August 25, 1986

Donald Strait
NRDC
122 East 42nd St
NY, NY 10168

Dear Donald:

After I spoke with you on the phone, I spent the next evening going through my collection of FLUORIDE, the quarterly journal of the International Society for Fluoride Research. (I have subscribed since 1968, and have all the issues back to the first one.) I searched through that one journal for reports on skeletal fluorosis, or related research topics.

The enclosures are copies of much of what I found. This pile of papers is almost exclusively from FLUORIDE. (I've also made copies of a few other papers I had handy, but only half a dozen of the encloures are from sources other than FLUORIDE.)

I went through this exercise primarily to show how easy it is to come up with a large amount of literature pertinent to an assessment of skeletal effects of fluoride. I believe the EPA has effectively overlooked essentially all of this literature. This pile, found in less than a day's searching, demonstrates that the literature exists and is quite easy to find; and with a little study it will be clear that it is very pertinent to the issue of the safety of a 4.0 ppm MCL.

Some at EPA (or elsewhere) might raise questions about the source of these papers, the journal FLUORIDE, and the society that publishes it. The ISFR is a multi-disciplinary scientific society with members in many countries; the scope of research interests of the society is very broad. Some of the American members of the ISFR are opponents of fluoridation; while that doesn't per se make them bad scientists, it's traditionally lowered their credibility in many scientific circles. However, the vast majority of ISFR members (and officers) are indifferent to the political controversy over fluoridation; it's simply not an issue in their countries.

The literature enclosed speaks for itself. Many of the authors are among the world's foremost authorities on skeletal fluorosis. As the bibliographies of their papers show, their work has appeared in many of the world's leading research publications. I read FLUORIDE because it focuses on issues like skeletal fluorosis. People who don't find FLUORIDE a very impressive journal could collect the same information from papers published in other journals, but it would take a lot more work to seek out all those papers.

Since this is a huge pile of literature, I've prepared a short guide to it, to help you select a few papers that may be of greatest value in responding to EPA. Some of the critical papers (in my estimation) are starred, to help you sort them out.

I hope this is helpful. There is such an overwhelming amount of scientific evidence on the issues related to EPA's fluoride MCL, and EPA has seemingly ignored almost all of it, so it is very hard to know where to start. However, I think skeletal fluorosis is one of the two key issues. (The other is the adverse health impact of dental fluorosis, and I think you have a strong case already on that one.)

I hope you have been able to follow up by calling Dr. Johnson at the Mayo Clinic, and Dr. Kleerekoper in Detroit. I have a feeling both should be very helpful.

Good luck with your effort.

Sincerely,

Edward Groth III, PhD

REBUTTAL TO EPA BRIEF AT pp 35-39.

(1) EPA DEFINES "CRIPPLING SKELETAL FLUOROSIS" AS THE EFFECT OF CONCERN

Skeletal fluorosis, like most chronic effects of cumulative toxic agents, is a progressive disease. Crippling skeletal fluorosis is the extreme, most debilitating stage of advanced disease. Long before crippling fluorosis is observed, there are detectable structural and functional changes in bone that are associated with lower doses of fluoride than those required to produce crippling. A continuum exists, from effects that are of no biological import, to those that may be functionally important but are not crippling, to those that produce severe and irreversible damage (crippling).

EPA's position that crippling fluorosis is the only effect that needs to be prevented is scientifically and morally bankrupt. It leaves no margin for error (provides an inadequate safety margin), and probably violates the mandate of the SDWA to protect against effects that may be adverse, even if not obviously debilitating.

(2) EPA REJECTS THE RELEVANCE OF FOREIGN STUDIES, ESPECIALLY THOSE DONE IN INDIA, FOR ASSESSING THE RISK OF SKELETAL FLUOROSIS IN THE US.

EPA rejects NRDC's contention that the epidemiological studies of skeletal fluorosis in India and other countries are relevant to an assessment of the risk of skeletal fluorosis in the United States. EPA's argument, however, contains numerous factual and conceptual errors that grossly distort the scientific substance of what the Indian research has shown.

