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January 5, 2004

Dockets Management Branch (HFA-305)  
Food and Drug Administration  
Room 1061  
5630 Fishers Lane  
Rockville, Maryland 20857

Re: Petition for Reconsideration and Stay of Action  
Final Monograph for OTC Antiperspirant Drugs  
68 Fed. Reg. 34273 (June 9, 2003)  
Docket No. 78N-0064

Revlon, Inc., submits this additional information in support of its Petition for Reconsideration and Stay of Action, dated July 7, 2003, with respect to this matter. Revlon has requested reconsideration and stay of the 24-hour limitation on a duration claim in the Final Monograph on Antiperspirant Drug Products for Over-the-Counter Human Use.

A. Current Studies Using the FDA-Approved Protocol Demonstrate 48-hour Effectiveness

In the preamble to the final regulation, FDA dismissed claims of duration longer than 24 hours stating only that the agency "has not received any data to demonstrate antiperspirant effectiveness for more than 24 hours according to the Panel's criteria." 68 Fed. Reg. 34273, 34278 (June 9, 2003). Although the FDA justification for this action is unlawful under the Administrative Procedure Act and the United States Constitution for the reasons set forth in the Petition, Revlon has nonetheless proceeded to conduct 48-hour effectiveness tests in accordance with the protocol set forth in the FDA guidelines referenced in 21 C.F.R. 350.60, and is submitting the results of those tests as supplemental information to support the Petition.

All of the 48-hour tests effectiveness previously conducted by Revlon (and by others in the industry as well) used a protocol that differs slightly from the protocol announced by FDA in the Final Monograph. Accordingly, it has been necessary to conduct new testing, in accordance with the new protocol, before relevant 48-hour data could be submitted for the administrative record. The results of the first two tests conducted by Revlon using the new FDA-approved protocol are as follows.

78N-0064

SUP 4

Dockets Management Branch (HFA-305)  
January 5, 2004  
Page 2

HTR Study No. 03-121791-112 (July 30, 2003): The test article demonstrated perspiration reductions of 36.39 percent at one hour, 42.99 percent at 24 hours, and 38.81 percent at 48 hours.

HTR Study No. 03-121794-112 (September 24, 2003): The test article demonstrated perspiration reductions of 45.88 percent at one hour, 38.26 percent at 24 hours, and 36.53 percent at 48 hours.

Copies of the two test reports are attached. All test products met the requirement in the Final Monograph that a minimum of 50 percent of the population demonstrate at least a 20 percent sweat reduction. It is virtually certain, indeed, that this requirement would have been met if the tests had been continued on for several hours after 48 hours.

B. Other Final and Tentative Final Monographs Authorize Claims Without Submission of Supporting Data to FDA

As noted above, the preamble to the Final Monograph states that 48-hour claims were denied because data from 48-hour tests were not submitted to FDA. As the Petition points out, FDA never asked for the submission of such data. Moreover, the new test protocol was not made final until the Final Monograph was published.

Even more important, FDA has on several occasions included in final and tentative final monographs testing requirements without a requirement that the test results be submitted to FDA. In fact, in none of these monographs has FDA required submission of supporting data to the agency. The supporting data which are required in order to justify making the claim, or even marketing the product, are retained in the manufacturer's files. Prior to enactment of the Food and Drug Administration Modernization Act of 1997, FDA had no legal authority to inspect those records. Since 1997, it has had this inspection authority under Section 704(a)(1) of the FD&C Act. The following OTC drug monographs and tentative final monographs contain performance testing standards with no requirement for submission of the resulting test data to FDA.

Final Monographs

1. Antacid Drug Products. Section 331.20 requires testing to determine the percent contribution of each active ingredient, calculated according to a formula set forth in the monograph.
2. Anticaries Drug Products. Section 355.70 provides that a fluoride dentifrice product must meet biological test requirements for animal carries reduction and either an enamel solubility reduction test or a fluoride enamel uptake test.

Dockets Management Branch (HFA-305)

January 5, 2004

Page 3

3. Sunscreen Drug Products. Subpart D of Part 352 sets forth testing procedures to determine the SPF value of the product and to determine the water resistance of the product.
4. Antiperspirant Products. Section 350.60 sets forth testing requirements to determine the effectiveness of final antiperspirant drug products to justify specific labeling claims.

Tentative Final Monographs

5. Topical Health-Care Antiseptic Drug Products. Section 333.470 proposes to require testing to demonstrate that the active ingredients provide in vitro activity against specified microorganisms and that the finished products demonstrate both in vitro and in vivo activity against specified microorganisms.<sup>1</sup>
6. Internal Analgesic Drug Products. Section 343.90 proposes to require dissolution testing requirements for final analgesic drug products.<sup>2</sup>
7. Oral Antiseptic Drug Products. Section 356.90 proposes to require final product testing demonstrating in vitro reduction of specified bacteria.<sup>3</sup>

We reiterate that in none of the above instances has FDA found it necessary or appropriate to require the submission of data to the agency to justify the use of the claims involved. In each instance, it has been sufficient that the manufacturer of the drug product has in fact conducted the required testing in accordance with the FDA-specified protocol and has achieved the required results. FDA is then free to examine those results at any time, if it wishes to do so.

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<sup>1</sup> 59 Fed. Reg. 31402, 31444-31452 (June 17, 1994).

<sup>2</sup> 53 Fed. Reg. 46204, 46260 (November 16, 1988).

<sup>3</sup> 59 Fed. Reg. 6084, 6122-6124 (February 9, 1994).

Dockets Management Branch (HFA-305)  
January 5, 2004  
Page 4

C. Conclusion

For the reasons set forth above, Revlon reiterates its request for reconsideration and stay of the 24-hour limitation on a duration claim in the Final Monograph on Antiperspirant Drug Products for Over-the-Counter Human Use. Revlon requests that this limitation be deleted and that any duration claim, of any length, be permitted as long as it is justified by testing conducted in accordance with the FDA-approved protocol under 21 C.F.R. 350.60.



Peter Barton Hutt  
Counsel for Revlon, Inc.

cc: Charles J. Ganley, M.D. (HFD-560)  
Daniel E. Troy, Esquire (GCF-1)

**CONFIDENTIAL**  
**REPORT FOR**  
**ANTIPERSPIRANT EFFICACY STUDY**

**HTR STUDY NO. 03-121794-112**

**SPONSOR NO. 03-7331-081**

**Final Report**

**September 24, 2003**

**FOR**  
**REVLON RESEARCH CENTER**  
**2121 ROUTE 27**  
**EDISON, NJ 08818**

**BY**  
**HILL TOP RESEARCH, INC.**  
**3225 N. 75<sup>TH</sup> ST.**  
**SCOTTSDALE, AZ 85251**

## 1.0 SUMMARY

- The objective of this study was to evaluate antiperspirant efficacy of the test articles on axillary sweating at specified post-treatment intervals. The study followed a paired comparison test design of one pair of antiperspirant test articles (A hydro-solid stick antiperspirant and B hydro-stick placebo). Within the pair of test articles, one test article was randomly assigned to either the right or left axilla and the opposite axilla received the remaining test article. There was a 17 to 21-day conditioning period during which no antiperspirants were used in the axillary area. Thirty-two female subjects completed the study.
- The following test articles were used in this study.

HTR Code	Sponsor Code	Description
A	509-016/A	Hydro-solid antiperspirant
B	509-016/B	Hydro-solid placebo

- No adverse events were reported during the course of this study.
- Based on the results of this study, hydro-solid antiperspirant 509-016/A (HTR Code A) was significantly effective in reducing axillary perspiration at 1, 24 and 48 hours after eight daily applications. The test article demonstrated reductions of 45.88 % at 1 hour, 38.26% at 24 hours and 36.53% at 48 hours.

At each interval antiperspirant 509-016/A (HTR Code A) satisfied the OTC antiperspirant final monograph requirements [§ 250.60 (21 CFR 350.60) of the final monograph (final rule) for OTC antiperspirant drug products, published in the FEDERAL REGISTER on June 9, 2003 (68 FR 34273)] that a minimum of 50% of the population demonstrate at least a 20% sweat reduction.

**2.0 TABLE OF CONTENTS**

1.0 SUMMARY.....1

2.0 TABLE OF CONTENTS .....2

3.0 SPONSOR PERSONNEL.....3

4.0 INVESTIGATIVE PERSONNEL.....3

5.0 CLINICAL RESEARCH STANDARDS.....3

6.0 PROTOCOL.....3

    6.1. STUDY PROCEDURES.....4

    6.2. PROTOCOL AMENDMENTS.....4

7.0 SUBJECTS .....4

8.0 STUDY SCHEDULE.....4

9.0 TEST ARTICLES.....4

10.0 ADVERSE EVENTS.....5

11.0 METHOD OF STATISTICAL ANALYSIS.....5

12.0 RESULTS OF STATISTICAL ANALYSIS .....7

13.0 CONCLUSIONS .....8

14.0 SIGNATURE(S).....8

15.0 QUALITY ASSURANCE STATEMENT .....9

APPENDICES

- Appendix I/Protocol
- Appendix II/Deviations
- Appendix III/Statistical Tables
- Appendix IV/Temperature and Humidity Charts

RECORD RETENTION AND PUBLICATION NOTICE

### **3.0 SPONSOR PERSONNEL**

Michael Dickens, Ph.D.  
Director of Biological Sciences  
Revlon Research Center

There was no on-site monitor visit.

### **4.0 INVESTIGATIVE PERSONNEL**

Investigator:	Linda P. Oddo, B.S.
Study Manager:	JoAnne Jubinville
Biostatistician:	James P. Bowman, M.S.
Manager Biostatistics:	Barbara M. Fath
Study Coordinator:	Dianna Christensen

### **5.0 CLINICAL RESEARCH STANDARDS**

The study was conducted in compliance with applicable Good Clinical Practice Regulations (investigator responsibilities, test article accountability, informed consent, study documentation, AE reporting), the Standard Operating Procedures of the Hill Top Research, Inc., and the study protocol. Informed consent was obtained in accordance with Title 21 of the Code of Federal Regulation, Part 50.

### **6.0 PROTOCOL**

The study protocol was followed (see Appendix I) with the exception of the deviations summarized below.

- Product was over-applied to the axillary vault on 25 occasions. The study coordinator and trained technicians reported that the test articles (especially HTR code A) were slightly “crumbly” and often small pieces were lost in the process of application.
- The humidity fell out of range briefly on Days 9 and 10 during the warm-up period, but was within range during the B and C collections.

A complete listing of deviations is available in Appendix II. In the opinion of the Investigator, the deviations did not compromise the integrity of the study.

### 6.1. Study Procedures

Subjects participated in a conditioning period for 17 to 21 days prior to enrollment. Subjects that read and signed the consent form, qualified during screening and sweat a minimum of 100mg of sweat/20 minutes/axilla were enrolled. Enrolled subjects also received a test article application on Day 1.

On days 2, 3, 4, 5, 6 and 7 subjects reported for axillary evaluation (irritation, if any, was assessed), supervised wash and test article application. On day 8 subjects also participated in sweat collection. On days 9 and 10 subjects had axillary evaluations and participated in sweat collection.

### 6.2. Protocol Amendments

There were no amendments to the protocol.

## 7.0 SUBJECTS

Forty female subjects were screened and signed the Consent Form. Thirty-two subjects who met the study criteria were enrolled. All enrolled subjects completed the study.

## 8.0 STUDY SCHEDULE

Conditioning Period: August 14 through September 3, 2003  
Date Initiated: September 4, 2003  
Date Completed: September 13, 2003

## 9.0 TEST ARTICLES

The following test articles were received by Hill Top Research on August 26, 2003:

HTR Code	Label Information	Description
A	New Improved Formula 509-016/A 1.8 oz Co-Brand Test	31 green transparent containers with green transparent lid containing solid test material
B	New Improved Formula 509-016/B 1.8 oz Co-Brand Test	30 green transparent containers with green transparent lids containing white solid test material. Two containers had labels that were no longer legible and therefore, were not used.

Each subject received eight test article applications of each product to the axillary areas according to the randomization. The test articles were applied to uniformly cover approximately a 4x6-inch area centered in the axillary vault at the rate of at least 0.35gm per axilla/treatment.

Remaining test articles will be returned to the study sponsor upon issue of the final report.

## 10.0 ADVERSE EVENTS

There were no adverse events reported during the course of the study.

## 11.0 METHOD OF STATISTICAL ANALYSIS

### 11.1 Antiperspirant Analysis - Signed Rank Test

The first method used to evaluate the data was the Wilcoxon Signed Rank Test, which is recommended in the guidelines for Effectiveness Testing of OTC Antiperspirant Drug Products, June 2003. The source data used for these analyses were the adjusted ratios, Z-values, which were calculated from the pre-treatment and post-treatment average B and C collections for each individual (shown in Table 4AB).

$$Z = (PC \times T) / (PT \times C)$$

Where Z was the adjusted ratio, PC was the pre-treated measure of moisture for the control axilla, PT was the pre-treatment measure for the test axilla, T was the treated measure for the test axilla, and C was the corresponding quantity for the control axilla.

