TABLE B-9 Estimated Average Daily Water Ingestion (mL/kg of Body Weight per Day) from All Sources During 1994-1996 by Consumers of Water

Population	Mean	50th Percentile	90th Percentile	95th Percentile	99th Percentile	Sample Size	Population
All consumers	21	17	38	50	87	14,726	253,667,688
<0.5 year	92	87	169	196	239	149	1,465,837
0.5-0.9 year	65	58	120	164	185	147	1,688,423
1-3 years	31	26	60	74	118	1,732	11,603,245
4-6 years	27	23	51	68	97	1,103	11,556,872
7-10 years	20	17	36	44	70	873	14,329,604
11-14 years	16	14	33	40	60	786	15,116,291
15-19 years	15	12	29	38	66	806	17,564,502
20-24 years	18	14	34	44	86	668	18,224,524
25-54 years	20	17	37	46	69	4,813	110,938,819
55-64 years	20	18	35	42	59	1,513	20,646,201
≥ 65 years	21	19	34	39	54	2,136	30,533,370
Males (all)	20	16	38	49	86	7,532	125,266,552
<1 year	77	66	164	173	233	147	1,538,210
1-10 years	25	20	48	62	91	1,882	19,480,513
11-19 years	16	13	32	42	69	794	16,642,651
≥ 20 years	19	16	34	43	67	4,709	87,605,178
Females (all)	22	18	39	50	88	7,194	128,401,136
<1 year	79	72	158	170	200	149	1,616,050
1-10 years	26	21	50	66	104	1,826	18,009,208
11-19 years	15	13	29	36	56	798	16,038,142
≥ 20 years	21	18	37	45	69	4,421	92,737,736
Lactating women	28	25	53	57	70	40	1,141,186
Pregnant women	21	19	39	44	61	69	1,729,947
Women aged 15-44 years	20	16	36	46	77	2,258	57,164,907

Source: EPA 2000a.

5% drink 50 mL/kg/day x 70 kg (150 lb) = 3,500 mL/day =
3.5 liters/day x 1 mg of Fluoride per liter = 3.5 mg of Fluoride per day

1% drink 87 mL/kg/day x 70 kg (150 lb) = 6,090 mL/day =
6.09 liters/day x 1 mg of Fluoride per liter = 6.09 mg of Fluoride per day

High Intake Population Subgroups

EPA, in its report to Congress on sensitive subpopulations (EPA 2000b), defines sensitive subpopulations in terms of either their response (more severe response or a response to a lower dose) or their exposure (greater exposure than the general population). Hence, it is appropriate to consider those population subgroups whose water intake is likely to be substantially above the national average for the corresponding sex and age group. These subgroups include people with high activity levels (e.g., athletes, workers with physically demanding duties, military personnel); people living in very hot or dry climates, especially outdoor workers; pregnant or lactating women; and people with health conditions that affect water intake. Such health conditions include diabetes mellitus, especially if untreated or poorly controlled; disorders of water and sodium metabolism, such as diabetes insipidus; renal problems resulting in reduced clearance of fluoride; and short-term conditions requiring rapid rehydration, such as gastrointestinal upsets or food poisoning (EPA 2000a). (While the population sample described in Appendix B [Water Ingestion and Fluoride Intakes] included some of these individuals, the study did not attempt to estimate means or distributions of intake for these specific subgroups.)

As shown in Appendix B (Tables B-4 to B-9), some members of the U.S. population could have intakes from community water sources of as much as 4.5-5 L/day (as high as 80 mL/kg/day for adults). Some infants have intakes of community water exceeding 200 mL/kg/day. Heller et al. (1999), using the same data set as EPA (2000a), reported that 21 of 14,640 people (of all ages) had water intakes over 6 standard deviations from the mean (greater than 249 mL/kg/day). Whyte et al. (2005) describe an adult woman who consistently consumed 1-2 gallons (3.8-7.6 L) of fluid per day (instant tea made with well water); no specific reason for her high fluid consumption is given.

Fluid requirements of athletes, workers, and military personnel depend on the nature and intensity of the activity, the duration of the activity, and the ambient temperature and humidity. Total sweat losses for athletes in various sports can range from 200 to 300 mL/hour to 2,000 mL/hour or more (Convertino et al. 1996; Horswill 1998; Cox et al. 2002; Coyle 2004). Most recommendations on fluid consumption for athletes are concerned with matching fluid replacement to fluid losses during the training session or competition to minimize the detrimental effects of dehydration on athletic performance (Convertino et al. 1996; Horswill 1998; Coris et al. 2004; Coyle 2004). Depending on the nature of the sport or training session, the ease of providing fluid, and the comfort of the athlete with respect to content of the gastrointestinal tract, fluid intake during exercise is often only a fraction (e.g., one-half) of the volume lost, and losses of 2% of body weight or more might occur during an exercise session in spite of fluid consumption during the session (Convertino et al. 1996; Cox et al. 2002; Coris et al. 2004; Coyle 2004).

Total daily fluid consumption by athletes generally is not reported; for many athletes, it is probably on the order of 5% of body weight (50 mL/kg/day) or more to compensate for urinary and respiratory losses as well as sweat losses. For example, Crossman (2003) described a professionally prepared diet plan for a major league baseball player that includes 26 cups (6.2 L) of water or sports drink on a workout day and 19 cups (4.5 L) on an off-day; this is in addition to 9-11 cups (2.1-2.6 L) of milk, fruit juice, and sports drink with meals and scheduled snacks (total fluid intake of 6.8-8.8 L/day, or 52-67 mL/kg/day for a 132-kg player[7]). While some players and

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[7] The player's weight was obtained from the 2003 roster of the Cleveland Indians baseball team (http://cleveland.indians.mlb.com).

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ARTICLE 1

COVER STORY

THE SCIENCE AND PRACTICE OF CARIES PREVENTION

JOHN D.B. FEATHERSTONE, M.SC., PH.D.

ABSTRACT

Background and Overview. Dental caries is a bacterially based disease. When it progresses, acid produced by bacterial action on dietary fermentable carbohydrates diffuses into the tooth and dissolves the carbonated hydroxyapatite mineral—a process called demineralization. Pathological factors including acidogenic bacteria (mutans streptococci and lactobacilli), salivary dysfunction, and dietary carbohydrates are related to caries progression. Protective factors—which include salivary calcium, phosphate and proteins, salivary flow, fluoride in saliva, and antibacterial components or agents—can balance, prevent or reverse dental caries.

Conclusions. Caries progression or reversal is determined by the balance between protective and pathological factors. Fluoride, the key agent in battling caries, works primarily via topical mechanisms: inhibition of demineralization, enhancement of remineralization and inhibition of bacterial enzymes.

Clinical Implications. Fluoride in drinking water and in fluoride-containing products reduces caries via these topical mechanisms. Antibacterial therapy must be used to combat a high bacterial challenge. For practical caries management and prevention or reversal of dental caries, the sum of the preventive factors must outweigh the pathological factors.

Although the prevalence of dental caries in children has declined markedly over the last 20 years in most countries in the Western world, the disease continues to be a major problem for both adults and children everywhere.

The trends in caries in U.S. children during the last 30 years were recently summarized[1] on the basis of results of four national surveys.[2-5] By the late 1980s, although approximately 75 percent of children aged 5 to 11 years were caries-free, about 70 percent of the 12- to 17-year-olds still had caries. Approximately 25 percent of children and adolescents in the 5- to 17-year age range accounted for 80 percent of the caries in permanent teeth. By age 17 years, however, 40 percent of the population accounted for 80 percent of the caries.[1-6] These findings illustrate the need for management of caries by individual risk assessment and for measures more specifically directed to high-risk people and populations.

Although these prevalence rates still leave much to be desired, the overall caries prevalence in children has indeed declined in the United States. Smaller epidemiologic studies in recent years indicate, however, that the decline in caries has not continued during the 1990s and that it may have plateaued.[6]

The reasons for the reductions in caries prevalence during the last 20 years are difficult to pinpoint. Strong evidence exists, however, that the near universal use of fluoride-containing products such as dentifrice, mouthrinses and topical gels applied in the dental office have been major contributors.[7,8] Earlier caries reductions of 40 to 70 percent (before the 1970s) had resulted from the fluoridation of public water supplies in many communities.[9-12]

Dental caries in adults also continues to be a major problem, as illustrated by a recent U.S. survey.[13] The survey reported that 94 percent of all dentate adults (aged 18 years or older) had evidence of treated or untreated coronal caries.

Caries obviously still is a major problem in adults, as well as children, and we need an improved approach to prevention and therapy. This article reviews and summarizes the scientific basis for and practice of successful intervention in the caries process.

THE CARIES PROCESS

Bacterial plaque and acid production. The caries process is now well-understood; much of it has been described extensively in the dental literature. Some details of the caries process remain to be unraveled, but, in general, we understand the process well enough to initiate better-targeted methods of caries prevention and intervention.

The mechanism of dental caries formation is essentially straightforward.[1] Plaque on the surface of the tooth consists of a bacterial film that produces acids as a byproduct of its metabolism.[14,15] To be specific, certain bacteria within the plaque are acidogenic—that is, they produce acids when they metabolize fermentable carbohydrates.[12,14,15] These acids can dissolve the calcium phosphate mineral of the tooth enamel or dentin in a process known as demineralization.[16-18] If this process is not halted or reversed via remineralization—the redeposition of mineral via saliva—it eventually becomes a frank cavity.

Dental caries of the enamel typically is first observed clinically as a so-called "white-spot lesion." This is a small area of subsurface demineralization beneath the dental plaque. The body of the subsurface lesion may have lost as much as 50 percent of its original mineral content and often is covered by an "apparently intact surface layer."[19] The surface layer forms by remineralization. The process of demineralization continues each time there is carbohydrate taken into the mouth that is metabolized by the bacteria. The saliva has numerous roles, including buffering (neutralizing) the acid and remineralization by providing minerals that can replace those dissolved from the tooth during demineralization.[1,20,21]

The mutans streptococci and the lactobacilli, either separately or together, are the primary causative agents of dental caries.

Any fermentable carbohydrate (such as glucose, sucrose, fructose or cooked starch) can be metabolized by the acidogenic bacteria and create the aforementioned organic acids as byproducts.[22] The acids diffuse through the plaque and into the porous subsurface enamel (or dentin, if exposed), dissociating to produce hydrogen ions as they travel.[17,23] The hydrogen ions readily dissolve the mineral, freeing calcium and phosphate into solution, which can diffuse out of the tooth. Most importantly, lactic acid dissociates more readily than the other acids, producing hydrogen ions that rapidly lower the pH in the plaque.[17] As the pH is lowered, acids diffuse rapidly into the underlying enamel or dentin.

The two most important groups of bacteria that predominantly produce lactic acid are the mutans streptococci and the lactobacilli.[14] Each group contains several species, each of which is cariogenic. Mutans streptococci include *Streptococcus mutans* and *S. sobrinus.* The lactobacilli species also are prolific producers of lactic acid and appear in plaque before caries is clinically observed.[24,25] These two groups of bacteria, either separately or together, are the primary causative agents of dental caries.

HOW FLUORIDE COMBATS THE CARIES PROCESS

The ability of fluoride to prevent and arrest caries has been researched extensively. Fluoride has three principal topical mechanisms of action:

- inhibiting bacterial metabolism after diffusing into the

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bacteria as the hydrogen fluoride, or HF, molecule when the plaque is acidified;

- inhibiting demineralization when fluoride is present at the crystal surfaces during an acid challenge;
- enhancing remineralization and thereby forming a low-solubility veneer similar to the acid-resistant mineral fluorapatite, or FAP, on the remineralized crystals.

Inhibiting bacterial metabolism. Several investigators have studied the possible effects of fluoride on oral bacteria.[26-28] The most significant finding reported is that the ionized form of fluoride, or F^-, cannot cross the cell wall and membrane but can rapidly travel into the cariogenic bacterial cells in the unchanged form as HF.[26-28]

When the pH in the plaque falls as the bacteria produce acids, a portion of the fluoride present in the plaque fluid then combines with hydrogen ions to form HF and rapidly diffuses into the cell, effectively drawing more HF from the outside.[1,26-28] Once inside the cell, the HF dissociates, acidifying the cell and releasing fluoride ions that interfere with enzyme activity in the bacterium. For example, fluoride inhibits enolase, an enzyme necessary for the bacteria to metabolize carbohydrates. As fluoride is trapped in the cell, the process becomes cumulative.

In summary, fluoride from topical sources is converted partially to HF by the acid that the bacteria produce and diffuses into the cell, thereby inhibiting essential enzyme activity.

Inhibiting demineralization. The mineral of our teeth (enamel, cementum, dentin) and bones is a carbonated hydroxyapatite[29] that can be approximately represented by this simplified formula:

$$Ca_{10-x}(Na)_x(PO_4)_{6-y}(CO_3)_z(OH)_{2-u}(F)_u$$

The substitutions in the hydroxyapatite crystal lattice (the arrangement of atoms and ions in the crystal) occur as the mineral is first laid down during tooth development, with the carbonate (CO_3) ion in particular causing major disturbances in the regular array of ions in the crystal lattice.[30,31] During demineralization, the carbonate is lost, and during remineralization it is excluded from the newly formed mineral. The calcium-deficient, carbonate-rich regions of the crystal are espe-

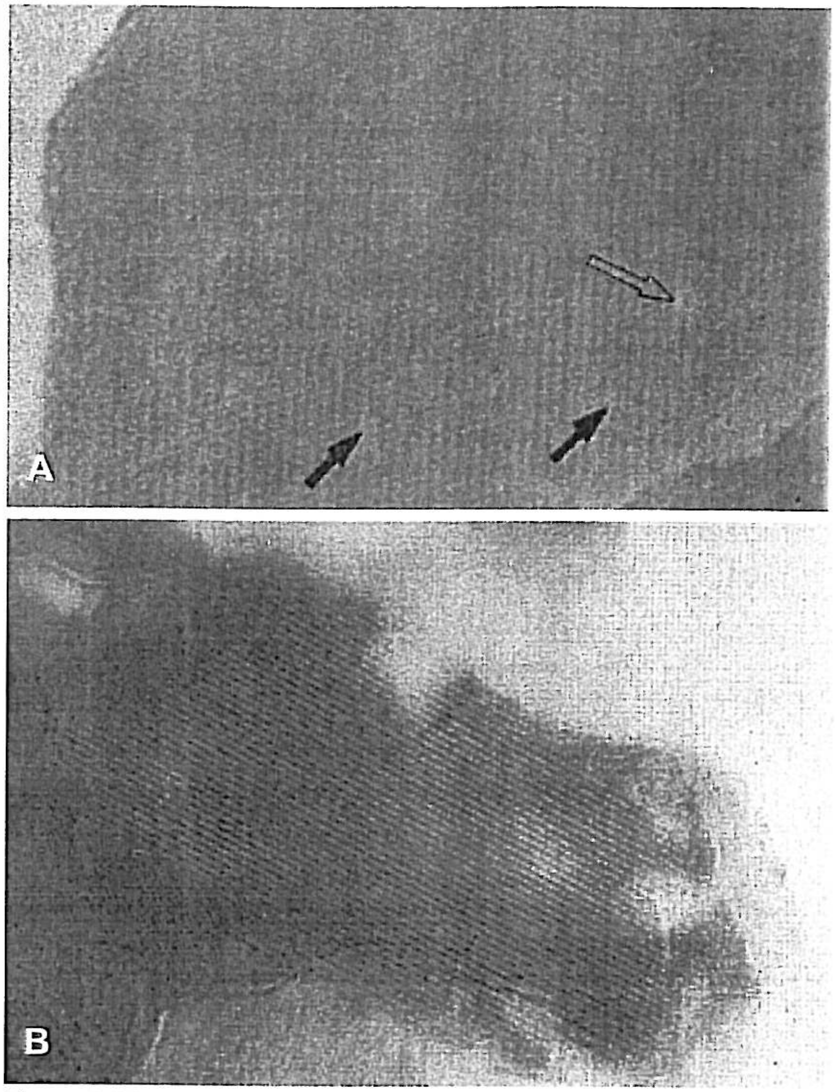

Figure 1. High-resolution electron microscope images (magnification approximately ¥2,000,000) of individual enamel crystals. The black lines are rows of calcium atoms, which are visualized by this technique. A. Normal enamel crystal showing white patches (arrows), which are calcium-deficient and carbonate-rich defect regions. B. Demineralized crystal from the body of a natural caries lesion showing "large" hexagonal holes coinciding with the "small" defect regions seen in normal enamel. (Adapted from Featherstone and colleagues[30,31] with permission from Karger, Basel.)

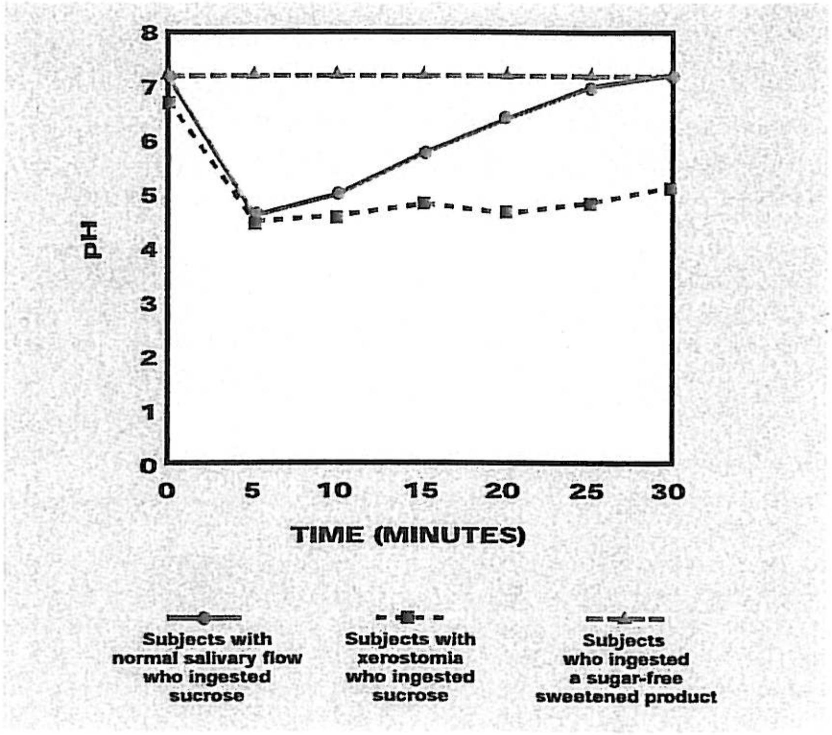

Figure 2. Typical pH curves for normal subjects with normal salivary flow and for subjects with xerostomia (mean for each group) after ingestion of sucrose. A curve for ingestion of a sugar-free sweetened product is shown for comparison. (Reproduced from Featherstone[1] with permission of the publisher. Copyright ©1999, Munksgaard.)

cially susceptible to attack by the acid hydrogen ions during demineralization, as has been shown by several investigators.[21,29-33] High-resolution lattice imaging, which images crystals almost to atomic resolution (viewed at about ×2,000,000 magnification), was used to illustrate the appearance of hexagonal holes in the early stages of enamel crystal dissolution in dental caries (Figure 1), which coincided with the calcium-deficient, carbonate-substituted regions of the crystal.[30-33]

The carbonated hydroxyapatite, or CAP, of our teeth is much more soluble in acid than hydroxyapatite, or HAP (HAP = $Ca_{10}(PO_4)_6(OH)_2$), and that in turn is much more soluble than fluorapatite, or FAP (FAP = $Ca_{10}(PO_4)_6F_2$),[21] in which the OH^- ion in pure hydroxyapatite is completely replaced by an F^- ion. The resulting mineral FAP is highly resistant to dissolution by acid.

Fluoride inhibits demineralization. Sound enamel, except in its outer few micrometers, generally contains fluoride at levels of about 20 to 100 parts per million, or ppm, depending on the fluoride ingestion during tooth development.[34] Teeth in children who lived in areas with fluoridated drinking water during tooth development have fluoride content toward the higher end of this range. The outer few micrometers of enamel can have fluoride levels of 1,000 to 2,000 ppm.[34]

Fluoride in the solution surrounding CAP crystals has been shown to be much more effective in inhibiting demineralization than fluoride incorporated into the crystals at the levels found in enamel.[21,35] Ten Cate,[21] Nelson and colleagues[35] and Featherstone and colleagues[36,37] found no measurable reduction in the acid solubility of synthetic CAP (3 percent CO_3 by weight, comparable to that of dental enamel mineral) with about 1,000 ppm fluoride incorporated. Importantly, this means that fluoride incorporated during tooth mineral development at normal levels of 20 to 100 ppm (even in areas that have fluoridated drinking water or with the use of fluoride supplements) does not measurably alter the acid solubility of the mineral. Even when the outer enamel has higher fluoride levels, such as 1,000 ppm, it does not measurably withstand acid-induced dissolution any better than enamel with lower levels of fluoride. Only when fluoride is concentrated into a new crystal surface during remineralization is it sufficient to beneficially alter enamel solubility. The fluoride incorporated developmentally—that is, systemically into the normal tooth mineral—is insufficient to have a measurable effect on acid solubility.[21,38]

In contrast to the lack of effect of fluoride incorporated into the CAP crystals of tooth mineral developmentally, as little as 1 ppm in the acid solution reduced the dissolution rate of CAP to a rate equivalent to that of HAP.[35] Further increases in fluoride in the acid solution in contact with the CAP mineral surface decreased the solubility rate logarithmically. These results indicate that if fluoride is present in the aqueous solution surrounding the crystals, it is adsorbed strongly to the surface of CAP carbonated apatite (enamel mineral) crystals and thus acts as a potent protection mechanism against acid dissolution of the crystal surface in the tooth's subsurface region. If fluoride is in the plaque fluid at the time that the bacteria generate acid, it will travel with the acid into the subsurface of the tooth and, therefore, adsorb to the crystal surface and protect it against being dissolved.

In summary, fluoride present in the water phase at low levels among the enamel or dentin crystals adsorbs to these crystal surfaces and can markedly inhibit dissolution of tooth mineral by acid.[21,36] Fluoride that acts in this way comes from the plaque fluid via topical sources such as drinking water and fluoride products. Fluoride incorporated during tooth development is insufficient to play a significant role in caries protection. Fluoride is needed regularly throughout life to protect teeth against caries.

Enhancing remineralization. As the saliva flows over the plaque and its components neutralize the acid, raising the pH (Figure 2), demineralization is stopped and reversed. The saliva is supersaturated with calcium and phosphate, which can drive mineral back into the tooth.[21,39] The partially demineralized crystal surfaces within the lesion act as "nucleators," and new surfaces grow on the crystals (Figure 3). These processes constitute remineralization—the replacement of mineral in the partially demineralized regions of the carious lesion of enamel or dentin (including the tooth root).[20,21] Fluoride enhances remineralization by adsorbing to the crystal surface and attracting calcium ions, followed by phosphate ions, leading to new mineral formation. The newly formed "veneer" excludes carbonate and has a composition somewhere between HAP and FAP as described above (Figure 4). FAP contains approximately 30,000 ppm F and has a very low solubility in acid. The new

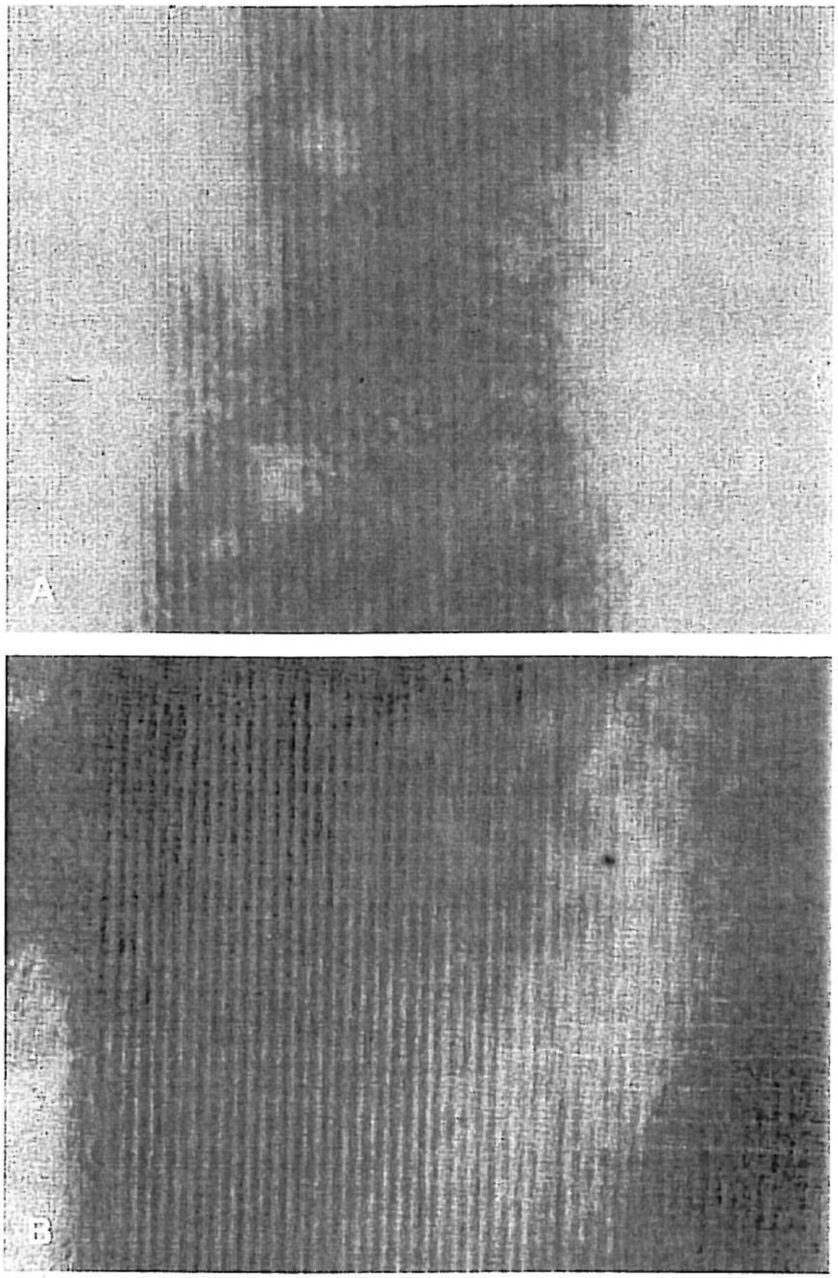

Figure 3. High-resolution electron microscope images (magnification approximately ×2,000,000) of individual enamel crystals that visualize remineralization at the atomic level. The black lines are rows of calcium atoms, which are visualized by this technique. A. Normal enamel crystal dissected from the inner region of enamel, showing "small" white patches of calcium-deficient, carbonate-rich regions. B. Crystal on which a "remineralized" surface veneer has been grown after treatment with fluoride, calcium and phosphate. (Adapted from Featherstone and colleagues, 1981[20] with permission from Karger, Basel.)

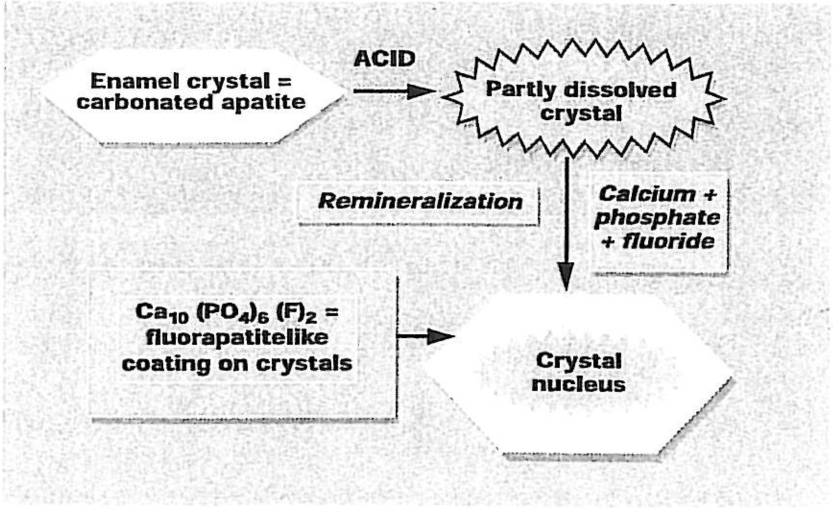

Figure 4. Schematic representation of demineralization followed by remineralization in the caries process. If remineralization is successful, the final result is a crystal with a surface veneer of "fluorapatitelike" mineral of low solubility. (Reproduced from Featherstone[1] with permission of the publisher. Copyright ©1999, Munksgaard.)

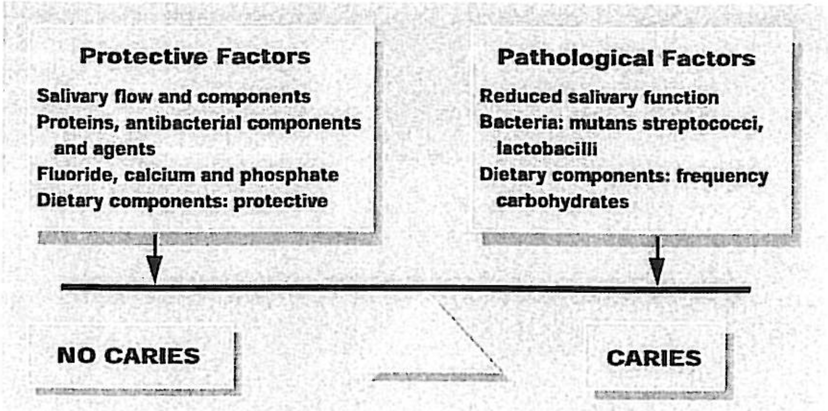

Figure 5. The caries balance: a schematic diagram of the balance between pathological and protective factors in the caries process. (Reproduced from Featherstone[1] with permission of the publisher. Copyright ©1999, Munksgaard.)

remineralized crystal now will behave like low-solubility FAP rather than the highly soluble CAP of the original crystal surface.[36]

In summary, fluoride in solution from topical sources enhances remineralization by speeding up the growth of a new surface on the partially demineralized subsurface crystals in the caries lesion. The new crystal surface veneer is FAP-like, with much lower solubility than the original CAP tooth mineral. Subsequent acid challenges must be quite strong and prolonged to dissolve the remineralized enamel.

Saliva and caries. Saliva has a critical role in the prevention or reversal of the caries process; it provides calcium, phosphate, proteins that maintain supersaturation of calcium in the plaque fluid, proteins and lipids that form a protective pellicle on the surface of the tooth, antibacterial substances and buffers.[40] The saliva components neutralize the acids produced by bacterial metabolism in the plaque, raise the pH and reverse the diffusion gradient for calcium and phosphate. Thereby, they return calcium and phosphate to the subsurface lesion, where these ions can regrow new surfaces on the crystal remnants that were produced by demineralization. These so-called "remineralized" crystals have a veneer of much less soluble mineral. Saliva also clears carbohydrates and acids from the plaque.

In the case of salivary dysfunction,[41] all of the above benefits of saliva are reduced or eliminated (as is illustrated partially in Figure 2 by the pH profile of the subjects with xerostomia).

THE CARIES BALANCE

Fluoride's three extensively studied and documented principal mechanisms of action rely on the presence of fluoride in saliva, in the plaque at the tooth surface and in the fluid among the crystals in the subsurface of the enamel or dentin. The clinical effects of fluoride, therefore, can be optimized by using delivery methods that bring fluoride to the surface of the tooth and into the plaque rather than incorporating fluoride into the tooth mineral crystals during tooth development. These topical delivery methods are equally applicable to adults and children and include fluoride in beverages and foods, dental products and drinking water. The benefits of continually providing low levels of fluoride in the saliva and plaque from the aforementioned topical sources are described more fully

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in a recent review article.[1]

Pathological and protective factors in the caries balance. Caries progression, as opposed to reversal, consists of a delicate balance between the aforementioned factors—namely, a bacterially generated acid challenge and a combination of demineralization inhibition and reversal by remineralization.[1,42] The balance between pathological factors (such as bacteria and carbohydrates) and protective factors (such as saliva, calcium, phosphate and fluoride) is a delicate one that swings either way several times daily in most people (Figure 5).

Protective factors. Saliva is essential for the protection of the tooth against dental caries and provides many natural protective factors summarized earlier,[40,41] including calcium, phosphate, antibacterial components and other proteins with various functions. Extrinsic antibacterial agents such as chlorhexidine also can be considered as protective factors in this balance, as can fluoride from external sources. The mechanisms of action of fluoride described in this article apply primarily to fluoride from topical sources; systemically incorporated fluoride has only a minor role in protecting against dental caries. This conclusion is supported not only by laboratory data as described previously, but also by epidemiologic studies. For example, a four-year study in England found a 27 percent lower caries incidence among children who were 12 years old when water fluoridation began in their communities, relative to the incidence in control subjects of the same age in nonfluoridated areas.[43] This was a well-conducted study, and it clearly showed the posteruptive (topical) effects of fluoride in the drinking water. Other studies have illustrated the weak preeruptive effects of fluoride. For example, in two groups of Okinawa nursing students aged 18 to 22 years, there was no difference in caries status between those who had received fluoridated water only until about 5 to 8 years of age (and none thereafter) and those who had never received fluoridated drinking water.[44]

The cariostatic effects of fluoride are, in part, related to the sustained presence of low concentrations of ionic fluoride in the oral environment,[1,21,38] derived from foods and beverages, drinking water and fluoride-containing dental products such as toothpaste. Prolonged and slightly elevated low concentrations of fluoride in the saliva and plaque fluid decrease the rate of enamel demineralization and enhance the rate of remineralization.[21,36,38,45-48] For example, fluoride at 0.04 ppm in saliva can enhance remineralization. Remineralization of early lesions also requires calcium and phosphate, which are derived primarily from saliva and plaque fluid.

> **There is the mistaken belief that drilling out a caries lesion and placing a restoration eliminates the bacteria and thereby stops caries progression.**

Pathological factors. Pathological factors obviously include cariogenic bacteria and the frequency of ingestion of fermentable carbohydrates that sustain these bacteria. The importance of mutans streptococci (which includes *S. mutans* and *S. sobrinus*) in the development of dental caries has been reviewed extensively.[12,14,15,49,50] Numerous cross-sectional studies in humans have shown that greater numbers of mutans streptococci and lactobacilli in saliva or plaque are associated with high caries rates.[15,25,49,51-54] Longitudinal studies have shown that an increase over time in numbers of both of these bacterial groups is associated with caries onset and progression.[24,55,56]

CARIES INTERVENTION

The methods of caries intervention can be summarized by joining the principal components of the caries process with the interventional possibilities (Table).

