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J.T. Fruin, DVM, PhD, LTC, VC; M.A. Hanes, DVM, CPT, VC; K. Black, MD, LTC, MC; and V.L. Gildengor PhD, DAC	
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TECHNICAL NOTE NO. 82-29TN

DERMAL SENSITIZATION POTENTIAL OF CANDIDATE INSECT

**REPELLENTS: LAIR Formulation (CHF1)** 

N-(n-octyl) glutarimide (CHR2)

N-(n-hexyl) glutarimide (CHR3)

(E) 1,2,3,4-tetrahydro-6-methyl-1-(2-methyl-1-oxo-2-butenyl)quinoline (CHR5) 1,2,3,4-tetrahydro-6-methyl-1-(3-methyl-1-oxo-2-butenyl) quinoline (CHR6)

JOHN T. FRUIN, DVM, PhD, LTC VC MARTHA A. HANES, DVM, CPT VC KENNETH BLACK, MD, LTC MC and VIRGINIA L. GILDENGORIN, PhD

TOXICOLOGY GROUP, DIVISION OF RESEARCH SUPPORT DIVISION OF CUTANEOUS HAZARDS and INFORMATION SCIENCES GROUP

 FEBRUARY 1982
 Toxicology Series 12

 Image: Control of the series of the serie

LETTERMAN ARMY INSTITUTE OF RESEARCH PRESIDIO OF SAN FRANCISCO CALIFORNIA 94129

## Toxicology Series 12 - Fruin, Hanes, Black, and Gildengorin

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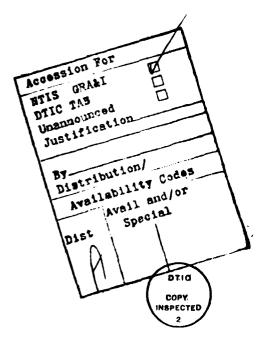
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In conducting the research described in this report, the investigation adhered to the "Guide for the Care and Use of Laboratory Animals," as promulgated by the Committee on Revision of the Guide for Laboratory Animal Facilities and Care, Institute of Laboratory Animal Resources, National Research Council.

This material has been reviewed by Letterman Army Institute of Research and there is no objection to its presentation and/or publication. The opinions or assertions contained herein are the private views of the author(s) and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense. (AR 360-5)

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(Signature and date)



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PREFACE

Dermal Sensitization GLP Study Report

TESTING FACILITY: Letterman Army Institute of Research Presidio of San Francisco, CA 94129

SPONSOR: Letterman Army Institute of Research Presidio of San Francisco, CA 94129

PROJECT: Prevention of Military Disease Hazards 3M1677ØA871

GLP STUDY NUMBER: 81008

STUDY DIRECTOR: LTC (P) John T. Fruin, DVM, PhD, VC, Diplomate of American College of Veterinary Preventive Medicine

PRINCIPAL INVESTIGATOR: CPT Martha A. Hanes, DVM, VC

DERMATOLOGIST: LTC Kenneth Black, MD, MC Diplomate of American Board of Dermatology

STATISTICIAN: Virginia L. Gildengorin, PhD, DAC

RAW DATA: A copy of the final report, study protocol, as amended, raw data, and standard operating procedures will be retained in the LAIR Archives.

TEST SUBSTANCES: A. LAIR formulation consisting of 50% N,Ndiethyl-m-toluamide (m-DEET), 25% Dow Corning 200 Fluid 1000 cs. viscosity and 25% isopropyl alcohol (CHF1).

B. N-(n-octyl)glutarimide (CHR2).

C. N-(n-hexyl)glutarimide (CHR3).

- D. (E) 1,2,3,4-tetrahydro-6-methyl-1-(2-methyl-1-21-oxo-2-butenyl)quinoline (CHR5).
- E. 1,2,3,4-tetrahydro-6-methyl-1(3-methyl-1-oxo-2-butenyl)quinoline (CHR6).
- WORK UNIT: 201 Development of Repellents Against Medically Important Arthropods.
- PURPOSE: The purpose of this study was to determine the dermal sensitization potential of the test substances listed above.

### ACKNOWLEDGMENTS

The authors wish to thank MAJ George H.G. Eisenberg, PhD, MS; SSG Lance White; SP5 Leonard Sauers, BA; SP4 Thomas P. Kellner, BA; SP4 Larry Mullen, BS; PFC Evelyn Zimmerman; John Dacey; and Carolyn Lewis, MS, for their assistance in performing the research, administration, and support in planning, executing, and reporting the study. We also wish to thank Dr. A. McCreesh of the U.S. Army Environmental Health Agency for advice in establishing the test procedures and interpretation of results.

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## Signatures of Principal Scientists Involved in the Study

We, the undersigned, believe the study, GLP Study No. 81008, described in this report to be scientifically sound and the results and interpretations to be valid. The study was conducted to comply, to the best of our ability, with the Good Laboratory Practice Regulations for Non-clinical Laboratory Studies outlined by the Food and Drug Administration.

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MARTHA A. HANES, DVM /DATE CPT, VC Principal Investigator

JOHN T. FRUIN, DVM, PhD /DATE LTC (P), VC Study Director

hermette Back Maine Unaima à 1911 de mar 7 Jan 82

KENNETH BLACK, MD /DATE LTC, MC Dermatologist

VIRGINIA L. GILDENGORIN, PhD/DATE DAC, GS-12 Statistician

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#### DEPARTMENT OF THE ARMY

LETTERMAN ARMY INSTITUTE OF RESEARCH PRESIDIO OF SAN FRANCISCO, CALIFORNIA 94129

REPLY TO ATTENTION OF

SGRD-ULZ-QA

25 June 1981

MEMORANDUM FOR RECORD

SUBJECT: Report of GLP Compliance

1. I hereby certify that in relation to LAIR GLP study 81008 the following inspections were made:

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2. The report and raw data for this study were audited on 18 Aug 81.

3. Inspection findings were reported to the Study director on 15 May 81, 28 May 81, and 8 Jun 81. These inspections are also included in the July 1981 report to Management and the Study Director.

John C Johnson

JOHN C. JOHNSON CPT, M: Quality Assurance Officer

DERMAL SENSITIZATION POTENTIAL OF CANDIDATE INSET REPELLECTS: CHF1, CHR2, CHR3, CHR5, CHR6

Letterman Army Institute of Research (LAIR) has been directed to participate in the development of better insect repellents for the protection of soldiers from insects and insect-borne diseases in the field. In the last several years, investigators in the Division of Cutaneous Hazards at LAIR have tested a large number of chemical compounds submitted by SRI-International, the U.S. Department of Agriculture (USDA), and private industry against a variety of mosquitoes, sand flies, fleas, bugs, ticks, and mites in animal and in in vitro test systems. Several of these materials have shown sufficient repellent activity and persistence on the skin of animals to warrant consideration for use in lieu of, or in conjunction with, the current troop-issue repellent, 71.25% diethyl-toluamide (n-DEET) The investigators also evaluated a number of new in ethanol. formulations of m-DEET prepared at LAIR or submitted by private industry. Several of these new formulations have been more persistent on the skin in tests on animals than the current troop-issue repellent.

We now plan to test on human volunteers the most promising of the new compounds and formulations to confirm the results that have been obtained in the in vitro and animal tests and to evaluate the performance of these agents under conditions of actual use. Before this can be done, it is necessary to obtain certain toxicity data on each compound or formulation to insure that it is safe for application to the skin. The basic toxicity tests required for experimental use of the new compounds and formulations on human volunteers are prescribed by the LAIR and U.S. Army Medical Research and Development Command (USAMRDC) Human Use Committees. If adverse toxicity data are obtained in these tests, the respective material(s) will be eliminated from consideration, and the prospective tests on human volunteers will not be carried out. The toxicity testing program thereby serves both as a safety factor and secondary screen in the repellent development scheme.

### Objective of the Study

The objective of this study was to determine the dormal

sensitization potential of candidate insect repellents CHF1, CHR2, CHR3, CHR5, and CHR6.

## METHODS

Historical Listing of Study Events

22 Apr 81	Guinea pigs arrived at LAIR. They were observed for signs of clinical illness, sexed, ear-tagged, weighed, and housed individually in cages in room AS1410 for a one-week guarantine period.
29 Apr 81	Animals were removed from quarantine status and weighed.
30 Apr 81	Animals received the first sensitizing dose of Ø.05 ml of Ø.1% test substance. Injection sites were scored and the values recorded after 24 and 48 hr.
2,5,7,9,12, 14,16,19 and 21 May 81	Animals received sensitizing doses of Ø.1 ml of test substance. Injections were scored and the values recorded 24 and 48 hr after each injection.
5,12,19, 26 May and 4 Jun 81	The animals were weighed.
4 Jun 81	The animals received the challenge dose of $\emptyset.1$ ml of $\emptyset.1$ % test substance.
5 Jun 81	Injection sites were scored and the values recorded for the 24-hr reaction.
6 Jun 81	Injection sites were scored and the values recorded for the 48-hr reaction.

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Chemical Data

A. CHF1 - a formulation of 50% N,N-diethyl-m-toluamide (m-DEET) in 25% Dow Corning 200 Fluid and 25% isopropyl alcohol. The formulation is a suspension that must be agitated to maintain homogeneity (1,2).