The hypotheses tested in the signed rank test ( $\alpha=0.05$ ) are stated as follows:

$$H_0: \text{median } Z \geq 0.80$$

$$H_a: \text{median } Z < 0.80$$

The following hypotheses were also tested in the signed rank test ( $\alpha=0.05$ ):

$$H_0: \text{median } Z \geq 0.70$$

$$H_a: \text{median } Z < 0.70$$

## 11.2 Antiperspirant Analysis - Ratio Method

The efficacy of the test material was evaluated by calculating A/B ratios from the milligram data for each subject (509-016/A Hydro-solid antiperspirant - HTR Code A, 509-016/B Hydro-solid placebo - HTR Code B). Let  $R_{ij}$  equal the  $i^{\text{th}}$  A/B ratio for the  $j^{\text{th}}$  subject.  $R_{ij}$  measured prior to the first treatment represents baseline ratios ( $CR_{ij}$ ) and  $R_{ij}$  measured after individual treatments represents treatment ratios ( $TR_{ij}$ ). Since baseline ratios are dependent upon the individual subject, treatment effects were estimated from the  $TR_{ij}$  after  $TR_{ij}$  had been adjusted from  $CR_{ij}$  by calculating an adjusted ratio ( $AR_{ij}$ ) for each subject. The following formula was used for this calculation:

$$AR_{ij} = \frac{TR_{ij}}{\text{Avg. } CR_j}$$

The average  $CR_{ij}$  ( $CR_j$ ) for the  $j^{\text{th}}$  subject was calculated using the following formula:

$$\overline{CR_j} = \sum_{i=1}^n CR_{ij} / n$$

Where  $n$  = number of baseline ratios to be averaged.

The adjusted ratio (A/B) was used to evaluate treatment effect in the statistical models described below and reflects the activity of HTR Code A relative to that of the placebo side. If the activities of HTR Code A and placebo are equal, the ratio is 1.000. When the adjusted ratio is greater than or less than 1.000, the activity of HTR Code A is proportionately less than the untreated side or greater than the placebo side, respectively.

The mean adjusted sweating ratio is the arithmetic mean of the adjusted post-treatment ratios (A/B) for that post-treatment interval. This value is converted to an estimate of percent reduction in sweating using the following formula:

$$\% \text{ Reduction} = (100) (1.000 - \text{mean adjusted ratio})$$

The 95% Confidence Interval (CI) for this %Reduction is computed in the following manner:

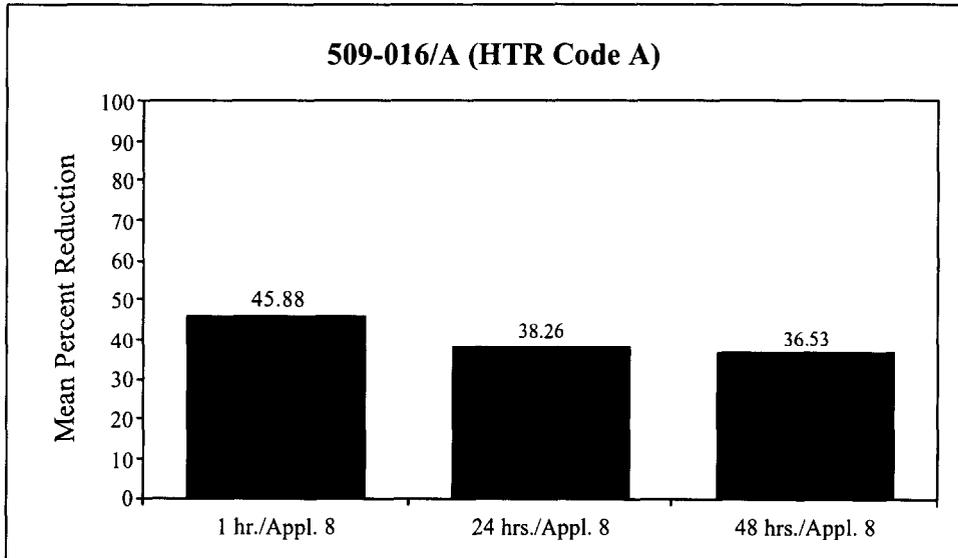
$$95\% \text{ CI} = \pm (\text{Standard error of the mean adjusted ratio}) (t_{0.05, n-1}) (100)$$

Where  $(t_{0.05, n-1})$  is the Student's  $t$  critical value for 95% significance and  $n-1$  degrees of freedom.

The number of subjects with  $\geq 20\%$  reduction in sweating based on the adjusted ratios were also calculated.

**12.0 RESULTS OF STATISTICAL ANALYSIS**

Based on the results of the signed rank test, HTR Code A was significantly effective in reducing perspiration at 1 hour, 24 hours and 48 hours after Application No. 8. The mean percent reductions in sweat, the 95% confidence intervals, the significance levels derived from the distribution-free signed rank test and the number of subjects showing  $\geq 20\%$  reduction are presented below.



Evaluation	% Reduction ± Conf. Int.	Significance Level		No. Subjects Showing ≥ 20% Reduction
		Ha: Z<.80	Ha: Z<.70	
1-Hr. after Appl. 8	45.88 ± 7.89	<0.0001*	<0.0001*	30/32
24-Hrs. after Appl. 8	38.26 ± 8.12	<0.0001*	0.0023*	27/32
48-Hrs. after Appl. 8	36.53 ± 7.31	<0.0001*	0.0227*	26/32

\* HTR Code A was significantly effective (signed rank test).

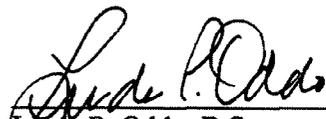
### 13.0 CONCLUSIONS

Based on the results of this study, hydro-solid antiperspirant 509-016/A (HTR Code A) was significantly effective in reducing axillary perspiration at 1, 24 and 48 hours after eight daily applications. The test article demonstrated reductions of 45.88 % at 1 hour, 38.26% at 24 hours and 36.53% at 48 hours.

At each interval antiperspirant 509-016/A (HTR Code A) satisfied the OTC antiperspirant final monograph requirements [§ 250.60 (21 CFR 350.60) of the final monograph (final rule) for OTC antiperspirant drug products, published in the FEDERAL REGISTER on June 9, 2003 (68 FR 34273)] that a minimum of 50% of the population demonstrate at least a 20% sweat reduction.

### 14.0 SIGNATURE

HILL TOP RESEARCH, INC.

  
Linda P. Oddo, B.S.  
Investigator

9-24-03  
Date

**15.0 QUALITY ASSURANCE STATEMENT**

To assure compliance with the study protocol and standard operating procedures (SOPs) of Hill Top Research, Inc., the Quality Assurance Unit performed an in phase audit during the conduct of the study on 09/06/2003, completed an audit of the study records on 09/21/2003, and audited the final report on 09/24/2003.

Any observations found during the course of the audit were reported (as applicable) to the Site Director, Study Director, Principal Investigator, Study Manager, Study Coordinator, Report Writer, and/or HTR Management.

Report reviewed by:

Valerie Fallert      September 24, 2003  
Valerie Fallert, B.S. CCRA      Date  
Quality Assurance Auditor

HTR Study No. 03-121794-112  
Sponsor No. 03-7331-081

Final Report

## **APPENDIX I**

Total number of pages = 18

**Protocol and Consent Form**

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II

  
HILL TOP RESEARCH, INC.

**PROTOCOL FOR**  
**Antiperspirant Efficacy Study**  
**(Monograph)**

**For: Revlon Research Center**

**Sponsor No.: 03-7331-081**

**Hill Top Research Project No.: 03-121794-112**

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## TABLE OF CONTENTS

1.0	INTRODUCTION.....	1
2.0	OBJECTIVE.....	1
3.0	STUDY SPONSOR AND MONITOR.	1
4.0	INVESTIGATIVE ORGANIZATION AND PERSONNEL.	1
5.0	CLINICAL RESEARCH STANDARDS .....	...2
6.0	EXPERIMENTAL DESIGN	.2
7.0	TEST ARTICLES.	.2
8.0	SUBJECT SELECTION.....	...2
8.1	Instructions.....	...2
8.2	Inclusion Criteria...	...3
8.3	Exclusion Criteria.	...3
9.0	SUBJECT WITHDRAWAL.	.3
10.0	PROCEDURE.....	...4
10.1	Conditioning Period .....	...4
10.2	Axillary Examinations.....	...4
10.3	Baseline .....	...4
10.4	Supervised Washes .....	...4
10.5	Treatment Assignment/Application	...4
	EVALUATIONS .....	.5
11.1	Sweat Collection Intervals	.5
11.2	Sweat Stimulation .....	.5
11.3	Sweat Collections.....	.5
	TEST SCHEDULE	.6
	ADVERSE EXPERIENCES....	...6
13.1	Definitions.....	...6
13.2	Follow-up .....	...7
13.3	Notification.....	...7
13.4	Anticipated Reactions	...7
	STATISTICAL ANALYSIS.	.8
	REPORT	...9
16.0	NOTICE	9
17.0	PROTOCOL APPROVAL	.9

HTR Study No.: 03-121794-112  
Sponsor No.: 03-7331-081  
Confidential

## 1.0 INTRODUCTION

An antiperspirant product is an OTC (over the counter) drug and is regulated by the Food and Drug Administration (FDA). In order to be labeled an antiperspirant, a product must be formulated within the Category I guidelines of the Antiperspirant Drug Products for Over-the-Counter Human Use: Final Monograph (68 FR 34273), June 9, 2003. The product must reduce axillary perspiration to a level that is statistically significantly greater than 20% reduction, or 30% reduction for a claim of extra effective.

If the product is not formulated within the guidelines, the product will require submission of a New Drug Application (NDA) and be tested under an Investigational New Drug exemption (IND).

The following test is carried out to determine the effectiveness of the test article in reducing axillary (underarm) sweating.

## 2.0 OBJECTIVE

To evaluate antiperspirant efficacy of the test articles on axillary sweating at specified post-treatment intervals.

## 3.0 STUDY SPONSOR AND MONITOR

Revlon Research Center  
2121 Route 27  
Edison, NJ 08818

Michael Dickens, Ph.D.  
Director of Biological Sciences  
Telephone No.: (732) 287-7715  
Fax No.: (732) 287-7784

## 4.0 INVESTIGATIVE ORGANIZATION AND PERSONNEL

Organization:	Hill Top Research, Inc.
Location:	3225 N. 75 <sup>th</sup> St. Scottsdale, AZ 85251
Telephone No:	480-949-7766
Fax No.:	480-946-2179
Investigator:	Linda P. Oddo
Study Manager:	JoAnne Jubinville
Study Coordinator:	Dianna Christensen

### CLINICAL RESEARCH STANDARDS

The study will be conducted in compliance with applicable Good Clinical Practice Regulations (investigator responsibilities, test article accountability, informed consent, study documentation, AE reporting), the Standard Operating Procedures of the Hill Top Research, Inc., study protocol and protocol amendment(s). Informed consent will be obtained in accordance with Title 21 of the Code of Federal Regulations, Part 50.

### EXPERIMENTAL DESIGN

The study will follow a paired comparison test design of one pair of antiperspirant test articles (A- hydro-solid stick antiperspirant and B-hydro-solid stick placebo). Within the pair of test articles, one test article will be randomly assigned to either the right or left axilla and the opposite axilla will receive the remaining test article. It will include a 17 - 21-day conditioning period during which no antiperspirants will be used in the axillary area..

A baseline sweat collection, treatment regimen and post-treatment sweat collections will follow the conditioning period.

### **7.0** TEST ARTICLES

The Study Sponsor will supply an adequate amount of the test articles for treatment of all subjects

HTR Code	Sponsor Code	Description
A	509-016/A	Hydro-solid antiperspirant
B	509-016/B	Hydro-solid placebo

All test articles will be returned to the Sponsor following the completion of the study.

### SUBJECT SELECTION

A sufficient number of subjects will be recruited to participate in the conditioning period to assure that approximately 30 complete the study.

8. **Instructions:** To participate in the study the subjects must agree to observe the following instructions:
- a. Abstain from the use of all antiperspirants for the entire conditioning and test periods.
  - b. Use only the deodorant product issued by Hill Top Research, Inc. or

HTR Study No.: 03-121794-112  
Sponsor No.: 03-7331-081  
Confidential

# 5

- nothing during the conditioning period.
- c. All axillary washing will be confined to the laboratory during the test period.
- d. Abstain from shaving the axillae two days prior to and during the test period.

8.2 **Inclusion Criteria**: To participate in the test period of the study each subject must satisfy the following inclusion criteria:

- a. Female, age 18-65, in good general health
- b. Has had an annual medical screening, which qualifies them for antiperspirant testing
- c. Has participated in at least a 17-21-day conditioning period
- d. Has given signed informed consent (Exhibit A)
- e. Has participated in and satisfied the established requirements of a brief medical screening just prior to enrollment ( $\leq 100$  pulse,  $\leq 99.2^{\circ}\text{F}$  temperature,  $\leq 150$  systolic,  $\leq 90$  diastolic)
- f. Produces at least 100 mg of sweat/20 minutes/axilla during baseline sweat collection

8.3 **Exclusion Criteria**: A subject will be excluded from participation in the test period for any of the following exclusion criteria:

- a. Has axillary irritation
- b. Has a history of irritation or sensitivity to axillary antiperspirant, deodorant or soap products
- c. Has a recurring history of infections, boils, abscesses, or lymph node enlargement in the axilla
- d. Has active psoriasis, eczema, skin cancer or a dermatological condition that may interfere with the conduct of the study
- e. Has heart disease, uncontrolled hypertension, kidney disease, significant respiratory disease, epilepsy, heat intolerance
- f. Taking any medication or has a significant disease that may interfere with the study results or present the subject as unhealthy
- g. Insulin dependent diabetic
- h. Taken a systemic antibiotic or used a topical antibiotic medication in the axillary area within two weeks prior to the enrollment  
Pregnant or lactating

## 9.0 **SUBJECT WITHDRAWAL**

After admission to the study, the subject may withdraw at any time for any reason. The reason for withdrawal will be reported fairly and accurately.