Cariogenic bacteria and high bacterial challenge. Dental caries is a transmissible, bacterially generated disease. There is the mistaken belief that drilling out a caries lesion and placing a restoration eliminates the bacteria and thereby stops caries progression. Although traditional restorative work may eliminate the bacteria at the site of the restoration, the remainder of the mouth is left untouched, caries continues unchecked in the remainder of the mouth and recolonization commences rapidly at the margins.[57]

It is logical, therefore, to use

TABLE

SUMMARY: THE CARIES PROCESS AND METHODS OF CARIES INTERVENTION.

CARIES COMPONENT	INTERVENTION METHOD
Bacteria	Antibacterial therapy such as treatment with chlorhexidine gluconate (see text)
Carbonated Hydroxyapatite	Make the mineral less soluble by transforming it to other crystalline forms such as hydroxyapatite without carbonate (future caries-preventive treatments by specific laser irradiation will enable this to be done[69,70])
Fermentable Carbohydrates	Reduce the frequency of ingestion; substitute with noncariogenic sweeteners (this method is well-accepted and used in patient education) Recommend use of sugar-free chewing gum, which reduces frequency of fermentable carbohydrate ingestion and also enhances remineralization
Organic Acids Produced by Oral Bacteria	Neutralize the acid by providing extra buffering or enhancing saliva; sugar-free gum assists in this as well
Saliva	Enhance the saliva flow and function
Fluoride	Exploit its known effects on bacteria, inhibition of demineralization and enhancement of remineralization by using "topical" fluoride delivery by means of dental products, drinking water, beverages and foods

antibacterial therapy—such as treatment with chlorhexidine gluconate rinse—as a caries-preventive measure. Although this has been proposed for many years[58-60] and used in several European countries, an antibacterial approach almost never is used in the United States for the prevention of the progression of dental caries.

One of the difficulties in persuading clinicians to use the antibacterial approach is that there have not been rapid and accurate methods of determining the levels of cariogenic bacteria in the mouth. Furthermore, although numerous studies have indicated that mutans streptococci and lactobacilli definitely are risk factors for dental caries, there is no one-to-one direct correlation between levels of these bacteria and caries progression.[24,49] However, it now is well-established that high levels of mutans streptococci, high levels of lactobacilli or both constitute a "high bacterial challenge."[24] This bacterial challenge can be balanced by the protective factors described earlier, which include salivary components—especially calcium, phosphate and fluoride—and the amount of saliva present.[42]

Figure 5 illustrates the balance between pathological factors (including cariogenic bacteria, reduced salivary function and frequency of use of fermentable carbohydrates) and protective factors. If these pathological and protective factors are in balance, caries does not progress. If they are out of balance, caries either progresses or reverses.

Antibacterial therapy for caries control. Currently, the most successful antibacterial therapy against cariogenic bacteria is treatment by chlorhexidine gluconate rinse or gel.[47,61] Chlorhexidine is available by prescription in the United States. Studies have shown that a daily dose of chlorhexidine rinse for two weeks can markedly reduce the cariogenic bacteria in the mouth and that, as a result, recolonization takes place in three to six months rather than immediately.[58] In patients with high levels of bacteria, therefore, chlorhexidine treatments at three-month

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intervals are indicated.

The problem faced by clinicians is how to determine, in a timely fashion, whether the bacterial challenge is high, medium or low. For many years, commercial "dip slides" have been available in Europe, and they recently became available in the United States.[58] A saliva sample is taken from the patient and incubated on the dip slide; two days later, a result is provided of the levels of *S. mutans* and lactobacilli bacteria in the mouth.[58] Although these slides are a major advance in convenience and are the best tools available at the time of this writing, it has been shown that this technology is not well-correlated with traditional bacterial plating. It is anticipated that methods of rapid chairside assessment of bacterial challenge, based on molecular biology, will be available in the future.

Several investigators have explored the possibility of using modern molecular biology for better and more rapid methods of bacterial assessment,[62] but they were unable to overcome a number of complications. An exciting development is work by Shi and colleagues,[63] who recently published a method using species-specific monoclonal antibodies that recognize the surface of cariogenic bacteria. With this technology, it is not necessary to split open the bacterial cells to assess the internal DNA or RNA. These probes can be tagged either with a fluorescent molecule or with a marker that can be measured quantitatively in a simple spectrophotometer.

It is anticipated that these probes will be available commercially in the near future, and that clinicians will be able to use them chairside and obtain results within a few minutes. This will enable clinicians to determine the quantitative levels of bacteria in a patient's mouth while he or she is in the operatory and to factor these numbers into an overall risk assessment of caries for that patient. It is envisaged that computer programs will be available that will include the assay numbers, as well as other data. The practitioner will receive guidance as to the level of caries risk and what regimen or regimens to use to prevent further caries and to reduce the bacterial challenge. With the new monoclonal antibody probes, the levels of bacteria and success of the intervention could readily be followed over time. This is an exciting, innovative tool that may become widely used and accepted within a few years.

Methods of rapid chairside assessment of bacterial challenge, based on molecular biology, will be available in the future.

CARIES RISK ASSESSMENT

Several studies have attempted to determine risk factors that can be reliably used to assess the level of risk of caries progression in individual patients. Studies still are under way, and there is no definitive formula yet available. The status of risk assessment was summarized, however, by the authors of a special supplement to The Journal of the American Dental Association in 1995; this publication can be used as a guide until more definitive information is available.[64] Figure 5 represents a basis for determining caries risk with the information currently available.

It has been established that high-risk patients include those who have a high bacterial challenge, which may consist of a combination of high numbers of mutans streptococci, lactobacilli or both. Although fluoride has excellent properties in terms of balancing caries challenge, if the challenge is too high, then fluoride—even at increased concentrations, with increased use or both—cannot balance that challenge. Therefore, in the case of high bacterial challenge, the bacterial infection must be dealt with, typically with a chlorhexidine rinse, as well as the enhancement of salivary action by topical delivery of fluoride. These principles apply equally well to adults and children. Accurate detection of early caries can increase the reliability of caries risk assessment, particularly if those measurements are made at three- or six-month intervals and caries progression can be measured. In the case of caries progression, obviously, intervention is needed either antibacterially, with fluoride or

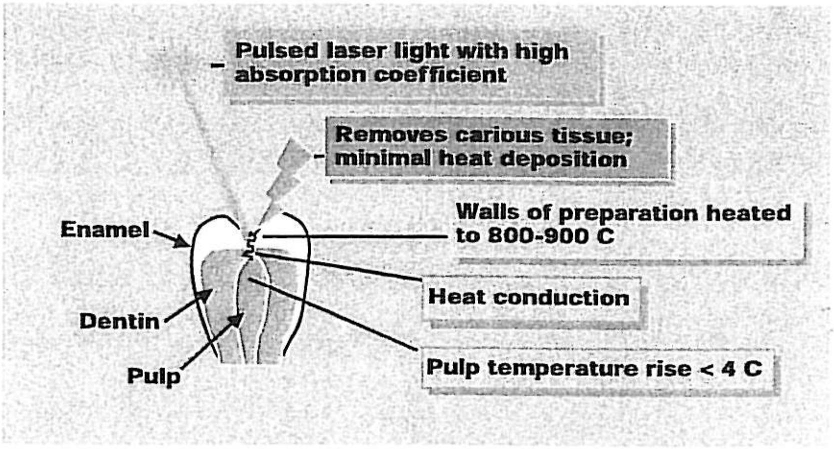

Figure 6. Schematic diagram showing the potential use of specific lasers for precise removal of carious enamel and modification of the surrounding enamel for prevention of further caries progression after restoration. The laser would be set first to remove a minimum of carious tissue. Then the walls and base of the cavity preparation would be treated with the laser to inhibit subsequent caries progression. (Reproduced from Featherstone[71] with the permission of the publisher. Copyright © 2000 Indiana University School of Dentistry.)

with other techniques, some of which are described in the following material.

Caries management by risk assessment. As the caries risk assessment methodologies are refined, we will have more definitive biological and chemical risk assessment measures to guide clinical decision making. These measures form the basis for assessing the direction in which the caries balance is likely to move for a particular patient. Early caries detection, especially in occlusal surfaces, is an essential part of caries management by risk assessment.

Caries management by risk assessment now is receiving considerable attention, and software programs are being developed that will aid practitioners in assessing risk and lead them to the use of current and new technologies by specifying treatments recommended for the various risk categories.[59,60] As we move into the future, tooth restorations will become less and less desirable as a treatment and will be used only as a final resort when new intervention measures have failed or when people have not participated in caries intervention programs such as those indicated previously.

CARIES MANAGEMENT TOOLS FOR THE FUTURE

Several technological advancements are currently close to clinical reality and will be embraced if they are proven successful.

Assessment of bacterial challenge by chairside molecular probes. The use of chairside bacterial probes for assessing a patient's cariogenic bacterial challenge will be an essential component of caries management by risk assessment.

Caries immunization. In a program of caries management by risk assessment, it is logical that all available tools should be used. One such tool that has been investigated for many years is an immunization against caries. There are many obstacles to the success of immunization, as caries is not a systemic infection that can be dealt with simply by administering a specific antibiotic. The infection must be dealt with in the mouth, where the internal body fluids do not pass and, therefore, the normal immune response is not relevant. However, IgA that is produced by the saliva naturally can interfere with the colonization of the surface of the tooth by specific bacteria.

Recent studies by Ma and colleagues[65,66] have illustrated the effectiveness of specific IgA in the inhibition of recolonization of mutans streptococci. The next logical step is to use this technology as one of the tools for caries intervention. It is possible to use genetically engineered plants, such as tobacco or alfalfa, to produce immunoglobulins.[66,67] A study is in progress at the University of California, San Francisco, to test IgA that has been produced using genetically engineered tobacco plants. At press time, the results were not known, but if the trial is successful, this IgA can be applied to the teeth after chlorhexidine treatment has removed the cariogenic bacteria, with the aim of inhibiting future recolonization by mutans streptococci.

Early caries detection and intervention. Successful use of the innovative methods described here for caries intervention will require accurate methods for the early detection of dental caries in enamel and dentin. Early-detection methods such as fluorescence, optical coherence tomography, electrical impedance and

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ultrasonography are likely to become available for use by clinicians in the near future.[68] It will be possible to detect lesions in the occlusal surface and to determine whether they have progressed into the dentin and, if so, how far. This is not possible with current radiographic technology.

Once new methods are introduced for the early detection of caries, they can be used in two opposing fashions. Clinicians with traditional training are likely to use these methods to intervene physically at an earlier stage with carious lesions—drilling, filling and placing restorations. This outcome is of concern, as many more restorations would be placed than may be necessary, which weakens the tooth structure. Early detection and intervention by placing a restoration also does not take advantage of the body's natural protective mechanisms of inhibition of demineralization and enhancement of remineralization via saliva.

Alternatively, early detection of caries can be used as an opportunity to promote remineralization via salivary enhancement, use of topical fluoride and chlorhexidine and meticulous oral hygiene. In addition, as innovative methods for early caries intervention are introduced, the need for restorations may be eliminated for many patients, thereby preserving the tooth structure and halting or reversing progression of dental caries.

Caries prevention by laser treatment. In May 1997, the U.S. Food and Drug Administration approved the use of an erbium:yttrium-aluminum-garnet, or Er:YAG, laser for use on teeth. This was the first approval for laser use on dental hard tissues. This approval by the FDA was for this particular laser to be used for the removal of dental caries and the cutting of sound tissue before the placement of restorations. This event has ushered in a new era for lasers in dentistry. Since then, other lasers have been approved for the same purpose, and additional hard-tissue uses are likely to be approved in the future, including the use of lasers for the inhibition of progression of dental caries by altering the composition of surface enamel or dentin mineral.

As innovative methods for early caries intervention are introduced, the need for restorations may be eliminated for many patients.

Kantorowitz and colleagues[69] and Featherstone and colleagues[70] have studied the effects of lasers on hard tissues for almost 20 years. The overall objective of these studies is to establish the scientific basis for the choice of laser parameters that can be used clinically for the prevention, removal or treatment of caries lesions. Their studies have demonstrated that specific pulsed carbon dioxide, or CO_2, laser treatment of dental enamel can inhibit subsequent carieslike progression in a severe demineralization-remineralization model in the laboratory by up to 85 percent. They have demonstrated that carbonate is lost from the CAP mineral of the tooth during specific laser irradiation, making the mineral highly resistant to dissolution by acid. Although they have demonstrated in the laboratory, using pH cycling models, that as little as 20 pulses of 100 microseconds each can produce a preventive effect similar to daily use of fluoride dentifrice, these promising and exciting results have not yet been tested in human mouths.[70]

For practical purposes, it would be desirable to develop a laser that can remove carious tissue and subsequently be used to treat the walls of the area from which carious tissue is removed to make them resistant to subsequent caries challenge[71] (Figure 6). Fried and colleagues[72] recently published a report on a new CO_2 laser that efficiently removes carious tissue. After caries and a minimal amount of surrounding tissue are removed, it will be possible to change the laser parameters to perform caries-preventive treatment on the same area. This would be followed by placement of a resin-based composite restoration, thereby inhibiting subsequent caries around that restoration. For example, if an early occlusal lesion was detected (by the new methods described previously) that was deemed to be beyond hope of remineralization, this lesion could be conservatively removed with an appropriate laser. Then the surrounding cavity preparation walls could be treated for caries prevention by the laser and a small conservative restoration placed. The cavity walls will be highly resistant to acid attack and therefore resistant to secondary caries. Providing bacterial intervention via chlorhexidine rinse was also part of the treatment in the same patient, future caries would be unlikely.

SUMMARY AND CONCLUSIONS

The mechanism of dental caries is well-established to the point where new approaches are being made for caries prevention based on a scientific understanding of the processes involved. Several existing methodologies are available to enable successful management of dental caries by risk assessment. Understanding the balance between pathological factors and protective factors is the key. Beyond the well-established and currently used methods, some innovative and exciting techniques have shown early research successes that most likely will be used for early caries intervention in the future. These methods include fluoride therapy for inhibition of demineralization and enhancement of remineralization, molecular probes for the quantitative detection of cariogenic bacteria at chairside, computerized caries risk assessment programs, genetically engineered IgA for inhibition of recolonization of cariogenic bacteria, specific lasers for conservative removal of carious tissue and specific lasers for the prevention of caries progression.

The use of these technologies will require extensive retraining of clinical dentists. But it will dramatically alter the way in which dentists diagnose, intervene, treat and manage caries, with major benefits to the oral health of their patients. ■

Dr. Featherstone is a professor and the chair, Department of Preventive and Restorative Dental Sciences and Department of Dental Public Health and Hygiene, University of California, San Francisco, 707 Parnassus Ave., Box 0758, San Francisco, Calif. 94143, e-mail "jdbf@itsa.ucsf.edu". Address reprint requests to Dr. Featherstone.

The author sincerely acknowledges contributions from numerous colleagues over many years to much of the work reviewed here.

1. Featherstone JD. Prevention and reversal of dental caries: role of low level fluoride. Community Dent Oral Epidemiol 1999; 27(1):31-40.
2. Kaste LM, Selwitz RH, Oldakowski RJ, Brunelle JA, Winn DM, Brown LJ. Coronal caries in the primary and permanent dentition of children and adolescents 1-17 years of age: United States, 1988-1991. J Dent Res 1996;75:631-41.
3. National Institute of Dental Research, Epidemiology and Oral Disease Prevention Program. Oral health of United States children: The National Survey of Dental Caries in U.S. School Children, 1986-1987—national and regional findings. Bethesda, Md.: U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health; 1989. NIH publication 89-2247.
4. The prevalence of dental caries in United States children 1979-1980: The National Dental Caries Prevalence Survey. Bethesda, Md.: U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health; 1981. NIH publication 82-2245.
5. National Center for Health Statistics. Decayed, missing and filled teeth among youths, 12-17 years: United States, 1974. Vital and Health Statistics, Series 11-No. 144. Washington: Government Printing Office; 1974. DHEW publication (HRA) 75-1626.
6. Speechley M, Johnston DW. Some evidence from Ontario, Canada, of a reversal in the dental caries decline. Caries Res 1996; 30(6):423-7.
7. Jenkins GN. Recent changes in dental caries. Br Med J 1985;291(6505):1297-8.
8. Hargreaves JA, Thompson GW, Wagg BJ. Changes in caries prevalence in Isle of Lewis children between 1971 and 1981. Caries Res 1983;17(6):554-9.
9. Burt BA, Fejerskov O. Water fluoridation. In: Fejerskov O, Ekstrand J, Burt BA, eds. Fluoride in dentistry. Copenhagen, Denmark: Munksgaard; 1996:275-90.
10. Murray JJ. Fluorides in caries prevention. 3rd ed. Oxford, England; Boston: Butterworth-Heinemann; 1991.
11. Newbrun E. Effectiveness of water fluoridation. J Public Health Dent 1989;49: 279-89.
12. Newbrun E. Cariology. 3rd ed. Chicago: Quintessence; 1989:63-87, 331-49.
13. Winn DM, Brunelle JA, Selwitz RH, et al. Coronal and root caries in the dentition of adults in the United States, 1988-1991. J Dent Res 1996;75:642-51.
14. Loesche WJ. Role of *Streptococcus mutans* in human dental decay. Microbiol Rev 1986;50(4):353-80.
15. Loesche WJ, Hockett RN, Syed SA. The predominant cultivable flora of tooth surface plaque removed from institutionalized subjects. Arch Oral Biol 1972;17(9):1311-25.
16. Featherstone JD. An updated understanding of the mechanism of dental decay and its prevention. Nutr Q 1990;14:5-11.
17. Featherstone JD, Rodgers BE. Effect of acetic, lactic and other organic acids on the formation of artificial carious lesions. Caries Res 1981;15(5):377-85.
18. Featherstone JD, Mellberg JR. Relative rates of progress of artificial carious lesions in bovine, ovine and human enamel. Caries Res 1981;15(1):109-14.
19. Silverstone LM. Structure of carious enamel, including the early lesion. Oral Sci Rev 1973;3:100-60.
20. ten Cate JM, Duijsters PP. Influence of fluoride in solution on tooth demineralization. II. Microradiographic data. Caries Res 1983; 17(6):513-9.
21. ten Cate JM, Featherstone JD. Mechanistic aspects of the interactions between fluoride and dental enamel. Crit Rev Oral Biol Med 1991;2(3):283-96.
22. Geddes DA. Acids produced by human dental plaque metabolism in situ. Caries Res 1975;9(2):98-109.
23. Featherstone JD. Diffusion phenomena and enamel caries development. In: Guggenheim B, ed. Proceedings of the Cariology Today International Congress, September 1983, Zurich, Switzerland. Basel, Switzerland: Karger; 1984:259-68.
24. Leverett DH, Proskin HM, Featherstone JD, et al. Caries risk assessment in a longitudinal discrimination study. J Dent Res 1993;72(2):538-43.
25. Leverett DH, Featherstone JD, Proskin HM, et al. Caries risk assessment by a cross-sectional discrimination model. J Dent Res 1993;72(2):529-37.
26. Hamilton IR, Bowden GH. Fluoride effects on oral bacteria. In: Fejerskov O, Ekstrand J, Burt BA, eds. Fluoride in dentistry. Copenhagen, Denmark: Munksgaard; 1996:230-51.
27. Whitford GM, Schuster GS, Pashley DH, Venkateswarlu P. Fluoride uptake by *Streptococcus mutans* 6715. Infect Immunol 1977;18(3):680-7.
28. Van Louveren C. The antimicrobial action of fluoride and its role in caries inhibition. J Dent Res 1990;69:676-81.
29. LeGeros RZ. Calcium phosphates in oral biology and medicine. In: Myers HM, ed. Monographs in oral science. Basel, Switzerland: Karger; 1991:1-201.
30. Featherstone JD, Nelson DG, McLean JD. An electron microscope study of modifications to defect regions in dental enamel and synthetic apatites. Caries Res 1981;15(4): 278-88.
31. Featherstone JD, Goodman P, McLean JD. Electron microscope study of defect zones in dental enamel. J Ultrastruc Res 1979;67: 117-23.
32. Nelson DG, McLean JD. High-resolution electron microscopy of octacalcium phosphate and its hydrolysis products. Calcif Tissue Int 1984;36(2):219-32.
33. Nelson DG, McLean JD. Direct observation of near-atomic details in synthetic and biological apatite crystallites. In: Fearnhead RW, Suga S, ed. Tooth enamel IV: Proceedings of the Fourth International Symposium on the Composition, Properties, and Fundamental Structure of Tooth Enamel.

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Amsterdam, Netherlands: Elsevier Science Publishers; 1984:47-51.

34. Robinson C, Kirkham J, Weatherell JA. Fluoride in teeth and bone. In: Fejerskov O, Ekstrand J, Burt BA, eds. Fluoride in dentistry. Copenhagen, Denmark: Munksgaard; 1996:69-87.

35. Nelson DG, Featherstone JD, Duncan JF, Cutress TW. Effect of carbonate and fluoride on the dissolution behaviour of synthetic apatites. Caries Res 1983;17(3):200-11.

36. Featherstone JD, Glena R, Shariati M, Shields CP. Dependence of in vitro demineralization of apatite and remineralization of dental enamel on fluoride concentration. J Dent Res 1990;69:620-5.

37. Featherstone JD, Shields CP, Khademazad B, Oldershaw MD. Acid reactivity of carbonated apatites with strontium and fluoride substitutions. J Dent Res 1983; 62(10):1049-53.

38. Fejerskov O, Thylstrup A, Larsen MJ. Rational use of fluorides in caries prevention. A concept based on possible cariostatic mechanisms. Acta Odont Scand 1981;39(4):241-9.

39. Moreno EC, Kresak M, Zahradnick RT. Physicochemical aspects of fluoride-apatite systems relevant to the study of dental caries. Caries Res 1977;11:142-71.

40. Lamkin MS, Oppenheim FG. Structural features of salivary function. Crit Rev Oral Biol Med 1993;4:251-9.

41. Mandel ID. Relation of saliva and plaque to caries. J Dent Res 1974;53(2): 246-66.

42. Featherstone JD. Clinical implications: New strategies for caries prevention. In: Stookey GK, ed. Indiana Conference 1996: Early Detection of Dental Caries. Indianapolis: Indiana University School of Dentistry; 1996:287-95.

43. Harwick JL, Teasdale J, Bloodworth G. Caries increments over 4 years in children aged 12 at the start of water fluroridation. Br Dent J 1982;153:217-22.

44. Kobayashi S, Kawasaki K, Takagi O, et al. Caries experience in subjects 18-22 years of age after 13 years' discontinued water fluoridation in Okinawa. Community Dent Oral Epidemiol 1992;20:81-3.

45. ten Cate JM, Mundorff-Shrestha SA. Working group report: laboratory models for caries (in vitro and animal models). Adv Dent Res 1995;9:332-4.

46. Zero DT. In situ caries models. Adv Dent Res 1995;9:214-30.

47. Featherstone JD, Zero DT. Laboratory and human studies to elucidate the mechanism of action of fluoride-containing dentifrices. In: Embery G, Rolla R, eds. Clinical and biological aspects of dentifrices. Oxford, England: Oxford University Press; 1992: 41-50.

48. Arends J, Nelson DG, Dijkman AG, Jongebloed WL. Effect of various fluorides on enamel structure and chemistry. In: Guggenheim B, ed. Proceedings of the Cariology Today International Congress, September 1983, Zurich, Switzerland. Basel, Switzerland: Karger; 1984:245-58.

49. Krasse B. Biological factors as indicators of future caries. Int Dent J 1988;38(4): 219-25.

50. Ellen RP. Microbiological assays for dental caries and periodontal disease susceptibility. Oral Sci Rev 1976;(8):3-23.

51. Alaluusua S, Kleemola-Kujala E, Nystrom M, Evalahti M, Gronroos L. Caries in the primary teeth and salivary *Streptococcus mutans* and lactobacillus levels as indicators of caries in permanent teeth. Pediatr Dent 1987;9(2):126-30.

52. Klock B, Krasse B. Microbial and salivary conditions in 9- to 12-year-old children. Scand J Dent Res 1977;85(1):56-63.

53. Klock B, Emilson CG, Lind SO, Gustavsdotter M, Olhede-Westerlund AM. Prediction of caries activity in children with today's low caries incidence. Community Dent Oral Epidemiol 1989;17(6):285-8.

54. Seppa L, Hausen H. Frequency of initial caries lesions as predictor of future caries increment in children. Scand J Dent Res 1988;96(1):9-13.

55. Loesche WJ, Eklund S, Earnest R, Burt B. Longitudinal investigation of bacteriology of human fissure decay: epidemiological studies in molars shortly after eruption. Infect Immunol 1984;46(3):765-72.

56. Kingman A, Little W, Gomez I, et al. Salivary levels of *Streptococcus mutans* and lactobacilli and dental caries experiences in a U.S. adolescent population. Community Dent Oral Epidemiol 1988;16(2):98-103.

57. Wright JT, Cutter GR, Dasanayake AP, Stiles HM, Caufield PW. Effect of conventional dental restorative treatment on bacteria in saliva. Community Dent Oral Epidemiol 1992;20(3):138-43.

58. Anderson MH, Bales DJ, Omnell KA. Modern management of dental caries: the cutting edge is not the dental bur. JADA 1993;124(6):37-44.

59. Anusavice KJ. Treatment regimens in preventive and restorative dentistry. JADA 1995;126(6):727-43.

60. Anusavice KJ. Efficacy of nonsurgical management of the initial caries lesion. J Dent Educ 1997;61(11):895-905.

61. Lagerlof F, Oliveby A. Clinical implications: new strategies for caries treatment. In: Stookey GH, Beiswanger B, eds. Indiana Conference 1996: Early Detection of Dental Caries. Indianapolis: Indiana University School of Dentistry; 1996.

62. Cangelosi GA, Iversen JM, Zuo Y, Oswald TK, Lamont RJ. Oligonucleotide probes for mutans streptococci. Mol Cell Probes 1994;8(1):73-80.

63. Shi W, Jewett A, Hume WR. Rapid and quantitative detection of *Streptococcus mutans* with species-specific monoclonal antibodies. Hybridoma 1998;17(4):365-71.

64. Caries diagnosis and risk assessment: a review of preventive strategies and management. JADA 1995;126(suppl):1-24S.

65. Ma JK, Hunjan M, Smith R, Lehner T. Specificity of monoclonal antibodies in local passive immunization against *Streptococcus mutans*. Clin Exp Immunol 1989;77(3):331-7.

66. Ma JK, Hikmat BY, Wycott K, et al. Characterization of a recombinant plant monoclonal secretory antibody and preventive immunotherapy in humans. Nat Med 1998;4(5):601-6.

67. Ma JK, Lehner T, Stabila P, Fux CI, Hiatt A. Assembly of monoclonal antibodies with IgG1 and IgA heavy chain domains in transgenic tobacco plants. Eur J Immunol 1994;24(1):131-8.

68. Stookey GK. Practical applications of early caries detection methods. In: Stookey GK, ed. Early detection of dental caries II: 1999. Indianapolis: Indiana University School of Dentistry (in press).

69. Kantorowitz Z, Featherstone JD, Fried D. Caries prevention by CO_2 laser treatment: dependency on the number of pulses used. JADA 1998;129:585-91.

70. Featherstone JD, Barrett-Vespone NA, Fried D, Kantorowitz Z, Seka W. CO_2 laser inhibitor of artificial caries-like lesion progression in dental enamel. J Dent Res 1998; 77(6):1397-403.

71. Featherstone JD. Innovative methods for early caries intervention. In: Stookey GK, ed. Early detection of dental caries II: 1999. Indianapolis: Indiana University School of Dentistry (in press).

72. Fried D, Murray MW, Featherstone JD, et al. Dental hard tissue modification and removal using sealed TEA lasers operating at $\lambda = 9.6$ and 10.6 µm. Proceedings of Lasers in Dentistry V: Jan. 24-25, 1999, San Jose, Calif. Bellingham, Wash.: SPIE Press; 1999:196-203.

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Background: Infant Formula and the Risk for Enamel Fluorosis

The proper amount of fluoride from infancy through old age helps prevent and control tooth decay. In a minority of children, fluoride exposure during the ages when teeth are forming (from birth through age 8) also can result in a range of changes within the outer surface of the tooth called enamel fluorosis. Recent evidence suggests that mixing powdered or liquid infant formula concentrate with fluoridated water on a regular basis may increase the chance of a child developing the faint white markings of very mild or mild enamel fluorosis. This occurs on baby and permanent teeth while they are forming under the gums. Once the teeth come into the mouth, they are no longer able to develop this condition. Typically, very mild or mild fluorosis is barely noticeable, if noticed at all. Studies have not shown that teeth are likely to develop more esthetically noticeable forms of fluorosis, even with regular mixing of formula with fluoridated water.

In children younger than 8 years of age, combined fluoride exposure from all sources—water, food, toothpaste, mouth rinse, or other products—contributes to enamel fluorosis. Currently one-third (33%) of children aged 12 to 15 years in the United States have very mild to mild forms of this condition. It is important to understand that some fluoride exposure to developing teeth also plays a long-term role in preventing tooth decay. Parents and health providers should weigh the balance between a child's risk for very mild or mild enamel fluorosis and the benefit of fluoride for preventing tooth decay and the need for dental fillings.

The possibility of an association between fluoride in infant formula and the risk for enamel fluorosis has been studied for many years. Until now, most researchers concluded that fluoride intake during a child's first 10 to12 months had little impact on the development of this condition in permanent teeth. A recent study, however, has raised the possibility that fluoride exposure during the first year of life may play a more important role on fluorosis development than was previously understood. It now appears that the amount of the fluoride contained in the water used for mixing infant formula may influence a child's risk for developing enamel fluorosis, particularly if the child's sole source of nutrition is from reconstituted infant formula.

CDC will continue to assess the science regarding the use of fluoride in preventing tooth decay while limiting enamel fluorosis, and will modify its recommendations as warranted. CDC believes that community water fluoridation is safe and healthy and promotes its use for people of all ages.

- What is the best source of nutrition for infants?
- What type of water does CDC recommend for mixing infant formula?
- Why is there a focus on infant formula as a source of fluoride?
- What types of infant formula may increase the risk for enamel fluorosis?
- What is enamel fluorosis?
- Should all parents consider mixing formula with water from sources other than tap water?
- How can I find out what the concentration of fluoride is in my tap water?
- My city has community water fluoridation (adjusted fluoride in the public water supply). Is it safe to use this tap water for my baby?
- Is all bottled water low in fluoride?
- Can mixing formula with optimally fluoridated tap water cause moderate or severe fluorosis?
- Are children today at greater risk for developing fluorosis from infant formula mixed with fluoridated water than children in the past?
- Will using only low fluoride water to mix formula eliminate the risk for fluorosis?
- What can be done to reduce my child's chance of developing fluorosis?

What is the best source of nutrition for infants?

Breastfeeding is ideal for infants. CDC is committed to increasing breastfeeding rates throughout the United States and to promoting optimal breastfeeding practices. Both babies and mothers gain many benefits from breastfeeding. Breast milk is easy to digest and contains antibodies that can protect infants from bacterial and viral infections. More can be learned about this subject at http://www.cdc.gov/breastfeeding/.
If breastfeeding is not possible, several types of formula are available for infant feeding. Parents and caregivers are encouraged to speak with their pediatrician about which type of infant formula is best suited for their child.

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What type of water does CDC recommend for mixing infant formula?

Parents should follow the advice of the formula manufacturer and their child's doctor for the type of water appropriate for the formula they are using. Parents and caregivers of infants fed primarily with formula from concentrate who are concerned about the effect that mixing their infant's formula with fluoridated water may have in developing enamel fluorosis can lessen this exposure by mixing formula with low fluoride water most or all of the time. This may be tap water, if the public water system is not fluoridated (check with your local water utility). If tap water is fluoridated or has substantial natural fluoride (0.7 mg/L or higher), a parent may consider using a low-fluoride alternative water source. Bottled water known to be low in fluoride is labeled as purified, deionized, demineralized, distilled, or prepared by reverse osmosis. Most grocery stores sell these types of low-fluoride water. Ready to feed (no-mix) infant formula typically has little fluoride and may be preferred for use at least some of the time.

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Why is there a focus on infant formula as a source of fluoride?

Infant formula manufacturers take steps to assure that infant formula contains low fluoride levels—the products themselves are not the issue. Although formula itself has low amounts of fluoride, when infant formula concentrate is mixed with fluoridated water and used as the primary source of nutrition, it may introduce fluoride at levels above the amount recommended to minimize the risk for fluorosis. Infants consume little other than breast milk or formula during the first four to six months of life, and continue to have a high intake of liquids during the entire first year. Therefore, proportional to body weight, fluoride intake from liquids is generally higher for younger or smaller children than for older children, adolescents, or adults. Mixing concentrate with fluoridated tap water on an occasional basis is unlikely to be of much risk. However, when used consistently as the primary source of nutrition over longer periods of the first year, a child may receive enough fluoride to increase his/her chances of developing very mild or mild fluorosis.

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What types of infant formula may increase the risk for enamel fluorosis?

There are three types of formula, including powder, which comes in bulk or single serve packets, concentrated liquid, or ready-to-feed formula. Ready-to-feed formula is more convenient, but also more expensive. Powder formula is usually the least expensive, but requires mixing with water, as does the liquid concentrate.

Ready-to-feed formula contains little fluoride and does not contribute to enamel fluorosis. Those types of formula that require mixing with water—powdered or liquid concentrates—can be the child's main source of fluoride intake (depending upon the water source) and may contribute to this condition.

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What is enamel fluorosis?

Enamel fluorosis is a hypomineralization of the enamel surface of the tooth that develops during tooth formation. Clinically, this appears as a range of cosmetic changes varying from barely noticeable white lines or spots to pitting and staining of the outer enamel layer. More cosmetically objectionable forms of this condition can occur when young children consume excess fluoride from all sources during critical periods of tooth development. More can be learned about enamel fluorosis at http://www.cdc.gov/fluoridation/safety/enamel_fluorosis.htm.

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Should all parents consider mixing formula with water from sources other than tap water?

There is no evidence that water containing low concentrations of fluoride introduces a risk for enamel fluorosis in the developing teeth of young children. Some tap water and most bottled water contain low concentrations of fluoride. Mixing concentrate with fluoridated tap water on an occasional basis is unlikely to be of much consequence. For infants whose primary nutrition source is formula from concentrates, parents should take into consideration the fluoride concentration in their water source when making decisions about mixing formula.

