



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

SEP 5 2000

OFFICE OF  
WATER

The Honorable Ken Calvert  
Chairman Subcommittee on Energy and The Environment  
Committee on Science  
House of Representatives  
Washington, D.C. 20515-6310

Dear Mr. Chairman:

This is in reply to the questions posed in your May 8, 2000, letter to Carol M. Browner, Administrator of the United States Environmental Protection Agency (EPA). Your questions primarily deal with fluoride and EPA's management of fluoride through our current regulatory programs. I apologize for the delay in this response. The detailed nature of many of the questions required both significant fact finding and inter-office coordination.

The Office of Water, Office of Air, Office of Solid Waste, Office of Pollution Prevention and Toxics, Office of Pesticide Programs, and the Office of Research and Development contributed information on the activities of their programs related to fluoride. The answers to the technical questions were provided by the Office of Water and the Office of Pesticide Programs and reviewed by the Office of Research and Development. We have included recent references on the health effects of fluoride and other materials (memoranda, communications) as requested. The scientific publications provided are either those cited in the enclosures or those published over the past five years and collected by EPA as part of its routine surveillance of the fluoride literature.

We hope the information provided addresses your concerns. If you have any additional questions, please feel free to contact me or have your staff call Dr. Joyce Donohue, at (202) 260-1318.

Sincerely,

A handwritten signature in black ink, appearing to read "JCF", written over a large, stylized flourish.

J. Charles Fox  
Assistant Administrator

Enclosures

**CONGRESSMAN CALVERT INQUIRY  
OF MAY 8, 2000  
RESPONSE TO QUESTIONS**

**Question 1**

On November 18, 1998, two EPA scientists, Drs. James Murphy and William Hirzy, wrote a memorandum to Dr. Oscar Hernandez, Director of the Risk Assessment Division, Office of Pollution Prevention and Toxics (OPPT) on the subject of the pending Children's Health Test Rule. Drs. Murphy and Hirzy cited six recent studies that indicated that fluoride might pose a risk of neurotoxicity for children. They also pointed out that a Reference Dose (calculated using standard EPA methodology) and the cited studies would have a range of 0.000007 mg/kg/day to 0.003 mg/kg/day. They noted that no chronic studies of any kind appear to have been conducted on hydrofluosilicic acid or its sodium salt – which are used in around 90% of water fluoridation systems in the U.S. – and that the potential for those substances to form complexes with heavy metals (such as lead) has not been studied.

Given the extremely wide spread exposure of millions of American children to fluoride, and in particular, to hydrofluosilicic acid and its sodium salt, along with the Administrator's concern for the health of children, and these two scientists' positions at EPA, surely EPA has responded to their November 18, 1998, memorandum. Please provide a copy of EPA's response, and what action EPA has taken to deal with the concerns raised in the November 18, 1998, memorandum.

**Response**

The response to Question 1 is divided into two segments. The first is the response from OPPT regarding the memorandum to Dr. Hernandez from Drs. Murphy and Hirzy. The second part provides information on recent publications that discuss the potential for fluorosilicates to form complexes with heavy metals.

**I OPPT Response**

On November 18, 1998, Drs. James Murphy and William Hirzy wrote a memorandum to Dr. Oscar Hernandez which cited six studies that indicated that fluoride might pose a concern for neurotoxicity in children. In addition, they suggested in their memorandum that fluoride would be a good candidate chemical for a regulation which-was under development at the time. That regulation was intended to develop health effects data for chemicals to which children are exposed. The proposed regulation or test rule was targeted to be completed December 30, 1998. A formal response to the memorandum was not drafted because shortly thereafter EPA decided to put the test rule on hold in order to develop, on a cooperative basis with interested stakeholders, a Voluntary Children's Chemical Evaluation Program which was intended to serve

the same purpose as the rule. This decision was publicized widely and it effectively preempted consideration of any testing issues related to the test rule.

A voluntary program to obtain exposure and hazard information pertinent to the analysis of children's risks evolved from series of stakeholder meetings over the past year. Participants in this process were selected through an open process to ensure balanced participation from a spectrum of stakeholders. The interested public was also encouraged to participate in these stakeholder meetings. After considering the feedback from these meetings, OPPT has contemplated using a set of improved criteria, different from those used in the test rule, to select chemicals for the program. These new criteria emphasize biomonitoring data which demonstrate that a chemical is present in human blood/tissues/exhaled breath, and that this chemical is found in indoor air, food or drinking water. Dr. Hirzy requested and was granted an opportunity to address the attendees at a recent stakeholder meeting regarding his views on fluoride toxicity and to reiterate his early suggestion that this chemical be considered for inclusion in the program. EPA is evaluating all comments received through this activity and will determine whether the chemical which is of interest to Dr. Hirzy is appropriate for inclusion in the voluntary program. The launch of the voluntary program is expected later this year.

Drs. Murphy and Hirzy also stated in their memorandum that the Agency's Integrated Risk Information System (IRIS) had developed a Reference Dose (RfD) for fluoride, and that the value for the RfD may be reduced if the new studies that they cited were considered. As discussed in the response to Question 9, EPA is required by the Safe Drinking Water Act to review the MCLG/MCL for fluoride. That review will take place over the next two years. These studies will be considered in that review and, as appropriate, changes to the RfD and/or the MCLG/MCL will proceed based on this and all other available information.

