MICHIGAN DEPARTMENT OF ENVIRONMENT, GREAT LAKES, AND ENERGY

INTEROFFICE COMMUNICATION

TO: File for *tert*-Butyl alcohol (CAS # 75-65-0)

FROM: Doreen Lehner, Toxics Unit, Air Quality Division

DATE: July 19, 2023

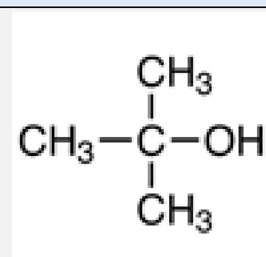
SUBJECT: Screening Level for *tert*-Butyl alcohol (CAS # 75-65-0)

Summary

The initial risk screening level (IRSL) for *tert*-butyl alcohol is 7 μg/m^3 (annual averaging time) and the secondary screening level (SRSL) is 70 μg/m^3 (annual averaging time).

Uses and Physical Chemical Properties

Tert-Butyl alcohol is the simplest tertiary alcohol and had been found in chickpeas, cassava, and beer. *Tert*-butyl alcohol is used: as a solvent for paints, a denaturant for ethanol, an ingredient in paint remover; in gasoline octane booster and oxygenate; an agent for dehydrating; in the manufacture of flotation agents; in fruit essences; in perfumes; and as a chemical intermediate in the production of methyl *tert*-butyl ether (MTBE), ethyl *tert*-butyl ether (ETBE), and *tert*-butyl hydroperoxide (TBHP) (EPA, 2021).

Table 1. Physical/Chemical Properties of *tert*-Butyl alcohol	
Structure	
CAS Number	75-65-0
Synonyms	t-Butanol; 2-Methyl-2-propanol; 1,1-Dimethylethanol; Trimethylcarbinol; t-Butyl hydroxide
Appearance/Odor	Colorless oily liquid with a sharp alcohol odor
Odor Threshold	219 mg/m^3

Molecular Weight	74.12 g/mol
Melting Point	25.81°C
Boiling Point	82.4 °C @ 760 mmHg
Flash Point	11 °C (closed cup)
Autoignition Temperature	478 °C
Solubility: Water	1000 mg/mL @ 25°C
Density	0.7886 g/cm^3 @ 20°C
Vapor Pressure	40.7 mm Hg at 25°C
Heat of Vaporization	39.07 kJ/mol
Log Kow	0.35
Henry's Law Constant	9.05 x 10^{-6} atm-m^3 /mole at 25°C

Literature Search

The literature was searched to find relevant data to assess the toxicity of *tert*-butyl alcohol. The following references or databases were searched: U.S. Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS), Registry for Toxic Effects of Chemical Substances (RTECS), American Conference of Governmental and Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs), National Institute for Occupational Safety and Health (NIOSH) Recommended Exposure Levels (RELs), International Agency for Research on Cancer (IARC) Monographs, Chemical Abstract Service (CAS) SciFinder (searched 3/6/2023), U.S. EPA ChemView, California Office of Environmental Health Hazard Assessment (OEHHA), the U.S. Department of Health and Human Services Agency for Toxic Substances and Disease Registry (ATSDR), European Chemical Agency (ECHA), and the U.S. National Toxicology Program (NTP).

IRSL Derivation

The IRSL was based on the EPA IRIS oral slope factor of 5 x 10^{-4} per mg/kg-day. "Under EPA Cancer Guidelines [EPA, 2005], there is *suggestive evidence of carcinogenic potential* for *tert*-butanol. *tert*-Butanol induced kidney tumors in male (but not female) rats and thyroid tumors (primarily benign) in male and female mice following long-term administration in drinking water (NTP, 1995). The potential for carcinogenicity applies to all routes of human exposure" (EPA, 2021).

"In accordance with EPA's guidance on alpha 2µ-globulin [EPA, 1991], rat kidney tumors are unsuitable for quantitative analysis because not enough data are available to determine the relative contribution of alpha 2µ-globulin nephropathy and other processes to the overall kidney tumor response. A quantitative estimate of carcinogenic potential from oral exposure to *tert*-butanol was based on the increased incidence of thyroid follicular cell adenomas in female B6C3F1 mice and thyroid follicular cell adenomas and carcinomas in male B6C3F1 mice (NTP, 1995). The study included histological examinations for tumors in many different tissues, contained three exposure levels and controls, contained adequate numbers of animals per dose group (~50/sex/group), treated animals for up to 2 years, and included detailed reporting of methods and results" (EPA, 2021).

