MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

MARCH 8, 1994

TO: File for Sodium Nitrite (7632-00-0)

FROM: Marco Bianchi

SUBJECT: Review of ITSL for Sodium Nitrite

A review of the sodium nitrite ITSL (10 µg/m^3) was conducted with the recent addition of a chronic oral mouse study. This study entitled, Chronic Low-Dose Exposure of Sodium Nitrite in VM-Strain Mice: Central Nervous System Changes (Hawkes 1992), examined the incidence of cerebral gliomas in glioma sensitive VM-strain mice. A total of 300 animals were exposed to 0.2% sodium nitrite in their drinking water. One hundred of this group were exposed both in utero and throughout their adult lives. The remaining 200 animals received nitrite from the time of weaning. A further 200 mice were used as controls and received distilled water. All animals were maintained until their natural death and were then subjected to autopsy and routine histological examination. There was no excess of nervous system tumors in the experimental group. This study was discussed with AQD staff and compared with the ITSL setting study. Although there were no significant adverse toxicological effects in the reviewed study, it was thought the ITSL setting study provided better toxicological endpoints with a greater degree of safety. It was decided by staff to keep the current ITSL of 10 µg/m^3.

Hawkes CH, et al., 1992. Chronic Low—Dose Exposure of Sodium Nitrite in VM Strain Mice: Central Nervous System Changes. Human Experimental Toxicology. 11:279—281.

MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

February 3, 1994

TO: Sodium Nitrite File (CAS # 7632-00-0)

FROM: Gary Butterfield

SUBJECT: ITSL for Sodium Nitrite

The ACGIH has no TLV, NIOSH has no REL, and EPA has no RfC or RfD for sodium nitrite. A CAS-on-line and NLM search was conducted in September 1993. No inhalation toxicity studies were found in those searches, or in any other reference sources reviewed.

It has been speculated by some that ingestion of sodium nitrite and materials with amines could be converted, by conditions in the stomach, to a nitrosoamine compound. Nitrosoamine compounds are generally considered to be fairly strong carcinogens. It's not clear what relevance to identification of an inhalation hazard the issue of potential carcinogenicity following ingestion has. There were no toxicity studies found that were conducted by the inhalation route of exposure. Several authors have investigated the potential for carcinogenic effects from ingestion of sodium nitrite in animals. The majority of these studies found no clear evidence of increased carcinogenic potential. Because there is no clear evidence of carcinogenicity following oral doses and there is no reason to suspect inhalation exposure is a route that would lead to generation of a carcinogenic species, carcinogenic effects are not considered in the development of a screening level.

Among the studies investigating non-carcinogenic effects, that were able to identify a NOAEL, are those that looked at changes in reproductive abilities. Roth et al (1987) was able to identify a NOAEL of 0.5 g/L (or 65 mg/kg) during their investigation of Long-Evans rat reproductive changes. At doses of 1 g/L, rat pups had hematological changes. While even higher doses, of 2 or 3 g/L, caused the pups to have reduced body weight, become severely anemic, and have an increased mortality rate.

Vorhees et al (1984) examined the behavioral changes in Sprague-Dawley rats that were exposed to diets containing sodium nitrite at concentrations of 0, 0.0126, 0.025, 0.05 % (which converts to doses of 0, 10, 20 and 40 mg/kg) during gestation, lactation and until 90 days of age. Besides behavioral changes, the higher two doses increased the preweaning mortality and also decreased preweaning body weight gain. Behavioral tests detected consistent changes at those dose levels, as decreases in swimming development and open field activity.

The ITSL for sodium nitrite is being based on the NOAEL, of 10 mg/kg, identified by Vorhees et al (1984), because this study evaluated effects on a sensitive endpoint (newborn survival, body weight and behavioral changes), on the apparent most sensitive population (fetus and newborn), over a longer exposure period than any of the other available studies. The ITSL is calculated from the equation in Rule 232 (1)(e) as follows.

$$ITSL = \frac{\frac{10mg}{kg}}{10\ x\ 100}\ x \frac{1kg}{0.9m^3} = 10 \frac{\mu g}{m^3}\ annual\ average$$

Where, uncertainty factor of 10 replaces the 35 factor in, Rule 232 (1)(e) to account for the length of the study being 90 days, and the default breathing rate for rats of 0.9 m3 per kg body weight was used.

References

Roth et al. 1987. Evaluation of the developmental toxicity of sodium nitrite in Long-Evans rats. Fund Appl Toxicol 9:668-677.

Vorhees et al. 1984. Developmental toxicity and psychotoxicity of sodium nitrite in rats. Fd Chem Toxicol 22:1—6.