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How can I find out what the concentration of fluoride is in my tap water?

The best source of information on fluoride levels in your water system is your local water utility. Other knowledgeable sources may be a local public health authority, dentist, dental hygienist, or physician. My Water's Fluoride on the CDC Web site allows consumers in currently participating states to learn the fluoridation status of their water system. Nearly all tap water contains some natural fluoride, but, depending on the water system, the concentration can range from very low (0.2 mg/L fluoride or less) to very high (2.0 mg/L fluoride or higher). Approximately 69% of all public water systems serving about 184 million people have optimally adjusted fluoride in their water—that is between 0.7 and 1.2 mg/L fluoride.

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My city has community water fluoridation (adjusted fluoride in the public water supply). Is it safe to use this tap water for my baby?

Water fluoridation is safe, effective, and healthy. Water fluoridated at a level optimal for oral health poses no known health risks for infants. However, some children may develop enamel fluorosis, a cosmetic condition. All persons should know whether the fluoride concentration in their primary source of drinking water is below optimal (less than 0.7 mg/L fluoride), optimal (0.7–1.2 mg/L fluoride), or above optimal (greater than 1.2 mg/L fluoride). Use of water below 0.7 mg/L fluoride contributes to a very small risk of developing this condition. The risk increases with an increasing level of fluoride and depends on other factors, such as age and weight of the child and how much formula they drink each day. Knowledge of the fluoride level in the drinking water is also the basis for other individual and professional decisions regarding use of fluoride products by children, such as fluoride toothpaste, mouth rinses, or dietary supplements. In addition, people living in areas where naturally occurring fluoride levels in drinking water are greater than 2 mg/L should consider an alternative water source or home water treatments to reduce the risk of fluorosis for young children. Contact your local water company or utility to learn the fluoride level in your water supply.

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Is all bottled water low in fluoride?

Most bottled water contains low fluoride concentrations; however, much variation exists—some brands may contain optimal or higher levels. Because there currently is no requirement to display the fluoride concentration on bottle labels, you may need to contact the bottler to learn the level of fluoride in bottled drinking water. Certain types of bottled water are, by definition, always low in fluoride and can reliably be used for mixing formula. Water labeled as purified, distilled, deionized, demineralized, or produced through reverse osmosis are always low in fluoride.

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Can mixing formula with optimally fluoridated tap water cause moderate or severe fluorosis?

For decades, parents have been mixing infant formula with optimally fluoridated tap water (a level determined by the U.S. Public Health Service between 0.7 mg/L fluoride and 1.2 mg/L fluoride and maintained by your water utility to maximize decay prevention and limit fluorosis potential) and no association has been observed between infant formula use and an increased risk for moderate or severe fluorosis. There is no clear evidence that using infant formula from concentrates as the primary souce of nutrition increases a child's chances of developing the more severe forms of fluorosis; however, there may be an increased risk for very mild to mild forms.

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Are children today at greater risk for developing fluorosis from infant formula mixed with fluoridated water than children in the past?

Children today are at no greater risk of developing enamel fluorosis from infant formula than children in previous generations. Little has changed with regard to the amount of fluoride consumed or the concentration of fluoride in the formula. There has always been some level of very mild and mild fluorosis in children, but it was thought to be caused by fluoride intake after age one. However, new evidence indicates that fluoride exposure during the first year of life may play a greater role in developing fluorosis than was previously thought, so parents may consider reducing the potential for this condition by limiting fluoride from this source.

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Will using only low fluoride water to mix formula eliminate the risk for fluorosis?

Using only water with low fluoride levels to mix formula will not eliminate the risk of enamel fluorosis. But following such a practice may reduce the chance of fluorosis occurring. This condition occurs among some children in all communities, even in communities with a low natural concentration of fluoride in the water. Other factors that contribute to developing fluorosis include swallowing of toothpaste and use of dietary supplements that include fluoride (tablets or drops). Learn more about simple steps to take care of children's teeth. (PDF–170K)

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What can be done to reduce my child's chance of developing fluorosis?

CDC has developed recommendations to reduce the risk for enamel fluorosis. Remember, fluorosis can only occur during the time of enamel formation, before the teeth come into the mouth. Young children who use multiple sources of fluoride such as fluoride toothpaste, dietary supplements, and water with optimal or higher natural fluoride have a higher risk for this condition. Community water fluoridation is a safe, effective, and inexpensive way to prevent tooth decay, and CDC recommends continuing and extending this practice. Steps can be taken to reduce the potential for enamel fluorosis associated with drinking water and other fluoride products. Learn more about recommendations on how to reduce the risk for enamel fluorosis.

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Date last reviewed: August 28, 2009
Date last modified: August 28, 2009
Content source: Division of Oral Health, National Center for Chronic Disease Prevention and Health Promotion

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MMWR

Weekly

October 22, 1999 /48(41);933-940

Achievements in Public Health, 1900-1999: Fluoridation of Drinking Water to Prevent Dental Caries

Fluoridation of community drinking water is a major factor responsible for the decline in dental caries (tooth decay) during the second half of the 20th century. The history of water fluoridation is a classic example of clinical observation leading to epidemiologic investigation and community-based public health intervention. Although other fluoride-containing products are available, water fluoridation remains the most equitable and cost-effective method of delivering fluoride to all members of most communities, regardless of age, educational attainment, or income level.

Dental Caries

Dental caries is an infectious, communicable, multifactorial disease in which bacteria dissolve the enamel surface of a tooth (1). Unchecked, the bacteria then may penetrate the underlying dentin and progress into the soft pulp tissue. Dental caries can result in loss of tooth structure and discomfort. Untreated caries can lead to incapacitating pain, a bacterial infection that leads to pulpal necrosis, tooth extraction and loss of dental function, and may progress to an acute systemic infection. The major etiologic factors for this disease are specific bacteria in dental plaque (particularly *Streptococcus mutans* and lactobacilli) on susceptible tooth surfaces and the availability of fermentable carbohydrates.

At the beginning of the 20th century, extensive dental caries was common in the United States and in most developed countries (2). No effective measures existed for preventing this disease, and the most frequent treatment was tooth extraction. Failure to meet the minimum standard of having six opposing teeth was a leading cause of rejection from military service in both world wars (3,4). Pioneering oral epidemiologists developed an index to measure the prevalence of dental caries using the number of decayed, missing, or filled teeth (DMFT) or decayed, missing, or filled tooth surfaces (DMFS) (5) rather than merely presence of dental caries, in part because nearly all persons in most age groups in the United States had evidence of the disease. Application of the DMFT index in epidemiologic surveys throughout the United States in the 1930s and 1940s allowed quantitative distinctions in dental caries experience among communities--an innovation that proved critical in identifying a preventive agent and evaluating its effects.

History of Water Fluoridation

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Soon after establishing his dental practice in Colorado Springs, Colorado, in 1901, Dr. Frederick S. McKay noted an unusual permanent stain or "mottled enamel" (termed "Colorado brown stain" by area residents) on the teeth of many of his patients (6). After years of personal field investigations, McKay concluded that an agent in the public water supply probably was responsible for mottled enamel. McKay also observed that teeth affected by this condition seemed less susceptible to dental caries (7).

Dr. F. L. Robertson, a dentist in Bauxite, Arkansas, noted the presence of mottled enamel among children after a deep well was dug in 1909 to provide a local water supply. A hypothesis that something in the water was responsible for mottled enamel led local officials to abandon the well in 1927. In 1930, H. V. Churchill, a chemist with Aluminum Company of America, an aluminum manufacturing company that had bauxite mines in the town, used a newly available method of spectrographic analysis that identified high concentrations of fluoride (13.7 parts per million [ppm]) in the water of the abandoned well (8). Fluoride, the ion of the element fluorine, almost universally is found in soil and water but generally in very low concentrations (less than 1.0 ppm). On hearing of the new analytic method, McKay sent water samples to Churchill from areas where mottled enamel was endemic; these samples contained high levels of fluoride (2.0-12.0 ppm).

The identification of a possible etiologic agent for mottled enamel led to the establishment in 1931 of the Dental Hygiene Unit at the National Institute of Health headed by Dr. H. Trendley Dean. Dean's primary responsibility was to investigate the association between fluoride and mottled enamel (see box). Adopting the term "fluorosis" to replace "mottled enamel," Dean conducted extensive observational epidemiologic surveys and by 1942 had documented the prevalence of dental fluorosis for much of the United States (9). Dean developed the ordinally scaled Fluorosis Index to classify this condition. Very mild fluorosis was characterized by small, opaque "paper white" areas affecting less than or equal to 25% of the tooth surface; in mild fluorosis, 26%-50% of the tooth surface was affected. In moderate dental fluorosis, all enamel surfaces were involved and susceptible to frequent brown staining. Severe fluorosis was characterized by pitting of the enamel, widespread brown stains, and a "corroded" appearance (9).

Dean compared the prevalence of fluorosis with data collected by others on dental caries prevalence among children in 26 states (as measured by DMFT) and noted a strong inverse relation (10). This cross-sectional relation was confirmed in a study of 21 cities in Colorado, Illinois, Indiana, and Ohio (11). Caries among children was lower in cities with more fluoride in their community water supplies; at concentrations greater than 1.0 ppm, this association began to level off. At 1.0 ppm, the prevalence of dental fluorosis was low and mostly very mild.

The hypothesis that dental caries could be prevented by adjusting the fluoride level of community water supplies from negligible levels to 1.0-1.2 ppm was tested in a prospective field study conducted in four pairs of cities (intervention and control) starting in 1945: Grand Rapids and Muskegon, Michigan; Newburgh and Kingston, New York; Evanston and Oak Park, Illinois; and Brantford and Sarnia, Ontario, Canada. After conducting sequential cross-sectional surveys in these communities over 13-15 years, caries was reduced 50%-70% among children in the communities with fluoridated water (12). The prevalence of dental fluorosis in the intervention communities was comparable with what had been observed in cities where drinking water contained natural fluoride at 1.0 ppm. Epidemiologic investigations of patterns of water consumption and caries experience across different climates and geographic regions in the United States led in 1962 to the development of a recommended optimum range of fluoride concentration of 0.7-1.2 ppm, with the lower concentration recommended for warmer climates (where water consumption was higher) and the higher concentration for colder climates (13).

The effectiveness of community water fluoridation in preventing dental caries prompted rapid adoption of this public health measure in cities throughout the United States. As a result, dental caries declined precipitously during the second half of the 20th century. For example, the mean DMFT among persons aged 12 years in the United States declined 68%, from 4.0 in 1966-1970 (14) to 1.3 in 1988-1994 (CDC, unpublished data, 1999) (Figure 1). The American Dental Association, the American Medical Association, the World Health Organization, and other professional and scientific organizations quickly endorsed water fluoridation. Knowledge about the benefits of water fluoridation led to the development of other modalities for delivery of fluoride, such as toothpastes, gels, mouth rinses, tablets, and drops. Several countries in Europe and Latin America have added fluoride to table salt.

Effectiveness of Water Fluoridation

Early studies reported that caries reduction attributable to fluoridation ranged from 50% to 70%, but by the mid-1980s the mean DMFS scores in the permanent dentition of children who lived in communities with fluoridated water were only 18% lower than among those living in communities without fluoridated water (15). A review of studies on the effectiveness of water fluoridation conducted in the United States during 1979-1989 found that caries reduction was 8%-37% among adolescents (mean: 26.5%) (16).

Since the early days of community water fluoridation, the prevalence of dental caries has declined in both communities with and communities without fluoridated water in the United States. This trend has been attributed largely to the diffusion of fluoridated water to areas without fluoridated water through bottling and processing of foods and beverages in areas with fluoridated water and widespread use of fluoride toothpaste (17). Fluoride toothpaste is efficacious in preventing dental caries, but its effectiveness depends on frequency of use by persons or their caregivers. In contrast, water fluoridation reaches all residents of communities and generally is not dependent on individual behavior.

Although early studies focused mostly on children, water fluoridation also is effective in preventing dental caries among adults. Fluoridation reduces enamel caries in adults by 20%-40% (16) and prevents caries on the exposed root surfaces of teeth, a condition that particularly affects older adults.

Water fluoridation is especially beneficial for communities of low socioeconomic status (18). These communities have a disproportionate burden of dental caries and have less access than higher income communities to dental-care services and other sources of fluoride. Water fluoridation may help reduce such dental health disparities.

Biologic Mechanism

Fluoride's caries-preventive properties initially were attributed to changes in enamel during tooth development because of the association between fluoride and cosmetic changes in enamel and a belief that fluoride incorporated into enamel during tooth development would result in a more acid-resistant mineral. However, laboratory and epidemiologic research suggests that fluoride prevents dental caries predominately after eruption of the tooth into the mouth, and its actions primarily are topical for both adults and children (1). These mechanisms include 1) inhibition of demineralization, 2) enhancement of remineralization, and 3) inhibition of bacterial activity in dental plaque (1).

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Enamel and dentin are composed of mineral crystals (primarily calcium and phosphate) embedded in an organic protein/lipid matrix. Dental mineral is dissolved readily by acid produced by cariogenic bacteria when they metabolize fermentable carbohydrates. Fluoride present in solution at low levels, which becomes concentrated in dental plaque, can substantially inhibit dissolution of tooth mineral by acid.

Fluoride enhances remineralization by adsorbing to the tooth surface and attracting calcium ions present in saliva. Fluoride also acts to bring the calcium and phosphate ions together and is included in the chemical reaction that takes place, producing a crystal surface that is much less soluble in acid than the original tooth mineral (1).

Fluoride from topical sources such as fluoridated drinking water is taken up by cariogenic bacteria when they produce acid. Once inside the cells, fluoride interferes with enzyme activity of the bacteria and the control of intracellular pH. This reduces bacterial acid production, which directly reduces the dissolution rate of tooth mineral (19).

Population Served by Water Fluoridation

By the end of 1992, 10,567 public water systems serving 135 million persons in 8573 U.S. communities had instituted water fluoridation (20). Approximately 70% of all U.S. cities with populations of greater than 100,000 used fluoridated water. In addition, 3784 public water systems serving 10 million persons in 1924 communities had natural fluoride levels greater than or equal to 0.7 ppm. In total, 144 million persons in the United States (56% of the population) were receiving fluoridated water in 1992, including 62% of those served by public water systems. However, approximately 42,000 public water systems and 153 U.S. cities with populations greater than or equal to 50,000 have not instituted fluoridation.

Cost Effectiveness and Cost Savings of Fluoridation

Water fluoridation costs range from a mean of 31 cents per person per year in U.S. communities of greater than 50,000 persons to a mean of $2.12 per person in communities of less than 10,000 (1988 dollars) (21). Compared with other methods of community-based dental caries prevention, water fluoridation is the most cost effective for most areas of the United States in terms of cost per saved tooth surface (22).

Water fluoridation reduces direct health-care expenditures through primary prevention of dental caries and avoidance of restorative care. Per capita cost savings from 1 year of fluoridation may range from negligible amounts among very small communities with very low incidence of caries to $53 among large communities with a high incidence of disease (CDC, unpublished data, 1999). One economic analysis estimated that prevention of dental caries, largely attributed to fluoridation and fluoride-containing products, saved $39 billion (1990 dollars) in dental-care expenditures in the United States during 1979-1989 (23).

Safety of Water Fluoridation

Early investigations into the physiologic effects of fluoride in drinking water predated the first community field trials. Since 1950, opponents of water fluoridation have claimed it increased the risk for cancer, Down syndrome, heart disease, osteoporosis and bone fracture, acquired immunodeficiency syndrome, low intelligence, Alzheimer disease, allergic reactions, and other health conditions (24). The safety and effectiveness of water fluoridation have been re-evaluated

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frequently, and no credible evidence supports an association between fluoridation and any of these conditions (25).

21st Century Challenges

Despite the substantial decline in the prevalence and severity of dental caries in the United States during the 20th century, this largely preventable disease is still common. National data indicate that 67% of persons aged 12-17 years (26) and 94% of persons aged greater than or equal to 18 years (27) have experienced caries in their permanent teeth.

Among the most striking results of water fluoridation is the change in public attitudes and expectations regarding dental health. Tooth loss is no longer considered inevitable, and increasingly adults in the United States are retaining most of their teeth for a lifetime (12). For example, the percentage of persons aged 45-54 years who had lost all their permanent teeth decreased from 20.0% in 1960-1962 (28) to 9.1% in 1988-1994 (CDC, unpublished data, 1999). The oldest post-World War II "baby boomers" will reach age 60 years in the first decade of the 21st century, and more of that birth cohort will have a relatively intact dentition at that age than any generation in history. Thus, more teeth than ever will be at risk for caries among persons aged greater than or equal to 60 years. In the next century, water fluoridation will continue to help prevent caries among these older persons in the United States.

Most persons in the United States support community water fluoridation (29). Although the proportion of the U.S. population drinking fluoridated water increased fairly quickly from 1945 into the 1970s, the rate of increase has been much lower in recent years. This slowing in the expansion of fluoridation is attributable to several factors: 1) the public, some scientists, and policymakers may perceive that dental caries is no longer a public health problem or that fluoridation is no longer necessary or effective; 2) adoption of water fluoridation can require political processes that make institution of this public health measure difficult; 3) opponents of water fluoridation often make unsubstantiated claims about adverse health effects of fluoridation in attempts to influence public opinion (24); and 4) many of the U.S. public water systems that are not fluoridated tend to serve small populations, which increases the per capita cost of fluoridation. These barriers present serious challenges to expanding fluoridation in the United States in the 21st century. To overcome the challenges facing this preventive measure, public health professionals at the national, state, and local level will need to enhance their promotion of fluoridation and commit the necessary resources for equipment, personnel, and training.

Reported by Div of Oral Health, National Center for Chronic Disease Prevention and Health Promotion, CDC.

References

1. Featherstone JD. Prevention and reversal of dental caries: role of low level fluoride. Community Dent Oral Epidemiol 1999;27:31-40.
2. Burt BA. Influences for change in the dental health status of populations: an historical perspective. J Public Health Dent 1978;38:272-88.
3. Britten RH, Perrott GSJ. Summary of physical findings on men drafted in world war. Pub Health Rep 1941;56:41-62.
4. Klein H. Dental status and dental needs of young adult males, rejectable, or acceptable for military service, according to Selective Service dental requirements. Pub Health Rep

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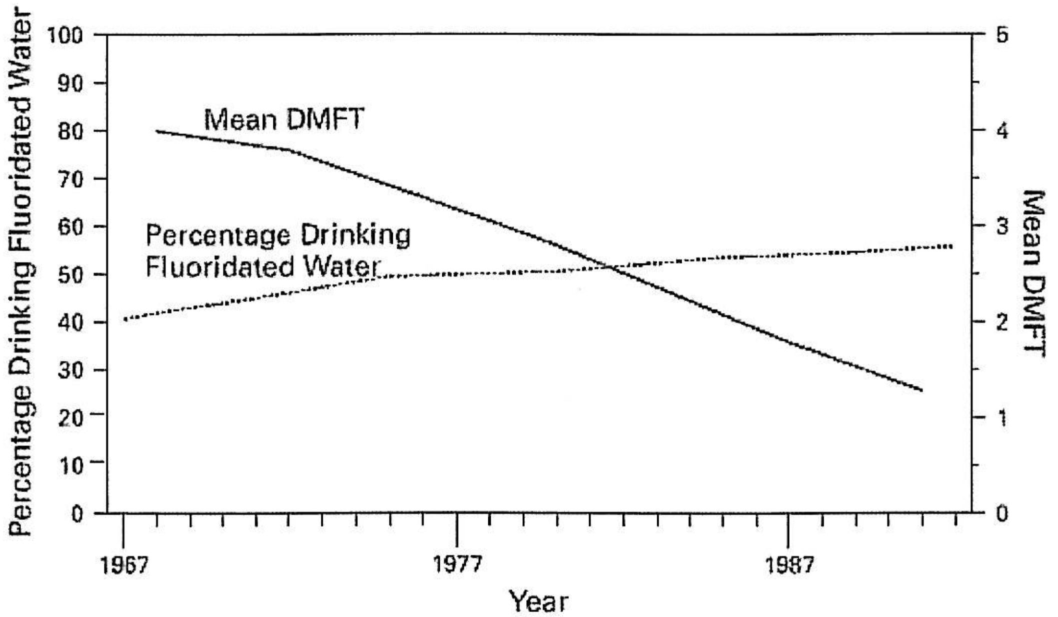
1941; 56:1369-87.

5. Klein H, Palmer CE, Knutson JW. Studies on dental caries. I. Dental status and dental needs of elementary school children. Pub Health Rep 1938;53:751-65.
6. McKay FS, Black GV. An investigation of mottled teeth: an endemic developmental imperfection of the enamel of the teeth, heretofore unknown in the literature of dentistry. Dental Cosmos 1916;58:477-84.
7. McKay FS. Relation of mottled enamel to caries. J Am Dent A 1928;15:1429-37.
8. Churchill HV. Occurrence of fluorides in some waters of the United States. J Ind Eng Chem 1931;23:996-8.
9. Dean HT. The investigation of physiological effects by the epidemiological method. In: Moulton FR, ed. Fluorine and dental health. Washington, DC: American Association for the Advancement of Science 1942:23-31.
10. Dean HT. Endemic fluorosis and its relation to dental caries. Public Health Rep 1938;53:1443-52.
11. Dean HT. On the epidemiology of fluorine and dental caries. In: Gies WJ, ed. Fluorine in dental public health. New York, New York: New York Institute of Clinical Oral Pathology, 1945:19-30.
12. Burt BA, Eklund SA. Dentistry, dental practice, and the community. 5th ed. Philadelphia, Pennsylvania: WB Saunders, 1999.
13. Public Health Service. Public Health Service drinking water standards--revised 1962. Washington, DC: US Department of Health, Education, and Welfare, 1962. PHS publication no. 956.
14. National Center for Health Statistics. Decayed, missing, and filled teeth among youth 12-17 years--United States. Rockville, Maryland: US Department of Health, Education, and Welfare, Public Health Service, Health Resources Administration, 1974. Vital and health statistics, vol 11, no. 144. DHEW publication no. (HRA)75-1626.
15. Brunelle JA, Carlos JP. Recent trends in dental caries in US children and the effect of water fluoridation. J Dent Res 1990;69:723-7.
16. Newbrun E. Effectiveness of water fluoridation. J Public Health Dent 1989;49:279-89.
17. Horowitz HS. The effectiveness of community water fluoridation in the United States. J Public Health Dent 1996;56:253-8.
18. Riley JC, Lennon MA, Ellwood RP. The effect of water fluoridation and social inequalities on dental caries in 5-year-old children. Int J Epidemiol 1999;28:300-5.
19. Shellis RP, Duckworth RM. Studies on the cariostatic mechanisms of fluoride. Int Dent J 1994;44(3 suppl 1):263-73.
20. CDC. Fluoridation census 1992. Atlanta, Georgia: US Department of Health and Human Services, Public Health Service, CDC, National Center for Prevention Services, Division of Oral Health, 1993.
21. Ringelberg ML, Allen SJ, Brown LJ. Cost of fluoridation: 44 Florida communities. J Public Health Dent 1992;52:75-80.
22. Burt BA, ed. Proceedings for the workshop: cost effectiveness of caries prevention in dental public health. J Public Health Dent 1989;49(5, special issue):251-344.
23. Brown LJ, Beazoglou T, Heffley D. Estimated savings in U.S. dental expenditures, 1979-89. Public Health Rep 1994;109:195-203.
24. Hodge HC. Evaluation of some objections to water fluoridation. In: Newbrun E, ed. Fluorides and dental caries. 3rd ed. Springfield, Illinois: Charles C. Thomas, 1986:221-55.
25. National Research Council. Health effects of ingested fluoride. Washington, DC: National Academy Press, 1993.
26. Kaste LM, Selwitz RH, Oldakowski RJ, Brunelle JA, Winn DM, Brown LJ. Coronal caries in the primary and permanent dentition of children and adolescents 1-17 years of

age: United States, 1988-1991. J Dent Res 1996;75:631-41.
27. Winn DM, Brunelle JA, Selwitz RH, et al. Coronal and root caries in the dentition of adults in the United States, 1988-1991. J Dent Res 1996;75:642-51.
28. National Center for Health Statistics. Decayed, missing, and filled teeth in adults--United States, 1960-1962. Rockville, Maryland: US Department of Health, Education, and Welfare, Public Health Service, Health Resources Administration, 1973. Vital and health statistics vol 11, no. 23. DHEW publication no. (HRA)74-1278.
29. American Dental Association Survey Center. 1998 consumers' opinions regarding community water fluoridation. Chicago, Illinois: American Dental Association, 1998.

Figure 1

FIGURE 1. Percentage of population residing in areas with fluoridated community water systems and mean number of decayed, missing (because of caries), or filled permanent teeth (DMFT) among children aged 12 years — United States, 1967–1992



Sources:

1. CDC. Fluoridation census 1992. Atlanta, Georgia: US Department of Health and Human Services, Public Health Service, CDC, National Center for Prevention Services, Division of Oral Health, 1993.
2. National Center for Health Statistics. Decayed, missing, and filled teeth among youth 12–17 years—United States. Rockville, Maryland: US Department of Health, Education, and Welfare, Public Health Service, Health Resources Administration, 1974. Vital and health statistics, vol 11, no. 144. DHEW publication no. (HRA)75-1626.
3. National Center for Health Statistics. Decayed, missing, and filled teeth among persons 1–74 years—United States. Hyattsville, Maryland: US Department of Health and Human Services, Public Health Service, Office of Health Research, Statistics, and Technology, 1981. Vital and health statistics, vol 11, no. 223. DHHS publication no. (PHS)81-1673.
4. National Institute of Dental Research. Oral health of United States children: the National Survey of Dental Caries in U.S. School Children, 1986–1987. Bethesda, Maryland: US Department of Health and Human Services, Public Health Service, National Institutes of Health, 1989. NIH publication no. 89-2247.
5. CDC, unpublished data, third National Health and Nutrition Examination Survey, 1988–1994.

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Disclaimer All *MMWR* HTML versions of articles are electronic conversions from ASCII text into HTML. This conversion may have resulted in character translation or format errors in the HTML version. Users should not volume > 2.5 L/day, and up to 12% have frank nephrogenic diabetes insipidus characterized by a urine volume > 3 L/day (Mukhopadhyay et al. 2001).

Five papers described dental fluorosis in association with diabetes insipidus or polydipsia (Table 2-3). Two of the papers described cases of dental fluorosis in the United States resulting from fluoride concentrations of 1, 1.7, or 2.6 mg/L in drinking water (Juncos and Donadio 1972; Greenberg et al. 1974). The two individuals drinking water with fluoride at 1.7 and 2.6 mg/L also had roentgenographic bone changes consistent with "systemic fluorosis"[8] (Juncos and Donadio 1972). These patients and four other renal patients in the U.S. "in whom fluoride may have been the cause of detectable clinical and roentgenographic effects" were also reported by Johnson et al. (1979); most of the patients had urine volumes exceeding 3 L/day and drinking water with fluoride concentrations around 1.7-3 mg/L.

Moderate and severe dental fluorosis have been reported in diabetes insipidus patients in other countries with drinking water containing fluoride at 0.5 mg/L (Klein 1975) or 1 mg/L (Seow and Thomsett 1994), and severe dental fluorosis with skeletal fluorosis has been reported with fluoride at 3.4 mg/L (Mehta et al. 1998). Greenberg et al. (1974) recommended that children with any disorder that gives rise to polydipsia and polyuria[9] be supplied a portion of their water from a nonfluoridated source.

Table 2-4 provides examples of fluoride intake by members of several population subgroups characterized by above-average water consumption (athletes and workers, patients with diabetes mellitus or diabetes insipidus). It should be recognized that, for some groups of people with high water intakes (e.g., those with a disease condition or those playing indoor sports such as basketball or hockey), there probably will be little correlation of water intake with outdoor temperature—such individuals in northern states would consume approximately the same amounts of water as their counterparts in southern states. However, fluoridation still varies from state to state (Appendix B), so that some individuals could consume up to 1.7 times as much as others for the same water intake (1.2 versus 0.7 mg/L).

Background Food

Measured fluoride in samples of human breast milk is very low. Dabeka et al. (1986) found detectable concentrations in only 92 of 210 samples (44%) obtained in Canada, with fluoride ranging from <0.004 to 0.097 mg/L. The mean concentration in milk from mothers in fluoridated communities (1 mg/L in the water) was 0.0098 mg/L; in nonfluoridated communities, the mean was 0.0044 mg/L). Fluoride concentrations were correlated with the presence of fluoride in the mother's drinking water. Spak et al. (1983) reported mean fluoride concentrations in colostrum of 0.0053 mg/L (0.28 μM/L) in an area in Sweden with fluoride at 0.2 mg/L in drinking water and 0.0068 mg/L (0.36 μM/L) in an area with fluoride at 1.0 mg/L in the drinking water; in the fluoridated area, the mean fluoride concentration in mature milk was 0.007 mg/L

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[8] These two individuals also had impaired renal function, which could have increased their retention of fluoride (see Chapter 3).

[9] Greenberg et al. (1974) listed "central diabetes insipidus, psychogenic water ingestion, renal medullary disease, including hypercalemic nephropathy, hypokalemic nephropathy and anatomic and vascular disturbances and those diseases causing solute diuresis" as disorders associated with "excessive" consumption of water and therefore the possibility of "fluoride toxicity in a community with acceptable fluoride concentration."

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TABLE 2-3 Case Reports of Fluorosis in Association with Diabetes Insipidus or Polydipsia

Study Subjects	Exposure Conditions	Comments	Reference
(a) 18-year-old boy, 57.4 kg (b) 17-year-old girl, 45.65 kg (United States)	(a) "high" intake of well water containing fluoride at 2.6 mg/L since early childhood; current intake, 7.6 L/day (0.34 mg/kg/day) (b) "high" intake of water containing fluoride at 1.7 mg/L since infancy; current intake, 4 L/day (0.15 mg/kg/day)	Dental fluorosis and roentgenographic bone changes consistent with "systemic fluorosis," attributed to the combination of renal insufficiency and polydipsia (the latter resulting from the renal disease); reported by the Mayo Clinic	Juncos and Donadio 1972
2 boys (ages 10 and 11) with familial nephrogenic diabetes insipidus (United States)	Fluoridated communities in the U.S. (1 mg/L); one child since birth, one since age 4; fluid intake ranged from 2.6 to 6 times normal daily intake for age (approximately 1.25-3 L/day at time of study)	Dental fluorosis; fluoride concentrations in deciduous teeth (enamel layer 50-100 µm from surface) 3-6 times those in controls (normal boys aged 10-14 residing in an area with fluoride at 1 mg/L)	Greenberg et al. 1974
Mother and four children with familial pituitary diabetes insipidus (Israel)	Water had "lower than accepted" fluoride content (0.5 mg/L); water consumption by mother and two teenage daughters (none used vasopressin) was 10-15 L/day each; two younger children treated for diabetes insipidus from ages 3 and 5	Dental fluorosis in all four children: severe in the older two who were not treated for diabetes insipidus, milder in the two younger children who were treated for diabetes insipidus. Mother also had diabetes insipidus and fluorosis; she had grown up in Kurdistan with an unknown water fluoride content	Klein 1975
Six cases of familial pituitary diabetes insipidus (Australia)	Children had average water intake of 8-10 L/day; two of the children lived in fluoridated areas (1 mg/L)	Moderate (one child) or severe (one child) dental fluorosis in the two children who lived in fluoridated areas	Seow and Thomsett 1994
Two brothers with pituitary diabetes insipidus (ages 17 and 7) (India)	Well water with fluoride at 3.4 mg/L	Severe dental fluorosis, skeletal deformities, and radiological evidence of skeletal fluorosis	Mehta et al. 1998

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TABLE 2-4 Examples of Fluoride Intake from Drinking Water by Members of Selected Population Subgroups Living in Fluoridated Areas[a]

	Typical Consumers[b]				High Consumers[c]			
	Water Consumption		Fluoride Intake[d]		Water Consumption		Fluoride Intake[d]	
Population Subgroup (Weight)	mL/day	mL/kg/day	mg/day	mg/kg/day	mL/day	mL/kg/day	mg/day	mg/kg/day
Athletes, workers, military (50 kg)	2,500	50	1.8-3.0	0.035-0.06	3,500	70	2.5-4.2	0.049-0.084
Athletes, workers, military (70 kg)	3,500	50	2.5-4.2	0.035-0.06	4,900	70	3.4-5.9	0.049-0.084
Athletes, workers, military (100 kg)	5,000	50	3.5-6.0	0.035-0.06	7,000	70	4.9-8.4	0.049-0.084
Athletes and workers (120 kg)	6,000	50	4.2-7.2	0.035-0.06	8,400	70	5.9-10	0.049-0.084
DM patients (20 kg)	1,000	50	0.7-1.2	0.035-0.06	2,000	100	1.4-2.4	0.07-0.12
DM patients (70 kg)	3,500	50	2.5-4.2	0.035-0.06	4,900	70	3.4-5.9	0.049-0.084
NDI patients (20 kg)	1,000	50	0.7-1.2	0.035-0.06	3,000	150	2.1-3.6	0.11-0.18
NDI patients (70 kg)	3,500	50	2.5-4.2	0.035-0.06	10,500	150	7.4-13	0.11-0.18

Abbreviations: DM, diabetes mellitus; NDI, nephrogenic diabetes insipidus

[a] Assumes all drinking water is from fluoridated community (municipal) sources.

[b] Based on a typical consumption rate for the population subgroup.

[c] Based on a reasonably high (but not upper bound) consumption rate for the population subgroup; some individual exposures could be higher.

[d] Based on fluoride concentrations of 0.7-1.2 mg/L.

(0.37 µM/L). No statistically significant difference in milk fluoride concentration between the two areas was found.

Hossny et al. (2003) reported fluoride concentrations in breast milk of 60 mothers in Cairo, Egypt, ranging from 0.002 to 0.01 mg/L [0.1-0.6 µM/L; median, 0.0032 mg/L (0.17 µM/L); mean, 0.0046 mg/L (0.24 µM/L)]. Cairo is considered nonfluoridated, with a reported water fluoride concentration of 0.3 mg/L (Hossny et al. 2003). Opinya et al. (1991) found higher fluoride concentrations in mothers' milk (mean, 0.033 mg/L; range, 0.011-0.073 mg/L), but her study population was made up of mothers in Kenya with an average daily fluoride intake of 22.1 mg. However, even at very high fluoride intakes by mothers, breast milk still contains very low concentrations of fluoride compared with other dietary fluoride sources. No significant correlation was established between the fluoride in milk and the intake of fluoride in the Kenyan study (Opinya et al. 1991).

