride acids, plants have been known to accumulate fluoride to toxic levels for livestock (Groth, 1975). Other plants also concentrate fluoride. For example, it is estimated that a single cup of green tea may have 1 – 4 mg of fluoride (Richmond, 1985).

D. Fluoride in Surface Waters and Aquifers

Fluoride ions enter surface waters from soil leeching, precipitation, and human emissions. The concentration in river water varies with the geology of the drainage basins, but an average of 0.1 ppm has been determined (cited in Olausson and Cato, 1980). Phosphate mining of fluoroapatite, $CaF_2(PO4)_6$, results in the production of fluoride as a byproduct, often resulting in its addition to surface waters at concentrations high enough to be considered a pollutant. Once in surface waters or aquifers, complexing of fluoride with magnesium and calcium is negatively affected by

increasing sodium concentrations. For high alkalinity river water, fluoride exists predominantly as free ion (98%), magnesium fluoride ion pair (1.2%) and calcium fluoride ion pair (0.7%). In low alkalinity river water or acidic groundwaters, the percentage of ion pair complexes would be lower. Thus, for ECUA supply well water from the sand and gravel aquifer (pH 5.3), most fluorine will be present as free ion (>99%). For most groundwaters free fluoride ion concentrations are below 1 ppm. Precipitation of fluoride with $AlOH_3$ tends to control the fluoride concentration of ground water (Vengosh and Pankratov, 1998). Fluoride concentrations in ECUA water supply wells are presented in **Table 2** (**APPENDIX C**) and show values typical for aquifers. Fluoride in wastewater treatment plant effluents recharged to aquifers is quickly absorbed into the sediment matrix (Vengosh and Pankratov, 1998). Fluoride contamination from industrial activity that results in much higher loading rates can overwhelm the ability of the sediment matrix to bind the compound. This type of effect is seen in the fluoride plume from the Agrico site, Escambia County, where elevated levels of fluoride are detected at considerable distances (Ma et al., 1999).

E. Fluoride in Estuaries and Seawater

In seawater, fluoride is naturally present at a concentration around 1.32 ppm, with some variation in different ocean basins. Thus, anyone who spends a significant amount of time in the Gulf/Ocean, consumes seafood, or uses sea salt for food preparation / consumption instead of NaCl, already experiences levels of fluoride near that which will be added to the municipal drinking water supply. In seawater, fluorine is present mostly as a free anion F^- (50.5%), a cation pair with magnesium (MgF^+, 47.7%), and as a cation pair with calcium (CaF^+, 1.8%) (Bodek et al., 1988; Rude and Adler, 1993). In marine sediments, fluoroapatite precipitation, carbonate mineral reactions, and alumino-silicate reactions occur and will sequester fluoride. Adsorption of F^- by amorphous iron oxyhydroxide (FeOOH), MnO_2 and SiO_2*nH_2O are facilitated by the presence of Mg^{2+} ions, through the formation of the MgF^+ ion pair prior to adsorption or as a co-adsorption. The adsorption process is reversible and in equilibrium with free F^-. F^- adsorption at low pH is inhibited by the lower adsorption of Mg^{+2} under these conditions (Rude and Adler, 1993).

In estuaries, seawater is diluted by fresh river water, and seawater chemistry tends to dominate river water chemistry above salinities of 5 parts per thousand. Below this point the constants for ion dissociation are not stable, but change with the ion balances as influenced by river drainage geology. This transition is also observed in the complexing of fluoride ion with magnesium and calcium, with 98-99% of fluorine existing as free ion in river water changing to 51% in seawater. The formation of a cation pair with magnesium is not as strong as the tendency to form complexes with aluminum ($Al(OH)_3$, $Al(OH)_4^-$) and thorium ($Th(OH)_3^+$, $Th(OH)_4$), but the magnitude of the concentration difference in seawater for these compounds ensures most of the fluorine not present as free ion will be complexed with magnesium (Dyrssen and Wedborg, 1980).

F. Ecosystem Impacts

Whole ecosystem studies of the impact of fluoridated water supplies are rare. In the wastewater treatment processes, fluoride concentrations are reduced by precipitation and by organic complexing during biological treatment. In the Chesapeake Bay, fluoride additions from natural and supplemented waters could not be found accumulating in the system, and the compound was presumably flushed out to sea (Berkowitz et al., 1978). In some estuaries, sediment pore water may retain higher concentrations than the water column, likely due to inorganic and organic complexes (Windom, 1971). In the St. Lawrence River, a freshwater system, fluoride is quickly diluted to natural background levels upon addition of effluents to the river (Osterman, 1990). Fluoride could not be found accumulating in aquatic plants as has been reported for some terrestrial forage crops, but it was concentrated in the skin, exoskeletons, and shells of aquatic organisms as has also been reported for marine systems (Wallis et al., 1996). These authors concluded that fluoridated effluents added to the river system would pose no environmental risks, as the compound is apparently not toxic to aquatic organisms at the exposure levels from for municipal fluoridation. They did note, however, that synergistic effects are possible with aluminum toxicity.

G. Ecotoxicology

LC50s (lethal concentrations that produce 50% mortality) for fluoride ions for two species of trout range from 64 – 136 ppm (Camargo and Tarazona, 1991), well above the levels encountered in the fluoridation of municipal water supplies. Growth of algae in cultures has been shown to be enhanced with fluoride at concentrations up to 110-200 mg/L, with inhibition of some forms occurring at lower levels (Anta and Klut, 1981; Joy and Balakrishnan, 1990). For two estuarine amphipods, fluoride concentrations of 2.64 mg/L enhanced growth, with increased levels of 5.0 mg/L resulting in the same growth as background levels (1.3 to 1.7 mg/L) (Connell and Airey, 1982). Fluoride has been shown to inhibit photosynthesis, respiration, protein synthesis and enzyme activities of higher plants, green algae, cyanobacteria, and bacteria, at levels encountered from industrial fluoride pollution, but not at the levels encountered in municipal fluoridation or in seawater.

Some reports have indicated that fluoride can ameliorate aluminum toxicity to trout by the formation of fluoride-aluminum complexes, but other studies suggest that fluoride can act synergistically to enhance aluminum toxicity. Under acidified conditions (e.g., acid rain impacted waters), the rate of aluminum fluoride complex formation is controlled by the concentration of aluminum (Radic and Bralic, 1995). AlF_4^- has a molecular structure that interferes with phosphate binding to GDP to form GDP-AlF_4^-, which in turn binds to G-protein binding sites such as found on actin molecules and associated with microtubules and inhibits activity normally induced by GTP (Rai et al.,

1996). AlF_4^- has also been implicated in interfering with ATP energy storage compounds (Rai et al., 1996) by binding to ADP. It has also been suggested that phosphate inhibits movement of aluminum into algae cells, while fluoride enhances it, presumably through a similar binding effect as described above (Rai et al., 1998). Toxic effects on algae from these proposed mechanisms all involve levels of fluoride greatly exceeding the amounts found in marine waters or used in fluoridating water supplies.

