

MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

October 21, 1994

TO: File for 4-hydroxytetramethyl piperadine free radical
(4-OH-TEMPO) CAS# (65402-65-5)

FROM: Marco Bianchi

SUBJECT: Initial Threshold Screening Level

The initial threshold screening level (ITSL) for 4-OH-TEMPO is $4 \mu\text{g}/\text{m}^3$ based on an annual averaging time.

The following references or databases were searched to identify data to determine the ITSL: IRIS, HEAST, NTP Management Status Report, RTECS, EPB-CCD, EPB library, CAS-online, NLM-online, IARC, NIOSH Pocket Guide, and ACGIH Guide.

A complete reference check was conducted for 4-OH-TEMPO, but only limited information was available. Upjohn provided an in-house oral LD50 study for 4-OH-TEMPO. A total of four groups of four male albino rats were orally dosed at 625, 1250, 2500, and 5000 mg/kg of 4-OH-TEMPO suspended in a 0.25% methylcellulose aqueous solution.

At a dose of 2500 or 5000 mg/kg, all rats in both groups, except for one in the 5000 mg/kg dose group, developed toxic signs including decreased activity, salivation, dried material around the mouth, tactile hyperesthesia, mild convulsions prostrations and death. Necropsy of the dead rats revealed dark pink lungs, dark red livers and tannish-yellow stomach lining. The remaining rat had similar clinical signs, but fully recovered by day seven post dosing, and thereafter for the remainder of the 14 day study. Body weight exceeded its pre-fasting weight, and necropsy at the 14-day euthanasia did not reveal any gross lesions.

At a dose of 1250 mg/kg, two rats appeared normal for approximately one to two hours post dosing and then became tactually hyperesthetic and had mild convulsions. These rats were found dead at approximately one and four hours post dosing, respectively. Necropsy of the two rats revealed yellow liquid stomach contents and dark red livers. On day one after dosing, the two survivors had diarrhea. At day two post dosing, one of the two rats had dried red material on the muzzle and lacked normal fecal discharge while the remaining rat appeared normal. After day two, both rats appeared normal and gained weight for the remainder of the 14-day study period. Necropsy of the two rats at the 14-day sack did not reveal any gross lesions.

At a dose of 625 mg/kg, all four rats appeared normal and gained body weight throughout the 14-day study period. Necropsy of the four rats at the end of the study period did not reveal any gross lesions.

The LD₅₀ for this study was determined to be 1250 mg/kg.

The ITSL was derived as follows:

LD₅₀ = 1250 mg/kg

$$\text{ITSL} = \frac{1}{500} \times \frac{1}{40} \times \frac{1}{100} \times \frac{1250}{0.167 \times 0.900} = 0.004 \text{ mg/kg}$$

0.0041 mg/kg x 1000 = 4 $\mu\text{g}/\text{m}^3$ based on annual averaging.

The ITSL for 4-OH-TEMPO = 4 $\mu\text{g}/\text{m}^3$ based on annual averaging.

MB:ma