

WM. T. BURNETT & COMPANY

Non Clickable Polyester Foam
Lot No.: S82s Run 270

Closed Patch Sensitization
(ANSI/AAMI/ISO 10993-10:2010)
Direct Contact
(GLP)

December 11, 2013

JN13J0757

JN13J0757

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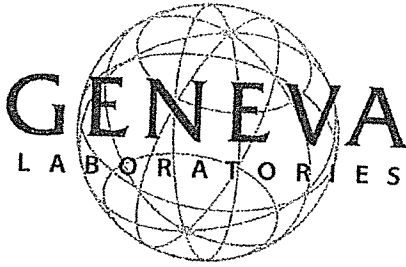
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SECTION 1

TEST PROTOCOL

GLP0002*



JN13J0757

FOR THE MEDICAL INDUSTRY WORLDWIDE

P.O. Box 140 • 1001 Proctor Drive • Elkhorn, WI 53121-0140

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www.genevalabs.com

GLP PROTOCOL

Closed Patch Sensitization
(ANSI/AAMI/ISO 10993-10:2010)
(Direct Contact)

SPONSOR: Wm. T. Burnett & Company
2112 Montevideo Road
Jessup, MD 20794

P.O. NO.: 714120

TEST ARTICLE: Non Clickable Polyester Foam

X AND LOT/ID: 5825 Run 270

Signing of this protocol constitutes sponsor's approval of the procedure outlined on the following pages, and sponsor's confirmation that the conduct of this study does not unnecessarily duplicate previous work.

STUDY DIRECTOR: _____

Sandy Ott
Study Director/Toxicology
Geneva Laboratories, Inc.

STUDY
INITIATION

DATE: 10-15-13

SPONSOR: _____

Wm. T. Burnett & Company

DATE: 10-16-13

GENEVA LABORATORIES, INC.

**PROTOCOL FOR CLOSED PATCH SENSITIZATION TEST
(ANSI/AAMI/ISO 10993-10:2010)**

Title 21 CFR 58
Good Laboratory Practice for a Nonclinical Laboratory Study

§58.120 PROTOCOL

1). TITLE

Closed Patch Sensitization Test
(ANSI/AAMI/ISO 10993-10:2010)
Geneva Laboratories Proc. No.: CL1014*

2). PURPOSE

To assess the potential of the material under test to produce delayed contact hypersensitivity in guinea pigs.

3). IDENTIFICATION OF

	<u>Name</u>	<u>CAS/Code (Lot No.)</u>
Test Article:	Non Clickable Polyester Foam	S82s Run 270
Control Article:	Gauze	Current Mfr. & Lot

16-17-13

4). SPONSOR NAME

Wm. T. Burnett & Company
2112 Montevideo Road
Jessup, MD 20794
ATTN: Mr. Scott Magness

5). TEST FACILITY

Geneva Laboratories, Inc.
Proctor Drive at McKenzie Lane
P.O. Box 140
Elkhorn, WI 53121-0140

6). TEST SYSTEM

Number:	Twenty-five (25) [ten (10) test, five (5) control, ten (10) positive control from historical data]
Weight Range:	300g - 500g
Sex:	Female, nulliparous and not pregnant
Source of Supply:	Charles River Laboratories
Species:	Cavia porcellus (Guinea Pig)
Strain:	Hartley
Age:	1 - 5 months

7). TEST SYSTEM IDENTIFICATION

- A. Each guinea pig within an enclosure will be identified with an individually numbered ear tattoo.
- B. Guinea pigs will be observed daily for health irregularities.

8). DESCRIPTION OF EXPERIMENTAL DESIGN TO INCLUDE METHODS FOR CONTROL OF BIAS

A. Closed Patch Sensitization Test

Ten (10) healthy female guinea pigs will be used, with an additional five (5) as the negative control. Ten (10) positive controls will be referenced from historical data.

