MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

TO: File for Allyl alcohol (CAS# 107-18-6)

FROM: Doreen Lehner, Toxics Unit, Air Quality Division

DATE: January 25, 2017

SUBJECT: Allyl alcohol (CAS# 107-18-6) ITSL change in the averaging time from 24 hours to annual

The initial threshold screening level (ITSL) for allyl alcohol is 18 µg/m^3 based on an annual averaging time. The ITSL was originally established on 8/30/1995 and was set at 18 µg/m^3 based a 24-hour averaging time. The ITSL was based on an EPA (1987) oral reference dose (RfD) of 5E-3 mg/kg/day derived from a 15 week oral rat study by Carpanini et al., (1978). Carpanini et al., exposed groups of Wistar rats (15/sex/dose) to allyl alcohol in drinking water at doses of 0, 4.8, 8.3, 14.0, or 48.2 mg/kg/day (males) and 0, 6.2, 6.9, 17.1, or 58.4 mg/kg/day (females). The critical effects were determined to be impaired renal function and increased liver and kidney weights. The NOAEL for this study is 4.8 mg/kg/day. 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.

Carpanini FMB, Gaunt IF, Hardy J, Gangalli SD, Butterworth KR, and Lloyd HG. 1978. Short-term toxicity of allyl alcohol in rats. Toxciology 9:29-45.

EPA. 1987. Integrated Risk Information System. Allyl Alcohol; CASRN 107-18-6. Available online at: https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=4

MICHIGAN DEPARTMENT OF NATURAL RESOURCES

INTEROFFICE COMMUNICATION

August 30, 1995

TO: File for Allyl Alcohol (107-18-6)

FROM: Marco Bianchi

SUBJECT: Initial Threshold Screening Level

Allyl alcohol was initially evaluated by AQD staff in 1993, using interim ITSL procedures to derive a value of 50 ug/m^3 (8 hr) and 17.5 ug/m^3 (24 hr). In an effort to finalize all interim chemical screening levels, this chemical was re-reviewed to set a final ITSL. 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.

Review of the literature revealed acute and subchronic animal studies in addition to occupational exposure information.

In acute animal studies, Smyth et al., determined an oral rat LD_{50} of 64 mg/kg for allyl alcohol, which was corroborated by Dunlap et al., who reported an oral rat LD_{50} for this compound at 71 mg/kg. Dunlap et al., also determined rat inhalation LC_{50} levels for 1-, 4-, and 8-hour exposures, which were 1060, 165, and 76 ppm, respectively. Toxic responses included apathy, excitability, tremors, convulsions, diarrhea, coma, pulmonary, and visceral congestion, and varying degrees of hepatic injury.

Occupational studies have shown that allyl alcohol is an intense human irritant to skin, eye, nose, and throat. It causes burns on contact, and may cause pulmonary edema if inhaled. It is poisonous in small quantities. Dunlap et al., found that a significant effect of allyl alcohol exposure at 25 ppm is severe eye irritation, while 5 ppm is slightly irritating to some individuals. Skin absorption may lead to serious systemic injury (visceral congestion, periportal congestion of the liver, hematuria, and nephritis); skin contact may cause first and second degree burns of the skin and blister formation. Sensory threshold studies indicate recognition of allyl alcohol by most individuals at about 0.8 ppm. Lacrimatory effects have persisted for some hours following exposure, but neither increased sensitivity nor tolerance appear to develop. There is no evidence of histamine release following allyl alcohol exposure.

The EPA established a Reference Dose (RfD) of 5×10^{-3}, using a subchronic oral rat study (drinking water) by Carpanini et al. This value was used to derive the interim ITSL of 17.5 ug/m3 (24 hr averaging time). In this study, Carpanini et al., (1978) exposed groups of Wistar rats (15/sex/dose) to drinking water equivalent dosages of 0, 4.8, 8.3, 14.0, and 48.2 mg/kg/day (males) and 0, 6.2, 6.9, 17.1, and 58.4 (females) allyl alcohol for 15 weeks. Results of hematologic and clinical chemistry tests were unremarkable. There were no histopathologic lesions attributable to treatment in any of the organs examined; however, the relative organ weights of the liver, kidney, and spleen were significantly increased in a dose-related fashion for all except the 4.8- and 6.2 mg/kg-day level. The EPA defined the NOAEL at 4.8 mg/kg-day, resulting in a RfD of 5×10^{-3}. The critical effect was determined to be impaired renal function and increased liver and kidney weights. Confidence in the RfD was low.