Cows' milk likewise contains very low fluoride concentrations, compared with other dietary sources such as drinking water. Dairy milk samples measured in Houston contained fluoride at 0.007 to 0.068 mg/L (average, 0.03 mg/L) (Liu et al. 1995). Milk samples in 11 Canadian cities contained 0.007-0.086 mg/L (average, 0.041 mg/L) (Dabeka and McKenzie 1987). A sample of soy milk contained much more fluoride than a sample of dairy milk, with a measured concentration of 0.491 mg/L (Liu et al. 1995).

Infant formulas vary in fluoride content, depending on the type of formula and the water with which it is prepared. Dabeka and McKenzie (1987) reported mean fluoride concentrations in ready-to-use formulas of 0.23 mg/L for formulas manufactured in the United States and 0.90 mg/L for formulas manufactured in Canada. Van Winkle et al. (1995) analyzed 64 infant formulas, 47 milk-based and 17 soy-based. For milk-based formulas, mean fluoride concentrations were 0.17 mg/L for ready-to-feed, 0.12 mg/L for liquid concentrates reconstituted with distilled water, and 0.14 mg/L for powdered concentrates reconstituted with distilled water. Mean fluoride concentrations for soy-based formulas were 0.30, 0.24, and 0.24 mg/L for ready-to-feed, liquid concentrates, and powdered concentrates, respectively (the latter two were reconstituted with distilled water). Obviously, the fluoride concentration in home-prepared formula depends on the fluoride concentrations in both the formula concentrate and the home drinking water. Fomon et al. (2000) have recommended using low-fluoride water to dilute infant formulas.

Heilman et al. (1997) found 0.01 to 8.38 µg of fluoride per g of prepared infant foods. The highest concentrations were found in chicken (1.05-8.38 µg/g); other meats varied from 0.01 µg/g (veal) to 0.66 µg/g (turkey). Other foods—fruits, desserts, vegetables, mixed foods, and cereals—ranged from 0.01 to 0.63 µg/g. The fluoride concentrations in most foods are attributable primarily to the water used in processing (Heilman et al. 1997); fluoride in chicken is due to processing methods (mechanical deboning) that leave skin and residual bone particles in the meat (Heilman et al. 1997; Fein and Cerklewski 2001). An infant consuming 2 oz (about 60 g) of chicken daily at 8 µg of fluoride per g would have an intake of about 0.48 mg (Heilman et al. 1997).

Tea can contain considerable amounts of fluoride, depending on the type of tea and its source. Tea plants take up fluoride from soil along with aluminum (Shu et al. 2003; Wong et al. 2003). Leaf tea, including black tea and green tea, is made from the buds and young leaves of the tea plant, the black tea with a fermentation process, and the green tea without. Oolong tea is intermediate between black and green tea. Brick tea, considered a low-quality tea, is made from old (mature) leaves and sometimes branches and fruits of the tea plant (Shu et al. 2003; Wong et

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al. 2003). Fluoride accumulates mostly in the leaves of the tea plant, especially the mature or fallen leaves. Measured fluoride concentrations in tea leaves range from 170 to 878 mg/kg in different types of tea, with brick tea generally having 2-4 times as much fluoride as leaf tea (Wong et al. 2003). Commercial tea brands in Sichuan Province of China ranged from 49 to 105 mg/kg dry weight for green teas and 590 to 708 mg/kg dry weight for brick teas (Shu et al. 2003). Infusions of Chinese leaf tea (15 kinds) made with distilled water have been shown to have fluoride at 0.6-1.9 mg/L (Wong et al. 2003). Brick teas, which are not common in the United States, contain 4.8-7.3 mg/L; consumption of brick teas has been associated with fluorosis in some countries (Wong et al. 2003).

Chan and Koh (1996) measured fluoride contents of 0.34-3.71 mg/L (mean, 1.50 mg/L) in caffeinated tea infusions (made with distilled, deionized water), 1.01-5.20 mg/L (mean, 3.19 mg/L) in decaffeinated tea infusions, and 0.02-0.15 mg/L (mean, 0.05 mg/L) in herbal tea infusions, based on 44 brands of tea available in the United States (Houston area). Whyte et al. (2005) reported fluoride concentrations of 1.0-6.5 mg/L in commercial teas (caffeinated and decaffeinated) obtained in St. Louis (prepared with distilled water according to label directions). Warren et al. (1996) found fluoride contents of 0.10-0.58 mg/L in various kinds and brands of coffee sold in the United States (Houston area), with a slightly lower mean for decaffeinated (0.14 mg/L) than for caffeinated (0.17 mg/L) coffee. Instant coffee had a mean fluoride content of 0.30 mg/L (all coffees tested were prepared with deionized distilled water). Fluoride concentrations of 0.03 mg/L (fruit tea) to 3.35 mg/L (black tea) were reported for iced-tea products sold in Germany primarily by international companies (Behrendt et al. 2002).

In practice, fluoride content in tea or coffee as consumed will be higher if the beverage is made with fluoridated water; however, for the present purposes, the contribution from water for beverages prepared at home is included in the estimated intakes from drinking water, discussed earlier. Those estimates did not include commercially available beverages such as fruit juices (not including water used to reconstitute frozen juices), juice-flavored drinks, iced tea beverages, carbonated soft drinks, and alcoholic beverages. Kiritsy et al. (1996) reported fluoride concentrations in juices and juice-flavored drinks of 0.02-2.8 mg/L (mean, 0.56 mg/L) for 532 different drinks (including five teas) purchased in Iowa City (although many drinks represented national or international distribution); frozen-concentrated beverages were reconstituted with distilled water before analysis. White grape juices had the highest mean fluoride concentration (1.45 mg/L); upper limits on most kinds of juices exceeded 1.50 mg/L. Stannard et al. (1991) previously reported fluoride concentrations from 0.15 to 6.80 mg/L in a variety of juices originating from a number of locations in the United States. The variability in fluoride concentrations is due primarily to variability in fluoride concentrations in the water used in manufacturing the product (Kiritsy et al. 1996). The high fluoride content of grape juices (and grapes, raisins, and wines), even when little or no manufacturing water is involved, is thought to be due to a pesticide (cryolite) used in grape growing (Stannard et al. 1991; Kiritsy et al. 1996; Burgstahler and Robinson 1997).

Heilman et al. (1999) found fluoride concentrations from 0.02 to 1.28 mg/L (mean, 0.72 mg/L) in 332 carbonated beverages from 17 production sites, all purchased in Iowa. In general, these concentrations reflect that of the water used in manufacturing. Estimated mean intakes from the analyzed beverages were 0.36 mg/day for 2- to 3-year-old children and 0.60 mg/day for 7- to 10-year-olds (Heilman et al. 1999). Pang et al. (1992) estimated mean daily fluoride intakes from beverages (excluding milk and water) for children of 0.36, 0.54, and 0.60 mg, for

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DMFT (Decayed, Missing & Filled teeth) Status for 12 year olds by Country
- World Health Organization Data (2004) -

Country	DMFTs	Year	Status*
Germany	0.7	2005	No water fluoridation, but salt fluoridation is common
Australia	0.8	1999	More than 50% of water is fluoridated; no salt fluoridation
Denmark	0.8	2006	No water fluoridation or salt fluoridation
Netherlands	0.8	2002	No water fluoridation or salt fluoridation
Zurich, Switzerland	0.9	2000	No water fluoridation, but salt fluoridation is common
UK *(England & Wales)*	0.9	2000	11% of water supplies are fluoridated; no salt fluoridation
Austria	1.0	2002	No water fluoridation, but salt fluoridation is available to a limited extent.
Sweden	1.0	2005	No water fluoridation or salt fluoridation
Italy	1.1	2004	No water fluoridation or salt fluoridation
Belgium	1.1	2002	No water fluoridation or salt fluoridation
Ireland	1.1	1997	More than 50% of water is fluoridated; no salt fluoridation
Finland	1.2	2006	No water fluoridation or salt fluoridation
US	1.28	1992-1994	More than 50% of water is fluoridated; no salt fluoridation
Iceland	1.4	2005	No water fluoridation or salt fluoridation
New Zealand	1.7	2005	More than 50% of water is fluoridated; no salt fluoridation
Norway	1.7	2004	No water fluoridation or salt fluoridation
France	1.9	1998	No water fluoridation, but salt fluoridation is common

Data from WHO Oral Health Country/Area Profile Programme Department of Noncommunicable Diseases Surveillance/Oral Health WHO Collaborating Centre, Malmö University, Sweden http://www.whocollab.od.mah.se/euro.html

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Two of the 12 members of the committee did not agree that severe enamel fluorosis should now be considered an adverse health effect. They agreed that it is an adverse dental effect but found that no new evidence has emerged to suggest a link between severe enamel fluorosis, as experienced in the United States, and a person's ability to function. They judged that demonstration of enamel defects alone from fluorosis is not sufficient to change the prevailing opinion that severe enamel fluorosis is an adverse cosmetic effect. Despite their disagreement on characterization of the condition, these two members concurred with the committee's conclusion that the MCLG should prevent the occurrence of this unwanted condition.

Enamel fluorosis is also of concern from an aesthetic standpoint because it discolors or results in staining of teeth. No data indicate that staining alone affects tooth function or susceptibility to caries, but a few studies have shown that tooth mottling affects aesthetic perception of facial attractiveness. It is difficult to draw conclusions from these studies, largely because perception of the condition and facial attractiveness are subjective and culturally influenced. The committee finds that it is reasonable to assume that some individuals will find *moderate* enamel fluorosis on front teeth to be detrimental to their appearance and that it could affect their overall sense of well-being. However, the available data are not adequate to categorize moderate enamel fluorosis as an adverse health effect on the basis of structural or psychological effects.

Since 1993, there have been no new studies of enamel fluorosis in U.S. communities with fluoride at 2 mg/L in drinking water. Earlier studies indicated that the prevalence of moderate enamel fluorosis at that concentration could be as high as 15%. Because enamel fluorosis has different distribution patterns among teeth, depending on when exposure occurred during tooth development and on enamel thickness, and because current indexes for categorizing enamel fluorosis do not differentiate between mottling of anterior and posterior teeth, the committee was not able to determine what percentage of moderate cases might be of cosmetic concern.

Musculoskeletal Effects

Concerns about fluoride's effects on the musculoskeletal system historically have been and continue to be focused on skeletal fluorosis and bone fracture. Fluoride is readily incorporated into the crystalline structure of bone and will accumulate over time. Since the previous 1993 NRC review of fluoride, two pharmacokinetic models were developed to predict bone concentrations from chronic exposure to fluoride. Predictions based on these models were used in the committee's assessments below.

Skeletal Fluorosis

Skeletal fluorosis is a bone and joint condition associated with prolonged exposure to high concentrations of fluoride. Fluoride increases bone density and appears to exacerbate the growth of osteophytes present in the bone and joints, resulting in joint stiffness and pain. The condition is categorized into one of four stages: a preclinical stage and three clinical stages that increase in severity. The most severe stage (clinical stage III) historically has been referred to as the "crippling" stage. At stage II, mobility is not significantly affected, but it is characterized by

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epidemiologic, and clinical data on fluoride—particularly data published since the NRC's previous (1993) report—and exposure data on orally ingested fluoride from drinking water and other sources. On the basis of its review, the committee was asked to evaluate independently the scientific basis of EPA's MCLG of 4 mg/L and SMCL of 2 mg/L in drinking water and the adequacy of those guidelines to protect children and others from adverse health effects. The committee was asked to consider the relative contribution of various fluoride sources (e.g., drinking water, food, dental-hygiene products) to total exposure. The committee was also asked to identify data gaps and to make recommendations for future research relevant to setting the MCLG and SMCL for fluoride. Addressing questions of artificial fluoridation, economics, risk-benefit assessment, and water-treatment technology was not part of the committee's charge.

THE COMMITTEE'S EVALUATION

To accomplish its task, the committee reviewed a large body of research on fluoride, focusing primarily on studies generated since the early 1990s, including information on exposure; pharmacokinetics; adverse effects on various organ systems; and genotoxic and carcinogenic potential. The collective evidence from in vitro assays, animal research, human studies, and mechanistic information was used to assess whether multiple lines of evidence indicate human health risks. The committee only considered adverse effects that might result from exposure to fluoride; it did not evaluate health risk from lack of exposure to fluoride or fluoride's efficacy in preventing dental caries.

After reviewing the collective evidence, including studies conducted since the early 1990s, the committee concluded unanimously that the present MCLG of 4 mg/L for fluoride should be lowered. Exposure at the MCLG clearly puts children at risk of developing severe enamel fluorosis, a condition that is associated with enamel loss and pitting. In addition, the majority of the committee concluded that the MCLG is not likely to be protective against bone fractures. The basis for these conclusions is expanded upon below.

Exposure to Fluoride

The major sources of exposure to fluoride are drinking water, food, dental products, and pesticides. The biggest contributor to exposure for most people in the United States is drinking water. Estimates from 1992 indicate that approximately 1.4 million people in the United States had drinking water with natural fluoride concentrations of 2.0 to 3.9 mg/L, and just over 200,000 people had concentrations equal to or exceeding 4 mg/L (the presented MCL). In 2000, it was estimated that approximately 162 million people had artificially fluoridated water (0.7 to 1.2 mg/L).

Food sources contain various concentrations of fluoride and are the second largest contributor to exposure. Beverages contribute most to estimated fluoride intake, even when excluding contributions from local tap water. The greatest source of nondietary fluoride is dental products, primarily toothpastes. The public is also exposed to fluoride from background air and from certain pesticide residues. Other sources include certain pharmaceuticals and consumer products.

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conclusions. Overall, the results are mixed, with some studies reporting a positive association and others no association.

On the basis of the committee's collective consideration of data from humans, genotoxicity assays, and studies of mechanisms of action in cell systems (e.g., bone cells in vitro), the evidence on the potential of fluoride to initiate or promote cancers, particularly of the bone, is tentative and mixed. Assessing whether fluoride constitutes a risk factor for osteosarcoma is complicated by the rarity of the disease and the difficulty of characterizing biologic dose because of the ubiquity of population exposure to fluoride and the difficulty of acquiring bone samples in nonaffected individuals.

A relatively large hospital-based case-control study of osteosarcoma and fluoride exposure is under way at the Harvard School of Public Health and is expected to be published in the summer of 2006. That study will be an important addition to the fluoride database, because it will have exposure information on residence histories, water consumption, and assays of bone and toenails. The results of that study should help to identify what future research will be most useful in elucidating fluoride's carcinogenic potential.

DRINKING-WATER STANDARDS

Maximum Contaminant Level Goal

In light of the collective evidence on various health end points and total exposure to fluoride, the committee concludes that EPA's MCLG of 4 mg/L should be lowered. Lowering the MCLG will prevent children from developing severe enamel fluorosis and will reduce the lifetime accumulation of fluoride into bone that the majority of the committee concludes is likely to put individuals at increased risk of bone fracture and possibly skeletal fluorosis, which are particular concerns for subpopulations that are prone to accumulating fluoride in their bones.

To develop an MCLG that is protective against severe enamel fluorosis, clinical stage II skeletal fluorosis, and bone fractures, EPA should update the risk assessment of fluoride to include new data on health risks and better estimates of total exposure (relative source contribution) for individuals. EPA should use current approaches for quantifying risk, considering susceptible subpopulations, and characterizing uncertainties and variability.

Secondary Maximum Contaminant Level

The prevalence of severe enamel fluorosis is very low (near zero) at fluoride concentrations below 2 mg/L. From a cosmetic standpoint, the SMCL does not completely prevent the occurrence of moderate enamel fluorosis. EPA has indicated that the SMCL was intended to reduce the severity and occurrence of the condition to 15% or less of the exposed population. The available data indicate that fewer than 15% of children will experience moderate enamel fluorosis of aesthetic concern (discoloration of the front teeth) at that concentration. However, the degree to which moderate enamel fluorosis might go beyond a cosmetic effect to create an adverse psychological effect or an adverse effect on social functioning is not known.

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Summary

Under the Safe Drinking Water Act, the U.S. Environmental Protection Agency (EPA) is required to establish exposure standards for contaminants in public drinking-water systems that might cause any adverse effects on human health. These standards include the maximum contaminant level goal (MCLG), the maximum contaminant level (MCL), and the secondary maximum contaminant level (SMCL). The MCLG is a health goal set at a concentration at which no adverse health effects are expected to occur and the margins of safety are judged "adequate." The MCL is the enforceable standard that is set as close to the MCLG as possible, taking into consideration other factors, such as treatment technology and costs. For some contaminants, EPA also establishes an SMCL, which is a guideline for managing drinking water for aesthetic, cosmetic, or technical effects.

Fluoride is one of the drinking water contaminants regulated by EPA. In 1986, EPA established an MCLG and MCL for fluoride at a concentration of 4 milligrams per liter (mg/L) and an SMCL of 2 mg/L. These guidelines are restrictions on the total amount of fluoride allowed in drinking water. Because fluoride is well known for its use in the prevention of dental caries, it is important to make the distinction here that EPA's drinking-water guidelines are not recommendations about adding fluoride to drinking water to protect the public from dental caries. Guidelines for that purpose (0.7 to 1.2 mg/L) were established by the U.S. Public Health Service more than 40 years ago. Instead, EPA's guidelines are maximum allowable concentrations in drinking water intended to prevent toxic or other adverse effects that could result from exposure to fluoride.

In the early 1990s at the request of EPA, the National Research Council (NRC) independently reviewed the health effects of ingested fluoride and the scientific basis for EPA's MCL. It concluded that the MCL was an appropriate interim standard but that further research was needed to fill data gaps on total exposure to fluoride and its toxicity. Because new research on fluoride is now available and because the Safe Drinking Water Act requires periodic reassessment of regulations for drinking-water contaminants, EPA requested that the NRC again evaluate the adequacy of its MCLG and SMCL for fluoride to protect public health.

COMMITTEE'S TASK

In response to EPA's request, the NRC convened the Committee on Fluoride in Drinking Water, which prepared this report. The committee was charged to review toxicologic,

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RCW 70.119A.080

(1) The department [Department of Health] shall administer a drinking water program which includes, but is not limited to, those program elements necessary to assume primary enforcement responsibility for part B, and section 1428 of part C of the federal safe drinking water act. …

(2) The department shall enter into an agreement of administration with the department of ecology and any other appropriate agencies, to administer the federal safe drinking water act.

(3) The department is authorized to accept federal grants for the administration of a primary program.

RCW 43.21A.445

The department of ecology, the department of natural resources, the department of health, and the oil and gas conservation committee are authorized to participate fully in and are empowered to administer all programs of Part C of the federal Safe Drinking Water Act (42 U.S.C. Sec. 300h et seq.), as it exists on June 19, 1986, contemplated for state participation in administration under the act.

40 C.F.R. 42.10

A State has primary enforcement responsibility for public water systems in the State during any period for which the Administrator determines … that such State, pursuant to appropriate State legal authority:

> (a) Has adopted drinking water regulations which are no less stringent than the national primary drinking water regulations (NPDWRs) in effect under part 141 of this chapter….

Fact Sheet on Questions About Bottled Water and Fluoride

Some consumers use bottled water as a beverage for various reasons, including as a convenient means of hydration during their activities or as a taste preference. Besides having a cost that is between one-to-five thousand times more expensive than tap water, bottled water may not have a sufficient amount of fluoride, which is important for good oral health. Some bottled waters contain fluoride, and some do not. Fluoride can occur naturally in source waters used for bottling or be added. Most bottled waters contain fluoride at levels that are less than optimal for oral health. This fact sheet covers common questions about bottled water and fluoride.

Is the amount of fluoride in bottled water listed on the label?
The U.S. Food and Drug Administration (FDA) does not require bottlers to list the fluoride content in a bottle of water, but does require fluoride additives to be listed. In 2006, the FDA approved labeling with the statement, "Drinking fluoridated water may reduce the risk of tooth decay," if the bottled water contains greater than 0.6 milligrams per liter (mg/L) and up to 1.0 mg/L.

How can I find out the level of fluoride in bottled water?
You must contact the manufacturer to ask about the fluoride content of a particular brand of bottled water.

Will the fluoride content change if the water is stored in a bottle for a lengthy period of time?
Fluoride will not react with other minerals in the water during storage, or with its plastic or glass container. The FDA considers bottled water to be safe indefinitely if produced in accordance with quality standard regulations and if stored in an unopened, properly sealed container without subsequent damage. However, many bottlers list an expiration date. If there is no expiration date, it is a reasonable practice not to consume water 2 years after the date of purchase because undetected deterioration of the packaging may have occurred.

Does consuming bottled water lead to more cavities?
Your oral health—specifically how many cavities you have—depends on many factors, only one of which is how much fluoride you get in the form of toothpaste, mouthwash, water, food, and applications by dental professionals (other factors include how often and how well you brush and floss, what you eat, and whether you get good dental care). If you mainly drink bottled water with no or low fluoride and you are not getting enough fluoride from other sources, you may get more cavities than you would if fluoridated tap water were your main water source.

Does the FDA regulate fluoride in bottled water?
Yes. The federal Food, Drug, and Cosmetic Act provides FDA with broad regulatory authority over food, including bottled water, that is introduced or delivered for interstate commerce (produced and sold in more than one state). Bottled water that is in intrastate commerce (produced and sold only in one state) is under the jurisdiction of the state in which the bottled water is produced and sold. You

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need to contact the manufacturer to ask if their product is under FDA jurisdiction or state jurisdiction.

What FDA regulations apply to bottled water?
The FDA regulations for governing the standards of "quality and identity" for bottled water are found in the Code of Federal Register 21 CFR 165.110. The FDA standards of quality state that domestic bottled water with no added fluoride may contain between 1.4 and 2.4 mg/L fluoride, depending on the annual average of maximum daily air temperatures at the location where the bottled water is sold at retail. Imported bottled water with no added fluoride may not contain fluoride in excess of 1.4 mg/L. Domestic bottled water with added fluoride can contain between 0.8 and 1.7 mg/L fluoride, depending on the annual average of maximum daily air temperatures at the location where the bottled water is sold at retail. Imported bottled water with added fluoride may not contain more than 0.8 mg/L fluoride. The labeling requirements by the FDA do not stipulate listing the actual fluoride content, so you will still need to contact the manufacturer to inquire about verified fluoride levels of their product.

Does the EPA have jurisdiction over the quality of bottled water?
The EPA does not have jurisdiction over the quality of bottled water. The U.S. Environmental Protection Agency (EPA) and the FDA have a 1979 Memorandum of Agreement specifying that the EPA regulates safe drinking water in accordance with the Safe Drinking Water Act, and the FDA regulates bottled water as a consumer beverage under the Food, Drug, and Cosmetic Act (Federal Register, Volume 44, No. 141, July 20, 1979). The FDA has its own regulations on standards of quality, identity, and good manufacturing practices that bottled water must meet.

Can I use fluoridated water for preparing infant formula?
Yes, you can use fluoridated water for preparing infant formula. However, if your child is exclusively consuming infant formula reconstituted with fluoridated water, there is an increased potential for mild dental fluorosis, which is a white spotting on teeth. Additional information can be found in the **Fact Sheet on Infant Formula.**

Related Links

- **FDA Bottled Water Regulations**
- **Ask the Regulators – Bottled Water Regulation and the FDA**
- **National Sanitation Foundation Types and Treatment of Bottled Water***

* Links to non-Federal organizations are provided solely as a service to our users. Links do not constitute an endorsement of any organization by CDC or the Federal Government, and none should be inferred. The CDC is not responsible for the content of the individual organization Web pages found at this link.

Date last reviewed: December 9, 2009
Date last updated: December 9, 2009
Content source: **Division of Oral Health, National Center for Chronic Disease Prevention and Health Promotion**
Page Located on the Web at
http://www.cdc.gov/FLUORIDATION/fact_sheets/bottled_water.htm

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MOU 225-79-2001
http://www.fda.gov/AboutFDA/PartnershipsCollaborations/MemorandaofUnderstandingMOUs/DomesticMOUs/ucm116216.htm

Memorandum of Understanding
Between
The Environmental Protection Agency
and
The Food and Drug Administration

I. Purpose:
This Memorandum of Understanding establishes an agreement between the Environmental Protection Agency (EPA) and the Food and Drug Administration (FDA) with regard to the control of direct and indirect additives to and substances in drinking water.

EPA and FDA agree:

A. That contamination of drinking water from the use and application of direct and indirect additives and other substances poses a potential public health problem;

B. That the scope of the additives problem in terms of the health significance of these contaminants in drinking water is not fully known;

C. That the possibility of overlapping jurisdiction between EPA and FDA with respect to control of drinking water additives has been the subject of Congressional as well as public concern;

D. That the authority to control the use and application of direct and indirect additives to and substances in drinking water should be vested in a single regulatory agency to avoid duplicative and inconsistent regulation;

E. That EPA has been mandated by Congress under the Safe Drinking Water Act (SDWA), as amended, to assure that the public is provided with safe drinking water;

F. That EPA has been mandated by Congress under the Toxic Substances Control Act (TSCA) to protect against unreasonable risks to health and the environment from toxic substances by requiring, inter alia, testing and necessary restrictions on the use, manufacture, processing, distribution, and disposal of chemical substances and mixtures;

G. That EPA has been mandated by Congress under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, to assure, inter alia, that when used properly, pesticides will perform their intended function without causing unreasonable adverse effects on the environment; and,

H. That FDA has been mandated by Congress under the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended, to protect the public from, inter alia, the adulteration of food by food additives and poisonous and deleterious substances.
It is the intent of the parties that:

A. EPA will have responsibility for direct and indirect additives to and other substances in drinking water under the SDWA, TSCA, and FIFRA; and,

B. FDA will have responsibility for water, and substances in water, used in food and for food processing and responsibility for bottled drinking water under the FFDCA.

II. Background:

A. FDA Legal Authority

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"Food" means articles used for food or drink for man or other animals and components of such articles. (FFDCA Section 201(f)). Under Section 402, inter alia, a food may not contain any added poisonous or deleterious substance that may render it injurious to health, or be prepared, packed or handled under unsanitary conditions. Tolerances may be set, under Section 406, limiting the quantity of any substance which is required for the production of food or cannot be avoided in food. FDA has the authority under Section 409 to issue food additive regulations approving, with or without conditions, or denying the use of a "food additive." That term is defined in Section 201(s) to include any substance the intended use of which results or may reasonable be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food, if such substance is not generally recognized as safe.

In the past, FDA has considered drinking water to be a food under Section 201(f). However, both parties have determined that the passage of the SDWA in 1974 implicitly repealed FDA's authority under the FFDCA over water used for drinking water purposes. Under the express provisions of Section 410 of the FFDCA, FDA retains authority over bottled drinking water. Furthermore, all water used in food remains a food and subject to the provisions of the FFDCA. Water used for food processing is subject to applicable provisions of FFDCA. Moreover, all substances in water used in food are added substances subject to the provisions of the FFDCA, but no substances added to a public drinking water system before the water enters a food processing establishment will be considered a food additive.

B. EPA Legal Authority

The SDWA grants EPA the authority to control contaminants in drinking water which may have any adverse effect on the public health, through the establishment of maximum contaminant levels (MCLs) or treatment techniques, under Section 1412, which are applicable to owners and operators of public water systems. The expressed intent of the Act was to give EPA exclusive control over the safety of public water supplies. Public water systems may also be required by regulation to conduct monitoring for unregulated contaminants under Section 1445 and to issue public notification of such levels under Section 1414(c).

EPA's direct authority to control additives to drinking water apart from the existence of maximum contaminant levels or treatment techniques is limited to its emergency powers under Section 1431. However, Section 1442(b) of the Act authorizes EPA to "collect and make available information pertaining to research, investigations, and demonstrations with respect to providing a dependably safe supply of drinking water together with appropriate recommendations therewith."

TSCA gives EPA authority to regulate chemical substances, mixtures and under some circumstances, articles containing such substances or mixtures. Section 4 permits EPA to require testing of a chemical substance or mixture based on possible unreasonable risk of injury to health or the environment, or on significant or substantial human or environmental exposure while Section 8 enables EPA to require submission of data showing substantial risk of injury to health or the environment, existing health and safety studies, and other data. For new chemical substances, and significant new uses of existing chemical substances, Section 5 requires manufacturers to provide EPA with pre-manufacturing notice. Under Section 6 the manufacture, processing, distribution, use, and disposal of a chemical substance or mixture determined to be harmful may be restricted or banned. Although Section 3(2)(B) of TSCA excludes from the definition of "chemical substance" food and food additives as defined under FFDCA, the implicit repeal by the SDWA of FDA's authority over drinking water enables EPA to regulate direct and indirect additives to drinking water as chemical substances and mixtures under TSCA.

The FIFRA requires EPA to set restrictions on the use of pesticides to assure that when used properly, they will not cause unreasonable adverse effects on the environment. EPA may require, inter alia labeling which specifies how, when, and where a pesticide may be legally used. In addition, EPA has, under Section 409 of the FFDCA, required FIFRA registrants at times to obtain a food additive tolerance before using a pesticide in or around a drinking water source. Such tolerances establish further restrictions on the use of a pesticide which are enforceable against the water supplier as well as the registrant of the pesticide.

III. Terms of Agreement:

A. EPA's responsibilities are as follows:
1. To establish appropriate regulations, and to take appropriate measures, under the SDWA and/or TSCA, and FIFRA, to control direct additives to drinking water (which encompass any substances purposely added to the water), and indirect additives (which encompass any substance which might leach from paints, coatings or other materials as an incidental result of drinking water contact), and other substances.

2. To establish appropriate regulations under the SDWA to limit the concentrations of pesticides in drinking water; the limitations on concentrations and types of pesticides in water are presently set by EPA through tolerances under Section 409 of the FFDCA.

3. To continue to provide technical assistance in the form of informal advisory opinions on drinking water additives under Section 1442(b) of the SDWA.

4. To conduct and require research and monitoring and the submission of data relative to the problem of direct and indirect additives in drinking water in order to accumulate data concerning the health risks posed by the presence of these contaminants in drinking water.

B. FDA's responsibilities are as follows:
1. To take appropriate regulatory action under the authority of the FFDCA to control bottled drinking water and water, and substances in water, used in food and for food processing.

2. To provide assistance to EPA to facilitate the transition of responsibilities, including:
a) To review existing FDA approvals in order to identify their applicability to additives in drinking water.
b) To provide a mutually agreed upon level of assistance in conducting literature searches related to toxicological decision making.
c) To provide a senior toxicologist to help EPA devise new procedures and protocols to be used in formulating advice on direct and indirect additives to drinking water.

IV. Duration of Agreement:
This Memorandum of Understanding shall continue in effect unless modified by mutual consent of both parties or terminated by either party upon thirty (30) days advance written notice to the other.
This Memorandum of Understanding will become effective on the date of the last signature.

Approved and Accepted
for the Environmental Protection Agency
Signed by: Douglas P. Costle
Administrator
Environmental Protection Agency
Date: June 12, 1979
Approved and Accepted
for the Food and Drug Administration
Signed by: Donald Kennedy
Administrator
Food and Drug Administration

NSF International
Ann Arbor, MI • Sacramento, CA • Washington, D.C. • Brussels, Belgium

July 7, 2000

The Honorable Ken Calvert
Chairman Subcommittee on Energy and the Environment
Committee on Science
U. S. House of Representatives
Suite 232O, Rayburn House Office Building
Washington, DC 20515-6301

Dear Mr. Chairman:

Thank you for your letter of May 8, 2000 to Dr. Joseph Cotruvo wherein you request information from NSF International (NSF) on fluoride containing compounds. We appreciate having received an extension in order to allow NSF staff sufficient time to provide a comprehensive response to your request.

This response is comprised of a general information section entitled *Background on NSF and the Drinking Water Additives Program* and a section that answers the 8 questions in your letter. I have attached additional documents that will also assist in answering your questions.

It is important to note that your questions relate to two separate issues, and departments, within NSF – standards and product certification. First, ANSI/NSF Standard 60 – the American National Standard developed by NSF and a consortium of major stakeholders consisting of the American Water Works Association (AWWA), the AWWA Research Foundation (AWWARF), the Association of State Drinking Water Administrators (ASDWA), and the now inactive Conference of State Health and Environmental Managers (COSHEM) was developed from 1985 to 1987. Second, NSF operates a separate product testing, certification and listing program based on the requirements of the standard.

The health based principles of Standard 60 were originally developed by the NSF Health Advisory Board (HAB) which is a panel of non-NSF health science experts. This group continues its role in an advisory and oversight function to NSF and its Toxicology staff to assure that ANSI/NSF Standards are consistent with current public health principles.

The standard and the certification program are recognized and utilized by AWWA and its member utilities, and adopted in most state regulations. More than 43 states have regulations in place requiring product compliance with ANSI/NSF Standard 60. (See Attachment 14). The program provides a product quality and safety assurance that aims to prevent addition of harmful levels of contaminants from treatment chemicals.

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Fluorosilicate products are comprised of a fluoride entity as well as a silicate entity. Based on previously published studies, there is virtually complete dissociation of the fluoride and silicate entities in dilute solutions. As such, the toxicological evaluation of fluorosilicate products is conducted through the evaluation of each entity separately.

ANSI/NSF Standard 60 requires, when available, that the U.S. EPA regulated Maximum Contaminant Level (MCL) be used to determine the acceptable level for a contaminant. The MCL for fluoride is 4 mg/L of drinking water. As such, NSF has not independently developed toxicology data to support this level of human exposure. The Maximum Allowable Level (MAL) for fluoride ion in drinking water from NSF Certified treatment chemicals is 1.2 mg/L, or less than one-third the EPA's MCL. The product Maximum Use Level (MUL) certified by NSF ranges from 4 - 6.6 mg/L.

There is no EPA MCL for silicate in drinking water. When an MCL does not exist for a contaminant, ANS/NSF Standard 60 provides criteria to conduct a toxicological risk assessment of the contaminant and the development of a Maximum Drinking Water Level (MDWL). NSF has established a Maximum Drinking Water Level of silicate at 16 mg/L. A fluorosilicate product MUL of 4-6.6 mg/L results in silicate drinking water levels substantially below the 16 mg/L MAL established by NSF for silicates. Attachment 15 outlines the derivation of the NSF MAL for silicates.

