

## US NATIONAL RESEARCH COUNCIL SUBCOMMITTEE ON FLUORIDE IN DRINKING WATER

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Many readers of this journal who do research on fluoride and/or live in countries that do not fluoridate their drinking water probably cannot begin to understand the frustration of scientists who are opposed to this measure but live in countries that practice it. It is incredibly frustrating because, for over 50 years, it has proved virtually impossible in fluoridated countries to get this issue arbitrated by an independent scientific body without interference from government agencies, who appear more eager to protect their policy than to engage in an honest scientific examination of the evidence. August 12, 2003, however, may have been a turning point in the United States for the beginning of a genuine examination of this controversial policy.

On that day, a new Subcommittee on Fluoride in Drinking Water of the United States National Research Council (NRC) held its first public hearing to review the drinking water standard for fluoride at the request of the US Environmental Protection Agency (EPA). At the National Academy of Sciences building in Washington, DC, the meeting panel heard from four people: Dr Joyce M Donohue, toxicologist of the EPA's Office of Water; Dr Bernard Wagner of Wagner Associates, who chaired an earlier panel; Dr William R Maas, director of the division of oral health at the Centers for Disease Control and Prevention (CDC); and me. In this report I will summarize and comment on the presentations, particularly my own.

This is the second time that the NRC has been asked to review the standard for fluoride in drinking water. Its last review was published in 1993<sup>1</sup> and is frequently cited by fluoridation proponents. Indeed, other than a chapter in a textbook written in 1985, it was the only health reference cited by the CDC in its 1999 report claiming that water fluoridation was one of the top ten public health achievements of the twentieth century.<sup>2</sup> Studies published during the six years after 1993 raising new concerns about health impacts of fluoride were not cited by the CDC. Clearly, however, the EPA is concerned about these and other recent studies and hence this new review.

### PROBLEM AT ISSUE

*The question posed to the panel is essentially twofold:*

Is the maximum contaminant level (MCL) standard for fluoride in drinking water (set by the EPA in 1986 at 4 ppm) protective of all health outcomes, with a reasonable margin of safety for the most vulnerable members of society?

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If it is not, what maximum contaminant level goal (MCLG) should be recommended?

A key point is the difference between an MCL and an MCLG. An MCLG is a safe level *goal* based on the lowest levels of exposure that show damage in toxicological, animal, or human studies, with an appropriate safety margin applied to protect all members of society, including vulnerable subsets like children, the elderly, and those who are already sick. This is the level society would want from an ideal perspective, which should be based on the best science available and the best scientific judgment.

The MCL on the other hand, is the regulator's determination of how close society can get to that goal from a practical (usually economic) perspective. One can illustrate this difference with the MCLG and the MCL for arsenic. In the US, the MCLG for arsenic is zero, because arsenic has been shown to be a human carcinogen, and the EPA has a policy that there is no safe level for a human carcinogen. However, to get down to a level of zero for this naturally occurring contaminant in drinking water would be too costly. Thus the current compromise is an MCL of 10 ppb (parts per billion) for arsenic, and even this has caused concern in states with levels higher than this in some of their water supplies, since they will have to spend money to reduce those levels.

For fluoride the issue becomes more complicated, not only because it is a "contaminant" like arsenic, but also because it is an "additive" in communities that practice water fluoridation.

#### AN HISTORICAL NOTE

When the EPA established its 4 ppm MCL for fluoride in 1986, it was unusual for a contaminant level standard to be raised rather than lowered. Most often, MCLs tend to get lowered as new evidence of harm is discovered. At the time professionals at the US EPA were appalled by what they saw as a blatant political attempt to manipulate the findings of a blue ribbon panel whose discussions included the memorable phrase, "You would have to have rocks in your head...to allow your child much more than 2 ppm."<sup>3</sup> However, despite the EPA being taken to court by the Natural Resources Defense Council (NRDC), the 4 ppm standard prevailed. Our neighbors to the North (Canada) and to the South (Mexico) both have a 1.5 ppm standard.

Years earlier, in 1939, two professional water-treatment engineers of the American Water Works Association recommended a fluoride standard of 0.1 ppm to provide an adequate margin of safety to protect against dental fluorosis.<sup>4</sup> That suggestion, however, was made before the idea of water fluoridation had taken off, and was quickly forgotten.