1. Chemical Name: N,N-diethyl-m-toluamide

Chemical Abstracts Service Registry No.: 134-62-3

CH2

Molecular formula/structure:  $C_{1,2}H_{1,7}NO$ 

Molecular weight: 191.3

pH: N/A nonaqueous

Physical state: Liquid

Boiling range: 288-292C

Compound density: 0.996

Compound refractory index:  $n_D^{20} = 1.5212$ 

Contaminants: Contains ortho and para isomers

Manufacturer: Aldrich Chemical Co., Inc., Milwaukee, WI 53233

Manufacturer Lot No.: Ø32697 (purity at purchase was 98%, April 1979)

Published Toxicity Data:

Oral LD<sub>50</sub> (rat) 2000 mg/ky

Dermal  $LD_{50}$  (rabbit) 3180 mg/kg

Other information:

Listed as an irritant to eyes and mucous membranes. Can cause central nervous system distrubances.

2. Chemical Name: Dow Corning 200 Fluid, 1000 cs. viscosity (Dimethylsiloxane polymer)

Chemical Abstracts Service Registry No.: None.

Molecular formula: linear polydimethyl siloxanes

Molecular weight: about 25,000

pH: N/A nonaqueous

Physical state: fluid

Specific gravity: 0.971

Stability: high thermal stability — manufacturer says unlimited useful life when stored at 25 C

Compound refractory index:  $n_D^{20} = 1.403$ 

Manufacturer: Dow Corning Corp., Midland, MI 48640

Manufacturer Lot No.: MA 129889

Other information:

Water repellent, low surface tension, low toxicity, essentially non-toxic and nonirritating (although discomfort may result if rubbed into the eye).

3. Chemical Name: isopropanol(3)

Chemical Abstracts Service Registry No.: 67-63-0

Molecular structure: CH<sub>3</sub>CHOHCH<sub>3</sub>

Molecuar weight: 60.09

pH: N/A nonaqueous

Physical state: clear colorless liquid

Boiling point: 82.5C

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Compound density: 0.7854

Manufacturer: VWR Scientific Products, San Francisco, CA 94119

Manufacturer's Control Code: A17

Published toxicity data:

Oral  $LD_{50}$  (rat) = 5840 mg/kg

Dermal LD<sub>50</sub> (rabbit) = 16,000 mg/kg

Other information:

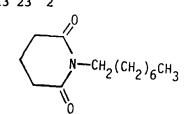
Listed as an irritant to eyes; acts as a local irritant and in high concentration as a narcotic. It can cause corneal burns and eye damage. Acts much like ethanol in regard to absorption and metabolism and elimination, but with a stronger narcotic action.

- B, CHR2
  - 1. Chemical Name: N(n-octyl)glutarimide

Chemical Abstracts Service Registry Information No.: Unknown

Molecular formula/structure: C13H23NO2

Molecular weight: 225.3



pH: N/A nonaqueous

Physical state: liquid

Boiling Point: 134 @ Ø.5 mm Hg

Compound density: unknown

Compound refractory index: unknown

Stability: unknown

Names of contaminants and percentages: unknown

Manufacturer: SRI International 333 Ravenswood Ave. Menlo Park, CA 94025

Manafacturer Lot No.: unknown

C. CHR3

1. Chemical name: N-(n-hexyl)glutarimide

Chemical Abstracts Service Registry No.: Unknown

Molecular formula/structure:  $C_{11}H_{19}NO_2$ 

N-сн<sub>2</sub>(сн<sub>2</sub>)<sub>4</sub>сн<sub>3</sub>

Molecular weight: 197.3

pH: N/A nonaqueous

Physical state: liquid

Boiling point: 115 C @ Ø.5 mm Hg

Compound density: unknown

Compound refractory index: unknown

Stability: unknown

Names of contaminants and percentages: unknown

Manufacturer: SRI Intenational 333 Ravenswood Ave. Menlo Park, CA 94025

Manufacturer Lot. No.: 3905H23/31

D. CHR5

1. Chemical Name: (E) 1,2,3,4-tetrahydro-6-methyl-1-(2-methyl-1-oxo-2-butenyl)quinoline

Chemical Abstracts Service Registry No.: Unknown

Molecular formula/structure: C<sub>15</sub>H<sub>19</sub>NO

Molecular weight: 229

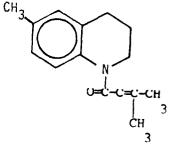
Physical state: liquid

Boiling point: unknown

Compound density: unknown

Compound refractory index: unknown

Stability: unknown



Names of contaminants and percentages: unknown

Manufacturer: SRI International 333 Ravenswood Ave. Menlo Park, CA 94025

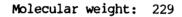
Manufacturer Lot No.: 4214H31

E. CHR6

1. Chemical Name: 1,2,3,4-tetrahydro-6-methyl-1-(3-methyl-1-oxo-2-butenyl)quinoline

Chemical Abstracts Service Registry No.: Unknown

Molecular structure: C<sub>15</sub>H<sub>19</sub>NO



pH: N/A nonaqueous

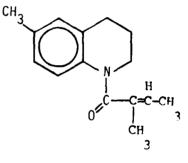
Physical state: liquid

Boiling range: unknown

Compound density: unknown

Compound refractory index: unknown

Stability: unknown



Names of Contaminants and Pecentages: unknown

Manufacturer: SRI International 333 Ravenswood Ave. Menlo Park, CA 94025

Manufacturer Lot No.: 3905H83

Animal Data

Animal: albino guinea pig

Sex: male

Justification: The albino guinea pig is a proven acceptable model to determine dermal sensitization potential.

Source: Charles River Laboratories

Pre-test conditioning:

- 1. Quarantine from 22-29 April 1981
- 2. Animals' backs were close clipped.

Method of randomization: Manual, random numbers table

Number of animals on test: 10 animals per test substance

Age of animals at start of study: Young adults

Animal weight range at start of study: 250-400 g start, 550-750 g end Condition of animals at start of study: Normal

## Environmental conditions

- <u>Caging</u>: Number/cage = 1; type cage used = stainless steel, wire mesh bottom, battery type, no bedding, automatic flushing
- Diet: Purina Guinea Pig Chow No. 5025 ad libitum supplemented with about 100 cm<sup>2</sup> of fresh lettuce daily
- <u>Water</u>: Central line to cage battery with automatic lick dispensers

Temperature:  $70 \pm 5 F (21 \pm 3 C)$ 

Relative Humidity: 70 + 10%

Photoperiod: 0530-2000 hr/day (14-1/2 hr light)

## Dosing Levels

The test substance concentration throughout the study was  $\emptyset$ .1%.

- A. CHF1 initial dose Ø.Ø5 ml; 9 sensitizing doses of Ø.1 ml and challenge dose of Ø.1 ml
- B. CHR2 initial dose Ø.Ø5 ml; 9 sensitizing doses of Ø.1 ml and challenge dose of Ø.1 ml
- C. CHR3 initial dose 0.05 ml; 9 sensitizing doses of 0.1 ml and challenge dose of 0.1 ml
- D. CHR5 initial dose 0.05 ml, 9 sensitizing doses of 0.1 ml and challenge dose of 0.1 ml

E. CHR6 - initial dose Ø.05 ml, 9 sensitizing doses of Ø.1 ml and challenge dose of Ø.1 ml

## Treatment for Infectious Diseases

During the course of this study, no animal required treatment of infectious disease.

### Rationale for Selection of Vehicle

Saline and propylene glycol have been used successfully as vehicles for this test and were compatible with the test substance.

### Test Substance Preparation

A 3% stock solution of each test substance was prepared by adding  $\emptyset.3 \text{ ml}$  of test substance to 9.7 ml of propylene glycol and refrigerated in Room LR1155. Just before sensitization injections,  $\emptyset.5 \text{ ml}$  of stock solution was added to 14.5 ml of physiologic saline to achieve  $\emptyset.1$ % test substance preparation.

## Animal Preparation

The hair was removed by close-clipping a strip running from the posterior flank to the scapular region on each side and across the back prior to initial dosing. Clipping was repeated as necessary for injection and accurate scoring.

### Route of Administration

The test substance and carrier vehicle were injected intradermally using a 26-gauge needle and a tuberculin syringe.

### Dosing

An initial dose of  $\emptyset.05 \text{ ml}$  of 0.1% solution of test substance was injected intradermally in the right scapular area. Two days later, an

injection of  $\emptyset$ .1 ml of  $\emptyset$ .1% test substance was given. Injections were repeated three times weekly on alternate days for three weeks, starting in the right lumbosacral area. Similar injections of carrier solution (3.3% propylene glycol in physiologic saline) were injected at corresponding locations on the left side of the animal's back. Two weeks following the final injection, a challenge dose of  $\emptyset$ .1 ml of  $\emptyset$ .1% solution of test compound and carrier solution were administered on the right and left sides, respectively.

### Scoring of Skin Reaction

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The most recent injection sites (test substance, right side; vehicle control, left side) were scored at 24 and 48 hr after injection. The scoring system was designed so that the intensity of the skin reaction was represented by a proportionate numerical value. The product of the width and length (in millimeters) of the lesion was multiplied by the following reaction scores:

$\emptyset$ = needle puncture	5 = bright red
1 = very faint pink - no wheal	6 = edema < 1 mm in height
2 = faint pink	$7 \approx \text{edema} > 1 \text{ mm}$ in height
3 = pink	8 ≈ necrosis < 1 sq mm
4 = red	9 = necrosis > 1 sq mm

The width and length of the reaction was measured with an adjustable micrometer.

CHANGES TO ORIGINAL METHODS AND OBJECTIVES

- . Compound purity and stability were not monitored because definitive analytical methods for monitoring test substance purity and stability have not been developed.
- Complete chemical characterization of test substance will be reported when it becomes available.
- Experience at the Army Environmental Health Agency (AEHA), Edgewood Arsenal, MD, has shown that a Ø.1% solution of test substance reduces chemical irritation and is sufficient for dermal sensitization. The recommendations of AEHA for

injecting the test substance at a concentration of 0.1% were followed.

