Appendix 1-C. FAN submission to NRC 2006 on F adverse effects including cancer

Submission to:
National Research Council Committee:
Toxicologic Risk of Fluoride in Drinking Water; BEST-K-02-05-A

Wednesday, March 30, 2005.

Dear NRC panel members,

By now, we hope that you have had time to digest our submissions (part I & II) on Bassin's thesis and the ramifications for other studies on osteosarcoma.

To date, the panel has spent countless hours over the past two years to digest a mountain of material. The panel contains experts from many fields and with differing points of view. We sincerely hope that all this knowledge will be used to produce a comprehensive report on the state of knowledge of fluoride's toxicity.

Crucial to the utility of the report will be detailed discussions of NOAELs (No Observed Adverse Effect Levels), LOAELs (Lowest Observed Adverse Effect Levels), and safety margins for each adverse endpoint. Unanimity may not always be achieved, but science and the public interest are not advanced by limiting the final report to recommendations for which there is unanimous agreement.

Finally, having spent so much of our own time and energy on this issue, we hope you will give consideration to this summation of what, we believe, are the most important points for determining a truly protective MCLG.

EPA's MCLG - Bone

We believe that there is one overwhelming and undeniable truth and that is the 4 ppm MCLG is not protective of health. This is most clearly evident when re-visiting EPA's own rationale for the 4 ppm MCLG.

The rationale utilized by EPA in 1985 to set the MCLG is deficient on all three components used in the calculation (the LOAEL, the safety factor, and the exposure estimate).

Before we address the problems, however, with each of these three components, here is EPA's own explanation of the MCLG as presented in 2004 by EPA's office of Prevention, Pesticides and Toxic Substances.

> "... For fluoride, both the MCL and the MCLG have been set at 4.0 ppm in order to protect against crippling skeletal fluorosis. The MCLG was established in 1986 [FR 51 (63)] and is based on an LOAEL of 20 mg/day, a safety factor of 2.5, and an adult drinking water intake of 2 L/day. The use of a safety factor of 2.5 ensures public health criteria while still allowing sufficient concentration of fluoride in water to realize its beneficial effects in protecting against dental caries. The typical 100X factor used by

> the HED [Health Effects Division] to account for inter- and intra-species variability have been removed due to the large amounts of human epidemiological data surrounding fluoride and skeletal fluorosis (EPA 2004, p. 16)."

Below we address what we see as the weaknesses of each component of the EPA's determination and have recommended more appropriate calculations which, when combined, produce the **highest** MCLG which could be defended scientifically.

The LOAEL

20 mg/day of fluoride is an inadequate and outdated LOAEL for chronic lifetime fluoride exposure.

First, it is based on data gathered on a small set of adult cryolite workers in the 1930s (Roholm 1937), and is therefore not an appropriate "threshold" dose to utilize for all members of the population, particularly children, people with chronic malnutrition, people with kidney disease and all other subsets of the population not represented in the cryolite study.

Second, the dose is based on only "10 to 20 years" of exposure, not lifetime exposure.

Third, the scientist who first derived the 20 mg/day estimate (Hodge 1950) from the cryolite worker study, eventually revised his estimate to 10-25 mg/day (Hodge 1979).

The NRC's 1993 report recognized the outdated status of the 20 mg/day LOAEL when they wrote:

> "Crippling skeletal fluorosis might occur in people who have ingested 10-20 mg of fluoride per day for 10-20 years."

Moreover, Cao (2003) verified that a daily intake of 12 mg/day (from all sources combined) was associated with a markedly high prevalence of crippling fluorosis in Tibet.

Hence, the LOAEL for crippling fluorosis should be at most 10-12 mg/day. The 20 mg/day LOAEL for crippling fluorosis should therefore be lowered by a factor of 2.

