

**Comments on**  
***Evidence on the Carcinogenicity of***  
***Fluoride and Its Salts***

Prepared for the  
California Environmental Protection Agency  
Reproductive and Cancer Hazard Assessment Branch  
Office of Environmental Health Hazard Assessment  
and Carcinogenicity Identification Committee

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## Summary

Fluoride Action Network (FAN) is pleased that the Carcinogen Identification Committee (CIC) will consider fluoride and its salts for listing under the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65) at its next meeting scheduled for 12-13 October 2011. We are also delighted that the Office of Environmental Health Hazard Assessment (OEHHA) has chosen qualified scientists, including toxicologists and epidemiologists, to produce and review the recent document on which our comments are based.

We fully support the listing of this chemical, based on the hypotheses presented in OEHHA's current document:

“that fluoride is incorporated into bones (especially rapidly growing bones), where it can i) stimulate cell division of osteoblasts via direct mitogenicity and indirectly via effects on thyroid function and parathyroid function; ii) induce genetic changes; iii) induce other cellular changes leading to malignant transformation, and iv) alter cellular immune response, resulting in increased inflammation and/or reduced immune surveillance, thereby increasing the risk of development of osteosarcomas.”

We would also like to bring attention to the following points:

1. Valid and *unrefuted* scientific evidence exists regarding the potential for fluoride to increase the risk for development of osteosarcoma in boys and young men
2. Numerous human and animal studies have found associations between fluoride exposure and the increased incidence of various other types of cancer
3. Issues exist regarding the potential carcinogenicity of silicofluorides used in the majority of artificial water schemes
4. Various interests may act to delay or prevent a positive finding regarding the carcinogenicity of fluoride

We have full faith that the CIC and OEHHA will deliberate this issue with impartiality and integrity. After having reviewed all of the science available to date, we have no doubt that the Committee will return with a final decision that fluoride and its salts meets the California EPA's description of a chemical that is “known to the state to cause cancer.”

## 1. Introduction

This submission by FAN is in response to the request for comments on the document *Evidence on the Carcinogenicity of Fluoride and Its Salts*, released July 2011 by the OEHHA's Reproductive and Cancer Hazard Assessment Branch of the California Environmental Protection Agency.

Fluoride is virtually ubiquitous today, with the major source for most people in the United States being artificially fluoridated municipal drinking water (NRC, 2006). As of 2008 over 60% of the U.S. population was receiving fluoridated water (CDC, 2010). Per California State law, all public water systems serving over 10,000 connections must artificially fluoridate the water supply (CDPH, 2010), and thus over 21 million California residents were receiving artificially fluoridated water in 2008 (CDC, 2010).

Residents of fluoridating communities not only drink this water, but also use this water to prepare foods and beverages. Perhaps most disturbing is that an infant consuming formula reconstituted with fluoridated water (1 mg F/L) will receive approximately 250 times more fluoride than a breastfed infant (NRC, 2006), meaning that the most susceptible of our population may be consistently exposed to levels of fluoride well above that considered "safe" by the U.S. Environmental Protection Agency (EPA, 2010). Persons may also be exposed to fluoride via dermal routes (e.g. showering, bathing). This artificially fluoridated water is not restricted to use by residents of fluoridating communities, but is also a source of fluoride for those consuming products processed using this municipal water.

Far too long have the proponents of artificial fluoridation touted the benefits, and minimized or completely ignored the risks of ingesting fluoride. It has been determined that "the major anticaries benefit of fluoride is topical and not systemic" (NRC, 2006, p.16). This predominant mode of action is now also accepted by the Centers for Disease Control and Prevention (CDC, 2001), as well as numerous researchers (e.g. Zero et al., 1992; Rölla and Ekstrand, 1996; Featherstone, 1999; Limeback, 1999; Clarkson and McLoughlin, 2000; Warren and Levy, 2003; Fejerskov, 2004; Hellwig and Lennon, 2004; Pizzo et al., 2007; Cheng et al., 2007). Thus, any dietary guidelines (e.g. "Adequate Intake," AI), such as those proposed by the Institute of Medicine in 1997 (IOM, 1997) should now be considered irrelevant.

