MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

November 19, 2015

To: File for Vinyl Bromide (CAS # 593-60-2)

From: Mike Depa, Toxics Unit, Air Quality Division

Subject: Initial Threshold Screening Level

The Initial Threshold Screening Level (ITSL) for vinyl bromide is 30 µg/m^3 with an annual averaging time.

U.S. Environmental Protection Agency (EPA, 1993) reviewed the toxicity database and summarized the key study used to derive a Reference Concentration (RfC) for vinyl bromide. Groups of 120 male and female Sprague-Dawley rats were exposed via inhalation to target concentrations of 0, 10, 50, 250, and 1250 ppm [actual concentrations were 0, 9.7, 52, 247, or 1235 ppm (0, 43, 230, 1095, or 5474 mg/m^3), respectively] vinyl bromide vapor for 6 hours/day, 5 days/week (duration adjusted to 0, 7.7, 41, 196, or 977 mg/m^3) for 6, 12, 18, or 24 months (Busey, 1978, 1979; Huntington Research Center, 1977a,b); and in a peer-reviewed publication (Benya et al., 1982). Increased mortality occurred in animals exposed to 50, 250, and 1250 ppm. At 18 months, eosinophilic foci and basophilic foci were increased in groups exposed to 50, 250, and 1250 ppm. Focal hypertrophy and peliosis (atelectasia) were increased in all exposed groups. Bile duct proliferation was also slightly increased in all exposed groups. In male rats examined at the terminal sacrifice, eosinophilic foci were seen in 19, 42, and 39% of control, 10-ppm and 50-ppm animals, respectively. Basophilic foci were seen in 12, 31, and 39%, and clear cell foci were seen in 1, 12, and 25% of animals in the control, 10-ppm and 50- ppm groups, respectively (n = 74, 52, and 28, respectively). Similar results were obtained when animals dying during the last 6 months of the study were included with the terminal sacrifice. No exposure-related nonneoplastic histopathology was observed in sites other than the liver at the terminal sacrifice. Incidences of these lesions in the groups exposed to 250 and 1250 ppm were lower than in the controls, but the interpretation of this finding is confounded by the high incidence of neoplasms in these groups, the early termination of the 1250-ppm group, and the small numbers of animals surviving to terminal sacrifice for which livers were examined (n = 6 and 19 for the 250- and 1250-ppm groups, respectively). The 10 ppm dose level was identified as the LOAEL[1]. A NOAEL[2] was not identified. The critical effect was “Hypertrophy, basophilic and eosinophilic foci, in the liver.” (EPA, 1993).

[1] Lowest-observed-adverse-effect-level
[2] No-observed-adverse-effect-level

EPA (1993) converted the LOAEL of 10 ppm to mg/m^3 using the molecular weight of vinyl bromide (106.9g) as follows:

LOAEL (mg/m^3) = 9.7 ppm x 106.9/24.12
LOAEL (mg/m^3) = 43 mg/m^3

The LOAEL was duration adjusted for continuous exposure:

LOAEL(ADJ) = 43 x 6 hours/24 hours x 5 days/7 days
LOAEL(ADJ) = 7.7 mg/m^3

The LOAEL human equivalent concentration (HEC) was calculated for a gas:extrarespiratory effect assuming periodicity was attained. The blood:gas partition coefficient (b:a lambda) was used to calculate the HEC. For the rat, b:a lambda(a) = 4.05, for the human, b:a lambda(h) = 2.27 (Gargas et al., 1989). Since b:a lambda(a) is greater than b:a lambda(h), a default value of 1 is used for this ratio.

LOAEL(HEC) = LOAEL(ADJ) x (b:a lambda(a)/b:a lambda(h))
LOAEL(HEC) = 7.7 mg/m^3 x 1
LOAEL(HEC) = 7.7 mg/m^3

The total uncertainty factor (UF) of 3000 was used by EPA (1993) to derive their RfC, composed of 10 for protection of sensitive human subjects, 3 for interspecies extrapolation, 10 for extrapolation from a LOAEL to a NOAEL and UF of 10 for database deficiencies, including lack of data for a second species, and lack of any developmental or reproductive toxicity data. Since there was no chemical specific reason for applying the database deficiency UF of 10, it was not used to derive the final RfC.

RfC = LOAEL(HEC)/(10x3x10)
RfC = 7.7 mg/m^3/300
RfC = 0.0256 x 1000µg/mg
RfC = 30 $\mu g/m^3$ (rounding to 1 significant figure)

Pursuant to Rule 232(1)(a) the ITSL is equal to the RfC. The current file review also concludes that the averaging time for the chronic RfC derived ITSL may appropriately be set at annual, based on the nature and duration of the key study and the ITSL value derivation, as allowed under Rule 229(2)(b).

References

Benya, T.J., W.M. Busey, M.A. Dorato, and P.E. Berteau. 1982. Inhalation carcinogenicity bioassay of vinyl bromide in rats. Toxicol. Appl. Pharmacol. 64(3): 367-379.

Busey, W.M. 1978. HRC Project 7511-253. 18-Month sacrifice. Pathology report. Huntington Research Center, New City, NY. EPA/OTS No. 0200461.

Busey, W.M. 1979. Oncogenic potential of vinyl bromide during chronic inhalation exposure - rats: Pathology Report. EPA/OTS 8EHQ-0479-0281.

EPA. 1993. Vinyl bromide; CASRN 593-60-2. Chemical Assessment Summary. Integrated Risk Information System (IRIS). National Center for Environmental Assessment. U.S. Environmental Protection Agency. http://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/0671_summary.pdf#nameddest=rfc

Gargas, M.L., R.J. Burgess, D.E. Voisard, G.H. Cason, and M.E. Anderson. 1989. Partition coefficients of low-molecular-weight volatile chemicals in various liquids and tissues. Toxicol. Appl. Pharmacol. 98: 87-99.

Huntington Research Center. 1977a. Oncogenic potential of vinyl bromide during chronic inhalation exposure. Twelve month interim report. Volume 1. Project Number 7511-253. NTIS PB87-207460.

Huntington Research Center. 1977b. Oncogenic potential of vinyl bromide during chronic inhalation exposure. Twelve month interim report. Volume 2. Project Number 7511-253. NIOSH No. 00152540, NTIS PB87-207478.