## **II Fluorosilicate Complexes with Heavy Metals**

Two recent papers have reviewed the issues of fluorosilicate chemistry as applied to drinking water fluoridation. These publications conclude that fluorosilicate hydrolysis and dissociation are greater than 99.9% complete and that complexes of metals with fluorosilicates are negligible, with concentrations below 1 part per trillion (Urbansky and Schock, 2000a,b)

### **Question 2**

Given that normal healthy teeth do not display fluorosis, does EPA consider the appearance of dental fluorosis as a sign of too much exposure to fluoride? If not, why not? If so, at what incidence level would EPA consider that the population is receiving too much fluoride?

## Response

When EPA regulated fluoride levels in drinking water in 1986 by setting a Maximum Contaminant Level (MCL), it was regulated on the basis of the opinion of a group of experts that mild dental fluorosis was not an adverse health effect. Thus, in the judgment of the experts, mildly fluorotic teeth are still healthy. When dental fluorosis causes cracks and fissures, tooth function is considered to be impaired. Therefore, following the logic of the fluoride drinking water regulation, levels of fluoride ingestion sufficient to cause severe dental fluorosis in individuals would be too much fluoride.

EPA Secondary Maximum Contaminant Level (SMCL) was established to warn the public regarding the potential for development of dental fluorosis as a result of drinking water with fluoride concentrations greater than 2 mg/L. Based on the data available in the mid-1980s, the incidence of severe fluorosis was negligible at fluoride concentrations less than 2 mg/L (NAS, 1993). However, based on evidence from recent studies that relate the concentrations of fluoride in drinking water to the incidence of severe dental fluorosis, the number of cases has increased in the years since fluoride was regulated by EPA (Bothwell and Limeback, 1999; Ishii and Suckling, 1991; NAS, 1993). At least a part of the increase appears to be due to the increased fluoride exposure from dental products, processed foods, etc. (Bothwell and Limeback, 1999; NAS, 1993).

Because of considerable variability in the results of studies of dental fluorosis in the population and the fact that those studies generally measure only the fluoride in the drinking water rather than total fluoride exposure, it is not possible to provide an exposure value for the total fluoride intake that causes severe dental fluorosis. In the recent review of the fluoride data by the National Academy of Sciences (1997), the following upper limits on fluoride intakes for infants and children vulnerable to dental fluorosis were proposed:

- 0 through 6 months                      0.7 mg/day
- 7 through 12 months                      0.9 mg/day
- 1 through three years                      1.3 mg/day
- 4 through 8 years                          2.2 mg/day

The NAS values are intended to protect against all dental fluorosis, not just severe dental fluorosis. Accordingly, intakes that would protect against severe dental fluorosis would be greater than the values above.

### Question 3

What regulations does EPA have – either promulgated, under development, or under consideration – to control fluoride emissions to the air, water, soil? Regarding emissions of hydrofluosilicic acid, which EPA has characterized as a water and air pollutant, how does EPA explain its willingness to allow this substance to be bled into drinking water systems (especially in the absence of any chronic toxicity studies on it) as long as the fluoride level does not exceed 4 mg/L? Is it EPA’s policy that the “solution to pollution is dilution” as long as the pollutant is applied directly into drinking water systems and not into fresh surface water?

### Response

The response to this question is divided into several sections. The first section deals with regulations (promulgated, under development, or under consideration). That section is subdivided by the responsible office within EPA. The second section deals with fluoridation chemicals, i.e., hydrofluosilicic acid.

#### I. Regulations (Promulgated, Under Development or Under Consideration)

#### Office of Air

The following is a list of EPA regulations that control fluoride emissions to the air:

#### New Source Performance Standards 40 CFR 60: Promulgated Standards

Subpart S - Standards of Performance for Primary Aluminum Reduction Plants

Subpart T - Standards of Performance for the Phosphate Fertilizer Industry: Wet-Process Phosphoric Acid Plants

Subpart U - Standards of Performance for the Phosphate Fertilizer Industry: Superphosphoric Acid Plants

Subpart V - Standards of Performance for the Phosphate Fertilizer Industry: Diammonium Phosphate Plants

Subpart W - Standards of Performance for the Phosphate Fertilizer Industry: Triple Superphosphate Plants

Subpart X - Standards of Performance for the Phosphate Fertilizer Industry: Granular Triple Superphosphate Storage Facilities

National Emission Standards for Hazardous Air Pollutants 40 CFR 61      None

National Emission Standards for Hazardous Air Pollutants for Source Categories  
40 CFR 63: Promulgated Standards

Subpart AA - National Emission Standards for Hazardous Air Pollutants from Phosphoric Acid Manufacturing Plants

Subpart BB - National Emission Standards for Hazardous Air Pollutants from Phosphate Fertilizers Production Plants

Subpart LL - National Emission Standards for Hazardous Air Pollutants for Primary Aluminum Reduction Plants

Subpart YY - National Emission Standards for Hazardous Air Pollutants for Source Categories Generic Maximum Achievable Control Technology Standards: Hydrogen Fluoride Production

National Emission Standards for Hazardous Air Pollutants for Source Categories

<u>Source Category</u>	<u>Status</u>
• Alumina Processing	(b)
• Clay Products Manufacturing	
- Clay Minerals Processing	(b)
- Brick, Structural Clay Products and Ceramics Manufacturing	(b)
- Lightweight Aggregate Production	(b)
• Uranium Hexafluoride Production	(b)
• Refractory Products Manufacturing	
- Clay Refractory Manufacturing	(b)

