Free Executive Summary

Fluoride in Drinking Water: A Scientific Review of EPA's Standards

Committee on Fluoride in Drinking Water, National Research Council

ISBN: 0-309-10128-X, 576 pages, 6 x 9, paperback (2006)

This free executive summary is provided by the National Academies as part of our mission to educate the world on issues of science, engineering, and health. If you are interested in reading the full book, please visit us online at http://www.nap.edu/catalog/11571.html . You may browse and search the full, authoritative version for free; you may also purchase a print or electronic version of the book. If you have questions or just want more information about the books published by the National Academies Press, please contact our customer service department toll-free at 888-624-8373.

This executive summary plus thousands more available at www.nap.edu.

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,

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.

Highly exposed subpopulations include individuals who have high concentrations of fluoride in drinking water, who drink unusually large volumes of water, or who are exposed to other important sources of fluoride. Some subpopulations consume much greater quantities of water than the 2 L per day that EPA assumes for adults, including outdoor workers, athletes, and people with certain medical conditions, such as diabetes insipidus. On a per-body-weight basis, infants and young children have approximately three to four times greater exposure than do adults. Dental-care products are also a special consideration for children, because many tend to use more toothpaste than is advised, their swallowing control is not as well developed as that of adults, and many children under the care of a dentist undergo fluoride treatments.

Overall, the committee found that the contribution to total fluoride exposure from fluoride in drinking water in the average person, depending on age, is 57% to 90% at 2 mg/L and 72% to 94% at 4 mg/L. For high-water-intake individuals, the drinking-water contribution is 86% to 96% at 2 mg/L and 92% to 98% at 4 mg/L. Among individuals with an average water-intake rate, infants and children have the greatest total exposure to fluoride, ranging from 0.079 to 0.258 mg/kg/day at 4 mg/L and 0.046 to 0.144 mg/kg/day at 2 mg/L in drinking water. For high-water-intake individuals exposed to fluoride at 4 mg/L, total exposure ranges from 0.294 mg/kg/day for adults to 0.634 mg/kg/day for children. The corresponding intake range at 2 mg/L is 0.154 to 0.334 mg/kg/day for adults and children, respectively.

Dental Effects

Enamel fluorosis is a dose-related mottling of enamel that can range from mild discoloration of the tooth surface to severe staining and pitting. The condition is permanent after it develops in children during tooth formation, a period ranging from birth until about the age of 8. Whether to consider enamel fluorosis, particularly the moderate to severe forms, to be an adverse health effect or a cosmetic effect has been the subject of debate for decades. In previous assessments, all forms of enamel fluorosis, including the severest form, have been judged to be aesthetically displeasing but not adverse to health. This view has been based largely on the absence of direct evidence that severe enamel fluorosis results in tooth loss; loss of tooth function; or psychological, behavioral, or social problems.

Severe enamel fluorosis is characterized by dark yellow to brown staining and discrete and confluent pitting, which constitutes enamel loss. The committee finds the rationale for considering severe enamel fluorosis only a cosmetic effect to be much weaker for discrete and confluent pitting than for staining. One of the functions of tooth enamel is to protect the dentin and, ultimately, the pulp from decay and infection. Severe enamel fluorosis compromises that health-protective function by causing structural damage to the tooth. The damage to teeth caused by severe enamel fluorosis is a toxic effect that is consistent with prevailing risk assessment definitions of adverse health effects. This view is supported by the clinical practice of filling enamel pits in patients with severe enamel fluorosis and restoring the affected teeth. Moreover, the plausible hypothesis concerning elevated frequency of caries in persons with severe enamel fluorosis has been accepted by some authorities, and the available evidence is mixed but generally supportive.

Severe enamel fluorosis occurs at an appreciable frequency, approximately 10% on average, among children in U.S. communities with water fluoride concentrations at or near the current MCLG of 4 mg/L. Thus, the MCLG is not adequately protective against this condition.

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

sporadic pain, stiffness of joints, and osteosclerosis of the pelvis and spine. Whether EPA's MCLG of 4 mg/L protects against these precursors to more serious mobility problems is unclear.