B. Preparation of Test Article and Extracts

1. For direct application of test article, the procedure outlined in ANSI/AAMI/ISO 10993-10:2010, Annex A is followed.
2. Test Article extracts are prepared according to sponsor recommendations or according to ANSI/AAMI/ISO 10993-12.

C. Procedure

1. Induction Phase I consists of topical applications on the clipped left shoulder to the ten (10) test guinea pigs with the test article or its extract. Patches are removed after six (6) hours \pm 30 minutes. Five (5) guinea pigs are maintained as a control group which are treated similarly using a control article. This procedure is repeated for two (2) more days for a total of three (3) applications per week.
2. Induction Phase II begins approximately seven (7) days following Phase I. Test article or its extract is topically applied and taped to the same freshly clipped site as the Phase I application sites. The control group is treated similarly using a control article. Patches are removed after six (6) hours \pm 30 minutes. This procedure is repeated for two (2) more days for a total of three (3) applications per week.
3. Induction Phase III begins approximately 14 days following Phase I. Test article or its extract is topically applied and taped to the same freshly clipped site as the Phase I and II applications sites. The control group is treated similarly using a control article. Patches are removed after six (6) hours \pm 30 minutes. This procedure is repeated for two (2) more days for a total of three (3) applications per week.
4. Challenge Phase IV begins fourteen (14) days (\pm 1 day) after the last induction phase. Test article or its extract is topically applied to the clipped left posterior quadrant of the side and back (virgin site) of the ten (10) test and five (5) control group animals. Patches are removed after six (6) hours \pm 30 minutes.

5. Observations

Scoring occurs at twenty-four (24) and forty-eight (48) hours after Challenge patch removal. (See Table II, below, Scoring Criteria for Skin Reactions.)

Table II
Scoring Criteria for Skin Reactions

Magnusson and Kligman Scale	
Patch Test Reaction	Grading Scale
No visible change	0
Discrete or patchy erythema	1
Moderate and confluent erythema	2
Intense erythema and swelling	3

6. Results

Grades of 1 or greater in the test group generally indicate sensitization, provided grades of less than 1 are seen on control animals. If grades of 1 or greater are noted on control animals, then the reactions of test animals which exceed the most severe control reaction are presumed to be due to sensitization.

7. Rechallenge

Occasionally, the test group has a greater number of animals showing a response than the controls, although the intensity of the reaction is not greater than that exhibited by the controls. In these instances, a rechallenge may be necessary to define the response clearly. If necessary a rechallenge shall be carried out approximately 7 days after the first challenge. The method used shall be as described for the first challenge, using an untested area on the flank of the animal.

**9) . DESCRIPTION/IDENTIFICATION OF THE DIET TO INCLUDE
ACCEPTABLE LEVELS OF CONTAMINANTS**

Diet: Teklad Certified Guinea Pig Diet 7006C (fed ad libitum)

A Certificate of Analysis and mill date is retained on file at Geneva Laboratories.

10) . DOSAGE OF TEST AND CONTROL ARTICLES

A. Phases I, II and III

Ten (10) test guinea pigs, one (1) topical application on the left shoulder on three (3) days per week of:

a. 2.5 cm x 2.5 cm patch of test article

or

b. 2.5 cm x 2.5 cm patch of filter paper or gauze saturated with 0.4 mL of test article or its extract.

Five (5) control guinea pigs, one (1) topical application of control on the left shoulder on three (3) days per week.

B. Phase IV

Ten (10) test and five (5) control guinea pigs, one (1) topical application on the left posterior quadrant of:

a. 2.5 cm x 2.5 cm patch of test article

or

b. 2.5 cm x 2.5 cm patch of filter paper or gauze saturated with 0.4 mL of test article or its extract.

11) . METHOD AND FREQUENCY OF ADMINISTRATION

- A. Induction Phase I -- Week one (1) - three (3) topical applications
- B. Induction Phase II -- Week two (2) - three (3) topical applications
- C. Induction Phase III -- Week three (3) - three (3) topical applications
- D. Challenge Phase IV -- Week five (5) - one (1) topical application
- E. Necropsy

A necropsy will be performed on any guinea pig that dies or is withdrawn from the study before the end of the observation period.