(a) proposed, (b) under development, or (c) under consideration

**Office of Solid Waste**

The Office of Solid Waste is in the process of proposing revisions to the fluoride and cyanide treatment standards applicable to spent potliners from primary aluminum reduction (EPA hazardous waste K088) under its Land Disposal Restrictions (LDR) program. The standards are based on a relatively new type of K088 vitrification technology that also recovers fluoride. If the proposal is promulgated, it will result in the extraction, recovery and reuse of fluoride, the destruction of toxic cyanide in the waste, and a reduction in the volume of treated K088 residuals that are land disposed. The proposal is under review by OMB and will shortly enter final review for signature by the Administrator.

## Office of Water

Under the Clean Water Act, EPA has promulgated effluent limitation's guidelines and standards for fluoride in eight point source categories. The following list summarizes the location of these fluoride regulations by part and subpart from the Code of Federal Regulations. In addition to the regulations already promulgated and summarized below, EPA is considering effluent limitations for fluoride for two additional point source categories: (1) Iron and Steel Manufacturing and (2) Metal Products and Machinery. Both of these regulations are under development and have not yet been proposed. EPA is not yet certain whether the regulations for these two point source categories will include fluoride effluent limitations.

### Summary of Effluent Limitations and Standards for Fluoride

#### Part 415 - Inorganic Chemicals Manufacturing Point Source Category

Subpart H	Hydrofluoric Acid Production Subcategory
Subpart W	Aluminum Fluoride Production Subcategory
Subpart BC	Sodium Fluoride Production Subcategory

#### Part 418 - Fertilizer Manufacturing Point Source Category

Subpart A	Phosphate Subcategory
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#### Part 421 - Nonferrous Metals Manufacturing Point Source Category

Subpart B	Primary Aluminum Smelting Subcategory
Subpart C	Secondary Aluminum Smelting Subcategory
Subpart I	Metallurgical Acid Plants Subcategory
Subpart K	Primary Columbium-Tantalum Subcategory
Subpart O	Primary Beryllium Subcategory
Subpart P	Primary and Secondary Germanium and Gallium
Subpart S	Primary Molybdenum and Rhenium Subcategory
Subpart AA	Secondary Tin Subcategory
Subpart AD	Secondary Uranium Subcategory

#### Part 422 - Phosphate Manufacturing Point Source Category

Subpart D	Defluorinated Phosphate Rock Subcategory
Subpart E	Defluorinated Phosphoric Acid Subcategory
Subpart F	Sodium Phosphates Subcategory

#### Part 426 - Glass Manufacturing Point Source Category

Subpart K	Television Picture Tube Envelope Manufacturing Subcategory
Subpart L	Incandescent Lamp Envelope Manufacturing Subcategory
Subpart M	Hand Pressed and Blown Glass Manufacturing Subcategory

Part 436 - Mineral Mining and Processing Point Source Category

Subpart D Industrial Sand Subcategory

Part 469 - Electrical and Electronic Components Point Source Category

Subpart A Semiconductor Subcategory  
Subpart B Electronic Crystals Subcategory  
Subpart C Cathode Ray Tube Subcategory  
Subpart D Luminescent Materials Subcategory

Part 471 - Nonferrous Metals Forming and Metal Powders Point Source Category

Subpart B Magnesium Forming Subcategory  
Subpart C Nickel-Cobalt Forming Subcategory  
Subpart E Refractory Metals Forming Subcategory  
Subpart F Titanium Forming Subcategory  
Subpart G Uranium Forming Subcategory  
Subpart I Zirconium-Hafnium Forming Subcategory

II. Fluoridation Chemicals

EPA is not involved with the decision of any drinking water system to fluoridate its water supply. Those decisions are made by States and local communities. Individual systems make the decisions regarding which fluoridation chemical to use, if fluoridation is practiced. Most States require that systems select fluoridation chemicals certified against ANSI/NSF Standard 60: Drinking Water Treatment Chemicals - Health Effects. The acronym ANSI/NSF indicated that the Standard was developed by NSF International (formerly the National Sanitation Foundation) and approved by American National Standards Institute.

EPA supported the development of the Standards for Drinking Water Additives (ANSI/NSF Standard 60 and 61) to insure that the chemicals used for fluoridation (sodium fluoride, sodium silicofluoride, and hydrofluosilicic acid) did not contain impurities that might be deleterious to health and were evaluated against the Standard. Standard 60 requires that all fluoridation chemicals be analyzed for the presence of regulated heavy metals (ANSI/NSF, 1998).

**Question 4**

What has EPA done to investigate the charges of science fraud made in the amicus curia brief submitted by your headquarters professionals union in 1986 in the NRDC v. EPA law suit over drinking water standards that was filed in that year (and subsequently reiterated by Drs. Robert Carton and William Hirzy of the union in a 1998 National Association of Environmental Professionals publication)?

## **Response**

In our attempt to answer this question, we consulted with our Office of General Counsel. Based on the limited amount of information provided in the citation to the case, and the time that has passed and associated turnover of key staff, we have not been able to locate the brief containing the allegations of science fraud. If you have more detailed information regarding the case, we would be pleased to further research the question.

