



Health and Environmental
Sciences Department

Closed-Patch Repeated Insult Dermal Sensitization Study of Tertiary Amyl Methyl Ether (TAME) in Guinea Pigs (Buehler Method)

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One of the most significant long-term trends affecting the future vitality of the petroleum industry is the public's concerns about the environment. Recognizing this trend, API member companies have developed a positive, forward-looking strategy called STEP: Strategies for Today's Environmental Partnership. This program aims to address public concerns by improving our industry's environmental, health and safety performance; documenting performance improvements; and communicating them to the public. The foundation of STEP is the API Environmental Mission and Guiding Environmental Principles.

API ENVIRONMENTAL MISSION AND GUIDING ENVIRONMENTAL PRINCIPLES

The members of the American Petroleum Institute are dedicated to continuous efforts to improve the compatibility of our operations with the environment while economically developing energy resources and supplying high quality products and services to consumers. The members recognize the importance of efficiently meeting society's needs and our responsibility to work with the public, the government, and others to develop and to use natural resources in an environmentally sound manner while protecting the health and safety of our employees and the public. To meet these responsibilities, API members pledge to manage our businesses according to these principles:

- ❖ To recognize and to respond to community concerns about our raw materials, products and operations.
- ❖ To operate our plants and facilities, and to handle our raw materials and products in a manner that protects the environment, and the safety and health of our employees and the public.
- ❖ To make safety, health and environmental considerations a priority in our planning, and our development of new products and processes.
- ❖ To advise promptly, appropriate officials, employees, customers and the public of information on significant industry-related safety, health and environmental hazards, and to recommend protective measures.
- ❖ To counsel customers, transporters and others in the safe use, transportation and disposal of our raw materials, products and waste materials.
- ❖ To economically develop and produce natural resources and to conserve those resources by using energy efficiently.
- ❖ To extend knowledge by conducting or supporting research on the safety, health and environmental effects of our raw materials, products, processes and waste materials.
- ❖ To commit to reduce overall emission and waste generation.
- ❖ To work with others to resolve problems created by handling and disposal of hazardous substances from our operations.
- ❖ To participate with government and others in creating responsible laws, regulations and standards to safeguard the community, workplace and environment.
- ❖ To promote these principles and practices by sharing experiences and offering assistance to others who produce, handle, use, transport or dispose of similar raw materials, petroleum products and wastes.

FOREWORD

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API STAFF CONTACT

Richard Rhoden, Ph.D., Health and Environmental Sciences Department

MEMBERS OF THE AIR/FUELS TOXICOLOGY HEALTH EFFECTS WORKGROUP

Russell D. White, Ph.D., *Chairman*, Chevron Research & Technology, Inc.

Rudolph J. Breglia, Ph.D., BP America, Inc.

Charles R. Clark, Ph.D., Unocal

Wayne Daughtrey, Ph.D., Exxon Biomedical Sciences, Inc.

David Duncan, Texaco, Inc.

Francis J. Koschier, Ph.D., ARCO

Charles A. Lapin, Ph.D., ARCO

David C. Logan, M.D., Mobil Corporation

John H. Mitchell, M.D., Amoco Corporation

Susan A. Rodney, Ph.D., Texaco, Inc.

Ceinwen A. Schreiner, Ph.D., Stonybrook Laboratories

David R. Steup, Ph.D., Shell Oil Company

Michael S. Wells, Ph.D., Amoco Corporation

American Petroleum Institute
Health and Environmental Sciences Department

QUALITY ASSURANCE STATEMENT

Study Title: Closed Patch Repeated Insult Dermal Sensitization
Study of TAME in Guinea Pigs

Testing Facility: Bio/dynamics, Now Pharmaco LSR

Testing Facility Number: 92-6222

This study was reviewed by API Quality Assurance personnel under the direction of API Management on the dates indicated below. This study was not required or intended to be in strict compliance with GLP Regulations.

<u>Date(s) of Inspection/Review</u>	<u>Type of Inspection</u>	<u>Date of Report to Management</u>
8/92	Protocol Evaluation	8/92
10/26/92	Laboratory Inspection and Data Audit	10/27/92
2/23/93	Draft Report Audit	2/23/93
9/12/94	Amended Final Report Review	9/12/94
9/19/94	Final Report Acceptance	9/19/94

Christine Sexsmith
Christine Sexsmith
Quality Assurance Coordinator

9/19/94
Date

PHARMACO::LSR

Pharmacology LSR Study No.: 92-6222

Closed-Patch Repeated Insult Dermal Sensitization
Study of Tertiary Amyl Methyl Ethyl (TAME) in Guinea Pigs
(Buehler Method)

ABSTRACT

This study was conducted for American Petroleum Institute in order to evaluate the allergic contact sensitization potential of Tertiary Amyl Methyl Ether (TAME) in guinea pigs. This study was performed at Pharmacology LSR Inc., Toxicology Service North America, P.O. Box 2360, Mettlers Road, East Millstone, New Jersey 08875-2360.