Few clinical cases of skeletal fluorosis in healthy U.S. populations have been reported in recent decades, and the committee did not find any recent studies to evaluate the prevalence of the condition in populations exposed to fluoride at the MCLG. Thus, to answer the question of whether EPA's MCLG protects the general public from stage II and stage III skeletal fluorosis, the committee compared pharmacokinetic model predictions of bone fluoride concentrations and historical data on iliac-crest bone fluoride concentrations associated with the different stages of skeletal fluorosis. The models estimated that bone fluoride concentrations resulting from lifetime exposure to fluoride in drinking water at 2 mg/L (4,000 to 5,000 mg/kg ash) or 4 mg/L (10,000 to 12,000 mg/kg ash) fall within or exceed the ranges historically associated with stage II and stage III skeletal fluorosis (4,300 to 9,200 mg/kg ash and 4,200 to 12,700 mg/kg ash, respectively). However, this comparison alone is insufficient for determining whether stage II or III skeletal fluorosis is a risk for populations exposed to fluoride at 4 mg/L, because bone fluoride concentrations and the levels at which skeletal fluorosis occurs vary widely. On the basis of the existing epidemiologic literature, stage III skeletal fluorosis appears to be a rare condition in the United Sates; furthermore, the committee could not determine whether stage II skeletal fluorosis is occurring in U.S. residents who drink water with fluoride at 4 mg/L. Thus, more research is needed to clarify the relationship between fluoride ingestion, fluoride concentrations in bone, and stage of skeletal fluorosis before any conclusions can be drawn.

Bone Fractures

Several epidemiologic studies of fluoride and bone fractures have been published since the 1993 NRC review. The committee focused its review on observational studies of populations exposed to drinking water containing fluoride at 2 to 4 mg/L or greater and on clinical trials of fluoride (20-34 mg/day) as a treatment for osteoporosis. Several strong observational studies indicated an increased risk of bone fracture in populations exposed to fluoride at 4 mg/L, and the results of other studies were qualitatively consistent with that finding. The one study using serum fluoride concentrations found no appreciable relationship to fractures. Because serum fluoride concentrations may not be a good measure of bone fluoride concentrations or long-term exposure, the ability to show an association might have been diminished in that study. A meta-analysis of randomized clinical trials reported an elevated risk of new nonvertebral fractures and a slightly decreased risk of vertebral fractures after 4 years of fluoride treatment. An increased risk of bone fracture was found among a subset of the trials that the committee found most informative for assessing long-term exposure. Although the duration and concentrations of exposure to fluoride differed between the observational studies and the clinical trials, bone fluoride content was similar (6,200 to more than 11,000 mg/kg ash in observational studies and 5,400 to 12,000 mg/kg ash in clinical trials).

Fracture risk and bone strength have been studied in animal models. The weight of evidence indicates that, although fluoride might increase bone volume, there is less strength per unit volume. Studies of rats indicate that bone strength begins to decline when fluoride in bone ash reaches 6,000 to 7,000 mg/kg. However, more research is needed to address uncertainties associated with extrapolating data on bone strength and fractures from animals to humans. Important species differences in fluoride uptake, bone remodeling, and growth must be

considered. Biochemical and physiological data indicate a biologically plausible mechanism by which fluoride could weaken bone. In this case, the physiological effect of fluoride on bone quality and risk of fracture observed in animal studies is consistent with the human evidence.

Overall, there was consensus among the committee that there is scientific evidence that under certain conditions fluoride can weaken bone and increase the risk of fractures. The majority of the committee concluded that lifetime exposure to fluoride at drinking-water concentrations of 4 mg/L or higher is likely to increase fracture rates in the population, compared with exposure to 1 mg/L, particularly in some demographic subgroups that are prone to accumulate fluoride into their bones (e.g., people with renal disease). However, three of the 12 members judged that the evidence only supports a conclusion that the MCLG *might not* be protective against bone fracture. Those members judged that more evidence is needed to conclude that bone fractures occur at an appreciable frequency in human populations exposed to fluoride at 4 mg/L and that the MCLG is not *likely* to be protective.

There were few studies to assess fracture risk in populations exposed to fluoride at 2 mg/L in drinking water. The best available study, from Finland, suggested an increased rate of hip fracture in populations exposed to fluoride at concentrations above 1.5 mg/L. However, this study alone is not sufficient to judge fracture risk for people exposed to fluoride at 2 mg/L. Thus, no conclusions could be drawn about fracture risk or safety at 2 mg/L.

