



Consumer Product Testing Co.

EST. 1975

FINAL REPORT


CLIENT: Applied Dental Sciences
481 Pleasant Street
Lee, Massachusetts 01238

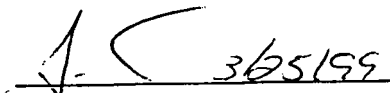
AUTHORIZING AGENT: Beth A. McGowan
Technical Director

TEST: Acute Oral LD₅₀ in Rats

TEST ARTICLE: Hydrogen Peroxide Gel, Lot#: 1/14/99, ID#: 98-305-27

**EXPERIMENT
REFERENCE NUMBER:** T99-0017-3


Kathleen Alworth, B.A.
Director of Quality Assurance


Steven Nitka
Laboratory Director
Vice President

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Consumer Product Testing Co.

QUALITY ASSURANCE UNIT STATEMENT

Study No.: T99-0017-3

The objective of the Quality Assurance Unit (QAU) is to monitor the conduct and reporting of nonclinical laboratory studies. These studies have been performed under Good Laboratory Practice principles (including government regulations to the extent applicable) and in accordance to standard operating procedures and applicable standard protocols. The QAU maintains copies of study protocols and standard operating procedures and has inspected this study on the date(s) listed below. The findings of these inspections may have been reported to management and the Study Director.

Dates of data inspections: March 25, 1999

Professional personnel involved:

Steven Nitka, B.S.

Vice President

Laboratory Director

(Study Director)

Lillian Deniza, B.S.

Laboratory Supervisor

Melissa Pandorf, B.S.

Technician

OnChi Cheung, B.S.

Quality Assurance Associate

The representative signature of the Quality Assurance Unit on the front page signifies that this study has been performed in accordance with standard operating procedures, study protocols and the Good Laboratory Practice principles.



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Final Report Summary

CLIENT: Applied Dental Sciences

STUDY NO.: T99-0017-3

REFERENCE: B.A. McGowan

TEST ARTICLE: Hydrogen Peroxide Gel, Lot#: 1/14/99, ID#: 98-305-27

TEST ARTICLE RECEIPT DATE: January 21, 1998

EXPERIMENTAL INTERVAL: January 29, 1999 to March 16, 1999

Acute Oral LD₅₀ in Rats

Method: Albino rats, 200 – 252 g, sexes as indicated below, were dosed singly at range finding levels and in groups of ten (5M:5F) per test level. Each animal received a single oral dose of the test article. Animals were observed for pharmacological activity and drug toxicity 1, 3, 6, and 24 hours after treatment, and daily thereafter for a total of 14 days. Animals sacrificed at the end of the 14 day observation period, as well as non-survivors, were subjected to gross necropsy, with all findings noted. The test article was used as received (Sp.g. = 1.11).

Results:

	Dose Level (g/kg)	Sex	No. Dead/No. Dosed (M:F)	Mortality (%)
Range Finding:	1.00	1M	0/1	0
	5.00	1M	0/1	0
	10.00	1F	0/1	0
	20.00	1F	0/1	0
	40.00	1M	1/1	100
Test Dose Levels:	18.89	5M:5F	1/5:0/5	10
	23.80	5M:5F	1/5:2/5	30
	25.30	5M:5F	4/5:5/5	90
	26.78	5M:5F	4/5:5/5	90
	30.00	5M:5F	4/5:5/5	90

Conclusion: Under the conditions of this test, this test article elicited the following oral LD₅₀ in rats: LD₅₀ = 24.5 (22.28 – 26.95) g/kg.

Acute Oral LD₅₀ in Rats

This test was designed to determine the acute oral LD₅₀ of the test article in rats. The methods described by Hagan¹ served as a guide.

Wistar-strain, albino rats were used for this test. Animals were obtained from Ace Animals in Boyertown, Pennsylvania, in equal numbers of each sex and approximately six to nine (6 to 9) weeks of age. Upon receipt, the animals were carefully checked for respiratory difficulty, ocular or nasal lacrimation, dehydration, diarrhea, and general condition.

The animals were acclimated for at least seven (7) days prior to test initiation. They were housed in stainless steel cages with indirect bedding, in a room with a 12 hour light/dark cycle. The room temperature was controlled, to provide for the health and comfort of the animals with an approximate range of 65° to 75° F. The humidity was also monitored. Diet consisted of Lab Diet Certified Rodent Diet #5002, as well as water, *ad libitum*.

Prior to test initiation, the test article's mass to volume relationship (specific gravity) was determined to facilitate volumetric dosing.

An initial phase of the test, a dosage level range finding, was performed to determine a possible range for the LD₅₀. One (1) rat was dosed at each of several dose levels, with a wide spread between successive levels. The lowest dose level at which mortality occurred served as the guide for choosing the first of several graded dose levels used for the LD₅₀ calculation.

Twenty-four (24) hours prior to dosing, all rats were reexamined for general condition as described above. A group of rats, sexes equally distributed, and of sufficient weight to assure a fasted body weight between 200 and 300 grams, was labeled and set aside.

The following day, after approximately 18 hours of fasting, each rat was weighed and marked with an ear clip. Individual doses, calculated on the basis of body weight and the dose level being administered, were given using a stainless steel intragastric feeding needle of sufficient bore to allow even passage of the test article in its dosing form. Rats were then returned to their cages, where food and water were available *ad libitum*. Each cage was uniquely labeled with respect to job number, test article, dose level, sex, animal number(s), and date of dosing.

The animals were observed for signs of pharmacological activity and drug toxicity at 1, 3, 6, and 24 hours post-dosage. Observations were made at least once daily thereafter for a total of 14 days.

¹E.C. Hagan, "Acute Toxicity", *Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics*, (The Association of Food and Drug Officials of the United States. 1959). pp. 17 - 25.

Animals sacrificed at the end of the 14 day observation period, as well as non-survivors, were weighed and subjected to complete gross necropsy, with all findings noted. Sacrificing was accomplished via carbon dioxide asphyxiation.

The oral LD₅₀, including 95% confidence limits, was calculated using the method of Litchfield and Wilcoxon².

²J.T. Litchfield and F. Wilcoxon, "A Simplified Method of Evaluating Dose-Effect Experiments", *Journal of Pharmacology and Experimental Therapeutics*, 96, (1949), pp. 99 - 107.