12) . TYPE AND FREQUENCY OF TEST MEASUREMENTS

Evaluation of dermal reaction will be twenty-four (24) and forty-eight (48) hours following patch removal of the Challenge Phase.

13) . RECORDS TO BE MAINTAINED

All raw data resulting from original observations and activities of the study that are necessary for the reconstruction and evaluation of this study will be maintained in the Geneva Laboratories archives.

14) . PROPOSED STATISTICAL METHODS

None.

15) . REVISIONS TO APPROVED PROTOCOLS

All changes and/or revisions of an approved protocol and the reasons for changes will be documented, signed and dated by the Study Director and maintained with the protocol.

SECTION 2

TEST REPORT/STUDY PERSONNEL

GENEVA

LABORATORIES

JN13J0757

TP13886

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CLOSEPAT-A

P.O. NO.: 714120

REPORT TO: Mr. Scott Magness
Wm. T. Burnett & Company
2112 Montevideo Road
Jessup, MD 20794

TEST ARTICLE: Non Clickable Polyester Foam
Lot No. S82s Run 270

DATE RECEIVED: 10-15-13

TEST INITIATION DATE: 11-05-13

TEST COMPLETION DATE: 12-06-13

TEST PROCEDURE: Closed Patch Sensitization Test (GLP)
ANSI/AAMI/ISO 10993-10:2010
Ref. Geneva Laboratories Proc. No.: CL1014K

OBJECTIVE: To assess the potential of the material under test to produce delayed contact hypersensitivity in guinea pigs.

CONCLUSION: Under the conditions of this study, the test article is a:

X Non-sensitizer
N/A Sensitizer

For a detailed description of test methods and findings, see pages 2-7.

ANALYST:

Scott M Roberts

DATE:

12-6-13

ACCEPTED BY:

[Signature]
Technical Reviewer

DATE:

12-9-13

QA SIGNATURE:

[Signature]

DATE:

12/10/13

Page 1 of 7

STATISTICAL METHODS: None.

CONTROL ARTICLE: When applicable, a gauze patch with 0.4 mL of extracting or diluting media, prepared without the test article is used for control. For direct application, a plain, dry gauze patch is utilized.

N/A 0.9% Sodium Chloride USP

Mfg.:
Lot No.:
Exp.:

N/A Cottonseed Oil

Mfg.:
Lot No.:
Exp.:

X Gauze

Mfg.: Medline
Lot No.: 4505042314
Exp.: N/A

TEST SYSTEM: Clinically healthy, Hartley Strain Albino Guinea Pigs were received from Charles River Labs with individually numbered ear tattoos. Each animal's number was recorded in the raw data and referred to in Table II of this report.

Housing: Animals were group housed in box cages identified by sex, arrival date, supplier and number per cage.

Approximate age at test initiation: 1 - 5 months

Animal weight range at test initiation: 300 g to 500 g

Low Weight: 310 grams

High Weight: 375 grams

Sex of animal: Female, nulliparous and not pregnant

Diet fed ad libitum through test: Teklad Certified

Guinea Pig Diet No. #7006

Water: Municipal source, ad libitum, monitored monthly for microbial content

Number of animals used for study:

-- Ten (10) test and five (5) negative control

-- Ten (10) positive controls reference in historical data (HCA* used as positive control sensitizer)

JUSTIFICATION OF TEST SYSTEM: The Hartley albino guinea pig has been utilized historically in sensitization studies and is believed to be the most appropriate animal model for this study.

STABILITY: Test article was stored at room temperature until use unless otherwise requested by sponsor. When applicable, the control and test article extract was applied within twenty-four (24) hours of the time they were decanted.

