MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

November 8, 1996

TO: File for 3-Picoline (CAS# 108-99-6)

FROM: Michael Depa, Toxics Unit, Air Quality Division

SUBJECT: Screening Level Determination

The initial threshold screening level (ITSL) for 3-picoline (also called 3-methylpyridine) is 80 $\mu g/m^3$ based on an annual averaging time.

The following references or databases were searched to identify data to determine the ITSL: IRIS, RTECS, ACGIH Threshold Limit Values, NIOSH Pocket Guide to Hazardous Chemicals, Environmental Protection Bureau Library, IARC Monographs, CAS Online (1967 - May 8, 1996), National Library of Medicine, Health Effects Assessment Summary Tables, and NTP Status Report. Review of these sources found that EPA has not established an RfD of RfC for 3-picoline.. The ACGIH or NIOSH have not established occupational exposure limits (OELs) for 3-picoline. The pertinent toxicological studies are summarized below.

The oral LD50 for 3-picoline in male and female Sprague-Dawley rats was determined to be 710 mg/kg (confidence limits: 620 - 820) (Monsanto, 1972). Groups of 5 male or female Sprague-Dawley rats were exposed to 501, 631, 794 or 1000 mg/kg 3-picoline in a single oral dose and observed for 7 days. Toxic signs included reduced appetite and activity (for one to four days in survivors), ocular discharge containing blood, increasing weakness, collapse, and death. At autopsy there was hemorrhagic lungs, liver discoloration, and acute gastrointestinal inflammation.

In another single dose oral toxicity study, groups of 3 male Fischer 344 rats were dosed with 320, 1300, 2000, 3200, or 5000 mg/kg 3-picoline and observed for 2 weeks (Dow, 1992). The Oral LD50 was determined to be ~630 mg/kg. The authors reported the following in-life signs of toxicity: lethargy (320-2000 mg/kg), loss of motor coordination (630-2000 mg/kg), watery eyes (320-3200 mg/kg), excessive salivation (630-3200 mg/kg), rapid shallow breathing (630-5000 mg/kg) and unconsciousness (630-5000 mg/kg). Deaths were observed in 0/3 in the 320 mg/kg dose and 1/3 in the 630 mg/kg dose. All other doses had 100% mortality.

In a 28 day feeding study, rats were fed a diet resulting in a dose of 500 mg/kg/day 3-picoline (Du Pont, 1992). Unfortunately, the strain and number of animals per dose level were not reported. Furthermore, no information concerning the toxicological investigation was reported except for the following: slight growth inhibition and an increase in liver fat content were observed. The poor reporting of information in this study make this study unsuitable for a quantitative risk assessment.

An acute inhalation study was performed in groups of 6 male Crl:CD®(SD)BR rats with 4 hour doses of 1300 or 3300 ppm 3-picoline (Du Pont, 1985). The observation period was 14 days post-exposure. There was 0/6 deaths in the 1300 ppm dose group and 6/6 deaths in the 3300 ppm dose group. During the recovery period, rats exposed to 1300 ppm had severe weight loss for 1 or 2 days, followed by normal weight gain. Some rats exposed to 1300 ppm had dry red nasal, ocular and oral discharges, wet perineum, decreased muscle tone, general paralysis, no righting reflex, hunched posture and were cold to the touch. The majority of clinical signs were observed 1 day post exposure, and all signs were absent 4 days post exposure.

In a subacute inhalation study, groups of 10 male CD rats were exposed to 0 or 290 ppm (1,105 mg/m^3) 3-picoline 6 hours per day for 10 days (Du Pont, 1984). Urinalysis was performed on urine samples taken prior to each exposure. Blood chemistry tests were performed on blood taken 3 days prior to the first exposure and immediately following the tenth exposure. Hematological and serum enzyme analysis were also performed. Five rats from each groups were sacrificed for pathologic evaluation following the last day of exposure. Following a 13 day recovery period, the hematologic and clinical chemical (serum and urine) measurements were repeated on the five surviving rats in each group. Significance was judged at the 5% probability level using the Dunnett criteria. Only statistically significant results are presented. Male rats exposed ten times to 1,105 mg/m^3 3-picoline had increased hematocrit values, absolute numbers of eosinophils and decreased serum concentrations of urea nitrogen and cholesterol. These rats excreted a higher volume of more alkaline urine than the controls. Urine osmolality was decreased. Decreased serum cholesterol concentrations persisted following a 13 day recovery period. Absolute numbers of lymphocytes were higher than the controls. The authors stated, "The clinical chemical and hematologic changes shown to be statistically significantly affected in Table V were within the range of expected biological variation and were therefore not interpreted to be biologically significant or related to exposure to 3-methylpyridine." The dose administered in this study was determined to be a free standing NOAEL.

The ITSL was based on the 10 day inhalation study (Du Pont, 1984) pursuant to Rule 232(1)(d). The ITSL was calculated as follows:

ITSL = NOAEL/(35 x 100) x (hours exposed per day)/(24 hours per day)

ITSL = (1105 mg/m^3)/(35 x 100) x 6/24

ITSL = 7.89×10^{-2} mg/m^3

ITSL = 80 μg/m^3 (based on an annual averaging time)

The ITSL for 3-picoline is 80 μg/m^3 based on an annual averaging time.

REFERENCES

Du Pont. 1992. Letter from E I Du Pont de Nemours and Co., to USEPA submitting enclosed risk assessment on 3-picoline with attachments. Obtained from EPA/OTS, Doc# 86-920000737.

Du Pont. 1985. Lethal concentration(s) by inhalation of pyridine and 3-methylpyridine. E. I. du Pont de Nemours and Co., Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Elkton Rd., PO Box 50, Newark, Delaware 19714. Obtained from the EPA/OTS, Doc# 878214921.

Du Pont. 1984. Clinical pathology report: Subacute inhalation toxicity of 3-methylpyridine and pyridine. E. I. Du Pont de Nemours and Company, Inc., Haskell laboratory for Toxicology and Industrial Medicine, Elkton Rd., Newark, Delaware 19711. Obtained from the EPA/OTS, Doc# 87-8214922.

Monsanto. 1972. Toxicological investigation of 0.4 mole fraction 3-methylpyridine. Study performed by Younger Laboratories, Inc. for Monsanto Company, St. Louis, Missouri. Monsanto Project Number Y-72-75. Obtained form the EPA via EPA/OTS, Doc# 88-920000371.

MD:slb