- Certified feed was not available for the animals (guinea pigs in this study; however, fresh lettuce supplemented the guinea pig chow. The study was short (22 April-8 June 1981); experience has shown that certified feed is desirable but not necessary.
- The challenge dose was given as two 0.05 ml interdermal injections approximately 3 hr apart in the same site, equaling the correct dose of 0.1 ml of test substance.

#### RESULTS AND DISCUSSION

Scores were taken 24 and 48 hr after the initial sensitizing and challenge doses. The data are recorded as tabular average and final score values (Tables 1A-C through 5A-C for CHF1, CHR2, CHR3, CHR5, and CHR6, respectively).

Average final scores for CHFI, CHR2, and CHR3, i.e., test substance score minus diluent scores, remained under 10 throughout the sensitizing period and the challenge dose. The data collected clearly showed no indication of sensitization potential at this dose level for these three test substances.

The grand average final scores for CHR5 ranged from -0.2 on the first dose to 220.4 on dose number 7. Scores on later doses were lower and the grand average of the challenge dose was 126. The data collected did not present the classic picture of a dermal sensitizing agent, but there was clearly a dosage carryover effect. The linear correlation coefficient of the combined average score compared to dose number was low ( $r^2 = 0.55$ ).

Substances that produce dermal sensitization classically cause higher scores after 48 hr than after 24 hr. A comparison of individual and average final 24 and 48-hr scores was inconclusive in determining which scores were higher.

There are no proven statistical techniques available for data of this type; consequently, classification must be made on the experience

and scientific judgement of the investigator. Substance CHk5 shows some characteristics of a sensitizing agent and some characteristics of a dermal irritant.

The grand average final scores for CHR6 ranged from 0.15 on the first dose to 114 on dose number 7. Scores on later doses were lower and the grand average of the challenge dose was 3.05. The data were similar to that collected for CHR5 in that the classical dose response was not evident. The correlation coefficient was quite low ( $r^2 = 0.07$ ) and the 48-hr score appears to be less than the 24-hr score.

### CONCLUSION

We believe that test substances CHF1, CHR2, and CHR3 are non-sensitizing. These conclusions are based on the low scores throughout the dosing and for the challenge dose.

Scores were considerably higher for CHR5 and CHR6. There was a progressive increase in test scores as the number of doses increased up to dose number 7; then the scores declined and did not increase with the challenge dose. The low correlation coefficient and the fact that the 48-hr scores were not greater than the 24-hr scores, indicate that no definite conclusions can be reached regarding the dermal sensitization potential of CHR5 and CHR6.

#### RECOMMENDATIONS

We recommend that compounds CHF1, CHR2, and CHR3 undergo further toxicological testing with the eventual goal being Federal clearance for general use as an insect repellent. We also recommend the dermal sensitization testing of compounds CHR5 and CHR6 be repeated with efforts made to test these compounds at a dose below the irritation level.

### **BIBLIOGRAPHY**

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- The Merck Index. An Encyclopedia of Chemicals and Drugs (Ninth edition), edited by W. Windholz. Rahway, NJ: Merck & Co., Inc., 1976
- 3. Dangerous Properties of Industrial Materials (Fifth edition). N. Irving Sax Van Nostrand Reinhold Company. New York: Litton Educational Publishing, Inc., 1979

# APPENDIX A

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Table	1C.	•	•	٠	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	21
Table	2A.	•	•	•	•	٠	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	22
Table	2B.	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	23
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Table	3A.	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	25
Table	ЗВ.	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	26
Table	3C.	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	27
Table	4A.	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	28
Table	4B.	•	•	•	•	•	•	•	٠	•	•	•	•	٠	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	29
Table	4C.	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	٠	•	٠	•	3Ø
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Table	5B.	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	32
Table	5C.	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	33

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TABLE 1A GLP STUDY # 81008

GUINEA PIG SENSITIZATION TEST

7 c 2 0 с 12 48hr -24 -46 40 4.3 - 19.6 - 12.3 = Challenge: -2 -J 2 24hr 0 |--30 15 1 4 19 -56 -17: 0 -12 4 48hr Q  $\sim$ C J 55 21 cυ ~ Initial & Challenge Date: 30 APR - 4 JUNE Diluent: Propylene Glycol:Saline (1:30) 6 5 24hr 78 -10 36 4 -20 36 -18 4 33 7 Max Max Max 0.3 2122 à .... 43hr C ~ œ 0 22 C 0 1 7 T ÷ പ്പെട്ട 7\_+-- ; jo 1.0 24hr 0 0 4 9 C Ci 7 20 Ann 20 May 20 May 20 May 20 May 0.4 0 48hr 0 0 ام o ap 0 4  $\sim_{i}$ 4 . G 0.9 24hr 0 Q  $\sim$ 2 0 0 0 4 7 - ci m dia 0.0 -0.3 -0.2 -1.5 -0.7 Injection dates: **4**8hr ÷  $\mathbf{m}_{i}^{t}$  $\circ$ <†1 C C C ~  $\sim$  $\sim$ i. - L -16  $\sim$ 9 24hr œ 2 12 00 0 7 • 18 43hr 0 0 0 o C 0 0 φ. 4 oi 24hr 9 0 0 0 2 O'  $\infty$ 0 0 0 0 ł SCORE 48hr 0 0 7 0 0 0 5 0 0 FINAL 0.4 24hr | 4 C 0  $\sim$ 0 0 0 0 0 o 2 9.6 48hr 0 0 8 ~ 4 0 0 \_ 0 0 0.0 . 1.2. Þ 24hr 0 4 0 0 0 20 C 0 сł -0.25 -1.10 0.65 5.20 48hr 0i  $\circ$ 0 ~ 0 0 C 0 00 20 40 -10.1-10.0 in 24hr C 0 σ  $\sim$  $\sim$ 0 <u>- 36</u> 2 4 -16.0 HANES 48hr oÌ 0 0 0 0 0 0 0 oi c í CP1 12 Challenge: . 1. 0.05 . 2. 0.00 3. -0.80 5. 0.20 5. 0.20 0.01 24hr RED 0 0 o 0 1 0 0 0 0 0 0 • Principal Investigator: 0.0 CHF1 48hr d ol O 0 0 0 0 0 0 oj Sensitizing Dose: 1 for 0.1 24hr 0 0 0 0  $\overline{}$ 0 0 0 0 Chemical Name: Average Score Average Score Animals # E3100018 E3100029 Ed100046 Ed100015 E8100024 E8100027 E3100033 E3100044 E3100045 E8100053 Average Score 19

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TABLE 15 GLP STUDY #\_\_\_\_\_\_\_0003\_\_\_\_

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GUINEA PIG SENSITIZATION TEST

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Chemical Name:		Ciff 1	RED					l					_	Initial	•ð	Challenge Date:	Date:_	30 APR		4 JUNE		
Principal Investigator:	Invest	igator		CPT HANES	ES				TFST S	SHR STANCE	IC F			Diluent		<u>pylen</u>	Propylene Glycol:		Saline (1:30)	: 30)		i
Sensitizing Dose:	ng Dose	-	5		٣		4			2	9	•			1		6		10		Challienge	enge:
Animals #	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	43hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	4Ehr	24hr	48hr	24hr	43h.
E3120015	0	0	0	0		C	C	0	0	0	0	0	<u>ເ</u>	4		0	-	0	96	0	72	~
E3100018	0	0	0	a	ä	a	0	0	2	0	0	0	0	0	0	0	4	5	2	ω	18	¢
E3100024	0	0		-0	لر ا		0	6	0	0			0	4	9	4	0	0	216	105	12	2
E8100327	0	5	0	0	~	0	4			0	0	0	j 16	4	4	4	-	3	-0	0		
E&100029		5		0	2	C	20	4	0	C		0		0	-	0	-	C	6	6	တ	ੇ ਹੈ  
E310033	C	0	0	0	6	0	0	0	0	0	0	0	4	4	с С	œ	-		0	್	9	Ļ.
E8100044	0	0	0	0	0	0	-	-		0	0	0	12	0	-	2	-	C	36	œ	48	12
E3100045	0	0	0	e		0	0	0	0	 	8	4		0	0	ω	2	0	4	2	4	C
Ed100046		3	0	0	<del>ः च</del> 	0	0	0	0	0	0			0	0	-	8	C	-0	0	140	4
E8100053	0	0	0	0		-	0	0	10		0		0	0	4	8	0	0	-0	0	N	
Average Score	0.1	0.0	0.0	0.0	2.0	0.2	2.5	9.6	0.4		d	6 0 4	4 7		2.5	3 5	~ ~ ~		35. 4			
Average Score for Challenge: Average Score for 1. 0.05 2. 0.00 3. 1.10 5. 0.25	core fo	r Chall 2. 3. 5.	lenge: 0.05 0.00 1.10 6.05 0.25	16.60			0.65 3.15 3.20 2.25 2.25 2.25	1 t + 1			• • •		sction	date	- 0 - 40		4 .	6. 12 9. 16 213 0. 213	M W W M			

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TABLE 1C GLP STUDY # \_\_\_\_\_\_81008

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GUINEA PIG SENSITIZATION TEST