*Hexylcinnamaldehyde

TEST METHOD:

A. X Direct Application

The test article was prepared into 2.5 cm x 2.5 cm patches, not greater than 0.5 cm in thickness. For liquid test samples, 0.4 mL was directly applied to 2.5 cm x 2.5 cm patches.

B. N/A Extract Preparation:

The test article extracted on separate occasions, prior to each application.

The test article was subdivided into portions as recommended in the current USP <88>, ANSI/AAMI/ISO 10993-12, or as requested by Sponsor.

Test article was placed in a clean extraction container and the appropriate extracting medium was added.

One blank control for parallel comparison was prepared for each extraction.

Extract was prepared for:

- N/A One (1) hour at 121°C
- N/A Twenty-four (24) hours at 70°C
- N/A Seventy-two (72) hours at 50°C
- N/A Other: hours at °C

Sample Preparation Ratio: N/A

Extracting Media:

- N/A 0.9% Sodium Chloride Injection USP
- N/A Cottonseed Oil
- N/A Other:

Condition of Extract and Test Article after extraction:

N/A

Extract Mfg., Lot No. and Exp. Date were the same as controls unless otherwise noted.

The extract was cooled to room temperature, but not below 20°C and agitated for several minutes. Then the extract was immediately decanted into a sterile syringe using aseptic techniques.

C. Test Procedure

1. Induction Phase I, II, III

The test article was administered by topical application to the clipped left upper back region of each of ten (10) test animals. When necessary, filter paper or gauze saturated with 0.4 mL of test material or extract was administered. The area was covered with an appropriate dressing. After six (6) hours, the test article and dressing were removed. Five (5) guinea pigs were maintained as the negative control group and were treated similarly using the control article. This procedure is repeated on two (2) more days for a total of three (3) applications per week. Phases II and III were conducted similarly on week two (2) and week three (3) for a total of nine (9) induction applications.

2. Induction Phase I -- Date Conducted: November 5, 6, 7, 2013

3. Induction Phase II -- Date Conducted: November 12, 13, 14, 2013

4. Induction Phase III -- Date Conducted: November 19, 20, 21, 2013

5. Challenge Phase IV -- Date Conducted: December 4, 2013

Challenge Phase IV began approximately fourteen (14) days following Phase III. The test article was administered by topical application to a clipped untested area of all test and control animals. When necessary, filter paper or gauze saturated with 0.4 mL of test article or extract was administered. The area was covered with an appropriate dressing. After six (6) hours, the test article and dressing were removed.

6. Observations

Scoring occurred at approximately twenty-four (24) and forty-eight (48) hours after the removal of the challenge phase patch using the criteria listed in Table I.

7. Evaluation of Results

Grades of 1 or greater in the test group generally indicate sensitization, provided grades of less than 1 are seen on negative control animals. If grades of 1 or greater are noted on control animals, then the reactions of the test animals which exceed the most severe control reaction are presumed to be due to sensitization.

Occasionally, the test group has a greater number of animals showing a response than the negative controls, although the intensity of the reaction is not greater than that exhibited by the controls. In these instances, a rechallenge may be necessary to define the response clearly. If necessary, a rechallenge shall be carried out one (1) to two (2) weeks after the first challenge. The method used shall be as described for the first challenge, using an untested area on the flank of the animal.

TABLE I
Scoring Criteria for Skin Reactions

Magnusson and Kligman Scale	
Patch Test Reaction	Grading Scale
No visible change	0
Discrete or patchy erythema	1
Moderate and confluent erythema	2
Intense erythema and swelling	3

DOSAGE OF TEST ARTICLE:

Phase I, II, & III -- Ten (10) test guinea pigs received one (1) topical application on the left shoulder on three (3) days per week for three (3) weeks of the following:

-- 2.5 cm x 2.5 cm patch of test article, or

-- 2.5 cm x 2.5 cm gauze or filter paper patch saturated with 0.4 mL of test article or extract.

-- Five (5) negative control guinea pigs received one (1) topical application of appropriate control on the left shoulder on three (3) days per week for three (3) weeks.