H. Hydrofluosilicic acid

This compound is widely used in fluoridating municipal water supplies. Guidelines for its safe and effective use have been established (updated 1999) and are available in the CDC Engineering and Administrative Recommendations of Water Fluoridation, 1995. US Department of Health and Human Services, Public Health Service, Centers for Disease control and Prevention, Morbidity and Mortality Weekly Report Recommendations and Reports Vol. 44, No. RR-13 on the Internet at:

http://www.cdc.gov/epo/mmwr/preview/mmwrhtml/00039178.htm.

In addition to this report, this project will analyze the raw hydrofluosilicic acid to be used by ECUA for the concentrations of impurities such as heavy metals that may affect human health. Results of these analyses will be presented in the final report.

III. HUMAN HEALTH

The debate over fluoridation of community water supply includes a long history of assertions that fluoride causes just about every ailment known to humankind. One Internet posting lists over 150 symptoms and diseases that are alleged to result from "fluoride poisoning" (http://www.bruha.com/fluoride/html/symptoms_hypo_f.htm). Such lists are essentially meaningless in that they are comprised of references to symptoms taken out of the context of either original scientific literature or the popular press (e.g., news periodicals). A substantial body of research exists to demonstrate that these concerns are largely unwarranted; in work where adequate controls have been used, placebo treatments generate as many side effects as do fluoride treatments.

It is also important to understand the difference between correlated events and causally related events. Correlation means that two events co-occur; it does not mean that one event is caused by the other. For example, there is a statistical correlation between watching TV and cancer; it does not mean that TV causes cancer, only that the two are related, possibly to a sedentary lifestyle. Cause and effect relationships are more difficult to establish in that doing so requires carefully designed studies to eliminate spurious correlations. Much of the anti-fluoridation information is based on studies and extrapolations that do not conform to this standard.

Fluoride bioavailability. Bioavailability is the quality of a substance that renders it capable of interacting with and affecting biological processes. Materials with low bioavailability are neutral; materials with high bioavailability may serve as food sources, toxins, or regulatory substances for biological organisms. For example, a toxic substance may be present at high concentration, but if it is bound up in a biologically inert unreactive form, it will have low bioavailability and thus no toxic effect. Between 35 and 50% of the fluoride that enters the human body from any source is retained (World Health Organization, 1984; U.S. Environmental Protection Agency, 1988; Public Health Service, 1991), and the remainder is primarily excreted in urine. Ingested fluorine, in the form of sodium fluoride or sodium monofluorophosphate is highly soluble (dissociates to F^- form) and would readily disperse in the aqueous fluids of an animal. However, of the fluoride retained within a human, most will be sequestered in the bones and teeth, and its bioavailability, as defined by its ability of affect biological processes in the body would be considered rather low.

A. Benefits

The U.S. Environmental Protection Agency (1988) published a summary review of health effects associated with hydrogen fluoride and related compounds. This peer-reviewed document was compiled by the Oak Ridge National Laboratory and contracted by the U.S. Environmental Protection Agency (EPA). The major findings were:

- Exposure to fluoride from ambient air outside of industrial settings was negligible
- There are conflicting reports on the mutagenicity of fluoride; however, most reports of mutagenicity are from in vitro studies in which cultured cells were exposed to very high concentrations of fluoride
- There is essentially no evidence of a relationship of fluoride compounds to cancer.
- EPA asserts the safety of fluoridation of community water at 1.0 ppm (Public Health Service, 1991). Subsequently, caveats for specific age and gender groups have been applied to ensure Adequate Intake (AI) values for fluoride (National Academy Press, 1999; also on the Internet at http://www.nap.edu/books/0309063507/html/288.html)

In October of 1999, the preeminent chronicler of reportable disease and public health issues for the U.S. Government Center for Disease Control and Prevention, the Morbidity and Mortality Weekly Report (1999a, 1999b), cited community water fluoridation as one of the most important "Achievements in Public Health." The article outlines how the fluoridation of community drinking water is a major factor in the decline of tooth decay. Fluoridation of the drinking water supply has been proven to be the most cost effective method of preventing dental caries. However, while fluoridation is highly effective it has not continued to be widely promoted because the general public does not believe that dental disease is a health risk any longer, much as immunization against infectious diseases is perceived as no longer necessary after the success of immunization programs. The lack of perceived benefits often limits the political will to place fluoride in a community's drinking water. The text of this article is available online at:
http://www.cdc.gov/epo/mmwr/preview/mmwrhtml/mm4841a1.htm.

One of the best comprehensive reviews of the scientific bases for benefits and risks of fluoridation is the *Report of the Ad Hoc Subcommittee on Fluoride* of the *Committee to Coordinate Environmental Health and Related Programs*, which was published by the Public Health Service, Department of Health and Human Services (Public Health Services, 1991). This report addressed virtually all aspects of fluoridation, pro and con, it provides a good review of the fate of fluoride inside the mammalian body. The Public Health Service report (1991) unequivocally recommended continued use of fluoride to promote dental health and the optimal fluoridation of water supplies.

The EPA primary maximum contaminant level (MCL), which is enforceable, is 4 mg/L; the secondary MCL, which is not enforceable, is 2 mg/L (Public Health Service, 1991; U.S. Environmental Protection Agency, 1999). However, public notification of exceedances of the secondary MCL is required (U.S. Environmental Protection Agency, 1999; the entire text of the proposed rule, as published in the Federal Register, can be found at http://www.epa.gov/ogwdw000/pws/pn/proposal.pdf).

The American Dietetic Association has recently strongly reaffirmed their position on the efficacy of fluoride supplementation to optimal levels either through the fluoridation of the community water supply or by other means (Journal of the American Dietetic Association, 1989; 1994). The earlier (1989) paper on the current status of fluoridation endorses fluoridation of the water supply to an optimal concentration of 0.7 to 1.2 ppm with the expected result of a 40 to 60% reduction in dental caries. This report also addresses the then current status of community water fluoridation, safety issues, and cost factors. The American Dietetic Association concludes that fluoride reduces dental caries and aids in the remineralization of teeth. The 1994 Position Paper relates the history of fluoridation practice and effect, and also describes the function of fluoride in dental health as follows:

A. promotes new mineralization of incipient lesions
B. increases resistance to acid demineralization
C. interferes in the formation of dental plaque microorganisms
D. increases the rate of posterruptive maturation and improves morphology.