In light of current scientific evidence of harm, the CIC and OEHHA should seriously consider the ethical and legal ramifications that refusing to identify fluoride and its salts as a potential or probable carcinogen would place upon the State of California—especially if its decision to do so is based upon the desire to protect the water fluoridation program and those who promote this outdated and unethical practice.

## 2. Comments of the Fluoride Action Network

FAN is pleased that OEHHA has selected fluoride and its salts for consideration by the Carcinogen Identification Committee (CIC) under Proposition 65. We applaud OEHHA for recruiting qualified scientists, including toxicologists and epidemiologists, in the preparation and review of the document *Evidence on the Carcinogenicity of Fluoride and Its Salts*.

We fully support the listing of this chemical, based on the hypotheses presented in OEHHA's current document:

“that fluoride is incorporated into bones (especially rapidly growing bones), where it can i) stimulate cell division of osteoblasts via direct mitogenicity and indirectly via effects on thyroid function and parathyroid function; ii) induce genetic changes; iii) induce other cellular changes leading to malignant transformation, and iv) alter cellular immune response, resulting in increased inflammation and/or reduced immune surveillance, thereby increasing the risk of development of osteosarcomas.”

We would also like to bring attention to the following:

### 2.1. *CIC and OEHHA must consider the valid and unrefuted scientific evidence of the potential for fluoride to cause osteosarcoma.*

There should be no further delay for a weight of evidence analysis of fluoride's potential to cause osteosarcoma (a frequently fatal bone cancer) in boys and young men. Such an analysis is likely to show that fluoride meets the California EPA's description of a chemical that is “known to the state to cause cancer.”

In reference to the potential of fluoride to promote cancer, the National Research Council of the National Academies, in the report *Fluoride in Drinking Water: A Scientific Review of EPA's Standards*, wrote in 2006:

Fluoride appears to have the potential to initiate or promote cancers, particularly of the bone, but the evidence to date is tentative and mixed (Tables 10-4 and 10-5). As noted above, osteosarcoma is of particular concern as a potential effect of fluoride because of (1) fluoride deposition in bone, (2) the mitogenic effect of fluoride on bone cells, (3) animal results described above, and (4) pre-1993 publication of some positive, as well as negative, epidemiologic reports on associations of fluoride exposure with osteosarcoma risk. (p. 336)

In 2001, Elise Bassin, a graduate student at the Harvard Dental School, successfully defended her doctoral thesis, which included a case-control study that found young boys were at a 5- to 7-fold increased risk for developing osteosarcoma by the age of 20 when exposed to fluoridated water between 6 and 8 years of age (Bassin, 2001; also see Connett et al., 2005a).

In response to the study by Bassin, NRC (2006) stated:

A unique feature of the analysis published in the literature so far was an exploratory analysis of ORs (odds ratios) for each specific year of age. Bassin found elevated ORs for the highest tertile compared with the lowest centering on ages 6 to 8. At age 7, the respective ORs (and 95% confidence intervals) were 7.2 (1.7 to 30.0) for males and 2.0 (0.43 to 9.28) for females. For the highest tertile, graphed results for males indicated a gradual increase and then a decrease of estimated relative risk from exposure at ages 0 to 15 with peaks at age 7, with the middle tertile, compared with the lowest, showing stable ORs across all ages...

...the highest ORs at ages 6 to 8, during what the author describes as the “midchildhood growth spurt for boys,” are consistent with some previous ecologic or semiecologic studies (Hoover et al. 1991; Cohn 1992) and with a hypothesis of fluoride as an osteosarcoma risk factor operating during these ages.

A publication based on the Bassin thesis is expected in the spring/summer of 2006 (E. Bassin, personal communication, Jan. 5, 2006). If this paper provides adequate documentation and analyses or the findings are confirmed by another study, more weight would be given to an assessment of fluoride as a human carcinogen. (p. 329)

Bassin did indeed publish her findings in 2006, in the international medical journal *Cancer Causes and Control*.