In general, NSF Certified fluoridation products have been tested and found to comply with the requirements of ANSI/NSF Standard 60 for 12 additional inorganic chemicals. Additional testing of these products for radionuclides has resulted in no measurements above the detection limits. The specific answers below provide additional detail.

If there is any more information that you need, please do not hesitate to contact me.

Sincerely.

Stan Hazan

Stan Hazan
General Manager
Drinking Water Additives Certification Program
734-769-5105
hazan@nsf.org

cc: Dr. Joe Cotruvo, NSF
Dr. Lori Bestervelt, NSF

List of Attachments

Attachment	Description
1	FR Notice 5/17/84 - Disposition of the Federal DWA Advisory Program
2	FR Notice 7/7/88 - Termination of the Federal DWA Program, Notice
3	ANSI/NSF Standard 60 - DW Treatment Chemicals- Health Effects
4	ANSI/NSF Standard 61 - DW System Components- Health Effects
5	NSF Standards Development and Maintenance Policies
6	Standards Update - Flowchart of the Standards Development Process
7	1987 NSF DWA Joint Committee Membership List
8	1987 NSF Council of Public Health Consultants List
9	NSF Certification Policies for DW Treatment Chemicals - Standard 60
10	Toxicology Data Review Submission Form - Part A
11	Toxicology Data Review Submission Form - Part B
12	NSF DWA Listings Book
13	NSF DWA Certification Process - 7 Steps
14	ASDWA State Survey of Adoption of ANSI/NSF Standards 60 and 61
15	NSF MAL Derivation for Silicates in Drinking Water

Background on NSF and the Drinking Water Additives Program.

NSF International was established in 1944, as an independent, not-for-profit, third party organization dedicated to the protection of public health and safety. NSF has more than 300 employees consisting of engineers, chemists and toxicologists who develop U.S. national standards and provide independent product testing and certification services for products that impact food, air, water and the environment. NSF is a World Health Organization (WHO) Collaborating Center on Drinking Water Safety and Treatment, as well as for Food Safety.

NSF involvement in the evaluation of drinking water chemicals, including fluoride-based chemicals, began in 1985, when the U.S. EPA granted an NSF-led consortium of stakeholders the responsibility to develop consensus, health-based, quality specifications for drinking water treatment chemicals and drinking water system components (Attachment 1). EPA also requested development of a product testing and certification program that would allow for independent product evaluations for use by states, cities, and water utilities, as a basis for product acceptance and use.

The original goal of the standard and certification program was to develop a preventative mechanism for selecting treatment chemicals that would not contribute harmful levels of contaminants to drinking water. The standards and the certification program were designed to be dynamic, to change as regulations change, and to constantly be tied to the requirements of the Safe Drinking Water Act and its drinking water quality regulations. In 1988, EPA terminated its informal chemical additives advisory program upon completion of the NSF standards and successful launch of the NSF product certification program (Attachment 2). We believe that the NSF standards and certification program have succeeded in achieving the goals of the original mandate.

The NSF Certification program consists of seven steps for initial product certification, and 4 steps on an annual basis. (See Attachment 13).

Today, NSF provides testing and certification services for thousands of products from more than 30 countries. NSF publishes its listings on its web site at www.nsf:org as well as in hardcopy (Attachment 12). In addition, attached is a copy of the NSF Certification Policies for Drinking Water Treatment Chemicals (Attachment 9). This document outlines the rules that govern the product certification program, over and above the requirements of the standard.

This section provides responses to the 8 questions in your letter.

Question 1. Please provide the identification and affiliation of each member of the committee or committees contributing to the policies established for each of the fluorine-bearing additives destined for the public water supplies, both current committee members and those responsible for establishing product standards for fluoride.

In response to an identified need for health-based standards dealing with drinking water contact products, a consortium led by the National Sanitation Foundation (now NSF) worked to develop voluntary third-party consensus standards for all direct and indirect drinking water additives. Other consortium members were the American Water Works Association (AWWA), the American Water Works Association Research Foundation (AWWARF), the Association of State Drinking Water Administrators (ASDWA) and the Conference of State Health and Environmental Managers (COSHEM, now inactive).

ANSI/NSF 60 *Drinking water treatment chemicals – Health effects* was initially adopted in December 1987, and was last revised in May 2000. It establishes minimum human health effects requirements for the chemicals that are added directly to drinking water for its treatment or other purposes. The standard was developed using a consensus standards development process with representation of the major stakeholder interests, including product manufacturers, product users such as consultants and water utilities, and representatives from the regulatory/public health sectors. As an American National Standard, each revision to ANSI/NSF 60 also undergoes a public comment review. This public comment process allows for any interested party to obtain a copy of the proposed revision and to submit comments or objections to NSF. All comments received are handled in accordance with the due-process requirements set forth in the ANSI procedures and NSF policies.

Each edition of ANSI/NSF 60 contains a list of the committee members who oversee the development and review of that edition of the standard. These committees consist of the NSF Joint Committee for Drinking Water Additives, the balanced group of approximately 36 representatives from the user, regulatory and manufacturing sectors, and the NSF Council of Public Health Consultants, which is a group of approximately 45 independent, public health experts from government, academia and the environmental health community. The current version of ANSI/NSF 60 (2000) is enclosed for your review (Attachment 3), as well as a list of the membership of these committees when the Standard was first adopted in 1987 (Attachments 7 and 8). Copies of the NSF *Standards Development and Maintenance Policies* (Attachment 5) and "Standards Update" (Attachment 6) are also enclosed to provide further detail on the standards development process.

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Question 2. Under General Requirements 3.2.1, formulation submission and review, ANSI/NSF 60 -1999, are manufacturers of hydrofluosilicic acid and silicofluorides required to "submit for each product, when available, a list of published and unpublished toxicological studies relevant to the treatment chemical and the chemicals and impurities present in the treatment chemical?"
The standard requires that the manufacturer of a product submitted for certification provide toxicological information, (if available.) NSF requires that manufacturers seeking certification to the standard submit this information as part of their formulation or ingredient supplier submission. ✓

Has your document, General Requirements 3.2.1, Formulation submission and review, ANSI/NSF 60 - 1999, been peer reviewed for accuracy? If so, please provide the names, affiliations and contact information for the peer reviewers.
The document (ANSI/NSF Standard 60) has been peer reviewed for accuracy. Joint Committee and CPHC members and contact information are contained in Attachments 3, 7, and 8.

Please provide:
All lists complying with the above requirement submitted by manufacturers of hydrofluosilicic acid and silicofluorides.
NSF has based its certification on the product use not exceeding the EPA's MCL for fluoride. Separately, NSF has developed an MAL for silicates of 16 mg/L that supports the silicate portion of the products in question. In addition, potential contaminants are also limited by the standard. The supporting rationale for the silicate MAL is enclosed in Attachment 15.

The complete record of all tests of each fluorine-bearing additive using ion chromatography, atomic absorption spectroscopy, and scintillation counting.
NSF toxicology review and testing of fluorosilicate compounds looks for potential trace contaminants such as heavy metals and radionuclides. The formulation review step examines not only the product formulation, but also considers potential contaminants from the ingredients, processing aids, and any other factors impacting contaminants in the finished drinking water. Contaminants in the finished drinking water are not permitted to exceed one-tenth of the EPA's regulated MCL (Maximum Contaminant Level) when the product is added to drinking water at its Maximum Use Level, unless it can be documented that a limited number of sources of the contaminant occur in drinking water.

NSF has reviewed its files and has compiled a summary of our findings (Table 1) in lieu of complete test reports. Individual test reports, as well as formulation information are protected by nondisclosure agreements with certification clients.

NSF searched its files to determine the level of contaminants found in these fluoridation products, when the product is dosed to water at the Maximum Use Level (MUL). The exact number of laboratory tests performed is not readily available because we maintain records only on those tests where a contaminant was detected. The results in Table 1 include initial product tests as well as annual product monitoring tests. In total, these products have been tested more than 100 times in our laboratories. Table 1 indicates that metals contamination of drinking water as a result of fluoride chemical use is not an issue. There has not been a single fluoride product tested with a metal concentration in excess of its corresponding MAL.

Silica and silicates, which make up a portion of the fluoridation chemicals mentioned above, are addressed by the certification of sodium silicates to a level of 16 mg/L under ANSI/NSF Standard 60. (See Attachment 15).

Beginning in early 1998, NSF went beyond Standard 60 requirements and voluntarily began testing fluoridation chemicals for the presence of radionuclides (alpha and beta emitters) utilizing EPA Test Method 900.0, as specified in Annex B of ANSUNSF Standard 60. To date, we have not found any sample with a positive (detected) result, with detection limits of 4 pCi/liter and 3 pCi/liter for gross alpha and gross beta, respectively.
Table 1

	Number of Fluoride Samples with Positive Test Results	Average Contaminant Concentration in Samples with Positive Test Results* (ppb)	Maximum Contaminant Concentration in Samples with Positive Test Results (ppb)	ANSI/NSF Standard 60 Maximum Allowable Level (MAL) (ppb)	US EPA Maximum Contaminant Level (MCL) (ppb)
Antimony	0	NA	NA	0.6	6
Arsenic	39	0.43	1.66	2.5**	50
Barium	1	0. 19	0.17	200	2000
Beryllium	5	0.21	0.3	0.4	4
Cadmium	3	0.06	0.1	0.5	5
Chromium	3	0.14	0.2	10	100
Copper	8	0.49	0.55	130	1300
Lead	7	0.4	1.1	1.5	15
Mercury	5	0.013	0.015	0.2	2
Nickel	0	NA	NA	NA	NA
Selenium	I	0.60	0.6	5	50
Thallium	6	0.03	0.05	0.2	2
Radionuclides	0	NA	NA	-	-

**Only those samples where a contaminant was detected contribute to the average. The average contaminant concentration for all samples tested is significantly lower, and is affected by detection limits and number of detections.*
*** ANSI/NSF Std 60 utilizes Canadian MACs and EPA MCLs in determination of MALs.*

A true and complete copy of all tests that identify the full composition of each fluorine-bearing additive, including all attendant organic substances, radionuclides and other chemicals.

Compositional analyses are not required by the NSF standard. The verification of composition is performed during the annual unannounced plant inspection by NSF auditors who verify sources and ratios of labeled ingredients. Separately, there are industry standards from AWWA (American Water Works Association) (ANSI/AWWA B702-99 for Sodium Fluorosilicate and ANSI/AWWA B703a-97 for Fluosilicic Acid) that provide for compositional requirements.

Copies of any and all tests or studies of each of the fluorine-bearing additives that consider or indicate degree of dissociation.

The standard requires testing for contaminants that are likely to be present in the product. A study by N.T. Crosby, published in 1969 in the Journal of Applied Chemistry (Volume 19), establishes dissociation of fluorosilicates at 99% for 1ppm fluoride concentrations in drinking water.

Copies of any and all studies that have been performed on laboratory animals using hydrofluosilicic acid or silicofluorides.

NSF does not perform animal testing, although these may be required under Standard 60 if hazard/risk based action levels are exceeded. NSF toxicologists may review animal studies during the toxicology evaluation step of the product certification process.

Copies of any risk assessment documents in NSF International files that pertain to fluorine-bearing pesticides, such as cryolite.

Fluorine-containing pesticides such as cryolite are not required analyses under the standard, unless it is determined to be part of the formulation, or a potential contaminant. NSF would test for this or any other contaminants if indicated during the formulation review step.

Question 3. Have any studies on hydrofluosilicic acid or silicofluorides been submitted to NSF under claimed Confidential Business Information protection?

There have not been any studies on hydrofluosilicic acid or silicofluorides submitted to NSF under claimed Confidential Business Information protection.

Question 4. What are the Maximum Contaminant Levels, or any other regulatory standards, established for the following contaminants (either singularly, in combination with another substance, or in the elements' various forms) or any other contaminants reported as present in the fluorine-bearing substances hydrofluosilicic acid and other silicofluorides used in fluoridation programs?

Maximum Contaminant Levels (MCLs) can be found in Annex E of the enclosed copy of ANSI/NSF 60. Annex E of Standard 60 lists the federally regulated MCLs. Of the contaminants listed in your letter, MCLs exist for arsenic, barium, beryllium, cadmium, chromium, fluoride, lead, mercury, selenium, and dioxin (as 2,3,7,8-TCDD). Federal regulatory standards have not been established for the remaining contaminants listed in your letter.

Question 5. What tests are performed to identify the full and exact consistency of the fluorine-bearing product and determine the concentrations of each of the contaminants or combination of contaminants in a sample? Upon what occasion or frequency are these tests performed? Are Certificates of Analysis provided with each shipment of such products from the manufacturer?

NSF tests certified products at least annually for prospective contaminants (See response to Question 2). An NSF Certified company may produce many shipments during the course of the year, but the company is contractually bound to not change the formulation ratios, ingredients or add unauthorized sources of supply. Certificates of Analyses are typically provided by the vendor to the utility on a per shipment basis. There are industry standards from AWWA (American Water Works Association) (ANSI/AWWA B702-99 for Sodium Fluorosilicate and ANSI/AWWA B703a-97 for Fluosilicic Acid) that provide for affidavits and Certificates of Analyses.

Question 6. What is the purpose of establishing a maximum allowable level (MAL) for additives, restricting the contribution to drinking water of any one product to 10% of the Maximum Contaminant Level (MCL)?

The purpose of establishing a maximum allowable level (MAL) for individual drinking water additives products at 10% of the MCL is to recognize that contaminants may enter drinking water from other points throughout the system, including the source water, during the treatment and distribution process, and either through direct addition or surface contact. Limiting individual products to a contribution of 10% of the MCL for a given contaminant provides an extra margin of safety so that it is unlikely that the summation of the contributions from all potential sources will exceed the MCL at the tap.

Question 7. Under what circumstances or authority is an additive certified when the MAL of 10% of the established MCL is exceeded?

An MAL of greater than 10% of the MCL can be established by the certification body in limited cases if it can be reasonably documented that there are no other significant sources of the same contaminant, that together, would result in the finished drinking water contaminant concentration exceeding the MCL. Fluoride has an MAL of 1.2 mg / liter, which is 30% of the MCL. This is justified on the basis of the limited number of other potential sources of fluoride ion to drinking water. For example, water that naturally contains sufficient fluoride is not additionally fluoridated, and fluoride is seldom present in other additives.

Question 8. What tests and how often are they performed by NSF International to determine the exact consistency and concentrations of all contaminants in hydrofluosilicic acid, silicofluorides and sodium fluoride products? What is the ratio of NSF International tests to shipments by manufacturers of the additives? Are NSF International test results compared with Certificates of Analyses as a quality assurance measure?

As indicated in question 2, the testing required by the standard is for regulated metals. NSF additionally performs radionuclides analysis. Contaminant testing is performed initially upon application, and at least annually thereafter. Samples are collected during unannounced inspections by NSF auditors.

As mentioned previously, NSF tests products at least once per year. A contract signed by the NSF Certified manufacturer precludes production or process changes without written consent from NSF.

NSF test results are not routinely compared to Certificate of Analyses results. Certificates of Analyses often report on parameters not required under ANSVNSF Standard 60. For example, the AWWA standards mentioned previously require testing for fluoride content, moisture, impurities, etc. The AWWA standards also incorporate the option of additional purchaser specifications.

Please provide the committee with copies of any NSF International publications, studies, and reports relating to fluoride.

As mentioned earlier, NSF relies on the U.S. EPA MCL and its supporting documentation, as specified in the standard. See attachments listed in the cover letter.

Fluorine-containing pesticides and pharmaceuticals also contribute to total fluorine exposures and are considered separately. Fluoride in food and drinking water usually is considered in terms of total fluorine content, assumed to be present entirely as fluoride ion (F^-). Information on exposures to fluorosilicates and aluminofluorides is also included.

SOURCES OF FLUORIDE EXPOSURE

Drinking Water

General Population

The major dietary source of fluoride for most people in the United States is fluoridated municipal (community) drinking water, including water consumed directly, food and beverages prepared at home or in restaurants from municipal drinking water, and commercial beverages and processed foods originating from fluoridated municipalities. On a mean per capita basis, community (public or municipal) water constitutes 75% of the total water ingested in the United States; bottled water constitutes 13%, and other sources (e.g., wells and cisterns) constitute 10% (EPA 2000a). Municipal water sources that are not considered "fluoridated" could contain low concentrations of naturally occurring fluoride, as could bottled water and private wells, depending on the sources.

An estimated 162 million people in the United States (65.8% of the population served by public water systems) received "optimally fluoridated"[1] water in 2000 (CDC 2002a). This represents an increase from 144 million (62.1%) in 1992. The total number of people served by public water systems in the United States is estimated to be 246 million; an estimated 35 million people obtain water from other sources such as private wells (CDC 2002a,b). The U.S. Environmental Protection Agency (EPA) limits the fluoride that can be present in public drinking-water supplies to 4 mg/L (maximum contaminant level, or MCL) to protect against crippling skeletal fluorosis, with a secondary maximum contaminant level (SMCL) of 2 mg/L to protect against objectionable dental fluorosis (40CFR 141.62(b)[2001], 40CFR 143.3[2001]).

Of the 144 million people with fluoridated public water supplies in 1992, approximately 10 million (7%) received naturally fluoridated water, the rest had artificially fluoridated water (CDC 2002c). Of the population with artificially fluoridated water in 1992, more than two-thirds had a water fluoride concentration of 1.0 mg/L, with almost one-quarter having lower concentrations and about 5% having concentrations up to 1.2 mg/L (CDC 1993; see Appendix B).

Of the approximately 10 million people with naturally fluoridated public water supplies in 1992, approximately 67% had fluoride concentrations $\leq$ 1.2 mg/L (CDC 1993; see Appendix B). Approximately 14% had fluoride concentrations between 1.3 and 1.9 mg/L and another 14% had between 2.0 and 3.9 mg/L; 2% (just over 200,000 persons) had natural fluoride

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[1] The term optimally fluoridated water means a fluoride level of 0.7-1.2 mg/L; water fluoride levels are based on the average maximum daily air temperature of the area (see Appendix B).

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NEWS COVERAGE

Public health bodies slam new fluoride tolerance levels

FoodNavigator-USA.com, Anthony Fletcher
Published October 2, 2005

Environmental organizations claim that new food tolerances for the fluoride-based pesticide sulfuryl fluoride could be potentially damaging to public health.

The new Environmental Protection Agency (EPA) tolerances were requested by Dow AgroSciences following the firm's expansion of its pesticide sulfuryl fluoride - trade name ProFume - which is used to fumigate food processing facilities and storage areas.

The product targets stored product pests, as well as those insects that may be transported from the field on food commodities. But some environmental groups argue that the new levels are potentially dangerous.

Indeed, the Environmental Working Group, Beyond Pesticides and the Fluoride Action Network (FAN) said that the maximum legal limits for the fluoride-based pesticide in foods have been set at levels that dwarf the amount allowed in tap water.

For example, the EPA is allowing 900 parts per million (ppm) of fluoride in dried eggs, as opposed to the maximum 4 ppm allowed in tap water. One third of the nation's eggs are sold and consumed in dried, reconstituted form.

The groups also noted that 900 ppm set for dried eggs is extremely close to that used in toothpaste (1,000 ppm), a level that is considered toxic if consumed in greater than pea sized portions.

"How can the EPA consider 900 ppm in eggs safe, while the Food and Drug Administration directs parents to call poison control centers if their children consume more than a pea sized portion of toothpaste with fluoride at 1,000 ppm?" asked Paul Connett, executive director of FAN.

"Unlike toothpaste, eggs are meant to be eaten, not spat out."

It isn't just powdered eggs that could contain dangerous but legal levels of fluoride under the new regime. Fluoride Action Network (FAN) researcher Chris Neurath claims that all processed foods will be allowed 70 ppm fluoride residues, including everything from breakfast cereal to cake mix.

"Wheat flour is allowed up to 125 ppm," he said. "For comparison, the maximum level of fluoride allowed in drinking water is 4 ppm and the natural level of fluoride in mothers' milk is approximately 0.008 ppm. The potential for a significant number of acute poisoning cases every year is very real."

Dow AgroSciences however believes that the establishment of new accepted fluoride levels is great news for millers and food processors. "With the label amendments and additional tolerances, ProFume brings unprecedented flexibility and effective, reliable control of stored product pests to more markets segments and broadens its use pattern," said Drew Ratterman, marketing specialist, Dow AgroSciences.

"We appreciate the continued support of many throughout the industry during this registration process and are pleased to be able to offer a product that meets their fumigation needs."

However Richard Wiles, senior vice-president of the Environmental Working Group (EWG,), contends that EPA is relying on outdated science to support this increase in fluoride exposure.

"In our view [the EPA] has not discharged its legal duty to thoroughly consider the effects of fluoride on infants and children, from all routes of exposure, based on a thorough review of the most recent peer-reviewed science," he said.

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At EWG, our team of scientists, engineers, policy experts, lawyers and computer programmers pores over government data, legal documents, scientific studies and our own laboratory tests to expose threats to your health and the environment, and to find solutions. Our research brings to light unsettling facts that you have a right to know.

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Fluorine-containing pesticides and pharmaceuticals also contribute to total fluorine exposures and are considered separately. Fluoride in food and drinking water usually is considered in terms of total fluorine content, assumed to be present entirely as fluoride ion (F^-). Information on exposures to fluorosilicates and aluminofluorides is also included.

SOURCES OF FLUORIDE EXPOSURE

Drinking Water

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The major dietary source of fluoride for most people in the United States is fluoridated municipal (community) drinking water, including water consumed directly, food and beverages prepared at home or in restaurants from municipal drinking water, and commercial beverages and processed foods originating from fluoridated municipalities. On a mean per capita basis, community (public or municipal) water constitutes 75% of the total water ingested in the United States; bottled water constitutes 13%, and other sources (e.g., wells and cisterns) constitute 10% (EPA 2000a). Municipal water sources that are not considered "fluoridated" could contain low concentrations of naturally occurring fluoride, as could bottled water and private wells, depending on the sources.

An estimated 162 million people in the United States (65.8% of the population served by public water systems) received "optimally fluoridated"[1] water in 2000 (CDC 2002a). This represents an increase from 144 million (62.1%) in 1992. The total number of people served by public water systems in the United States is estimated to be 246 million; an estimated 35 million people obtain water from other sources such as private wells (CDC 2002a,b). The U.S. Environmental Protection Agency (EPA) limits the fluoride that can be present in public drinking-water supplies to 4 mg/L (maximum contaminant level, or MCL) to protect against crippling skeletal fluorosis, with a secondary maximum contaminant level (SMCL) of 2 mg/L to protect against objectionable dental fluorosis (40CFR 141.62(b)[2001], 40CFR 143.3[2001]).

Of the 144 million people with fluoridated public water supplies in 1992, approximately 10 million (7%) received naturally fluoridated water, the rest had artificially fluoridated water (CDC 2002c). Of the population with artificially fluoridated water in 1992, more than two-thirds had a water fluoride concentration of 1.0 mg/L, with almost one-quarter having lower concentrations and about 5% having concentrations up to 1.2 mg/L (CDC 1993; see Appendix B).

Of the approximately 10 million people with naturally fluoridated public water supplies in 1992, approximately 67% had fluoride concentrations ≤ 1.2 mg/L (CDC 1993; see Appendix B). Approximately 14% had fluoride concentrations between 1.3 and 1.9 mg/L and another 14% had between 2.0 and 3.9 mg/L; 2% (just over 200,000 persons) had natural fluoride

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[1] The term optimally fluoridated water means a fluoride level of 0.7-1.2 mg/L; water fluoride levels are based on the average maximum daily air temperature of the area (see Appendix B).

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Sulfuryl fluoride

From Wikipedia, the free encyclopedia

Sulfuryl fluoride is the chemical compound with the formula SO_2F_2. This inorganic gas has properties more similar to sulfur hexafluoride than sulfuryl chloride, being resistant to hydrolysis even up to 150 °C. So inert is this material that suspended molten "sodium metal retains its shiny metallic appearance."[1]

Contents

- 1 Structure and preparation
- 2 Use as a fumigant
- 3 Safety considerations
- 4 Environmental fate
- 5 References
- 6 External links

Structure and preparation

The molecule is tetrahedral with C_{2v} symmetry. The S-O distance is 140.5 pm, S-F is 153.0 pm. As predicted by VSEPR, the O-S-O angle is more open than the F-S-F angle, 124° and 97°, respectively.[1]

It is prepared by direct reaction of fluorine with sulfur dioxide:

$$SO_2 + F_2 \rightarrow SO_2F_2$$

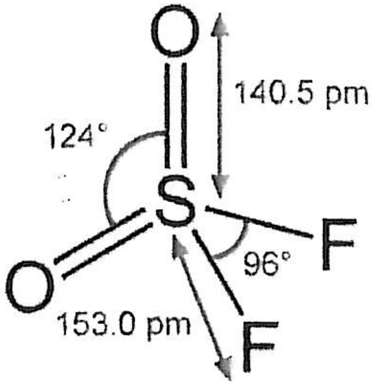
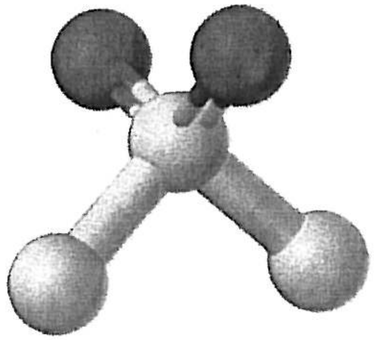
A laboratory-scale synthesis begins with the preparation of potassium fluorosulfite:[2]

$$SO_2 + KF \rightarrow KSO_2F$$

This salt is then chlorinated to give sulfuryl chloride fluoride:

$$KSO_2F + Cl_2 \rightarrow SO_2ClF + KCl$$

Further heating (180 °C) of potassium fluorosulfite with the sulfuryl chloride fluoride gives the desired product:[3]

Sulfuryl fluoride	
	
	
IUPAC name Sulfuryl fluoride	
other names Sulfonyl fluoride; Sulfur dioxide difluoride; Sulphuryl fluoride; Sulfuryl difluoride	
Identifiers	
CAS number	2699-79-8
Properties	
Molecular formula	SO_2F_2
Molar mass	102.06 g/mol
Appearance	colourless gas
Density	1.623 g/cm³ at 0 °C
Melting point	-135.7 °C
Boiling point	-55.2 °C
Solubility in water	low
Solubility in other solvents	SO_2
Structure	
Coordination geometry	tetrahedral
Hazards	

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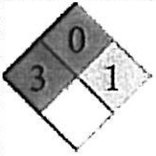
$$SO_2ClF + KSO_2F \rightarrow SO_2F_2 + KCl + SO_2$$

Heating metal fluorosulfonate salts also gives this molecule:[1]

$$Ba(OSO_2F)_2 \rightarrow BaSO_4 + SO_2F_2$$

Main hazards	toxic
NFPA 704	 0 3 1
Related compounds	
Related compounds	SO_2Cl_2, SO_2ClF, SF_6, SO_3
Except where noted otherwise, data are given for materials in their standard state (at 25 °C, 100 kPa)	
Infobox references	

Use as a fumigant

SO_2F_2 is of interest as a fumigant with the phase-out of methyl bromide and in view of the risks of phosphine.[4]

Originally developed by the Dow Chemical Company, SO_2F_2 (sulfuryl fluoride) is in widespread use as a structural fumigant insecticide to control drywood termites, particularly in warm-weather portions of the southwestern and southeastern United States and in Hawaii. Less commonly, it can also be used to control rodents, powderpost beetles, bark beetles, and bedbugs.

Sulfuryl fluoride is currently marketed by three distinct manufacturers, under four different brand names. *Vikane* (Dow) (EPA Reg. No. 62719- 4-ZA) has been commercially available since the early 1960s, with *Zythor* (marketed by competitor EnSystex II of North Carolina) (EPA Reg. No. 81824- 1-AA) being more recently introduced gradually as its use is approved by individual states (in Florida circa 2004, but not in California until October 2006, for example). Dow recently has begun marketing sulfuryl fluoride as a post-harvest fumigant for dry fruits, nuts, and grains under the trade name *ProFume* (EPA Reg. No. 62719- 376-AA). [1] Most recently Drexel Chemical Company has registered *Master Fume* (EPA Reg. No. 19713-596-AA) for the structural market, competing against *Vikane* and *Zythor*. [5]

During application, the building is enclosed in a tight tent and filled with the gas for a period of time, usually at least 16-18 hours, sometimes as long as 72 hours. The building must then be ventilated, generally for at least 6 hours, before occupants can return. Sulfuryl fluoride is colorless, odorless, and leaves no residue. During the fumigation process, a warning agent called Chloropicrin (similar to tear gas, but more toxic) is first released into the building to ensure that no occupants remain.

Some pest control experts claim sulfuryl fluoride is the only effective treatment for drywood termites. (Heat is the only other approved method for whole structure treatment for termites in California.[6]) Because it leaves no residue sulfuryl fluoride provides no protection from future infestations, although heavy reinfestation can take several years since drywood termites have slower growing colonies than ground termites.

Safety considerations

Sulfuryl fluoride is toxic in humans and following inhalation may cause symptoms of fluoride poisoning. Symptoms may include weakness, nausea, vomiting, hypotension, metabolic acidosis, hypocalcemia, cardiac dysrhythmia, pulmonary edema, and death.[7][8][9] Medical treatment may consist of giving calcium, correcting acidosis with sodium bicarbonate, and hemodialysis.[7]

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Sulfuryl fluoride must be transported in a vehicle marked with "Inhalation Hazard 2" placards. Most U.S. states also require a license or certification for the individual applying the fumigant.

Environmental fate

Based on the first high frequency, high precision, in situ atmospheric and archived air measurements of sulfuryl fluoride it was determined that sulfuryl fluoride has an atmospheric lifetime of 30-40 years [10], much longer than the 5 years earlier estimated [11]. Moreover, sulfuryl fluoride has been reported to be a greenhouse gas which is about 4000-5000 times more efficient in trapping infrared radiation (per kg) than carbon dioxide (per kg).[12] [10] [13]. It is important to note, however, that amounts of sulfuryl fluoride released into the atmosphere (about 2000 metric tons per yr[10]) are far, far lower than the amounts of CO_2 released by hydrocarbon-burning vehicles, industry, and other processes (about 30 billion metric tons per year). The most important loss process of sulfuryl fluoride is dissolution of atmospheric sulfuryl fluoride in the ocean followed by hydrolysis [10][14].

References

1. ^ *a b c* Holleman, A. F.; Wiberg, E. "Inorganic Chemistry" Academic Press: San Diego, 2001. ISBN 0-12-352651-5.
2. ^ Seel, F. "Potassium Fluorosulfite" Inorganic Syntheses 1967, IX, pages 113-115.
3. ^ Seel, F. "Sulfuryl Chloride Fluoride and Sufluryl Fluoride" Inorganic Syntheses 1967, IX, pages 11-113.
4. ^ Bell, C. H. "Fumigation in the 21st century" "Crop Protection, 2000, 19, 563-569. ISSN 0261-2194. AN 2000:895590
5. ^ Output Reporting
6. ^ Termites Fact Sheet
7. ^ *a b* Schneir A, Clark RF, Kene M, Betten D (November 2008). "Systemic fluoride poisoning and death from inhalational exposure to sulfuryl fluoride". *Clin Toxicol (Phila)* **46** (9): 850-4. PMID 18608259.
8. ^ Centers for Disease Control (CDC) (Sep 18 1987). "Fatalities resulting from sulfuryl fluoride exposure after home fumigation--Virginia". *MMWR Morb Mortal Wkly Rep* **36** (36): 602-4, 609-11. PMID 3114607.
9. ^ Scheuerman EH (1986). "Suicide by exposure to sulfuryl fluoride". *J Forensic Sci* **31** (3): 1154-8. PMID 3734735.
10. ^ *a b c d* Mühle, J., J. Huang, R.F. Weiss, R.G. Prinn, B.R. Miller, P.K. Salameh, C.M. Harth, P.J. Fraser, L.W. Porter, B.R. Greally, S. O'Doherty, and P.G. Simmonds, Sulfuryl Fluoride in the Global Atmosphere, Journal of Geophysical Research, 114, D05306, doi:10.1029/2008JD011162, 2009
11. ^ KEMI, SULFURYL FLUORIDE (PT8), Competent Authority Report, Document III-A7, Ecotoxicological Profile Including Environmental Fate and Behaviour, Swedish Chemicals Agency, Sweden, 2005.
12. ^ Papadimitriou, V.C., R.W. Portmann, D.W. Fahey, J. Mühle, R.F. Weiss, and J.B. Burkholder, Experimental and Theoretical Study of the Atmospheric Chemistry and Global Warming Potential of SO2F2, Journal of Physical Chemistry A, 112 (49), 12657-12666, doi:10.1021/jp806368u, 2008.
13. ^ Sulbaek Andersen, M.P., D.R. Blake, F.S. Rowland, M.D. Hurley, and T.J. Wallington, Atmospheric Chemistry of Sulfuryl Fluoride: Reaction with OH Radicals, Cl Atoms and O3, Atmospheric Lifetime, IR Spectrum, and Global Warming Potential, Environmental Science & Technology, doi:10.1021/es802439f, 2009.
14. ^ Cady, G.H., and S. Misra, Hydrolysis of Sulfuryl Fluoride, Inorganic Chemistry, 13 (4), 837-841, 1974.

External links

- Sulfuryl Fluoride Technical Fact Sheet - National Pesticide Information Center
- Sulfuryl Fluoride General Fact Sheet - National Pesticide Information Center

February 2008

NSF Fact Sheet on Fluoridation Chemicals

Introduction

This fact sheet provides information on the fluoride containing water treatment additives that NSF has tested and certified to NSF/ANSI Standard 60: Drinking Water Chemicals - Health Effects. According to the latest Association of State Drinking Water Administrators Survey on State Adoption of NSF/ANSI Standards 60 and 61, 45 states require that chemicals used in treating potable water must meet Standard 60 requirements. If you have questions on your state's requirements, or how the NSF/ANSI Standard 60 certified products are used in your state, you should contact your state's Drinking Water Administrator.

Water fluoridation is the practice of adjusting the fluoride content of drinking water. Fluoride is added to water for the public health benefit of preventing and reducing tooth decay and improving the health of the community. The U.S. Centers for Disease Control and Prevention is a reliable source of information on this important public health intervention. For more information please visit www.cdc.gov/fluoridation/.

NSF certifies three basic products in the fluoridation category:

1. Fluorosilicic Acid (aka Fluosilicic Acid or Hydrofluosilicic Acid).
2. Sodium Fluorosilicate (aka Sodium Silicofluoride).
3. Sodium Fluoride.