Phase IV -- Ten (10) test and five (5) control guinea pigs received topical applications of:

-- 2.5 cm x 2.5 cm patch of test article, or

-- 2.5 cm x 2.5 cm gauze or filter paper patch saturated with 0.4 mL of test article or extract.

COMMENTS: None.

DESCRIPTION OF CALCULATIONS PERFORMED ON DATA:

The percentage of test animals that were sensitized and the percentage of negative control animals that received a score was calculated.

RESULTS: See Table II (page 7) for test and control reactions.

0/10 (0 %) of the test animals were sensitized

0/5 (0 %) of the negative control animals received a score

10/10 (100%) of the positive control animals were sensitized

TABLE II

Closed Patch Sensitization Reactions

Cage & Animal Number	Hours Following Patch Removal	
	24 Hours	48 Hours
23/1	0	0
23/2	0	0
23/3	0	0
24/4	0	0
24/5	0	0
25/6	0	0
25/7	0	0
25/8	0	0
26/9	0	0
26/10	0	0
Negative Control Animals		
27/11	0	0
27/12	0	0
27/13	0	0
28/14	0	0
28/15	0	0
Positive Control Animals Reference Data: (10-02-13)		
11/637	1	1
11/638	3	1
11/639	2	1
12/640	1	1
12/641	2	1
13/642	1	1
13/643	2	2
13/644	1	2
14/645	1	0
14/646	3	2

GENEVA LABORATORIES, INC.
Toxicology Department Personnel

Dr. Colleen Stewart -- Director of Veterinary Medicine

Sandra Ott -- Study Director

Scott Roberts -- Analyst

Samantha Johnson -- Analyst

Erin Dennis -- QA Toxicology

Justin Lien -- QA/QC Supervisor

SECTION 3

***QUALITY ASSURANCE AUDIT
REPORT & STATEMENT***

JN13J0757

GLP0006*
Attachment 2-1/2

GENEVA LABORATORIES, INC.
GLP AUDIT SCHEDULE REPORT, TEST ID AND CERTIFICATION

SPONSOR: Wm. T. Burnett & Company
2112 Montevideo Road
Jessup, MD 20794

TEST ARTICLE: Non Clickable Polyester Foam
Lot No.: S82s Run 270

NATURE OF STUDY: Closed Patch Sensitization
(ANSI/AAMI/ISO 10993-10:2010) (Direct Contact)

REFERENCE: Geneva Laboratories Proc. No.: CL1014K

TEST SYSTEM: Hartley Albino Guinea Pigs

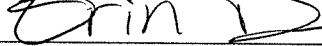
TEST STATUS: Study Initiated: 10-15-13
Test Initiated: 11-05-13
Test Completed: 12-06-13
Study Completed: 12-11-13

AUDIT DATES: See Table I

COMMENTS INCLUDING DEVIATIONS AND PROBLEMS: Under the conditions of this study, the test article is a non-sensitizer.

My review of the study documents indicates that the facilities, equipment, personnel, methods, practices, records and controls are in conformance with the GLP Regulations. This final report accurately describes the methods and standard operating procedures used and the raw data generated during the course of the study.

The copies of the protocols and records of Quality Assurance inspections have been transferred to the Geneva Laboratories GLP archive and will be maintained as long as indicated in 21 CFR Part 58 §58.195 paragraph a) and b).