## **Question 5**

What has EPA done to investigate charges made by Office of Ground Water and Drinking Water Senior Science Advisor, Dr. William Marcus, that data were tampered with and conclusions improperly downgraded in the National Toxicology Program (NTP) cancer study on sodium fluoride? Regarding the NTP study, mandated by Congress in 1977 to specifically exclude the Public Health Service and National Institute of Health from involvement with it (because they would not be unbiased), how is it that EPA did not challenge the down grading of the study conclusions?

## **Response**

The allegations were heard and discussed by Agency staff. The allegations were not substantiated. There was no evidence that the NTP conducted its review by other than its standard, rigorous review process, or that there was any downgrading of findings. Enclosed is a copy of the peer review panel discussion on the study taken from the NTP report. This panel was a subcommittee of the NTP Board of Scientific Counselors. Also enclosed is a copy of the NTP process for quality control of its studies. In addition to quality control of study conduct, the steps include reading of the pathology slides by independent, expert pathologists followed by independent scientific peer review of report findings by a subcommittee of the Board. The Board and its subcommittees are composed of experts whose integrity has not been challenged, and was not challenged in the case of the fluoride study.

## **Question 6**

What disciplinary action has been taken against the EPA employees involved in firing Dr. Marcus (and thereby incurring unwarranted expenses to the tax payer)? What personnel actions have been taken against those involved including promotions, awards, transfers, demotions, firing, etc.?

## **Response**

Based on the Agency's review of the Department of Labor (DOL) decision issued in Dr. Marcus' case, no disciplinary action was required or taken with regard to relevant Agency employees. With regard to any other personnel actions involving relevant EPA employees as

cited in your letter, including promotions, awards and transfers, such actions would be effected in the routine course of Agency business and in compliance with appropriate Office of Personnel Management regulations and EPA policy and practice.

### **Question 7**

Fluoride is well recognized as a general enzyme poison (arising from its powerful hydrogen bonding propensity that disrupts protein [and DNA/RNA structures] and it displays high acute toxicity (ca. 5 mg/kg a threshold lethal dose), ranking as acute toxicant lying between lead and arsenic. A host of chronic toxic effects of lead and arsenic are acknowledged by EPA (e.g. hematopoietic effects, cardiovascular effects, neurologic effects, carcinogenicity, etc.). The EPA view of fluoride toxicity appears to be that ingested fluoride strengthens teeth, or it will kill, or will inflict skeletal fluorosis, but has no other chronic toxic effects as its neighbors arsenic and lead do. How does EPA explain this unique toxicological behavior of fluoride, especially in light of its known effect on enzymes?

### **Response**

The response to the question first considers the statements regarding fluoride's hydrogen bonding potential and its potential effects on enzymes, and then respond to the portion of the question relative to acute and chronic fluoride toxicity.

#### **II. Fluoride and Hydrogen Bonding**

There are several scientific problems with the statements made about the hydrogen bonding potential of fluoride and its effects on enzymes. Hydrogen bonds are electrostatic interactions between partially positive hydrogen atoms in molecules and partially negative atoms in the same or neighboring molecules (Lehninger et al., 1993). Partial positive and negative charges within a molecule are the product of differences in the affinity of covalently bonded atoms for electrons resulting in bond polarity. Hydrogen fluoride, the simplest hydrogen-containing inorganic fluorine compound, has a  $pK_a$  of 3.5. This means that the molecule can only participate in hydrogen bond formation to any significant extent at pH values of less than about 4.5. The pH maintained in most mammalian cells is about 7 to 7.3, a pH range where only about one in 1,000 to one in 10,000 of the fluorines is present as hydrogen fluoride. The remainder of the fluorines are present as monovalent, negative fluoride ions. The acid secreting cells of the stomach are an exception to this generalization. The low pH of the gastric secretions would favor the presence of the undissociated hydrogen fluoride, and hydrogen fluoride is capable of hydrogen bonding. The primary interactions that would be displayed by the fluoride ion would be ion-ion interactions or ion-dipole interactions rather than hydrogen bond interactions.

The distinction made above regarding the types of interactions expected between fluoride and cellular constituents is more than simply semantic. For example, interactions of fluoride ions with the hydrogen bonds in DNA are very unlikely since the negative charges on the DNA phosphate-sugar backbone and the pi-bonds of the DNA bases would tend to repel fluoride anion

preventing its disruption of the DNA hydrogen bonds. Interaction of the fluoride ion with the positively charged DNA-associated polyamines or histone proteins would be more likely. However, to the knowledge of EPA, there has been no experimental investigation of fluoride ion interactions with DNA-polyamines or histone proteins.

The results from studies of fluoride's mutagenicity and genotoxicity are consistent with the hypothesis that the effects of fluoride on chromosomes and DNA are indirect rather than direct. Most of the mutagenicity studies, particularly those using the Ames Assay, are negative (NAS, 1993). Although *in vitro* mouse Lymphoma mutagenicity assays have some positive results, this assay detects chromosomal damage as well as gene mutations. The results from many of the *in vitro* studies of chromosomal effects are positive but the *in vivo* assays have approximately equal numbers of positive and negative results (NAS, 1993). Thus, the effects of fluoride on DNA appear to occur at the level of the chromosomes rather than the DNA bases.

