MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

January 15, 2016

TO: Chloroprene File (CAS # 126-99-8)

FROM: Mike Depa, Toxics Unit, Air Quality Division

SUBJECT: Initial Threshold Screening Level

The Initial Threshold Screening Level (ITSL) for chrloroprene is 20 µg/m³ with annual averaging time. The Initial Risk Screening Level (IRSL) and Secondary Risk Screening Level (SRSL) are 0.002 and 0.02 µg/m³, respectively; both with annual averaging time.

Inhalation Non-carcinogenic Risk

The ITSL was based on the U.S. Environmental Protection Agency (EPA) Reference Concentration (RfC) of 20 µg/m³ (EPA, 2010).

ITSL/RfC Critical Effect: Nervous, Immune, Respiratory.

ITSL/RfC Basis: Increase in incidence of olfactory atrophy, alveolar hyperplasia, and splenic hematopoietic proliferation in male F344/N rats, female F344/N rats, and female B6C3F1 mice, respectively BMDL[1] (HEC[2]): 2 mg/m³

Total Uncertainty Factor: 100

Previously, the averaging time (AT) assigned to chloroprene was 24 hours, as per the default methodology. The current file review concludes that the AT 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). Therefore, the AT is set to annual.

Inhalation Carcinogenic Risk

Regarding the basis and derivation of the inhalation unit risk, the following paragraph was taken from EPA (2010):

> Given the multiplicity of tumor sites observed in female mice exposed to chloroprene for 2 years (NTP, 1998[3]), the derivation of the inhalation unit risk of 3.0×10^{-4} per µg/m^3 is based on the incidence of tumors in multiple organ systems: alveolar/bronchiolar adenoma or carcinoma; hemangioma/hemangiosarcoma (all organs); mammary gland adenocarcinoma, carcinoma, or adenoacanthoma; forestomach squamous cell papilloma or carcinoma; hepatocellular adenoma or carcinoma; Harderian gland adenoma or carcinoma; skin sarcoma; and Zymbal's gland carcinoma (NTP, 1998), (NTP, 1998), (NTP, 1998), (NTP, 1998). The dose metric used in the

[1] Benchmark dose lower 95% confidence limit
[2] Human Equivalent Concentration
[3] See EPA, 2010 for reference citations

current estimate of the human equivalent concentration (HEC) is the applied or external dose because the only PBPK model available (Himmelstein et al., 2004) was determined to be inadequate for application for calculation of internal dose metrics or interspecies dosimetry extrapolations. As there is evidence that chloroprene and/or its metabolite are distributed systemically (i.e., the observation of tumors in multiple organ systems), there is the potential that chloroprene is redistributed to the lungs. For this reason, and because of chloroprene's low water solubility, low reactivity and distribution of lesions, it is most appropriately treated as a Category 3 gas for which blood-borne delivery plays a critical role. Hence, as was done for noncancer lesions, all tumors were treated as systemic effects and, since the blood:air partition coefficient for chloroprene is greater in rats than in humans, a DAF[4] of 1.0 was applied.

Because a mutagenic mode of action for chloroprene carcinogenicity is supported by in vivo and in vitro data and relevant to humans (EPA, 2010), and in the absence of chemical-specific data to evaluate the differences in susceptibility, increased early-life susceptibility is assumed and the age-dependent adjustment factors (ADAFs) should be applied, as appropriate, along with specific exposure data in accordance with EPA's Supplemental Guidance for Assessing Susceptibility From Early-Life Exposure to Carcinogens (EPA, 2005).

Risk for birth through < 2 yr = 3×10^{-4} per $\mu g/m^3 \times 10 \times 2yr/70yr = 8.6\times10^{-5}$ per $\mu g/m^3$
Risk for ages 2 through < 16 = 3×10^{-4} per $\mu g/m^3 \times 3 \times 14yr/70yr = 1.8\times10^{-4}$ per $\mu g/m^3$
Risk for ages 16 until 70 = 3×10^{-4} per $\mu g/m^3 \times 1 \times 54yr/70yr = 2.3\times10^{-4}$ per $\mu g/m^3$

To calculate the lifetime risk estimate for continuous exposure from birth for a population with default life expectancy of 70 years, the risk associated with each of the three relevant time periods is summed:

Total Risk = $8.6\times10^{-5} + 1.8\times10^{-4} + 2.3\times10^{-4} = 5.0\times10^{-4}$ per $\mu g/m^3$

The Initial Risk Screening Level (IRSL) and Secondary Risk Screening Level (SRSL) are calculated pursuant to Rule 231(1) as follows:

IRSL = 1E-6/inhalation unit risk
IRSL = 1E-6/5.0×10^{-4} per $\mu g/m^3$
IRSL = 0.002 $\mu g/m^3$

SRSL = 1E-5/inhalation unit risk
SRSL = 1E-5/5.0×10^{-4} per $\mu g/m^3$
SRSL = 0.02 $\mu g/m^3$

Annual averaging time was assigned to the IRSL and SRSL, pursuant to Rule 231(4).

Reference:

EPA, 2005. Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens. Risk Assessment Forum U.S. Environmental Protection Agency Washington, DC. EPA/630/R-03/003F March 2005
http://www3.epa.gov/ttn/atw/childrens_supplement_final.pdf

EPA. 2010. Chloroprene; CASRN: 126-99-8. Integrated Risk Information System (IRIS) U.S. Environmental Protection Agency. Chemical Assessment Summary National Center for

[4] Dosimetric adjustment factor

Environmental Assessment.
http://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/1021_summary.pdf