According to Bassin et al. (2006):

“It is biologically plausible that fluoride affects the incidence rate of osteosarcoma, and that this effect would be strongest during periods of growth, particularly in males. First, approximately 99% of fluoride in the human body is contained in the skeleton with about 50% of the daily ingested fluoride being deposited directly into calcified tissue (bone or dentition). Second, fluoride acts as a mitogen, increasing the proliferation of osteoblasts and its uptake in bone increases during periods of rapid skeletal growth. In the young, the hydroxyapatite structure of bone mineral exists as many extremely small crystals each surrounded by an ion-rich hydration shell, providing a greater surface area for fluoride exchange to occur.”

In the same volume of *Cancer Causes and Control* in which Bassin published her research, Chester Douglass (Bassin's thesis advisor) published a letter promising a larger study that would negate Bassin's findings (Douglass and Joshipura, 2006).

NRC (2006) commented on this related study by Douglass and colleagues:

A relatively large hospital-based case-control study of osteosarcoma and fluoride exposure is under way (Douglass, 2004) and is expected to be reported in the summer of 2006 (C. Douglass, Harvard School of Dental Medicine, personal communication, January 3, 2006). (p. 329)

The results of the Douglass et al. multicenter osteosarcoma study (expected in the summer of 2006) could add important data to the current body of literature on fluoride risks for osteosarcoma because the study includes bone fluoride concentrations for cases and controls. When this study is published, it should be considered in context with the existing body of evidence to help determine what follow-up studies are needed. (p. 338)

Promoters of fluoridation in several countries have used this unpublished, un-peer-reviewed claim to deflect attention from Bassin's finding, sometimes giving the impression that Douglass's claim in the letter to *Cancer Causes and Control* was actually a published study.

Five years later the paper promised by Douglass has finally been published (Kim et al., 2011). However, the results of this study by Douglass's group were not published in a medical journal, as were Bassin's findings (Bassin et al., 2006), but in a dental journal (*Journal of Dental Research*). There are numerous weaknesses inherent in this study by Douglass's group, ultimately leading to the conclusion that this study is incapable of refuting Bassin's (2006) findings of an increased risk of osteosarcoma in young boys exposed to fluoride in drinking water.

Some weaknesses of the Kim et al. (2011) study include:

1. *Smaller study with much lower statistical power than Bassin et al. (2006).*

For years, Douglass and colleagues have been promising that this study would be larger than the one by Bassin, but it is actually only a fraction of the size. This study simply doesn't have the statistical power to detect an effect of fluoride on osteosarcoma. Many researchers, including Bassin, have suggested that the link between fluoride and osteosarcoma may be most apparent in younger people, such as those under age 20. Bassin restricted her study subjects to this age range. Douglass's group, however, was unable to recruit many subjects under 20 years old (<100 cases, <20 controls). The gross disparity between the number of cases and controls is unusual, because statistically the power of the study is limited by the small number of controls.

Kim et al. (2011) acknowledge that “this study did not have sufficient power for a subgroup analysis among patients <20 years old.”

## *2. Study abandoned matching on age, sex, and distance from hospital.*

One of the most basic requirements of a case-control study design is that the cases and controls be as similar as possible in all factors except the exposure of interest. When they are not, it can be difficult—if not impossible—to adjust for differences, and these differences can lead to large biases in the results. Presumably due to the trouble in obtaining sufficient numbers of subjects, however, Kim et al. (2011) abandoned matching on age, sex, and distance from hospital—all of which were planned in the original study design. In contrast, Bassin et al. (2006) was able to maintain matching on all of these key variables, which are known or likely confounding factors. After abandoning matching, Douglass and colleagues ended up with a control group that was very different from the case group in several of the key variables. Bassin et al. (2006) states that “studies with larger numbers of osteosarcoma patients, with incidence under age 20, that examine age-specific and sex-specific associations are required to confirm or refute the findings of the current study.” The study by Douglass’s group (Kim et al., 2011) does not meet these requirements, and thus cannot possibly refute Bassin’s study.

