

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY

INTEROFFICE COMMUNICATION

May 26, 2016

TO: File for Methyl Tert-Butyl Ether (CAS No. 1634-04-4)  
FROM: Mike Depa, Toxics Unit, Air Quality Division  
SUBJECT: Initial Threshold Screening Level

The Initial Threshold Screening Level (ITSL) for methyl tert-butyl ether (MTBE) is 3000  $\mu\text{g}/\text{m}^3$ , with annual averaging time.

Previously, the averaging time (AT) assigned to MTBE 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.

The ITSL is based on the U. S. Environmental Protection Agency (EPA, 1993) Reference Concentration (RfC) of 3  $\text{mg}/\text{m}^3$ . The RfC was based on 2-year rat inhalation study by Chun et al. (1992). In a chronic inhalation study (Chun et al., 1992), Fischer 344 rats (50 males, 50 females/group) were exposed to analytical mean concentrations of 403, 3023, or 7977 ppm MTBE vapors (1453, 10,899, or 28,760  $\text{mg}/\text{m}^3$ ) 6 hours/day, 5 days/week for 24 months (duration-adjusted<sup>1</sup> values are 259, 1946, and 5136  $\text{mg}/\text{m}^3$ , respectively). The No-Observed-Adverse-Effect-Level (NOAEL) was identified at 1453  $\text{mg}/\text{m}^3$  (403 ppm). The NOAEL human equivalent concentration (HEC) or NOAEL(HEC) = 259  $\text{mg}/\text{m}^3$ , was calculated for a gas:extrarrespiratory effect in rats assuming periodicity was attained. Since the blood-gas partition coefficient or lambda values are unknown for the experimental species (a) and humans (h), a default value of 1.0 is used for this ratio.

At the Lowest-Observed-Adverse-Effect-Level (LOAEL) there was increased absolute and relative liver and kidney weights and increased severity of spontaneous renal lesions (females), increased prostration (females), and swollen periocular tissue (males and females). The LOAEL(ADJ) = 1946  $\text{mg}/\text{m}^3$  = LOAEL(HEC).

EPA (1993) used a total uncertainty factor ( $UF_{\text{tot}}$ ) of 100 to calculate the RfC. The  $UF_{\text{tot}}$  was composed of an uncertainty factor of 10 to account for extrapolation to sensitive human subpopulations. An additional factor of 3 was used to account for interspecies extrapolation<sup>2</sup>. EPA (1993) applied an uncertainty factor of 3 for database deficiencies because of the lack of certain information from the chronic exposure bioassay (e.g., urinalysis results, serum chemistry, and limited reporting of motor activity/clinical signs during exposure).

$RfC = \text{NOAEL(HEC)} / (UF_{\text{tot}})$   
 $RfC = 259 \text{ mg}/\text{m}^3 / (100)$   
 $RfC = 2.59 \text{ mg}/\text{m}^3 \approx 3 \text{ mg}/\text{m}^3$  (EPA rounds to 1 significant figure).  
 $RfC = 3 \text{ mg}/\text{m}^3 \times 1000 \mu\text{g}/\text{mg} = 3000 \mu\text{g}/\text{m}^3$ ; with annual averaging time

<sup>1</sup>  $\times 6 \text{ hours}/24 \text{ hours} \times \text{days}/7 \text{ days}$  to convert to continuous exposure

<sup>2</sup> A full 10-fold adjustment for interspecies extrapolation was not deemed necessary due to the use of dosimetric adjustments.

## References

Chun, J.S., H.D. Burleigh-Flayer, and W.J. Kintigh. 1992. Methyl tertiary butyl ether: vapor inhalation oncogenicity study in Fischer 344 rats (unpublished material). Prepared for the MTBE Committee by Bushy Run Research Center, Union Carbide Chemicals and Plastics Company Inc. Docket No. OPTS- 42098.

U.S. Environmental Protection Agency (EPA). 1993. Methyl tert-butyl ether (MTBE); CASRN 1634-04-4. Integrated Risk Information System (IRIS) U.S. Environmental Protection Agency. Chemical Assessment Summary. National Center for Environmental Assessment.

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