These Position Papers cite various surveys and case studies of fluoridation and conclude that fluoride use by either systemic or topical means promotes a healthy life. The following sections will expand our discussion of some focal points relative to human and public health.

Intake of Fluoride

Cerklewski (1997) reviewed scientific literature addressing fluoride bioavailability. Although fluoride is not actively transported into animal cells, it is second only to iron in concentration in the human body, and thus should not be classified as a micro-trace element for humans.

Indeed, fluoride has been considered as meeting many of the criteria for a recommended daily allowance (RDA) substance. The total fluoride found in a typical adult human body is approximately 2.6 g, which puts it above the concentration range for micro-trace elements. Unlike a dietary non-essential trace element like lead, high fluoride intake does not result in accumulation in the soft tissues where its toxicity becomes manifest. Normal fluoride soft-tissue levels are in the micromolar range (1.0 μM = 19 parts per billion), whereas enzyme inhibition typically requires millimolar concentrations (1.0 mM = 19 parts per million). The combined effects of skeletal uptake and urinary excretion maintain a loose homeostatic balance of the ion in selected tissues, a behavior that would be expected of a nutritionally required ion rather than that of a toxic element such as lead. Although fluoride does not bioaccumulate in tissues other than those of bones and teeth, its internal concentration is only crudely regulated by the balance between intake and urinary excretion requiring a continual intake of the substance. However, in cases of high exposure levels or with renal deficiencies (Public

Health Service, 1991) fluoride will increase in soft tissues somewhat in proportion to intake.

Caries Prevention

Since U.S. communities began fluoridation of water in 1945, the prevalence of dental caries in such communities has decreased dramatically and the average number of decayed, missing and filled permanent teeth has declined from an estimated seven to three. Excellent reviews of the science in this area are available (Richmond, 1985; Easley, 1990; National Academy Press, 1999 and papers cited therein; also on the Internet at http://www.nap.edu/books/0309063507/html/288.html).

Mechanism of anti-caries activity. Oral bacteria in dental plaque ferment sugars to produce a range of organic acids (acetic, lactic, propionic) that promote dissolution of tooth enamel leading to formation of caries. Fluoride decreases demineralization of the enamel and promotes re-mineralization by physicochemical mechanisms. These well-established mechanisms are reviewed in Cerklewski (1997) and the papers cited therein.

The effects on plaque bacteria involve inhibition of several enzymes, which limits the uptake of sugars and reduces the amount of acid produced (National Academy Press, 1999 and papers cited therein; also on the Internet at http://www.nap.edu/books/0309063507/html/288.html). In addition, recent evidence (Cox et al., 1999) demonstrates a direct effect of fluoride on the ability of caries-causing streptococci to colonize tooth enamel surfaces. Streptococci that cause caries bind glucan on tooth enamel surfaces by means of glucan-binding molecules called lectins. Fluoride interferes with this specific binding and thus inhibits biofilm formation by the streptococci that demineralize enamel. The fluoride ion also inhibits chain formation (growth) in streptococci, and affects the physiological capabilities of the microorganism to metabolize sucrose (Embleton et al., 1998). However, these effects are manifest only at high fluoride concentrations, making the role of fluoride in mineralization the likely process for caries reduction.

Free fluoride ion has direct topical effects on the ability of tooth enamel to resist decay in erupted teeth. These effects have been categorized as 1) a reduction of the acid solubility of enamel; 2) promotion of remineralization of incipient enamel lesions at the ultra-structural level; 3) increasing the deposition of mineral phases of plaque, which may under acidic conditions increase remineralization and retard demineralization of the enamel surface; and, 4) fluoride is incorporated into the hydroxyapatite in tooth enamel to increase the proportion of fluoroapatite, which is less-easily dissolved by mouth acids than is hydroxyapatite, and therefore more resistant to decay (Public Health Service, 1991; Cerklewski, 1997).

$$Ca_{10}(PO_4)_6 + 2F^- \rightarrow Ca_{10}(PO_4)_6F_2 + 2OH^-$$

Thus, evidence exists for several mechanisms by which free fluoride ion can prevent or retard dental caries; these mechanisms, impinging both on the causal agents of decay (bacteria and the acidic metabolites they produce) and on the physicochemical structure of tooth enamel, are discussed in depth in a number of reviews (see, National Academy Press, 1999 and papers cited therein; also on the Internet at http://www.nap.edu/books/0309063507/html/288.html)..

Dietary Requirement

Fluoride has been recognized by the National Academy of Science as a beneficial mineral element for humans based on its role in the mineralization of teeth (National Academy Press, 1999 and papers cited therein; also on the Internet at http://www.nap.edu/books/0309063507/html/288.html). Current best estimates recommend up 0.05-mg/kg of body weight up to 40 kg and up to 2 mg per day thereafter. There is no recommended increase or decrease during pregnancy or lactation, as fluoride does not easily pass placental or mammary barriers.

Chlubek et al., (1998) dispute the contention that fluoride does not bioaccumulate in placental tissues. Their study attempted to assess the fluoride levels of maternal plasma, and the marginal- and central-placentas of 30 pregnant women, ages ranging from 19 to 40 years old, living in an area with relatively low water and air fluoride (fluorine) content. They concluded that the placenta could accumulate fluoride in healthy women who are exposed in pregnancy to relatively low fluoride concentrations in water and in the air. However, an examination of their data show that in Table 1 and Table 2, they shift units between "μM/L" (a meaningless unit: it should be either μmol/L or μM) and μg fluoride/g of tissue ash (a unit that is impossible to relate to any point of reference in their publication) makes their findings meaningless, and makes one wonder whether these workers are competent in elementary chemistry. Moreover, their study included no controls that would allow the study to be related to how much exposure these women actually experienced.

Six types of evidence support the establishment of an RDA or an AI (Adequate Intake):

1) intake of fluoride by normally healthy people is documented in the literature with no ill effects;
2) hundreds of epidemiological studies in which the clinical consequences of low fluoride intake (dental decay) were safely corrected by dietary supplementation with fluoride;
3) balance studies that measure fluoride status in relation to intake (more data needed here; see "**Uncertainty**," below);
4) children who started in non-fluoridated area, received fluoridation benefits, and then were subjected to fluoride withdrawal showed an increase in dental decay;

5) extrapolation of numerous animal studies that are consistent with benefits of fluoridation;
6) a valid mechanism for mineralization and re-mineralization has been established.

One argument that is made against providing RDA status for fluoride is that it does not serve as a catalytic center for any known enzyme, as do a number of other vitamins and minerals that have achieved RDA status. However, other essential ions such as chloride and iodide for which RDAs have been established also do not serve as catalytic centers.

