Comments in response to

Evidence on the Carcinogenicity of Fluoride and Its Salts
July 2011

As prepared and available for public comment by

Reproductive and Cancer Hazard Assessment Branch
Office of Environmental Health Hazard Assessment
California Environmental Protection Agency

Submitted

September 6, 2011

By
David Kennedy, DDS
Preventive Dental Health Association
1068 Alexandria Drive
San Diego, CA 92107
Email: davidkennedy-dds@cox.net
Phone: (619) 222-8177

Summary

The conclusion drawn by OEHHA concerning the Kim/Douglass 2011 study, in which OEHHA minimizes the scientific data drawn from the Bassin study, cannot withstand scientific scrutiny.

Kim/Douglass 2011 does not, and cannot, significantly alter the probable carcinogen finding of the CIC for the following reasons:

#1. Kim/Douglass 2011 presents too small of a subject base for a comparison to the age-sex-related effects presented in the larger Bassin study.

#2. Kim/Douglass 2011 did not present adequate controls for a disease that occurs more often in males than females.

#3. Kim/Douglass 2011's use of bone cancer controls, using older patients, are inappropriate controls for bone cancers in younger patients.

#4. Numerous conflicts of interest are disclosed in the OEHHA presentation of evidence, which call into question the scientific objectivity of the authors.

Utilizing the best available science, considering the mechanisms identified, the site of the cancers, and the increased sensitivity of young males, clearly the weight of the evidence favors a determination of fluoride's carcinogenicity.

Discussion

In vivo studies have identified the mechanism, and the site of the cancer, showing that toxin accumulation in bone is logical.

The CIC has previously received analyses of the F/bone cancer link from both Drs. Thiessen and Mullenix, and since these earlier submissions there is an additional report by Colgate's editor Douglas that was highly touted in the dental press as disproving the cancer/F link. However, Kim/Douglass does not, and cannot, disprove the cancer/F link based upon their study design. It is so seriously flawed that it was not even published in a reputable medical journal. (Kim/Douglass et al. *An Assessment of Bone Fluoride and Osteosarcoma* Journal of Dental Research July 28, 2011.)

A dental journal such as JDR obviously does not have a peer review faculty with an adequate knowledge of epidemiology or normal case-controlled research. It is highly inappropriate to publish a complex cancer epidemiological study in a dental journal. The touting of this be-all, end all study even in the previous Proposition 65 considerations accentuates the shortcomings of both the study and its peer review. I've attached and appended a brief analysis of why a study that used an inappropriate metric (bone fluoride) and inappropriate controls (other bone cancers) is simply a study designed to muddy an already very clear issue. Fluoride obviously can and does cause cancer. Bottom line.....Douglass's study does not negate Bassin's work.

A brief summary of the bone cancer fluoride link: NTP study in 1989 found a clear link to bone and liver cancers.

In 1990 these findings were downgraded, without scientifically logical explanation, to equivocal by the US Public Health Service.

Dr. William Marcus, Senior Toxicologist at EPA's Office of Drinking Water, won with punitive damages two whistleblower lawsuits over the unjustified alterations of the NTP study by the US Public Health Service. His "May Day Memo" that was a key piece of evidence in both the trials is attached.

In Cohn, PD, *Association of Drinking Water Fluoridation and the Incidence of Osteosarcoma Among Young Males*, Environmental Health Services, New Jersey Nov 8, 1992, the authors state,

> "Recently, a national study of drinking water fluoridation at the county level found a significant association with osteosarcoma incidence among males under 20 years of age (Hoover et al., 1991). However, the meaning of the association was questioned by the authors because of the absence of a linear trend of association with the duration of time for which the water supplies were fluoridated. Furthermore, the simple study design used did not have individual information on the average amount of water ingested daily, use of dental fluoride supplements, long term residence, other potentially confounding (or causal) exposures, or genetic involvement."

And found,

> "Osteosarcoma incidence between 1979 and 1987 was compared by ecologic epidemiology methods to water supply fluoridation in seven counties in central New Jersey. Twelve cases were diagnosed among males under age 20 in fluoridated municipalities vs. eight cases in non-fluoridated municipalities.
>
> The rate ratio of incidence in fluoridated vs. nonfluoridated municipalities was 3.4 with a 95% statistical confidence interval (95%CI) between 1.8 and 6.0. All twelve cases in fluoridated municipalities resided in a three county area with the greatest prevalence of fluoridation. The rate ratio of incidence in fluoridated vs. nonfluoridated municipalities in the three county area was 5.1 (95%CI 2.7-9.0). Among 10-19 year old males in those three counties, the rate ratio was 6.9 (95%CI 3.3-13). No other age/sex groups exhibited significant association with fluoridation."

Although they did not have individual information on type or amount of water consumed and the other sources of F exposure such as bottled water, toothpaste, dental office-applied fluoride treatments and/or F mouthwash, Cohn had again found an age/sex specific cancer of bone.

Specific evidence of the unsustainable opinion and weight that OEHHA has presented for Kim/Douglass:

Point #1. Kim/Douglass et al. (JDR 2011) quote: "If fluoride levels were related to bone cancer in general, the current study design would be unable to detect this. There is no published evidence of such an association."

Carl Sagan stated that, "Absence of evidence is not evidence of absence". It is equally true that there is also no published evidence to disprove such an association--in fact; there are almost no studies of this issue. However, the Hoover 1991 study (an appendix in the PHS report) does report an excess of Ewing's sarcoma (a type of bone cancer) in fluoridated counties vs. nonfluoridated counties and the authors speculated this was an artifact. Perhaps it was not an artifact.