### THE NRC MEETING

Appearing as the first speaker at the recent August 12 hearing, Dr Joyce Donohue of the EPA Water Division gave an overview of the agency's regulatory history concerning fluoride and explained why the EPA had asked the NRC to review their MCL and SMCL for fluoride in drinking water. (The SMCL refers to the secondary maximum contaminant level—a non-enforceable standard to protect against moderate and severe dental fluorosis.) Since the 1993 NRC review there have been a number of important new studies. Donohue mentioned concerns about increased rates of dental fluorosis, bone fractures, and other health concerns in very general terms.

There was one point that Donohue made with which I disagreed. She stated that the Food and Nutrition Board of the Institute of Medicine (IOM) had come around to accepting fluoride as a "nutrient".<sup>5</sup> In the comment period I pointed out that at the IOM meeting in September 1997, Dr Vernon Young, chairman of the Food and Nutrition Board, stated quite clearly that fluoride was not a nutrient but a "beneficial element". Subsequent to this IOM meeting, the presidents of the IOM and of the National Academy of Sciences wrote in a letter to the editor of this journal that if anyone at that meeting had described fluoride as a nutrient, they had "misspoke".<sup>6</sup>

Donohue noted that the MCLG and the MCL are now set at the same level—4 ppm—but stressed that the main concern was to determine an appropriate MCLG. The chairman, Dr John Doull, stated that the brief to the subcommittee asked them to review both the MCL and the SMCL—the secondary maximum contaminant level (now 2.0 ppm), which pertains only to fluoride levels that are thought to lead to the adverse effects of moderate and severe dental fluorosis. Donohue explained that both moderate and severe dental fluorosis were viewed by the EPA as not being "health" effects but "cosmetic" effects. This secondary goal is not a federal standard but exists so states can use it as their MCL if they so wish. Some of the panel members were clearly uneasy that moderate/severe dental fluorosis was not considered an adverse health effect.

### SUPPORT FOR THE 1993 NRC REPORT

Following Donohue, Dr Bernard Wagner, who had chaired the earlier 1993 NRC fluoride review panel, spoke in favor of the recommendations of this earlier report. In his presentation, however, he made a number of serious mistakes summarizing the NRC's 1993 review. Thus, he dismissed the NTP (National Toxicology Program) cancer bioassay, which showed a dose response increase in osteosarcoma in male rats,<sup>7</sup> with comments that actually pertained to a study sponsored by Procter & Gamble.<sup>8</sup> This latter study was indeed problematic, but the irony is that the 1993 NRC review used the P&G study to "dilute" the findings of the NTP study!

Another glaring mistake made by Wagner occurred when he stressed how “large” the fluoride concentrations were in the NTP study. (In fact, they were not large compared to the typical concentrations used to tease out a suspected human carcinogen using a *small* number of animals.) He repeated the same mistake made ten years earlier. In the executive summary of the 1993 NRC report, the authors reported concentrations for sodium fluoride, not fluoride ion. This might make it appear that the concentrations were over two times higher in fluoride ion than were actually used, *i.e.*, 100 and 175 ppm concentrations of sodium fluoride, which correspond to 45 and 79 ppm fluoride ion. After ten years Dr Wagner has still not corrected this elementary error. Another mistake was his assertion that there has been no increase in osteosarcoma in young males over the period in which fluoridation has been practiced in the US. Dr Charles Poole, a member of the panel, corrected him on this.<sup>9,10,11</sup>

The panel then heard from Dr William R Maas, DDS, MPH, Director, Division of Oral Health at the CDC. Dr Maas hardly touched on health concerns other than dental fluorosis. Early in his lengthy presentation he made it known that he thought that the 1993 NRC review was a good one and its conclusions could still be relied upon. Maas even cited the highly criticized Fluoridation Forum report from Ireland,<sup>12</sup> which devoted only 17 pages (out of 295) to health concerns, and of these 17 pages only two pages dealt with primary studies.

The rest of Maas's talk essentially promoted the benefits of fluoridation (exaggerated in my view) and downplayed the significance of the enormous increase in dental fluorosis in the US and other fluoridated countries. He discussed, at some length, studies which have tried to understand children's psychological response to fluorosed teeth. What stood out in his presentation, however, was the overwhelming impression that the CDC is far more interested in promoting water fluoridation than giving any consideration to adverse health effects from exposure to fluoride.