Another criterion that fluoride does not achieve is unequivocal evidence that fluorine deficiency impairs growth (Cerklewski, 1997), however, that criterion has not been applied to riboflavin. A new criterion of *essentiality* has been entertained — to be taken in consideration with the six listed above: that nutritional intake of the nutrient in question reduces the occurrence of a chronic disease. (publications in support of and in opposition to this criterion are cited in Cerklewski, 1997). At this point it seems that the fluoride AI status in the National Health Dietary Reference Intakes will be 3.0 and 4.0 mg F per day for female and male adults, respectively. See the National Academy of Sciences Internet site (http://www.nutritionhealthreports.com/RDA.html), which covers the issue of RDA and AI. Although RDAs are currently under revision, it is unlikely that the recommendations for fluoride will change in the near future based on available information.

Studies on the dietary intake are reviewed by the National Academy of Science publication on Dietary Reference Intakes of (National Academy Press, 1999 and papers cited therein; also on the Internet at http://www.nap.edu/books/0309063507/html/288.html). Some of the salient points documented in that review regarding fluoride intake include:

- Ten independent U.S. and Canadian studies published from 1956 to 1987 show that dietary fluoride intakes by adults range from 1.4 to 3.4 mg/day in areas where water fluoridation was 1.0 mg/L.
- There is no evidence that dietary fluoride intake in the 1970s and 1980s had increased over that of the 1950s.
- Most foods are low in fluoride; exceptions include some teas, some seafood, beverages and infant formula formulated with fluoridated water
- The Canadian Paediatric Society, American Dental Association, and the American Academy of Pediatrics agreed to recommend dietary supplementation of fluoride for children 6 months and older in areas with water fluoride content below 0.3 mg/L.
- Intake from dental products such as fluoride-containing toothpastes must be carefully monitored in young children, as children aged 7 years or younger ingest 0.8 mg fluoride with each brushing.

Effects of Inadequate Fluoride Intake

Early studies support that communities having approximately 1.0 mg/L fluoride in their water supply had 40 to 60% lower incidence of dental caries. However, more recent studies (1986 – 1987), such as that of the National Caries Program of the National Institute of Dental Research (reviewed by Brunelle and Carlos, 1990) show an overall difference of 18% between areas with fluoridated water and those with non-fluoridated water. However, when the data were adjusted to exclude children with a history of dietary fluoride supplementation or topical fluoride treatment, the difference increased to 25%, which is still highly significant. The reduction in efficacy levels may reflect an increase in fluoride intake in areas with non-fluoridated water from foods and beverages that are produced in fluoridated areas. Also, the level fluoridation in various EPA Regions of the study was proportionate to the efficacy of fluoridation in reduction of incidence of caries. The World Health Organization's recent publication on "Water Quality and Health" (Helmer, 1999) acknowledges that either inadequate or excess fluoride levels can affect health and urges correction of either condition.

B. Risks

Effects on Enzymes

There are numerous reports of stimulatory or inhibitory effects on enzymes in soft tissues. These have doubtful physiological meaning in that the fluoride concentrations required for these effects are in the millimolar range when normal tissue levels are 1000 times lower. Such is the case of both the documented inhibition of cariogenic bacteria (cited in Cox et al., 1999) or the stimulation and other effects on G-binding protein (Murthy and Makhlouf, 1994; Codina and Birnbaumer, 1994; Rai et al., 1996). Enzymes are catalytic proteins that must maintain their tertiary shape (3D structure) to be effective; a broad variety of ions, elements, salts, and physicochemical parameters when present far in extreme of normal physiological conditions will affect enzymatic function. Thus, this in vitro inhibition, or stimulation, of enzymes or membrane function by 100 to 1000 times the fluoride concentrations seen in vivo can not be physiologically meaningful. In this context the mitogenic (growth-stimulating) effect of fluoride on osteoblasts (cells that grow bone) at higher than physiological concentrations has been taken as a potential for fluoride to treat osteoporosis, or may suggest its potential to promote bone cancer. Both interpretations are unwarranted extrapolations of the scientific results.

Fluoride and Osteoporosis

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 a lifetime of fluoride exposure was associated with increased hip fractures has not been supported by others.

Toxicity and Interaction with Aluminum

A toxic condition related to fluoride intake is termed "fluorosis." Three types of fluorosis are recognized in human beings: 1) acute poisoning, 2) crippling fluorosis, and 3) mottling of tooth enamel (Cerklewski, 1997). In acute poisoning, death is likely within 2 – 4 hours when an average adult consumes 5 g of sodium fluoride. Crippling fluorosis results from long-term exposure (10 – 20 years) to high concentrations (20 – 80 mg/day); in the United States, there have been only five reported cases of crippling skeletal fluorosis in over 35 years (Richmond, 1985; Public Health Service, 1991; National Academy Press, 1999 and papers cited therein; also on the Internet at http://www.nap.edu/books/0309063507/html/288.html), and acute poisoning by ingestion is likewise extremely rare. Numerous studies of patients who were accidentally or purposefully subjected to long-term dosing (10 years or more) at 30 to 60 mg fluoride/day with little or essentially no side effects (cited in Richmond, 1985). These doses are much higher than the proposed 0.8 mg/L for the water supply.

Dental fluorosis is a non-life-threatening condition that occurs in children under 6 years of age who ingest 2 – 3 times the recommended amount. There is a relatively narrow margin of safety between optimal dose and doses that will produce dental fluorosis in children (Cerklewski, 1997). Enamel fluorosis is caused by excessive fluoridation only if the children are exposure during the preeruptive development of teeth (National Academy Press, 1999 and papers cited therein; also on the Internet at http://www.nap.edu/books/0309063507/html/288.html).

One argument for the fluoridation of community water supplies is that relative to the administration of fluoride supplements, it *lessens* the likelihood of dental fluorosis in children. Pendrys and coworkers (1996) found that children living in low-fluoride water areas that were given fluoride supplements or exposed to fluoridated toothpaste during ages 2 through 8 years had an increased risk in developing enamel fluorosis. Subsequently Ismail and Bandekar (1999) prepared a systematic review of the dental literature to investigate the positive and adverse effects of fluoride supplements in non-fluoridated communities. Of 24 studies, 10 were cross-sectional/case-control studies and four were follow up studies. The review confirmed that in non-fluoridated communities, those using fluoride supplements during the first 6 years of life had an increase in the risk of developing dental fluorosis.