Initial & Challenge Date: 30 APR - 4 JUNE

Chemical Name: CHF1 - RED

d 48hr 14.4 Challenge: 50.7 24hr 8.8 48hr ŝ ~ ł Saline (1:30) 29.3 24hr g ~ 48hr ¢ α --6.000 1.7 Diluent: Propylene Glycol: ~ -~ -24hr <u>с.</u> 48hr N  $\omega$ -Apr May May May 1.6 24hr ~~ o 2.3 Injection dates: 48hr  $\infty$ \_\_\_ 6.2 24hr ( S ø  $\sim$ 0.6 48hr Q ÷ 1.2 24hr 0.1 48hr  $\circ$ ---.Э DILUENT 0.0 24hr 48hr o. 0.8 24hr c ì 7.90 4.25 2.35 19.05 0.2 o c 48hr 90.00 'n 3.6 24hr HARES 0.0 48hr c CPT 1~ 0.0 Challenge: 1. 0.00 2. 0.00 3. 1.90 4. 0.40 5. 0.05 24hr Ċ C Príncipal Investigator: 0.0 **48hr** for Dose: 0.0 o 24hr Score Score Sensitizing Animals # E8100027 E8100015 E8100018 E8100053 E8100024 E3100029 E8100033 Average Average Score

TABLE 2A

GLP STUDY # <u>31008</u> GUINEA PIG SENSITIZATION TEST

Chemical Name: <u>CHR2 - BLUE</u>	lame:	CHR2	- BLUE					}					I	nitial	Initial & Challenge Date:	lenge	Date:	30 APR	•	4 JUNE	1	
Principal Investigator:	Invest	igator	- {	CPT HANES	S			1			140		Q	Diluent:		ylene	Propylene Glycol: Saline (1:30)	Salir	le (1:3	(0		1
													:	•	;				į			
Sensitizing Dose:	1g Dose	-		2	m		4		-	, 2	9		~ 1		8		6		2		Challenge	rde :
Animals #	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	43hr	24hr	48hr	24hr	48hr	24hr	45hr
E8100012	0	0	0	0	c.	0	ę	8	0	0	- 1	0	ω	0	0	0	0	C	4	C	02	1
E3100013	0	0	0	0	20	ςο	0	-	0	0	0	0	8	0	0	0	0		 	> 0	-55-	-14
E3100014	7	0	0	0	-	-	0	0	0	0	0	0	0	0	0	7	0	0	10	n m	- 120	
E8100023	0	0	0	0	0	0	0	-	C	2	2	17	0	0	0		- -	0	4	တ	232	10.
E3100034	0	0	0	0	0	0	8	4	0	0	0	8	7	-2	0	r.)	0	C	24	C	- 40	- 12
E8100037	0	0	0	0	12	2	0	-	0	0	0	0	2	2	0	0	0	C	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0	c	
E8100039	C	0	0	0	4		0	-	-	0	-2	0	ۍ ۱	- 14	۳. ۲			4	1	α	-24	, v
E8100041	C	0	0	0	8	14	-	2	0	0	0	0	0	0	4-	-5-	68	24	C		ye.	4
E8100052	0	0	0	0	12	2	0	0	0	9	0	4	<i>.</i> -	-8	-	0	-	-5	-4	0	12	61-
E3100060	0	0	0	0	-	-	0	0	0	0	0	0	-3 -3			0	0		0	-2	-2-	2-
																+-	+-	+-			+-	
Average Score	-0.1	0.0	0.0	0.0	6.4	3.3	2	×		C	-	0	°	· · ·				0	1			
Average Score for Challenge: Average Score for 10.05 2. 0.00 3. 4.90 4. 1.65 5. 0.55	ore fo ore fo	r - Chal 	lenge: -0.05 4.90 1.65 0.55			6. 1.40 71.75 30.40 9. 4.30					-	Injec	-1 0	_1		30 Apr 2 May 5 May 7 May 9 May		21 12	A A A May May May			-6.2

TABLE 28 GLP STUDY # 81008

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GUINEA PIG SENSITIZATION TEST

CHR2 - BLUE Chemical Name:

Initial & Challenge Date: 30 APR - 4 JUNE

Principal Investigator:_	Invest	igator		CPT HANES	S			۲ 	0110 L01	TECT CUDCTANCE			Ö	iluent	Prop	ylene	Diluent: Propylene Glycol: Saine	Saìın	e (1:30)	()		I
Sensitizing Dose:	g Dose		2	2	• <b>m</b> •		4			5	9	• • • • •	7	•	က		6		10	H4	Chall	Challenge: <sup>1</sup>
Animals #	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr
E8100012	0	0	0	0	24	9	و	8	0	0	0	0	တ	0	С	0	0	0	0	0	196	4
E8100013	0	0	0	0	40	12	0	-	0	0	0	0	12	0	0	0	4	4	-	0	45	2
E8100014	0	0	0	0	-		0	0	0	0	0	0	0	0	0	-	_	C	12	4	40	4
E3100023	0	0	0	0	2	-	0	-	0	2	12	18	18	0	0	2	-	0	4	တ	294	12
E8100034	d	a	9	0	0	0	00	4	0	0	0	8	0	0	0	2	-	0	24	0	48	4
E8100037	0	0	0	0	12	æ	0	-	0	0	0	0	2	2	-	0	-	-	4	C	က	0
E3100039	0	0	0	0	4	-	0	-	-	0	0	0	15	4	-	0	+	4	12	ω	24	8
E8100041	0	0	0	0	င၁	16	-	2	0	0	0	0	4	4	0	2	72	24	0	6	60	4
E3100052	0	0	C	C	12	~	0	0	0	6	0	4	C	G	c	0	0	0	0	0	48	- 2
E8100060	0	0	0	0		-	0	0	0	0	0	0	0	0	-	0	~	~	4	0	48	0
													_				- +				-	
Average Score	0.0	0.0	0.0	0.0	10.4	4.8	1-5	1.8	1.0	- 0	1.2	3.0	5.9	0	0.3	0.7	3.2	- <b>A</b> -	e. 1 9	2.0	81.1	4.0
Average Sc Average Sc	ore fo ore fo	Score for Challenge: Score for 1. 0.00 2. 0.00 3. 7.60 4. 1.65 5. 0.55	allenge: 0.00 7.60 1.65 0.55		42.50	6. 2.10 7. 3.45 3. 0.50 9. 5.80	10 50 05 05					Injer	Injection dates:	da tes :	- ~ ~ 40 w	30 Apr 2 May 5 May 7 May 9 May	-	000 8 16 12 1000 21 21 000 12	Max Max Vois 19 Max Vois 19 Vois 19 Vo			

TABLE 2C GLP STUDY = <u>81008</u>

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GUINEA PIG SENSITIZATION TEST