Reproductive and Developmental Effects

A large number of reproductive and developmental studies in animals have been conducted and published since the 1993 NRC report, and the overall quality of that database has improved significantly. Those studies indicated that adverse reproductive and developmental outcomes occur only at very high concentrations that are unlikely to be encountered by U.S. populations. A few human studies suggested that high concentrations of fluoride exposure might be associated with alterations in reproductive hormones, effects on fertility, and developmental outcomes, but design limitations make those studies insufficient for risk evaluation.

Neurotoxicity and Neurobehavioral Effects

Animal studies designed to test motor coordination, performance of species-typical behaviors, and some forms of learning and memory have reported deficits in performance related to fluoride exposure. A few epidemiologic studies of Chinese populations have reported IQ deficits in children exposed to fluoride at 2.5 to 4 mg/L in drinking water. Although the studies lacked sufficient detail for the committee to fully assess their quality and relevance to U.S. populations, the consistency of the results appears significant enough to warrant additional research on the effects of fluoride on intelligence.

A few animal studies have reported alterations in the behavior of rodents after treatment with fluoride, but the committee did not find the changes to be substantial in magnitude. More compelling were studies on molecular, cellular, and anatomical changes in the nervous system found after fluoride exposure, suggesting that functional changes could occur. These changes might be subtle or seen only under certain physiological or environmental conditions. More research is needed to clarify the effect of fluoride on brain chemistry and function.

Endocrine Effects

The chief endocrine effects of fluoride exposures in experimental animals and in humans include decreased thyroid function, increased calcitonin activity, increased parathyroid hormone activity, secondary hyperparathyroidism, impaired glucose tolerance, and possible effects on timing of sexual maturity. Some of these effects are associated with fluoride intake that is achievable at fluoride concentrations in drinking water of 4 mg/L or less, especially for young children or for individuals with high water intake. Many of the effects could be considered subclinical effects, meaning that they are not adverse health effects. However, recent work on borderline hormonal imbalances and endocrine-disrupting chemicals indicated that adverse health effects, or increased risks for developing adverse effects, might be associated with seemingly mild imbalances or perturbations in hormone concentrations. Further research is needed to explore these possibilities.

Effects on Other Organ Systems

The committee also considered effects on the gastrointestinal system, kidneys, liver, and immune system. There were no human studies on drinking water containing fluoride at 4 mg/L in which gastrointestinal, renal, hepatic, or immune effects were carefully documented. Case reports and in vitro and animal studies indicated that exposure to fluoride at concentrations greater than 4 mg/L can be irritating to the gastrointestinal system, affect renal tissues and function, and alter hepatic and immunologic parameters. Such effects are unlikely to be a risk for the average individual exposed to fluoride at 4 mg/L in drinking water. However, a potentially susceptible subpopulation comprises individuals with renal impairments who retain more fluoride than healthy people do.

Genotoxicity and Carcinogenicity

Many assays have been performed to assess the genotoxicity of fluoride. Since the 1993 NRC review, the most significant additions to the database are in vivo assays in human populations and, to a lesser extent, in vitro assays with human cell lines and in vivo experiments with rodents. The results of the in vivo human studies are mixed. The results of in vitro tests are also conflicting and do not contribute significantly to the interpretation of the existing database. Evidence on the cytogenetic effects of fluoride at environmental concentrations is contradictory.

Whether fluoride might be associated with bone cancer has been a subject of debate. Bone is the most plausible site for cancer associated with fluoride because of its deposition into bone and its mitogenic effects on bone cells in culture. In a 1990 cancer bioassay, the overall incidence of osteosarcoma in male rats exposed to different amounts of fluoride in drinking water showed a positive dose-response trend. In a 1992 study, no increase in osteosarcoma was reported in male rats, but most of the committee judged the study to have insufficient power to counter the evidence for the trend found in the 1990 bioassay.

Several epidemiologic investigations of the relation between fluoride and cancer have been performed since the 1993 evaluation, including both individual-based and ecologic studies. Several studies had significant methodological limitations that made it difficult to draw

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.

