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Memorandum

Date October 2, 1981
From EIS Officer, Task Force on Kaposi's Sarcoma and Opportunistic Infections
Subject Conversations with Drs. Frank Vocci (FDA) and Paul Newberne (MIT) about Nitrites: Animal and Possibly Human Effects
To Coordinator, Task Force on Kaposi's Sarcoma and Opportunistic Infections

Darrow

Frank Vocci (FTS 8-443-3504), of the Neuropharmacology Branch, has been interested in nitrites for many years, and has been with the FDA for 3½ years. He had recently spoken with Harold Jaffe, M.D., of the KSOI task force, and is forwarding some printed material to us, including a state-of-knowledge paper written at FDA on this subject within the past 2 years. He confirmed that very little inhalation toxicology has been performed on nitrites, and that the possibility that nitrites are now being implicated in human disease might very well stimulate renewed interest in new nitrite research. He was familiar with the work of Newberne on ingested nitrite and lymphoma in rats, and the extensive controversy over those findings.

I spoke with Newberne at MIT and discussed his work with him. He acknowledges that there is controversy, although he labels it "semantics" (over calling the tumors "lymphomas"). However, he argues that one finding (which he has not published) is incontrovertible, namely that the rats had excess angiosarcomas when exposed to oral nitrites compared to controls. His findings were submitted to FDA and were included in a volume called "Re-evaluation of pathology studies of nitrite and cancer: Contract #223079-2263," U.A.R.E.P., and in a companion volume by the Inter Agency Regulatory Liaison Group (IARLG) (perhaps in more detail). Both have now been requested by me from the FDA.

After reading extensively on health effects of nitrites both in humans and animals, several conclusions appear to me:

1. There have been no inhalation studies on nitrites that address the major issues of interest to us, especially the effects of the chemical upon the immunologic status of the host.
2. While it makes sense for inhaled nitrite to react in vivo the same way as ingested nitrite, the measurements of serum nitrite, nitrate and nitrosamine levels have not been reported in the literature.
3. The estimates of nitrite intake by inhalation from the Toxicology Branch (Drs. Liddle and Hill) suggest that a heavy user could increase his daily intake of nitrite by anywhere from 2 to 10 times or more on days of use. Both from the point of view of nitrosation reactions in vivo and possible immunosuppression, these bursts of exposure are likely to be important biologically.
4. If concomitant exposures to sexually transmitted agents (including CMV among others) occurs, then not only would the combination of exposures be evident, but the exposure of, say, CMV to nitrite might alter it as a pathogen. Nitrous acid is known to alter the behavior of some microorganisms with respect to the rate of transformations of DNA, and CMV is a known immunosuppressor in its own right.