Besides calcium, fluoride forms insoluble complexes with the dietary non-essential element aluminum. Thus, aluminum and calcium salts are effective in decreasing the absorption of fluoride and are used in emergency treatment of fluoride poisoning. One

consequence of this interaction is that fluoro-aluminum complexes may increase the bioavailability of aluminum (see above, **ENVIRONMENTAL IMPACTS**). However, common antacids utilize aluminum carbonate without apparent ill effects.

Mutagenicity and Carcinogenicity

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 cereviseae*.

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 in vitro studies but in 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.

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 IACR found no correlation of cancer rates with fluoride exposure. Similar investigations performed by the EPA (U.S. Environmental Protection Agency, Federal Register, 1985b) and the National Research Council (1977) likewise found no correlation of fluoride levels with cancer.

The National Cancer Institute's online report on fluoridated water (Fluoridated Water, 1992; http://cacernet.nci.nih.gov/clinpdq/risk/Fluoridated_Water.html) acknowledges that virtually all water contains fluoride and those areas with water fluoridation are considered best for dental health. The NCI evaluated the relationship between fluoridation and cancer mortality in the U.S. 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 that 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.

Brain Effects

Varner et al. (1993) published a study of male rats treated with AlF_3 — 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 AlF_3 complex. In these experiments the AlF_3-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

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 a 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 to 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 lived for several generations in areas with natural fluoridation of drinking water at 2 to 10 mg/L (e.g., 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).

C. Uncertainty

Below are listed areas needing continued research to keep abreast of changing conditions and to clarify past findings:

Epidemiological monitoring should continue to keep up-to-date information on the relationships among fluoride exposures from all major sources and the prevalence of dental caries and enamel fluorosis at specific life stages.

Basic laboratory and epidemiological studies to further the understanding of effects of fluoride on biomechanical properties of bone and on calcification of soft tissues should be supported.

Clarification of the effects of metabolic and environmental variables on the absorption, retention, excretion and biological effects of fluoride should be further investigated; e.g., the interaction of fluoride with other elements and ions (Al, Mg, Ca) and how it affects their bioavailability needs further study.

IV. CONCLUSION

As of 1977, scientists had published approximately 35,000 papers over the preceding 30 years verifying the efficacy and safety of water fluoridation (reviewed by Richmond, 1985). Still, the issue of fluoridation of community water supplies often results in a polarized debate and a level of emotional acrimony that transcends scientific evaluation of risks and benefits. The controversy has been documented in a "Special Report" by *Chemical and Engineering News* (Hileman, 1988), and in a commentary piece in *Science*, the journal of the American Association for the Advancement of Science, entitled: *The Fluoride Debate: One More Time* (Marshall, 1990). Many of the sociological and emotional facets of the debate are brought out in these two articles. This is an issue that continues to be discussed and about which a preponderance of unsubstantiated assertions exist.

In the opinion of Easley (1990) the failure to attain the 1990 objectives of the U.S. Public Health Service for implementation of community water fluoridation occurred for a variety of reasons. Among them were 1) that fluoridation is a low priority issue within many local, State, and Federal health agencies; 2) there is inadequate funding to support fluoridation at all levels of government; 3) there is a lack of a coordinated and focused national fluoridation effort; 4) there has been little State or Federal governmental interest in mandating fluoridation of public water supplies; 5) there are public misconceptions about safety and efficacy of fluoridation; and, 6) there exists an unrelenting opposition by a highly vocal minority of the lay public.

The safety, health benefits, and risks of fluoridation of community water supplies have been studied for 50 years at the cost of many millions of dollars. This report is unlikely to resolve this controversy. However, it has attempted to provide a factual basis for evaluating the issue and provide a guide to the literature for further information.

V. ACKNOWLEDGMENTS

We thank Ms. Angela Harris for her assistance in conducting the literature search and in securing reprints and interlibrary loans of much of the literature upon which this report is based. We also appreciate the input and the many reprints and Internet site URLs provided by Mr. Kerry Culligan.

VI. APPENDICES

APPENDIX A: REFERENCES

Anta, N.J., and M.E. Klut. 1981. Fluoride addition effects on euryhaline phytoplankton growth in nutrient-enriched seawater at an estuarine level of salinity. Botanica Marina **24:**147-152.

Augenstein, W.L., D. Spoerke, and K. Kulig. 1991. Fluoride ingestion in children: a review of 87 cases. Amer. Acad. Pediatrics **88:**907-912.

Berkowitz, J.B., M.M. Goyer, J.C. Harris, W.J. Lyman, L.H. Nelken, and D.H. Rosenblatt. 1978. Chemistry, toxicology and potential enviromental effects of selected organic pollutants. Volume III, Final Report to the U.S. Army Toxic and Hazardous Materials Agency.

Birnbaumer, L., S.L. Pohl, and M. Rodbell. 1971. The Glucagon-sensitive adenyl cyclase sytem in plasma membranes of rat liver. J. Biol. Chem. **246:**1857-1880.

Bodek, I., W.J. Lyman, W.F. Reehl, and D.H. Rosenblatt. 1988. Environ. Inorg. Chem. Pergamon Press, NY.

Bower, C.A., and J.T. Hatcher. 1967. Adsorption of fluoride by soils and minerals. Soil Sci. **103:**151-164.

Brunelle, J.A., and J.P. Carlos. 1990. Recent trends in dental caries in U.S. children and the effect of water fluoridation. J. Dent. Res. **69:**723-727.

Calderon, R.L. 2000. The epidemiology of chemical contaminants of drinking water. Food Chem. Toxicol. **38:**S13-S20.

Camargo, J.A., and J.V. Tarazona. 1991. Short-term toxicity of fluoride (F^-) in soft water to rainbow trout and brown trout. Chemosphere. **22:**605-611.

Center for Disease Control and Prevention. 1995. Engineering and administrative recommendations for water fluoridation, 1995. CDC. **44(RR-13):**1-40.

Cerklewski, F.L. 1997. Fluoride bioavailability-- nutritional and clinical aspects. Nutritional Res. **17(5):**907-929.

Chen, X., and G.M. Whitford. 1999. Effects of caffeine on fluoride, calcium and phosphorus metabolism and calcified tissues in the rat. Arch. Oral Biol. **44:**33-39.

Chlubek, D., Poreba R., and Machalinski, B.. 1998. Fluoride and Calcium distribution in human placenta. Fluoride **31:** 131-136.

Codina, J., and L. Birnbaumer. 1994. Requirement for intramolecular domanin interaction in activation of G-protein a-subunit by aluminum fluoride and GDP but not by GTP gamma. S. J. Biol. Chem. **169:**29339-29342.

Connell, A.D., and D.D. Airey. 1982. The chronic effects of fluoride on the estuarine amphipods *Grandidierella lutosa* and *G. lignorum*. Water Res. **16:**1313-1317.