OTHER PUBLIC HEALTH ISSUES

The committee's conclusions regarding the potential for adverse effects from fluoride at 2 to 4 mg/L in drinking water do not address the lower exposures commonly experienced by most U.S. citizens. Fluoridation is widely practiced in the United States to protect against the development of dental caries; fluoride is added to public water supplies at 0.7 to 1.2 mg/L. The charge to the committee did not include an examination of the benefits and risks that might occur at these lower concentrations of fluoride in drinking water.

RESEARCH NEEDS

As noted above, gaps in the information on fluoride prevented the committee from making some judgments about the safety or the risks of fluoride at concentrations of 2 to 4 mg/L. The following research will be useful for filling those gaps and guiding revisions to the MCLG and SMCL for fluoride.

- Exposure assessment
  — Improved assessment of exposure to fluoride from all sources is needed for a variety of populations (e.g., different socioeconomic conditions). To the extent possible, exposures should be characterized for individuals rather than communities, and epidemiologic studies should group individuals by exposure level rather than by source of exposure, location of residence, or fluoride concentration in drinking water. Intakes or exposures should be characterized with and without normalization for body weight. Fluoride should be included in nationwide biomonitoring surveys and nutritional studies; in particular, analysis of fluoride in blood and urine samples taken in these surveys would be valuable.
- Pharmacokinetic studies
  — The concentrations of fluoride in human bone as a function of exposure concentration, exposure duration, age, sex, and health status should be studied. Such studies would be greatly aided by noninvasive means of measuring bone fluoride. Information is particularly needed on fluoride plasma and bone concentrations in people with small-to-moderate changes in renal function as well as in those with serious renal deficiency.
  — Improved and readily available pharmacokinetic models should be developed. Additional cross-species pharmacokinetic comparisons would help to validate such models.
- Studies of enamel fluorosis
  — Additional studies, including longitudinal studies, should be done in U.S. communities with water fluoride concentrations greater than 1 mg/L. These studies should focus on moderate and severe enamel fluorosis in relation to caries and in relation to psychological, behavioral, and social effects among affected children, their parents, and affected children after they become adults.
  — Methods should be developed and validated to objectively assess enamel fluorosis. Consideration should be given to distinguishing between staining or mottling of the anterior teeth and of the posterior teeth so that aesthetic consequences can be more easily assessed.
  — More research is needed on the relation between fluoride exposure and dentin fluorosis and delayed tooth eruption patterns.

• Bone studies

— A systematic study of clinical stage II and stage III skeletal fluorosis should be conducted to clarify the relationship between fluoride ingestion, fluoride concentration in bone, and clinical symptoms.

— More studies of communities with drinking water containing fluoride at 2 mg/L or more are needed to assess potential bone fracture risk at these higher concentrations. Quantitative measures of fracture, such as radiologic assessment of vertebral body collapse, should be used instead of self-reported fractures or hospital records. Moreover, if possible, bone fluoride concentrations should be measured in long-term residents.

• Other health effects

— Carefully conducted studies of exposure to fluoride and emerging health parameters of interest (e.g., endocrine effects and brain function) should be performed in populations in the United States exposed to various concentrations of fluoride. It is important that exposures be appropriately documented.

FLUORIDE IN DRINKING WATER:

A Scientific Review of EPA's Standards

Committee on Fluoride in Drinking Water

Board on Environmental Studies and Toxicology

Division on Earth and Life Studies

NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES

THE NATIONAL ACADEMIES PRESS
Washington, D.C.
www.nap.edu

THE NATIONAL ACADEMIES PRESS   **500 Fifth Street, NW**   **Washington, DC 20001**

THE NATIONAL ACADEMIES

Advisers to the Nation on Science, Engineering, and Medicine

The **National Academy of Sciences** is a private, nonprofit, self-perpetuating society of distinguished scholars engaged in scientific and engineering research, dedicated to the furtherance of science and technology and to their use for the general welfare. Upon the authority of the charter granted to it by the Congress in 1863, the Academy has a mandate that requires it to advise the federal government on scientific and technical matters. Dr. Ralph J. Cicerone is president of the National Academy of Sciences.

The **National Academy of Engineering** was established in 1964, under the charter of the National Academy of Sciences, as a parallel organization of outstanding engineers. It is autonomous in its administration and in the selection of its members, sharing with the National Academy of Sciences the responsibility for advising the federal government. The National Academy of Engineering also sponsors engineering programs aimed at meeting national needs, encourages education and research, and recognizes the superior achievements of engineers. Dr. Wm. A. Wulf is president of the National Academy of Engineering.