Chemical Name: CHR2 - BLUE

Propylene Slycol: Saline (1:30)         3       5       10         3       5       10         0       0       0       0         0       0       0       0         0       0       0       0         1       12       0       0         1       0       1       2       0         1       0       1       2       0         1       0       1       2       0         1       0       1       2       0         1       0       1       2       0         1       0       1       2       0         1       0       1       2       0         1       0       1       2       0         1       0       1       2       0         1       0       1       2       0         1       0       1       2       0         1       0       1       2       0         1       0       1       0       0       0         1       0       1       0       0       0 <th>Itility Dose:       I       Itility       Dillett:       Dilett:       Dillett:       Di</th> <th>incipal</th> <th>Invest</th> <th>instau.</th> <th></th> <th>718611</th> <th></th> <th></th> <th></th> <th></th> <th></th> <th></th> <th></th> <th></th> <th>1</th> <th>Initial &amp; Challenge Date:</th> <th>&amp; Cha</th> <th>llenge</th> <th>Date:</th> <th>30 Apr</th> <th>r - 4 Jun</th> <th>un</th> <th></th> <th></th>	Itility Dose:       I       Itility       Dillett:       Dilett:       Dillett:       Di	incipal	Invest	instau.		718611									1	Initial & Challenge Date:	& Cha	llenge	Date:	30 Apr	r - 4 Jun	un		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $			, marker											a	i luent		200						I
z $z$	z $z$	sitizin	a Dose	- -	,			1	÷		:	DILUENT	ļ					auarz	Traction	L PC :	le []:3	(0)		
1       24hr       48hr       24hr       24hr <t< th=""><th><math display="block"> \begin{array}{c c c c c c c c c c c c c c c c c c c </math></th><th></th><th></th><th></th><th>•  -  </th><th></th><th></th><th></th><th>+</th><th>4    </th><th></th><th>. n</th><th>9</th><th></th><th>!</th><th><u>}</u></th><th>3</th><th></th><th>5</th><th>}  </th><th>101</th><th></th><th></th><th></th></t<>	$ \begin{array}{c c c c c c c c c c c c c c c c c c c $				•  - 				+	4   		. n	9		!	<u>}</u>	3		5	} 	101			
1       0       0       0       1       0 <th0< th=""> <th0< th=""> <th0< th=""></th0<></th0<></th0<>	$ \begin{bmatrix} 2 & 0 & 0 & 0 & 0 & 18 & 6 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0$		24hr			48hr	24hr						+ ·	·	2444	104		-		-1	2	1	- la	- de
3       0	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	20012	0	0	0	0	18						+	+	5		c4nr	-+	24hr	•			+	Shr
4       1       0       1       150       0       0       150       1       150       0       0       0       0       1       1       0       0       0       1       150       0       0       1       1       0	4       1       0	51000	0	0	0	0	02			ļ	ļ	1-	-	0	0	0	0	0	0	0	4		126	16
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	0014	~	0	C					1_		Ĺ		0	4	0	0	0	4	2	2		100	16
a       b	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	0023	0	G	6		5 6	-		$\bot$	_	1.	0	0	0	0	0	2	-	C	2		163	24
7       0	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	0034					V	-		$\bot$			2		18	0	0	-	12	0	0	0	12	1
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9       0       1       0       1       2       4       0	v $0$	1000		2	-	-	0	~)	0		0	0	0	0	0	0	~	0	-					2
0       0	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	6500	0	0	0	0	0	0	0	0	0	0	~	0	24	q	-	, ,	-			5	x	N
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0       0       0       0       1       0       1       2       4       0       36         1       0       0       0       0       0       0       0       1       0       1       2       4       0       36       36       36       36       1       0       1       2       4       0       36       36       36       36       10       36	$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	052	0	0	0	0	0	C		c			5	5	4	4	4	4	4	0	0		24	0
3.1     0.0     0.0     0     0     0     0     0     1     0     4     2     50       3.1     0.0     0.0     0.0     0.0     0.0     0.0     0.0     1.3     0.1     7.1     3.3     1.0     0     0     2     50       5core for Challenge:     38.10     0.0     0.0     0.0     1.3     0.1     7.1     3.3     1.0     0.8     2.5     0.3     66.0     10       5core for 1.     0.05     6     0.70     1.3     0.1     7.1     3.3     1.0     0.8     2.5     0.3     66.0     10       5core for 1.     0.05     7     5.20     10.0     0.0     1.3     0.1     7.1     3.3     1.0     0.8     2.5     1.8     0.3     66.0     10       5core for 1.     0.05     7     5.20     10.0     1.0     0.0     3     5     0.4     7     14     0.3     66.0     10       5core for 1.     0.05     7     5     200     7     14     10     3     5     10     10     10     10     10     10     10     10     10     10     10     10     10	3.1     0.0     0.0     0.0     0.0     0.0     0.0     1     0     4     2     50       3.1     0.0     0.0     0.0     0.0     0.0     0.0     0.0     1     0     4     2     50       5.0     0.0     0.0     0.0     0.0     0.0     0.0     1.3     0.1     7.1     3.3     1.0     0.8     2.5     0.3     66.0     10       5.0     0.0     0.0     0.0     0.0     0.0     1.3     0.1     7.1     3.3     1.0     0.8     2.5     0.3     66.0     10       5.0     0.0     0.0     0.0     0.0     0.0     1.3     0.1     7.1     3.3     1.0     0.8     2.5     0.5     1.8     0.3     66.0     10       5.0     0.0     0.0     0.0     0.0     1.3     0.1     7.1     3.3     1.0     0.8     7.1     8     16     9       5.0     0.0     10.0     1.0     0.0     1.0     1.0     0.8     1.1     0.3     66.0     10       5.0     0.0     0.0     0.0     1.3     0.1     7.1     3.3     1.4     1.4       6.0	060	0	0	0		C							5	12	8	-	0	-	2	7		36	12.
3.1     0.0 <td>3.1     0.0<td></td><td></td><td> </td><td></td><td> </td><td>+</td><td></td><td></td><td>2</td><td>5</td><td></td><td>0</td><td>0</td><td>8</td><td>-†</td><td>0</td><td>0</td><td>-</td><td>0</td><td>4</td><td></td><td>50,</td><td>~</td></td>	3.1     0.0 <td></td> <td></td> <td> </td> <td></td> <td> </td> <td>+</td> <td></td> <td></td> <td>2</td> <td>5</td> <td></td> <td>0</td> <td>0</td> <td>8</td> <td>-†</td> <td>0</td> <td>0</td> <td>-</td> <td>0</td> <td>4</td> <td></td> <td>50,</td> <td>~</td>						+			2	5		0	0	8	-†	0	0	-	0	4		50,	~
3.1     0.0     0.0     0.0     1.5     0.0     0.0     0.0     1.3     0.1     7.1     3.3     1.0     0.8     2.5     0.5     1.8     0.3       Score for Challenge:     38.10     6.070     0.0     0.0     1.3     0.1     7.1     3.3     1.0     0.8     2.5     0.5     1.8     0.3       Score for 1.     0.05     7     5.20     1.3     0.1     7.1     3.3     1.0     0.8     2.5     0.5     1.8     0.3       Score for 1.     0.05     7     5.20     1.3     Apr     6     12     May       3.     2.55     9.0     10     1.55     1.5     1.8     0.3       5.     0.00     7     5.20     1.30     Apr     6     12     May       4.     0.00     10     1.55     1.55     1.55     3.2     2.7     14	3.1     0.0     0.0     0.0     4.0     1.5     0.0     0.0     0.0     1.3     1.0     0.8     2.5     0.5     1.8     0.3       Score for Challenge:     38.10     0.0     0.0     0.0     1.3     0.1     7.1     3.3     1.0     0.8     2.5     0.5     1.8     0.3       Score for 1     0.05     6.     0.70     0.0     1.3     0.1     7.1     3.3     1.0     0.8     2.5     0.5     1.8     0.3       Score for 1     0.05     6.     0.70     7.5     5.20     10.3     7.5     2.2     0.3     0.3       3.     2.75     3.     0.90     9.     1.65     1.6     1.6     1.8     0.3       5.     0.00     10.0     1.05     5.     9.09     1.55     1.9     0.3		<b> </b>	+		+	+							-+		-+							 	
Score for Challenge:       38.10       0.01       0.0       0.0       1.3       0.1       7.1       3.3       1.0       0.8       2.5       0.5       1.8       0.3         Score for 1.       0.05       6.       0.70       0.0       0.0       1.3       0.1       7.1       3.3       1.0       0.8       2.5       0.5       1.8       0.3         Score for 1.       0.05       6.       0.70       7       5.20       7       8       4       0.3         3.       2.75       3.       0.90       9       1.50       3.       5       7       7       7       7       7       14       May         4.       0.00       9       1.50       9       1.55       4.       0.00       9       16       9	Score for Challenge:       38.10       0.01       0.0       0.0       1.3       0.1       7.1       3.3       1.0       0.8       2.5       0.5       1.8       0.3         Score for 1.       0.05       6.070       0.0       0.0       1.3       0.1       7.1       3.3       1.0       0.8       2.5       0.5       1.8       0.3         Score for 1.       0.05       7       5.20       7       10       7       14       0.3         3.       2.75       3.       0.90       7       5.20       3.5       7       14       May         4.       0.00       9.1       1.50       9.150       3.5       9.19	ge		-	1							1		-+	-+									7-
Challenge:       38.10       6.070       1.06       0.31         1.005       6.070       7.5.20       Injection dates:       1.30 Apr       6.12 May         2.000       7.5.20       1.050       2.2 May       7.14 May       7.14 May         3.2.000       9.000       9.090       3.5 May       6.15 May       7.14 May         5.000       10.105       3.090       3.6 May       6.16 May	Challenge:       38.10       C.31       0.31         1. 0.05       6. 0.70       1.0       1.30         2. 0.00       7. 5.20       1.0       1.31         3. 2.75       3. 0.90       3. 5       2. 2         4. 0.00       9. 1.50       3. 5       3. 5         5. 0.00       10. 1.05       5. 9       13         6. 12 May       7. 14 May       7. 14 May         7. 5.20       3. 5       5       9. 16         9. 1.50       9. 1.50       3. 5       9. 19         9. 10. 1.05       10. 1.05       5. 9       19			0.0	i		4.0	1.5			0.0	0.0	1.3	0,1	7.1		0	8		ļ.		1	<u> </u> .	1-
	<sup>9</sup> Hay 10. 21	ge Scor ge Scor	e for	Challer 1. 0.00 2. 0.00 3. 2.75 5. 0.00 5. 0.00	; age ;	38	0 <u>1</u> 0 0 0 0		00000					Inject	ion da	1	1253	ay ay ay		12	×	m	0.10	2

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GUINEA PIG SENSITIZATION TEST TABLE 3A GLP STUDY # 81008

Chemical Name: CHR3 - BLACK

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Initial & Challenge Date: 30 APR - 4 JUNE

Sensitizing Dose: 1       Sensitizing Dose: 1       Animals 4 24hr 48hr 2       E3100025     0       E3100028     0       E3100030     0       E3100042     0       E3100042     0       E3100059     0       E3100059     0			ç																1
0000000000		ULL MANES				i				0	Diluent:		ylen (	Propylen Glycol:Saline (1:30	Saline	(02-1)	_		
						FIN	FINAL SCORE	RE		I						100.11			1
24hr 48hr 24hr 48hr 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2		e.	   	4	L:	2.5	9				3	•	, 6		0			
74hr 74hr		┢──	I	ł	<u> </u>			++			1		T					1 i Pilo	crid i lenge:
	24hr 48	48hr 2	24hr 4	48hr 24	24hr 48hr	ir 24hr	r 48hr	- 24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	<b>48hr</b>
	0	0	0	-3	0	13	0	-24		- 27	C	0	6	- 19	C		ſ	· +	
	0	0		~				 		;			, <del> </del>	2	5	 7	<b>v</b>		>
		-		 		 	1	1	5	12	0	0	-	14	9	0	2	4	46
0 0 0 0 0	-	0	16	0	0	-	0	0	0	0	-	-4	0	18	0	4	2	~	4
00000	0	a	0	-12	0	0	2 0	0	2	4	0	0	α	-12	C	α	c	c	
0 0 0 0	0	0		0	10 3	30	0	0	0	17	0	0	~	-50	× v	5	> u		
0 0 0	0	0	0	0	0	0	0	0	0	- ]4	0		<b>_</b>	10		12	f		
0 0	0			0	0	0 4	4	0	ø	-2	¢,		   C	c	> c	u c	+		י א
0	0	0	0	0		0 		с 	- -			+   -			 >	0	2	t -	×
	0		c				 				 3! 	-	 T	>	7	-	4	<del>6</del>	32
	, ,	 		>					D	- 5	2	0	0	-	ω	9	2	-27	-9
	0	0	0	0	0	0	2	0	С	8	8	0		2	m	80	16	4	4
	-+-		-+		•				+									<b> </b>	-
		-													 			+-	]
Average Score 0.0 0.0 (	0.0 0.	0.0	1.9 -1.4		.0 4.9	0.6	8.0	4		0		 c	-+	 , ,	i	•+	-4	-1_	
Average Score for Challenge: Average Score for 1. 0.00 2. 0.00 3. 0.25 4. 2.95 5. 0.70	nge: 200 35 70	- 3.60		-0.70 0.55 0.90 -1.10 2.95					Injec	. т с		6. 20 30 6. 30 6. 30 6. 30 7.	Apr May May	0.0 0.0 0.0	12 12 12	Z.3 May May May May	3.6 - 1	-16.5	<b>9.3</b>