## 10.0 PROCEDURE

**Conditioning Period:** Each subject will be provided with a deodorant product to use as needed for a period of at least 17-21 days prior to enrollment. To affect a washout (conditioning) of previously used axillary products, each subject will be instructed to discontinue using axillary antiperspirants during this period.

**Axillary Examinations:** Subjects will be screened for axillary irritation prior to being accepted on the study. A 100-watt blue incandescent light will be used for all examinations. Hill Top personnel will conduct axillary examinations daily according to the identified scoring procedure (Exhibit B).

**Baseline:** Baseline sweat volumes will be determined according to the procedures identified in 11.3. Baseline volumes will be used to compare differences between highest and lowest sweat volume among the subjects. If the difference between the highest and lowest rate does not exceed 600 milligrams of sweat/20 minutes/axilla the study will be discontinued. To be eligible for the treatment period, each subject must have a baseline perspiration level  $\geq$  100 milligrams of sweat/20 minutes/axilla.

Each Subject will be given a treatment assignment number after being accepted onto the treatment period.

**Supervised Washes:** Supervised washes will be conducted prior to each test article application according to the following procedure:

- 1 Wash right axilla for 10 seconds using a disposable towel saturated with a 2% aqueous solution of Camay soap.
- 2 Wet a fresh disposable towel under running water and rinse the axilla until all soap is removed.
- 3 Gently pat dry the axilla using a dry disposable towel.
- 4 Repeat for left axilla.

**Test Article Assignment/Application:** For each subject the determination of which axilla will receive which test article will be determined by the randomization schedule (Exhibit C). For replicate evaluations, treatment assignments to the right and left axillae of a specific subject will remain the same.

Each subject will receive eight (8) treatment applications to both axillae. The test articles will be applied to uniformly cover approximately a 4x6-inch area centered in the axillary vault. A qualified technician will make all applications.

Test articles A (509-016/A) hydro-solid antiperspirant and B (509-016/B) hydro-

HTR Study No.: 03-121794-112  
Sponsor No.: 03-7331-081  
Confidential

7 7

solid placebo; will be applied at a rate of  $0.350\text{g} \pm 0.02\text{g}$  per axilla/treatment. The amount of sample used will be determined by weighing each unit before and after each use.

Subjects will wait at the test facility for approximately twenty-minutes following each test article application to allow time for drying and absorption of test articles.

## 11.0 EVALUATIONS

11.1 Sweat Collection Evaluation Intervals: Evaluations will be conducted at baseline, one hour after no. 8, and 24 and 48-hours after application no. 8. A total of four collections, including baseline, will be conducted.

Sweat Stimulation: Sweating of the subjects is induced by having the subjects sit in a room maintained at  $100^{\circ}\text{F} \pm 2^{\circ}\text{F}$  and at a relative humidity of about 35%. The conditions in the room will be recorded.

Sweat Collections: During the first 40 minutes of the sweat stimulation period, the subject will hold unweighed pads of Webril (non-woven cotton padding fabric) in the axillae. This preliminary warm up period will be followed by two successive 20-minute collection periods, during which the subject will hold weighed Webril pads in the axillae.

The pads will be weighed in tightly capped polystyrene vials before and after use. The vials will be labeled with the subject's number, axilla and collection designation. To insure the correct assembly of the bottle, cap and pad after use, all three components of the right collection unit will be distinctively marked. The first collection made with weighed pads will be designated Collection B and the second Collection C. Hill Top personnel will insert and remove the weighed pads. The process will be conducted at approximately 15-second intervals between subjects.

During the collections with weighed pads, the subject will be required to sit in an erect position with both feet flat on the floor and with the arms at rest in a symmetrical manner. The subjects will be allowed to drink water as desired during the warm up period and between Collections B and C.

**TEST SCHEDULE**

EVENT	DAY									
	1	2	3	4	5	6	7	8	9	10
Informed Consent	X									
Inclusion/Exclusion	X									
Axillary Evaluation	X	X	X	X	X	X	X	X	X	X
Supervised Wash	X	X	X	X	X	X	X	X		
Sweat Collection	X <sup>a</sup>							X <sup>b</sup>	X <sup>c</sup>	X <sup>c</sup>
Test Article Application	X	X	X	X	X	X	X	X		

<sup>a</sup> Day 1 sweat collection (baseline) will be conducted prior to the test article application.

<sup>b</sup> Day 8 sweat collection will be conducted ~ one-hour following test article application no. 8.

<sup>c</sup> Days 9 and 10 sweat collections will be conducted ~ 24-hours and 48-hours following test article application no. 8, respectively.

**ADVERSE EXPERIENCES**

13.1 **Definitions:** An Adverse Event/Experience is any unexpected or undesirable experience occurring to a subject during a study, which may or may not be related to the test article. All adverse event/experiences will be recorded and reported according to Good Clinical Practice Regulations and the Standard Operating Procedures of Hill Top Research, Inc.

A **Serious Adverse Event/Experience** is any adverse experience that results in any of the following outcomes:

- \* death;
- \* a life-threatening adverse experience;
- \* inpatient hospitalization or prolongation of existing hospitalization;
- \* a persistent or significant disability/incapacity;
- \* a congenital anomaly/birth defect

Important medical event/experiences that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

An **Unexpected Adverse Event/Experience** is any adverse event/experience not listed in the current labeling for the test article, the current investigator's brochure or safety data. Where test article labeling, investigator's brochure, or safety data are not available, anticipated experience will be listed and explained in the protocol based on the pharmacological properties of the test article(s).

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II 9

All adverse events, regardless of severity or the causal/effect relationship, are to be recorded. The severity of the effect will be noted as "Mild", "Moderate", or "Severe" according the following definitions:

Mild	Awareness of signs or symptom, but easily tolerated
Moderate	Discomfort to a degree as to cause interference with normal daily life activities and /or requiring medication.
Severe	Incapacity with inability to work or do usual daily life activities and requiring medical attention/intervention.

**Causal Relationship of Adverse Event/Experience**

When determining the causal/effect relationship to the test article, the relationship will be described as "None," "Possible," "Probable," or "Definite."

The following definitions will be utilized:

None	No association to the test article. Related to other etiologies such as concomitant medications or conditions or subject's known clinical state.
Possible	Uncertain association. Other etiologies are also possible.
Probable	Clear-cut association with improvement upon withdrawal of the test article. Not reasonably explained by the subject's known clinical state but not a anticipated event.
Definite	An adverse event with a clear-cut temporal relationship.

**Follow-up:** If an adverse event/experience occurs, the subject under the direction of the Investigator (or designee), may be referred to Hill Top's consultant physician for treatment. Serious or Unexpected Event/Experience will be followed to resolution.

**Notification:** The sponsor will be notified of all adverse event/experiences. Any Serious or Unexpected Adverse Event/Experience which occurs during the study must be reported promptly by the investigator (or designee) to the sponsor and the reviewing IRB, where applicable, within 24 hours of the information being reported to Hill Top Research, Inc.

**Anticipated Reactions:** A reaction could be redness, rash, swelling, itching, burning sensation, cracking or peeling, or in rare cases, small blisters. Reactions usually occur only where the sample touches the skin. A detailed account of any adverse events will be documented on the appropriate case report form. The investigator will evaluate all adverse experiences as to severity and relatedness to the test material. If the event is considered significant to the study, whether or not it is considered related to the product treatment, Hill Top will notify the sponsor as soon as possible. For the purposes of this study, an adverse event is defined as an

HTR Study No.: 03-121794-112

Sponsor No.: 03-7331-081

Confidential

unexpected adverse experience that is not identified in nature or severity in the risk assessment section of the informed consent.

If an adverse event occurs, the subject, under the direction of the Investigator (or designee), may be referred to a consultant physician for treatment. All study related adverse events will be monitored by Hill Top staff until resolution. Hill Top will report all serious adverse events to the study sponsor within 24 hours. A serious adverse event is any experience that is fatal, life threatening, permanently disabling or requires hospitalization. Additionally, any event that involves cancer, a congenital anomaly or drug overdose is considered serious.

#### 14.0 STATISTICAL ANALYSIS

Individual post-treatment sweat collections, in milligrams, will be shown. The amount of sample, in grams, used for each application to each panelist will be shown.

Antiperspirant activity is evaluated by determining shifts in ratios of the sweat output by the treated axilla to the output of the placebo treated axilla for each panelist. Estimates of percent reduction and 95% confidence intervals will be calculated.

The data will be analyzed using the Wilcoxon Signed Rank Test, which is recommended in the Guidelines for Effectiveness Testing of OTC Antiperspirant Drug Products, June, 2003. The source data for this analysis are treated to control ratios adjusted for the ratio of right-to-left axillary sweating rates. These ratios are calculated using the post-treatment average B and C collections for each individual at each time period.

The adjusted treated to control ratios for this analysis will be calculated as follows:

$$Z = (PC \times T) / (PT \times C)$$

where Z is the adjusted ratio, PC is the pretreatment measure of moisture for the control axilla (placebo), PT is the pretreatment measure for the test axilla, T is the treated measure for the test axilla, and C is the corresponding quantity for the control axilla (placebo).

The study results are analyzed by comparing the adjusted ratio to 0.80, the ratio which corresponds to a 20 percent reduction in moisture due to treatment or to an adjusted ratio of 0.70, the value which corresponds to a 30 percent reduction in moisture due to treatment. The hypothesis that reduction in perspiration exceeds 20 percent is tested statistically by subtracting 0.80 from Z for all subjects and testing the resulting number with the Wilcoxon signed rank test. The hypothesis that reduction in perspiration exceeds 30 percent is tested statistically by subtracting 0.70 from Z for all subjects and testing the resulting number with the Wilcoxon signed rank test.

The hypotheses tested in the signed rank test are stated below.

HTR Study No.: 03-121794-112  
 Sponsor No.: 03-7331-081  
 Confidential

$H_0$ : Median  $Z \geq 0.80$   
 $H_a$ : Median  $Z < 0.80$   
 $H_0$ : Median  $Z \geq 0.70$   
 $H_a$ : Median  $Z < 0.70$

Hypothesis testing will be performed at the  $\alpha = 0.05$  level

Rejection of the null hypothesis will justify the conclusion that at least 50 percent of the target population will obtain a sweat reduction of at least 20 percent.

### REPORT

The final report will summarize the method, data and conclusions relative to the test articles, as well as any information regarding the subjects that would impact the study. Source data will be retained by the testing facility on microfilm. The original source data will be maintained according to the investigator's standard operating procedure. A copy of the source documents may be obtained upon request of the Study Sponsor. Copies of transcribed data will be incorporated in the report.

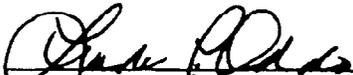
### NOTICE

No amendments to the protocol will be permitted without approval from the Study Sponsor and Investigator and where applicable, the Institutional Review Board. Such changes will be documented in writing. Approval by the Board must be obtained prior to initiation of the amendment.

### PROTOCOL APPROVAL

#### **HILL TOP RESEARCH, INC.**

Principal Investigator:

  
 Linda P. Oddo \_\_\_\_\_ 18-13-03  
 Technical Director Date

#### **REVLON RESEARCH CENTER, INC.**

Monitor:

  
 Michael Dickens, Ph.D. \_\_\_\_\_ 18/14/03  
 Director of Biological Sciences Date

Institution: Hill Top Research, Inc.  
Investigator: Linda P. Oddo  
Study Title: Antiperspirant Efficacy Study

HTR Study No. 03-121794-112

II 12  
Exhibit A

**CONSENT FORM**

**INTRODUCTION:** You are being asked to take part in a research study. Before you give your consent to be a subject, it is important that you take enough time to read and understand what your participation would involve. In preparing this consent form, it has been necessary to use some technical language. Please ask questions if there is anything you do not understand.

You will be given a signed copy of this consent form and any other necessary written information prior to the start of the study.

**PURPOSE:** The purpose of this research study is to determine if the test article is an effective antiperspirant formulation. Approximately thirty (30) females' 18-65 years of age will participate in the study. You will be testing one antiperspirant formulation and a placebo. You will receive treatment under both underarms.

**TEST ARTICLES:** One test article is a hydro-solid antiperspirant, the second test article is a hydro-solid placebo (contains no active ingredient).

