

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

February 9, 1998

TO: File for 2,2'-Bipyridyl (366-18-7)

FROM: Marco Bianchi, Toxics Unit, Air Quality Division

SUBJECT: Initial Threshold Screening Level

The initial threshold screening level (ITSL) for 2,2'-bipyridyl is 0.8 ug/m³ 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, and Patty's Industrial Hygiene and Toxicology.

A detailed database search was conducted for 2,2'-bipyridyl, but only limited information was available. This compound induces excretion of excessive amounts of iron in iron-overloaded rats by its iron-chelating properties. It is toxic when given interperitoneally (ip) in divided doses of 50 mg/kg in 0.25 ml of 25% ethanol, and produces hyperglycemia in rats at 10 mg/kg or higher doses.

Only one acute/subacute study (Groce and Kimbrough, 1982) was found to derive an ITSL for 2,2'-bipyridyl. In the acute portion of this study, 4 groups of 10 adult male or female Sherman rats were dosed by gavage with a 2% solution in 20% ethanol after fasting for 24 hours. The authors did not list a measured dose for this 2% solution. In additional acute studies, smaller doses of 90 or 155 mg/kg were given to 10 rats each by gavage to observe the effect of nonlethal doses. LD50 values were calculated by the method of Litchfield and Wilcoxon. The acute oral LD50 values of 2,2'-bipyridyl were 100 mg/kg in males and 107 mg/kg in females. Symptoms of toxicity included immediate subdued behavior, loss of muscle coordination, and red urine. Tremors were observed several hours later, and convulsions immediately before death occurred 1 or 2 days after dosing. Histopathological results revealed massive pulmonary hemorrhage. Microscopic lung changes included pulmonary edema, intra-alveolar hemorrhage, congestion, and atelectasis. Kidneys and spleen were also congested. The authors also observed a very small difference between the no-effect and 100% lethality doses for the compound. A dose of 75 mg/kg had no effect in male and female rats; while 150 mg/kg caused 100% mortality in males and 120 mg/kg caused 80% mortality in females.

In the subacute portion of the study, three groups of 6 male and 6 female Sherman rats received 0, 0.01 (7.13 mg/kg), or 0.05% (35.65 mg/kg) of 2,2'-bipyridyl in drinking water for 3 months. There were no symptoms of toxicity such as central nervous system effects or red urine, but the dosed animals did gain less weight and drink less water than controls. Microscopically, no lung changes were present. Kidney changes included calcium concretions in tubules of three rats and nephrosclerosis in one of six rats given 7.13 mg/kg. Bowman's glomerular capsule occasionally was thickened, and the tubular epithelium contained a brown pigment in one rat for each dose. The tubular epithelium occasionally had enlarged, atypical nuclei in 2 of ten rats receiving 35.65 mg/kg. No NOAEL was obtained for this study, but a LOAEL was determined to be 7.13 mg/kg, based on renal tubules containing calcium concretions and the formation of nephrosclerosis.

The ITSL was determined as follows:

LOAEL = 7.13 mg/kg/day.

NOAEL to LOAEL uncertainty factor of 10

Uncertainty factor of 35 reduced to 10 because of 13 week (90 day) study

$$I_a = 0.80(0.395)^{0.8206} = 0.3733\text{m}^3$$

$$\text{ITSL} = \text{NOAEL}/(10 \times 10 \times 100) \times W_a/I_a \times b/a$$

$$\text{ITSL} = 7.13 \text{ mg/kg/day}/(10,000) \times 0.395 \text{ kg}/0.3733\text{m}^3 = 0.000754 \text{ mg/m}^3$$

Conversion of mg/m³ to µg/m³

$$0.0008 \text{ mg/m}^3 \times 1000 = 0.8 \text{ µg/m}^3$$

The ITSL for 2,2'-bipyridyl = 0.8 g/m³ based on an annual averaging.

MB : SLB

cc: Mary Lee Hultin, Toxics Unit