

**National Toxicology Program**  
Toxicity Report Series  
Number 57

**NTP Technical Report**  
**on the Toxicity Studies of**  
**Benzyltrimethylammonium Chloride**

(CAS No. 56-93-9)

**Administered by Gavage**  
**to F344/N Rats and B6C3F<sub>1</sub> Mice**

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**U.S. Department of Health and Human Services**  
**Public Health Service**  
**National Institutes of Health**

## FOREWORD

The National Toxicology Program (NTP) is made up of four charter agencies of the U.S. Department of Health and Human Services (DHHS): the National Cancer Institute (NCI), National Institutes of Health; the National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health; the National Center for Toxicological Research (NCTR), Food and Drug Administration; and the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention. In July 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS. The NTP coordinates the relevant programs, staff, and resources from these Public Health Service agencies relating to basic and applied research and to biological assay development and validation.

The NTP develops, evaluates, and disseminates scientific information about potentially toxic and hazardous chemicals. This knowledge is used for protecting the health of the American people and for the primary prevention of disease.

The studies described in this Toxicity Study Report were performed under the direction of the NIEHS and were conducted in compliance with NTP laboratory health and safety requirements and must meet or exceed all applicable federal, state, and local health and safety regulations. Animal care and use were in accordance with the Public Health Service Policy on Humane Care and Use of Animals.

These studies are designed and conducted to characterize and evaluate the toxicologic potential of selected chemicals in laboratory animals (usually two species, rats and mice). Chemicals selected for NTP toxicology studies are chosen primarily on the bases of human exposure, level of production, and chemical structure. The interpretive conclusions presented in this Toxicity Study Report are based only on the results of these NTP studies. Extrapolation of these results to other species and quantitative risk analyses for humans require wider analyses beyond the purview of these studies. Selection *per se* is not an indicator of a chemical's toxic potential.

Listings of all published NTP reports and ongoing studies are available from NTP Central Data Management, NIEHS, P.O. Box 12233, MD E1-02, Research Triangle Park, NC 27709 (919-541-3419). Other information about NTP studies is available at the NTP's World Wide Web site: <http://ntp-server.niehs.nih.gov>.

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**to F344/N Rats and B6C3F<sub>1</sub> Mice**

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## PEER REVIEW

The draft report on the toxicity studies of benzyltrimethylammonium chloride was evaluated by the reviewers listed below. These reviewers serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, reviewers determine if the design and conditions of these NTP studies are appropriate and ensure that the Toxicity Study Report presents the experimental results and conclusions fully and clearly.

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## ABSTRACT



### BENZYLTRIMETHYLAMMONIUM CHLORIDE

CAS No. 56-93-9

Molecular Weight: 185.70

**Synonyms:** Ammonium, benzyltrimethyl-chloride (8Cl); BTM; BTMAC; N,N,N,-trimethyl-benzenemethanaminium chloride; trimethylbenzylammonium chloride (9Cl); TMBAC

Benzyltrimethylammonium chloride is widely used as a solvent for cellulose, a gelling inhibitor in polyester resins, a chemical intermediate, a paint dispersant, and an acrylic dyeing agent. It is also used in plant growth regulator compositions and synthetic processes. The National Institute of Environmental Health Sciences nominated benzyltrimethylammonium chloride for study due to its high production volume and the potential for occupational exposure, as well as the limited information on toxicity of this chemical. Male and female F344/N rats and B6C3F<sub>1</sub> mice received benzyltrimethylammonium chloride by gavage for 16 days or 13 weeks. Animals were evaluated for hematology, clinical chemistry, histopathology, neurotoxicity, and reproductive toxicity. Genetic toxicology studies were conducted in *Salmonella typhimurium* and in mouse peripheral blood erythrocytes.

In the 16-day studies, groups of five male and five female rats received 0, 16, 32, 63, 125, or 250 mg benzyltrimethylammonium chloride/kg body weight in deionized water by gavage, 5 days per week for 16 days. Groups of five male and five female mice received 0, 63, 125, 250, 500, or 1,000 mg/kg benzyltrimethylammonium chloride in deionized water by gavage, 5 days per week for 16 days. All rats in the 125 and 250 mg/kg groups, all mice in the 250, 500, and 1,000 mg/kg groups, and one 125 mg/kg female mouse died on day 1 of the studies. Clinical findings observed in 125 mg/kg male and female rats included abnormal breathing, ataxia, lethargy (males only), nasal and eye discharge, and tremors. Salivation was slightly increased in male and female rats in the 63 mg/kg groups. Female mice in the 125 mg/kg group had

a significantly greater absolute liver weight than that of the vehicle controls. No gross or microscopic changes observed in rats or mice were considered related to chemical administration.