GLF STUDY = 81008 TABLE 3B

Challenge:

43hr 9<del>0</del> 

24hr \$ 

 $\sim$ Q 

48hr 6.2 Initial & Challenge Date: <u>30 APR - 4 JU;E</u> Saline (1:30) ! 24hr တ ω 9.9 اف 12 May 14 May 16 May 19 May 21 May Į 43hr Q Q <del>د</del>ا 2.8 Diluent: Propylene Glycol: 24hr 7.9 April May May May Mav 48hr -00  $\sim$  $\infty$ N ~--2.9 24hr | C ~ Ç. Q. -- ~ ~ ~ ~ 48hr 1.21 Injection dates: ~ ω 24hr  $\sim$ 6.2 --- $\sim$ ∞ ł ŀ-0.8 0.01 1.01 48hr ~ ÷ ω C Q 24hr GUIMEA PIG SENSITIZATION TEST TEST SUBSTANCE + 48hr ~ cl ---'n, 48hr | 24hr 4.5 0.6  $\sim$ ~ 24hr 1.8 48hr 0.50 3.70 1.55 5.35 8.05 0.2  $\circ|$ ľ 10 m m m m 1.9 24hr -. ار CPT HANES 22,39 48hr 0.01  $\sim$ CHR3 - BLACK 24hr ç 0.0 11enge: 0.00 1.00 1.05 3.35 0.70 Principal Investigator: 0.0 48hr C C ~ Jose: 24hr for Chemical Name: 0.01 Score Score Sensitizing Animals # E8100020 Average Score Average Average 

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 $\sim$  23.61 21.01

TABLE 3C GLP STUDY # 81008 GUINEA PIG SENSITIZATION TEST

Chemical Name: CHR3 - BLACK

Initial & Challenge Date: <u>30 APR - 4 JUNE</u> Diluent: Provlene Glycol: Saline (1:30)

Principal Investigator:	Invest	igator		CPT HANES			1	-	DILUENT	L			Ū	Diluent:	Ì	ylene	Proylene Glycol:	: Saline	le (1:30)	(0)		1
Sensitizing Dose:	ng Dose	۱ ــــ		2	, M		4			2	و		7	1	3	┣ :	6		01		Chal	Challenge:
Animals #	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	43hr	24hr	48hr	24hr	48hr
E8100020	0	0	0	0	0	m	0	 C	0	0	24	0	36	0	0	0	32	9	16	4	80	4
E8100025	0	0	0	0	0		0	0	0	0	G	0	0	0	0	-	0	0	0	0	12	2
E8100028	~	0	0	0	0	0	0	0	0	0	0	0	t.1	3	4	4	 C   I	0	12	 	16	12
E3100030	0	0	0	0	0	12	0	0	0	0	0		2	0	0	0	12	Ċ	- C		36	4
E810036	0	0	0	0	0	0	0	0	 0	0	0	0		0.			- 20	<del>ا</del> ب ا			32	16
E8100040	0	0	0	0	0	0	0	0	0	0		ا بې	191	0			~1	C	23	ę	126	2-
E8100 <b>042</b>	0	0	0	0	0	0	8	0	0	0		0			6	5	4	Ŷ	28	12	- 25	
E8100043	0	0	0	0	0	0	0	0	0	0	0	T <sub>C</sub>		са	0	0		~	c	Ċ	<mark>+</mark> + +	
E8100059	0	0	0	0	0	0	0	C	0	0	0	10	0	<:	-4 	0	~~~		-01	C	10 10 10	24
Ed100061	0	0	0	0	0	0	0	0	0	0	с) 	0		· 0	с -	0		-	0	0	0	0
										- +-	· •• •• •	<b>**</b> *	•	· • • •	- -	•••••	- 4     		4			1
Average Score	0.0	0.0	0.0	0.0	0.0	ů, I	0.8	, d	1 0 0	C.G.	2.4	• C · C		2 6	<b>c</b> .0	0.8	11.4	1.5	7 6	و ح		
Average Score for Challenge: 0.00 Average Score for 1. 0.00 2. 0.00 3. 0.00 5. 0.00	core for	r Chall.	<b>)enge</b> : 0.000 0.45 0.05	25.90	~	6. 1.20 7. 3.15 3. 665 3. 6.45 9. 6.45 9. 9.10	1.20 3.15 5.65 6.45 9.10					Injec	Injection dates	late:	54 - 53 9 - 55	Apr Mar Nav Vav		6. 9. 5 2. 7. 5 7. 7. 5 7. 7. 5 7. 7. 5 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7. 7	May May May			

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TABLE 4A GLF STIGI 7 ALUVE

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OUREA FIG SENSIFIZATION TEST

Principal Investigator.         CPT MOLE         FINAL SCM         FINAL SCM </th <th>Chemical Hame:</th> <th>ame:</th> <th>CHR5</th> <th>CHR5 - GREEN</th> <th><u>ज</u></th> <th>l</th> <th></th> <th></th> <th></th> <th></th> <th></th> <th></th> <th></th> <th></th> <th>Instal</th> <th>% Cha</th> <th>&amp; Chailemic Date:</th> <th>Uate:</th> <th>30 200</th> <th>er. Gel</th> <th></th> <th>i I</th> <th>1</th>	Chemical Hame:	ame:	CHR5	CHR5 - GREEN	<u>ज</u>	l									Instal	% Cha	& Chailemic Date:	Uate:	30 200	er. Gel		i I	1
Ing Dose:         1         2         3         4         5         6         7         7         3         5         5         10           2 2arr         4 sin         24 r         4 r         24 r <th>Principal</th> <th>Invest</th> <th>igator</th> <th></th> <th>HANES</th> <th></th> <th></th> <th>:</th> <th></th> <th>F I NA</th> <th>L SCOF</th> <th>٤Ę</th> <th></th> <th>57</th> <th>il_ent</th> <th></th> <th><u>[]en_6]</u></th> <th>1007</th> <th>Saiine</th> <th>1:30</th> <th>7</th> <th></th> <th>4</th>	Principal	Invest	igator		HANES			:		F I NA	L SCOF	٤Ę		57	il_ent		<u>[]en_6]</u>	1007	Saiine	1:30	7		4
$ \begin{bmatrix} 2 4 nr & 4 3 nr & 2 4 nr & 2 $	Sensitizin	g Dose				~)		7	_		-0	2		7		ಲ		σ		0	• - •	Chall.	l : afiua
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Aninals≢	24nr	43hr	24hr	· · +	24hr	48hr	·		24hr	48hr	, ∩, ,		2465	43hr	24hr	{ ;	24hr			2 - A N		, J4c ;
5     0     0     6     18     35     86     84     84     72     60     68     11     10     11     245     12     24     24     24     24     25     25     25     25     25     25     25     25     25     25     25     26     23     175     31     126     135     31     27     25     26     23     137     35     156     31     126     31     37     35     156     31     35     35     35     35     35     35     35     35     35     35     35     35     35     35     35     35     35     35     36     37     35     36     37     35     36     35	E3100011	6	С	0	48	31	69	156	50	72	20	126	5	116	172	36	13	96	52	<b>म</b> ्ट	5	63	2
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	E3100016	0	0	0	60	18	35	36	84	84	72	60	68			16	10	all	245	21	44	25.	40
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	E8100019	0	0	0	32	26	62	34	140	140	120	192	. 16	420 1		4	30	138	140	. 611	69	5	
0         0         0         0         2         18         48         86         4         34         45	E3100021	0	0	0	32	60	24	126	75	70	84	60	112	5#2		53-		263	263	176	216	132	
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	E3100022	0	0	0	32	18	48		4	34	압	<u>မှ</u>	o; 	168	100		160	51 51	167	196	336	156	5
0 $0$	Ed10:0031	0	0	0	75	0	100	122	189	112	70	105	30	3.94	120	53 -	- 66	44	132	196	214	202	۳Ì
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	E2100047	0	0	0	0	12	56	36	75	84	(co 	90	180	392	210	48	171	295	194	80	48	96	55
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	E8103048	- 4	0	0	C	2	19	0	48	96	72	25	0	188	100	12	- 14	90	105		0	324	
0     0     36     4     35     98     39     108     192     56     420     54     256     210     324     380     224     329       -0.4     0.0     0.0     41.5     26.6     22.1     33.3     70.6     94.3     62.3     269.1     168, 7     33.8     90.8     147     154       -0.4     0.0     0.0     41.5     26.6     22.1     33.3     76.3     89.3     70.6     94.3     62.3     59.8     145     147     154       Score for Challenge:     126.0     .21     33.3     76.3     89.3     70.6     94.3     62.3     169.7     33.8     90.8     145     154       Score for Challenge:     126.0     .21     33.3     76.3     89.3     70.6     94.3     62.3     154     147     154       Score for 1     -0.2     20.8     7     188.7     33.8     90.8     145     147     154       3     39.4     8     64.8     3.5     7     3.5     5     33     9.6     147     154       5     30.2     8     8     90.8     169.7     168.7     38.9     90.8     90.8     90.8	E8100051	0	0	0	100	95	32	30	_ م	48	54	10 10	6	240	12	ω	12	113	4 <sup>1</sup>	252	-	138	234
-0.4     0.0     0.0     41.5     26.6     22.1     83.3     70.6     94.3     62.3     269.1     168.7     38.8     99.4     145     154       -0.4     0.0     0.0     41.5     26.6     22.1     83.3     70.6     94.3     62.3     269.1     168.7     38.8     99.4     145     154       score for Challenge:     126.0     .     87.6     .     31.6     14.7     154       score for 1     -0.2     .     87.6     .     10.0     62.3     269.1     168.7     38.8     99.4     147     154       score for 1     -0.2     .     87.6     .     10.6     94.3     62.3     269.1     168.7     38.8     99.4     147     154       score for 1     -0.2     2.1     83.3     70.6     94.3     62.3     269.1     168.7     38.8     99.4     147     154       score for 1     -0.2     2.0.2     .     .     91.6     142     154       3     39.4     3     64.8     3     5     80.7     169.4     147     154       4     70.8     9.157.1     5     30.2     10.145.4     5     30.7     16	E8100055	0	0	0	36	4	35	98 8	89	103	108	192	56	420	504	54	236	210	324	380	224	32.9	69
-0.4     0.0     0.0     41.5     26.6     32.1     83.3     70.6     94.3     62.3     269.1     168.7     33.8     99.8     145     144     147     154       Score for Challenge:     126.0      31.5      31.5     10.6     94.3     62.3     269.1     168.7     33.8     99.8     145     144     147     154       Score for Challenge:     126.0      31.5      10.5     10.8     7     13.4     147     154       Score for 1     -0.2      31.5      10.5     13.4     147     154       Score for 2       31.5      10.5     168.7     7     13.4     147     154       Score for 1     -0.2      31.6     14.8     7     144     147     154       3     39.4     3     30.4     3     36.4     3     36     37     5       4     70.8     157.1     5     30.2     10.145.4     5     7     37     90.7     10.2     134						·					-			1			·+···· !		· •	•- + -			
Core for Challenge:     126.0     Store for 1.     0.2     Store for 1.     3.1.6       Score for 1.     -0.2     3.1.6     -1.7.8     7.218.9       Score for 1.     -0.2     2.2.0.8     7.218.9       3.     3.0.4     3.64.8     3.64.8       4.     7.9.8     9.157.1       5.     30.2     10.145.4	verage core	-0.4	0.0			26.6	22.1	8 <b>3</b> .3	76.3	39-3 3	70.6		е£-3	269.1	168.7	38.8	90.8	145	169	] 44	147		0.66
	verage Sco verage Sco	ore for		1enge: -0.2 20.8 39.4 30.2		-		0 6 8 - 4					Inje	ction ,			3.3 Apr 2 May 7 May 9 May						