Common sense, however, should indicate that damage to skeletal health can occur before the crippling phase of skeletal fluorosis occurs. This fact, ignored by EPA when setting the MCLG in 1985, was acknowledged by the DHHS in 1991. In the DHHS' 1991 report, crippling fluorosis was reported to be preceded by "stiffness of joints," "chronic joint pain", "calcification of ligaments" and various effects on bone including osteosclerosis of trabecular bone and osteoporosis in the appendicular skeleton. Thus, the 20 mg/day LOAEL should be lowered by another safety factor of at least 2 in order to protect against the pre-crippling phase of skeletal damage.

The Safety Factor

The safety factor of 2.5 is unacceptably low. As the LOAEL was derived from a study of a small set of otherwise healthy workers (Roholm 1937) a factor of 2.5 cannot possibly be

expected to cover the full range of sensitivities in a human population. For example, it is completely inadequate to protect the most vulnerable members of society, particularly those suffering from kidney impairment. Nor can it be expected/assumed to protect those exposed through infancy and the full duration of childhood.

The first health study of children living in a fluoridated community found a statistically significant increase (13.5 versus 6.5%) in cortical bone defects in the fluoridated community (Newburgh, NY) compared with the unfluoridated community (Kingston, NY) after just ten years of fluoridation at 1 ppm fluoride (Schlesinger, 1956). While this observation prompted the NAS in 1977 to recommend looking for a possible connection between fluoridated water and osteosarcoma in young men, the observation should also be considered in terms of its ramifications for bone fractures, since the cortical layer (the outside layer of the bone) is critical in protection of the appendicular skeleton from fracture. Such a concern was greatly amplified with the recent findings of a linear correlation between the severity of dental fluorosis and the incidence of bone fracture in children (Alarcon-Herrera et al., 2001). With dental fluorosis rates now impacting approximately 30% of children living in artificially fluoridated water at 1 ppm and over 20% in non-fluoridated communities (Heller et al, 1997) this is not a matter that should be taken lightly.

Moreover, a well-conducted study by Mayo Clinic scientists (Johnson 1979), which was unfortunately overlooked by the NRC in 1993 and EPA in 1985, found strong evidence of skeletal fluorosis (e.g. histological evidence coupled with extremely elevated bone and blood fluoride levels) among people with kidney disease (not on dialysis) drinking water with just 1.7 to 2.0 ppm.

With these observations in mind, we can see no reason why the standard safety factor of 10 to cover intra-species variation should be abandoned for fluoride – especially when considering the growing recognition (not appreciated in 1985 when EPA established the fluoride standard) that extra safety factors are needed to protect children. Utilizing a MINIMAL safety factor of 10 instead of 2.5 leads to a lowering of the MCLG by another factor of 4.

Exposure Estimate

Finally, the assumption that people drink only two liters of water, underlines the fact that this standard at best was only designed to protect the average person - in this case the average water drinker. Some individuals drink far more water than this on a regular basis.

According to EPA's own water consumption data (EPA 1985), up to 5% of the population drinks 4 liters of water per day or more. (Athletes in my university classes drink about 5 liters of water a day.)

Moreover, the Institute of Medicine has recently recommended that men over the age of 19 drink **three liters of water per day** (IOM 2004). Thus, as it now stands, the EPA standard does not protect adult males drinking the IOM's recommended "adequate intake" of water.

Another problem with EPA's exposure estimate, is that it does not take into account other sources of fluoride (e.g. tea; Whyte 2005).

Thus, in order to protect individuals drinking up to 5 liters of water per day, and in order to protect individuals exposed to other sources of fluoride, the safety factor needs to be raised by AT LEAST another factor of 2.5.

Thus, this most elementary analysis of the deficiencies in the calculation of the 1986 MCLG for just one tissue (the bone) would require lowering the MCLG by a factor of at least 40:

2x (to update LOAEL with revised estimate for crippling fluorosis);
2x (to update LOAEL to protect against skeletal effects occurring prior to crippling fluorosis);
4x (to utilize standard safety factor of 10 instead of 2.5); and
2.5x (to protect individuals with high water consumption).

Applying these factors (2 x 2 x 4 x 2.5) to EPA's current MCLG of 4 ppm would yield an MCLG of 0.1 ppm.

