



Health and Environmental  
Sciences Department

# **Primary Skin Irritation Study in Rabbits of: API 91-01 and PS-6 Unleaded Test Gasolines**

**MARCH 1995**

TOXICOLOGY REPORT NUMBER 409  
CAIS ABSTRACT NO. 42-2014



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.



**Revised Final Report I**

**Primary Skin Irritation Study in Rabbits**

**of: API 91-01 and PS-6**

**for: American Petroleum Institute**

**Hill Top Biolabs Project No. 93-8177-21 (A)**

**HILL TOP BIOLABS, INC.**

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**The Hill Top Companies**

**Hill Top Research, Inc. · Hill Top Pharmatest, Inc. · Hill Top Biolabs, Inc.**



**Documents**

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American Petroleum Institute  
Health and Environmental Sciences Department

QUALITY ASSURANCE/GLP COMPLIANCE STATEMENT

Study Title: A Primary Skin Irritation Study in Rabbits of:  
API-9101 and PS-6 Unleaded Gasoline

Testing Facility: Hilltop, Biolabs, Inc.

Testing Facility Number: 93-8177-21 (A)

This study was reviewed by API Quality Assurance personnel under the direction of API Management on the dates indicated below.  
**This study was not intended to be in compliance with EPA TSCA GLP regulations.**

Copies of reports by API Quality Assurance personnel are available upon written request to the Director of the Health and Environmental Sciences Department of the American Petroleum Institute or his designee.

| <u>Date(s) of</u><br><u>Inspection/Review</u> (Reported to Management) | <u>Type of</u><br><u>Inspection</u> |
|------------------------------------------------------------------------|-------------------------------------|
| 10-18-93 (10-21-93)                                                    | Protocol Evaluation                 |
| 1-11-94 (1-12-94)                                                      | In-life inspection                  |
| 2-28-94 (2-28-94)                                                      | and data audit                      |
| 7-28-94 (7-28-94)                                                      | Draft Report Audit                  |
|                                                                        | Second Draft Report                 |
|                                                                        | Audit                               |
| 1-4-94 (1-4-94)                                                        | Final Report                        |
|                                                                        | Acceptance                          |

Christine Sexsmith  
Christine Sexsmith, B.S.  
Quality Assurance Coordinator

1/4/95  
Date

**American Petroleum Institute**  
1220 L Street, Northwest  
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202-682-8000

**Quality Assurance Final Report Acceptance**

**Study: Primary Dermal Irritation Study in Rabbits with API 91-01  
and PS-6 Unleaded Gasoline**

**Laboratory: Hill Top Biolabs, Inc.**

**Study Director: Theresa Morris**

The final report for the above-referenced study was recieved by  
API QA on January 4, 1995. The report is now final.

(It was noted that on each page, February 14, 1994 appears at the  
top of the page. This was the date of the first draft. Thinking  
this was an error, the laboratory was contacted. They indicated  
that it is their normal procedure to leave the original report  
date on each page.)

Prepared by:   
Chris Sexsmith

cc: R. Rhoden  
M. Mongillo

## FOREWORD

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## ACKNOWLEDGMENTS

THE FOLLOWING PEOPLE ARE RECOGNIZED FOR THEIR CONTRIBUTIONS OF TIME AND EXPERTISE DURING THIS STUDY AND IN THE PREPARATION OF THIS REPORT:

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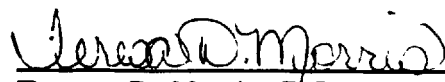
Ref.: 93-8177-21 (A)

February 1, 1995

**COMPLIANCE STATEMENT**

All aspects of this study, as defined in the Protocol and the Supplemental Instructions, were conducted in accordance with Good Laboratory Practice Standards (40 CFR).

HILL TOP BIOLABS, INC.