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TABLE 48 GLP STUDY # 31008

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GUINEA PIG SENSITIZATION TEST

Cnemical Name:	Name:	CHR5	CHR5 - GREEN	N				ļ					1	Initial		& Challenge Date	Date:	30 APR	& 4	JUNE		
Principal Investigator:	Invest	tigator		CPT HANES	<u>ves</u>			I	TEST	T SUBS	SUBSTANCE		Ď	Diluent:	Prop	<sup>P</sup> ropylene	Glycol: Saline (1:30	: Salir	ne (1:	30)		ŧ I
Sensitizing Dose: 1	ng Dose			5	3		4		·	. 2	ور		~		ന		6	• • • • • • • • • • • • • • • • • • •	01		Chall	Challenge:
Animals #	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	43hr	24hr	48nr	24hr	48hr
E3100011	C	0	0	43	40	60	162	54	72	70	126	50	140	180	36	16	72	60	36	14	175	53
E3130016	0	0	0	63	24	36	66	34	84	72	60	72	126	84	16	16	126	245	20	56	75	64
E3100019	0	C	0	32	27	72	34	140	140	- 120	192	105	448	245	54	80	108	140	135	150	06	64
E3100021	0	0	0	32	60	24	126	75	20		3	112	245	140	54	128	270	294	180	324	150	63
E3100022	0	0	0	32	- 13	54	6	4	84	48	43	C	168	100	νç	162	60	160	196	336	168	125
E8100031	0	0	0	75	0	100	126	189	112	<u>67</u>	105	30	384	120	27	10.7	150	144	196	516	210	64
E3100047	0	0	0	0	12	60	36	- 15	84	8	90	130	392	210	44 0)	175	283	200	60	48	000	64
E310043		0	C	0	2	20	- 6	45	96	- 22	25		200	001	12	4	06	175	0	c	336	<u>ب</u> آ
13000123	0	0	0	100	96	32	30	6	42	54	20	- 66	252	12	۰ ۳	12	120	48	252	140	200 -	242
52100022 	0		0	36	4	36	98	06	103	108	192	56	432	504	<b>57</b> 10	256	210	324	392	224	336	360
						- +		†			-•	 - 	•		•	• • •	· •• •		4	1		
Juerage Score	0.0	0.0	0.0	41.5 28.	28.3	54.4	85.1	76.8	59.8	70.6	94.8	69.5 2	278.7.1		39.5		149.411	72.0.148		152.8.184.0		110.7
Average Score for Challenge: Average Score for 1. 0.00 2. 20.75 3. 41.35 5. 80.20 5. 80.20	ore foi cre foi	7 1. Chall	allenge: 0.00 20.75 41.35 70.15 80.20		147.35 7.7 9.	5. 82.15 5. 82.15 7. 224.10 7. 66.85 0. 160.70 0. 143.75	15 15 70 75		,		- - - - -	Injec	Injection dates:		. 012/0	S S S S S S S S S S S S S S S S S S S	C					

TABLE 4C is P\_STUDY = \_\_\_\_\_\_

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۰ ۱ JUINER PIG SENSITIZATION TEST

$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Cnewical Name: CHR5 - SREEV		CHR5 -	GREEN	;		•	;	,					- 1	nitial	3 Cha	Initial & Challenge Date:	Date:	30 APR	4	2014		
Iny Doce:       1       2       4       5       6       7       3       9       15       15 $e^{-241r}$ 4.0 r       241r       24	Principal	investi	gator:		PT_nA0	S	ł	;	:	C	TU LIFUT			<i>د</i> ع	i)uent			lycol:	Saline	(1:39)			
Zahr     Zahr     Jahr     Zahr     Jahr     Zahr	Sensitizin	j Dose∶	-	2		ŝ		7	-+		5	e		1	τ ι		ı.	, '	<u>}</u>	ŝ.	-	Che Lienge:	enge:
$ \begin{bmatrix} 1 & 2 & 3 & 3 & 2 & 0 \\ 2 & 1 & 2 & 3 & 3 & 2 & 0 \\ 1 & 1 & 2 & 3 & 2 & 0 & 0 & 0 \\ 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 &$	Anjmals. = .	24hr	۱.	e :		24hr	18hr					• • • • • •		24hr	48hr	24hr		24hr	<del></del>	1.1.1.1	4 · · · •	24010 -	- tanr
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Ed100011	0	c	,	0	6	⊃'	<u>و</u>	4	0	+		С	24	ď	0	m	30		15	12	ן 21 <sup>י</sup>	40
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	E8120016	0		0	0	Q	-	4	0	C	ا +۰		4	م ا ا	0	0	9	0	C	3	12	53	54
$ \begin{bmatrix} 1 & 1 & 2 & 3 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0$	E3100019	. 0	с, <sup>с</sup>	0	<u>_</u> †		10	+	0	0	·			28	0	C	0	0	0	10	0	65	32
$ \begin{bmatrix} 2 & 0 & 0 & 0 & 0 & 0 & 0 & 6 & 4 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0$	<u>E3130021</u>	C	ы П	0	0	0	0	 	0	0		۱ ۱ ۱۰		0	0		0	0	0	4	œ	100 	<u>د</u> .
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	E3100022		0	Ũ	0	0	9	4	0	0			0	0	0	0	0	12	0	6	Cu	12	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	E8100031	۔ ان	0	c	0	0			C	0		 		0	0	-	8	9	121	-0	5	ά;	ا ہے۔ :
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	E8100047	0	0	0	0	6	4	0	0	0			0	0	0		4		9	C	0	4	21
1       0	E8100048	4	0	0	0		-	0	0	0		0	) 	12	0	0	15	°	0	0	0	12	ĉ
5 0 0 0 0 0 1 0 1 0 1 0 1 0 0 0 0 0 0 0	EU100051	-0	0	- 10	0	-	0		0	0				12	0	0	0		0	0	0	- 1 01 6- 1	9
0.4     0.0     0.0     0.0     0.0     0.0     0.0     0.0     1.2     9.6     0.8     0.2     5.2     3.4     2.0       Score for Challenge:     20.00     0.0     0.0     1.2     9.6     0.8     0.2     3.9     4.8     2.6     5.2     3.4     20       Score for Challenge:     20.00     0.0     0.0     1.2     9.6     0.8     0.2     3.9     4.8     2.6     5.2     3.4     20       Score for 1     0.20     3.2     0.0     3.2     5.2     3.4     20       3.     2.00     3.2     3.70     3.70     5.3     4.9     10.4     4.9       5.     3.00     10.4     4.30     5.4     9.4     9.7     9.4	E8100055		0	0	10		-	0	-	0		C	C	12	0	0	0	-61	0	15	0	'n	50
0.4     0.0     0.0     0.0     0.0     0.0     0.0     1.2     9.6     0.8     2.6     5.2     3.4     20       Score for Challenge:     20.0     0.0     0.0     0.0     1.2     9.6     0.8     0.2     5.2     3.4     20       Score for Challenge:     20.0     0.0     0.0     1.2     9.6     0.8     0.2     3.4     20       Score for 1     0.20     5.20     1.12     9.6     0.8     0.2     5.2     3.4     20       3     2.00     3     2.00     3.2     5     May     6.1     12     May       4.     1.15     3     3.70     3.70     3.70     5.3     4.9     10.2     10     10			+						, , ,								   			-			1
1       0.4       0.0       0.0       0.0       0.0       0.0       0.0       1.2       9.6       0.8       2.6       5.2       3.4       20         Score for Challenge:       20.00       7       5.20       1.3       0.5       0.0       0.0       1.2       9.6       0.8       2.6       5.2       3.4       20         Score for 1       0.20       7       5.20       1.3       0.0       7.1       1.30       Apr       6.1       1.8       2.4       20         2       0.00       7       5.20       5.20       3.4       5.3       3.4       20         3       2       0.00       7       5.20       5.20       3.4       5.3       4       20         3       2       0.00       7       5.20       5				•	4+     	•••	1			1						-						•	1
20.65       6.0.60       1.30 Apr       6.12         7.5.20       7.14         8.2.05       3.5 May       7.14         9.3.70       3.70       5.90         9.3.70       5.90       6.16         9.3.70       5.90       6.16         10.4.90       5.90       9.370	core	0.4	0.0	0.01	0.0-	1.7			0.	0.0	'			• 1	0		3.9		· · · ·	1	• 1	تەتى	
	verage Sco verage Sco	ore for ore for	Challe 2. 0. 3. 2. 0.	enge:	20.01			50 20 35 70 20	, , , ,				Inje	ction	dates:				12	a Va Va Va Va Va Va			

