MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

November 2, 2015

TO: 2-Chloroacetophenone File (CAS #532-27-4)

FROM: Mike Depa, Toxics Unit, Air Quality Division

SUBJECT: Screening level for 2-Chloroacetophenone

The initial threshold screening level (ITSL) for 2-chloroacetophenone is 0.6 µg/m³ with annual averaging time. Previously, the ITSL was 0.03 µg/m^3 with a 24-hr averaging time.

The ITSL is based on an U.S. Environmental Protection Agency (EPA, 1991) assessment of chronic inhalation risk. However, in order to derive the ITSL, the EPA's reference concentration (RfC; 0.03 µg/m^3) was modified to take into account recent advances in animal to human dosimetry. The EPA (2012) RfC methodology specifies that the dosimetric adjustment factor is "1" for gases that have extrathoracic (ET) effects (e.g., nasal) in rodents. This means that the dose in animals equals the dose in humans. Nasal effects were the critical effect observed in mice and rats in a chronic inhalation study (NTP, 1990) used to derive the RfC (see Table 1).

Table 1. Inhalation RfC Summary (adapted from Table B.1. from EPA, 1991)

Critical Effect	Exposures*	UF	MF	RfC
Squamous hyperplasia of the nasal respiratory epithelium Chronic rat Inhalation Study NTP, 1990	NOAEL: None LOAEL: 1 mg/m³ LOAEL(ADJ): 0.18 mg/m³ LOAEL(HEC): 0.18 mg/m³	300	1	6E-4 mg/m³ or 0.6 µg/m³

*Conversion Factors: MW = 154.6. The LOAEL(HEC) was calculated using a default dosimetric adjustment factor of 1 for gas:respiratory effect in the ExtraThoracic region (EPA, 2012)

The lowest-observed-adverse-effect-level (LOAEL) was then adjusted to account for the intermittent exposure.

$$LOAEL_{ADJ} = LOAEL \times (6 \text{ hours})/(24 \text{ hours}) \times (5 \text{ days})/(7 \text{ days})$$

$$LOAEL_{ADJ} = 1.0 \text{ mg/m}^3 \times 6/24 \times 5/7$$

$$LOAEL_{ADJ} = 0.18 \text{ mg/m}^3$$

Since the dose in animals equals the dose in humans:

$$LOAEL_{HEC} = LOAEL_{ADJ}$$

$$LOAEL_{HEC} = 0.18\ mg/m^3$$

The RfC was then calculated as follows:

$$RfC = \frac{LOAEL_{HEC}}{UF_1 \times UF_2 \times UF_3}$$

Where,
UF_1 is an uncertainty factor of 3 for interspecies variability[1],
UF_2 is 10 to account for sensitive individuals (intraspecies variability),
UF_3 is 10 to account for the conversion of a LOAEL to NOAEL

$$RfC = \frac{0.18\ mg/m^3}{3 \times 10 \times 10}$$

$$RfC = 0.0006\ mg/m^3 \times 1000\ \mu g/mg$$

$$RfC = 0.6\ \mu g/m^3$$

Previously, the averaging time (AT) assigned to 2-chloroacetophenone was 24 hours, as per the default methodology (Rule 232(2)(b)). 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.

References

EPA, 1991. Chemical Assessment for 2-Chloroacetophenone; CASRN 532-27-4. Integrated Risk Information System (IRIS) U.S. Environmental Protection Agency. National Center for Environmental Assessment. http://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/0537_summary.pdf

EPA. 2012. Advances in Inhalation Gas Dosimetry for Derivation of a Reference Concentration (RfC) and Use in Risk Assessment. United States Environmental Protection Agency. September 2012. EPA/600/R-12/044

NTP (National Toxicology Program). 1990. Toxicology and carcinogenesis studies of 2-chloroacetophenone (CAS No. 532-27-4) in F344/N rats and B6C3F1 mice (inhalation studies). NTP Technical Report 379.

[1] The animal to human UF of 3 was used because of the decreased uncertainty in animal to human dosimetry (EPA, 1994). EPA used a factor of 3 for databased deficiency (lack of neurotoxicity and reproductive/developmental effects). Since there was no chemical specific rationale for using this database gaps uncertainty factor, it was not used in the development of the ITSL.