**STUDY PROCEDURES:** Approximately 17- 21 days ago you received a deodorant product to use at home. You were instructed to use this product exclusively or use nothing during this period. During the ten day study, you will come to Hill Top Research, Inc. each day. Product applications will be made on Days 1 through 8 of the study. During each product application visit, both underarms will be treated. You are expected to use only the test materials on your underarms throughout the study. Participation in the study will also require you, on Days 1, 8, 9 and 10 to spend about 80 minutes in a "hotroom" in which a temperature of approximately 100°F ± 2°F and a relative humidity of about 35% are maintained. The hotroom session will consist of a 40-minute warm-up period and two 20-minute sweat collections. Sweat collections will be conducted by placing absorbent pads in your underarms. You must remain seated with your feet flat on the floor throughout all sweat collections. You will be permitted to drink water during the 40-minute warm-up period and between the two 20-minute sweat collections. There will be a total of 10 visits to Hill Top Research.

Hill Top Research, Inc. personnel, will apply the test article. After these daily applications, you will be asked not to wash or otherwise wet your underarms or apply any deodorant/antiperspirant product until the following morning when you report to the laboratory.

Eligibility for participation in this study will be determined by the results of your annual medical screening as well as your present health state. This will be determined by a brief medical screening just prior to the start of the study.

**\*\*FEMALES OF CHILDBEARING POTENTIAL:** You may not participate in this study if you are pregnant, lactating, or planning a pregnancy. As part of giving your consent you must agree to have a urine pregnancy test at the start of the study.

Institution: Hill Top Research, Inc.  
Investigator: Linda P. Oddo  
Study Title: Antiperspirant Efficacy Study

HTR Study No. 03-121794-112

II 13  
Exhibit A

**RISKS:** The test product contains ingredients available in marketed antiperspirant/deodorant formulations. No problems are expected; however, since the test is being done, in part, to see how the test article affect human skin, it is possible that you might have a "reaction". A reaction could be redness, rash, swelling, itching, cracking or peeling, or in rare cases, small blisters. Reactions usually occur only where the sample touches the skin.

A technician will examine your underarms daily to see if you are reacting. Such reactions may be due to skin irritation or allergy. However, the chance of an allergy is considered unlikely.

No risk to study participants, other than those described above as "reactions", is anticipated during the study.

**BENEFITS:** You will not benefit from the applications of test articles, but the study results may allow a new or improved product to be marketed.

**ALTERNATIVE PROCEDURES/TREATMENTS:** Because you are not being treated for a medical condition, alternative treatments do not apply to this study.

**CONFIDENTIALITY:** Information concerning you that is obtained in connection with this study will be kept confidential by Hill Top Research, except that the Company whose product is being tested will receive a copy of the study. In addition, the Food and Drug Administration and others in certain legal actions may inspect the records of the study. Information obtained in the study may be used for medical or scientific publication, but your identity will remain confidential.

**MEDICAL TREATMENT:** If in the course of this study you experience illness, discomfort or injury that appears to be a result of the study, Hill Top Research will provide you with medical care at no cost to you. Providing such medical care is not an admission of legal responsibility. If such illness, discomfort or injury does occur, ask any staff member to arrange a meeting for you with the appropriate personnel.

In certain cases of illness or injury resulting from this study, insurance benefits may be available.

**WHO TO CONTACT:** If you have any questions about this study or in case of an emergency, contact Dianna, Study Coordinator, at (480) 949-7766 during business hours (M-F, 8:00 A.M. - 4:00 P.M.) or JoAnne, Study Manager, at (602) 270-6697 after hours and on weekends. In addition, if you have any questions as to your rights as a research subject, contact Linda Oddo, Investigator, at (602) 270-6997.

**VOLUNTARY PARTICIPATION/WITHDRAWAL:** Your participation in this research study is strictly voluntary. If you fail to follow study instructions, your participation may be ended.

If you agree to participate in this study, you are also agreeing to provide Hill Top Research with accurate information and to follow study instructions as given to you. If you fail to comply with study procedures, your participation may be terminated.

Institution: Hill Top Research, Inc.  
Investigator: Linda P. Oddo  
Study Title: Antiperspirant Efficacy Study

HTR Study No. 03-121794-112

# 14  
Exhibit A

**CONSENT TO PARTICIPATE**

I understand that I will be paid \$210.00 for completion of this study. I know that participation is voluntary and that I have the right to refuse to participate. I know that I may drop out at any time without penalty or loss of benefits to which I am otherwise entitled. If I drop out of my own accord for personal reasons or is dismissed for refusal to obey rules or follow directions, I will not be paid. If, in the judgement of the Investigator, it is best to discontinue my participation in the study for other reasons, I will either be paid in full or for that portion of the test already completed.

If I am a female of childbearing potential, I am not currently pregnant or nursing an infant. I am using an adequate means of birth control and, if I become pregnant or believe I have become pregnant, I will notify the Investigator immediately.

**CONSENT:** I have read all of the pages of this consent and have been given an opportunity to ask questions about this study. Answers to such questions (if any) were satisfactory. I am eighteen years of age or older and freely and without reservation give my consent to serve as a subject in this study. By signing this form, I have not given up any of my legal rights as a research subject.

Subject's Name Printed: First \_\_\_\_\_ Middle Initial \_\_\_\_\_ Last \_\_\_\_\_

Subject's Signature \_\_\_\_\_ Date \_\_\_\_\_

Signature of Person Conducting Consent Discussion \_\_\_\_\_ Date \_\_\_\_\_

SUBJECT PRE-TEST NO.

SUBJECT NO.

11/15

## AUTHORIZATION FOR USE AND DISCLOSURE OF PERSONAL HEALTH INFORMATION

We are asking you to take part in a research study that was described in the informed consent. To do this research, the study staff will need to collect health information that identifies you.

Your personal health information includes, but is not limited to, information that was collected for your entry into the study and information collected during the study. The purpose of collecting this information is to allow *Hill Top Research, Inc.* study staff to conduct the study.

Study records that identify you will be kept confidential as required by law. Federal Privacy Regulations provide safeguards for privacy, security, and authorized access. Except when required by law, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside *Hill Top Research, Inc.* For records disclosed outside of *Hill Top Research, Inc.*, we will use your initials and assign a unique code number to the information that is sent to the sponsor.

You may decide not to give permission for the release of your personal health information for the study. In that case, you will not be able to participate in the study.

Your permission to share your personal health information for this study does not have an expiration date. If you no longer want to share your personal health information, you may cancel your permission at any time by writing *Hill Top Research, Inc.* at the address below:

Louise B. Aust  
Hill Top Research, Inc.  
3225 N. 75<sup>th</sup> St.  
Scottsdale, AZ 85251

If you cancel your permission after you have started the study, *Hill Top Research, Inc.* will stop collecting your personal health information. Although they will stop collecting new information about you, they will need to use the information already collected to evaluate the study results. If you start the study, then cancel your permission, you will not be able to continue to participate in the study.

The Sponsor and *Hill Top Research, Inc.* will make every reasonable effort to keep your personal health information private. Once the study staff shares your personal health information from the study, federal privacy laws may not keep the information private. There may be state laws or other federal laws that would protect the privacy of this information.

By signing this form, you authorize the use and disclosure of your personal health information for this research study. You will receive a copy of this form after you have signed it.

\_\_\_\_\_  
Name of Subject or Subject's Representative

\_\_\_\_\_  
Signature of Subject or Subject's Representative

\_\_\_\_\_  
Date

\_\_\_\_\_  
If signed by Representative, explain authority to act for Subject

Exhibit B

Axilla Examination and Axillary Irritation Scoring

The axillary area of all subjects will be examined by a qualified person, capable of detecting a problem under the supervision of the investigator, before the initial exposure to the hotroom, and before receiving each daily treatment application. The examination will consist of a visual inspection of the axillae for "Axillary Irritation" (edema, broken or abraded skin, erythema or abnormal physical appearance). The grading scale is attached. All scores will be documented in the study diary.

A subject exhibiting "Axillary Irritation" (score 0.5 or greater) before the study start will not be eligible for participation in the study. The presence of "Axillary Irritation" during the test period will not automatically necessitate withdrawal from the study. Should such a condition arise, the investigator will determine if the subject will continue in the study. The condition will be followed closely and documented until remission of the symptoms. If the investigator decides to drop the subject from the study, the decision will be recorded in the diary, identified by the subject's name and number, axilla involved, date and the reason for their termination. If the symptoms still exist at the end of the test, the investigator will establish a follow-up procedure.

If "Axillary Irritation" (score 2.0 or greater) appears, the subject will be withdrawn from the test and the investigator will establish a follow-up procedure which will continue until remission. All procedures and medication will be documented in the diary and a final report issued by the Investigator.

Subjective Observations

Any voluntary comments from the subjects (such as itching and burning) will also be noted in the diary. As noted in the informed consent, a subject is free to withdraw from the study at anytime for any reason.

**AXILLARY IRRITATION SCALE**

- 0 = No visible reaction
- 0.5 = Slight, confluent<sup>1</sup> or patchy erythema
- 1.0 = Mild erythema (pink)
- 2.0 = Moderate erythema (definite redness)
- 3.0 = Strong erythema (very intense redness)

<sup>1</sup>confluent - flowing or running together

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18

03-121794-112

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STUDY RANDOMIZATION

EXHIBIT C

SUBJECT NUMBER	RIGHT	LEFT
1	B	A
2	B	A
3	A	B
4	A	B
5	B	A
6	B	A
7	B	A
8	A	B
9	B	A
10	A	B
11	B	A
12	B	A
13	A	B
14	A	B
15	A	B
16	B	A
17	B	A
18	A	B
19	B	A
20	A	B
21	A	B
22	A	B
23	A	B
24	B	A
25	B	A
26	B	A
27	A	B
28	A	B
29	B	A
30	A	B
31	A	B
32	B	A

HTR Study No. 03-121794-112  
Sponsor No. 03-7331-081

Final Report

## **APPENDIX I**

Total number of pages = 2

### **Deviations**

**Deviations**

<b>Subj. No.</b>	<b>Day No.</b>	<b>Deviation</b>
2	1	Application on the right side exceeded the amount stated in the protocol. (0.404 gm)
13	1	Application on the right side exceeded the amount stated in the protocol. (0.376 gm)
31	1	Application on the right side exceeded the amount stated in the protocol. (0.405 gm)
4	1	Application on the left side exceeded the amount stated in the protocol. (0.379 gm)
2	2	Application on the left side exceeded the amount stated in the protocol. (0.375 gm)
32	2	Application on the left side exceeded the amount stated in the protocol. (0.406 gm)
7	3	Application on the left side exceeded the amount stated in the protocol. (0.530 gm)
9	3	Application on the left side exceeded the amount stated in the protocol. (0.372 gm)
13	3	Application on the left side exceeded the amount stated in the protocol. (0.414 gm)
30	3	Application on the right side exceeded the amount stated in the protocol. (0.394 gm)
4	3	Application on the left side exceeded the amount stated in the protocol. (0.390 gm)
31	3	Application on the right side exceeded the amount stated in the protocol. (0.393 gm)
17	4	Application on the left side exceeded the amount stated in the protocol. (0.395 gm)
1	4	Application on the right side exceeded the amount stated in the protocol. (0.394 gm)
30	4	Application on the right side exceeded the amount stated in the protocol. (0.391 gm)
5	5	Application on the left side exceeded the amount stated in the protocol. (0.379 gm)
7	5	Application on the left side exceeded the amount stated in the protocol. (0.524 gm)
23	5	Application on the right side exceeded the amount stated in the protocol. (0.382 gm)
17	6	Application on the right side exceeded the amount stated in the protocol. (0.380 gm)

### Deviations

22	7	Application on the right side exceeded the amount stated in the protocol. (0.409 gm)
23	7	Application on the right side exceeded the amount stated in the protocol. (0.404 gm)
29	7	Application on the left side exceeded the amount stated in the protocol. (0.399 gm)
30	7	Application on the right side exceeded the amount stated in the protocol. (0.426 gm)
11	8	Application on the left side exceeded the amount stated in the protocol. (0.382 gm)
28	8	Application on the right side exceeded the amount stated in the protocol. (0.391 gm)
All	9	Humidity dropped to approximately 29%RH for approximately 5 to 8 minutes during the warm-up session. Humidity was in range during B and C collections.
All	10	Humidity approximately 30%RH upon entering hot room. Rose steadily to 36%RH in approximately 15 minutes of warm-up period. Humidity was in range during B and C collections.

## **APPENDIX III**

Total number of pages = 9

### **Statistical Tables**

Table 1AB	Presentation of the net milligrams for sweat collected at each evaluation and the averages of the B & C collection net milligrams of sweat
Table 2AB	Presentation of the baseline and adjusted post-treatment sweating ratios
Table 3AB	Summary statistics for post-treatment sweating ratios
Table 4AB	Wilcoxon signed rank test (Z 0.80)
Table 5AB	Summary of the results of the signed rank test (Z 0.80)
Table 6AB	Wilcoxon signed rank test (Z 0.70)
Table 7AB	Summary of the results of the signed rank test (Z 0.70)
Table 8AB	Grams of test article used at each application

HTR No. 03-121794-112 Sponsor No.: 03-7331-081

08:35 Wednesday, September 17, 2003 1

Table 1AB. Presentation of the net milligrams of sweat (final-initial weights) collected at each evaluation and the averages of the B & C collection net milligrams of sweat.