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TABLE 5A GLP STUDY # 81008

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GUINEA PIG SENSITIZATION TEST

Chemical Name: CHR6 - GRAY

Initial & Challenge Date: 30 APR & 4 JUNE
Diluent: Propylene Clycol:Saline (1:30)

Principal Investigator:	Invest	igator:		CPT HANES	ES			1		10000			Di	luent:	Propy	lene G	Diluent: Propylene Glycol:Saline (1:30)	Saline	(1:30)			1
Sensitizing Dose: 1	g_Dose			2			4			5 5	2	•	1		හ		6		10		Cha 1	Challenge.
Animals #	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	48hr	24hr	43hr	24hr	48hr	24hr	48hr
E3100017	-	0	0	80	96	Э	59	0	64	01	0	0	32	40	2	39	0	16	2	0	16	64
E810026	-	-	0	64	27	48	28	80	69	16	50	10	232	180	18	3J	16	42	0	0	56	30
E8100032	0	0	0	36	16	0	19	39	35	0	168	20	180	64	12	61	214	150	72	60	-53	4
E8100038	0	0	0	60	0	2	24	40	12	0	, 16	12	180	36	12	9	24	0	0	0	-15	0
E8100049	0	0	0	60	Ø	2	131	0	180	42	40	0	82	120	45	59	56	4	48	4	27	25
E810050	0		0	30	20	2	64	54	126	24	10	30	240	224	60	18	186	132	54	2	- £	46
E3100054	0	0	0	90	0	-	45	06	56	4	4	C	108	16	4	12	143	48	324	128	-40	- 16
E3100056	0	-	0	16	12	35	108	30	32	4	60	4	40	64	4	- 2	59	4	28	26	- 36	-28
E3100057	0	0	0	18	18	18	108	16	96	12	10/	0	219	9-	36	α	30	44	36	0	- 36	-10
E0100058	0	0	0	32	12	27	70	26	4	0	40	15	175		18	õ	59	- 55	96	UI	30	_ [5]
								+			· ·		·   -					4   				
Average	0.2	0.1	0.0	38.4	20.9	13.8	69.8	30.3	67.4	11.2	48.6		148.3	79.8.21.1	· •••- 1	22.4	79.2	55.2	65.0	22.0	2.6	
<pre>4verage Score for Challenge: Average Score for 1. 0.15 2. 19.20 3. 17.35 4. 50.75 5. 39.30</pre>	ore for ore for	Chall 2.2.	lenge: 0.15 19.20 17.35 50.75 39.36	3.05		6. 28 7. 114 3. 21 9. 65	28.85 28.85 114.30 21.75 65.70 44.00					Injec	Injection dates:	ates:	- 01 m 40 8 0 m n 0	Apr Hay May Hay	-φαγικικά (2. β. -φαγικικά (2. β.) -φαγικικά (2. β.)	4 K 8 6 7	May May May			

SUD1 = 70013 -715 TABLE 5B

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Cha, leu le: 45nr S 27-7. 30.7 . 24hr j ŧ 39.4 57.0 20.4 23.6 ė 30 APP & 4 104E 43hr V Propylene Glyco::Saline (1:30) 43hr | 24hr May May May 4 K 6 6 6 6 \_ luitial & Challence Date: \_ (J) Ċ. 24hr 39.4 67.5 11.6 51.8 9.7 h63.2 91.0 21.1 25.1 Apr May May May 48hr တ  $\sim$ 24hr | 48hr | 24hr in the mass Diluent: Injection dates: ~ 24hr 48hr R ف C GUINER PIG SENSIFIZATION TEST TEST SUBSTANCE ŧ 24hr | 48hr 이 S 48hr • i  $\circ$  $\infty$ 24nr \_ 71.3 30.75 82.10 23.10 73.20 47.00 ļ 1. 48hr  $\sim$  $\sim$ ----~ 14.3  $\sim$ 21.0 24hr -1 G3 CPT HARES ..... 24hr 48hr 38.4 i CHR6 - GRAL Challenge: 1. 0.20 2. 19.20 3. 13.25 4. 55.35 5. 39.55 0.0 c o С Principal Investigator: 13hr 0.2 C ~ C ~ ---Sensitizing Dose: Average Score for Average Score for Cnemical Name: -1 ---C O, 0.2 Aninals = 64hr  $\odot$ 0) £8100026 E3100017 E8100038 E8100049 E3100050 E8100054 E8100056 E8100053 E8100057 Average Score

TABLE 5C

GLP STUDY # RIDOG GUINEA PIG SENSITIZATION TEST

idme: CHRG - GRAY

Cheinica

Challenge: 24hr | 43hr 4 q 40 4 5 32.1 0 2  $\sim$ 16.0 0 9 88 2 19 50 40 40 - 19 ÷ 36.3 48hr Initial & Challenge Date: 30 APR & 4 JULE C 9 1 0 9 d ~ C, 4 C C) 0.6 Probylene Glycol:Saline (1:30) 01 24hr N 0 5.4 0 2 d eu 3 21 22  $\odot$ i 5. 72 Mav 7. 16 Mav 9. 16 Mav 9. 19 Mar 10. 21 May 48hr 0 0 4.8 0 d d 18 2 1 4 2  $\sim$ en 0 24hr 20 10.2 0 50 a 27  $\sim$ 04 48hr 7 8 2 0 0 2.7 04 0 N 30 Apr 2 May 5 May 7 May 3 24hr 0 0 0 0, ¢ | 4 9 Ċ  $\sim$ c-C C Diluent: in di mini 18hr 00 1 0 0 d 1 9  $\subset$ 0  $\infty$ 96  $^{\circ}$ injec⁺ion dates: 7.6 14 11.2 1 20 24hr  $\infty$ 03 -3 0 d 4 0 36 ٤... 48hr 0 0 0 وً 0 0 0 0 0 0 24hr | 48hr | 24hr | . . 0 c  $\circ|$ 112 ام ا 0 0 3.2 00 0 0  $\infty$ 1  $O_1^{\dagger}$ 4 0 0 0 S 0 a DILUENT C 0 9.1.1.0.1 0.4 ي م C 0 0 0 0 C 0 Ċ 0 1 48hr 1 ; 01 0 j  $\infty$ 2 0 0 0 ി i 1 24hr C  $\sim$ 0 1.5.1 0 4 2 6, 0 0 48hr 1.90 12.50 2.50 3.00 ~ 0 ----0 0 ~ 0 ~ 0 0 0.5 ŝ 24t.r 0 0 6.000 0 , ..... 0 0.1 0 0 0 C HANES 0 43hr 0 15 0 0 0 0 0 2 CPT 0 eľ 5 56 0.0  $\sim$ 24hr 0 0 0 0 r Challenge: r 1. 5.05 2. 9.00 3. 0.30 4. 5.30 5. 0.25 0.0 11.0.1 6.0  $\odot$ 0 0 0 0 0 investigator: 48hr 0 0 0 0 -1 "ng Dose: 1 0 0 0 0 oi 24hr 0 0 0 0 i the for 0 0 0 0 0 Ċ, ł <sup>o</sup>rincip<sub>A</sub> E8100C11 E812005 E810003: E810004 -E8100010 Animals. E81000.1.L Sensit. 000183 E8100.0 E8100053 E8100C; Average iverage verage