Lack of hydrogen bonding potential of fluoride at physiological pH's would also determine the nature of its interaction with proteins. Fluoride ions could influence protein structure and, thus, enzyme activity by disrupting the electrostatic interactions between the acidic and basic amino acids, or by interrupting hydrogen bond interactions of polar amino acid side chains. Fluoride's ability to exert such an influence would be shared by other negative ions (i.e., chloride anions) and would be concentration and enzyme-specific. Fluoride would also have to compete with chloride and other intracellular negative ions for protein interaction sites. The small ionic radius of fluoride would be a factor favoring interaction with positively charged amino acid side chains that might not be accessible to larger ions.

It has been hypothesized (Spittle, 1994) that formation of relatively insoluble calcium or magnesium complexes might disrupt the activities of enzymes using these divalent cations as cofactors. This is a possible mechanism that might account for inhibition of some enzymes but divalent cation complex formation would be an enzyme-specific rather than a general effect.

To the knowledge of EPA, there has been no systematic evaluation of the ability of fluoride to inhibit enzyme activities, or of the mechanism for such inhibition. Data on the specific enzymes inhibited and the dose-response for the effects would be required for the data to be used for quantitative risk assessment. An NAS (1993) report on the health effects of ingested fluoride endorsed conducting research on the mechanism by which fluoride interacted with cells and biomolecules, including enzymes, and research on specific mechanisms of enzyme inhibition would be beneficial.

## II Fluoride Toxicity

There have been independent evaluations of the toxicity of fluoride by the Public Health Service (1991), EPA (1985), NAS (1993; 1998), and ATSDR (1993). In each of these reviews, the critical adverse effects of fluoride ingestion were identified as the effects on bone and teeth rather than other adverse effects. Brief descriptions of these evaluations are provided below.

In 1991, the Department of Health and Human Services (DHHS) completed a review of the benefits and risks of fluoride. Among other points, the DHHS review concludes that optimal fluoridation of drinking water to about 1 mg/L does not pose a detectable cancer risk in humans and recommended that the U. S. Public Health Service continue to support optimal fluoridation.

In 1993, the Agency for Toxic Substances and Disease Registry, a division within the Centers for Disease Control (CDC), published the *Toxicological Profile for Fluorides, Hydrogen Fluoride and Fluorine*. A Minimum Risk Level (MRL) of 0.05 mg/kg/day (3.5 mg/day for a 70-kg adult) was calculated for chronic oral exposure to fluoride. The study used as the basis of the MRL was a study of women with osteoporosis who received a 75-mg/day sodium fluoride supplement, a dose of about 0.48 mg/kg/day, compared to a group who received a placebo. Background fluoride exposure (diet, drinking water, dental products) was not measured or considered in estimating the dose and there was no comparison of the experimental group and the placebo group for their total fluoride exposure. Accordingly, the MRL applies to exposures to fluoride in excess of the background levels, rather than total fluoride exposure.

In 1998, the Institute of Medicine at NAS completed a review of fluoride as a nutrient. They concluded that the adequate intake for fluoride ranges from 0.01 mg/day for infants to 1 mg/day for children under age eight, the period when dental fluorosis can occur. For adults and children more than eight, the recommendation ranges from 2 to 4 mg/day. NAS also established an Upper Limit for a safe exposure in children older than age 8 and for adults of 10 mg/day.

There is general agreement among these publications regarding critical effects and the quantitative estimates of risk for effects on both bone and teeth. None of the publications listed above have ignored data on other acute or chronic effects of fluoride including its relatively low acutely toxic dose.

EPA understands that CDC is presently completing an assessment of fluoride and fluoridation. CDC is the principal Federal agency involved in research on fluoridation in this country.

### **Question 8**

How many individuals in the nation does EPA estimate fall into the category depicted as “unusually susceptible” in the *Toxicological Profile for Fluorides, Hydrogen Fluoride, and Fluorine*, published by the Agency for Toxic Substances and Disease Registry? What measures does EPA recommend for these unusually susceptible individuals who live in fluoridated communities or communities whose water contains fluoride at the MCL?

## Response

Table 1 below summarizes those populations that the ATSDR Toxicological Profile (1993; Section 2.7) identifies as sensitive and includes data on the prevalence in the United States of the underlying physiological, nutritional, or age-related condition. It is important to note that the population values in Table 1 are numbers of individuals that fall in each category. There are no data to suggest that these individuals as a group are, or would be, sensitive to fluoride at the levels found in the environment.

The demographic information for cardiovascular disease and renal disorders in Table 1 was collected by the Office of Water as a component of an effort to identify sensitive populations in the United States that might be sensitive to specific chemicals by virtue of their chronic disease state (O'Dey et al., 1998). Demographic data for the elderly come from a recently completed study of water intakes by the Office of Water (Jacobs et al., 2000). Prevalence values have been rounded to the nearest million and were extrapolated from the survey population to the U.S. population. Data on nutrient deficiencies are from the U.S. Department of Agriculture 1994-1996 Continuing Survey of Food Intake by Individuals (USDA, 1998). The values given are the percent of the population consuming less than 75% of the Recommended Dietary Allowance for the nutrient in question.