Cox, S.D., M.O. Lassiter, B.S. Miller, and R.J. Doyle. 1999. A new mechanism of action of fluoride on streptococci. Biochim. Biophys. Acta **1428:**415-423.

Da Motta, D.V., D.N. De Souza, and J. Nicolau. 1999. Effects of subtoxic doses of fluoride on some enzymes of the glucose metabolism in submandibular salivary glands of fed and overnight-fasted rats. Fluoride **32(1):**20-26.

Dean, H.T. 1936. Chronic endemic dental fluorosis (mottled enamel). J. Amer. Med. Assoc. **21:**1421-1426.

Dean, H.T. 1938. Endemic fluorosis and its relations to dental caries. Pub. Health Rep. **53:**1443-1452

Doyle, R. 1996. Fluoridation. Scientific American **274:**20.

Dunipace, A., C. Wilson, M. Wilxson, W. Zhang, A.H. Kafrawy, E.J. Brizendine, L.L. Miller, B.P. Katz, J.M. Warrick, and G.K. Stookey. 1996. Absence of detrimental effects of fluoride exposure in diabetic rats. Arch. Oral Biol. **41:**191-203.

Dyrssen, D., and M. Wedborg. 1980. Chemical speciation in estuarine waters. Chemistry and Biogeochemistry of Esutaries. Wiley-Interscience, NY.

Easley, M.W. 1990. The status of community water fluoridation in the United States. Pub. Health Rec. **105:**348-353.

Embleton, J.V., H.N. Newman, and M. Wilson. 1998. Influence of Growth mode and sucrose on susceptibility of streptococcus sanguis to amine fluorides and amine fluoride-inorganic fluoride combinations. Appl. Environ. Microbiol. **64:**3503-3506.

Flühler, H.J., J. Polomski, and P. Blaser. 1982. Retention and movement of fluoride in soils. J. Environ. Qual. **11:**461-468.

Gaciri, S.J., and T.C. Davies. 1993. The occurrence and geochemistry of fluoride in some natural waters of Kenya. J. Hydrol. (Amst). **143:**395-412.

Groth, E., III. 1975. Fluoride pollution. Environment **17:**29-38.

Hamilton, S.J., and T.A. Haines. 1995. Influence of fluoride on aluminum toxicity to Atlantic salmon (*Salmo salar*). Can. J. Fish Aquatic Sci. **52:**2432-2444.

Harley, B. and A. Schilling. 1972. Ineffectiveness of fluoride therapy on multiply myeloma. New Eng. J. Med. **286:**1283-1288.

Helmer, R. 1999. Water quality and health. The Enviornmentalist **19:**11-16.

Hichour, M., F. Persin, J. Molenat, and J. Sandeaux, and C. Gavach 1999. Fluoride removal from diluted solutions by donnan dialysis with anion-exchange membranes. Desalination **122:**53-62.

Hileman, B. 1988. Fluoridation of water: Questions about health risks and benefits remain after more than 40 years. Chem. Eng. News: 26-42.

Huang, P.M., and M.L. Jackson. 1965. Mechanism of reaction of neutral fluoride solution with layer of silicates and oxides of soils. Soil Sci. Soc. Amer. Proc. **29:**661-665.

International Agency for Research on Cancer. 1982. Inorganic fluorides used in drinking-water and dental preparations. In: IARC monographs of the evaluation of the carcinogenic risk of chemicals to humans: v 27, some aromatic amines, anthraquinones and nitroso compounds, and inorganic fluorides used in drinking-water and dental preparations. Lyon, France: World Health Organization: 237-303.

Ismail, A.I., and R.R. Bandekar. 1999. Fluoride supplements and fluorisis: a meta-analysis. Community Dent. Oral Epidemiol. **27:**48-56.

Joseph, E.M., F.M. Morel, and N.M. Price. 1995. Effects of aluminum and fluoride on phosphorus acquisition by *Chlamydomonas reinhardtii*. Can. J. Fish Aquatic Sci. **52:**353-357.

Journal of the American Dietetic Association. 1994. Position of the American Dietetic Association: the impact of fluoridation on dental health. Amer. Dietetic Assoc. **94:**1428.

Journal of the American Dietetic Association. 1989. Position of the American Dietetic Association: the impact of fluoridation on dental health. Amer. Dietetic Assoc. **89:**971-974.

Joy, C.M., and K.P. Balakrishnan. 1990. Effect of fluoride on axenic cultures of diatoms. Water Air Soil Pollution **49:**241-249.

Kyle, R.A., J. Jowsey, P.J. Kelly, D.R. Taves. 1975. Multiple myeloma bone disease. The comparative effect of sodium fluoride and calcium carbonate or placebo. New Eng. J. Med. **286:**1283-1288.

Laghzizil, A., N. Elhrech, O. Britel, A. Bouhaouss and M. Ferhat. 2000. Removal of fluoride from moroccan phosphate and synthetic fluoroapatites. J. Fluorine Chem. **101:**69-73.

Ma, T., T.R. Pratt, J. Dukes, R.A. Countryman, and G. Miller. 1999. Susceptibility of public supply wlls to ground water contamination in southern Escambia County, Florida. Water Resources Special Report 99-1. Northwest Florida Water Management District.

Marshall, E. 1990. The fluoride debate:one more time. Science **247:**276-277.

Maurer, J., M. Cheng, B. Boysen, and R. Anderson. 1990. Two-year carcinogenicity study of sodium fluoride in rats. J. Nat. Cancer Inst. **82:**1118-1126.

Morbidity and Mortality Weekly Report. 1999a. Ten great public health achievements--United States, 1990-1999. CDC-MMWR. **48:**241-243.

Morbidity and Mortality Weekly Report. 1999b. Achievements in public health, 1900-1999: fluoridation of drinking water to preven dental caries. CDC-MMWR. **48:**933-940.

Morbidity and Mortality Weekly Report. 1992. Public health focus:fluoridation of community water systems. CDC-MMWR. **41:**372-375.

Murthy, K.S., and G.M. Makhlouf. 1994. Fluoride activates G-protein-dependent and independent pathways in dispersed intestinal smooth muscle cells. Biochem. Biophys. Res. Commun. **202:**1681-1687.

National Academy Press. 1999. Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutrition Board, Institute of Medicine.

National Research Council. 1977. Inorganic solutes. In: Drinking water and health. National Academy of Sciences. Washington D.C. 205-488.

National Toxicology Program. 1990. TR-393 Toxicology and carcinogenesis studies of sodium fluoride (CAS No. 7681-49-4) in F344/N rats and B6C3F mice (Drinking water studies). Nat. Toxicol. Prog. TR-393.