#### MY PRESENTATION

It was then my turn to speak. In its invitation the NRC specifically asked that I not present arguments about water fluoridation but to focus on concerns about health impacts of fluoride. This is what I did, although after hearing from Dr Maas, who spent so much time defending water fluoridation, I was eager to get into the debate about fluoridation itself. However, I bit my tongue and stuck to my prepared presentation titled: “A safe drinking water standard for fluoride: LOAELs and protecting the most vulnerable.” My rationale was that all the health effects should be examined comprehensively and scientifically, before any benefits are considered.

The LOAEL is the “lowest observed adverse effect level (or dose)” observed in any study, whether it be an animal study, a clinical trial, or an epidemiological study, which produces some adverse effect. It is this dose which is used by regulatory agencies like the EPA to determine an allowable daily intake level (or reference dose). To do this, regulatory officials have to apply an appropriate safety factor to take into account such considerations as extrapolating from animal data to human data and allowing for a range of sensitivity in people to any drug or toxic substance. This latter factor is used to protect the most vulnerable members in society, which include the very young, the very old, and the sick. Too often in the past, when it comes to safe levels of fluoride, regulatory officials have only considered the “average” person not the “most vulnerable”.

My paper and power point presentation were both co-authored with my son Michael Connett and can be found at <http://www.fluoridealert.org/nrc-paper.pdf> and <http://www.fluoridealert.org/nrc-final.ppt>.

After reviewing the inadequacies of the 1993 NRC review, we summarized studies (mostly published since 1993) which indicate that fluoride can cause damage to either animals or humans. From these we identified the LOAELs and applied what we consider to be appropriate safety margins to arrive at a series of MCLGs for eight different outcomes in addition to dental fluorosis:

- 1 Accumulation in the human pineal gland;<sup>13</sup>
- 2 Neurotoxic effects:
  - brain damage in rats;<sup>14</sup>
  - increased uptake of lead into children’s blood associated with the use of silicofluorides as water fluoridating agents;<sup>15-16</sup>
  - lowering of IQ in children;<sup>17-18</sup>
- 3 Lowering of human thyroid gland activity;<sup>19-20</sup>
- 4 Osteosarcoma in young men;<sup>11</sup>
- 5 Bone fractures in children;<sup>21</sup>
- 6 Increased hip fractures in the elderly;<sup>22-26</sup>
- 7 Lowering of human fertility;<sup>27</sup>
- 8 Hypersensitivity to fluoride.<sup>28</sup>

All these outcomes except the hypersensitivity endpoint are listed in the following table.

**Table.** Lowest observed adverse effect level (LOAEL) and maximum contaminant level goal (MCLG) calculations for fluoride in drinking water

Endpoint	Author	LOAEL ppm	Safety factor	MCLG ppm
Pineal gland	Luke <sup>13</sup>	<1.0	100	<0.01
Neurotoxicity	Varner <sup>14</sup>	1.0	1000	0.001
Thyroid	Bachinskii <sup>19</sup>	2.3	100	0.02
	Galletti <sup>20</sup>	1.0 <sup>a</sup>	100	0.01
Osteosarcoma	Cohn <sup>11</sup>	1.0	100	0.01
Bone fracture, children	Alarcon-Herrera <sup>21</sup>	1.0 <sup>b</sup>	10	0.1
Hip fracture, elderly	Li and others Li <sup>22-26</sup>	1.0-1.5	10	0.1
Reproduction	Freni <sup>27</sup>	3.0	10	0.3

<sup>a</sup>The fluoride dose used in this study (2.3-4.5 mg/day) is within the range of doses expected in fluoridated communities (1.6-6.6 mg/day). <sup>b</sup>Increased fractures were associated with mild dental fluorosis occurring elsewhere with 1-ppm fluoride in drinking water.