EPA asserts that differences between conditions in India and those in the US make Indian research irrelevant to the risk of skeletal fluorosis here. But in fact, India's experience with skeletal fluorosis serves as an enormous natural "experiment" that has given medical science an almost unparalleled opportunity to study the disease. Indian research has provided detailed dose-response relationships (between fluoride in water and the incidence of skeletal fluorosis); extensive knowledge of interacting risk factors (e.g., dietary calcium); and many insights into basic biochemical and physiological mechanisms of the disease, including its early stages.

Most of EPA's statements about the Indian research are simply wrong, indicating either ignorance or willful distortion of the scientific facts. To wit:

1. EPA asserts that there are "four studies associating fluoride in drinking water with crippling fluorosis in India" (at p. 38). In fact, more than one million people in India are afflicted with skeletal fluorosis, and the

extensive epidemiological investigations of this disease have been published in several hundred research reports, dating from 1937 to the present, which appeared in many of the world's leading medical journals.

EPA then goes on to list several reasons why "epidemiological studies in India are not predictive of effects in the U.S. population," to wit:

1. Indians are believed to have higher fluoride content in their foods..."

   FACT: Systematic measurements of fluoride levels in the diet have not been made in most studies of fluorosis in India. Where they have been made, the authors concluded that drinking water was the primary source of fluoride. Furthermore, dietary fluoride intake varies in the United States. No detailed comparisons have been published that show that Indians customarily consume more fluoride in foods than Americans do; some overlap in the ranges of food fluoride exposure in the two countries is very likely.

2. "Indians are believed to have...greater consumption of water...."

   FACT: India's climate is hotter than the US's, on average, and many of the Indian patients with skeletal fluorosis are manual laborers whose work spurs great water consumption. However, there are parts of the US that have a hot climate, and populations of manual laborers in the US who work in the hot sun all day long. Water consumption varies widely within any population, and it is a certainty that there is considerable overlap between the water intake of Indians and that of at least some segments of the US population.

3. "Indians are believed to have higher fluoride levels in drinking water...."

   FACT: Levels of fluoride in drinking water in India range from less than 1 ppm to over 20 ppm in some villages; the range found in US waters is quite similar. Skeletal fluorosis has been reported in populations using waters with as little as 0.6 ppm F^- (Teotia and Teotia, 1984), and is fairly common (afflicting as many as 3 to 5 percent of the population) in some villages with 1 to 2 ppm F^- (several reports by Jolly). Contrary to EPA's assertion, skeletal fluorosis in India is quite common at levels below EPA's RMCL of 4 mg/l. (It is even more common at levels above 4 mg/l.) In some villages with water fluoride levels of 10 mg/l or more, skeletal fluorosis is evident in children exposed to the water for only a few years.

4. "Indians are believed to have...poorer diets than US citizens...."

FACT: EPA distorts what researchers have found. Calcium in the diet is a well-documented protective factor against the more severe manifestations of skeletal fluorosis. Indian studies have compared populations that get adequate dietary calcium (over 600 mg/day) with populations that get less calcium in the diet; those with calcium-deficient diets are much more likely to develop skeletal fluorosis. However, no evidence has ever been presented which demonstrates that Indians in general have poor diets, compared to those in the US. Poor nutrition is one of the more serious American public health problems, and inadequate dietary calcium is a widely recognized and very common nutritional deficiency in this country. (Average estimated intake for adult females in the US is about 480 mg/day, compared to the RDA of 800 mg/day, according to Consumer Reports, 10/84, p. 578.)

In short, the dietary risk factor most clearly identified by Indian researchers -- insufficient calcium intake -- is well known to be widespread in the US population. Rather than show a difference between Indians and Americans, this factor shows a striking similarity.