  
Teresa D. Morris, B.S. 2.2-95  
Study Director  
Acute Toxicology

American Petroleum Institute

Revised Final Report I

Ref.: 93-8177-21 (A)

February 1, 1995

**TITLE:** Primary Skin Irritation Study in Rabbits**CHEMICAL  
NAME:** API 91-01 and PS-6**AUTHOR:** Teresa D. Morris, B.S.**COMPLETION  
DATE:** December 20, 1994**PERFORMING  
LABORATORY:** Hill Top Biolabs, Inc.  
Main and Mill Streets  
Miamiville, OH 45147**STUDY NO.:** 93-8177-21 (A)**SPONSORED BY:** American Petroleum Institute  
1220 L Street, Northwest  
Washington, D.C. 20005**SUBMITTED BY:****DATE  
SUBMITTED:****EPA DATA  
REQUIREMENT:**

American Petroleum Institute

Revised Final Report I

Ref.: 93-8177-21 (A)

February 1, 1995

**HILL TOP BIOLABS, INC.****IMPORTANT NOTICE**

Hill Top Biolabs, Inc., submits this report with the understanding that no portion of it will be used for advertising or promotion without obtaining our prior written consent to the specific proposed use. When such use is desired we will be glad to assist in the preparation of mutually acceptable excerpts or summaries.

**TABLE OF CONTENTS**

|                                             |    |
|---------------------------------------------|----|
| Compliance Statement .....                  | 2  |
| Important Notice .....                      | 3  |
| Report Approval .....                       | 6  |
| Contributors .....                          | 7  |
| General Information .....                   | 8  |
| Sample Characterization and Stability ..... | 8  |
| Data Retention .....                        | 8  |
| Summary/Conclusions .....                   | 9  |
| Methods .....                               | 10 |
| Results .....                               | 12 |
| Protocol Deviation .....                    | 12 |
| Reference .....                             | 12 |

**TABLES**

|                                                                                                                   |    |
|-------------------------------------------------------------------------------------------------------------------|----|
| 1. Primary Skin Irritation in Rabbits Following a 4 Hour Dermal<br>Application of API 91-01 - Occluded .....      | 13 |
| 2. Primary Skin Irritation in Rabbits Following a 4 Hour Dermal<br>Application of API 91-01 - Semi-Occluded ..... | 14 |
| 3. Primary Skin Irritation in Rabbits Following a 4 Hour Dermal<br>Application of PS-6 - Occluded .....           | 15 |
| 4. Primary Skin Irritation in Rabbits Following a 4 Hour Dermal<br>Application of PS-6 - Semi-Occluded .....      | 16 |

American Petroleum Institute

Revised Final Report I

Ref.: 93-8177-21 (A)

February 1, 1995

**QUALITY ASSURANCE STATEMENT**

|                                   |    |
|-----------------------------------|----|
| Quality Assurance Statement ..... | 17 |
|-----------------------------------|----|

**APPENDICES**

|                                                         |    |
|---------------------------------------------------------|----|
| 1. Appendix 1 Cover Sheet .....                         | 18 |
| a. Copy of Protocol and Supplemental Instructions ..... | 19 |
| 2. Appendix 2 Cover Sheet .....                         | 31 |
| a. Copies of Raw Data .....                             | 32 |
| 3. Appendix 3 Cover Sheet .....                         | 46 |
| a. Report Amendment I .....                             | 47 |

American Petroleum Institute

Revised Final Report I

Ref.: 93-8177-21 (A)

February 1, 1995

REPORT APPROVAL

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American Petroleum Institute

Revised Final Report I

Ref.: 93-8177-21 (A)

February 1, 1995

**CONTRIBUTORS**

The following members of Hill Top Biolabs, Inc., contributed to the conduct and reporting of Project No. 93-8177-21 (A):

| <b><u>Name</u></b> | <b><u>Title</u></b>                                          | <b><u>Function</u></b>              |
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American Petroleum Institute

Revised Final Report I

Ref.: 93-8177-21 (A)

February 1, 1995

**GENERAL INFORMATION**

Project No.: 93-8177-21 (A)

Test/Protocol No.: Primary Skin Irritation Study in Rabbits  
2-4-2/03-09-90/REV 3

Testing Facility: Hill Top Biolabs, Inc.  
Main and Mill Streets  
Miamiville, OH 45147

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

Sample Identification: API 91-01 and PS-6

Source of Animals: Myrtle's Rabbitry Incorporated  
4678 Bethesda Road  
Thompson Station, Tennessee 37179

Date Study Initiated: January 7, 1994

Date Project Started: January 11, 1994

Date Project Completed: January 25, 1994

**SAMPLE CHARACTERIZATION AND STABILITY**

The Sponsor has assumed responsibility for test substance derivation, characterization, and stability testing.

The test material, API 91-01 unleaded gasoline (EPL #470), 40 ML Sample, Sampled 11/9/93, was received from Experimental Pathology Laboratories, Inc., on November 11, 1993, for use in this study. The test material was a clear pink liquid and was stored at room temperature in a brown glass jar with a brown plastic screw top. The test material was disposed of following the completion of testing.