In order to evaluate the effects of chronic exposure to allyl alcohol, Dunlap et al., (1958) conducted a series experiments using various routes of administration and species. In a series of 3 inhalation

experiments, groups of 10 male rats were exposed to levels of 1, 2, 5, 20, 40, 60, 100, and 150 ppm for 7 hrs/day, 5 days/wk for a total of 60 exposures (90 days). Control groups were similarly exposed to uncontaminated air. In the first experiment, levels of 1, 2, 5, and 20 ppm failed to produce gross or microscopic signs of toxicity. The 40 and 60 ppm groups resulted in slight pale and spotted lungs, hemorrhagic liver, air and mucus filled enteric tract, and the enteric vessels engorged. Microscopically, slight congestion of the lungs and liver was the only finding. Signs, lesions, and microscopic findings were similar at the 100 and 150 ppm experiment, but more intense. A concentration of 150 ppm proved highly lethal.

In another study by Torkelson et al., rats, rabbits, dogs, and guinea pigs were exposed by inhalation to allyl alcohol for 7 hrs/day, 5 days/wk for 35 days at 7 ppm, and 7 hrs/day, 5 days/wk for 6 months at 2 ppm. Rats numbered 24 animals/sex/group, and the control group was divided into an air-exposed group and an unexposed group each with 24 animals per sex. Torkelson et al., reported that rats, along with all animals in the 7 ppm group showed no evidence of ill-effects as judged by growth, behavior, mortality, gross appearance and final average body and organ weights. However, there was degeneration observed in the kidneys and livers of almost all animals under microscopic examination. This was characterized in the liver by dilation of the sinusoids, cloudy swelling and focal necrosis. In the kidney the changes were similar to those commonly seen in the glomerulonephritis, necrosis of the epithelium of the convoluted tubules and proliferation of the interstitial tissue. These changes appeared to be mild and reversible. In the 2 ppm group, both sexes of all animals showed no evidence of ill-effect as judged by growth, behavior, mortality and final average body and organ weights. Although Torkelson et al., did not establish 2 ppm as a NOEL, they did suggested a TWA of 2 ppm (4.8 mg/m^3) for daily 7- to 8-hr exposures.

Each of the studies presented above have strengths and weaknesses that make them equal in weight for ITSL derivation. An RfC could be developed from the Torkelson study which would likely be protective, however, only two dose ranges were used each covering a different length of time. Using the OEL would comply with standard practice, but the TLV is based on the Torkelson study and would present the same problems as previously mentioned. The Dunlap study used a variety of exposure routes, species and dose ranges, but when it came to the subchronic inhalation study, only one sex was used, and the LOAEL was higher than Torkelson's. This leaves the RfD study by Carpanini. Although this is an oral drinking water study, this study has the same critical endpoint as the Torkelson study, in addition to adequate doses and number of animals used. Because each of the studies are relatively equal in weight, the RfD will be used to derive an ITSL based on the hierarchical selection criteria listed in Rule 232. It appears that this study would be protective of inhalation endpoints. Therefore, the ITSL will be 18 ug/m^3 based on a 24 hour averaging time.

References:

ACGIH Documentation. 1994. Documentation of the TLV's and the BEI's.

IRIS EPA 1992. Allyl alcohol.

Dunlap et al., 1958. *The Toxicity of Allyl Alcohol; I. Acute and Chronic Toxicity.* A.M.A. Archives of Industrial Health. 18:303-310.

Torkelson et al., 1959. *Vapor Toxicity of Allyl Alcohol as Determined on Laboratory Animals.* American Industrial Hygiene Association Journal. 20:224-228

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