EPA goes on to assert that there are not large numbers of undetected cases of crippling fluorosis in the US. (Emphasis added). With that emphasis, the statement is probably true. However, crippling fluorosis is only the most obvious, unambiguous, extreme stage of the disease. In the past 20 years, the Indian researchers (and others, in other countries), have done landmark studies that have helped to define many of the early, more subtle stages of skeletal fluorosis. There have never been any surveys in the US that looked for early, less obvious signs of fluorosis. The US studies cited by EPA were done long ago and were sufficient only to rule out the widespread occurrence of severe skeletal fluorosis. No evidence EPA has cited can support the position that skeletal fluorosis, in degrees short of crippling debility, may be occurring in large numbers of Americans whose water contains high natural fluoride levels.

The MCL for fluoride in India is 1.0 ppm. At least one team of Indian experts on skeletal fluorosis has called for lowering the limit to 0.5 ppm, because in their view 1.0 ppm poses an unreasonable risk of skeletal fluorosis (Teotia & Teotia, 1984). Rather than disparage, dismiss, and disregard the vast amount of evidence on skeletal fluorosis amassed in India, EPA should be studying that evidence intently in an honest scientific effort to draw appropriate inferences about the risk of this disease in Americans.

SKELETAL FLUOROSIS:

OUTLINE OF MAJOR LINES OF INVESTIGATION

In assessing potential skeletal effects of raising the MCL for fluoride to 4.0 ppm, EPA could and should have drawn on a wide range of epidemiological and experimental evidence. The world literature includes multiple approaches to the study of fluoride's skeletal effects. Each approach has its own value for an assessment of the possible effects of 4.0 ppm F^- in water on skeletal physiology of exposed populations. Below, I have briefly outlined several major lines of evidence that contribute to understanding of skeletal fluorosis; each one represents a separate and sizeable literature. If EPA failed to consider any or all of these areas of investigation, it may be evidence of a superficial, inadequate, or biased assessment of the potential health consequences of its proposed MCL.

NO RMCL!

(I) EPIDEMIOLOGICAL STUDIES

(A) Populations Exposed to Fluoride in Water

1. Indian Research
2. Studies in Other Countries

(B) Populations Exposed Occupationally

1. Work of Franke et al in East Germany
2. A variety of literature over the past 50 years

(C) Populations Exposed to Other Sources (Food, Wine, etc.)

1. A Variety of Reports Over the Years

(II) CLINICAL STUDIES

(A) Hemodialysis with Fluoridated Water
(B) Treatment of Osteoporosis with Large Doses of F^-

(III) ANIMAL STUDIES

(A) Experimental Research on Skeletal Fluorosis
(B) Veterinary Reports on Pollution-Afflicted Livestock

(IV) OTHER EVIDENCE

NOTES ON THE OUTLINE

(I) EPIDEMIOLOGICAL STUDIES

(A) Populations Exposed to Fluoride in Water

(1) INDIAN RESEARCH

Skeletal fluorosis is a widespread public health problem in India, where more than 1,000,000 people are afflicted with the disease. While conditions in India are not strictly comparable to those in the USA, (e.g., hotter climate, likely nutritional deficiencies, genetic differences), India's skeletal fluorosis cases provide an enormous "natural laboratory" that has enabled medical science to describe the disease in great detail. The Indian medical researchers who have studied endemic fluorosis include most of the world's leading authorities on the disease, and their research has been published in many of the world's top medical journals. Among other things the Indian research has shown is that skeletal fluorosis can occur where water fluoride concentrations are below 1 ppm, if other factors that aggravate the disease are present. The Indian experience is very highly relevant to an assessment of potential effects of fluoride exposures in the range of 4 ppm.