Point #2. Kim/Douglass et al. (JDR 2011) use of bone fluoride levels at the time of diagnosis/surgery (snap shot) is not the appropriate metric for a disease that was initiated at least a few years earlier. Bassin's carefully controlled study showed that osteosarcoma was associated with the amount of fluoride exposure at the time of the specific growth spurts in young males, and thus the timing of exposure was highly significant. The amount of fluoride exposure during those earlier years is not necessarily represented adequately by the bone fluoride level at the time of surgery.

Most cancers have a "lag time" of at least 5 years, often 10 or more, between the probable time that the cancer began (was initiated) and the time that the cancer is diagnosed. Put simply, it takes a while for one aberrant cell to grow into something big enough to get noticed.

It is therefore obvious that bone fluoride could conceivably be quite low in a young male osteosarcoma cancer victim's bone at the time of cancer initiation (7 years-old) and substantially higher in non-cancerous bone and in cancerous bone some years later.

As we have discussed above, the bone fluoride at a point in time is in effect a measure of time-integrated exposure, and it is not the correct measure of exposure to use for something for which an age-specific susceptibility has been observed that may cause a cancer.

Kim's PhD thesis conclusion in Chapter 2, unpublished at this time and currently in the rare books library at Harvard: The correlation between bone F levels and cumulative F exposure from water as well as from F supplements was only moderately positive.

Thus, clearly drinking water F measures may not accurately reflect the total body burden of F.

What Bassin did was look at the F exposure level each year of a child's life, and found there was a relationship between exposure at a given age and the appearance of osteosarcoma some years later.

What Kim did was look at the cumulative fluoride exposure (more or less) at the time the cancer was found. Fluoride exposure between the time a cancer is initiated and the time the cancer is diagnosed contributes to the cumulative fluoride exposure that Kim measured, but did not likely contribute to cancer causation.

Point #3. If fluoride is a carcinogen and causes more than one type

of bone cancer then the measure of fluoride in bone from other bone cancer patients is an inappropriate control.

Nevertheless it is noteworthy that the bone fluoride in the cases (median age ~17) and "controls" (median age ~41) were not remarkably different. "The median cumulative lifetime water F levels did not differ between cases and controls (14.4 ppm vs. 16.5 ppm, p=0.17)." Given the great age difference (2.41 fold), it does strongly suggest that the cases had generally higher exposures per unit time. For accurate analysis, ideally the Kim/Douglass authors should have given all of the age related data range, standard deviation as well as the mean.

Point #4. Kim/Douglass et al. (JDR 2011) did not look for an association of risk with age-of-exposure that Elise Bassin previously found nor did they do an age specific analysis of the 137 of cases they used in this study. In fact, they point out "if risk is related to exposures at a specific time in life, rather than total accumulated dose, this metric would not be optimal."

Point #5. Kim/Douglass et al. (JDR 2011) cohort had a median age of about 17, with 28 of 137 cases being 30 or older (37 cases up to age 14, 72 more up to age 29, and not enough < 20 years old for statistical analysis, according to the authors.

Bassin's paper carefully limited the analysis to 103 cases diagnosed before the age of 20 (median age 14). Bassin had a bigger group of relevant cases than Kim/Douglass had, and more appropriate controls.

Point #6. There is a detailed discussion by the NRC of the Bassin thesis in two parts. They addressed this concern, especially in the manner of exposure. This is a unique contribution to exposure analysis. In the analysis performed by the NRC study group, white males at 5 and 7 years of age are at highest risk for osteosarcoma (see NRC Fluoride in Drinking Water 2006). It makes sense because growth spurts occur at those times and F exerts its adverse effects on the osteoclasts during times of maximum bone growth.

This is the very analysis that is lacking in the Kim/Douglass et al. (JDR 2011) recent publication, and thus the weight of the evidence is still tipped in favor of the young male bone cancer/fluoride link.

Scientific omission or distortion

The almost decade of opinion and assault on Bassin's conclusions presented by Douglass, with statements that the (now) Kim/Douglass study would show decisively that Bassin's evidence and conclusions could not prevail, highlights some obvious questions that, coupled with the non-medical publication without appropriate peer review of their study, call into question the political rather than scientific intent of their findings, which may equally apply to the OEHHA placing any weight on the quality of this specific source of evidence:

Question #1. What purpose could Kim/Douglass et al. (JDR 2011) have had in combining data on men and women if they were looking for a male linked cancer?

Question #2. How does one combine two groups--male and female--with median ages of 17.0 to get a median for the whole group of 17.6? Kim/Douglass et al. (JDR 2011) does give medians for the whole group and by sex. However, the digit after the decimal does not always agree between the paper and the values from the Kim dissertation.

Question #3. Kim/Douglass et al. (JDR 2011) states they adjusted for age in their analyses. They never say explicitly how this adjustment was made.

Conclusion

In summary, a link to fluoride and bone cancer in young males in both animals and humans has been found. The F was significantly associated when both age of exposure and sex was considered. Laboratory studies have confirmed genetic aberrancies with increasing F exposure that make it likely a carcinogen.

Current legislation requires OEHHA to set safe exposure standards for carcinogens on health effects without regard to cost impacts and shall be set at levels which OEHHA has determined do not pose any significant risk to health.

In cases of scientific ambiguity, OEHHA shall use criteria most protective of public health.

Furthermore OEHHA shall consider the existence of groups in the population that are more susceptible to adverse effects of the contaminants than a normal healthy adult, which in this case would be especially a young growing boy.

Adherence to the intent of the law, and consideration of the evidence without political distortion is essential to public confidence in this scientific process that was established by law for the benefit of the public

David Kennedy, DDS