### *Age Distribution:*

Most importantly, control subjects tended to be much older than case subjects in the study by Kim et al. (2011). Approximately 80% of subjects in the case group were under age 30, but only 41% of controls were under age 30. Subjects over age 45 made up only 11% of the case group, but comprised 41% of the control group. Although Kim et al. (2011) claim to have adjusted for age in the statistical analysis of the data, a serious problem was seemingly ignored: age is not only a very strong risk factor for development of osteosarcoma, but also heavily influences the fluoride levels in bones, with older individuals having higher bone fluoride levels. So, age is strongly influencing not only the risk of disease under study, but also the exposure metric chosen for this study. It is virtually impossible, with the data available, to adequately adjust for both of these effects. Thus it is likely that the results of this study are biased by the dramatic difference in age distribution between the cases and controls.

Even with this potentially strong bias, the final results showed that those with higher bone fluoride were 20-30% more likely to have osteosarcoma, although this finding did not reach “statistical significance.” Furthermore, Kim et al. (2011) found that “The median cumulative lifetime water F levels did not differ between cases or controls.” This strongly suggests that the (younger) case subjects had generally higher fluoride exposures per unit time than did the (older) control subjects. As bone fluoride level at any given

time is in effect a measure of time-integrated exposure, it is not the correct metric to use when an age-specific susceptibility is being investigated. Nevertheless, if we estimate average water fluoride level during the exposure period as cumulative bone fluoride level divided by median age of subjects:

Controls: (16.5 ppm F / 41.3 years) = 0.40 ppm F/year

Cases: (14.4 ppm F / 17.6 years) = 0.82 ppm F/year

If these estimates are correct, this indicates a factor of 2 higher average time-specific exposure for the case subjects than for the controls.

*Sex Distribution:*

Additionally, there was a large disparity in the sex ratio between cases and controls in the Kim et al. (2011) study, which was not adequately controlled for. Only 53% of the case subjects were male, compared with 71% of the control subjects. As males may tend to accumulate higher levels of fluoride in their bones than females, this disparity could lead to a bias for the controls having higher bone fluoride levels, which would obscure any true effect on osteosarcoma rates. However, not enough data are presented to know whether the males in this study tended to have higher levels of bone fluoride than the females.

*Residency Distribution:*

Another variable that was abandoned by Douglass's group (which was maintained by Bassin) was that of urban/rural residence, and distance that the subject lived from the hospital where he/she was recruited into the study. Kim et al. (2011) reports that there were almost twice as many case subjects who "never lived in an urban area" than were control subjects, suggesting that the cases tended to come from further away than controls, and were more likely to have lived their entire lives in rural areas. The majority of hospitals were in large metropolitan areas that artificially fluoridate the municipal water. Thus, urban residents living closer to the hospitals may have been more likely to have been exposed to fluoridated water, whereas rural residents may have been more likely to have been exposed to water from unfluoridated private wells or smaller municipal water systems, which are less likely to fluoridate. This difference between the case and control groups is again likely to bias the results so that any real risk of osteosarcoma related to bone fluoride levels is obscured.

*3. The control group for this study was comprised solely of subjects with other types of malignant bone tumors.*

Despite that hundreds of non-tumor control subjects were initially recruited into the Kim et al. (2011) study, with detailed data collected from each regarding fluoride exposure history, there is a rather glaring admission that



the only controls used in this study were those who had malignant bone tumors of types other than osteosarcoma.

The exposure data for the non-tumor (“orthopedic”) controls, however, seem to have been completely ignored by Douglass’s group, even though this group was much larger than the set of tumor controls, and is the only group which supplies data pertinent to Bassin’s study design. Douglass’s group argues that bone fluoride measurements, which were not obtained from the non-tumor controls, may provide a more accurate estimate of total, averaged, lifetime fluoride exposure. However, this metric provides no information about specific timing of exposure to fluoride that may increase one’s risk for developing osteosarcoma (e.g. ages 6-8), which was at the heart of Bassin’s findings.