In the 13-week studies, groups of 10 male and 10 female rats and mice received benzyltrimethylammonium chloride in deionized water by gavage at doses of 0, 12.5, 25, 50, or 100 mg/kg, 5 days per week for 13 weeks. Benzyltrimethylammonium chloride generally had little effect on the body weights of rats or mice. Final mean body weights of dosed animals were within 8% (rats) or 3% (mice) of the control group body weights. The deaths of two female rats and one male and one female mouse administered 100 mg/kg were the result of pharmacologic effects on the cardiovascular system. Some cholinergic effects including chromodacryorrhea, lacrimation, salivation, pupillary constriction, altered gait, and mild tremors were observed at nonlethal doses in rats; these effects were accompanied by alterations in body position. No significant target organ toxicity was observed in dosed rats or mice.

Benzyltrimethylammonium chloride was not mutagenic in *S. typhimurium* strain TA97, TA98, TA100, or TA1535, with or without S9 metabolic activation enzymes. However, significant increases in the frequency of micronucleated normochromatic erythrocytes were found in the peripheral blood of male and female mice administered benzyltrimethylammonium chloride by gavage for 13 weeks.

Based on the mortality observed in the 16-day and 13-week studies, rats and mice appeared to be equally sensitive to benzyltrimethylammonium chloride. The minimally toxic dose for rats and mice was estimated to be 50 mg/kg.

**NTP TECHNICAL REPORTS ON TOXICITY STUDIES  
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<b>TOX No.</b>	<b>Chemical</b>	<b>TOX No.</b>	<b>Chemical</b>
1	Hexachloro-1,3-butadiene	28	Tetrachlorophthalic Anhydride
2	<i>n</i> -Hexane	29	Cupric Sulfate
3	Acetone	30	Dibutyl Phthalate
4	1,2-Dichloroethane	31	Isoprene
5	Cobalt Sulfate Heptahydrate	32	Methylene Bis(thiocyanate)
6	Pentachlorobenzene	33	2-Chloronitrobenzene and 4-Chloronitrobenzene
7	1,2,4,5-Tetrachlorobenzene	34	1-Nitropyrene
8	D & C Yellow No. 11	35	Chemical Mixture of 25 Groundwater Contaminants
9	<i>o</i> -Cresol, <i>m</i> -Cresol, and <i>p</i> -Cresol	36	Pesticide/Fertilizer Mixtures
10	Ethylbenzene	37	Sodium Cyanide
11	Antimony Potassium Tartrate	38	Sodium Selenate and Sodium Selenite
12	Castor Oil	39	Cadmium Oxide
13	Trinitrofluorenone	40	$\beta$ -Bromo- $\beta$ -nitrostyrene
14	<i>p</i> -Chloro- $\alpha$ , $\alpha$ , $\alpha$ -trifluorotoluene	42	1,3-Diphenylguanidine
15	<i>t</i> -Butyl Perbenzoate	43	<i>o</i> -, <i>m</i> -, and <i>p</i> -Chloroaniline
16	Glyphosate	44	<i>o</i> -Nitrotoluene and <i>o</i> -Toluidine Hydrochloride
17	Black Newsprint Ink	45	Halogenated Ethanes
18	Methyl Ethyl Ketone Peroxide	50	Cyclohexanone Oxime
19	Formic Acid	51	Methyl Ethyl Ketoxime
20	Diethanolamine	52	Urethane
21	2-Hydroxy-4-methoxybenzophenone	53	<i>t</i> -Butyl Alcohol
22	N, N-Dimethylformamide	54	1,4-Butanediol
23	<i>o</i> -Nitrotoluene, <i>m</i> -Nitrotoluene, and <i>p</i> -Nitrotoluene	58	60-Hz Magnetic Fields
24	1,6-Hexanediamine	59	Chloral Hydrate
25	Glutaraldehyde	65	3,3',4,4'-Tetrachloroazobenzene
26	Ethylene Glycol Ethers	66	3,3',4,4'-Tetrachloroazoxybenzene
27	Riddelliine		