509-016/A Hydro-solid antiperspirant (HIR Code A) vs 509-016/B Hydro-solid placebo (HIR Code B)

HIR Code A		BASELINE		APPLN 8-1 HOUR		APPLN 8-24 HOUR		APPLN 8-48 HOUR					
Collection		Collection		Collection		Collection		Collection					
B		C		average		B		C		average			
Subject	Axilla												
1	L	368	453	410.5	75	94	84.5	161	245	203.0	217	228	222.5
2	L	439	455	447.0	93	122	107.5	161	246	203.5	338	282	310.0
3	R	470	674	572.0	336	230	283.0	325	602	463.5	391	476	433.5
4	R	286	656	471.0	158	307	232.5	435	403	419.0	470	568	519.0
5	L	568	403	485.5	176	156	166.0	191	605	398.0	158	261	209.5
6	L	336	387	361.5	166	125	145.5	151	222	186.5	178	309	243.5
7	L	367	432	399.5	377	315	346.0	170	258	214.0	350	460	405.0
8	R	617	524	570.5	196	308	252.0	547	886	716.5	618	934	776.0
9	L	332	424	378.0	149	194	171.5	406	450	428.0	446	416	431.0
10	R	238	344	291.0	61	57	59.0	120	140	130.0	135	193	164.0
11	L	332	301	316.5	97	87	92.0	157	185	171.0	111	188	149.5
12	L	303	443	373.0	72	78	75.0	108	119	113.5	118	154	136.0
13	R	356	404	380.0	75	87	81.0	127	213	170.0	108	90	99.0
14	R	765	881	823.0	755	696	725.5	887	1673	1280.0	1647	1107	1377.0
15	R	670	638	654.0	207	263	235.0	389	470	429.5	500	626	563.0
16	L	615	494	554.5	55	63	59.0	201	206	203.5	409	244	326.5
17	L	432	353	392.5	75	79	77.0	151	193	172.0	148	173	160.5
18	R	353	510	431.5	83	136	109.5	221	221	221.0	211	300	255.5
19	L	644	843	743.5	215	205	210.0	383	377	380.0	232	399	315.5
20	R	356	797	576.5	159	64	111.5	172	82	127.0	271	207	239.0
21	R	360	429	394.5	121	131	126.0	171	190	180.5	146	255	200.5
22	R	355	323	339.0	240	181	210.5	374	339	356.5	449	358	403.5
23	R	738	988	863.0	164	287	225.5	626	724	675.0	612	1005	808.5
24	L	168	259	213.5	90	107	98.5	105	216	160.5	181	205	193.0
25	L	310	364	337.0	57	159	108.0	156	183	169.5	109	188	148.5
26	L	293	340	316.5	69	96	82.5	227	154	190.5	144	306	225.0
27	R	503	490	496.5	113	111	112.0	338	682	510.0	228	298	263.0
28	R	231	332	281.5	77	110	93.5	198	237	217.5	238	299	268.5
29	L	399	597	496.0	180	334	257.0	247	262	254.5	285	280	282.5
30	R	856	745	800.5	150	144	147.0	281	278	279.5	246	195	220.5
31	R	1048	709	878.5	74	114	94.0	217	203	210.0	182	424	303.0
32	L	763	716	739.5	320	543	431.5	685	747	716.0	736	798	767.0
Mean		464.7	522.1	493.4	163.6	187.0	175.3	284.0	375.3	329.7	331.6	382.1	356.8
Std		206.4	189.2	182.7	136.5	141.4	134.1	185.7	314.3	243.3	292.0	255.2	263.0
N		32	32	32.0	32	32	32.0	32	32	32.0	32	32	32.0

HIR No. 03-121794-112 Sponsor No.: 03-7331-081

08:35 Wednesday, September 17, 2003 2

Table 1AB. Presentation of the net milligrams of sweat (final-initial weights) collected at each evaluation and the averages of the B & C collection net milligrams of sweat.

509-016/A Hydro-solid antiperspirant (HIR Code A) vs 509-016/B Hydro-solid placebo (HIR Code B)

HIR Code B		BASELINE			APPLN. 8-1 HOUR			APPLN. 8-24 HOUR			APPLN. 8-48 HOUR		
		Collection			Collection			Collection			Collection		
		B, C, average			B, C, average			B, C, average			B, C, average		
Subject	Axilla												
.1	R	452	505	478.5	190	285	237.5	372	477	424.5	432	355	393.5
.2	R	498	545	521.5	287	329	308.0	389	626	507.5	615	465	540.0
.3	L	431	614	522.5	441	447	444.0	514	796	655.0	835	858	846.5
.4	L	307	547	427.0	192	382	287.0	515	489	502.0	494	703	598.5
.5	R	491	408	449.5	402	328	365.0	381	1158	769.5	308	412	360.0
.6	R	499	463	481.0	336	489	417.5	405	512	458.5	484	675	579.5
.7	R	542	740	641.0	415	381	398.0	419	518	468.5	754	686	720.0
.8	L	803	640	721.5	649	537	593.0	914	944	929.0	850	1170	1010.0
.9	R	222	363	292.5	174	261	217.5	517	497	507.0	432	526	479.0
.10	L	192	327	259.5	51	91	71.0	375	379	377.0	404	485	444.5
.11	R	370	321	345.5	212	206	209.0	268	479	373.5	206	290	248.0
.12	R	394	478	436.0	198	293	245.5	301	358	329.5	247	416	331.5
.13	L	289	458	373.5	120	143	131.5	191	283	237.0	127	124	125.5
.14	L	562	603	582.5	846	714	780.0	775	1136	955.5	1276	1321	1298.5
.15	L	613	547	580.0	418	572	495.0	677	736	706.5	737	1031	884.0
.16	R	492	340	416.0	119	198	158.5	326	413	369.5	805	604	704.5
.17	R	474	362	418.0	168	248	208.0	254	344	299.0	240	311	275.5
.18	L	363	531	447.0	202	249	225.5	352	342	347.0	435	460	447.5
.19	R	485	774	629.5	485	410	447.5	687	638	662.5	277	553	415.0
.20	L	225	529	377.0	288	170	229.0	447	175	311.0	562	423	492.5
.21	L	337	428	382.5	192	303	247.5	288	356	322.0	263	416	339.5
.22	L	369	345	357.0	348	342	345.0	573	528	550.5	462	402	432.0
.23	L	552	692	622.0	401	733	567.0	874	1117	995.5	804	1203	1003.5
.24	R	233	251	242.0	161	298	229.5	210	241	225.5	244	292	268.0
.25	R	223	296	259.5	65	140	102.5	207	267	237.0	142	255	198.5
.26	R	435	524	479.5	227	414	320.5	791	125	458.0	362	1117	739.5
.27	L	339	458	398.5	155	189	172.0	442	522	482.0	275	322	298.5
.28	L	186	303	244.5	81	206	143.5	338	304	321.0	316	391	353.5
.29	R	521	867	694.0	363	828	595.5	382	649	515.5	523	511	517.0
.30	L	491	451	471.0	210	317	263.5	550	402	476.0	383	350	366.5
.31	L	878	585	731.5	140	460	300.0	652	582	617.0	422	1051	736.5
.32	R	1019	878	948.5	465	716	590.5	696	829	762.5	729	938	833.5
.Mean		446.5	505.4	475.9	281.3	365.3	323.3	471.3	538.2	504.8	482.7	597.4	540.0
.Std		191.7	162.5	161.6	175.2	187.7	168.8	198.3	270.1	208.9	256.8	319.9	271.3
.N		32	32	32.0	32	32	32.0	32	32	32.0	32	32	32.0



HTR No. 03-121794-112 Sponsor No.: 03-7331-081  
 Table 3AR Summary statistics for post treatment sweating ratios.  
 509-016/A Hydro-solid antiperspirant (HIR Code A) vs 509-016/B Hydro-solid placebo (HIR Code B)

	PERCENT REDUCTION	CONFIDENCE INTERVAL	20% REDUCTION	n
APPLN 8-1 HOUR	45.88	7.89	30	32
APPLN 8-24 HOUR	38.26	8.12	27	32
APPLN 8-48 HOUR	36.53	7.31	26	32

Table 4AB. Wilcoxon signed rank test.

509-016/A Hydro-solid antiperspirant (HIR Code A) vs 509-016/B Hydro-solid placebo (HIR Code B)

SUBJECT	APPLN. 8-1 HOUR						APPLN. 8-24 HOUR						APPLN. 8-48 HOUR					
	PC	PT	C	T	Z	Z-0.80	PC	PT	C	T	Z	Z-0.80	PC	PT	C	T	Z	Z-0.80
	Z=(PC x T)/(PT x C)																	
1	478.5	410.5	237.5	84.5	0.41	-0.39	478.5	410.5	424.5	203.0	0.56	-0.24	478.5	410.5	393.5	222.5	0.66	-0.14
2	521.5	447.0	308.0	107.5	0.41	-0.39	521.5	447.0	507.5	203.5	0.47	-0.33	521.5	447.0	540.0	310.0	0.67	-0.13
3	522.5	572.0	444.0	283.0	0.58	-0.22	522.5	572.0	655.0	463.5	0.65	-0.15	522.5	572.0	846.5	433.5	0.47	-0.33
4	427.0	471.0	287.0	232.5	0.73	-0.07	427.0	471.0	502.0	419.0	0.76	-0.04	427.0	471.0	598.5	519.0	0.79	-0.01
5	449.5	485.5	365.0	166.0	0.42	-0.38	449.5	485.5	769.5	398.0	0.48	-0.32	449.5	485.5	360.0	209.5	0.54	-0.26
6	481.0	361.5	417.5	145.5	0.46	-0.34	481.0	361.5	458.5	186.5	0.54	-0.26	481.0	361.5	579.5	243.5	0.56	-0.24
7	641.0	399.5	398.0	346.0	1.39	0.59	641.0	399.5	468.5	214.0	0.73	-0.07	641.0	399.5	720.0	405.0	0.90	0.10
8	721.5	570.5	593.0	252.0	0.54	-0.26	721.5	570.5	929.0	716.5	0.98	0.18	721.5	570.5	1010.0	776.0	0.97	0.17
9	292.5	378.0	217.5	171.5	0.61	-0.19	292.5	378.0	507.0	428.0	0.65	-0.15	292.5	378.0	479.0	431.0	0.70	-0.10
10	259.5	291.0	71.0	59.0	0.74	-0.06	259.5	291.0	377.0	130.0	0.31	-0.49	259.5	291.0	444.5	164.0	0.33	-0.47
11	345.5	316.5	209.0	92.0	0.48	-0.32	345.5	316.5	373.5	171.0	0.50	-0.30	345.5	316.5	248.0	149.5	0.66	-0.14
12	436.0	373.0	245.5	75.0	0.36	-0.44	436.0	373.0	329.5	113.5	0.40	-0.40	436.0	373.0	331.5	136.0	0.48	-0.32
13	373.5	380.0	131.5	81.0	0.61	-0.19	373.5	380.0	237.0	170.0	0.71	-0.09	373.5	380.0	125.5	99.0	0.78	-0.02
14	582.5	823.0	780.0	725.5	0.66	-0.14	582.5	823.0	955.5	1280.0	0.95	0.15	582.5	823.0	1298.5	1377.0	0.75	-0.06
15	580.0	654.0	495.0	235.0	0.42	-0.38	580.0	654.0	706.5	429.5	0.54	-0.26	580.0	654.0	884.0	563.0	0.56	-0.24
16	416.0	554.5	158.5	59.0	0.28	-0.52	416.0	554.5	369.5	203.5	0.41	-0.39	416.0	554.5	704.5	326.5	0.35	-0.45
17	418.0	392.5	208.0	77.0	0.39	-0.41	418.0	392.5	299.0	172.0	0.61	-0.19	418.0	392.5	275.5	160.5	0.62	-0.18
18	447.0	431.5	225.5	109.5	0.50	-0.30	447.0	431.5	347.0	221.0	0.66	-0.14	447.0	431.5	447.5	255.5	0.59	-0.21
19	629.5	743.5	447.5	210.0	0.40	-0.40	629.5	743.5	662.5	380.0	0.49	-0.31	629.5	743.5	415.0	315.5	0.64	-0.16
20	377.0	576.5	229.0	111.5	0.32	-0.48	377.0	576.5	311.0	127.0	0.27	-0.53	377.0	576.5	492.5	239.0	0.32	-0.48
21	382.5	394.5	247.5	126.0	0.49	-0.31	382.5	394.5	322.0	180.5	0.54	-0.26	382.5	394.5	339.5	200.5	0.57	-0.23
22	357.0	339.0	345.0	210.5	0.64	-0.16	357.0	339.0	550.5	356.5	0.68	-0.12	357.0	339.0	432.0	403.5	0.98	0.18
23	622.0	863.0	567.0	225.5	0.29	-0.51	622.0	863.0	995.5	675.0	0.49	-0.31	622.0	863.0	1003.5	808.5	0.58	-0.22
24	242.0	213.5	229.5	98.5	0.49	-0.31	242.0	213.5	225.5	160.5	0.81	0.01	242.0	213.5	268.0	193.0	0.82	0.02
25	259.5	337.0	102.5	108.0	0.81	0.01	259.5	337.0	237.0	169.5	0.55	-0.25	259.5	337.0	198.5	148.5	0.58	-0.22
26	479.5	316.5	320.5	82.5	0.39	-0.41	479.5	316.5	458.0	190.5	0.63	-0.17	479.5	316.5	739.5	225.0	0.46	-0.34
27	398.5	496.5	172.0	112.0	0.52	-0.28	398.5	496.5	482.0	510.0	0.85	0.05	398.5	496.5	298.5	263.0	0.71	-0.09
28	244.5	281.5	143.5	93.5	0.57	-0.23	244.5	281.5	321.0	217.5	0.59	-0.21	244.5	281.5	353.5	268.5	0.66	-0.14
29	694.0	498.0	595.5	257.0	0.60	-0.20	694.0	498.0	515.5	254.5	0.69	-0.11	694.0	498.0	517.0	282.5	0.76	-0.04
30	471.0	800.5	263.5	147.0	0.33	-0.47	471.0	800.5	476.0	279.5	0.35	-0.45	471.0	800.5	366.5	220.5	0.35	-0.45
31	731.5	878.5	300.0	94.0	0.26	-0.54	731.5	878.5	617.0	210.0	0.28	-0.52	731.5	878.5	736.5	303.0	0.34	-0.46
32	948.5	739.5	590.5	431.5	0.94	0.14	948.5	739.5	762.5	716.0	1.20	0.40	948.5	739.5	833.5	767.0	1.18	0.38





HTR No. 03-121794-112 Sponsor No.: 03-7331-081

08:35 Wednesday, September 17, 2003 8

Table 7AB Summary of the results of the signed rank test.