Olausson, E. and I. Cato, eds. 1980. Chemistry and geochemistry of estuaries. Wiley-Interscience, NY.

Osterman, J.W. 1990. Evaluating the impact of municipal water fluoridation on the aquatic environment. Amer. J. Pub. Health. **80:**1230-1235.

Pendrys, D.G., R.V. Katz, and D.E. Morse. 1996. Risk factors for enamel fluorosis in a nonfluoridated population. Amer. J. Epidemiol. **143:**808-815.

Penman, A.D. 1993. Outbreak of acute fluoride poisoning caused by a fluoride overfeed, Mississippi, 1993. Pub. Health Rec. **112:**403-410.

Petersen, L.R., D. Denis, D. Brown, and J.L. Hadler. 1988. Community health effects of a municipal water supply hyperfluoridation accident. Amer. J. Pub. Health **78:**711-713.

Public Health Services. 1991. Review of fluoride: benefits and risks. Report of the Ad Hoc Subcommittee on Fluoride of the Committee to Coordinate Environmental Health and Related Programs. Department of Health and Human Services.

Radic, N., and M. Bralic. 1995. Aluminum fluoride complexation and its ecological importance in the aquatic environment. Science of the Total Environment. **172:**237-243.

Rai, L.C., Y. Husaini, and N. Mallick. 1998. pH-altered interaction of aluminum and fluoride on nutrient uptake, photosynthesis and other variables of Chlorella vulgaris. Aquatic Toxicol. 67-84.

Rai, L.C., Y. Husaini, and N. Mallick. 1996. Physiological and biochemical responses of Nostoc linckia to combined effects of aluminum, fluoride and acidification. Environ. Exp. Bot. **36:**1-12.

Richmond, V.L. 1985. Thirty years of fluoridation: a review. Amer. J. Clin. Nutr. **41:**129-138.

Rosalen, P., W. Bowen, and S. Pearson. 1997. Influence of fluoride co-crystallized with sugar on caries development in desalivated rats. Arch. Oral Biol. **42:**317-322.

Rude, P.D., and R.C. Aller. 1993. The influence of Mg super (2^+) on the adsorption of fluoride by hydrous oxides in seawater. Amer. J. Science. **293:**1-24.

Rzeuski, R., D. Chlubek, and Z. Machoy. 1998. Interactions between fluoride and biological free radical reactions. Fluoride **31:** 43-45.

Schatz, A. 1976. Increased death rates in Chile associated with artificial fluoridation of drinking water, with implications for other countries. J. Arts Sci. Humanities **2:**1-15.

Shaw, J.H. 1954. Effect of nutritional factors on bones and teeth. Ann. NY Acad. Sci. **60:**733-762.

Skjelkvaale, B.L. 1994. Factors influencing fluoride concentrations in Norwegian lakes. Water Air Soil Pollution. **77:**151-167.

Sowers, M.R., M. Clark, M. Jannausch, and R.B. Wallace. 1991. A prospective study of bone mineral content and fracture in communities with differential fluoride exposure. Amer. J. Epidemiol. **133:**649-660.

Suarez-Almazor, M.E., G. Flowerder, and D.L. Saunders. 1993. The fluoridation of drinking water and hip fracture hospitalization rates in two Canadian communities. Amer. J. Pub. Health. **83:**689-693.

Tsutsui, T., N. Suzuki, M. Ohmori, and H. Maizumi. 1984a. Cytotoxicity, chromosome aberrations and unscheduled DNA synthesis in cultured human diploid fibroblasts induced by sodium fluoride. Mutation Res. **139:**193-198.

Tsutsui, T., K. Ide, and H. Maizumi. 1984b. Induction of unscheduled DNA synthesis in cultured human diploid fibroblasts by sodium fluoride. Mutation Res. **140:**43-48.

Tsutsui, T., N. Suzuki, and M. Ohmori. 1984c. Sodium fluoride-induced morphological and neoplastic transformation, chromosome aberrations, sister chromatid exchanges, and unscheduled DNA synthesis in cultured Syrian hamster embryo cells. Cancer Res. **44:**938-941.

Turner, C., I. Owan, J. Brizendine, W. Zhang, M.E.Wilson, and A.J. Dunipace. 1996. High fluoride intakes cause osteomalacia and diminished bone strength in rats with renal deficiency. Bone **19:**595-601.

U.S. Dept. of Health and Human Services. 1993. A toxicological profile by the US Dept of Health and Human Services, Public Health Service. Agency for Toxic Substances and Disease Registry. TP-91/17:112.

U.S. Environmental Protection Agency, 1999. **Federal Register**. 1999. 40 CFR, Parts 141, 142, 143; National Primary Drinking Water Regulations. Federal Register. **64:**25963-26001.

U. S. Environmental Protection Agency, 1985. **Federal Register**. 1985. National primary drinking water regulations; fluoride [final rule]. Federal Register. **50:**47142-47171.

U.S. Environmental Protection Agency. 1988. Summary review of health effects associated with Hydrogen Fluoride and related compounds. Office of Health and Environmental Assessment. EPA, Research Triangle Park, NC.

Van der voet, G., O. Schijns, and F.A. deWolff. 1999. Fluoride enhances the effect of aluminum chloride on interconnections between aggregates of hippocampal neurons. Arch. Physiol. Biochem. **107:**15-21.

Varner, J.A., K.F. Jensen, W. Horvath, and R.L. Isaacson. 1998. Chronic administrationof aluminum-fluoride or sodium fluoride to rats in drinking water: alterations in neuronal and cerebrovascular integrity. Brain Res. **784:**284-298.

Varner, J.A., C.W. Huie, W. Horvath, K.F. Jensen, and R.L. Isaacson. 1993. Chronic AlF_3 administration: II. Selected histological observations. Neurosci. Res. Commun. **13:**99-104.

Vengosh, A., and I. Pankratov. 1998. Chloride/bromide and chloride/fluoride ratios of domestic sewage effluents and associated contaminated ground water. Ground Water. **36:**815-825.

Wallis, P., R. Gehr, and P. Anderson. 1996. Fluorides in wastewater discharges: toxic challenges to the St. Lawrence River biological community. Water Qual. Res. Journal Canada. **31:**809-838.

Wang, F., D. Zhang, R. Wang. 1998. Toxic effects of fluoride on beating myocardial cells cultured in vitro. Fluoride **31:**26-32.

Weisburger, J., G. Williams, E. Wynder. 1990. Fluoride safety and efficacy. J. Nat. Cancer Inst. **82:**1942-1943.

Whitford, G.M. 1989. The metabolism and toxicity of fluoride. Karger, Switzerland.