TAME was administered as received to twenty Dunkin Hartley guinea pigs (10/sex). Animals were clipped free of hair, the test material was applied to saturation (approximately 0.3 mls) beneath a Hilltop Chamber®. The chamber was occluded and left in place for six hours. This was performed once a week, for three weeks, for a total of three induction exposures. Twenty control animals (5/sex/control material) were similarly treated with Light Mineral Oil (control) or Dinitrochlorobenzene (DNCB; positive control). Challenge treatments followed the same administration procedure as the Induction Phase but at naive sites. In order to differentiate dermal reactions produced by irritation from those produced by sensitization, ten (5/sex) previously untreated animals were subjected to the same challenge procedures, with Light Mineral Oil, DNCB and TAME applied at three separate sites.

Observations for mortality were made twice daily. Body weights were obtained pretest and two days after challenge. Animals were also observed prior to treatment and weekly during the study for general health. Dermal evaluations were made approximately 24 and 48 hours after the first induction exposure and 24 and 48 hours after the challenge exposure.

All animals survived throughout the study. Most animals gained weight throughout the study; Animal No. 8082 (found dead one week after study termination) lost 18 grams of weight during the study.

All ten control animals challenged with 100% light mineral oil were free of significant dermal responses, as were the irritation control animals. The Incidence Index of sensitization to the mineral oil was 0%. The Severity Indices at 24 and 48 hours were 0, for both mineral oil-treated animals and irritation control animals.

All ten positive control animals treated with 0.3% DNCB exhibited clear dermal responses which were of greater incidence and severity than the responses seen in the irritation control animals to the same concentration. The Incidence Index of sensitization to DNCB was 100%. The Severity Indices at 24 and 48 hours were 1.8 and 2.1, respectively, for the positive control animals, compared the indices of 0.2 and 1.4 for the irritation control animals. This positive response to a known sensitizer demonstrated the susceptibility of this shipment of animals to sensitization.

All twenty animals challenged with 100% TAME were free of dermal responses as were the irritation control animals. The Incidence Index of sensitization to TAME was 0%. The Severity Indices at 24 and 48 hours were 0, for test material-treated animals and irritation control animals.

Under conditions of this study, TAME did not exhibit any potential to produce dermal sensitization in guinea pigs.



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PHARMACO LSR STUDY NO.: 92-6222

CLOSED-PATCH REPEATED INSULT DERMAL SENSITIZATION
STUDY OF TERTIARY AMYL METHYL ETHER (TAME) IN GUINEA PIGS
(Buehler Method)

Performed by: Pharmaco LSR Inc.
Toxicology Services North America
P.O. Box 2360, Mettlers Road
East Millstone, New Jersey 08875-2360

Submitted to: American Petroleum Institute
1220 L Street, Northwest
Washington, D.C. 20005

Attn: Robert T. Drew, Ph.D.

Date: October 8, 1993

Amended Report Date: September 8, 1994

I. INTRODUCTION

This study was conducted for American Petroleum Institute in order to evaluate the allergic contact sensitization potential of Tertiary Amyl Methyl Ether (TAME) in guinea pigs. This study was performed at Pharmaco LSR Inc., Toxicology Services North America, P.O. Box 2360, Mettlers Road, East Millstone, New Jersey 08875-2360, and used procedures based on the methods described by E.V. Buehler in "Delayed Contact Hypersensitivity in the Guinea Pig", Arch. Dermatol. 91: 171-175, (1965) and H.L. Ritz and E.V. Buehler in "Planning, Conduct and Interpretation of Guinea Pig Sensitization Patch Tests", in Current Concepts in Cutaneous Toxicity (Victor A. Drill and Paul Lazar, eds.), pp. 25-40; Academic Press, 1980.

This study was designed to follow the Buehler Test method which is the method specified in the following guideline:

TSCA (Toxic Substances Control Act): Health Effects Test Guidelines; Office of Toxic Substances; Office of Pesticides and Toxic Substances, United States Environmental Protection Agency, September 1985, Section 798.4100: Dermal Sensitization.

This report has been reviewed by the Quality Assurance Unit of Pharmaco LSR, Inc. to assure its conformance with the protocol and the raw data. All raw data and the original study protocol and final report will be retained on file in archives of the Testing Facility.

II. EXPERIMENTAL DESIGN

Group	Test/Control Material	Number of Animals	Concentration (%)	
			Induction	Challenge
IA	Light Mineral Oil ^a	10	100%	100%
IB	Light Mineral Oil (Irritation Control) ^d	10	-	100%
IIA	DNCB	10	0.5% ^b	0.3% ^c
IIB	DNCB (Irritation Control) ^d	10	-	0.3% ^c
IIIA	TAME	20	100%	100%
IIIB	TAME (Irritation Control) ^d	10	-	100%

^aSince TAME was administered at 100%, a sham control would have been adequate. However, because the protocol specified a vehicle control group, the vehicle used for the range-finding study was also used for the main study.

^bVehicle: 80% ethanol.

^cVehicle: acetone.

^dIrritation control groups were treated at challenge only. The same ten animals served as irritation controls for all three materials.