QA AUDITOR:  DATE: 12/11/13

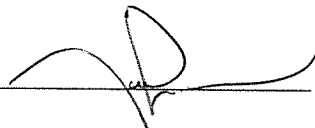
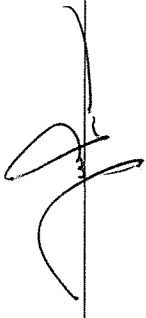
QA MANAGEMENT:  DATE: 12.11.2013

TABLE I
QUALITY ASSURANCE AUDIT DATES

INSPECTED BY INSPECTION DATE	STUDY SEGMENT INSPECTED	DATE FINDINGS WERE WRITTEN FOR MANAGEMENT AND STUDY DIRECTOR
E.D./11-05-13	Phase I: Day 1 Direct Application & 6 Hour Patches Removed	11-05-13
J.L.-E.D./ 11-06-13	Phase I: Day 2 Direct Application & 6 Hour Patches Removed	11-06-13
E.D./11-07-13	Phase I: Day 3 Direct Application & 6 Hour Patches Removed	11-07-13
E.D./11-12-13	Phase II: Day 1 Direct Application & 6 Hour Patches Removed	11-12-13
E.D./11-13-13	Phase II: Day 2 Direct Application & 6 Hour Patches Removed	11-13-13
E.D./11-14-13	Phase II: Day 3 Direct Application & 6 Hour Patches Removed	11-14-13
E.D./11-19-13	Phase III: Day 1 Direct Application & 6 Hour Patches Removed	11-19-13
E.D./11-20-13	Phase III: Day 2 Direct Application & 6 Hour Patches Removed	11-20-13
E.D./11-21-13	Phase III: Day 3 Direct Application & 6 Hour Patches Removed	11-21-13
E.D./12-04-13	Phase IV: Direct Application & 6 Hour Patches Removed	12-04-13
E.D./12-05-13	24 Hour Scoring	12-05-13
E.D./12-06-13	48 Hour Scoring	12-06-13
E.D./12-10-13	Raw Data Review	12-10-13
E.D./12-11-13	Final Report Review	12-11-13

*E.D. Erin Dennis
J.L. Justin Lien

QA AUDITOR:  DATE: 12/11/13

QA MANAGEMENT:  DATE: 12.11.2013

SECTION 4

***COMPLIANCE/ARCHIVE
STATEMENTS***

GENEVA LABORATORIES, INC.
STUDY DIRECTOR COMPLIANCE STATEMENT

SPONSOR: Wm. T. Burnett & Company
2112 Montevideo Road
Jessup, MD 20794

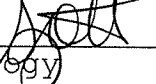
PROTOCOL: Closed Patch Sensitization Test
(ANSI/AAMI/ISO 10993-10:2010) (Direct Contact)

TEST ARTICLE: Non Clickable Polyester Foam
Lot No.: S82s Run 270

STUDY INITIATION DATE: 10-15-13 STUDY COMPLETION DATE: 12-11-13

After a review of the pertinent raw data, I am led to conclude the test results were accurately recorded and verified, correctly analyzed, interpreted and all applicable GLP regulations of 21 CFR Part 58 for Non-Clinical Laboratory Studies were followed.

All raw data, documentation, protocols, specimens and final reports are retained for orderly storage and expedient retrieval as recommended in the 21 CFR Part 58 §58.190.

STUDY DIRECTOR: _____ DATE: 12-11-13
Toxicology 

GENEVA LABORATORIES, INC.
GLP COORDINATOR ARCHIVE STATEMENT

SPONSOR: Wm. T. Burnett & Company
2112 Montevideo Road
Jessup, MD 20794

PROTOCOL: Closed Patch Sensitization
(ANSI/AAMI/ISO 10993-10:2010) (Direct Contact)

TEST ARTICLE: Non Clickable Polyester Foam
Lot No.: S82s Run 270

STUDY INITIATION DATE: 10-15-13 STUDY COMPLETION DATE: 12-11-13

For the purpose of information retrieval, we are informing you of our storage procedure of specimens and records.

Specimens and a copy of the final report are stored in the archives of Geneva Laboratories, Inc. Fragile specimens will be retained so long as the quality of the preparation affords evaluation.

Raw data for the above listed test compiled by Geneva Laboratories is stored at Geneva Laboratories, Inc. (or an alternate archive location) for not less than five (5) years.

GLP COORDINATOR: Janis Smith DATE: 12.11.13