Alternatively, applying a safety factor of 10 to the LOAEL findings of Alarcon- Herrera (2001), Johnson (1979), Juncos (1972), Ng (2004), and Schlessinger (1956) would yield an MCLG of 0.1 ppm – 0.17 ppm.

While we think there are arguments that these factors are not conservative enough, we would proffer here that 0.1 ppm is the **maximum MCLG** which could be rationally defended for potential damage to bone in children and those with kidney dysfunction. It might be possible to go lower than this but we cannot see how it could be any higher.

Turning to other health effects besides bone damage, we will now focus on what we consider to be two of the most important effects: neurotoxicity and osteosarcoma.

Non-Bone Endpoints – Neurotoxicity

Since 1993 there have been many studies on fluoride's impact on the brain in both animals and humans. We have listed most of these studies online at: http://www.fluoridealert.org/health/brain/.

With nearly 30 animal studies since 1993 finding that chronic fluoride exposure damages the brain, it is no longer possible to maintain (as the EPA did when establishing the MCLG in 1985) that bone is the only tissue adversely impacted by chronic exposure to fluoride. Thus, we would recommend that the NRC panel select an appropriate NOAEL or LOAEL from the fluoride/neurotoxicity literature and determine the corresponding MCLG.

For animal studies, we would recommend utilizing the series of studies from Guan at the Karolinksa Institute (Guan 1998, Long 2002, Chen 2003; Shan 2004). In this series of studies, 30 ppm fluoride has repeatedly been associated with adverse effects on the brain (e.g. reduced nicotinic acetylcholine receptors, reduced phospholipid content, etc). Thus, if we use 30 ppm as the LOAEL for neurotoxicity in rats, and apply the standard safety and uncertainty factors (10x for absence of NOAEL, 10x for extrapolation from animals to humans, and 10x for variation of sensitivity among humans) we arrive at an MCLG of 0.03 ppm.

For human studies, we would recommend starting with Xiang et al. (2003) who estimated that IQ is lowered at 1.8 ppm among children. Applying a safety factor of 10 to allow for the range of sensitivity within a human population and another factor of 2 to allow for other sources of fluoride would yield an MCLG of 0.09 ppm. Again it would be possible to go lower than this, with more conservative consumption figures, but we cannot see how an MCLG could be any higher for this serious end point.

Non-Bone Endpoints – Osteosarcoma

In light of the accepted biological plausibility of a fluoride/ osteosarcoma link, in light of previous findings in animals and humans, and in light of the recent case control study from Elise Bassin at Harvard, we believe the weight of evidence now suggests a probable relationship between fluoride exposure and osteosarcoma in young males. Such a conclusion would necessitate a recommendation that the MCLG be lowered to zero, since, according to EPA's water policy, there is no safe level for a human carcinogen. What happens with the MCL, of course, is the EPA's affair and like arsenic will be heavily influenced by economic considerations.

Due to the obvious importance of this issue (osteosarcoma is a serious, often deadly, form of childhood cancer) we would also ask that the panel, if it can not reach unanimity on this question, provide the EPA and the public with a full discussion covering all points of view represented on the panel. If necessary this might be a point at which a minority report would be helpful. In our view, no amount of recommendations for future study could compensate for a failure to acknowledge the implications of the current evidence presented by Bassin and others. If there are differences on this they need to be made visible and transparent.

Finally, recognizing the problem posed by the fact that we have two US agencies involved in recommending standards on this issue, namely the EPA which provides a standard based on treating fluoride as a contaminant (4 ppm) and the CDC which recommends a standard of 1 ppm based upon the arguable notion that fluoride reduces tooth decay when swallowed, we would hope that members of the panel would recommend - again, if necessary, as a minority report - that bearing in mind the seriousness of such end points as osteosarcoma and impacts on the central nervous system, that even if they cannot **precisely** define an MCLG for the purposes of removing naturally occurring fluoride, they can recommend that fluoride not be DELIBERATELY ADDED to the water supply at levels (1 ppm) that on average are 10X greater than typical natural fluoride water levels and 100X greater than that present in breast milk

Sincerely,

Paul Connett
Ellen Connett
Michael Connett
Chris Neurath

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