The **Institute of Medicine** was established in 1970 by the National Academy of Sciences to secure the services of eminent members of appropriate professions in the examination of policy matters pertaining to the health of the public. The Institute acts under the responsibility given to the National Academy of Sciences by its congressional charter to be an adviser to the federal government and, upon its own initiative, to identify issues of medical care, research, and education. Dr. Harvey V. Fineberg is president of the Institute of Medicine.

The **National Research Council** was organized by the National Academy of Sciences in 1916 to associate the broad community of science and technology with the Academy's purposes of furthering knowledge and advising the federal government. Functioning in accordance with general policies determined by the Academy, the Council has become the principal operating agency of both the National Academy of Sciences and the National Academy of Engineering in providing services to the government, the public, and the scientific and engineering communities. The Council is administered jointly by both Academies and the Institute of Medicine. Dr. Ralph J. Cicerone and Dr. Wm. A. Wulf are chair and vice chair, respectively, of the National Research Council.

www.national-academies.org

COMMITTEE ON FLUORIDE IN DRINKING WATER

Members

JOHN DOULL (*Chair*), University Kansas Medical Center, Kansas City
KIM BOEKELHEIDE, Brown University, Providence, RI
BARBARA G. FARISHIAN, Washington, DC
ROBERT L. ISAACSON, Binghamton University, Binghamton, NY
JUDITH B. KLOTZ, University of Medicine and Dentistry of New Jersey, Piscataway, NJ
JAYANTH V. KUMAR, New York State Department of Health, Albany
HARDY LIMEBACK, University of Toronto, Ontario, CANADA
CHARLES POOLE, University of North Carolina at Chapel Hill, Chapel Hill
J. EDWARD PUZAS, University of Rochester, Rochester, NY
NU-MAY RUBY REED, California Environmental Protection Agency, Sacramento, CA
KATHLEEN M. THIESSEN, SENES Oak Ridge, Inc., Oak Ridge, TN
THOMAS F. WEBSTER, Boston University School of Public Health, Boston, MA

Staff

SUSAN N. J. MARTEL, Project Director
CAY BUTLER, Editor
TAMARA DAWSON, Senior Program Assistant

Sponsor

U.S. ENVIRONMENTAL PROTECTION AGENCY

COMMITTEE ON TOXICOLOGY

Members

WILLIAM E. HALPERIN (*Chair*), New Jersey Medical School, Newark, NJ
LAWRENCE S. BETTS, Eastern Virginia Medical School, Norfolk, VA
EDWARD C. BISHOP, Parsons Corporation, Pasadena, CA
JAMES V. BRUCKNER, University of Georgia, Athens, GA
GARY P. CARLSON, Purdue University, West Lafayette, IN
MARION EHRICH, Virginia Tech, Blacksburg, VA
SIDNEY GREEN, Howard University, Washington, DC
MERYL KAROL, University of Pittsburgh, Pittsburgh, PA
JAMES MCDOUGAL, Wright State University School of Medicine, Dayton, OH
ROGER MCINTOSH, Science Applications International Corporation, Baltimore, MD
GERALD WOGAN, Massachusetts Institute of Technology, Cambridge, MA

Staff

KULBIR S. BAKSHI, Program Director
EILEEN N. ABT, Senior Program Officer for Risk Analysis
SUSAN N. J. MARTEL, Senior Program Officer
ELLEN K. MANTUS, Senior Program Officer
AIDA NEEL, Program Associate
TAMARA DAWSON, Senior Program Assistant
ALEXANDRA STUPPLE, Senior Editorial Assistant
SAMMY BARDLEY, Librarian

BOARD ON ENVIRONMENTAL STUDIES AND TOXICOLOGY[1]

---

[1]This study was planned, overseen, and supported by the Board on Environmental Studies and Toxicology.