Sensitive Population Group (ATSDR, 1991)	Estimated Population
Elderly	52,000,000 (>55 years)
Cardiovascular disease	22,000,000
Renal disorders	2,000,000
Vitamin C deficiency	27%
Magnesium deficiency	37%
Calcium deficiency	44%

Individuals that fall in each of the categories listed in Table 1 have a number of specific risk factors that impact their health status such as body weight, diet, and life style (e.g. smoking, alcohol consumption). Advice on beneficial life style changes for each condition is best provided by the medical community.

EPA is in the process of developing medical fact sheets to provide medical practitioners (doctors, nurses, dietitians, etc.) with health data relative to drinking water contaminants that can be then used in counseling patients. This work has just begun, and will initially focus on the elderly,

children and pregnant women. It will later be expanded to cover other at-risk populations. In addition, EPA has made it a requirement for public water systems to provide their clients with health effects information on contaminants in their water supply, including fluoride [Consumer Confidence Rule FR 63(160): 44512-44536].

Revised public notification language for fluoride has recently been proposed [FR 65(87): 25982-26049]. The new language suggests dental consultation in situations where there is a risk for dental fluorosis because the water provided by their drinking water system has exceeded the Secondary MCL for fluoride. The implementation manual for public notification is close to completion.

In addition, please refer to the answer to Question 11 and EPA advice regarding fluoride exposure and infants.

### **Question 9**

Do you interpret Section 101 (b)(4) of the Safe Drinking Water Act of 1996 as requiring EPA to set its MCL(G)s at a level that protects all persons, including sensitive populations, such as infants, children, people who drink 4 or more liters of water per day, people with allergies or hypersensitivity to fluoride and people with renal disease?

### **Response**

The Safe Drinking Water Act of 1996 does not have a Section 101(b)(4). Section 1412(b)(4)(a) states that “Each maximum contaminant level goal established under this subsection shall be set at the level at which no known or anticipated adverse effects on the health of persons occur and which allows an adequate margin of safety.”

As required by the SDWA [Section 1458(a)(1)], EPA is collecting information to identify groups within the general population with increased sensitivity to contaminants such as infants, children, the elderly, persons with allergies or hypersensitivity to chemicals. Some of the data that we have collected in this process are cited in the response to Question 8 above. If the MCL/MCLG for fluoride is selected for an in-depth evaluation as part of the six-year review of drinking water regulations, additional data on sensitive populations and their dose-response to fluoride will be collected and EPA will publish and seek public comment on its findings as required by the SDWA Section 1412(b)(3)(C)(i)(V).

### **Question 10**

Is EPA satisfied that fluoride doses delivered to the public via drinking water under an MCL(G) of 4 mg/L when added to the fluoride intake from dental products, pesticide residues, food and beverages will not cause adverse health effects?

## **Response**

EPA continues to support the MCLG as protective of public health. The Agency realizes that the use of fluoride in dental products has increased since fluoride was regulated in 1986. In 1998 the EPA commissioned an evaluation of the exposure data for fluoride, including data on amounts in foods and dental products. EPA found that the data published in the peer reviewed literature were limited, and did not differ substantially from the data available when fluoride was regulated. A copy of that draft report was included for your records when EPA responded to this question last year.

Over the past year we have collected recent publications covering the increased incidence of dental fluorosis and the factors other than drinking water fluoride that appear to be contributing to the increase (Barsden and Bjorvatn, 1999; Brothwell and Limeback, 1999; Den Besten, 1999; Fitzsimons et al., 1998; Horowitz, 1989; Ishii and Suckling, 1991; Villa et al.1998). The findings from those papers were used in making the proposed revision to the fluoride public notification language. If fluoride is selected for reevaluation of its MCL/MCLG, the Agency will look carefully at relative sources of exposure during the revision process.

## **Question 11**

What is the margin of safety for infants who consume drinking water containing 4 mg/L fluoride?

## **Response**

The Agency does not recommend that infants consume water containing 4 mg/L fluoride. The Agency requires that all families who receive water from a system with greater than 2 mg/L fluoride receive a public notification recommending that alternate sources of water be used for infants and children in that family [40CFR 143.5]. Copies of the present public notification statement and the proposed revision to that statement are enclosed for your records.

The Agency believes that the 2 mg/L SMCL protects children against dental fluorosis as well as adverse health effects in situations where there are no other significant sources of exposure. The Agency acknowledges that the MCL does not protect infants and children against dental fluorosis, a cosmetic effect rather than an adverse health effect.

## **Question 12**

What is the margin of safety for persons receiving kidney dialysis treatment, diabetics, or those who have a hypersensitivity or allergy to fluoride who consume drinking water containing 4 mg/L fluoride?

## **Response**

The 1993 NAS report on the health effects of ingested fluoride addressed the concern for fluoride retention in persons with impaired renal function, a group which includes individuals with diabetes. The NAS concluded that additional research was needed to adequately assess the risk.

EPA is not aware of recent data on the health effects of ingested fluoride in persons with impaired renal clearance that expand our knowledge on this issue.

The Agency regulations for potable water do not apply to water used in dialysis. The American Association for Medical Instruments (AAMI) establishes the standards that apply to dialysis waters. The address for a contact at AAMI is as follows:

Dr. Ronald H. Abrahams  
American Association of Medical Instruments  
Renal Disease and Detoxification Committee  
Suite 3330 Washington Boulevard  
Arlington, VA 22201-4598  
703 (525-4890)

Neither the NAS(1993) report, nor the ATSDR (1993) Toxicological Profile on fluoride provides data that identify any individuals with a fluoride-specific hypersensitivity or allergy. No judgement can be made regarding the effects of fluoride in drinking water on such a population without data from studies of such populations or knowledge of the mechanisms underlying the adverse response.