Perhaps an even more obvious problem with the use of other malignant bone tumors as the control group in Kim et al. (2011) is that there is strong biological plausibility that fluoride might increase the risk of *all* bone tumors, as fluoride reaches a very high concentration in the bones compared with all other tissues. The rationale by Douglass’s group that there is little scientific evidence linking any of the non-osteosarcoma types of bone tumors is deceptive. There have been virtually no studies on the relationship between fluoride and any types of bone tumors other than osteosarcoma. One exception is a study by Hoover et al. (1991), which actually provides evidence that fluoridation increased the rates of Ewing’s sarcoma, the second most common type of bone cancer after osteosarcoma. Additionally, a study by Sandhu et al. (2009) found that mean serum fluoride concentration was significantly higher in patients with osteosarcoma ( $p < 0.001$ ) *as well as in patients with other bone-forming tumors* ( $p < 0.05$ ), when compared to controls (patients with musculo-skeletal pain). This study also found that serum sialic acid concentration (reported to be a “sensitive index to detect fluoride toxicity at early stages in human and animal models”) was similarly significantly increased both in patients with osteosarcoma and other bone-forming tumors (Sandhu et al., 2009).

Any one of these weaknesses in the study by Douglass's group could have obscured a true link between fluoride exposure and osteosarcoma. The biases from these weaknesses are additive, so it is not surprising that Kim et al. (2011) was unable to confirm Bassin's study with such a weak study design and limited sample size.

If Bassin’s findings are indeed correct, young men with osteosarcoma are dying potentially because they were exposed to fluoridated water in their childhood. Despite the low overall incidence of osteosarcoma, the death of even a single person from this horrible cancer cannot be justified by the slight reduction of dental caries claimed by the proponents of fluoridation.

Bassin et al. (2006) and Cohn (1992) are not the only human studies that reveal an increased risk for osteosarcomas resulting from fluoride exposure, as indicated by OEHHA's current document. In fact, those epidemiological studies that have failed to find an association did not consider the age of exposure, and would not be able to detect an age-specific relationship between fluoride exposure and development of bone cancers in young males (EWG, 2009). Below are additional studies for which the data have indicated a positive relationship (See Connett et al., 2005b):

- Ecological study by Hoover et al. (1991) found a 79% increase in osteosarcoma in males <20 years in fluoridated counties, compared to a 4% decrease in non-fluoridated counties over time (33 Iowa and Seattle counties). However, Hoover discounted these findings based on analyses of the duration of exposure, rather than age at exposure, and thus was unable to detect an age-specific effect.
- Ecological, geographical correlation and time trend analysis by Freni and Gaylor (1992) revealed "significant increases in CR 10-29 [cumulative risk for 10-29 year olds] ( $p < 0.1$ ) were seen mainly in males and most frequently in the United States registry areas." Furthermore, US and Canada (40-60% fluoridated) had much larger significant increases in male CR 10-29 than Northern Europe or UK (<10% fluoridated).
- Ecological, geographical correlation and time trend analysis by Yiamouyiannis (1993) found that, when reanalyzing the Hoover et al. (1991) results, there were increased relative risks for fluoridated areas when female rates were subtracted from male rates for each area. This approach was chosen based on the rationale that most studies have found an effect of fluoride on males but not females, and thus females would act as a control for many factors that might influence osteosarcoma rates other than fluoride.
- Case-control study by Gelberg (1995) observed elevated risks of osteosarcoma, although the authors concluded that these were not large enough or consistent enough to be considered evidence for a positive association between fluoride and osteosarcoma. However, Gelberg failed to adjust for age, which may have biased the results towards the null, or no association, leading to an underestimation of the risk of osteosarcoma from drinking water fluoride.
- Similar to Hoover et al. (1991), Takahashi (2001) analyzed SEER data, using a methodology for assigning fluoridation status that allowed for the retention of all cases from each cancer registry. Bone cancer in males was positively associated with degree of fluoridation at  $p < 0.001$ .
- Analysis by Neurath (2005) of incidence rates of osteosarcoma (based on data from Bovill et al., 1985) and dental fluorosis (based on data from Chibole, 1987) for Kenya's eight provinces determined, via linear regression, a very strong positive association ( $p < 0.0003$ ) (Figure 1).