509-016/A Hydro-solid antiperspirant (HTR Code A) vs 509-016/B Hydro-solid placebo (HTR Code B)

EVALUATION	Standard Deviation		Z	p-value
	Mean	Deviation		
APPLN 8-1 HOUR	-0.1672	0.2242	32	<0.0001*
APPLN 8-24 HOUR	-0.0965	0.2069	32	0.0023*
APPLN 8-48 HOUR	-0.0649	0.2030	32	0.0227*

\* = Significance

HIR No. 03-121794-112 Sponsor No.: 03-7331-081  
 TABLE 8AB Grams of test article used at each application.

08:45 Thursday, September 18, 2003 9

509-016/A Hydro-solid antiperspirant (HIR Code A) VS. 509-016/B Hydro-solid placebo (HIR Code B)

SUBJECT NUMBER	AXILLA	(HIR CODE A) APPLICATION NUMBER								AXILLA	(HIR CODE B) APPLICATION NUMBER							
		1	2	3	4	5	6	7	8		1	2	3	4	5	6	7	8
1	L	0.35	0.35	0.36	0.36	0.36	0.37	0.36	0.36	R	0.35	0.36	0.35	0.39	0.35	0.36	0.36	0.36
2	L	0.35	0.38	0.36	0.35	0.36	0.36	0.36	0.36	R	0.40	0.36	0.35	0.35	0.35	0.37	0.34	0.34
3	R	0.34	0.34	0.34	0.34	0.36	0.37	0.36	0.34	L	0.34	0.36	0.33	0.34	0.35	0.34	0.35	0.35
4	R	0.35	0.37	0.34	0.36	0.36	0.37	0.35	0.37	L	0.38	0.35	0.39	0.34	0.36	0.36	0.34	0.36
5	L	0.34	0.36	0.36	0.37	0.38	0.36	0.34	0.36	R	0.34	0.36	0.35	0.34	0.35	0.35	0.34	0.35
6	L	0.37	0.34	0.36	0.33	0.34	0.35	0.36	0.36	R	0.37	0.35	0.34	0.37	0.34	0.35	0.34	0.36
7	L	0.35	0.36	0.53	0.34	0.52	0.37	0.36	0.35	R	0.35	0.35	0.36	0.34	0.36	0.34	0.36	0.34
8	R	0.36	0.36	0.36	0.34	0.37	0.36	0.37	0.36	L	0.34	0.35	0.36	0.34	0.35	0.35	0.35	0.36
9	L	0.34	0.37	0.37	0.36	0.37	0.37	0.36	0.37	R	0.35	0.36	0.35	0.37	0.34	0.35	0.35	0.35
10	R	0.37	0.36	0.37	0.37	0.35	0.35	0.35	0.37	L	0.36	0.36	0.34	0.37	0.37	0.35	0.37	0.37
11	L	0.36	0.36	0.35	0.37	0.37	0.37	0.34	0.38	R	0.37	0.36	0.33	0.35	0.35	0.37	0.36	0.35
12	L	0.36	0.37	0.36	0.35	0.34	0.37	0.36	0.36	R	0.36	0.37	0.34	0.34	0.35	0.35	0.36	0.34
13	R	0.38	0.34	0.35	0.34	0.35	0.36	0.35	0.37	L	0.36	0.36	0.41	0.35	0.36	0.34	0.36	0.35
14	R	0.35	0.36	0.35	0.35	0.37	0.37	0.35	0.35	L	0.35	0.36	0.35	0.35	0.35	0.36	0.37	0.35
15	R	0.36	0.35	0.34	0.36	0.37	0.36	0.37	0.36	L	0.35	0.35	0.35	0.36	0.34	0.36	0.37	0.36
16	L	0.35	0.37	0.33	0.35	0.35	0.37	0.34	0.36	R	0.35	0.36	0.34	0.34	0.35	0.34	0.35	0.35
17	L	0.36	0.36	0.34	0.40	0.36	0.35	0.36	0.36	R	0.35	0.35	0.35	0.37	0.36	0.38	0.36	0.34
18	R	0.35	0.36	0.35	0.34	0.36	0.35	0.37	0.37	L	0.36	0.35	0.35	0.34	0.35	0.35	0.34	0.35
19	L	0.35	0.35	0.37	0.35	0.34	0.37	0.36	0.36	R	0.34	0.35	0.35	0.35	0.35	0.36	0.35	0.36
20	R	0.35	0.35	0.35	0.34	0.37	0.35	0.34	0.36	L	0.35	0.35	0.34	0.35	0.36	0.35	0.36	0.35
21	R	0.35	0.34	0.35	0.37	0.35	0.37	0.37	0.37	L	0.37	0.36	0.35	0.36	0.36	0.36	0.35	0.37
22	R	0.35	0.36	0.35	0.36	0.36	0.36	0.41	0.36	L	0.36	0.36	0.33	0.34	0.34	0.36	0.35	0.36
23	R	0.36	0.34	0.34	0.34	0.38	0.37	0.40	0.35	L	0.36	0.35	0.34	0.33	0.34	0.35	0.36	0.35
24	L	0.37	0.37	0.36	0.34	0.36	0.34	0.34	0.35	R	0.35	0.35	0.35	0.36	0.35	0.35	0.34	0.35
25	L	0.34	0.36	0.35	0.34	0.35	0.35	0.36	0.35	R	0.36	0.35	0.35	0.35	0.36	0.34	0.35	0.36
26	L	0.37	0.36	0.35	0.37	0.35	0.37	0.35	0.34	R	0.36	0.34	0.35	0.35	0.35	0.35	0.36	0.35
27	R	0.36	0.35	0.34	0.33	0.36	0.35	0.35	0.35	L	0.36	0.37	0.35	0.35	0.36	0.34	0.36	0.35
28	R	0.37	0.37	0.35	0.35	0.37	0.37	0.36	0.39	L	0.35	0.37	0.34	0.35	0.36	0.37	0.35	0.34
29	L	0.36	0.36	0.35	0.34	0.37	0.37	0.40	0.36	R	0.37	0.37	0.35	0.35	0.35	0.37	0.37	0.35
30	R	0.35	0.36	0.39	0.37	0.34	0.34	0.43	0.36	L	0.35	0.36	0.36	0.37	0.36	0.37	0.36	0.36
31	R	0.41	0.36	0.39	0.36	0.35	0.36	0.34	0.35	L	0.35	0.36	0.35	0.34	0.37	0.37	0.34	0.36
32	L	0.37	0.41	0.34	0.33	0.36	0.37	0.37	0.35	R	0.36	0.37	0.35	0.37	0.34	0.34	0.37	0.36