## **Question 13**

Does the incidence of dental fluorosis among at least an estimated 22% of American children indicate that, at least among these children, an overdosing is occurring?

## **Response**

The National Survey of Dental Caries in US School Children (1986- 1987) reported a prevalence of dental fluorosis of 22.3%. Nearly all of the cases were mild to very mild. These data reflect exposures that occurred before the EPA MCL/MCLG was implemented.

A number of studies have been conducted since the National Survey of Dental Caries in US School Children as indicated in the response to Question 10. Some of these studies indicate that the prevalence of dental fluorosis appears to be increasing.

In 1993 NAS recommended that the most “effective approach to stabilizing the prevalence and severity of dental fluorosis without jeopardizing the benefits to human health, is likely to come from the more judicious control of fluoride in foods, processed beverages, and dental products,

rather than a reduction in the recommendation for fluoride in drinking water.” Control of fluoride from these other sources (foods, beverages, and dental products) would require action by the Food and Drug Administration.

#### **Question 14**

What steps has the Agency taken to address the hazards identified with fluoride exposure in the following publications that appeared since EPA reaffirmed its drinking water standards for fluoride? [Six publications are cited.]

#### **Response**

The Office of Water has reviewed each of the six references listed and participated in discussions with the EPA Office of Research and Development (ORD) regarding the strengths and weaknesses of each study. (See the enclosed memorandum from William Marcus dated 5/22/98 and the 6/3/98 response from Dr. Hugh Tilson of ORD.) The data presented in these publications will be utilized in the review of the MCL values for presently regulated compounds as discussed in the response to Question 9 above.

In 1999, EPA convened a group of experts to carefully consider the results of the Varner et al. (1998) study. A copy of the report of that conference is included. As a result of that conference, EPA has requested that the National Toxicology Program consider the possibility of conducting additional studies of the neurotoxicity of aluminum that include verification of the results observed in the Varner et al. study.

#### **Question 15**

Please provide copies of any risk assessment documents in EPA files that pertain to fluorine-bearing pesticides such as cryolite.

#### **Response**

A copy of the cryolite risk assessment by the Office of Pesticide Programs is enclosed with the references to this response.

Our understanding is that you are concerned about those fluorine-bearing pesticides that produce or act as free fluoride ion. You appear to be particularly concerned about the toxicity of hydrofluosilicic acid and its salts. We further understand that you are concerned about the use of fluorine-bearing pesticides that result in dietary exposures (i.e., through food or drinking water).

Our review of our pesticide chemical database indicates that there are three active ingredients in currently registered products that produce or act as free fluoride ion: sodium fluoride, sulfuryl

fluoride and cryolite. Hydrofluosilicic acid and its salts are not active ingredients in any currently or formerly registered pesticide products. Accordingly, we have not conducted any risk assessments on this chemical.

In 1993, EPA published a Reregistration Eligibility Document (RED) on sulfuryl fluoride. A fact sheet outlining the basis for EPA's reregistration decision is enclosed. This pesticide has no food uses and no other terrestrial uses. Accordingly, there is no dietary exposure through food or drinking water. The pesticide is used primarily to fumigate structures. The Agency has identified inhalation exposure as a possible hazard to persons who reenter treated structures. The Agency required submission of exposure data to support the retention of the current reentry level of 5 parts per million (ppm). (A reentry level is the concentration of sulfuryl fluoride in indoor air that the Agency judges to be safe for persons reentering treated structures.) The Agency announced in the RED that if these data were not submitted by August 1994, the Agency would change the reentry level to 1 ppm.

The Agency is currently reviewing exposure data and a 90-day inhalation toxicity study in rats required in the RED to characterize the neurotoxic effects of sulfuryl fluoride. EPA will reevaluate the reentry level for sulfuryl fluoride when it completes the review of these studies.

If the Agency finds that the use of sulfuryl fluoride results in significant exposures to infants and children, the Agency may require submission of developmental neurotoxicity and other neurotoxicity data on this compound. These studies were not routinely required before the passage of the Food Quality Protection Act (FQPA) of 1996. However, in an April 1999 draft report, an Agency task force recommended that such studies (among others) be routinely required for all pesticides used on food or in ways that significantly expose infants and children. In August 1999, EPA began to require developmental neurotoxicity and certain other neurotoxicity data on pesticides known or suspected to have neurotoxic effects. Initially, EPA required registrants of organophosphorus pesticides to submit such data, but the Agency plans to require developmental neurotoxicity and other neurotoxicity data for all food use pesticides that are known or suspected to have neurotoxic effects. Within a year, EPA will propose to amend its data requirements in Part 158 of Title 40 of the Code of Federal Regulations to require the developmental neurotoxicity and other neurotoxicity studies for all food use pesticides.

Sodium fluoride is used as a wood treatment to prevent rot. It is not used on food. The pesticide uses of sodium fluoride do not appear likely to result in dietary exposure through drinking water and it is not known whether the wood treatment use results in significant exposures to infants and children. The Agency plans to issue a RED on sodium fluoride in 2004. The Agency has not yet determined whether developmental neurotoxicity or other neurotoxicity studies should be required for this pesticide.