### Fluorosis Prevalence vs. Osteosarcoma Incidence in Kenyan Provinces

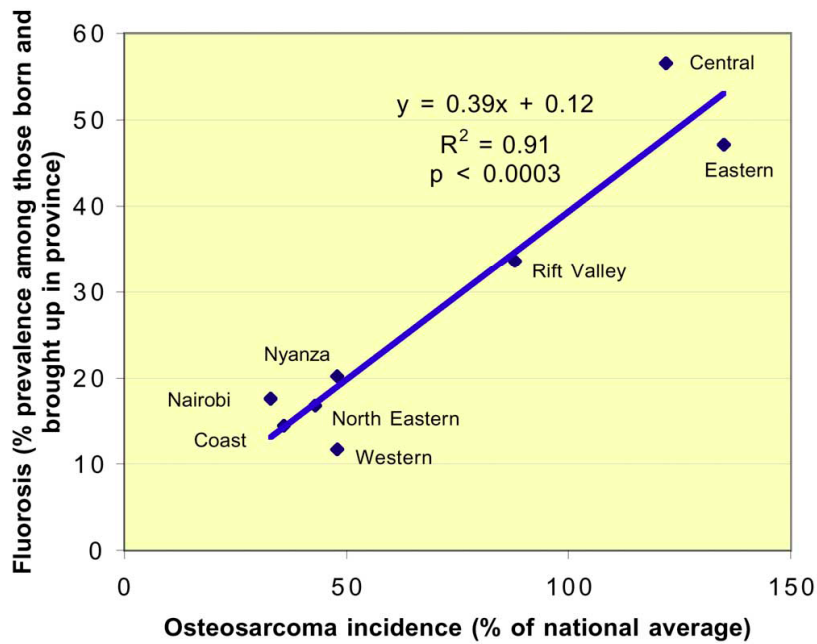


Figure 1. Prevalence of fluorosis (Chibole, 1987) versus osteosarcoma (Bovill et al., 1985) incidence for eight provinces in Kenya (Neurath, 2005).

- Case control-study by Sandhu (2009) found that the average serum fluoride level of osteosarcoma patients was 3.5 times greater than in controls.

Based on the current evidence for the increased risk of osteosarcoma in boys and young men associated with fluoride exposure, the CIC and OEHHA should not hesitate to include fluoride and its salts among the chemicals listed in Proposition 65, which are “known to the state to cause cancer.” Failure to do so now only prolongs this inevitable conclusion, and may allow the State of California to be held liable for willfully disregarding available scientific data at the peril of their residents.

*2.2. CIC and OEHHA must consider fluoride's potential to cause other types of cancer.*

In addition to osteosarcoma, fluoride exposure has been suggested as a factor in the etiology of several other types of cancer. As mentioned in Section 2.1., other bone and joint cancers (e.g. Ewing's sarcoma) are biologically plausible, as fluoride accumulates at higher levels in the bones than in any other tissue of the body and may act as a mitogen, increasing the proliferation of osteoblasts.

Hoover (one of the coauthors of the Kim et al. study), found a 79% increase in osteosarcoma and other bone and joint cancers (e.g. Ewing's sarcoma) in young males over time in fluoridated counties, compared with a 4% decrease over time in nonfluoridated counties (Hoover et al., 1991). However, Hoover used a new and unreliable method of analysis to dismiss these initial findings, claiming no link between fluoride and osteosarcoma or any other type of cancer (Connett et al., 2005b).

Hoover et al. (1991) not only revealed an increased rate of bone cancers for young males over time in fluoridated counties, but also found that several cancer site groups showed statistically significant increasing risk ratios for fluoridated counties with duration of fluoridation. These include colon and rectum cancers (p. E-21; in the Iowa counties,  $p < 0.001$  in both sexes), prostate cancers (p. E-21; Iowa and Seattle counties,  $p < 0.02$ ), and non-Hodgkin's lymphoma (p. E-22; Seattle counties,  $p = 0.01$  for both sexes combined). Hoover et al. (1991) also states that "a possible effect was seen in the incidence data for renal cancer. There was an increasing trend in the O/E ratios by duration of fluoridation for the sexes combined in both registries. The patterns in the sex-specific data were more variable, but the highest ratio was in the longest duration-of-fluoridation category for three of the four sex-registry groups."