I have enclosed 24 papers on epidemiological investigations of endemic skeletal fluorosis in India. All appeared in the same journal (FLUORIDE); a few are abstracts from works first published elsewhere. These are not all of the papers on this topic published, even in the one journal, over the period surveyed; I didn't copy everything. There's quite a bit of duplication, as is. However, I've included much of the work of several of the leading teams of investigators:

S.P.S. Teotia et al.: These investigators have 10 papers in the enclosed sample. Their work has gone farther than most other epidemiological research in India to define dose-effect and dose-response relationships; to elucidate the interactions among fluoride and other risk factors (such as nutrition, other environmental variables); and to suggest the underlying physiological mechanisms that produce the disease (e.g., secondary hyperparathyroidism). Several of their papers are starred (as things EPA should certainly not have overlooked.)

NOTE THAT SOME OF THEIR PAPERS APPEAR IN THE BIBLIOGRAPHY OF EPA'S CRITERIA DOCUMENT, BUT THE SCIENTIFIC SUBSTANCE OF THEIR FINDINGS IS COMPLETELY NEGLECTED BY EPA.

S.S. Jolly, et al.: Jolly's work extends over some three decades; by 1970, he was recognized as one of the world's top authorities on skeletal fluorosis, and was co-author of the chapter on that topic in the World Health Organization monograph, Fluorides and Human Health, published that year. His

work in the state of Punjab has described thousands of cases of skeletal fluorosis, and his surveys document the occurrence of the disease at a range of fluoride concentrations in water, some as low as 1.5 to 2.0 ppm. Although Jolly's forte is the field study, he has in recent years begun investigating some of the underlying mechanisms of effects (as have other Indian investigators, notably Teotia and Susheela.) Five of Jolly's papers from FLUORIDE are enclosed.

A.K. Susheela, et al.: Susheela is a toxicologist, not an epidemiologist. A couple of her papers have addressed epidemiological problems (copies enclosed), but most of her work has been done in experimental animals. Her group has for more than a decade been doing ground-breaking studies on the basic metabolic and physiological mechanisms that underlie the outward changes of skeletal fluorosis. That work is discussed in the section on Animal Studies (part III, below.)

Other Investigators: There are many; this is a huge public health problem in India, and has attracted a great deal of research attention. Seven papers by various authors not part of the research teams noted above are also enclosed.

NOTE THAT SKELETAL FLUOROSIS CONTINUES TO BE A "CURRENT" RESEARCH FIELD IN INDIA; MANY OF THE PAPERS HAVE BEEN PUBLISHED WITHIN THE LAST FEW YEARS.

(2) STUDIES IN OTHER COUNTRIES

Skeletal fluorosis is endemic in several other parts of the world, where the pattern of incidence is quite similar to that in India, but on a smaller scale. Reports (all from FLUORIDE) are enclosed on research on skeletal fluorosis in populations in the Sahara region of Africa; Algeria; Tanzania; and Turkey. The report by Pinet & Pinet is interesting, in that it covers 148 cases of skeletal fluorosis in a region where the water contained no more than 4.0 ppm F^-; Ca/Mg ratios of the water supplies in each area seemed to be a factor in the risk of fluorosis. The work of Elsair et al. (Algeria) is focused on biochemical changes that occur before radiologically obvious skeletal changes can be detected, so is of special interest for assessing "subclinical" effects.

NOTE THE ABSENCE OF RESEARCH FROM THE USA. Two things are enclosed that have to do with skeletal fluorosis in the US: An abstract of a paper by Juncos & Donadio (from 1972), reporting two cases at the Mayo Clinic; and a review by Waldbott, called "Hydrofluorosis in the USA." The Waldbott paper is of interest because it reviews and provides a bibliography of every case of skeletal fluorosis reported in the U.S. literature up to that date (1968). Waldbott also cited these same papers in his book (published in 1979), "Fluoridation: The Great Dilemma." Many people disregard Waldbott because of his anti-fluoridationism;

but regardless of his political views, his scientific and popular publications are a rich source of scientific bibliography of the fluoride literature, and his writings are very accessible. EPA's "literature search" overlooked several of the published reports of skeletal fluorosis cases in the US, despite their ready accessibility, here and elsewhere. This is further evidence of the superficial nature of EPA's attempt to assess the health impacts of its proposed MCL.