#### **Question 16**

Have any studies on hydrofluosilicic acid or silicofluorides been submitted to EPA under claimed Confidential Business Information Protection?

## **Response**

The Office of Pollution Prevention and Toxics has checked their Confidential Business Information files and cannot identify any studies of hydrofluosilicic acid or silicofluorides that were submitted to EPA under claimed Confidential Business Information Protection.

Through Mr. George Glasser from Florida, the Office of Water became aware of a nonconfidential submission in November 1992, by Rhone-Poulenc under TSCA Section 8(e). The submission includes data on hydrofluosilicic acid from three studies (skin irritation, eye irritation and acute oral LD-50). A copy of that submission has been included with this response.

## **Question 17**

Does the EPA support the recommendations made in the draft report of the Joint Science Advisory Board Scientific Advisory Panel Subcommittee on Data from Testing of Human subjects that states, "... in no case should developing humans be exposed to neurotoxic chemicals"?

## **Response**

The passage you have quoted appears in a draft report that has not been officially submitted to the Agency. We are not certain about the context of this passage or even whether it will appear in its current form when the report is presented to us. Accordingly, it would be premature to comment on it.

## **Question 18**

Has the so called "10x factor" been considered or applied in any way for fluorine-bearing pesticides under the FQPA?

## **Response**

Our understanding is that you are concerned about those fluorine-bearing pesticides that produce or act as free fluoride ion, so we have interpreted this question as applying only to those pesticides that produce or act as free fluoride. There are three fluoride pesticides: cryolite, sulfuric fluoride and sodium fluoride. Of these, only cryolite is used in or on food and, thus, is the only pesticide in the group that is subject to the requirements of section 408 of the Federal Food Drug and Cosmetic Act (FFDCA). The requirement to assess the need for a "10X factor" appears in section 408 of the FFDCA.

In a Federal Register notice of December 5, 1997 (62 FR 64294), EPA determined that a 10X factor was not required to account for completeness of data regarding infants and children's

exposures or toxicity or to reflect pre- or post-natal toxicity of the pesticide. This determination was based on current understanding of the information and procedures used to establish the need for a 10X factor.

About a year later, EPA convened an intra-agency task force to examine the kinds of studies and information needed to assess potential pre- and post-natal toxicity and exposure to infants and children from pesticides. In 1999, the 10X Task Force prepared two draft papers, "Toxicology Data Requirements for Assessing Risks of Pesticide Exposure to Children's Health" and "Exposure Data Requirements for Assessing Risks of Pesticide Exposure to Children." These papers supported the Office of Pesticide Programs' (OPP) draft policy guidance document on implementation of the additional 10X FQPA safety factor entitled, "The Office of Pesticide Programs' Policy on Determination of the Appropriate FQPA Safety Factor(s) for Use in the Tolerance-Setting Process." It was accompanied by the "Standard Operating Procedures (SOP) for Determining the Appropriate FQPA Safety Factor(s) for Use in Tolerance Assessment." All of these papers were presented in May 1999 to the Agency's Scientific Advisory Panel (chartered by the Federal Insecticide Fungicide and Rodenticide Act) and in July 1999, for public review and comment (Federal Register of July 9, 1999; 64 FR 37001).

EPA has not revisited the December 1997 decision on cryolite because no one has petitioned the Agency for a new tolerance for cryolite residues since then. The December 1997 action established a time-limited tolerance for cryolite residues on potatoes and the processed animal feed commodity potato waste which expires in November 2001. If the petitioner for the time-limited tolerance petitions the Agency for a permanent tolerance, EPA would follow its new SOP in making its 10X factor decision.

### **Question 19**

Have the final rule and resulting risk assessment found in FR, Vol. 62, No. 234, Friday, December 5, 1997, "Fluoride has been identified as the residue of toxicological concern in cryolite and synthetic fluoride and the available data show that these compounds which are approximately 52.8% fluoride, act as a free fluoride." been applied to any other substances?

### **Response**

No. As explained above, there are only two pesticides, in addition to cryolite, that produce or act as free fluoride: sodium fluoride and sulfuryl fluoride. EPA's 1993 reregistration eligibility review of sulfuryl fluoride preceded the 1997 tolerance assessment of cryolite, so the conclusions regarding cryolite were not available when EPA reviewed sulfuryl fluoride. EPA's reregistration eligibility review of sodium fluoride is scheduled for 2004. The Agency will consider the applicability of the findings on cryolite to sodium fluoride when it conducts the reregistration eligibility review of this compound.

## Question 20

What is the Water Quality Criterion under the Clean Water Act for protection of aquatic life (and for protection of human health) for fluoride?

## Response

There are no water quality criteria for fluoride either for the protection of aquatic life or for the protection of human health. Pollutants for which water quality criteria are developed are selected based on their toxicity, persistence, and exposure to target organisms. EPA has not developed an aquatic life criterion for fluoride because the risk associated with other pollutants is greater. The equations used to calculate human health criteria require that EPA have established an RfD or cancer risk value. Although there is an RfD for fluoride based on dental fluorosis, it is a cosmetic effect rather than an adverse health effect. Thus, the RfD is not an appropriate value to use for a human health water quality criterion.

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