

ARC201-13687A

**Test Plan
for
Tertiary Butanol
CAS Number 75-65-0**

USEPA HPV Challenge Program Submission

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Submitted by:

Propylene Carbonate / t-Butyl Alcohol HPV Committee

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I. Introduction

The Propylene Carbonate / t-Butyl Alcohol HPV Committee and its member companies have committed voluntarily to develop screening level human health effects, environmental fate and effects, and physicochemical test data for tertiary butyl alcohol under the Environmental Protection Agency's High Production Volume Challenge Program.

t-Butanol is manufactured in a closed system as part of the process of manufacture of propylene oxide. It is used primarily in the manufacture of methyl t-butyl ether, a gasoline oxygenate. During its manufacture and primary use, there is little human exposure to t-butanol. High purity t-butanol is used as a solvent. There are no known consumer markets for t-butanol.

Data Summary

	Data Available	Data Adequate	Testing Recommended
Melting point	Yes	Yes	No
Boiling point	Yes	Yes	No
Vapor Pressure	Yes	Yes	No
Partition Coefficient	Yes	Yes	No
Water Solubility	Yes	Yes	No
Stability in Water	No	No	Yes
Transport	No	No	Yes
Photodegradation	No	Yes	No
Biodegradation	Yes	Yes	No
Acute Toxicity to Fish	Yes	No	Yes
Acute Toxicity to Invert.	Yes	Yes	No
Acute Toxicity to aq. plants	No	No	Yes
Acute Tox – oral	Yes	Yes	No
Acute Tox – dermal	Yes	Yes	No
Gene tox in vivo – MN	Yes	Yes	No
Gene tox – vitro – Ames	Yes	Yes	No
Repeat dose- oral (90 day)	Yes	Yes	No
Repeat dos-inhal (90 day)	Yes	Yes	No
Repeat dose-derm (2 year)	Yes	Yes	No
Reproductive toxicity	Limited	No	Yes
Developmental tox	Yes	Yes	No

II. Test Plan and Rationale

A. Physical Chemical Data

The physical /chemical data for t-butanol are found in standard reference works. The underlying data were not found, but additional testing is not justified. No data on the photodegradation of t-butanol are available. Because t-butyl alcohol does not absorb light in the region of 290-800 nm, photodegradation testing is not required by guideline (see EPA 835.2310). Data on the transport of t-butanol between environmental compartments are not adequate.

A comparison of various biodegradation study designs was performed by Gerike and Fischer (1979). The results of studies of t-butanol were reported from the following: Zahn Wellens, MITI, AFNOR Test DOC, Sturm Test, OCED Screening Test, Closed Bottle Test, and Coupled Units Test. The authors did not provide detailed information about the methodologies used for each test; however, the paper provides an overall assessment of the biodegradability of TBA. Further testing is not warranted.

Recommended testing:

Transport and Distribution between Environmental Compartments (EQC Level I modeling)

The US EPA has acknowledged that computer modeling techniques are an appropriate method for estimating chemical partitioning among environmental compartments. A widely used fugacity model is the Equilibrium Criterion Model (EQC; Mackay et al., 1996). EPA has indicated that it accepts Level I fugacity data as an estimate of chemical distribution values. In EQC level I, distribution is calculated as percent partitioned to 6 compartments within a unit world. Level I data are basic partitioning data that allow for comparisons between chemicals and indicate the compartment(s) to which a chemical is likely to partition.

B. ECOTOXICITY

A study of limited value on the acute toxicity of TBA to goldfish (*Carassius auratus*) was published in 1979 (Bridie et al., 1979). The study does not meet EPA or OECD study guidelines, and does not contain details of study conduct or results. Therefore, an acute toxicity study in fish is recommended (**OECD guideline 203 or EPA guideline 850.1075**).

The government of Germany performed a study (Kühn et al., 1989) of the toxicity of a number of chemicals to Daphnia. While some study details are not reported, the study is generally sound. Therefore, no additional testing is recommended.

No studies of TBA toxicity to algae are available, an acute toxicity study in algae is recommended (**OECD guideline 201**).

Recommended testing:

Acute fish toxicity (**OECD Guideline 203**)

Algal toxicity (**OECD Guideline 201**)

C. MAMMALIAN TOXICITY

Acute Toxicity

Numerous acute toxicity tests are available on t-butyl alcohol. Oral, dermal and inhalation tests all meet OECD and EPA test guidelines. T-Butanol has low acute toxicity. The oral LD₅₀ is 2733 mg/kg; the dermal LD₅₀ is >20000 mg/kg. By inhalation, the LC50 is >14,100 ppm from a 4 hour whole body exposure to t-butanol vapor; ataxia and dyspnea were seen immediately post exposure at 9700 or 14,100 ppm. No further testing is recommended.

Repeated dose Toxicity

NTP performed short term and chronic carcinogenesis studies in both mice and rats by administration in drinking water. In rats, t-butanol caused kidney toxicity at concentrations of 1.25 to 5 mg/l and increased kidney tumors in male rats at 5 mg/l (420 mg/kg/day). In mice, t-butanol caused thyroid toxicity at concentrations of 10 to 20 mg/l and marginally increased thyroid tumors in females at 20 mg/l (2110 mg/kg). No further testing is recommended.

Mutagenesis Studies

There are two Ames assays; both are negative. There are two mouse lymphoma assays; both are negative. There is an in vitro sister chromatid exchange assay that was positive without activation, but negative with activation. Blood taken from mice in the 90 day NTP study were analyzed for micronuclei; TBA did not induce an increase in MN. The mutagenicity battery is satisfactory; no further mutagenicity testing is recommended.

Developmental Toxicity/Teratogenicity

Results from two developmental toxicity studies in mice are available; neither of the studies is compliant with either OECD or EPA guidelines for developmental toxicity

testing. However, there is sufficient information to determine that t-butyl alcohol has limited ability to cause malformations. No further developmental toxicity testing is recommended.

Toxicity to Reproduction

No studies of the effect of t-butanol on reproductive function are available. No adverse effects were observed in sex organs in rats or mice in the subchronic or chronic studies of t-butanol conducted by NTP. However, several observations (i.e., decreased fetal body weights in teratology studies, altered postnatal development) suggest that further study of reproductive toxicity is warranted. An enhanced OECD 421 study is proposed and would investigate the effect of t-butanol on mating behavior, preimplantation, embryonic and fetal development, parturition, and postnatal survival and development until weaning.

Recommended testing:

An enhanced **OECD Guideline 421** study on t-butyl alcohol is recommended. Key features include:

- exposure of F0 males 14 days pre mating for minimum of 72 days total,
- exposure of F0 female from 14 days pre mating through day 20 gestation and lactation days 5-21,
- no direct exposure of offspring
- mating allowed for 14 days of one male to one female
- special attention will be paid to thyroids in F0 and F1 animals
- sperm analysis will not be performed because it has already been evaluated in 90-day studies.