The question of why there is not more American research on skeletal fluorosis is worth examination. I think there are several reasons. First and foremost is the widespread perception that the disease does not occur in this country. That is a result of a few studies, done in the 1950's or 1960's for the most part, which effectively declared that the disease did not exist here. In contrast to the Indian research (and similar epidemiological studies in other countries), American studies were done with a political purpose -- to demonstrate that the fluoridation of water supplies would not pose any hazards to health. They were not done out of any strong scientific motivation to understand or prevent a potentially serious public health problem. By comparison to the other research you see enclosed here, the US studies were very crude. They looked only for the most obvious and unambiguous signs of harm (i.e., crippling skeletal fluorosis, or clear osteosclerosis). There was evidently no concern with potential subclinical changes that could occur at doses lower than those that cause obvious, unambiguous stages of the disease.

Subsequently, as research advanced in India and other parts of the world and skeletal effects of fluoride were linked with lower and lower levels of intake, few if any efforts were made to investigate the implications of such research for US populations exposed to high levels of fluoride (over 2 ppm, say). In talks with a variety of environmental health researchers about this void of good US fluoride research, I've encountered two explanations. First is the perception among researchers that fluoride is an "old" problem, one that was essentially fully studied decades ago. Many other topics, such as lead, PCB's, mercury, etc. were clamoring for research in the environmental health disciplines, and fluoride couldn't compete very well with a lot of the more "current" issues. Second, there has long been widespread awareness among environmental health scientists that any research that suggests possible harmful effects of fluoride will be used, perhaps out of context, by the antifluoridationists; at the same time, the research will probably be attacked in an effort to discredit it (often with personal disparagement of the researchers thrown in for good measure) by the pro-fluoridationists. The awareness that your research could embroil you in an emotional controversy, despite any effort you might make to avoid being so embroiled, may be a powerful disincentive to research on fluoride toxicity in this

country. In fact, my perception is that there is a strong pro-fluoridation bias on the part of most scientific institutions in the USA, because they've been recruited to the defense of fluoridation since the early days of the bitter political struggle the measure has engendered. Because the "official" scientific establishment is pro-fluoridation, any scientists who want to study toxic effects of fluoride in water are likely to be viewed as suspect -- if not anti-fluoridation, at least willing to give aid & comfort to the enemy. I think that open antipathy to the idea of hazards of F^- in water (at 1 ppm or at somewhat higher levels) has seriously discouraged more careful study of skeletal fluorosis in the US.

Whatever the explanation(s), the fact remains: There is a dearth of good scientific research on skeletal effects of fluoride in Americans. We have nothing comparable to the body of evidence the Indians have accrued to show how fluoride can affect the bones of people here. The few studies EPA does cite are limited and/or flawed to the point of being essentially useless for assessing potential effects of levels in the range of 1 to 4 ppm in drinking water. (See Waldbott's comments on the Stevenson and Watson survey, for instance -- in enclosed paper.)

(B) POPULATIONS WITH OCCUPATIONAL EXPOSURES

Occupational fluorosis has been a well-documented disease of workers in several industries since 1937, when Kaj Roholm, a Danish investigator, published a landmark monograph on the subject. Occupational exposure (in aluminum, steel, cryolite and other workers) usually involves inhalation of fluoride as dusts and vapors. Once in the blood, though, the fluoride is deposited in bones and has the same effects as fluoride from drinking water.

There is an enormous literature on industrial fluorosis, much of it several decades old. Once the disease had been defined and standards were set to protect workers in most countries, research more or less petered out. (There were, of course, many other occupational health hazards for researchers to pursue.) That has pretty much been the case in the USA; the major work on industrial fluorosis here was done by Hodge and Smith, at the U. of Rochester, in the 1940's and 1950's. In the late 1960's and 1970's, when research techniques began to advance into areas beyond the description of obvious, severe harm to define the subtler, early, subclinical manifestations of the disease, not much was being done here.