The study by Takahashi (2001) used SEER data consisting of nine areas with a total population of 22 million over 15 years to investigate a link between degree of water fluoridation and incidence of various cancers. Regression analysis found 23 of 36 cancer sites to be significantly positively associated with degree of fluoridation.

Importantly, NRC (2006) recommended that further research be conducted on the effects of fluoride on bladder cancer risk, and suggested that in vivo human genotoxicity studies be carried out within U.S. populations or populations having similar nutritional or sociodemographic variables.

Among animal studies, in addition to an increased rate of osteosarcoma in male rats, the NTP (1990) study also reported an increase in liver and oral cancers, and an increase in the incidence of thyroid follicular cell tumors. However, a government-review panel downgraded all of the non-bone cancers with a questionable rationale (Marcus, 1990).

2.3. *CIC and OEHHA must consider carcinogenicity issues associated with the use of silicofluorides for artificial water fluoridation.*

Approximately 75% of artificially fluoridating water systems, accounting for 90% of the people served, employ fluosilicic acid or sodium fluosilicate (i.e. fluorosilicates or silicofluorides) to raise the level of fluoride in drinking water to the recommended “optimal” level to “protect against dental caries” (NRC, 2006). Silicofluorides are a by-product from the manufacture of phosphate fertilizers (NRC, 2006, p. 15; Haneke and Carson, 2001). In fact, according to Thomas Reeves, former National Fluoridation Engineer for the CDC’s Oral Health Division, “All of the fluoride chemicals used in the U.S. for water fluoridation, sodium fluoride, sodium fluosilicate, and fluosilicic acid, are byproducts of the phosphate fertilizer industry” (Reeves, 2000).

Despite claims that the “standard toxicity database for fluoride is complete” (EPA, 2010a, p. 106), that of silicofluorides is sparse, and “essentially no studies have compared the toxicity of Silicofluorides with that of sodium fluoride” (NRC, 2006, p. 53). The U.S. EPA has admitted that it has no “empirical scientific data on the effects of fluosilicic acid or sodium silicofluoride on health and behavior” (Thurnau, EPA NRMRL, 2000).

A few studies that have looked at silicofluorides have found an association between exposure to silicofluorides in water and increased blood lead levels in children (Masters and Coplan, 1999). The four different human leukemic cell lines have been found to be more susceptible to the effects of sodium hexafluorosilicate than to NaF (Machalinski et al., 2003). NRC (2006) recommended that “Further research is needed to elucidate how fluorosilicates might have different biological effects from fluoride salts” (p. 221).

Hexafluorosilicic acid and sodium hexafluorosilicate were nominated in 2002 for review by the National Toxicology Program (NTP) for chemical and toxicological characterization (including chronic toxicity, carcinogenicity, neurotoxicity, and toxicokinetics), and mechanistic studies related to cholinesterase inhibition and lead bioavailability (NTP, 2002).

Sodium hexafluorosilicate and fluosilicic acid are both listed in Section 8(b) of the Toxic Substances Control Act, and EPA has referred to the “high inherent toxicity” of sodium hexafluorosilicate (EPA, 1999). In addition, fluosilicic acid can contain any number of other contaminants. These include heavy metals such as arsenic (Hazan, 2000; Weng et al., 2000) and lead (Hazan, 2000), and radioactive elements such as uranium (Guidry et al., 1986; IAEA, 1989; WISE online), radium-226, radium-222, polonium-210 and lead-210 (Guidry et al., 1986). All of these, including lead (van Wijngaarden, 2007; Wu et al., 2011) are known or suspected carcinogens.

After dilution of the hexafluorosilicic acid, the level of arsenic in the public water supply can reach 1 ppb (Wang et al, 2005), which has an incremental cancer risk of 1 in 1000 for lifetime consumption. In a bona fide cancer risk assessment, CIC and OEHHA must consider the cancer risks of deliberately adding arsenic—a known human carcinogen—above the US EPA’s MCLG of zero.

