MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Pyridine (CAS# 110-86-1)

FROM: Doreen Lehner, Toxics Unit, Air Quality Division

DATE: January 31, 2017

SUBJECT: Pyridine (CAS# 110-86-1) ITSL change in the averaging time from 24-hours to annual

The initial threshold screening level (ITSL) for pyridine is 3.5 µg/m^3 based on an annual averaging time. The ITSL was originally established on 12/13/1996 and was set at 3.5 µg/m^3 based on a 24-hour averaging time. The ITSL was based on an EPA (1987) RfC of 1 x 10^{-3} mg/kg/day based on an EPA (1986) 90-day oral rat study where the critical effect was increased liver weight. EPA determined the no observed adverse effect level (NOAEL) of 1.0 mg/kg/day and used an uncertainty factor (UF) of 1,000 (an UF of 10 for animal to human extrapolation; an UF of 10 for susceptible human populations; and an UF of 10 to extrapolate from a subchronic to chronic effect level). The current file review concludes that the averaging time may appropriately be set at annual, as the key study is a subchronic oral rat study. Therefore, the averaging time is being changed from 24-hours to annual.

References:

Act 451 of 1994, Natural Resources and Environmental Protection Act and Air Pollution Control Rules, Michigan Department of Environmental Quality.

EPA. 1986. Pyridine. 90-Day subchronic oral toxicity in rats. Sponsored by Office of Solid Waste, Washington, DC.

EPA. 1987. Integrated Risk Information System. Pyridine; CASRN 110-86-1. Available online at: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=261

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

December 13, 1996

TO: File for Pyridine (CAS# 110-86-1)

FROM: Michael Depa, Toxics Unit, Air Quality Division

SUBJECT: Screening Level Determination

The initial threshold screening level (ITSL) for pyridine is 3.5 $\mu g/m^3$ based on a 24 hour 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 - June 5, 1996), National Library of Medicine, Health Effects Assessment Summary Tables, and NTP Status Report. Review of these sources found that EPA has established an RfD for pyridine of 0.001 mg/kg/day. An RfC has not been developed. The ACGIH and NIOSH have established occupational exposure limits (OELs) for pyridine at 16 and 15 mg/m^3, respectively. The pertinent toxicological studies have been summarized in the attached AQD Interim Chemical Evaluation.

There was no data meeting the minimum requirement for establishing an RfC. Rule 232 hierarchy states that if an RfC is not available, the ITSL is to be based on an RfD. However, if it is clear that the effects observed in inhalation studies (i.e. effects of the lung) are not observed in oral studies then the ITSL will be based on other data if appropriate. With this in mind, the toxicological database was evaluated in order to determine if the RfD (a standard protective of oral effects) is appropriate to use for the protection of inhalation effects.

The RfD (0.001 mg/kg) was based on a subchronic oral animal study where there was a dose-related increase in the liver to body weight ratio of the female rats at 10, 25, and 50 mg/kg/day. From this study a NOAEL of 1.0 mg/kg was identified. The ACGIH (1991) cited a report that found neurological effects in humans (nausea, headache, insomnia, and nervousness) at 125 ppm pyridine (404 mg/m^3). The ACGIH also summarized an article cited in a Czechoslovakian journal where workplace exposures of 6 to 12 ppm pyridine over chronic periods were reported to cause mild symptoms of CNS injury. Animal inhalation studies show that there are effects in the nasal mucosa at 5 ppm when rats were exposed for 6 hours/day for 4 days (Nikula and Lewis, 1994; and Nikula et al., 1995); however, no neurological effects were noted. In another animal inhalation study, researchers found that exposure to 5 ppm for 1 or 4 days caused an increase in hepatic cytochrome P450IIE1 (Hotchkiss et al., 1993). Since these effects were observed at the ACGIH TLV of 5 ppm the TLV was deemed inappropriate to use the TLV to develop the ITSL.

The neurological and nasal effects from inhalation studies were not observed in the oral studies; however, the hepatic effects observed in the Hotchkiss et al (1993) study show that pyridine affects the liver via both routes of exposure. Since the toxic effects of pyridine from both oral and inhalation exposures are systemic in nature it was deemed appropriate to use the RfD to develop the ITSL. Furthermore, the ITSL, based on the RfD, would protect against the effects seen in the inhalation studies. Pursuant to Rule 232(1)(b) the ITSL was developed as follows:

ITSL = RfD x (70 kg)/(20 m^3)

ITSL = (0.001 mg/kg) x (70 kg)/(20 m^3)

ITSL = 0.0035 mg/m^3

ITSL = 3.5 $\mu g/m^3$ (24 hour averaging time)

The ITSL for pyridine is 3.5 $\mu g/m^3$ based on a 24 hour averaging time.

REFERENCES

ACGIH. 1991. Threshold limit values (TLVs) and biological exposure indices (BEI) documentation. American Conference of Governmental Industrial Hygienists. Cincinnati, OH, 45240-1634.

Hotchkiss JA, Kim SG, Novak RF, Dahl AR. 1993. Enhanced hepatic expression of P450IIE1 following inhalation exposure to pyridine. Toxicology and Applied Pharmacology. 118: 98-104.

Nikula KJ, Novak RF, Chang IY, Dahl AR, Kracko DA, Zanfar RC, Kim SG, Lewis JL. 1995. Induction of nasal carboxylesterase in F344 rats following inhalation exposure to pyridine. Drug Metabolism and Disposition. 23(5): 529-535.

Nikula KJ, Lewis JL. 1994. Olfactory mucosal lesions in F344 rats following inhalation exposure to pyridine at threshold limit value concentrations. Fundamental and Applied Toxicology. 23: 510-517.

MD:slb