OTHER REPORTS OF THE
BOARD ON ENVIRONMENTAL STUDIES AND TOXICOLOGY

Superfund and Mining Megasites—Lessons from the Coeur d'Alene River Basin (2005)
Health Implications of Perchlorate Ingestion (2005)
Air Quality Management in the United States (2004)
Endangered and Threatened Species of the Platte River (2004)
Atlantic Salmon in Maine (2004)
Endangered and Threatened Fishes in the Klamath River Basin (2004)
Cumulative Environmental Effects of Alaska North Slope Oil and Gas Development (2003)
Estimating the Public Health Benefits of Proposed Air Pollution Regulations (2002)
Biosolids Applied to Land: Advancing Standards and Practices (2002)
The Airliner Cabin Environment and Health of Passengers and Crew (2002)
Arsenic in Drinking Water: 2001 Update (2001)
Evaluating Vehicle Emissions Inspection and Maintenance Programs (2001)
Compensating for Wetland Losses Under the Clean Water Act (2001)
A Risk-Management Strategy for PCB-Contaminated Sediments (2001)
Acute Exposure Guideline Levels for Selected Airborne Chemicals (4 volumes, 2000-2004)
Toxicological Effects of Methylmercury (2000)
Strengthening Science at the U.S. Environmental Protection Agency (2000)
Scientific Frontiers in Developmental Toxicology and Risk Assessment (2000)
Ecological Indicators for the Nation (2000)
Waste Incineration and Public Health (1999)
Hormonally Active Agents in the Environment (1999)
Research Priorities for Airborne Particulate Matter (4 volumes, 1998-2004)
The National Research Council's Committee on Toxicology: The First 50 Years (1997)
Carcinogens and Anticarcinogens in the Human Diet (1996)
Upstream: Salmon and Society in the Pacific Northwest (1996)
Science and the Endangered Species Act (1995)
Wetlands: Characteristics and Boundaries (1995)
Biologic Markers (5 volumes, 1989-1995)
Review of EPA's Environmental Monitoring and Assessment Program (3 volumes, 1994-1995)
Science and Judgment in Risk Assessment (1994)
Pesticides in the Diets of Infants and Children (1993)
Dolphins and the Tuna Industry (1992)
Science and the National Parks (1992)
Human Exposure Assessment for Airborne Pollutants (1991)
Rethinking the Ozone Problem in Urban and Regional Air Pollution (1991)
Decline of the Sea Turtles (1990)

Copies of these reports may be ordered from the National Academies Press
(800) 624-6242 or (202) 334-3313
www.nap.edu

OTHER REPORTS OF THE COMMITTEE ON TOXICOLOGY

Review of the Department of Defense Research Program on Low-Level Exposures to Chemical Warfare Agents (2005)

Emergency and Continuous Exposure Guidance Levels for Selected Submarine Contaminants, Volume 1 (2004)

Spacecraft Water Exposure Guidelines for Selected Contaminants, Volume 1 (2004)

Toxicologic Assessment of Jet-Propulsion Fuel 8 (2003)

Review of Submarine Escape Action Levels for Selected Chemicals (2002)

Standing Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Chemicals (2001)

Evaluating Chemical and Other Agent Exposures for Reproductive and Developmental Toxicity (2001)

Acute Exposure Guideline Levels for Selected Airborne Contaminants, Volume 1 (2000), Volume 2 (2002), Volume 3 (2003), Volume 4 (2004)

Review of the US Navy's Human Health Risk Assessment of the Naval Air Facility at Atsugi, Japan (2000)

Methods for Developing Spacecraft Water Exposure Guidelines (2000)

Review of the U.S. Navy Environmental Health Center's Health-Hazard Assessment Process (2000)

Review of the U.S. Navy's Exposure Standard for Manufactured Vitreous Fibers (2000)

Re-Evaluation of Drinking-Water Guidelines for Diisopropyl Methylphosphonate (2000)

Submarine Exposure Guidance Levels for Selected Hydrofluorocarbons: HFC-236fa, HFC-23, and HFC-404a (2000)

Review of the U.S. Army's Health Risk Assessments for Oral Exposure to Six Chemical-Warfare Agents (1999)

Toxicity of Military Smokes and Obscurants, Volume 1(1997), Volume 2 (1999), Volume 3 (1999)

Assessment of Exposure-Response Functions for Rocket-Emission Toxicants (1998)

Toxicity of Alternatives to Chlorofluorocarbons: HFC-134a and HCFC-123 (1996)

Permissible Exposure Levels for Selected Military Fuel Vapors (1996)

Spacecraft Maximum Allowable Concentrations for Selected Airborne Contaminants, Volume 1 (1994), Volume 2 (1996), Volume 3 (1996), Volume 4 (2000)