HTR Study No. 03-121794-112  
Sponsor No. 03-7331-081

Final Report

## **APPENDIX IV**

Total number of pages = 4

**Temperature and Humidity Charts**



PROJECT NO.: 03-121794-112

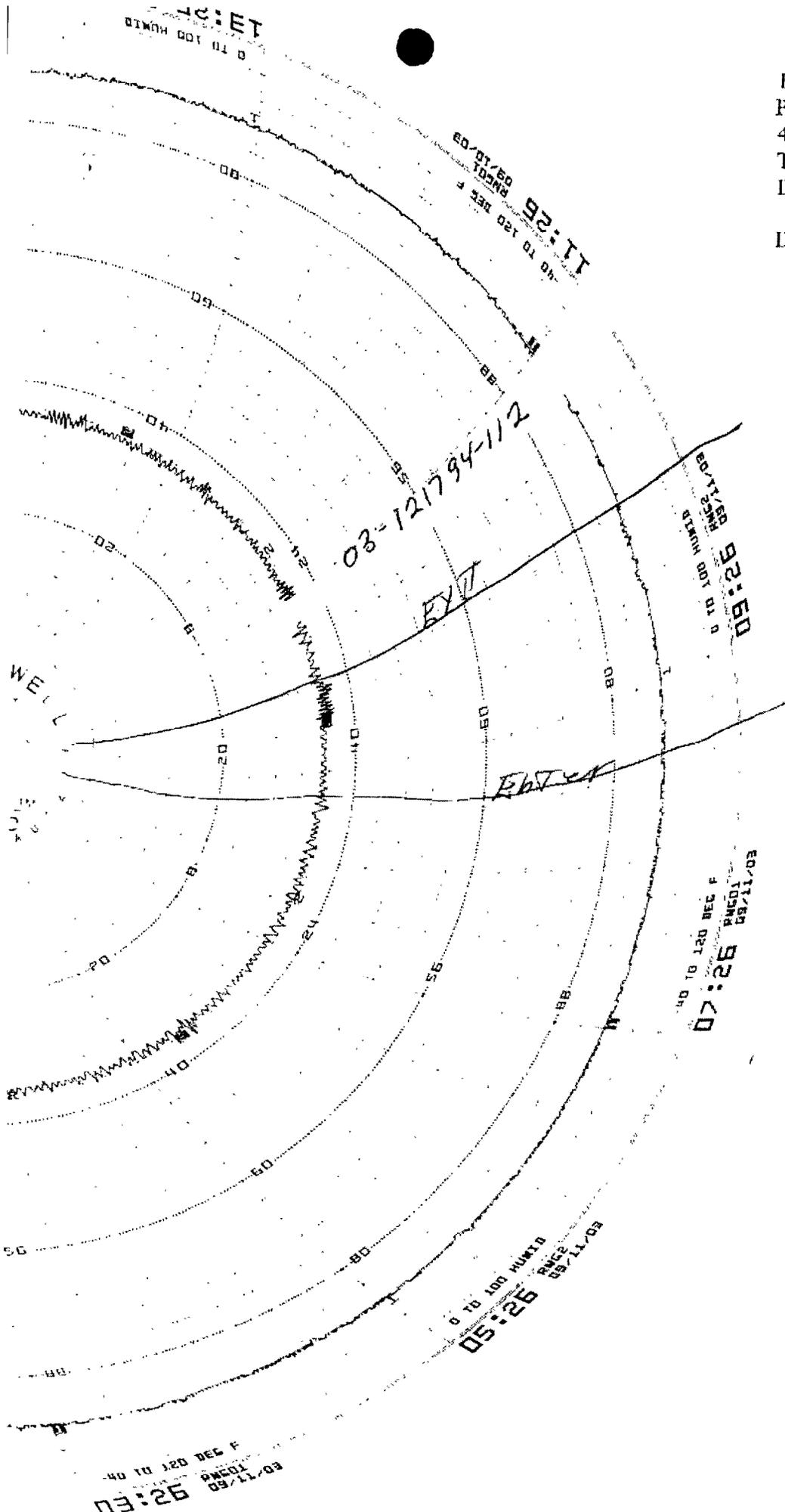
PAGE NO.: VI-93

40-minute warm-up period

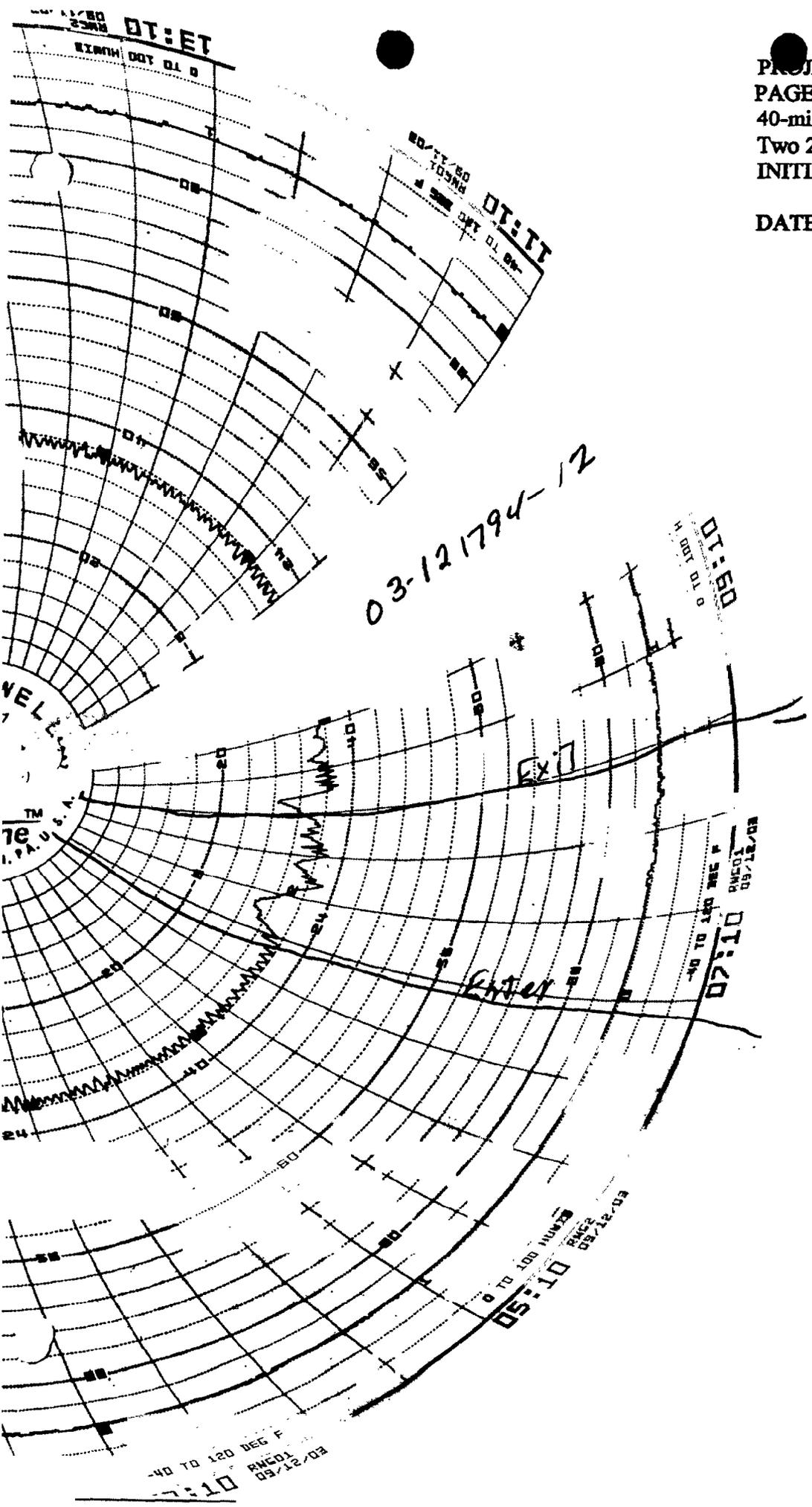
Two 20-minute collections

INITIALS RV

DATE 9-11-03



PROJECT NO.: 03-12794-112  
 PAGE NO.: VI-94  
 40-minute warm-up period  
 Two 20-minute collections  
 INITIALS Dr [Signature]  
 DATE 9-11-03  
9-12-03



PROJECT NO.: 03-121794-112

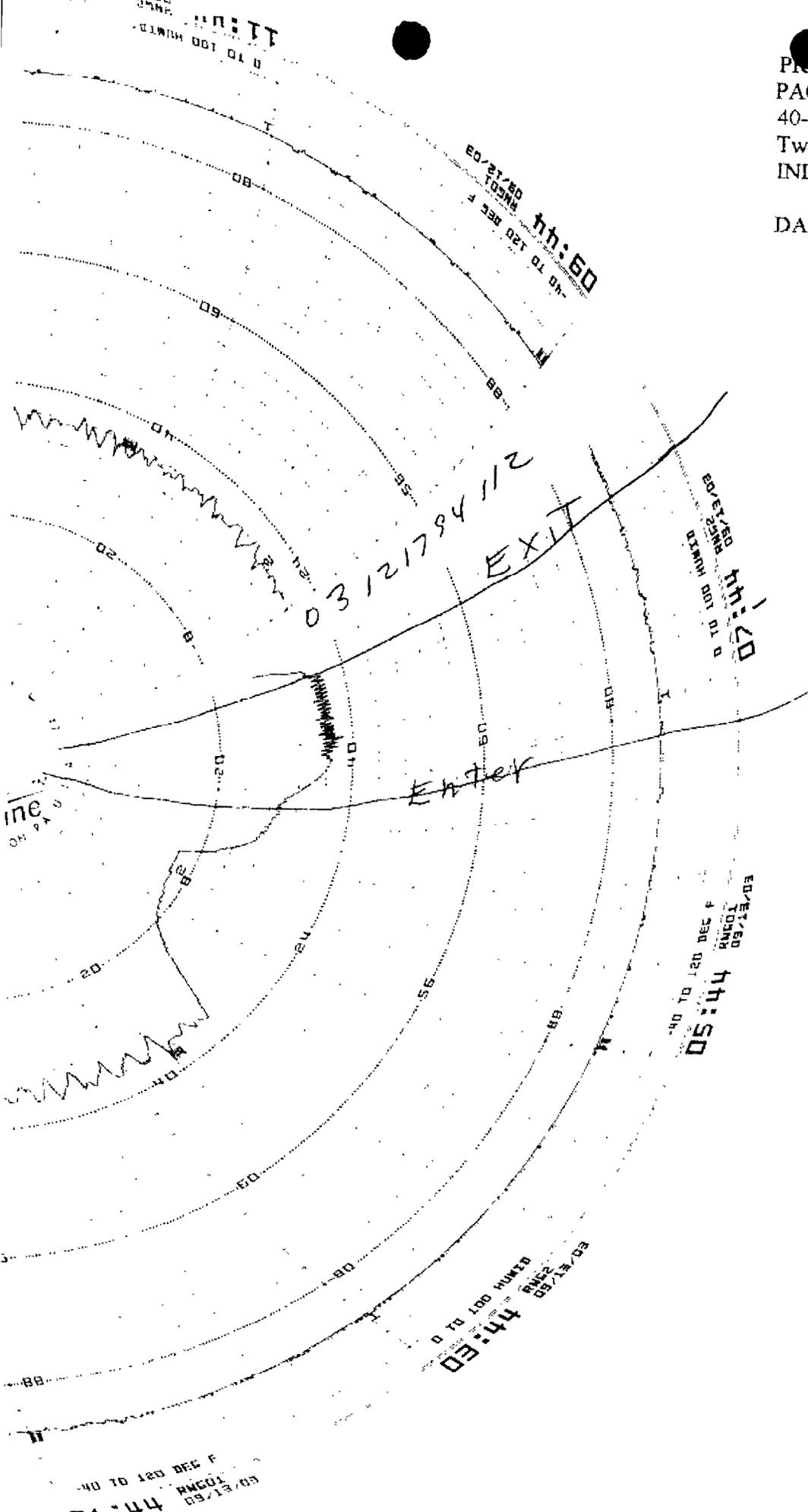
PAGE NO.: 01 95

40-minute warm-up period

Two 20-minute collections

INITIALS *[Signature]*

DATE 9-13-03



EO/ET/80  
RNG01  
40 TO 120 DEC F  
hh:50

EO/ET/80  
RNG01  
40 TO 100 HUND  
hh:50

EO/ET/80  
RNG01  
40 TO 120 DEC F  
hh:50

EO/ET/80  
RNG01  
40 TO 100 HUND  
hh:50

EO/ET/80  
RNG01  
40 TO 120 DEC F  
hh:44

HTR Study No. 03-121794-112  
Sponsor No. 03-7331-081

Final Report

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**CONFIDENTIAL**  
**REPORT FOR**  
**ANTIPERSPIRANT EFFICACY STUDY**

**HTR STUDY NO. 03-121791-112**

**SPONSOR NO. 03-7331-069**

**Final Report**

**July 30, 2003**

**FOR**  
**REVLON RESEARCH CENTER**  
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**EDISON, NJ 08818**

**BY**  
**HILL TOP RESEARCH, INC.**  
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**SCOTTSDALE, AZ 85251**

## 1.0 SUMMARY

- The objective of this study was to evaluate antiperspirant efficacy of the test articles on axillary sweating at specified post-treatment intervals. The study followed a paired comparison test design of one pair of antiperspirant test articles (A antiperspirant roll-on and B placebo roll-on). Within the pair of test articles, one test article was randomly assigned to either the right or left axilla and the opposite axilla received the remaining test article. There was a 21-day conditioning period during which no antiperspirants were used in the axillary area. Thirty-one subjects (6 male, 25 female) completed the study.
- The following test articles were used in this study.

HTR Code	Sponsor Code	Description
A	509-003/A	Antiperspirant roll-on
B	509-003/B	Placebo roll-on

- No adverse events were reported during the course of this study.
- Based on the results of this study, roll-on antiperspirant 509-003/A (HTR A) was significantly effective in reducing axillary perspiration at 1, 24 and 48 hours after eight daily applications. The test article demonstrated reductions of 36.39 % at 1 hour, 42.99% at 24 hours and 38.81% at 48 hours.

At each interval antiperspirant 509-003/A (HTR A) satisfied the OTC antiperspirant final monograph requirements [§ 250.60 (21 CFR 350.60) of the final monograph (final rule) for OTC antiperspirant drug products, published in the FEDERAL REGISTER on June 9, 2003 (68 FR 34273)] that a minimum of 50% of the population demonstrate at least a 20% sweat reduction.

## 2.0 TABLE OF CONTENTS

1.0	SUMMARY.....	1
2.0	TABLE OF CONTENTS .....	2
3.0	SPONSOR PERSONNEL.....	3
4.0	INVESTIGATIVE PERSONNEL.....	3
5.0	CLINICAL RESEARCH STANDARDS.....	3
6.0	PROTOCOL.....	3
6.1.	STUDY PROCEDURES.....	4
6.2.	PROTOCOL AMENDMENTS.....	4
7.0	SUBJECTS .....	4
8.0	STUDY SCHEDULE.....	4
9.0	TEST ARTICLES.....	5
10.0	ADVERSE EVENTS.....	5
11.0	METHOD OF STATISTICAL ANALYSIS.....	5
12.0	RESULTS OF STATISTICAL ANALYSIS.....	7
13.0	CONCLUSIONS .....	8
14.0	SIGNATURE(S).....	8
15.0	QUALITY ASSURANCE STATEMENT .....	9

## APPENDICES

Appendix I/Protocol

Appendix II/Statistical Tables

Appendix III/Temperature and Humidity Charts

RECORD RETENTION AND PUBLICATION NOTICE

### **3.0 SPONSOR PERSONNEL**

Michael Dickens, Ph.D.  
Director of Biological Sciences  
Revlon Research Center

There was no on-site monitor visit.

### **4.0 INVESTIGATIVE PERSONNEL**

Investigator:	Linda P. Oddo, B.S.
Study Manager:	JoAnne Jubinville
Biostatistician:	James P. Bowman, M.S.
Manager Biostatistics:	Barbara M. Fath
Study Coordinator:	Dianna Christensen

### **5.0 CLINICAL RESEARCH STANDARDS**

The study was conducted in compliance with applicable Good Clinical Practice Regulations (investigator responsibilities, test article accountability, informed consent, study documentation, AE reporting), the Standard Operating Procedures of the Hill Top Research, Inc., and the study protocol. Informed consent was obtained in accordance with Title 21 of the Code of Federal Regulation, Part 50.

### **6.0 PROTOCOL**

The study protocol was followed (see Appendix I) with the exception of the deviations summarized below.

- Due to an inability to maintain the proper humidity levels in the controlled sweat environment on enrollment day and the following day, the baseline sweat used for analysis occurred two days after consent and enrollment on July 9, 2003.
- Technician inadvertently started to treat the right axilla with Product A. Upon realizing her error she had subject 27 wash her axilla with soap, rinse and dry thoroughly. The correct product (B) was applied to the right axilla.

In the opinion of the Investigator, the deviations did not compromise the integrity of the study.

### **6.1. Study Procedures**

Subjects participated in a conditioning period for 21 days prior to enrollment. Subjects that read and signed the consent form, qualified during screening and sweat a minimum of 100mg of sweat/20 minutes/axilla were enrolled. Enrolled subjects also received a test article application on Day 1.

On days 2, 3, 4, 5, 6 and 7 subjects reported for axillary evaluation (assess irritation, if any), supervised wash and test article application. On day 8 subjects also participated in sweat collection. On days 9 and 10 subjects had axillary evaluations and participated in sweat collection.

### **6.2. Protocol Amendments**

There were no amendments to the protocol.

## **7.0 SUBJECTS**

Fifty-two subjects were screened and signed the Consent Form. Thirty-two subjects who met the study criteria were enrolled.

One subject withdrew from the study for personal reasons unrelated to the test product.

Thirty-one subjects (6 male and 25 female), ages 18-65, completed all phases of the study.