While it is understandable that the MCL for arsenic should be set higher than zero because of the very high economic costs of removing natural arsenic down to this level, this should not be used as an excuse for knowingly exceeding the MCLG by deliberately adding arsenic contaminated fluoridating agents to the drinking water.

As per Haneke and Carson (2001), no data were available at that time concerning short-term/subchronic exposure, chronic exposure, cytotoxicity, reproductive/teratological effects, or carcinogenicity of sodium hexafluorosilicate or fluorosilicic acid. To our knowledge, no new data on the long-term safety of silicofluorides have come available.

2.4. *OEHHA must consider the influence of those attempting to delay or prevent the determination of carcinogenicity for fluoride.*

Artificial water fluoridation in the United States has a long and controversial history (see Connett et al., 2010), with both sides still deeply entrenched in the battle. However, the proponents of fluoride and fluoridation are generally the ones who stand to gain from fluoride's (sometimes mandatory) use, and endorsements—not science—are often used as statements of fact by proponents to espouse the “safety and efficacy” of fluoride and fluoridation. Thus an impartial review of the carcinogenicity status of fluoride and its salts must take into consideration the influence that the often powerful proponents of fluoride and fluoridation have on the decision making process, and ultimately on the final outcome of such a deliberation.

The American Dental Association, one of the most prominent promoters of fluoridation, has long endorsed the use of fluoridated dental products and artificial water fluoridation. In March 2009 the California OEHHA solicited public comments on 38 chemicals selected for prioritization for evaluation by the state's Carcinogen Identification Committee (OEHHA, 2009a). “Fluoride and its salts” were included, and in October the state announced that fluoride was one of five chemicals selected for consideration (OEHHA, 2009b). A January 2010 bulletin from the Executive Director of the California Dental Association (CDA), states that the American Dental Association “granted CDA \$200,000 to assist in our effort *to prevent the placement* of ‘fluoride and its salts’ on the List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity that is produced by the State of California, Environmental Protection Agency; Office of Environmental Health Hazard Assessment (OEHHA).” (our emphasis) (CDA, 2010).

In Section 2.1. we discussed the weaknesses of the recent study published by Chester Douglass's research group (Kim et al., 2011). Nevertheless, proponents of fluoridation have jumped on the claimed findings of this study to once again tout artificial water fluoridation as “safe and effective” (e.g. ADA, 2011a, 2011b). However, Douglass has long had financial ties with those organizations that promote the use of fluoride in dental products and municipal water systems.

Douglass revealed an obvious bias towards water fluoridation—and against finding a link between fluoride and osteosarcoma—in a 1991 co-authored paper published as a cover article of the *Journal of the American Dental Association* (McGuire et al., 1991). This article made it very clear how a positive finding on osteosarcoma would end the water fluoridation program, as “Linkage of fluoride ingestion and cancer initiation could result in a large-scale defluoridation of municipal water systems under the Delaney clause,” an outcome the authors declared would be “detrimental to the oral health of most Americans, particularly those who cannot afford to pay for increasingly expensive restorative dental care” (McGuire et al., 1991). Furthermore, Douglass's numerous (claimed and unclaimed) financial ties make his involvement with any study related to fluoride and health effects a serious conflict of interest.

This brings into question not only the recent study by Douglass's group (Kim et al., 2011), but also the regulatory agencies that selected and funded a less-than objective oral health researcher to perform a pivotal study on osteosarcoma.

### **3. Conclusions**

While we understand that there will be tremendous pressure put on the CIC and OEHHA by the proponents of fluoride and fluoridation, we ask that the Committee continue to rely on its high level of scientific knowledge and integrity when deliberating and reaching a final conclusion on the carcinogenicity status of fluoride and its salts. After reviewing all of the science regarding the potential for fluoride to increase the incidence of cancer—especially that of osteosarcoma in boys and young men—we are confident that the Committee will return with a final decision to include fluoride and its salts among those chemicals “known to the state to cause cancer.”



#### 4. References

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