Preface

In 1986, the U.S. Environmental Protection Agency (EPA) established a maximum contaminant level goal (MCLG) of 4 mg/L and a secondary maximum contaminant level (SMCL) of 2 mg/L for fluoride in drinking water. These exposure values are not recommendations for the artificial fluoridation of drinking water, but are guidelines for areas in the United States that are contaminated or have high concentrations of naturally occurring fluoride. The goal of the MCLG is to establish an exposure guideline to prevent adverse health effects in the general population, and the goal of the SMCL is to reduce the occurrence of adverse cosmetic consequences from exposure to fluoride. Both the MCLG and the SMCL are non-enforceable guidelines.

The regulatory standard for drinking water is the maximum contaminant level (MLC), which is set as close to the MCLG as possible, with the use of the best technology available. For fluoride, the MCL is the same as the MCLG of 4 mg/L. In 1993, a previous committee of the National Research Council (NRC) reviewed the health effects of ingested fluoride and 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 exposures 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 evaluate the adequacy of its MCLG and SMCL for fluoride to protect public health. 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, epidemiologic, and clinical data on fluoride, particularly data published since 1993, and exposure data on orally ingested fluoride from drinking water and other sources. Biographical information on the committee members is provided in Appendix A.

This report presents the committee's review of the scientific basis of EPA's MCLG and SMCL for fluoride, and their adequacy for protecting children and others from adverse health effects. The committee considers the relative contribution of various sources of fluoride (e.g., drinking water, food, dental-hygiene products) to total exposure, and identifies data gaps and makes recommendations for future research relevant to setting the MCLG and SMCL for fluoride. Addressing questions of economics, risk-benefit assessment, or water-treatment technology was not part of the committee's charge.

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the NRC's Report Review Committee. The purpose of this independent review is to provide candid and

critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report: Kenneth Cantor, National Cancer Institute; Caswell Evans, Jr., University of Illinois at Chicago; Michael Gallo, University of Medicine and Dentistry of New Jersey; Mari Golub, California Environmental Protection Agency; Philippe Grandjean, University of Southern Denmark; David Hoel, Medical University of South Carolina; James Lamb, The Weinberg Group Inc.; Betty Olson, University of California at Irvine; Elizabeth Platz, Johns Hopkins Bloomberg School of Public Health; George Stookey, Indiana University School of Dentistry; Charles Turner, University of Indiana; Robert Utiger, Harvard Institute of Medicine; Gary Whitford, Medical College of Georgia; and Gerald Wogan, Massachusetts Institute of Technology.

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations, nor did they see the final draft of the report before its release. The review of this report was overseen by John C. Bailar, University of Chicago, and Gilbert S. Omenn, University of Michigan Medical School. Appointed by the NRC, they were responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

The committee gratefully acknowledges the individuals who made presentations to the committee at its public meetings. They include Paul Connett, St. Lawrence University; Joyce Donohue, EPA; Steve Levy, University of Iowa; William Maas, Centers for Disease Control and Prevention; Edward Ohanian, EPA; Charles Turner, Indiana University; and Gary Whitford, University of Georgia. The committee also wishes to thank Thomas Burke, Johns Hopkins University; Michael Morris, University of Michigan; Bernard Wagner, Wagner and Associates; and Lauren Zeise, California Environmental Protection Agency, who served as consultants to the committee.

The committee is grateful for the assistance of the NRC staff in preparing the report. It particularly wishes to acknowledge the outstanding staff support from project director Susan Martel. We are grateful for her persistence and patience in keeping us focused and moving ahead on the task and her expertise and skill in reconciling the differing viewpoints of committee members. Other staff members who contributed to this effort are James Reisa, director of the Board on Environmental Studies and Toxicology; Kulbir Bakshi, program director for the Committee on Toxicology; Cay Butler, editor; Mirsada Karalic-Loncarevic, research associate; Jennifer Saunders, research associate; and Tamara Dawson, senior project assistant.

Finally, I would like to thank all the members of the committee for their efforts throughout the development of this report.

John Doull, M.D., Ph.D., *Chair*
Committee on Fluoride in Drinking Water

Contents

Fluoride in Drinking Water:
A Scientific Review of EPA's Standards