NSF Standard 60

Products used for drinking water treatment are evaluated to the criteria specified in NSF/ANSI Standard 60. This standard was developed by an NSF-led consortium, including the American Water Works Association (AWWA), the American Water Works Association Research Foundation (AWWARF), the Association of State Drinking Water Administrators (ASDWA), and the Conference of State Health and Environmental Managers (COSHEM). This group developed NSF/ANSI Standard 60, at the request of the US EPA Office of Water, in 1988. The NSF Joint Committee on Drinking Water Additives continues to review and maintain the standard annually. This committee consists of representatives from the original stakeholder groups as well as other regulatory, water utility and product manufacturer representatives.

Standard 60 was developed to establish minimum requirements for the control of potential adverse human health effects from products added directly to water during its treatment, storage and distribution. The standard requires a full formulation disclosure of each chemical ingredient in a product. It also requires a toxicology review to determine that the product is safe at its maximum use level and to evaluate potential contaminants in the product. The standard requires testing of the treatment chemical products, typically by dosing these in water at 10 times the maximum use level, so that trace levels of contaminants can be detected. A toxicology evaluation of test results is required to determine if any contaminant concentrations have the potential to cause adverse human health effects. The standard sets criteria for the establishment of single product allowable concentrations (SPAC) of each respective contaminant. For contaminants regulated by the U.S. EPA, this SPAC has a default level not to exceed ten-percent of the regulatory level to provide protection for the consumer in the unlikely event of multiple sources of the contaminant, unless a lower or higher number of sources can be specifically identified.

NSF Certification

NSF also developed a testing and certification program for these products, so that individual U.S. states and waterworks facilities would have a mechanism to determine which products were appropriate for use. The certification program requires annual unannounced inspections of production and distribution facilities to ensure that the products are properly formulated, packaged, and transported with safe guards against potential contamination. NSF also requires annual testing and toxicological evaluation of each NSF Certified product. NSF Certified products have the NSF Mark, the maximum use level, lot number or date code and production location on the product packaging or documentation shipped with the product.

The use of this standard and the associated certification program have yielded benefits in ensuring that drinking water additives meet the health objectives that provide the basis for public health protection. NSF maintains listings of companies that manufacture and distribute treatment products at www.nsf.org. These listings are updated daily and list the products at their allowable maximum use levels. In recognition of the important safeguards that NSF Standard 60 provides to public drinking water supplies, 45 U.S. States and 10 Canadian Provinces and Territories require drinking water treatment chemicals to comply with the requirements of the standard.

Treatment products that are used for fluoridation are addressed in Section 7 of NSF/ANSI Standard 60. The products are allowed to be used up to concentrations that result in a maximum use level of 1.2 mg/L fluoride ion in water. The NSF standard requires that the treatment products added to drinking water, as well as any impurities in the products, are supported by toxicological evaluation. The following text explains the rationale for the allowable levels established in the standard for 1) fluoride, 2) silicate, and 3) other potential contaminants that may be associated with fluoridation chemicals.

Fluoride

NSF/ANSI Standard 60 requires, when available, that the US EPA regulated maximum contaminant level (MCL) be used to determine the acceptable level for a contaminant. The EPA MCL for fluoride ion in water is 4 mg/L. The NSF Standard 60 single product allowable concentration (SPAC) for fluoride ion in drinking water from NSF Certified treatment products is 1.2 mg/L, or less than one-third of the EPA's MCL. Based on this the allowable maximum use level (MUL) for the NSF Certified fluoridation products are:

1. Fluorosilicic Acid: 6 mg/L.
2. Sodium Fluorosilicate: 2 mg/L.
3. Sodium Fluoride: 2.3 mg/L.

Silicate

There is no EPA MCL for silicate in drinking water. When an MCL does not exist for a contaminant, NSF/ANSI Standard 60 provides criteria to conduct a toxicological risk assessment of the contaminant and the development of a SPAC. NSF has established a SPAC for silicate at 16 mg/L. A fluorosilicate product, applied at its maximum use level, results in silicate drinking water levels that are substantially below the 16 mg/L SPAC established by NSF. For example, a sodium fluorosilicate product dosed at a concentration into drinking water that would provide the maximum concentration of fluoride allowed (1.2mg/L) would only contribute 0.8 mg/L of silicate – or 5 percent of the SPAC allowed by NSF 60.

Potential Contaminants

The NSF toxicology review for a chemical product considers all chemical ingredients in the product as well as the manufacturing process, processing aids, and other factors that have an impact on the contaminants present in the finished drinking water. This formulation review identifies all the contaminants that need to be analyzed in testing the product. For example, fluosilicic acid is produced by adding sulfuric acid to phosphate ore. This is typically done during the production of phosphate additives for agricultural fertilizers. The manufacturing process is documented by an NSF inspector at an initial audit of the manufacturing site and during each annual unannounced inspection of the facility. The manufacturing process, ingredients, and potential contaminants are reviewed annually by NSF toxicologists, and the product is tested for any potential contaminants. A minimum test battery for all fluoridation products includes metals of toxicological concern and radionuclides.

Many drinking water treatment additives, including fluoridation products, are transported in bulk via tanker trucks to terminals where they are transferred to rail cars, shipped to distant locations or transferred into tanker trucks, and then delivered to the water treatment plants. These tanker trucks, transfer terminals and rail cars are potential sources of contamination. Therefore, NSF also inspects, samples, tests, and certifies products at rail transfer and storage depots. It is always important to verify that the location of the product distributor (the company that delivers the product to the water utility) matches that in the official NSF Listing for the product (available at www.nsf.org).

NSF has compiled data on the level of contaminants found in all fluoridation products that have applied for, or have been listed by, NSF. The statistical results in Table 1 (attached) include the test results for these products, as well as the annual monitoring tests from the period 2000 to 2006. This includes 245 separate samples analyzed during this time period. The concentrations reported represent contaminant levels that would be expected when the product is dosed into water at the Maximum Use Level (MUL). Lower product doses would produce proportionately lower contaminant concentrations (e.g. a 0.6 mg/L fluoride dose would produce one half the contaminant concentrations listed in Table 1.)

Table 1 documents that there is no contamination of drinking water from the fluoridation products NSF has tested and certified. NSF issued previous summaries of contaminant levels in fluoridation products for earlier reporting periods in 1999 and 2003. While some contaminant levels in those earlier periods were slightly higher than the current data for certain contaminants, there has not been a single fluoride product tested since the initiation of the program in 1988 with a contaminant concentration in excess of its corresponding SPAC. The documented reduction of impurities for this most current time period is due, at least in part, to the effectiveness of NSF/ANSI Standard 60 and the NSF certification program for drinking water treatment additives, and demonstrates the effectiveness of the program. The reduction in impurities is further attested to by an article in the Journal of the American Water Works Association entitled, "Trace Contaminants in Water Treatment Chemicals."[1]

Arsenic

The results in Table 1 indicate that the most common contaminant detected in these products is arsenic, but it is detected in only 43% of the product samples. This means that levels of arsenic

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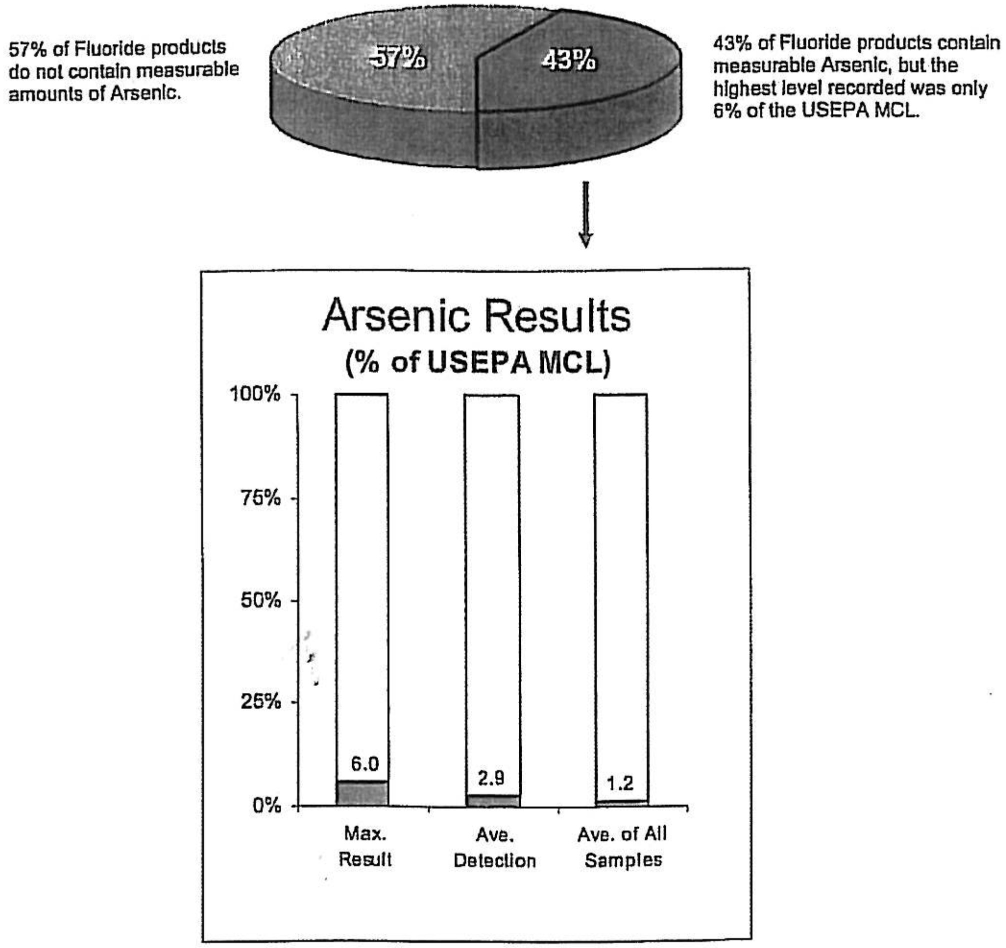
[1] Brown, R., et al., "Trace Contaminants in Water Treatment Chemicals: Sources and Fate." Journal of the American Water Works Association 2004: 96:12:111.

in 57% of the samples were non-detectable, even though products are tested at 10 times their maximum use level. All detections were at levels below the Single Product Allowable Concentration, if the product is added to drinking water at (or below) its maximum use level. The SPAC, as defined in NSF/ANSI Standard 60, is one tenth of the US EPA's MCL. The current MCL for arsenic is 10 ppb, the highest detection of arsenic from a fluoridation chemical was 0.6 ppb (shown on Table 1), and the average concentration was 0.12 ppb. Even the highest concentration of 0.6 ppb was only detected because the standard requires testing the chemical at 10 times its maximum use level to detect these trace levels of contaminants. Had the dose of fluoridation additives been tested in water at the maximum use level, instead of at 10 times their maximum use levels, the arsenic concentration measured would have been below the 1 ppb reporting limit for arsenic for 100 percent of the samples measured.

Figure A



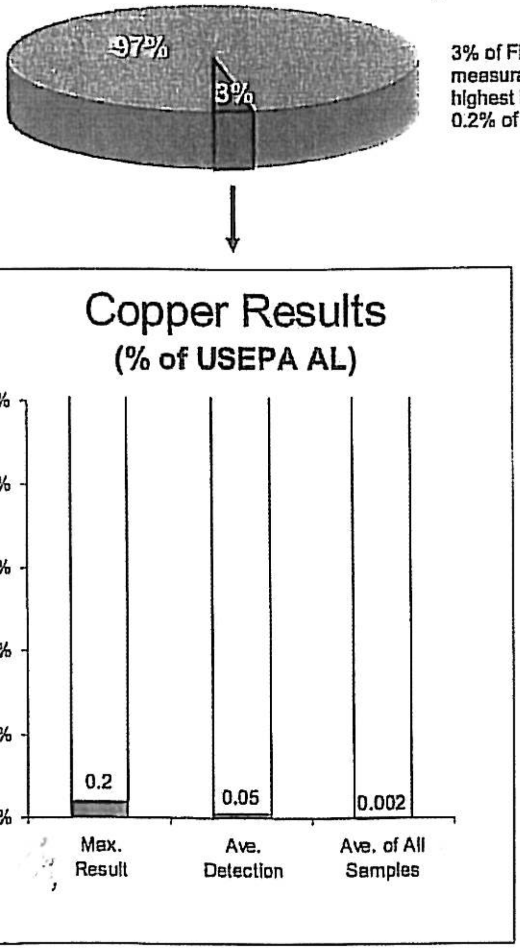
57% of Fluoride products do not contain measurable amounts of Arsenic.

43% of Fluoride products contain measurable Arsenic, but the highest level recorded was only 6% of the USEPA MCL.

Copper

The second most common contaminant found, and on a much less frequent basis, is copper, and 97% of all samples tested had no detectable levels of copper. The average concentration of copper has been 0.02 ppb with 2.6 ppb being the highest concentration detected. This is well below the 130 ppb SPAC requirement of NSF 60.

Figure B



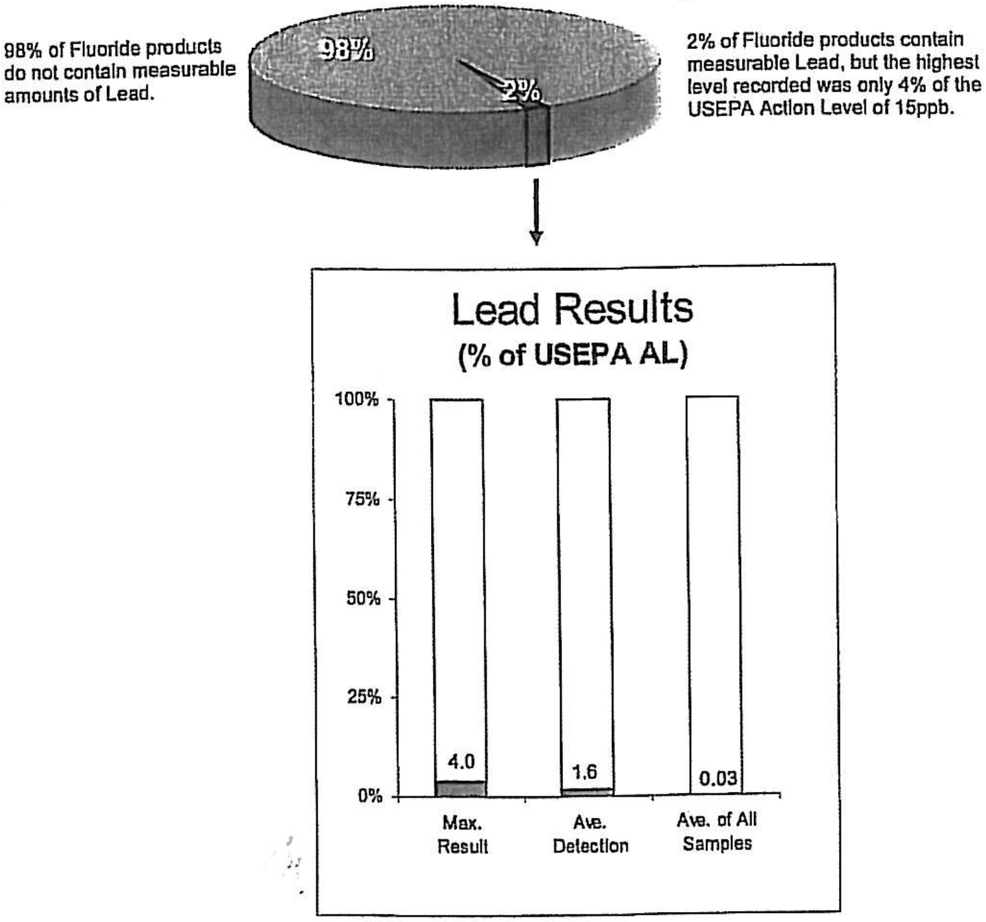
97% of Fluoride products do not contain measurable amounts of Copper.

3% of Fluoride products contain measurable Copper, but the highest level recorded was only 0.2% of the USEPA Action Level.

Lead

The third most common contaminant found is lead. It occurs on a much less frequent basis, and 98% of all samples tested had no detectable levels of lead. The average concentration of lead has been 0.005 ppb with 0.6 ppb being the highest concentration detected. This is well below the 1.5 ppb SPAC requirement of NSF 60.

Figure C



98% of Fluoride products do not contain measurable amounts of Lead.

2% of Fluoride products contain measurable Lead, but the highest level recorded was only 4% of the USEPA Action Level of 15ppb.

Radionuclides

Fluoridation products are also tested for radionuclides. All samples tested have not had any detectable levels of alpha or beta radiation.

Summary

In summary, the majority of fluoridation products as a class, based on NSF test results, do not add measurable amounts of arsenic, lead, other heavy metals, or radionuclide contamination to drinking water.

Additional information on fluoridation of drinking water can be found on the following web sites:

American Water Works Association (AWWA) Fluoridation Chemical Standards
http://www.awwa.org/Bookstore/producttopicsresults.cfm?MetaDataID=121&navItemNumber=5093

American Water Works Association (AWWA) position
http://www.awwa.org/Advocacy/pressroom/fluoride.cfm

American Dental Association (ADA) http://www.ada.org/public/topics/fluoride/index.asp

U.S. Centers for Disease Control and Prevention (CDC) http://www.cdc.gov/fluoridation

Table 1

	Percentage of Samples with Detectable Levels	Mean Contaminant Concentration in all samples (ppb)	Mean Contaminant Concentration in detectable samples (ppb)	Maximum Contaminant Concentration in detectable samples (ppb)	NSF/ANSI Standard 60 Single Product Allowable Concentration	US EPA Maximum Contaminant or Action Level
Antimony	0%	ND	ND	ND	0.6	6
Arsenic	43%	0.12	0.29	0.6 ✓	1	10
Barium	<1%	0.001	0.3	0.3	200	2000
Beryllium	0%	ND	ND	ND	0.4	4
Cadmium	1%	0.001	0.08	0.12	0.5	5
Chromium	<1%	0.001	0.15	0.2	10	100
Copper	3%	0.02	0.68	2.6	130	1300
Lead	2%	0.005	0.24	0.6 ✓	1.5	15
Mercury	<1%	0.0002	0.04	0.04	0.2	2
Radionuclides – alpha pCi/L	0%	ND	ND	ND	1.5	15
Radionuclides – beta mrem/yr	0%	ND	ND	ND	0.4	4
Selenium	<1%	0.016	1.95	3.2	5	50
Thallium	<1%	0.0003	0.04	0.06	0.2	2

<u>Abbreviations used in this Fact Sheet</u>

ANSI – American National Standards Institute

AWWA – American Water Works Association

AWWARF – American Water Works Association Research Foundation

ASDWA – Association of State Drinking Water Administrators

COSHEM – Conference of State Health and Environmental Managers

EPA – U.S. Environmental Protection Agency

MCL – maximum contaminant level

mrem/yr – millirems per year – measurement of radiation exposure dose

MUL – Maximum use level

NSF – NSF International (formerly the National Sanitation Foundation)

ppb – parts per billion

PCi/L – pico curies per liter – concentration of radioactivity

SPAC – Single Product Allowable Concentration

James Robert Deal

From: Stark, Blake [Stark@nsf.org]

Sent: Tuesday, July 15, 2008 12:55 PM

To: James Robert Deal

Subject: FW: need your help (fluoride issue)

As indicated in the fluoride fact sheet, NSF Standard 60 references the US EPA MCL for fluoride. You may be able to obtain toxicology studies from the US EPA or through their website.

Thank you,

-Blake Stark, NSF

****

****

From: James Robert Deal [mailto:JamesRobertDeal@jamesdeal.com]
Sent: Fri 7/11/2008 11:23 PM
To: Stark, Blake
Subject: need your help

Your Fact Sheet on water fluoridation mentions toxicological studies. Where would I find these?

I am looking for an assay of fluoridation materials in the raw, before dilution 240,000 times down to 1 ppm. Where would I find such an assay?

Sincerely,

James Robert Deal, Mortgage Broker
510-LO-25472, 510-MB-25306
James@DealMortgage.net
Deal Mortgage Corporation
P.O. Box 2370
Lynnwood WA 98036
425-771-1110 telephone
425-776-8081 fax
888-999-2022 toll-free
www.DealMortgage.net

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~~B-43~~

Hexafluorosilicic acid

From Wikipedia, the free encyclopedia
(Redirected from Fluorosilicic acid)

Hexafluorosilicic acid is the chemical compound with the formula H_2SiF_6. Hexafluorosilicic acid refers to an equilibrium mixture with hexafluorosilicate anion (SiF_6^{2-}) in an aqueous solution or other solvents that contain strong proton donors[1] at low pH.

Dihydrogen hexafluorosilicate	
IUPAC name	Dihydrogen hexafluorosilicate (2-)
Other names	Hexafluorosilicic acid Hydrofluorosilic acid Fluorosilicic acid Fluosilicic acid Silicofluoride
Identifiers	
CAS number	16961-83-4 ✓
EC number	241-034-8
UN number	1778
RTECS number	VV8225000
Properties	
Molecular formula	H_2SiF_6
Molar mass	144.09 g/mol
Appearance	colourless solution
Density	1.22 g/cm^3 (25% soln.) 1.38 g/cm^3 (35% soln.) 1.46 g/cm^3 (61% soln.)
Melting point	ca. 19 °C (60–70% soln.) <- 30 °C (35& soln.)
Structure	
Molecular shape	Octahedral SiF_6^{2-}
Hazards	
MSDS	External MSDS
EU Index	009-011-00-5
EU classification	Corrosive (**C**)
R-phrases	R34
S-phrases	(S1/2), S26, S27, S45
Flash point	Non-flammable
Related compounds	
Related hexafluorosilicates	Ammonium hexafluorosilicate Sodium hexafluorosilicate Potassium hexafluorosilicate Magnesium hexafluorosilicate
Related compounds	Hexafluorophosphoric acid Fluoroboric acid

✓ (what is this?) (verify)
Except where noted otherwise, data are given for materials in their standard state (at 25 °C, 100 kPa)

Contents

- 1 Nature of hexafluorosilicic acid
- 2 Production and principal reactions
- 3 Uses
  - 3.1 Niche applications
- 4 Safety
- 5 References

Nature of hexafluorosilicic acid

Like several related compounds, hexafluorosilicic acid does not exist as a discrete species, that is, a material with the formula H_2SiF_6 has not been isolated. Acids described similarly include chloroplatinic acid, fluoroboric acid, and hexafluorophosphoric acid, and, more commonly, carbonic acid. Distillation of hexafluorosilicic acid solutions produces no molecules of H_2SiF_6; instead the vapor consists of HF, SiF_4, and water. Aqueous solutions of H_2SiF_6 contain the hexafluorosilicate anion, SiF_6^{2-} and protonated water. In this octahedral anion, the Si-F bond distances are 1.71 Å.[2]

Production and principal reactions

H_2SiF_6 is mainly produced as a by-product from the production of phosphoric acid from apatite and fluorapatite. In the U.S. about 85% of fluorspar is used to produce hydrofluorosilic acid.[3] The

Infobox references

phosphoric and hydrofluoric acids are liberated from the mineral by the action of sulfuric acid. Some of the HF in turn reacts with silicate minerals, which are an unavoidable constituent of the mineral feedstock, to give silicon tetrafluoride. Thus formed, the silicon tetrafluoride reacts further with HF. The net process can be described as:[4]

$$SiO_2 + 6\ HF \rightarrow H_2SiF_6 + 2\ H_2O$$

Hexafluorosilicic acid can also be produced by treating silicon tetrafluoride and hydrofluoric acid.

Neutralization of solutions of hexafluorosilicic acid with alkali metal bases produces the corresponding alkali metal fluorosilicate salts:

$$H_2SiF_6 + 2\ NaOH \rightarrow Na_2SiF_6 + 2\ H_2O$$

The resulting salt Na_2SiF_6 is mainly used in water fluoridation. Related ammonium and barium salts are produced similarly for other applications. With excess base, the hexafluorosilicate undergoes hydrolysis, so the neutralization of the hexafluorosilicic acid must guard against this easy hydrolysis reaction:

$$Na_2SiF_6 + 4\ NaOH \rightarrow 6\ NaF + SiO_2 + 2\ H_2O$$

Uses

Hexafluorosilic acid is the feedstock for "virtually all organic and inorganic fluorine-bearing chemicals". [3] The majority of the hexafluorosilicic acid is converted to aluminium fluoride and cryolite.[4] These materials are central to the conversion of aluminium ore into aluminium metal. The conversion to aluminium trifluoride is described as:

$$H_2SiF_6 + Al_2O_3 \rightarrow 2\ AlF_3 + SiO_2 + H_2O$$

Hexafluorosilicic acid is also converted to a variety of useful hexafluorosilicate salts. The potassium salt is used in the production of porceleins, the magnesium salt for hardened concretes, and the barium salts for phosphors.

Hexafluorosilicic acid is also commonly used for water fluoridation in several countries including the United States, Great Britain, and Ireland. In the U.S., about 40,000 tons of fluorosilic acid is recovered from phosphoric acid plants, and then used primarily in water fluoridation, sometimes after being processed into sodium silicofluoride.[3]

Niche applications

H_2SiF_6 is a specialized reagent in organic synthesis for cleaving Si-O bonds of silyl ethers. It is more reactive for this purpose than HF. It reacts faster with t-butyldimethysilyl (TBDMS) ethers than triisopropylsilyl (TIPS) ethers.[5]

Hexafluorosilicic acid and the salts are used as wood preservation agents.[6]

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Safety

Hexafluorosilicic acid releases hydrogen fluoride when evaporated, so it has similar risks. It is corrosive and may cause fluoride poisoning; inhalation of the vapors may cause lung edema. Like hydrogen fluoride, it attacks glass and stoneware.[7]

References

1. ^ J. P. Nicholson (2005). "Electrodeposition of Silicon from Nonaqueous Solvents". *J. Electrochem. Soc.* **152** (12): C795–C802. doi:10.1149/1.2083227.
2. ^ Holleman, A. F.; Wiberg, E. "Inorganic Chemistry" Academic Press: San Diego, 2001. ISBN 0-12-352651-5.
3. ^ *a b c* USGS. Fluorspar.
4. ^ *a b* J. Aigueperse, P. Mollard, D. Devilliers, M. Chemla, R. Faron, R. Romano, J. P. Cuer, "Fluorine Compounds, Inorganic" in Ullmann's Encyclopedia of Industrial Chemistry, Wiley-VCH, Weinheim, 2005
5. ^ Pilcher, A. S.; DeShong, P. "Fluorosilicic Acid" in Encyclopedia of Reagents for Organic Synthesis, Copyright © 2001 John Wiley & Sons. DOI: 10.1002/047084289X.rf013
6. ^ Carsten Mai, Holger Militz (2004). "Modification of wood with silicon compounds. inorganic silicon compounds and sol-gel systems: a review". *Wood Science and Technology* 37 (5): 339. doi:10.1007/s00226-003-0205-5.
7. ^ Hexafluorosilicic acid Chemical Safety Card http://www.cdc.gov/niosh/ipcsneng/neng1233.html

Retrieved from "http://en.wikipedia.org/wiki/Hexafluorosilicic_acid"
Categories: Hydrogen compounds | Fluorides | Silicates | Acids | Coordination compounds

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STATE OF WASHINGTON
DEPARTMENT OF HEALTH
DIVISION OF ENVIRONMENTAL HEALTH
PO Box 47820 • Olympia, Washington 98504-7820

October 28, 2008

Dr. Eloise Kailin, MD
P.O. Box 1677
Sequim, WA 98382

Dear Dr. Kailin:

At the October 21, 2008 meeting of the Clallam County Board of Health you raised the question of whether or not the product used by the city of Port Angeles to fluoridate the city's water supply meets the regulatory requirements of the Washington State Department of Health. In follow-up we have confirmed that the city uses fluorosilicic acid provided from J. R. Simplot Company in Rock Springs, Wyoming. The product is NSF Standard 60 certified and does meet the requirements of our regulations.

At the Department of Health we do not have the resources that would allow us to do independent evaluations of water treatment products. As such we rely on national certification protocols to ensure the safety of water additives. Specifically, Washington Administrative Code 246-290-220 (3), requires that: "Any treatment chemicals, with the exception of commercially retailed hypochlorite compounds such as unscented Clorox, Purex, etc., added to water intended for potable use must comply with ANSI/NSF Standard 60. The maximum application dosage recommendation for the product certified by the ANSI/NSF Standard 60 shall not be exceeded in practice." Since the fluoridation product being used by the city of Port Angeles is certified under NSF Standard 60, the city's use of this product is in compliance with state law.

Attached is a July 2000 letter from Stan Hazan, general manager of the NSF Additives Certification Program, to US Representative Ken Calvert providing information on the NSF program. I hope you find this additional information useful.

Sincerely,

Gregg L. Grunenfelder, Assistant Secretary

Cc: Mary Selecky, Secretary of Health
Tom Locke, Clallam County Health Officer
Denise Clifford, Director Office of Drinking Water

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(10) 1,2-Dichloropropane
(11) Epichlorohydrin
(12) Ethylene dibromide
(13) Heptachlor
(14) Heptachlor epoxide
(15) Pentachlorophenol
(16) Polychlorinated biphenyls (PCBs)
(17) Tetrachloroethylene
(18) Toxaphene
(19) Benzo[a]pyrene
(20) Dichloromethane (methylene chloride)
(21) Di(2-ethylhexyl)phthalate
(22) Hexachlorobenzene
(23) 2,3,7,8-TCDD (Dioxin)

(b) MCLGs for the following contaminants are as indicated:

Contaminant	MCLG in mg/l
(1) 1,1-Dichloroethylene	0.007
(2) 1,1,1-Trichloroethane	0.20
(3) para-Dichlorobenzene	0.075
(4) Aldicarb	0.001
(5) Aldicarb sulfoxide	0.001
(6) Aldicarb sulfone	0.001
(7) Atrazine	0.003
(8) Carbofuran	0.04
(9) o-Dichlorobenzene	0.6
(10) cis-1,2-Dichloroethylene	0.07
(11) trans-1,2-Dichloroethylene	0.1
(12) 2,4-D	0.07
(13) Ethylbenzene	0.7
(14) Lindane	0.0002
(15) Methoxychlor	0.04
(16) Monochlorobenzene	0.1
(17) Styrene	0.1
(18) Toluene	1
(19) 2,4,5-TP	0.05
(20) Xylenes (total)	10
(21) Dalapon	0.2
(22) Di(2-ethylhexyl)adipate	.4
(23) Dinoseb	.007
(24) Diquat	.02
(25) Endothall	.1
(26) Endrin	.002
(27) Glyphosate	.7
(28) Hexachlorocyclopentadiene	.05
(29) Oxamyl (Vydate)	.2
(30) Picloram	.5
(31) Simazine	.004
(32) 1,2,4-Trichlorobenzene	.07
(33) 1,1,2-Trichloroethane	.003

[50 FR 46901, Nov. 13, 1985, as amended at 52 FR 20674, June 2, 1987; 52 FR 25716, July 8, 1987; 56 FR 3592, Jan. 30, 1991; 56 FR 30280, July 1, 1991; 57 FR 31846, July 17, 1992]

§ 141.51 Maximum contaminant level goals for inorganic contaminants.

(a) [Reserved]

(b) MCLGs for the following contaminants are as indicated:

Contaminant	MCLG (mg/l)
Antimony	0.006
Arsenic	zero[1]
Asbestos	7 Million fibers/liter (longer than 10 μm).
Barium	2
Beryllium	.004
Cadmium	0.005
Chromium	0.1
Copper	1.3
Cyanide (as free Cyanide)	.2
Fluoride	4.0
Lead	zero
Mercury	0.002
Nitrate	10 (as Nitrogen).
Nitrite	1 (as Nitrogen).
Total Nitrate+Nitrite	10 (as Nitrogen).
Selenium	0.05
Thallium	.0005

[1] This value for arsenic is effective January 23, 2006. Until then, there is no MCLG.

[50 FR 47155, Nov. 14, 1985, as amended at 52 FR 20674, June 2, 1987; 56 FR 3593, Jan. 30, 1991; 56 FR 26548, June 7, 1991; 56 FR 30280, July 1, 1991; 57 FR 31846, July 17, 1992; 60 FR 33932, June 29, 1995; 66 FR 7063, Jan. 22, 2001]

§ 141.52 Maximum contaminant level goals for microbiological contaminants.

MCLGs for the following contaminants are as indicated:

Contaminant	MCLG
(1) *Giardia lamblia*	zero
(2) Viruses	zero
(3) *Legionella*	zero
(4) Total coliforms (including fecal coliforms and *Escherichia coli*).	zero.
(5) *Cryptosporidium*	zero.

[54 FR 27527, 27566, June 29, 1989; 55 FR 25064, June 19, 1990; 63 FR 69515, Dec. 16, 1998]

§ 141.53 Maximum contaminant level goals for disinfection byproducts.