The test material, PS-6 unleaded gasoline, was received from CIIT at the direction of the American Petroleum Institute on December 14, 1993, for use in this study. The test material was a clear yellow liquid and was stored at room temperature throughout the study in a metal canister with a blue plastic lid. The test material was disposed of following the completion of testing.

**DATA RETENTION**

The raw data and the original final report will be sent to the Sponsor within six months following completion of the study. The testing facility will retain a copy of these study records in the form of microfilm.

**SUMMARY/CONCLUSIONS**

This study was designed to assess the potential of API 91-01 and PS-6 to cause irritation after a single topical application to the intact skin of New Zealand White Rabbits under occluded and semi-occluded conditions.

The primary skin irritancy of undiluted API 91-01 and PS-6, occluded and semi-occluded, was separately evaluated in compliance with the conditions specified in the regulation for the enforcement of the Federal Insecticide, Fungicide, and Rodenticide Act (40 CFR), the Toxic Substances Control Act (40 CFR), and the OECD Guidelines.

The Primary Irritation Index (PII) and classification criteria for the two occlusion methods for the two different test materials are presented in the following table:

| Test Material | Occlusion Method | Primary Irritation Index (PII) | Primary Irritation Category <sup>a</sup> | Skin and/or Coloration Changes                           | Irritation persisting 72 Hours following application | Irritation persisting 7 Days following application | Irritation Persisting 14 Days following application |
|---------------|------------------|--------------------------------|------------------------------------------|----------------------------------------------------------|------------------------------------------------------|----------------------------------------------------|-----------------------------------------------------|
| API 91-01     | Occluded         | 4.8                            | Moderate Irritant                        | desquamation on site                                     | well-defined                                         | very slight                                        | very slight                                         |
|               | Semi-Occluded    | 4.3                            | Moderate Irritant                        | desquamation on site and coriaceousness at edges of site | moderate                                             | very slight                                        | none                                                |
| PS-6          | Occluded         | 4.8                            | Moderate Irritant                        | desquamation on site                                     | moderate                                             | very slight                                        | none                                                |
|               | Semi-Occluded    | 3.7                            | Moderate Irritant                        | desquamation on site and coriaceousness at edges of site | moderate                                             | very slight                                        | none                                                |

<sup>a</sup>Draize et al.

Primary Irritation Index (PII) shown in the table above is based on the scores collected at the 24 and 72 hour readings.

Clinical observations of each animal noted at the time of scoring indicated normal appearance and behavior throughout the study.

No evidence of corrosion (necrosis) was found.

**METHODS** (See Appendix 1 for Protocol and Supplemental Instructions)

This standardized procedure was conducted according to the general conditions of the Protocol and specifically as designated in the Project Instruction Sheet and Supplemental Instructions, as applicable. As such, it satisfies the criteria established by the Federal Insecticide, Fungicide, and Rodenticide Act (40 CFR), the Toxic Substances Control Act (40 CFR), and the OECD Guidelines.

A total of four groups of six young adult, New Zealand White rabbits (three males and three females per group) were used in this study. The groups were divided into two groups per test material, each test material having an occluded group and a semi-occluded group.

Each animal in each occluded group received a 0.5 ml quantity of the appropriate undiluted test material onto a 1" x 1" gauze square. The patches were then held in place with adhesive tape. The test material was applied in this manner to one intact skin site per animal. After application of the patch, the trunk of each rabbit was wrapped with rubber dental dam which was secured with staples. An outer layer of gauze was then wrapped around the trunk of each animal and secured with tape. Each animal was fitted with an Elizabethan collar to prevent wrapping and patch removal. Following approximately 4 hours of exposure, the restraining device, wrapping, and patches were removed. The test sites were wiped free of residual test material by a gentle sponging using a paper towel moistened with tap water.

The semi-occluded method incorporated two Webri<sup>®</sup> pads, which were removed from the adhesive, and placed on top of each other. Each animal in each semi-occluded group received a 0.5 ml quantity of the appropriate undiluted test material applied to the pads. The pads were then held in place with adhesive tape. The test material was applied in this manner to one intact skin site per animal. After application of the pads each animal was fitted with an Elizabethan collar to prevent wrapping and patch removal. Following approximately 4 hours of exposure, the restraining device and pads were removed. The test sites were wiped free of residual test material by a gentle sponging using a paper towel moistened with tap water.