"Although *tert*-butanol was considered to have only *suggestive evidence of carcinogenic potential*, the National Toxicology Program (NTP) study was well conducted and suitable for quantitative analysis. Slope factors were derived for thyroid tumors in female or male mice. The modeled *tert*-butanol POD was scaled to human equivalent doses (HEDs) according to EPA guidance by converting the benchmark dose lower confidence limit corresponding to 10% extra risk ($BMDL_{10}$) on the basis of body weight scaling to the ¾ power ($BW^{3/4}$) [EPA, 2011, 2005]. Using linear extrapolation from the $BMDL_{10}$, a human equivalent oral slope factor was derived (slope factor = 0.1/$BMDL_{10}$). The resulting oral slope factor is 5 x 10^{-4} per mg/kg-day" (EPA, 2021).

In the NTP study, groups of 60 male and female B6C3F1 mice were given either 0, 5, 10, or 20 mg/ml (average daily doses of approximately 0, 540, 1,040, or 2,070 mg *tert*-butyl alcohol/kg body weight to males and approximately 0, 510, 1,020, or 2,110 mg *tert*-butyl alcohol/kg to females) in drinking water for 2 years. "Thyroid effects, specifically follicular cell hyperplasia and adenomas, were observed in mice of both sexes after 2 years of oral exposure via drinking water (NTP, 1995). NTP (1995) noted, '[p]roliferation of thyroid gland follicular cells is generally considered to follow a progression from hyperplasia to adenoma and carcinoma.' Both male and female mice exhibited a dose-related increase in the incidence of hyperplasia, and the average severity across all dose groups was minimal to mild with scores ranging from 1.2 to 2.2 (out of 4). Increased incidence of adenomas also was observed in the *tert*-butanol-treated female mice at the high dose, with the only carcinoma observed in high-dose males" (EPA, 2021). "The tumor response in male mice, adjusted for early mortality, showed a statistically significant increasing trend (Cochran-Armitage trend test, p=0.041; analysis performed by EPA). Although the response appeared nonmonotonic, with a slightly lower response at the high-dose level than at the mid-dose level, the increased mortality reported in the high-dose group occurred before tumors appeared; about 40% of the high-dose males died before the first tumor (a carcinoma) appeared in this group at Week 83. By comparison, only ~10% of the control group had died by this time, and the single tumor in the control group was observed at study termination. Mortality in the exposed female mice was similar to controls" (EPA, 2021).

Rule 231(1) was used to develop the IRSL, using the oral slope factor of 5 x 10^{-4} per mg/kg-day derived by the EPA for *tert*-butyl alcohol. But first, the oral slope factor is converted to an inhalation cancer value using the following equation:

$$q_1^*({}^{\mu g}/_{m^3})^{-1} = q_1^*({}^{mg}/_{kg/day})^{-1} \times \frac{20\ m^3}{70\ kg} \times \frac{1\ mg}{1{,}000\ \mu g} \times \frac{a}{b}$$

Where:
Unit Risk = q_1^*. q_1^* = The parameter expressed in units of (micrograms per cubic meter)$^{-1}$.

a = Absorption efficiency by inhalation route of exposure.
b = Absorption efficiency by the oral route of exposure.

Since it is unknown what the absorption efficiency of the inhalation route or the oral route, the value of 1 is substituted for both a and b. The value of q_1^* is the EPA carcinogenic oral slope factor of 5 x 10^{-4} per mg/kg-day. Inserting the value q_1^* in the equation above:

$$q_1^*({}^{\mu g}/_{m^3})^{-1} = 0.0005({}^{mg}/_{kg/day})^{-1} \times \frac{20\ m^3}{70\ kg} \times \frac{1\ mg}{1{,}000\ \mu g} \times \frac{1}{1}$$
$$= 0.000000143({}^{\mu g}/_{m^3})^{-1}$$

Under Rule 231(1), the IRSL is determined as follows:

$$IRSL = \frac{1 \times 10^{-6}}{Unit\ Risk}$$

Where:
Unit Risk = Additional lifetime cancer risk occurring in a population in which all individuals are exposed continuously for life to a concentration of 1 microgram per cubic meter of the chemical in the air. Using the q_1^* value determined above in the IRSL equation:

$$IRSL = \frac{0.000001}{0.000000143({}^{\mu g}/_{m^3})^{-1}} = 6.993006993\ {}^{\mu g}/_{m^3} \approx 7\ {}^{\mu g}/_{m^3}$$

According to Rule 231(3) the averaging time for an IRSL or SRSL is annual. Therefore, the IRSL for *tert*-butyl alcohol is 7 μg/m^3 with an annual averaging time and the SRSL is 70 μg/m^3 with an annual averaging time.

References:

Act 451 of 1994, Natural Resources and Environmental Protection Act and Air Pollution Control Rules, Michigan Department of Environment, Great Lakes, and Energy.

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