Thus, on the topic of industrial fluorosis, the work of Franke et al., in East Germany, stands out. Over the past two decades, they have worked out a detailed model of the physiological mechanisms of fluoride's effects, and elucidated effects

of smaller and smaller doses (looking for subclinical signs of toxicity, before radiologically obvious changes appear). Their work is comparable in many ways to the work of Teotia et al. in India, in that it provides one of the most comprehensive pictures of the disease researchers have compiled.

All but one of the enclosed papers from FLUORIDE on this topic (five in all) are Franke's work. He's the current president of the ISFR, which suggests the high esteem his colleagues around the world have for his research. His 1979 review (the starred paper, enclosed) shows his breadth of familiarity with the literature on many related topics; it's a superb overview not just of the occupational literature, but of the disease and all the evidence related to it.

NOTE: DOSE-RESPONSE DATA FROM OCCUPATIONAL STUDIES ARE NOT DIRECTLY APPLICABLE TO ENVIRONMENTAL STANDARDS, SUCH AS AN MCL FOR FLUORIDE IN DRINKING WATER. OCCUPATIONAL STUDIES DEAL WITH HEALTHY MALE WORKERS, FOR THE MOST PART, WHO ARE EXPOSED TO THE SOURCE OF FLUORIDE FOR 8 HOURS OR SO PER DAY. LEVELS THAT MAY BE BELOW THE THRESHOLD OF HARMFUL EFFECTS FOR SUCH POPULATIONS COULD STILL POSE HAZARDS FOR WOMEN, CHILDREN, AND OTHERS IN THE GENERAL POPULATION. HOWEVER, OCCUPATIONAL STUDIES ARE VERY USEFUL FOR SUGGESTING MECHANISMS OF EFFECTS, FACTORS THAT CAN REDUCE OR ENHANCE RISKS, ETC.

(C) POPULATIONS EXPOSED TO OTHER SOURCES

There is a small body of literature involving sources of F^- intake other than water or occupational exposures. This is a rather rare occurrence, represented in the enclosures by one series of reports on food-borne fluorosis from China, a study from Spain on wine-induced fluorosis, and a single case report from England on fluorosis from excessive tea intake.

This literature is a minor offshoot, but it does bring the insights of new investigators to bear on the disease. In that regard, the Chinese papers are somewhat interesting.

(II) CLINICAL STUDIES

Neither of the two major research areas under this heading (cases of skeletal fluorosis associated with hemodialysis using fluoridated water, and studies of the efficacy of fluoride as therapy for osteoporosis) has been very widely published in the journal FLUORIDE, so I have few papers along these lines to send you. There are excellent reviews of both topics in the AAAS book, "Continuing Evaluation of the Use of Fluorides," as we discussed on the phone.

FLUORIDE's editors have occasionally published abstracts on these research topics, and have written editorials reviewing the state of evidence for the beneficial effects of fluoride in osteoporosis (copies enclosed). They are skeptical of benefits (especially from drinking water @ 1 ppm), which seems to me to be the soundest scientific posture, based on studies I've seen.

(III) ANIMAL STUDIES

(A) Experimental Research

As in environmental health research on effects of any pollutant, toxicological studies on animals can complement the epidemiological evidence. Animal experiments may be able to provide a model of skeletal fluorosis, which can allow for the detailed study of mechanisms of the disease, specific physiological effects that underlie morphological changes, etc. For animal studies to be useful in assessing human risks, it is necessary to understand ways the human and animal responses to fluoride are the same (or, conversely, how they differ). But even with the caveat that animals aren't people, a great deal can be learned by studying animal models.

Among the enclosed papers (and in my judgment, in the world literature), the work of A.K. Susheela et al. stands out. Her work has been done in coordination with the human studies done in India, described in (I). Using rabbits as subjects, she and her colleagues have developed a number of investigative techniques and have learned a great deal about the biochemical, metabolic, and physiological changes that occur in bone with exposure to fluoride. Several papers summarizing her work have been published in FLUORIDE, and are enclosed.

