

## Fluoride and Its Salts

Fluoride is often added (as a fluoride salt) to municipal drinking water, toothpastes, mouthwashes, and other dental hygiene products to prevent dental caries. In certain regions of the world, naturally occurring fluoride and fluoride salts are present in the soil and water, and in plants grown in these regions. People may be exposed to fluoride and its salts through occupational exposures, through use and consumption of fluoridated drinking water, through use of fluoridated toothpastes, mouthwashes, or other dental treatments, and through consumption of foods grown in areas containing fluoride in the soil or water.

Fluoride and its salts passed the human data screen, underwent a preliminary toxicological evaluation, and is being brought to the Carcinogen Identification Committee for consultation. This is a compilation of the relevant studies identified during the preliminary toxicological evaluation.

### Epidemiological data

- Case-control studies of younger age groups
  - U.S. hospital-based case-control study of fluoride exposure and osteosarcoma in persons < 20 years of age: Bassin *et al.* (2006).
  - Population-based case-control study of the relationship between fluoride exposure and childhood osteosarcoma: Gelberg *et al.* (1995)
  - Case-control study of osteosarcoma in young persons: Operskalski *et al.* (1987)
- Case-control studies of general populations
  - Case-control study of fluoridated water and osteosarcoma in Massachusetts: McGuire *et al.* (1991)
- Cohort studies
  - Study of mortality and cancer incidence among aluminum reduction plant workers: Milham (1979)
  - Cancer mortality study among aluminum reduction plant workers exposed to hydrogen fluoride: Rockette and Arena (1983)
  - Cancer mortality study among cryolite processing plant workers exposed to fluoride: Grandjean *et al.* (1992)
- Ecological studies limited to younger age groups
  - Report from the New Jersey Department of Health examining the relationship between drinking water fluoridation and osteosarcomas in young men: Cohn (1992) [*The study has not been published in a peer reviewed journal*]

- Ecological studies of general populations
  - Cancer mortality study of 35 U.S. cities: Chilvers (1983)
  - Cancer mortality study in England: Chilvers and Conway (1985)
  - Study of international time-trends in the incidence of bone cancer: Freni and Gaylor (1992)
  - Study of fluoridation and cancer mortality in individuals  $\geq 45$  years of age in New Zealand: Goodall *et al.* (1980)
  - Study of the relationship between fluoridated drinking water and the occurrence of cancer in the U.S.: Hoover *et al.* (1976)
  - Study of the relationship between drinking water fluoridation and osteosarcoma in Alberta, Canada: Hrudley *et al.* (1990)
  - Study of cancer incidence in relation to fluoride level in water supplies: Kinlen (1975)
  - Time-trend study of bone cancer incidence rates in New York State related to fluoridation of drinking water: Mahoney *et al.* (1991)
  - Study of the relationship between the incidence of osteosarcomas in adult males and water fluoridation, using SEER data: Appendix F of DHHS (1991)
  - Study of osteosarcoma, seasonality and environmental factors in Wisconsin: Moss *et al.* (1995)
  - Global study of cancer incidence rates and environmental factors including fluoridated drinking water: Steiner (2002)
  - Study of fluoridated drinking water and cancer mortality in Taiwan: Yang *et al.* (2000)
  - Study of the relationship between cancers at 36 tissue/organ sites and exposure to fluoridated drinking water in the U.S., using data from the International Agency for Research on Cancer: Takahashi *et al.* (2001)

### **Animal carcinogenicity data**

- Two-year drinking water animal bioassays
  - B6C3F1 mice: NTP (1990)
  - F344/N rats: NTP (1990)
- Long-term diet animal bioassays
  - 97-week studies in CD-1 mice: Maurer *et al.* (1993)
  - 99-week studies in Sprague-Dawley rats: Maurer *et al.* (1990)

### **Other relevant data**

- Genotoxicity evidence: recent reviews and some individual studies:
  - Reviews: ATSDR (2003, pp. 132-136), NRC (2006, Chapter 6)
  - *Salmonella* reverse mutation assay: Li *et al.* (1987)
  - Mouse lymphoma cell thymidine kinase locus mutation assay: Caspary *et al.* (1987 and 1988)

- Human lymphoblast TK6 cells: Caspary *et al.* (1988)

## Reviews

- Agency for Toxic Substances and Disease Registry: ATSDR (2003)
- National Research Council: NRC (2006)

## References<sup>1</sup>

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<sup>1</sup> Copies of these listed references, as either the abstract, the relevant sections of the publication, or the complete publication, have been provided to members of the Carcinogen Identification Committee. These references have been provided in the order in which they are discussed in this document.

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