Windom, H.L. 1971. Fluoride concentration in coastal and estuarine waters of Georgia. Limnol. Oceanog. **16:**806-810.

World Health Organization. 1984. Fluorine and Fluorides. Geneva Switzerland, World Health Organization. Environ. Health Criteria: 36.

APPENDIX B: INTERNET WEBSITES

- **Achievements in Public Health, 1900-1999: Fluoridation of Drinking Water to Prevent Dental Caries.** 1999. CDC-MMWR. http://www.cdc.gov/epo/mmwr/preview/mmwrhtml/mm4841a1.htm

- **Association Fluoridation Policies.** American Dental Association News Daily. http://fluoride.oralhealth.org/papers/adaflpolicy.html

- **Chemfinder: Hydrofluosilicic acid.** ChemFinder. http://ChemFinder.com

- **Dental Health Facts Sheet**. Academy of General Dentistry. http://fluoride.oralhealth.org/papers/agdwhy_fluoride.html

- **Effects of subtoxic doses of fluoride on some enzymes of the glucose metabolism in submandibular salivary glands of fed and overnight-fasted rats.** 1999. Fluoride Journal Online. http://www.fluoride-journal.com/99-32-1/321-20.htm

- **Engineering and administrative recommendations for water fluoridation, 1995.** 1995. CDC-MMWR. http://www.cdc.gov/epo/mmwr/preview/mmwrhtml/00039178.htm

- **Fluoridated water.** 1992. National Cancer Institue Online. http://cancernet.nci.nih.gov/clinpdq/risk/Fluoridated_Water.html

- **Fluoridation of Public Water Supplies.** 1996. American Academy of Family Physicians. http://www.aafp.org/policy/camp/flouride.html

- **Fluoridation Facts.** British Columbia (Canada) Ministry of Health. http://fluoride.oralhealth.org/papers/bchfile28.html

- **Fluoride and Calcium distribution in human placenta.** 1998. Fluoride. http://www.fluoride-journal.com/98-31-3/313-131.htm

- **Fluoride fact sheet.** 1993. CDC. http://www.cdc.gov/nccdphp/oh/flintro.htm

- **Fluorides and fluoridation general information: articles and letters.** National Center for Fluoridation Policy and Research. http://fluoride.oralhealth.org/links.asp?pg=8

- **Fluorides and Fluoridation: published abstracts.** http://www.cadvision.com/fluoride/abstract.htm

- **Fluorides and Fluoridation: facts about fluoride.** 1999. ADA Online. http://www.ada.org/consumer/fluoride/articles/fa-01.html

- **Fluoridation Chemicals.** US Army Fluoridation Data and Chemical Sources, Orthodox Listing. http://members.xoom.com/_XMCM/trufax/fluoride/flchem.html

- **Fluoride journal instruction to authors submitting articles.** http://www.fluoride-journal.com/papers.htm

- **Interactions between fluoride and biological free radical reactions.** 1998. Fluoride. http://www.fluoride-journal.com/98-31-1/31143-45.htm

- **National Academy Press. Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride**. 1999. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, Food and Nutritional Board, Institute of Medicine. http://www.nap.edu/books/0309063507/html/288.html

- **National Institute of Dental and Cranofacial Research.** 2000. http://www.nidr.nih.gov/

- **Recommended Dietary Allowance.** Nutrition Health Reports. http://nutritionhealthreports.com/RDA.html

- **Review of fluoride: benefits and risks.** 1991. Department of Health and Human Services. http://fluoride.oralhealth.org/papers/dhhsflreviewhome.htm

- **Surgeon General's statement on community water fluoridation.** 1995. CDC. http://www.cdc.gov/nccdphp/oh/flintro.htm

- **Symptoms of Hypo/F.** http://www.bruha.com/fluoride/html/symptoms_hypo_f.htm

- **Toxic effects of fluoride on beating myocardial cells cultured in vitro.** 1998. Fluoride. http://www.fluoride-journal.com/98-31-1/31126-32.htm

- **U.S. Environmental Protection Agency, 1999. Federal Register. Parts 141, 142, 143: National Primary Drinking Water Regulations.** http://www.epa.gov/ogwdw000/pws/pn/proposal.pdf

- **Water Fluoridation and cavity prevention.** 1999. ADA Online. http://www.ada.org/consumer/fluoride/articles/fa-02.html

APPENDIX C: TABLES OF SUPPLEMENTAL INFORMATION

Table 1. Concentrations of selected inorganic constituents in ECUA water supply wells. All values are parts per million (ppm). Blank spaces indicate the compound was not detected.

	Nitrate	Fluoride	Aluminum	Iron	Manganese
EPA Standards					
Minimum Detection Level	0.10	0.01	0.10	0.05	0.01
Maximum Cotaminant Level	10.00	2.00	0.20	0.30	0.05
Well Identification					
West	4.5	0.01	0.10		0.01
#6 Well	2.8	0.01		0.30	
Montclair #2	2.8	0.01			
#9 Well	8.0		0.27	0.08	0.09
McAllister	2.1		0.20		0.03
Ensley	2.1	0.01	0.05		
East	5.1	0.3	0.41	0.21	0.10
Lillian	2.6		0.10	0.20	
9th Avenue	2.0	0.01			
Royce St.	2.3	0.01		0.20	
West Pensacola	1.7	0.01		0.20	
F & Scott	1.2	0.01		0.10	
OLF 4A	1.8	0.01		0.10	
Montclair #1	0.7	0.01			0.02
W & Avery	4.4	0.01		0.10	
Davis	1.1	0.01	0.10	0.20	
Sweeney	1.4				
Airport north	0.7				
Villa	0.5	0.01		0.20	
Olive Road	2.5	0.02	0.20		
Ellyson	2.4	0.01			
Avondale	1.2	0			
McCrory	1.5	0.01		0.40	
Montclair #3	1.1				
Broad St.	0.6				
Dunaway	0.2	0.01	0.10		
University	0.3	0.01			
Carriage Hills	0.7	0.01			
Cantonment	0.2	0.01			
Tennant	1.5	0.01		0.10	
Hagler	1.0	0.01			
Bronson #1	0.7	0.01			

Table 2. Common forms of fluorine in the environment.

Names	Chemical Formula
Fluoride	F^-
Hydrofluoric acid	HF
Fluorite, Fluorspar	CaF_2
Fluoroapitate	$CaF_2(PO4)_6$
Sodium Fluoride	NaF
Fluorosilicic (Fluosilicic; Hydrofluosilicic; Hydrofluorosilicic) acid	$2H_2SiF_6$
Sodium fluosilicate	Na_2SiF_6
Cryolite, Sodium Aluminum Fluoride	Na_3AlF_6
Aluminum Fluoride	ALF_3