In my presentation I stressed that while there was room for rationalizing different safety factors for different health endpoints, the basis for proposing them has to be made explicit. Moreover, I could see no scientific justification for having *NO* safety factor at all, as in the case of the UL (tolerable upper level intake) for fluoride proposed by the IOM in 1997<sup>5</sup> and repeated in the Irish Fluoridation Forum report in 2002.<sup>12</sup>

I also offered an alternative approach to arriving at a safe drinking water standard for fluoride. Traditionally, for setting a safety standard, one starts with levels which are known to cause harm, and, then works downward, using a safety factor, to levels which we hope will not cause harm. As a different method, I suggested we can jump directly to an assured safe level by using the concentration of fluoride found in mothers' milk. This level of 0.01 ppm,<sup>5</sup> *must* be a safe level, since evolutionary forces have worked so long at arriving at baby's first meal. This proposal generated some discussion from the panel, but I argued that the fluoride level in mothers' milk indicates two things: a) that fluoride is not a nutrient for the baby, and b) that there are sound biological reasons why fluoride is excluded from an infant's delicate biochemical machinery, especially in its earliest stages. (For a pertinent review of fluoride's interaction with G-proteins, see Li 2003.<sup>29</sup>)

I concluded with suggestions for future fluoride research needs. Hopefully, some who contribute to this journal will undertake or be called upon to conduct some of this research. Our suggestions include: 1) an independent review of the cancer slides in the controversial NTP animal study; 2) comprehensive monitoring of fluoride levels in bone and the pineal gland at

autopsy; 3) repetition of the 2001 Alarcon-Herrera study<sup>20</sup>; 4) more use of dental fluorosis as a biomarker for suspected end points in children; 5) introducing the study of skeletal fluorosis in relation to osteoarthritis in medical school curricula; 6) an up-to-date review of neuromuscular and gastrointestinal hypersensitivity to fluoride along the lines of the 1961 study by Feltman and Kosel<sup>27</sup>; 7) a comprehensive study of the toxicology of the silicofluorides used in water fluoridation programs; 8) an examination of possible synergistic effects of fluoride and other pollutants on the thyroid gland; and 9) a review of all organofluorine pharmaceuticals to determine how many are metabolized to free fluoride ion.

#### CLOSING COMMENTS

The panel members now have the task of examining the science behind the studies we have discussed and the safety margins we have recommended, and then making a judgment as to their validity and significance for setting a health-based standard for fluoride in drinking water. Only after they have done all this and agree upon a single MCLG should they then be confronted with the ramifications of what this number means for the practice of water fluoridation and for the controlling of other increasing sources of fluoride we are exposed to in our daily lives.

It is essential that the costs of removal of fluoride not influence a determination of an MCLG, even though they might be an important factor in moving from an MCLG to an MCL. Only after the MCLG has been determined by the very best scientific judgment should the panel examine the possible benefits of water fluoridation. At this point they should hear from scientists representing both sides of this controversial matter.

In my mind, the panel will be forced to conclude that the 4 ppm MCL has to be lowered. Simply by taking the NRC's own 1993 statement that skeletal fluorosis is likely to occur in someone consuming 10 mg of fluoride per day for 10 years or more, it is clear that the current MCL would not protect against this effect in high water consumers, or people with significant non-waterborne sources of fluoride exposure.

Moreover, if we consider the pre-clinical symptoms of skeletal fluorosis, which are virtually identical to arthritis,<sup>30-32</sup> even consumption of 1 ppm fluoride water by heavy water consumers, and people with kidney dysfunction, could present a risk for arthritic symptoms. Indeed, based on current data on bone concentrations in fluoridated, and even unfluoridated areas, it is evident that some people are accumulating levels of fluoride in their bone (>3,500 ppm)<sup>33-35</sup> that have been associated with the early stages of skeletal fluorosis.<sup>36</sup>

If a defensible scientific analysis indicates an MCLG lower than 1 ppm for arthritic symptoms and the other adverse effects discussed above, then a

recommendation is in order to halt the practice of deliberately adding fluoride (and especially industrial-grade silicofluorides) to public water supplies. It is hard to imagine that any panel that is not pre-ordained to endorse water fluoridation could possibly decide that the benefits of fluoridation justify the risks associated with any of the end points identified above, especially when extensive data from continental western Europe have conclusively shown that the decline of tooth decay in the western world is not dependent on the presence or absence of water fluoridation.<sup>37-38</sup>

For an independent report of this important NRC meeting, see the account by Bette Hileman, Senior Editor, in the August 25 issue of *Chemical and Engineering News*, an official weekly publication of the American Chemical Society.<sup>39</sup>

#### POSTSCRIPT

Since the meeting on August 12, we have learned that Dr Wagner has left the panel and has been replaced by Hardy Limeback, DDS, PhD, head of preventive dentistry at the University of Toronto.

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