MCLGs for the following disinfection byproducts are as indicated:

Disinfection byproduct	MCLG (mg/L)
Bromodichloromethane	Zero
Bromoform	Zero
Bromate	Zero
Dichloroacetic acid	Zero
Trichloroacetic acid	0.3
Chlorite	0.8
Dibromochloromethane	0.06

[63 FR 69465, Dec. 16, 1998, as amended at 65 FR 34405, May 30, 2000]

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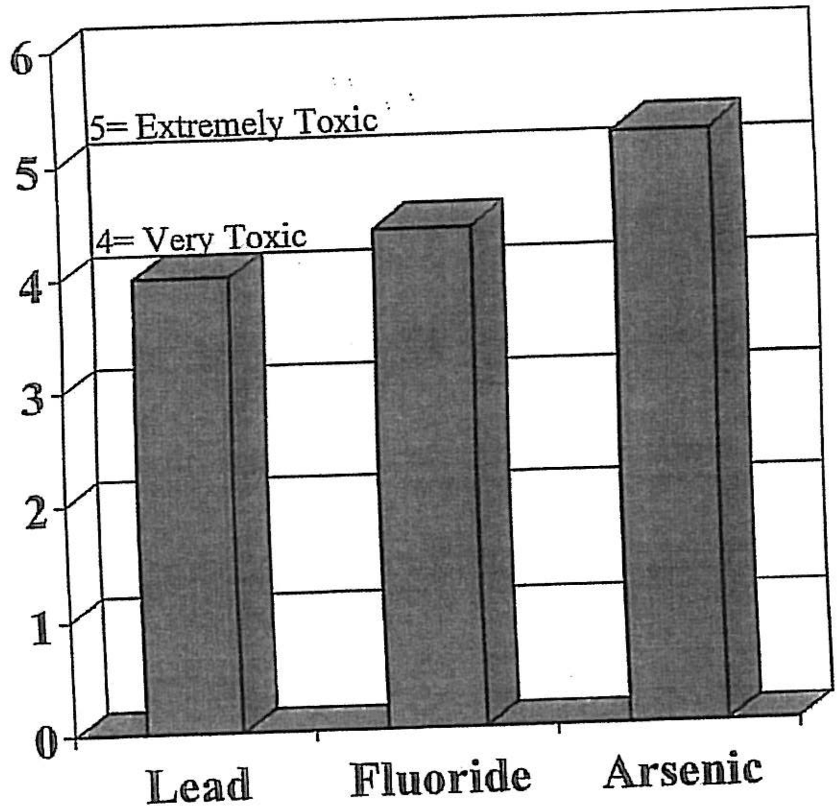
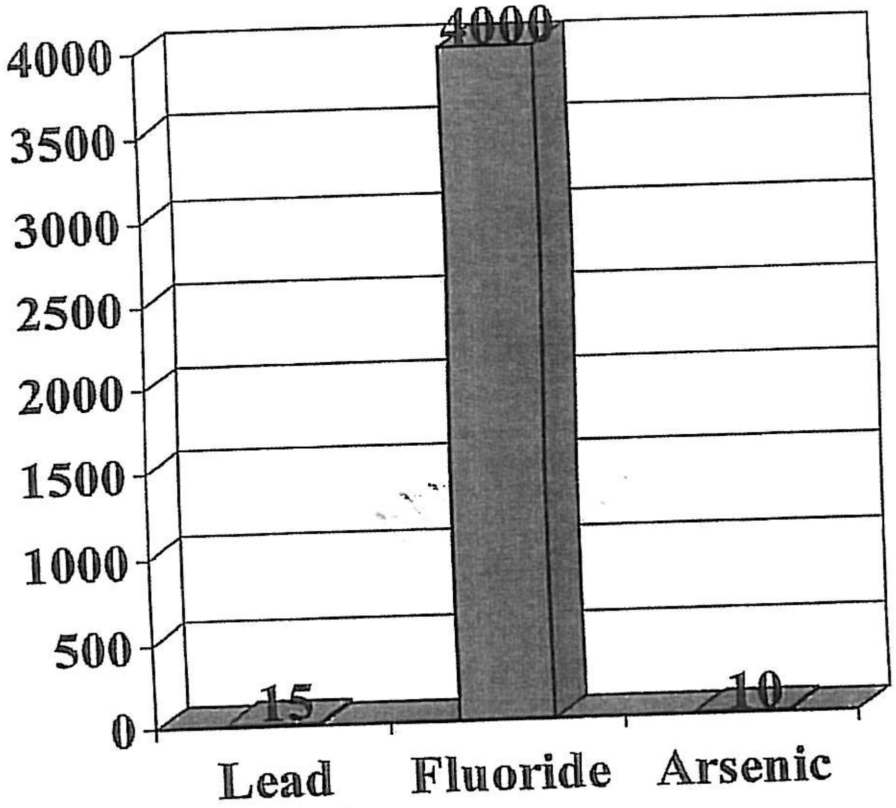
How Toxic is Fluoride compared to Lead & Arsenic.

Relative Toxicity



Source: *Clinical Toxicology of Commercial Products* LD50 data - 1984

EPA Maximum Contaminant Levels



ppb (Parts per Billion)

FDA National Pharmacy

A Community Pharmacy Technician's Role in Medication Reduction Strategies

This column was prepared by the Institute for Safe Medication Practices (ISMP). ISMP is an independent nonprofit agency that works closely with United States Pharmacopeia (USP) and Food and Drug Administration (FDA) in analyzing medication errors, near misses, and potentially hazardous conditions as reported by pharmacists and other practitioners. ISMP then makes appropriate contacts with companies and regulators, gathers expert opinion about prevention measures, and publishes its recommendations. To read about the recommendations for prevention of reported errors that you can put into practice today, subscribe to ISMP Medication Safety Alert!™ Community/Ambulatory Edition by visiting www.ismp.org. If you would like to report a problem confidentially to these organizations, go to the ISMP Web site (www.ismp.org) for links with USP, ISMP, and FDA. Or call 1-800/23-ERROR to report directly to the USP-ISMP Medication Errors Reporting Program. ISMP address: 200 Lakeside Dr, Horsham, PA 19044. Phone: 215/947-7797. E-mail: ismpinfo@ismp.org.

Pharmacy technicians play a major role in community pharmacy practice. The pharmacist relies on the technician to provide an extra layer of safety. It is important for technicians to follow system-based processes and inform the pharmacist when these processes do not work or are unmanageable.

Prescription Drop Off

The date of birth should be written on every hard copy prescription so the pharmacist has a second identifier readily available during verification. Allergy information should be questioned and updated at every patient encounter. Medical condition information, such as pregnancy, communicated to the technician at drop off should be updated in the computerized profile system to help the verification pharmacist determine counseling opportunities. Knowing a person's medical conditions also helps the pharmacist determine if prescriptions are written incorrectly or for the wrong drug.

Data Entry

Medication safety is enhanced when technicians know the particular language of pharmacy when entering a prescription.

New drugs are at a particular risk because it is more likely that the technician is not aware of the new drug and a more familiar drug is selected. Pharmacists and technicians should work together to determine the best method of distributing information regarding availability of new drugs on the market.

It is important that the technician understands the safety features of the computer system and does not create work-arounds to improve efficiency at the risk of decreasing accuracy and safety. Drug alerts can be numerous, and the technician may be inclined to override the alert and not "bother" the pharmacist. A better way to resolve too many alerts would be to establish protocol between the technician and the pharmacist to determine which level and type of alert needs pharmacist intervention.

Production

Mix-ups occur primarily due to incorrectly reading the label. The problem is aggravated by what is referred to as *confirmation bias*. Often a technician chooses a medication container based on a mental picture of the item, whether it be a characteristic of the drug label, the shape and size or color of the container, or the location of the item on a shelf. Consequently the wrong product is picked. Physically separating drugs with look-alike labels and packaging helps to reduce this contributing factor.

Point of Sale

Correctly filled prescriptions sold to a patient for whom it was not intended is an error that can be avoided by consistent use of a second identifier at the point of sale. Ask the person picking up the prescription to verify the address or in the case of similar names, the date of birth, and compare the answer to the information on the prescription receipt.

Internal errors should be discussed among all staff for training purposes. In addition, it is important to read about and discuss errors and methods of prevention occurring and being employed at other pharmacies within a chain and in other pharmacies, nationwide. ISMP Medication Safety Alert! Community/Ambulatory Edition offers this information to both pharmacists and technicians.

FDA's Effort to Remove Unapproved Drugs From the Market

Pharmacists are often not aware of the unapproved status of some drugs and have continued to unknowingly dispense unapproved drugs because the labeling does not disclose that they lack FDA approval. FDA estimates that there are several thousand unapproved drugs illegally marketed in the United States. FDA is stepping up its efforts to remove unapproved drugs from the market.

Background

There are three categories of unapproved drugs that are on the market. The first category consists of those that have been approved for safety, or that are identical, related, or similar to those drugs, and either have been found not to be effective, or for which FDA has not yet determined that they are effective. Between 1938 (passage of the Federal Food, Drug, and Cosmetic Act) and 1962, manufacturers were only required to demonstrate that drugs were safe; the requirement that they also demonstrate that drugs were effective was added in 1962. Drugs that fall in this category have been part of the DESI (Drug Efficacy Study Implementation) review, which was implemented to determine whether drugs approved between 1938 and 1962, or drugs that are identical, related, or similar to such drugs, met the new effectiveness requirements. While the DESI review is mostly completed, some parts of it are still continuing. The second category of unapproved drugs consists of those drugs that were on the market prior to 1938 (passage of the Federal Food, Drug, and Cosmetic Act). The third category, new unapproved drugs, comprises unapproved drugs that were first marketed (or changed) after 1962. Some also may have already been the subject of a formal agency finding that they are new drugs.

FDA's Concerns About Unapproved Drugs

FDA has serious concerns that drugs marketed without FDA approval may not meet modern standards for safety, effectiveness, manufacturing quality, labeling, and post-market surveillance. For example, FDA-approved drugs must demonstrate that their manufacturing processes can reliably produce drug products of expected identity, strength, quality, and purity. In addition, FDA's review of the applicant's labeling ensures that health care professionals and patients have the information necessary to understand a drug product's risks and its safety and efficacy.

Sponsors that market approved products are subject to more extensive reporting requirements for adverse drug events than sponsors of unapproved drugs. Reporting of adverse events by health care professionals and patients is voluntary, and under-reporting is well documented. FDA, therefore, cannot assume that an unapproved drug is safe or effective simply because it has been marketed for some period of time without reports of serious safety or effectiveness concerns.

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RCW 69.41.010

Definitions.

As used in this chapter, the following terms have the meanings indicated unless the context clearly requires otherwise:

(1) "Administer" means the direct application of a legend drug whether by injection, inhalation, ingestion, or any other means, to the body of a patient or research subject by:

(a) A practitioner; or

(b) The patient or research subject at the direction of the practitioner.

(2) "Community-based care settings" include: Community residential programs for the developmentally disabled, certified by the department of social and health services under chapter 71A.12 RCW; adult family homes licensed under chapter 70.128 RCW; and boarding homes licensed under chapter 18.20 RCW. Community-based care settings do not include acute care or skilled nursing facilities.

(3) "Deliver" or "delivery" means the actual, constructive, or attempted transfer from one person to another of a legend drug, whether or not there is an agency relationship.

(4) "Department" means the department of health.

(5) "Dispense" means the interpretation of a prescription or order for a legend drug and, pursuant to that prescription or order, the proper selection, measuring, compounding, labeling, or packaging necessary to prepare that prescription or order for delivery.

(6) "Dispenser" means a practitioner who dispenses.

(7) "Distribute" means to deliver other than by administering or dispensing a legend drug.

(8) "Distributor" means a person who distributes.

(9) "Drug" means:

(a) Substances recognized as drugs in the official United States pharmacopoeia, official homeopathic pharmacopoeia of the United States, or official national formulary, or any supplement to any of them;

(b) Substances intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in human beings or animals;

(c) Substances (other than food, minerals or vitamins) intended to affect the structure or any function of the body of human beings or animals; and

(d) Substances intended for use as a component of any article specified in (a), (b), or (c) of this subsection. It does not include devices or their components, parts, or accessories.

(10) "Electronic communication of prescription information" means the communication of prescription information by computer, or the transmission of an exact visual image of a prescription by facsimile, or other electronic means for original prescription information or prescription refill information for a legend drug between an authorized practitioner and a pharmacy or the transfer of prescription information for a legend drug from one pharmacy to another pharmacy.

(11) "In-home care settings" include an individual's place of temporary and permanent residence, but does not include acute care or skilled nursing facilities, and does not include community-based care settings.

(12) "Legend drugs" means any drugs which are required by state law or regulation of the state board of pharmacy to be dispensed on prescription only or are restricted to use by practitioners only.

(13) "Legible prescription" means a prescription or medication order issued by a practitioner that is capable of being read and understood by the pharmacist filling the prescription or the nurse or other practitioner implementing the medication order. A prescription must be hand-printed, typewritten, or electronically generated.

(14) "Medication assistance" means assistance rendered by a nonpractitioner to an individual residing in a community-based care setting or in-home care setting to facilitate the individual's self-administration of a legend drug or controlled substance. It includes reminding or coaching the individual, handing the medication container to the individual, opening the individual's medication container, using an enabler, or placing the medication in the individual's hand, and such other means of medication assistance as defined by rule adopted by the department. A nonpractitioner may help in the preparation of legend drugs or controlled substances for self-administration where a practitioner has determined and communicated orally or by written direction that such medication preparation assistance is necessary and appropriate. Medication assistance shall not include assistance with intravenous medications or injectable medications, except prefilled insulin syringes.

(15) "Person" means individual, corporation, government or governmental subdivision or agency, business trust, estate, trust, partnership or association, or any other legal entity.

(16) "Practitioner" means:

(a) A physician under chapter 18.71 RCW, an osteopathic physician or an osteopathic physician and surgeon under chapter 18.57 RCW, a dentist under chapter 18.32 RCW, a podiatric physician and surgeon under chapter 18.22 RCW, a veterinarian under chapter 18.92 RCW, a registered nurse, advanced registered nurse practitioner, or licensed practical nurse under chapter 18.79 RCW, an optometrist under

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chapter 18.53 RCW who is certified by the optometry board under RCW 18.53.010, an osteopathic physician assistant under chapter 18.57A RCW, a physician assistant under chapter 18.71A RCW, a naturopath licensed under chapter 18.36A RCW, a pharmacist under chapter 18.64 RCW, or, when acting under the required supervision of a dentist licensed under chapter 18.32 RCW, a dental hygienist licensed under chapter 18.29 RCW;

(b) A pharmacy, hospital, or other institution licensed, registered, or otherwise permitted to distribute, dispense, conduct research with respect to, or to administer a legend drug in the course of professional practice or research in this state; and

(c) A physician licensed to practice medicine and surgery or a physician licensed to practice osteopathic medicine and surgery in any state, or province of Canada, which shares a common border with the state of Washington.

(17) "Secretary" means the secretary of health or the secretary's designee.

[2009 c 549 § 1024; 2006 c 8 § 115. Prior: 2003 c 257 § 2; 2003 c 140 § 11; 2000 c 8 § 2; prior: 1998 c 222 § 1; 1998 c 70 § 2; 1996 c 178 § 16; 1994 sp.s. c 9 § 736; prior: 1989 1st ex.s. c 9 § 426; 1989 c 36 § 3; 1984 c 153 § 17; 1980 c 71 § 1; 1979 ex.s. c 139 § 1; 1973 1st ex.s. c 186 § 1.]

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Drugs

New Drug Application (NDA)

Introduction

For decades, the regulation and control of new drugs in the United States has been based on the New Drug Application (NDA). Since 1938, every new drug has been the subject of an approved NDA before U.S. commercialization. The NDA application is the vehicle through which drug sponsors formally propose that the FDA approve a new pharmaceutical for sale and marketing in the U.S. The data gathered during the animal studies and human clinical trials of an Investigational New Drug (IND) become part of the NDA.

The goals of the NDA are to provide enough information to permit FDA reviewer to reach the following key decisions:

- Whether the drug is safe and effective in its proposed use(s), and whether the benefits of the drug outweigh the risks.
- Whether the drug's proposed labeling (package insert) is appropriate, and what it should contain.
- Whether the methods used in manufacturing the drug and the controls used to maintain the drug's quality are adequate to preserve the drug's identity, strength, quality, and purity.

The documentation required in an NDA is supposed to tell the drug's whole story, including what happened during the clinical tests, what the ingredients of the drug are, the results of the animal studies, how the drug behaves in the body, and how it is manufactured, processed and packaged. The following resources provide summaries on NDA content, format, and classification, plus the NDA review process:

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Resources for NDA Submissions

The following resources have been gathered to provide you with the legal requirements of a new drug application, assistance from CDER to help you meet those requirements, and internal NDA review principles, policies and procedures.

Guidance Documents for NDAs

Guidance documents represent the Agency's current thinking on a particular subject. These documents are prepared for FDA review staff and applicants/sponsors to provide guidelines to the processing, content, and evaluation/approval of applications and also to the design, production, manufacturing, and testing of regulated products. They also establish policies intended to achieve consistency in the Agency's regulatory approach and establish inspection and enforcement procedures. Because guidances are not regulations or laws, they are not enforceable, either through administrative actions or through the courts. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both. For information on a specific guidance document, please contact the originating office.

For the complete list of CDER guidances, please see the Guidance Index. For information on a specific guidance document, please contact the originating office.

Guidance documents to help prepare NDAs include:

- Bioavailability and Bioequivalence Studies for Orally Administered Drug Products - General Considerations (Issued 10/2000, Posted 10/27/2000). This guidance should be useful for applicants planning to conduct bioavailability (BA) and bioequivalence (BE) studies during the IND period for an NDA, BE studies intended for submission in an ANDA, and BE studies conducted in the postapproval period for certain changes in both NDAs and ANDAs.

- Changes to an Approved NDA or ANDA [HTML] or [PDF] (Issued 11/1999, Posted 11/19/1999)
    - Changes to an Approved NDA or ANDA: Questions and Answers [HTML] or [PDF] (Issued 1/2001, Posted 1/22/2001)
- Container Closure Systems for Packaging Human Drugs and Biologics. (Issued 5/1999, Posted 7/6/1999)
- Format and Content of the Chemistry, Manufacturing and Controls Section of an Application. (Withdrawn as per FR notice, 6/1/2006)
- Format and Content of the Microbiology Section of an Application.
- Format and Content of the Clinical and Statistical Sections of an Application. (Issued 7/1988, Posted 5/21/1997)
- Format and Content of the Summary for New Drug and Antibiotic Applications. (Issued 2/1987, Posted 3/2/1998)
- Formatting, Assembling and Submitting New Drug and Antibiotic Applications. (Issued 2/1987, Posted 3/2/1998)
- Submitting Supporting Documentation in Drug Applications for the Manufacture of Drug Substances.
- Submitting Documentation for the Stability of Human Drugs and Biologics. (Issued 2/1987, Posted 3/2/1998)
- Submitting Samples and Analytical Data for Methods Validation.
- Submitting Supporting Documentation in Drug Applications for the Manufacture of Drug Products.
- NDAs: Impurities in Drug Substances (Issued 2/2000, Posted 2/24/2000)
- Format and Content of the Human Pharmacokinetics and Bioavailability Section of an Application. (Issued 2/1987, Posted 3/2/1998)
- Format and Content of the Nonclinical Pharmacology/Toxicology Section of an Application. (Posted 3/2/1998)
- Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products. Describes the quantity of evidence, and the documentation

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of the quality of evidence necessary to support a claim of drug effectiveness.

- Drug Master Files. A Drug Master File (DMF) is a submission to the FDA that may be used to provide confidential detailed information about facilities, processes, or articles used in the manufacturing, processing, packaging, and storing of one or more human drugs.
- Required Specifications for FDA's IND, NDA, and ANDA Drug Master File Binders
- Qualifying for Pediatric Exclusivity. Certain applications may be able to obtain an additional six months of patent exclusivity.

- PET Drug Applications - Content and Format for NDAs and ANDAs [HTML] or [PDF] (Issued 3/7/2000, Posted 3/7/2000)

- Refusal to File. (Issued 7/12/1993, Posted 11/26/99) Clarifies CDER's decisions to refuse to file an incomplete application.

Laws, Regulations, Policies and Procedures

The mission of FDA is to enforce laws enacted by the U.S. Congress and regulations established by the Agency to protect the consumer's health, safety, and pocketbook. *The Federal Food, Drug, and Cosmetic Act* is the basic food and drug law of the U.S. With numerous amendments, it is the most extensive law of its kind in the world. The law is intended to assure consumers that foods are pure and wholesome, safe to eat, and produced under sanitary conditions; that drugs and devices are safe and effective for their intended uses; that cosmetics are safe and made from appropriate ingredients; and that all labeling and packaging is truthful, informative, and not deceptive.

Code of Federal Regulations (CFR)

Code Of Federal Regulations (CFR) The final regulations published in the *Federal Register* (daily published record of proposed rules, final rules, meeting notices, etc.) are collected in the *CFR*. The *CFR* is divided into 50 titles which represent broad areas subject to Federal regulations. The FDA's

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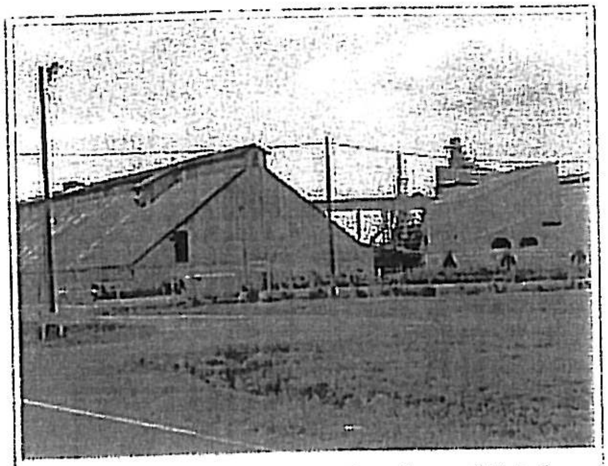
Bone Valley

From Wikipedia, the free encyclopedia
(Redirected from Bone valley)

The **Bone Valley** is a region of central Florida, encompassing portions of present-day Hardee, Hillsborough, Manatee, and Polk counties, in which phosphate is mined for use in the production of agricultural fertilizer. Florida currently contains the largest known deposits of phosphate in the United States.



Phosphate fertilizer processing plant -- Nichols, Florida.

Contents

- 1 Process
- 2 History
- 3 Rail Service
- 4 Risks of mining
- 5 External links

Process

Large walking draglines, operating twenty-four hours a day in surface mines, excavate raw pebble phosphate mixed with clay and sand (known as matrix) using huge buckets which can hold more than 40 cubic yards (30.58 m^3) of earth. The matrix contains a number of chemical impurities, including naturally occurring uranium at concentrations of approximately 100 ppm.

Rotary gondolas such as these are used by CSXT to transport phosphate rock from the Bone Valley region to transloading facilities along Tampa Bay -- Edison Junction, Florida.

The matrix is then dropped into a pit where it is mixed with water to create a slurry, which is then pumped through miles of large steel pipes to washing plants. These plants crush, sift, and separate the phosphate from the sand, clay, and other materials, and mix in more water to create a granular rock termed wetrock. The wetrock, which is typically of little use in raw form, is then moved largely by rail to fertilizer plants where it is processed. The final products include, but are not limited to, diammonium phosphate (DAP), monoammonium phosphate (MAP) and triple superphosphate (TSP).

Waste byproducts are stored in large phosphogypsum stacks and settling ponds, whose sizes are often measured in hundreds of acres, and can be up to 200 feet (60.96 m) tall in the case of large stacks. Phosphate processing produces significant amounts of fluorine gas, which must be treated by filtering through special scrubbers.

Most of the final product (known within the industry as 'dryrock') are then transported by rail to facilities along Tampa Bay, where they are transloaded onto ships destined for countries such as China.

Phosphate product intended for domestic use is assembled into long trains of covered hopper cars for

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northbound movement.

History

When the narrow gauge Florida Southern Railway reached Arcadia in 1886, it was only a sleepy little town and the builders paused only briefly before pushing the railroad south to Punta Gorda. Unknown to the railroad and the general public at this time, a great discovery had been made in 1881 by Captain Francis LeBaron of the United States Army Corps of Engineers, who was examining the lower Peace River area for the survey of a canal that would connect the headwaters of the Saint Johns River to Charlotte Harbor. Here he found and shipped to the Smithsonian Institution nine barrels of prehistoric fossils from the sand bars prevalent on the lower Peace River. He also noticed that there was a phosphatase quality to the fossils and the deposit they were found in was very valuable. The Smithsonian wanted him to return and lead an expedition for prospecting more fossils, but Captain LeBaron was unable to return due to his important duties at Fernandina where he was put in charge of harbor improvements.

Finally in December 1886, LeBaron was able to return to the Peace River where he dug some test pits and sent the samples to a laboratory for analysis. His suspicions were confirmed as the tests showed high quality bone phosphate of lime. LeBaron tried in vain to round up investors in New York, Boston and Philadelphia, but none were willing to invest in the project. Frustrated he left the United States for the ill-fated Nicaraguan Canal Project.

Meanwhile, the test results became known to Colonel G.W. Scott who owned the G.W. Scott Manufacturing Co. of Atlanta and he quickly sent a representative down to Arcadia who made several large purchases along the Peace River. Colonel T.S. Moorhead of Pennsylvania had also learned about the deposits from Captain LeBaron, but not the secret of their location, traveled to Arcadia where he luckily stumbled onto the famous sand bars. Mr. Moorhead formed the Arcadia Phosphate Company, with the Scott Mfg. Co. quickly agreeing to purchase the entire output. The very first shipment of Florida phosphate was made in May 1888 when the first ten car loads were dispatched to Scott's Fertilizer Works in Atlanta, Georgia. Soon after, G.W. Scott formed the Desoto Phosphate Co. at Zolfo where the Florida Southern Railway crossed the Peace River. However the biggest player was the Peace River Phosphate Co. (formed in January 1887) which was located in Arcadia by M.M. Knudson of New York and they quickly built a narrow gauge railroad from the works on the river to the interchange with the Florida Southern. It is this company and its railroad that is the first direct ancestor of the future Charlotte Harbor & Northern. The Peace River Phosphate Co. began mining in the Winter of 1889, and most of the ore was shipped to Punta Gorda via. the Florida Southern, where it was loaded onto boats for export to Europe.

Early mining methods was the pick and shovel method where the above water sand bars were mined by hand and loaded onto barges which were herded by shallow water tug boats to the drying works located nearby. Soon the use of suction dredges were put into use and the mining spread all along the lower Peace River.

Moorhead soon sold his Arcadia Phosphate Co. to Hammond & Hull of Savannah, Georgia a large fertilizer operation in that city. Moorhead then left Florida and returned to Pennsylvania, where he developed a phosphate mine in Juniata County, PA and formed the narrow gauge Tuscarora Valley Rail Road. Hammond & Hull also owned the Charlotte Harbor Phosphate Co. which had their works at Hull, connecting with the Florida Southern by a short branch line. Wanting to connect the two plants, Hammond & Hull built a narrow gauge railroad between Arcadia and Hull around 1890. The railroad served various load outs along the river where the barges full of pebble would be unloaded and raised to the railroad and loaded onto ore cars for the journey to the drying plants at Arcadia and Hull. Hammond dropped out around 1890 and the new firm was known as Comer & Hull.

The Peace River Phosphate Co. in the mean time had built a narrow gauge railroad north of Arcadia to their load-outs along the Peace River. Like the Comer & Hull operations, the ore was hauled to the drying plant at Arcadia where it was loaded into the narrow gauge boxcars of the Florida Southern. When the railroad converted it's Charlotte Harbor Division to standard gauge in 1892, both the Peace River Phosphate Co. and Comer & Hull operations converted their respective railroads. Joseph Hull of Comer & Hull purchased a half interest in the Peace River Phosphate Co. about this time.

In December 1894, Joseph Hull consolidated the Arcadia Phosphate Co., Charlotte Harbor Phosphate Co., Desota Phosphate & Mining Co. & Peace River Phosphate Co. into the Peace River Phosphate Mining Co.

Peter Bradley of New York was one of the fertilizer capitalists (Bradley Fertilzer Co.) that Captain LeBaron had first approached about the sand bars, but was initially rebuffed. In May 1899, he was involved in the merger of 22 fertilizer companies into the American Agricultural Chemical Co. becoming vice president and a director of the new corporation.

AACC began buying the stock of the Peace River Phosphate Mining Co. beginning in June 1899 and finishing up in January 1902.

The Peace River Phosphate Mining Company Railroad consisted of a mainline running south from Arcadia to Liverpool. A few short branches connected the railroad to the Florida Southern (later the Plant System in 1896 and the ACL after 1902) at Arcadia, Hull and Liverpool. At Hull was the washing plant where sand was removed. Liverpool housed the drying plant and barge loading facilities. A branch running north for about 3 miles (4.8 km) upstream from Arcadia served the many load outs along the river.

In the early years, phosphate from the Peace River area was barged to Punta Gorda, or shipped by rail to Port Tampa. Other important ports were later established at Seddon Island, Boca Grande, and Rockport.

Today, there are two companies which mine phosphate rock in the region, Mosaic Inc. (formed from the merger of IMC-Global and Cargill Crop Nutrition) as well as CF Industries. At present, Mosaic is seeking to mine properties further south, in Hardee and Manatee Counties.

With renewed interest in corn-based Ethanol fuel, the demand for fertilizer is expected to increase.

Rail Service

Throughout most of the twentieth century, the Bone Valley region received service from two major railroads, the Atlantic Coast Line and Seaboard Air Line. More than a few plants and mines saw the services of *both* railroad companies, such as the Ridgewood fertilizer plant located at Bartow, and the massive Pierce complex south of Mulberry. It was not until the 1967 Seaboard Coast Line merger that the bitter rivalry was put to rest. SCL itself was later absorbed into CSX, who have since pursued an aggressive strategy of abandoning redundant trackage.

Phosphate train enroute to a fertilizer plant. -- Pierce, Florida.

Risks of mining

Phosphate is a declining export to China. Previously, significant

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Phosphogypsum stack located near Fort Meade, Florida. These contain the waste byproducts of the phosphate fertilizer industry.

amounts of rock were shipped to China, where it was processed into phosphate fertilizer. The majority of phosphate mining in Florida is done in the Peace River watershed. Phosphate mining companies use draglines to remove surface soils up to 60 feet (18.29 m) deep over thousands of contiguous acres. Once land is mined, state law requires that it be reclaimed. Wetlands are reclaimed on an acre for acre, type for type basis. Most modern mining permits actually require companies to recreate more wetlands than were initially present on the land. More than 180,000 acres (728 km^2) have already been mined and reclaimed in the Peace River watershed. As reserves in the northern portion of the bone valley are depleting, mining companies are now seeking permits for another 100,000 acres (405 km^2), which will replace reclaimed mines to the north.

One byproduct of the extraction process is clay, which is stored in settling ponds and eventually comprise thirty to forty percent of a mine site. Some of these ponds can measure thousands of acres. Rain drains slower through these clay-laden ponds than typical soil. Critics argue that this, in turn, reduces baseflow to the Peace River. Some studies have indicated that reclaimed lands actually provide a more consistent baseflow because the sandier soils of the reclaimed land provide faster baseflow, while the clay provides a slower steady flow, creating more flow during dry periods than native land. Since the 1960s, the average annual flow of the middle Peace River has declined from 1,350 cubic feet (38.23 m^3) to 800 cubic feet (22.65 m^3) per second (38.23 to 22.65 m^3/s). Critics argue that this flow reduction is due to phosphate mining, but studies by the Southwest Florida Water Management District have shown that the reduction in flow is due to multidecadal oscillation in Atlantic Ocean temperatures.

Critics argue that each holding pond has been perceived as a risk that threatens water quality, public health, wildlife, and the regional economy. Dams restraining the ponds have overflowed or burst, sending a slurry of clay into the river, and coating the riverbed for many miles with a toxic clay slime that suffocates flora and fauna. One such incident in 1971 killed over three million fish when two million gallons of phosphate waste swept into the river, causing an estimated five foot tall tide of slime that spread into adjacent pastures and wetlands. Since the 1971 spill, clay settling areas are now constructed as engineered dams. No such spills have occurred from any settling areas built to these standards. The current dams even withstood three hurricanes which crossed directly over the Bone Valley in 2004.

Most recently, in 2004, during Hurricane Frances, a phosphogypsum stack was overwhelmed by hurricane rains and the levees were breached, sending over 18,000 US gal (68,137 L) of acidic process water into Tampa Bay. Cargill Crop Nutrition, who owned the stack, added lime into the affected areas in an attempt to neutralize the highly-acidic runoff. Due to the extraordinary amount of runoff created by the hurricane, the spill was quickly diluted and environmental damage was minimal. In a consent agreement with the Department of Environmental Protection, Cargill greatly increased its water treatment capacity at the facility. The facility is a no discharge facility and was overwhelmed by the above normal rainfall in 2004, in addition to being affected by three hurricanes.

On occasion, clay slime spills have prevented the *Peace River Manasota Water Supply Authority* from using river flows for drinking water, forcing municipalities to seek water supplies elsewhere, or rely on stored supplies. On several occasions, the effects of heavy rainfall have created sinkholes beneath the settling ponds.

External links

- CF Industries, Inc.
- Mosaic Co.
- The Phosphate Fertilizer Industry: An Environmental Overview
- Florida Phosphate Facts

Retrieved from "http://en.wikipedia.org/wiki/Bone_Valley"
Categories: Geography of Florida | Tampa Bay Area | History of Florida | Economic geology

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- This page was last modified on 12 November 2009 at 20:06.
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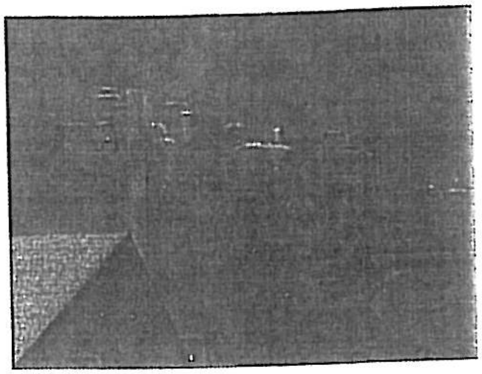
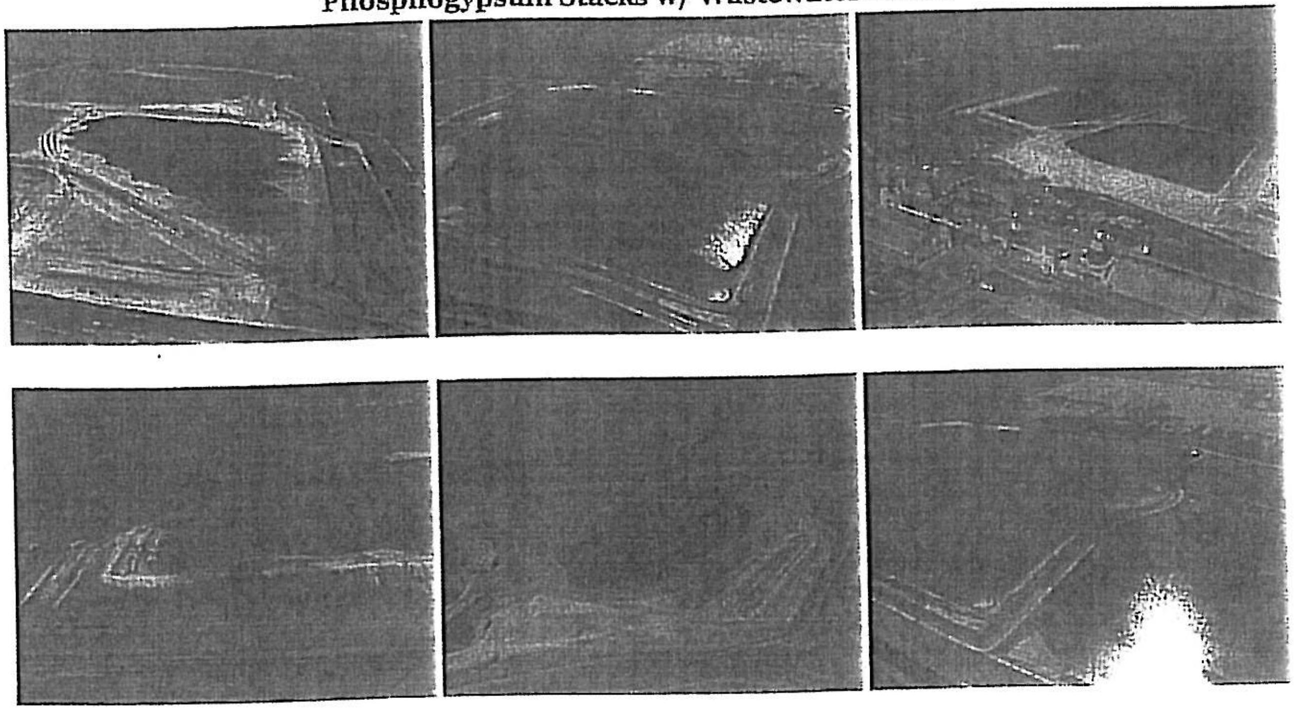


Photographs of Gypsum Stacks w/ Wastewater Ponds

All of the photographs on this page, except for the photos of the sinkhole, were taken by Michael and Paul Connett in Central Florida (the heart of the phosphate industry) in June 2001. They can be copied and distributed freely. Click on the photos to access larger copies of each. To learn more about the phosphate fertilizer industry, click here.