This research is of great importance. It provides a wholly new way of looking at skeletal fluorosis -- a variety of signs that disease is present, many of which can be detected long before obvious or crippling symptoms appear.

For EPA to have ignored this major body of work and to have defined crippling skeletal fluorosis as the biological marker of most concern is analagous to defining lead encephalopathy as the "threshold of concern" for lead toxicity, and ignoring all the readily detectable biochemical and metabolic changes that occur before obvious brain damage.

EPA's failure to review, interpret, and take into account the implications of this complex body of research shows its lack of competence in assessing the potential health effects of its fluoride MCL. No one who is familiar with research on the effects of fluoride can overlook Susheela's work.

(B) Veterinary Studies

There have been numerous incidents in which livestock (most often, cattle) have been injured by fluoride, which is a widespread air pollutant and accumulates in vegetation to levels that are toxic to animals. The animals get dental and skeletal fluorosis. Over three or four decades, fluorosis in animals has been very thoroughly decribed, and experimental research has been conducted (feeding fluoride to animals) to simulate the disease, understand its progressive development, and see what can be done to prevent it.

A few papers on veterinary studies are enclosed; one of them is not from FLUORIDE, but was something I had handy.

While cows are not people, and the way they handle fluoride may be different from how humans do, certain biochemical and physiological processes are similar among species. So what has been learned about the changes that occur in cattle bones when they are exposed to fluoride may be relevant, to some extent, in an assessment of possible effects on people. EPA could have learned a good deal about the basic biochemical effects of fluoride on bone by studying this literature.

Two of the world's leading experts on animal fluorosis are Lennart Krook, of Cornell, and J.L. Shupe, of Utah State U. A paper or two by each is enclosed.

(IV) OTHER STUDIES

There's only one paper enclosed under this heading, but it's an important one. It is a study on human bone grown in tissue culture, by Petrovic and Stutzmann. They took bone samples from boys living in towns with 0.6 and 1.0 ppm fluoride in the water, respectively, and found that the rate of calcium turnover was significantly lower in bones taken from people whose water had 1.0 ppm F^-.

Their research has focused on the potential beneficial effects of fluoride on osteoporosis. But in a larger context, it provides clear evidence that the normal physiological process of bone turnover is slowed appreciably by even 1.0 ppm F^- in water. Effects on osteoporosis aside, one can certainly ask whether inhibition of the normal physiology of bone in children (the subjects were 7 and 8 years old) is a potential effect EPA should disregard.

Several caveats are necessary here. The study was done in tissue culture; I don't know if comparable measurements could be made to see if the same effect occurs in living bones in

vivo. And it would be wise to see if other investigators can duplicate the result before accepting it as valid. Nevertheless, there are several issues that EPA must not ignore when setting an MCL: Do such effects occur at levels up to 4 ppm? If so, how much is the turnover of bone mineral slowed by the accumulation of fluoride? What effects could that have on other physiological processes that depend on bone as a source of minerals?

It appears to me that EPA has completely ignored this topic (and these researchers' work) -- more evidence of the superficiality and/or bias of its review.

MISCELLANEOUS ADDENDA

Also enclosed, should you find any use for them, are a list of the officers of the ISFR and the list of Editorial Advisors for FLUORIDE, and a Subject Index from the journal for the years 1968-1982.

I have also made a copy of sections of a report from the National Research Council of Canada, "Environmental Fluoride, 1977." I copied the chapter on fluoride's potential health effects on humans, and the list of references for the whole report. Compare the scope of these authors' review of the world literature, the scientific questions they identify as worthy of assessment, with EPA's superficial and slanted effort to examine the potential health impacts of the RMCL. I don't believe EPA even cited this report, let alone tried to emulate its scientific approach. If you need an example of how it "should have been done," this is the best one extant.