Phosphogypsum Stacks w/ Wastewater Ponds



Sinkhole in Gypsum Stacks

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Photographs of Gypsum Stacks w/ Wastewater Ponds

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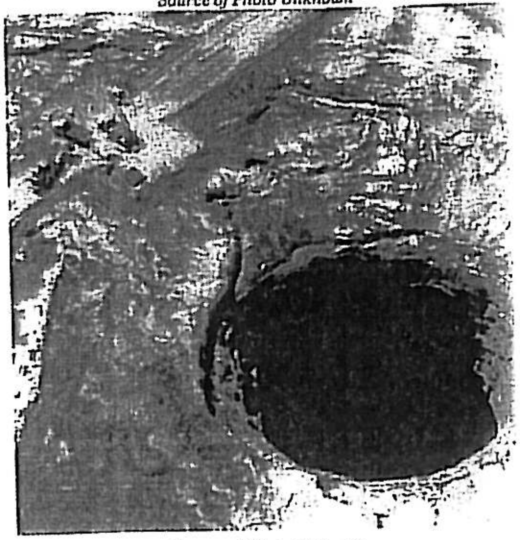

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See: <u>The Phosphate Fertilizer Industry: An Environmental Overview</u>

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IMC Agrico - Phosphate Processing Facility.
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The Phosphate Fertilizer Industry: An Environmental Overview

by Michael Connett
Fluoride Action Network
May 2003

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1) Introduction (back to top)

They call them "wet scrubbers" - the pollution control devices used by the phosphate industry to capture fluoride gases produced in the production of commercial fertilizer.

In the past, when the industry let these gases escape, vegetation became scorched, crops destroyed, and cattle crippled.

Today, with the development of sophisticated air-pollution control technology, less of the fluoride escapes into the atmosphere, and the type of pollution that threatened the survival of some communities in the 1950s and 60s, is but a thing of the past (at least in the US and other wealthy countries).

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However, the impacts of the industry's fluoride emissions are still being felt, although more subtly, by millions of people - people who, for the most part, do not live anywhere near a phosphate plant.

That's because, after being captured in the scrubbers, the fluoride acid (hydrofluorosilicic acid), a classified hazardous waste, is barreled up and sold, unrefined, to communities across the country. Communities add hydrofluorosilicic acid to their water supplies as the primary fluoride chemical for water fluoridation.

Even if you don't live in a community where fluoride is added to water, you'll still be getting a dose of it through cereal, soda, juice, beer and any other processed food and drink manufactured with fluoridated water.

Meanwhile, if the phosphate industry has its way, it may soon be distributing another of its by-products to communities across the country. That waste product is radium, which may soon be added to a roadbed near you - if the EPA buckles and industry has its way.

2) Effects of Fluoride Pollution (back to top)

Central Florida knows it well. So too does Garrison Montana, Cubatao Brazil, and any other community where phosphate industries have had inefficient, or non-existent, pollution control: Fluoride.

The Canadian Broadcasting Corporation (CBC) called the phophate industry a "pandora's box." That, while it brought wealth to rural communities, it also brought ecological devastation. The CBC described the effects of one particular phosphate plant in Dunville, Ontario:

> "Farmers noticed it first... Something mysterious burned the peppers, burned the fruit, dwarfed and shriveled the grains, damaged everything that grew. Something in the air destroyed the crops. Anyone could see it... They noticed it first in 1961. Again in '62. Worse each year. Plants that didn't burn, were dwarfed. Grain yields cut in half...Finally, a greater disaster revealed the source of the trouble. A plume from a silver stack, once the symbol of Dunville's progress, spreading for miles around poison - fluorine. It was identified by veterinarians. There was no doubt. What happened to the cattle was unmistakable, and it broke the farmer's hearts. Fluorosis - swollen joints, falling teeth, pain until cattle lie down and die. Hundreds of them. The cause - fluorine poisoning from the air."

Fluoride has been, and remains to this day, one of the largest environmental liabilities of the phosphate industry. The source of the problem lies in the fact that raw phosphate ore contains high concentrations of fluoride, usually between 20,000 to 40,000 parts per million (equivalent to 2 to 4% of the ore).

When this ore is processed into water-soluble phosphate (via the addition of sulfuric acid), the fluoride content of the ore is vaporized into the air, forming highly toxic gaseous compounds (hydrogen fluoride and silicon tetrafluoride).

In the past, when the industry had little, if any, pollution control, the fluoride gases were frequently emitted in large volumes into surrounding communities, causing serious environmental damage.

In Polk County, Florida, the creation of multiple phosphate plants in the 1940s caused damage to nearly 25,000 acres of citrus groves and "mass fluoride poisoning" of cattle. It is estimated that, as a result of fluoride contamination, "the cattle population of Polk County dropped 30,000 head" between 1953 and 1960, and "an estimated 150,000 acres of cattle land were abandoned" (Linton 1970).

According to the former president of the Polk County Cattlemen's Association:

> "Around 1953 we noticed a change in our cattle... We watched our cattle become gaunt and starved, their legs became deformed; they lost their teeth. Reproduction fell off and when a cow did have a calf, it was also affected by this malady or was a stillborn" (ibid).

In the 1960s, air pollution emitted by another phosphate plant in Garrison, Montana was severe enough to be branded "the worst in the nation" by a 1967 National Air Pollution Conference in Washington, D.C.

As in Polk County, and other communities downwind of fluoride emissions, the cattle in Garrison were poisoned by fluoride. As described in a 1969 article from *Good Housekeeping*:

> "The blight had afflicted cattle too. Some lay in the pasture, barely able to move. Others limped and staggered on swollen legs, or painfully sank down and tried to graze on their knees... Ingested day after day, the excessive fluoride had caused tooth and bone disease in the cattle, so that they could not tolerate the anguish of standing or walking. Even eating or drinking was an agony. Their ultimate fate was dehydration, starvation - and death."

3) Litigation from Fluoride Damage (back to top)

Damage to vegetation and livestock, caused by fluoride emissions from large industry, has resulted, as one might expect, in a great deal of expensive litigation. In 1983, Dr. Leonard Weinstein of Cornell University, stated that "certainly, there has been more litigation on alleged damage to agriculture by fluoride than all other pollutants combined" (Weinstein 1983). While Weinstein was referring to fluoride pollution in general, his comments give an indication of the problem facing the phosphate industry - one of the most notorious emitters of fluoride - in its early days.

So too does an estimate from Dr. Edward Groth, currently a Senior Scientist at Consumers Union. According to an article written by Groth, fluoride pollution between the years 1957 to 1968, "was responsible for more damage claims against industry than all twenty (nationally monitored air pollutants) combined."

The primary reason for the litigation against fluoride emitters was "the painful, economically disastrous, debilitating disease" that fluoride causes to livestock (Hodge & Smith 1977). As noted in a 1970 review by the US Department of Agriculture (USDA),

> "Airborne fluorides have caused more worldwide damage to domestic animals than any other air pollutant" (Lillie 1970).

Another review on air pollution reached the same conclusion. According to Ender (1969):

> "The most important problem concerning damage to animals by air pollution is, no doubt, the poisoning of domestic animals caused by fluorine in smoke, gas, or dust from various industries; industrial fluorosis in livestock is today a disorder well known by veterinarians in all industrialized countries."

According to a review discussing "Fluorine toxicosis and industry", Shupe noted that:

> "Air pollution damage to agricultural production in the United States in 1967 was estimated at $500,000,000. Fluoride damage to livestock and vegetation was a substantial part of this amount" (Shupe 1970).

4) Scrubbing away the problem (back to top)

Due to the inevitable liabilities that fluoride pollution presented, and to an increasingly stringent set of environmental regulations, the phosphate industry began cleaning up its act.

As noted by Ervin Bellack, a chemist for the US Public Health Service:

> "In the manufacture of super-phosphate fertilizer, phosphate rock is acidulated with sulfuric acid, and the fluoride content of the rock evolves as volatile silicofluorides. In the past, much of this volatile material was vented to the atmosphere, contributing heavily to pollution of the air and land surrounding the manufacturing site. As awareness of the pollution problem increased, scrubbers were added to strip particulate and gaseous components from the waste gas..." (Bellack 1970)

A 1979 review, published in the journal *Phosphorous & Potassium*, added:

> "The fluorine compounds liberated during the acidulation of phosphate rock are now rightly regarded as a menace and the industry is now obliged to suppress emissions-containing vapors to within very low limits in most parts of the world...
>
> In the past, little attention was paid to the emission of gaseous fluorine compounds in the fertilizer industry. But today fluorine recovery is increasingly necessary because of stringent environmental restrictions which demand drastic reductions in the quantities of volatile and toxic fluorine compounds emitted into the waste gases. These compounds now have to be recovered and converted into harmless by-products for disposal or, more desirably, into marketable products" (Denzinger 1979).

5) A Missed Opportunity: Little Demand for Silicofluorides (back to top)

Considering the great demand among big industry for fluoride chemicals as a material used in a wide variety of commercial products and industrial processes, the phosphate industry could have made quite a handsome profit selling its fluoride wastes to industry. This was indeed the hope among some industry analysts, including the authors of the review noted above (Denzinger 1979).

However, the US phosphate industry has thus far been unable to take advantage of this market. The principal reason for this failure stems from the fact that fluoride captured in the scrubbers is combined with silica. The resulting silicofluoride complex has, in turn, proved difficult for the industry to separate and purify in an economically-viable process.

As it now stands, silicofluoride complexes (hydrofluorosilicic acid & sodium silicofluoride) are of little use to industry.

Thus, while US industry continues to satisfy its growing demand for high-grade fluoride chemicals by importing calcium fluoride from abroad (primarily from Mexico, China, and South Africa), the phosphate industry continues dumping large volumes of fluoride into the acidic wastewater ponds that lie at the top of the mountainous waste piles which surround the industry.

In 1995, the Tampa Tribune summed up the situation as follows:

> "The U.S. demand for fluorine, which was 400,000 tons, is expected to jump 25 percent by next year... Even though 600,000 tons of fluorine are contained in the 20 million tons of phosphate rock mined in Florida, the fluorine market has been inaccessible because the fluorine is tied up with silica, a hard, glassy material."

Of course, not all of the phosphate industry's fluoride waste is disposed of in the ponds. As noted earlier, the phosphate industry has found at least one regular consumer of its silicofluorides: municipal water-treatment facilities.

According to recent estimates, the phosphate industry sells approximately 200,000 tons of silicofluorides (hydrofluorosilicic acid & sodium silicofluoride) to US communities each year for use as a water fluoridation agent (Coplan & Masters 2001).

6) Fluoridation: "An ideal solution to a long-standing problem"? (back to top)

In 1983, Rebecca Hanmer, the Deputy Assistant Administrator for Water at the US Environmental Protection Agency, described the policy of using the phosphate industry's silicofluorides for fluoridation as follows:

> "In regard to the use of fluosilicic acid as the source of fluoride for fluoridation, this agency regards such use as an ideal solution to a long standing problem. By recovering by-product fluosilicic acid from fertilizer manufacturing, water and air pollution are minimized, and water authorities have a low-cost source of fluoride available to them." (See letter)

Another EPA official, Dr. J. William Hirzy, the current Senior Vice-President of EPA Headquarters Union, recently expressed a different view on the matter. According to Hirzy:

> "'If this stuff gets out into the air, it's a pollutant; if it gets into the river, it's a pollutant; if it gets into the lake it's a pollutant; but if it goes right into your drinking water system, it's not a pollutant. That's amazing... There's got to be a better way to manage this stuff" (Hirzy 2000).

7) Recent Findings on Silicofluorides (back to top)

Adding to Hirzy's, and the EPA Union's, concerns are three recent findings.

First and foremost are two recent studies reporting a relationship between water treated with silicofluorides and elevated levels of lead in children's blood (Masters & Coplan 1999, 2000). The authors of these studies speculate that the silicofluoride complex may increase the uptake of lead (derived from other environmental sources, such as lead paint) into the bloodstream.

The second finding is the recent, and quite remarkable concession from the EPA, that despite 50 years of water fluoridation, the EPA has no chronic health studies on silicofluorides. All safety studies on fluoride to date have been conducted using pharmaceutical-grade sodium fluoride, not industrial-grade silicofluorides. A similar concession has also been obtained from the respective authorities in England.

The defense made by agencies promoting water fluoridation, such as the US Centers for Disease Control, to the lack of such studies, is that when the silicofluoride complex is diluted into water, it dissociates into free fluoride ions or other fluoride compounds (e.g. aluminum-fluoride), and thus the treated water, when consumed, will have no remaining silicofluoride residues (Urbansky & Schock, 2000).

This argument, while supported by a good deal of theoretical calculation is backed by a notable lack of laboratory data. Moreover, a recently obtained and translated PhD dissertation from a German chemist (Westendorf 1975) contradicts the claims. According to the dissertation, not only do the silicofluorides *not* fully dissociate, the remaining silicofluoride complexes are more potent inhibitors of cholinesterase, an enzyme vital to the functioning of the central nervous system.

The third finding, although perhaps of less concern, is that the silicofluorides, as obtained from the scrubbers of the phosphate industry, contain a wide variety of impurities present in the process water - including arsenic, lead, and possibly radionuclides. While these impurities occur at low concentrations, especially after dilution into the water, their purposeful addition to water supplies directly violates EPA

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public health goals. For instance, the EPA's Maximum Contaminant Level Goal for arsenic, a known human carcinogen, is 0 parts per billion. However, according to the National Sanitation Foundation, the addition of silicofluorides to the water supply will add, on average, about 0.1 to 0.43 ppb, and as much as 1.6 ppb, arsenic to the water.

As noted by the Salt Lake Tribune,

> "Those who had visions of sterile white laboratories when they voted for fluoride weren't thinking of fluorosilicic acid. Improbable as this sounds, much of it is recovered from the scrubbing solution that scours toxins from smokestacks at phosphate fertilizer plants."

8) Gypsum Stacks & 'Slime Ponds' (back to top)

To make 1 pound of commercial fertilizer, the phosphate industry creates 5 pounds of contaminated phosphogypsum slurry (calcium sulfate). This slurry is piped from the processing facilities up into the acidic wastewater ponds that sit atop the mountainous waste piles known as gypsum stacks. (See photos)

According to the EPA, 32 million tons of new gypsum waste is created each year by the phosphate industry in Central Florida alone. (Central Florida is the heart of the US phosphate industry). The EPA estimates that the current stockpile of waste in Central Florida's gypsum stacks has reached "nearly 1 billion metric tons." (The average gypsum stack takes up about 135 acres of surface area - equal to about 100 football fields - and can go as high as 200 feet.)

9) Radiation Hazard (back to top)

It is sort of a misnomer, however, to call these stacks "gypsum" stacks. Indeed, if the stacks were simply gypsum, they probably wouldn't exist, as gypsum can be readily sold for various purposes (e.g. as a building material). What can't be readily sold, however, is radioactive gypsum, which is about the only type of gypsum the phosphate industry has to offer.

The source of the gypsum's radioactivity is the presence of uranium, and uranium's various decay products (i.e. radium), in raw, phosphate ore. As noted by the Sarasota Herald Tribune

> "there is a natural and unavoidable connection between phosphate mining and radioactive material. It is because phosphate and uranium were laid down at the same time and in the same place by the same geological processes millions of years ago. They go together. Mine phosphate, you get uranium."

While uranium, and its decay-products, naturally occur in phosphate ore, their concentrations in the gypsum waste, after the extraction of soluble phosphate, are up to 60 times greater.

The gypsum has therefore been classified as a "Naturally Occurring Radioactive Material", or NORM waste, although some, including the EPA, have questioned whether this classification understates the problem. According to the Tampa Tribune, the gypsum "is among the most concentrated radioactive waste that comes from natural materials."

It is so concentrated, in fact, that "it can't be dumped at the one landfill in the country licensed to take only NORM waste."

Thus, according to US News & World Report, the EPA is currently "weighing whether to classify the gypsum stacks as hazardous waste under federal statutes, which would force the industry to provide strict safeguards" (to nearly 1 billion tons of waste).

One of EPA's main concerns with gypsum stacks centers around the fact that radium-

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226 breaks down into radon gas. When radon gas is formed, it can become airborne, leading to potentially elevated exposures downwind of the stacks. Such airborne exposures are of particular concern to areas like Progress Village, Florida, where "a new gypsum stack is rising a few hundred yards from a grade school."

According to US News & World Report, there is evidence to suggest that cancer rates downwind of the stacks may be elevated. A 1995 article in the magazine stated:

> "Some epidemiological studies suggest that lung cancer rates among nonsmoking men in the phosphate region are up to twice as high as the state average. Acute leukemia rates among adults are also double the average. An industry-sponsored study of male phosphate workers, however, found lung cancer rates no higher than the state average. There is no proof that mine wastes cause cancer, but the evidence is worrisome."

10) Will radioactive gypsum be added to roads? (back to top)

With the growing realization that gypsum stacks represent a serious environmental threat to Central Florida, both now and for generations to come, the phosphate industry has been looking into ways of reducing the size of the stacks (and the size of their liability.)

In an interesting parallel to fluoride, the phosphate industry is looking to turn its gypsum waste into a marketable product: as a potential cover for landfills, as a soil conditioner, and as a base material for roads.

According to Robert Vanderslice, head of Phosphate Management for Florida's Department of Environmental Protection, the gypsum is a "good material to replace lime rock in roads. Lime rock will run out at some time, and we're still building a lot of roads. Building roads with phosphogypsum would consume quite a bit of gypsum."

In 1995, a "Phosphogypsum Fact-Finding Forum" organized by the Florida Institute of Phosphate Research, presented a "message aimed straight at Washington: Relax the rules on using gypsum and the mountains will gradually disappear."

As of yet, however, the EPA does not appear willing to relax its rules and lift its ban on commercial uses of gypsum. According to the Tampa Tribune, "EPA's limit for use is 10 picocuries of radium per gram, well below the levels usually found in the mounds."

A recent statement from the EPA reads:

> "Only two uses (for the gypsum) are permitted: limited agricultural use and research. Other uses may be proposed, but otherwise the phosphogypsum must be returned to mines or stored in stacks."

11) Commercial Uranium Production (back to top)

While the presence of uranium decay-products makes gypsum a tough sell for the phosphate industry, the uranium has, at various times, presented the industry with a business opportunity of its own.

One of the lesser-known-facts about the phosphate industry is that its processing facilities have produced and sold sizeable quantities of uranium.

In 1997, just two phosphate plants in Louisiana produced 950,000 pounds of commercial uranium, which amounted to roughly 16% of the domestically produced uranium in the US.

In 1998, the same two plants produced another 950,000 pounds, but due to declining market prices for uranium, both plants have since ceased production.

If market prices improve, however, 4 US phosphate plants (2 in Louisiana & 2 in Florida) would have the capacity to produce a combined 2.75 million pounds of uranium per year, according to the Department of Energy (DOE). The DOE has termed these 4 facilities "Nonconventional Uranium Plants."

12) Cold War Secrets & Worker Health (back to top)

The Department of Energy has not always been so open about the uranium-making potential of the phosphate industry. During the Cold War, its predecessor institution, the Atomic Energy Commission (AEC), kept this fact closely under wraps - even to the workers who were, unknowingly, handling large quantities of the radioactive material.

In Joliet, Illinois, it has only recently come to light that the local phosphate plant had secretly produced some 2 million pounds of uranium for the US government in the years 1952 to 1962. According to local newspaper reports, the cancer rates of people who worked at the plant, especially "Building 55" where the uranium was processed, are unusually high.

"We used to kind of joke that if you worked for Blockson, you got cancer," quipped Vince Driscoll, the son of a cancer-stricken worker.

Today, with the Cold War over, it is becoming clear that workers in the phosphate industry need special protection. According to a report from the European Commission:

> " Processing and waste handling in the phosphate industry is associated with radiation levels of concern for workers and the public. The level of protection for these groups should be more similar to the level of protection that is state of the art in other industries, particularly the nuclear industry."

13) Wastewater Issues (back to top)

While the radioactivity of the gypsum stacks has probably been the key health concern of the EPA, it is not the only one.

Resting atop the phosphate industry's gypsum piles are highly-acidic wastewater ponds, littered with toxic contaminants, including fluoride, arsenic, cadmium, chromium, lead, mercury, and the various decay-products of uranium. This combination of acidity and toxins makes for a poisonous, high-volume, cocktail, which, when leaked into the environment, wreaks havoc to waterways and fish populations. As noted by the St. Petersburg Times, "Spills from these stacks have periodically poisoned the Tampa Bay environs. "

One spill, in 1997, from a now-defunct gypsum stack in Florida, "killed more than a million fish."

"Strike the Alafia River off your list of fishing spots," wrote one journalist after the spill. "It's gone, dead as a sewer pipe, killed by the carelessness of yet another phosphate company."

Today, the same gypsum stack which caused this particular spill, is considered by Florida's Department of Environmental Protection to be "the most serious pollution threat in the state." That's because tropical rains over the past couple of years have brought the wastewater to the edge of the stack's walls.

As noted by the Tampa Tribune, "The gypsum mound is near capacity, and a wet spring or a tropical storm could cause a catastrophic spill."

To prevent such a spill, which was all but inevitable, the EPA recently agreed to let Florida pursue "Option Z": To load 500-600 million gallons of the wastewater onto barges and dump it directly into the Gulf of Mexico.

The dumping of the wastewater into the Gulf represents the latest in a series of high-profile embarrasments for Florida's phosphate industry; one of the most dramatic of which happened on June 15, 1994.

On that day, a massive, 15-story sinkhole appeared in the middle of an 80 million ton gypsum stack. The hole was so big that, according to US News & World Report, it

> "could be as big as 2 million cubic feet, enough to swallow 400 railroad boxcars. Local wags call it Disney World's newest attraction – 'Journey to the Center of the Earth.'"

But, as US News noted,

> "there's nothing amusing about it. The cave-in dumped 4 million to 6 million cubic feet of toxic and radioactive gypsum and waste water into the Floridan aquifer, which provides 90 percent of the state's drinking water."

And so it goes.

As summarized by the Tampa Tribune:

> "It's not like you can padlock the doors and walk away. The complexities of keeping a phosphate processing plant operating are becoming clear to government regulators now overseeing two of them. Ponds full of 1.5 billion gallons of acid and three mountains of radioactive waste mean you just can't shut off the machinery and turn out the lights. The state could be stuck with the plants for years. And taxpayers would be stuck with the tab."

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14) REFERENCES (back to top)

Full citations of the studies listed above, can be accessed at:

http://www.fluoridealert.org/phosphate/overview-refs.htm

Note: Full-text copies of all newspaper articles cited in this article can be accessed by clicking on the links within the text.

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15) PHOTOGRAPHS OF THE PHOSPHATE INDUSTRY (back to top)

Photographs of the phosphate industry are available at:
http://www.fluoridealert.org/phosphate/photographs.htm

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16) FURTHER READING (back to top)

(Many thanks to Anita Knight for continually supplying FAN with newspaper articles on the phosphate industry in Florida.)

Fluoride Pollution Issues

- Wastewater Dump Seen As 'Lesser Of Two Evils' *The Tampa Tribune February 19, 2005*

Phosphate rich organic manure

From Wikipedia, the free encyclopedia

Phosphate rich organic manure is a type of fertilizer used as an alternative to diammonium phosphate and single super phosphate.

Phosphorus is required by all plants but is limited in soil, creating a problem in agriculture. In many areas phosphorus must be added to soil for the extensive plant growth that is required in crop production. Phosphorus was first added as a fertilizer in the form of single super phosphate (SSP) in the mid-nineteenth century, following research at Rothamsted Experimental Station in England.

The world consumes around 140 million tons of high grade rock phosphate mineral today, 90% of which goes into the production of diammonium phosphate (DAP). Excess application of chemical fertilizers in fact reduces the agricultural production as chemicals destroy natural soil flora and fauna. When DAP or SSP is applied to the soil only about 30% of the phosphorus is used by the plants, while the rest is converted to forms which cannot be used by the crops [x1,X2], a phenomenon which is known as phosphate problem to soil scientists.

Directly mixing finely ground rock phosphate mineral into organic manure produces a fertilizer known as **phosphate rich organic manure** (PROM). Research indicates that this substance may be a more efficient way of adding phosphorus to soil than applying chemical fertilizers.[1][2] Other benefits of PROM are that it supplies phosphorus to the second crop planted in a treated area as efficiently as the first, and that it can be produced using waste solids recovered from the discharge of biogas plants.

Phosphorus in rock phosphate mineral is mostly in the form of tricalcium phosphate, which is water insoluble. Phosphorus dissolution in the soil is most favorable at a pH between 5.5 and 7.[3] Ions of aluminum, iron, and manganese prevent phosphorus dissolution by keeping local pH below 5.5, and magnesium and calcium ions prevent the pH from dropping below 7, preventing the release of phosphorus from its stable molecule.[3] Microorganisms produce organic acids and heat, allowing the slow dissolution of phosphorus from rock phosphate dust added to the soil, allowing more phosphorus uptake by the plant roots. Organic manure can prevent ions of other elements from locking phosphorus into insoluble forms. The phosphorus in phosphate enhanced organic manure is water insoluble, so it does not run into ground water or runoff [x] any more than that from chemical fertilizers.

Most phosphate rocks can be used for phosphate rich organic manure. It was previously thought that only those rocks which have citric acid soluble phosphate and those of sedimentary origin could be used.[2] Rocks of volcanic origin can be used as long as they are ground to very fine size.

Organic manure should be properly prepared for use in agriculture, reducing the C:N ratio to 30:1 or lower. Alkaline and acidic soils require different ratios of phosphorus.

PROM is known as a green chemistry phosphatic fertilizer. Addition of natural minerals or synthetic oxides in water insoluble forms that contain micronutrients such as copper, zinc, and cobalt may improve the efficiency of PROM. Using natural sources of nitrogen, such as *Azolla*, may be more environmentally sound.[4]

References

1. ^ [1]
2. ^ a b [2]
3. ^ a b Brady, NC, Nature and Properties of Soils, Collier Macmillan, London,1984.
4. ^ [3]

[x] http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6V78-40CJYS8-17&_user=10&_rdoc=1&_fmt=&_orig=search&_sort=d&_docanchor=&view=c&_searchStrId=1048602170&_rerunOrigin=google&_acct=C000050221&_version=1&_urlV doi:10.1016/S0048-9697(00)00393-4

[x1] http://www.saber.ula.ve/bitstream/123456789/29069/1/mineral.pdf

[X2] http://www.uctm.edu/journal/j2006-3/05-Ivanova-297-302.pdf

Retrieved from "http://en.wikipedia.org/wiki/Phosphate_rich_organic_manure"
Categories: Organic fertilizers | Soil science

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MAR 30 1983

OFFICE OF
WATER

Leslie A. Russell, D.M.D.
363 Walnut Street
Newtonville, Mass. 02160

Dear Dr. Russell:

Thank you for your letter of March 9, 1983, in regard to the fluoridation of drinking water.

The information available to the Environmental Protection Agency is that fluoridation is a safe and effective means for reducing the occurrence of dental caries. The fluoridation process has been endorsed by several Presidents of the United States and by several Surgeons General, including the current Surgeon General, Dr. C. Everett Koop. A copy of Dr. Koop's statement on fluoridation is enclosed.

Water treatment chemicals, including fluosilicic acid, have been evaluated for their potential for contributing to the contamination of drinking water. The Water Treatment Chemicals Codex, published by the National Academy of Sciences, prescribes the purity requirements for fluosilicic acid and other fluoridation chemicals.

In regard to the use of fluosilicic acid as a source of fluoride for fluoridation, this Agency regards such use as an ideal environmental solution to a long-standing problem. By recovering by-product fluosilicic acid from fertilizer manufacturing, water and air pollution are minimized, and water utilities have a low-cost source of fluoride available to them. I hope this information adequately responds to your concern.

Sincerely yours,

Rebecca Hanmer

Rebecca Hanmer
Deputy Assistant Administrator
for Water

Enclosure

D-99 ~~B-69~~

Invoice 60147

Invoice Date 11/01/2006

Lucier Chemical Industries, Ltd.
PO Box 49000
Jacksonville Beach, FL 32250 USA

Telephone: 904/241-1200

Please remit to:
LCI, Ltd.
P.O. Box 790051
St. Louis, Mo 63179-0051

Bill To:

PORT ANGELES, CITY OF
P.O. BOX 1150
ATTN: WATER DIVISION
PORT ANGELES, WA 98362
USA

Ship To:

PORT ANGELES, CITY OF
3501 WEST 18TH STREET
FLUORIDATION PLANT
PORT ANGELES, WA 98363

Customer	Carrier	F.O.B.	Terms
PORT05	JJ WILLIAMS	DELIVERED	Net 30 Days

Purchase Order Number	Freight Terms	Our Order Number
Verbal	PREPAID BY LCI	11011601

Qty. Ordered	Qty. Shipped Qty. Adjusted	Item Item Description	Contract Price	Adjusted Price Discount	Tax	Extended Price
12,500	11.940	HFS	530.000@ 25%	520.46000		6214.29
	11.940	Fluorosilicic Acid, 8, Lot No. G20361 Analysis: 24.550				

Ordered 25,000 #

Nontaxable Subtotal	6214.29
Taxable Subtotal	0.00
Tax	0.00
Total Invoice	6214.29

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

DEC 21 2000

The Honorable Ken Calvert
Chairman
Subcommittee on Energy and Environment
Committee on Science
House of Representatives
Washington, D.C. 20515-6301

Dear Mr. Chairman:

Thank you for the letter of May 8, 2000, to Dr. Jane E. Henney, Commissioner of Food and Drugs, regarding the use of fluoride in drinking water and drug products. We apologize for the delay in responding to you.

We have restated each of your questions, followed by our response.

1. **If health claims are made for fluoride-containing products (e.g. that they reduce dental caries incidence or reduce pathology from osteoporosis), do such claims mandate that the fluoride-containing product be considered a drug, and thus subject the product to applicable regulatory controls?**

Fluoride, when used in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or animal, is a drug that is subject to Food and Drug Administration (FDA) regulation. FDA published a final rule on October 6, 1995, for anticaries drug products for over-the-counter (OTC) human use (copy enclosed). This rule establishes the conditions under which OTC anticaries drug products are generally recognized as safe and effective and not misbranded. The rule has provisions for active ingredients, packaging conditions, labeling, and testing procedures that are required by manufacturers in order to market anticaries products. A new drug application (NDA) may be filed for a product containing fluoride that does not meet the provisions stated in the final rule. As you know, the Environmental Protection Agency regulates fluoride in the water supply.

2. **Are there any New Drug Applications (NDA) on file, that have been approved, or that have been rejected, that involve a fluoride-containing product (including fluoride-containing vitamin products) intended for ingestion with the stated aim of reducing dental caries? If any such NDA's have been rejected, on what grounds were they rejected? If any such NDA have been approved, please provide the data on safety and efficacy that FDA found persuasive.**

No NDAs have been approved or rejected for fluoride drugs meant for ingestion. Several NDAs have been approved for fluoride topical products such as dentifrices and gels. Fluoride products in the form of liquid and tablets meant for ingestion were in use prior to enactment of the Kefauver-Harris Amendments (Drug Amendments of 1962) to the Food, Drug, and Cosmetic Act in which efficacy became a requirement, in addition to safety, for drugs marketed in the United States (U.S.). Drugs in use prior to 1962 are being reviewed under a process known as the drug efficacy study implementation (DESI). The DESI review of fluoride-containing products has not been completed.

3. **Does FDA consider dental fluorosis a sign of over exposure to fluoride?**

Dental fluorosis is indicative of greater than optimal ingestion of fluoride. In 1988, the U.S. Surgeon General reported that dental fluorosis, while not a desirable condition, should be considered a cosmetic effect rather than an adverse health effect. Surgeon General M. Joycelyn Elders reaffirmed this position in 1994.

4. **Does FDA have any action-level or other regulatory restriction or policy statement on fluoride exposure aimed at minimizing chronic toxicity in adults or children?**

The monograph for OTC anticaries drug products sets acceptable concentrations for fluoride dentifrices, gels and rinses (all for topical use only). This monograph also describes the acceptable dosing regimens and labeling including warnings and directions for use. FDA's principal safety concern regarding fluoride in OTC drugs is the incidence of fluorosis in children. Children under two years of age do not have control of their swallowing reflex and do not have the skills to expectorate toothpaste properly. Young children are most susceptible to mild fluorosis as a result of improper use and swallowing of a fluoride toothpaste. These concerns are addressed in the monograph by mandating maximum concentrations, labeling that specifies directions for use and age restrictions, and package size limits.

Thanks again for contacting us concerning this matter. If you have further questions, please let us know.

Sincerely,

Melinda K. Plaisier
Associate Commissioner
for Legislation

Enclosure
"Final Rule/Federal Register - October 6, 1995
Over-the-Counter Anticaries Drug Products"

Web site administrator's note:
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