## **8.0 STUDY SCHEDULE**

Conditioning Period: June 16 through July 8, 2003  
Date Initiated: July 7, 2003  
Date Completed: July 18, 2003

Subjects were consented, screened and enrolled on July 7, 2003. Upon entering the environmentally controlled room, the humidity went out of range. Study staff was unable to bring the humidity back into range. The same problem occurred on July 8. The room was fixed on July 9, 2003 and the humidity remained stable throughout the study. The study ran for two days longer than planned due to this problem.

## 9.0 TEST ARTICLES

The following test articles were received by Hill Top Research on June 25, 2003:

HTR Code	Label Information	Description
A	509-003/A	32 dark green containers with dark green lids, containing liquid roll-on test article
B	509-003/B	32 dark green containers with dark green lids, containing liquid roll-on test article

Each subject received eight test article applications of each product to the axillary areas according to the randomization. The test articles were applied to uniformly cover approximately a 4x6-inch area centered in the axillary vault at the rate of at least 0.40gm per axilla/treatment.

Remaining test articles will be returned to the study sponsor upon issue of the final report.

## 10.0 ADVERSE EVENTS

There were no adverse events reported during the course of the study.

## 11.0 METHOD OF STATISTICAL ANALYSIS

### 11.1 Antiperspirant Analysis - Signed Rank Test

The first method used to evaluate the data was the Wilcoxon Signed Rank Test, which is recommended in the guidelines for Effectiveness Testing of OTC Antiperspirant Drug Products, August 1982. The source data used for these analyses were the adjusted ratios, Z-values, which were calculated from the pre-treatment and post-treatment average B and C collections for each individual (shown in Table 4AB).

$$Z = (PC \times T) / (PT \times C)$$

Where Z was the adjusted ratio, PC was the pre-treated measure of moisture for the control axilla, PT was the pre-treatment measure for the test axilla, T was the treated measure for the test axilla, and C was the corresponding quantity for the control axilla.

The hypotheses tested in the signed rank test ( $\alpha=0.05$ ) are stated as follows:

$$H_0: \text{median } Z \geq 0.80$$

$$H_a: \text{median } Z < 0.80$$

## 11.2 Antiperspirant Analysis - Ratio Method

The efficacy of the test material was evaluated by calculating A/B ratios from the milligram data for each subject (509-003/A antiperspirant roll-on - HTR Code A, 509-003/B Placebo roll-on - HTR Code B). Let  $R_{ij}$  equal the  $i^{\text{th}}$  A/B ratio for the  $j^{\text{th}}$  subject.  $R_{ij}$  measured prior to the first treatment represents baseline ratios ( $CR_{ij}$ ) and  $R_{ij}$  measured after individual treatments represents treatment ratios ( $TR_{ij}$ ). Since baseline ratios are dependent upon the individual subject, treatment effects were estimated from the  $TR_{ij}$  after  $TR_{ij}$  had been adjusted from  $CR_{ij}$  by calculating an adjusted ratio ( $AR_{ij}$ ) for each subject. The following formula was used for this calculation:

$$AR_{ij} = \frac{TR_{ij}}{\text{Avg. } CR_j}$$

The average  $CR_{ij}$  ( $CR_j$ ) for the  $j^{\text{th}}$  subject was calculated using the following formula:

$$\overline{CR_j} = \sum_{i=1}^n CR_{ij} / n$$

Where  $n$  = number of baseline ratios to be averaged.

The adjusted ratio (A/B) was used to evaluate treatment effect in the statistical models described below and reflects the activity of HTR Code A relative to that of the placebo side. If the activities of HTR Code A and placebo are equal, the ratio is 1.000. When the adjusted ratio is greater than or less than 1.000, the activity of HTR Code A is proportionately less than the untreated side or greater than the placebo side, respectively.

ratios (A/B) for that post-treatment interval. This value is converted to an estimate of percent reduction in sweating using the following formula:

$$\% \text{ Reduction} = (100) (1.000 - \text{mean adjusted ratio})$$

The 95% Confidence Interval (CI) for this %Reduction is computed in the following manner:

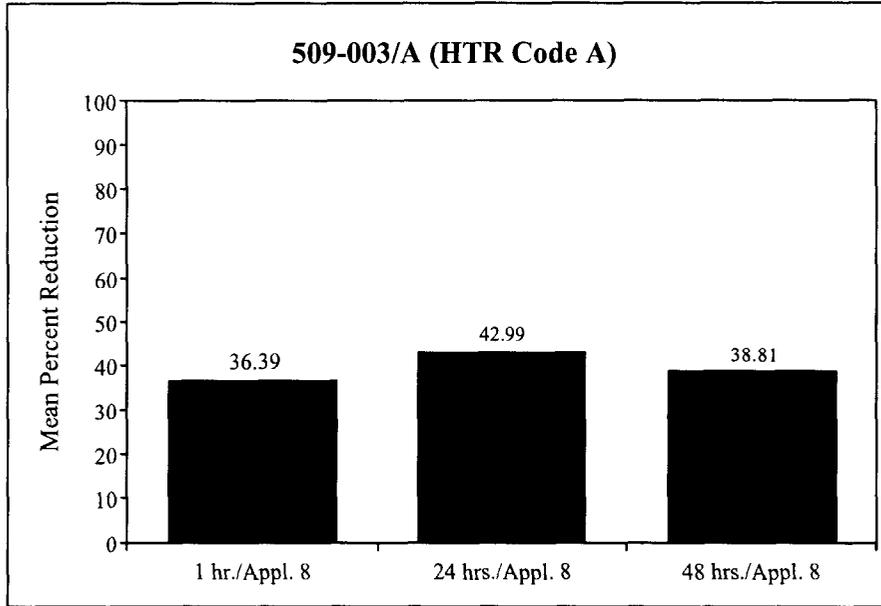
$$95\% \text{ CI} = \pm (\text{Standard error of the mean adjusted ratio}) (t_{0.05, n-1}) (100)$$

Where  $(t_{0.05, n-1})$  is the Student's  $t$  critical value for 95% significance and  $n-1$  degrees of freedom.

The number of subjects with  $\geq 20\%$  reduction in sweating based on the adjusted ratios were also calculated.

**12.0 RESULTS OF STATISTICAL ANALYSIS**

Based on the results of the signed rank test, HTR Code A was significantly effective in reducing perspiration at 1 hour, 24 hours and after 48 hours after Application No. 8. The mean percent reductions in sweat, the 95% confidence intervals, the significance levels derived from the distribution-free signed rank test and the number of subjects showing  $\geq 20\%$  reduction are presented below.



Evaluation	% Reduction ± Conf. Int.	Signed Rank p-value	No. Subjects Showing ≥ 20% Reduction
1-Hr. after Appl. 8	36.39% ± 7.72	<0.0001*	23/31
24-Hrs. after Appl. 8	42.99% ± 7.24	<0.0001*	26/31
48-Hrs. after Appl. 8	38.81% ± 6.90	<0.0001*	28/31

\* HTR Code A was significantly effective (signed rank test).

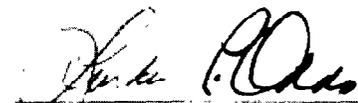
**CONCLUSIONS**

Based on the results of this study, roll-on antiperspirant 509-003/A (HTR A) was significantly effective in reducing axillary perspiration at 1, 24 and 48 hours after eight daily applications. The test article demonstrated reductions of 36.39 % at 1 hour, 42.99% at 24 hours and 38.81% at 48 hours.

At each interval antiperspirant 509-003/A (HTR A) satisfied the OTC antiperspirant final monograph requirements [§ 250.60 (21 CFR 350.60) of the final monograph (final rule) for OTC antiperspirant drug products, published in the FEDERAL REGISTER on June 9, 2003 (68 FR 34273)] that a minimum of 50% of the population demonstrate at least a 20% sweat reduction.

**SIGNATURE(S)**

HILL TOP RESEARCH, INC.



Linda P. Oddo, B.S.  
Investigator

7-30-03

Date

**15.0 QUALITY ASSURANCE STATEMENT**

To assure compliance with the study protocol and standard operating procedures (SOPs) of Hill Top Research, Inc., the Quality Assurance Unit completed an audit of the study records on 07/24/2003 and audited the final report on 07/29/2003.

Any observations found during the course of the audit were reported (as applicable) to the Site Director, Study Director, Principal Investigator, Study Manager, Study Coordinator, Report Writer, and/or HTR Management.

Report reviewed by:

Valerie Fallert      July 30, 2003  
Valerie Fallert, B.S. CCRA      Date  
Quality Assurance Auditor

HTR Study No. 03-121791-112  
Sponsor No. 03-7331-069

Final Report

## **APPENDIX I**

Total number of pages = 21

**Protocol and Consent Form**

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**HILL TOP RESEARCH, INC.**

**PROTOCOL FOR**  
**Antiperspirant Efficacy Study**  
**(Monograph)**

**For: Revlon Research Center**

**Sponsor No.: 03-7331-069**

**Hill Top Research Project No.: 03-121791-112**

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## TABLE OF CONTENTS

1.0	INTRODUCTION.....	1
2.0	OBJECTIVE.....	1
3.0	STUDY SPONSOR AND MONITOR.....	1
4.0	INVESTIGATIVE ORGANIZATION AND PERSONNEL.....	1
5.0	CLINICAL RESEARCH STANDARDS.....	2
6.0	EXPERIMENTAL DESIGN.....	2
7.0	TEST ARTICLES.....	2
8.0	SUBJECT SELECTION.....	2
8.1	Instructions.....	2
8.2	Inclusion Criteria.....	3
8.3	Exclusion Criteria.....	3
9.0	SUBJECT WITHDRAWAL.....	3
	PROCEDURE.....	4
10.1	Conditioning Period.....	4
10.2	Axillary Examinations.....	4
10.3	Baseline.....	4
10.4	Supervised Washes.....	4
10.5	Treatment Assignment/Application.....	4
	EVALUATIONS.....	5
11.1	Sweat Collection Intervals.....	5
11.2	Sweat Stimulation.....	5
11.3	Sweat Collections.....	5
	TEST SCHEDULE.....	6
	ADVERSE EXPERIENCES.....	6
13.1	Definitions.....	6
13.2	Follow-up.....	7
13.3	Notification.....	7
13.4	Anticipated Reactions.....	7
	STATISTICAL ANALYSIS.....	8
	REPORT.....	9
	NOTICE.....	9
	PROTOCOL APPROVAL.....	9

HTR Study No.: 03-121791-112  
Sponsor No.: 03-7331-069  
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## 1.0 INTRODUCTION

An antiperspirant product is an OTC (over the counter) drug and is regulated by the Food and Drug Administration (FDA). In order to be labeled an antiperspirant, a product must be formulated within the Category I guidelines of the Antiperspirant Drug Products for Over-the-Counter Human Use: Tentative Final Monograph (Federal Register, Volume 47, No. 162, August 20, 1982). The product must reduce axillary perspiration to a level that is statistically significantly greater than 20% reduction.

If the product is not formulated within the guidelines, the product will require submission of a New Drug Application (NDA) and be tested under an Investigational New Drug exemption (IND).

The following test is carried out to determine the effectiveness of the test article in reducing axillary (underarm) sweating.

### OBJECTIVE

To evaluate antiperspirant efficacy of the test articles on axillary sweating at specified post-treatment intervals.

## 3.0 STUDY SPONSOR AND MONITOR

Revlon Research Center  
2121 Route 27  
Edison, NJ 08818

Michael Dickens, Ph.D.  
Director of Biological Sciences  
Telephone No.: (732) 287-7715  
Fax No.: (732) 287-7784

### INVESTIGATIVE ORGANIZATION AND PERSONNEL

Organization:	Hill Top Research, Inc.
Location:	3225 N. 75 <sup>th</sup> St. Scottsdale, AZ 85251
Telephone No:	480-949-7766
Fax No.:	480-946-2179
Investigator:	Linda P. Oddo
Study Manager:	JoAnne Jubinville
Study Coordinator:	Dianna Christensen

HTR Study No.: 03-121791-112  
 Sponsor No.: 03-7331-069  
 Confidential

## 5.0 CLINICAL RESEARCH STANDARDS

The study will be conducted in compliance with applicable Good Clinical Practice Regulations (investigator responsibilities, test article accountability, informed consent, study documentation, AE reporting), the Standard Operating Procedures of the Hill Top Research, Inc., study protocol and protocol amendment(s). Informed consent will be obtained in accordance with Title 21 of the Code of Federal Regulations, Part 50.

## 6.0 EXPERIMENTAL DESIGN

The study will follow a paired comparison test design of one pair of antiperspirant test articles (A- antiperspirant roll-on and B-placebo roll-on). Within the pair of test articles, one test article will be randomly assigned to either the right or left axilla and the opposite axilla will receive the remaining test article. It will include a 21-day conditioning period during which no antiperspirants will be used in the axillary area..

A baseline sweat collection, treatment regimen and post-treatment sweat collections will follow the conditioning period.

## 7.0 TEST ARTICLES

The Study Sponsor will supply an adequate amount of the test articles for treatment of all subjects.

HTR Code	Sponsor Code	Description
A	509-003/A	Antiperspirant roll-on
B	509-003/B	Placebo roll-on

All test articles will be returned to the Sponsor following the completion of the study.

## 8.0 SUBJECT SELECTION

A sufficient number of subjects will be recruited to participate in the conditioning period to assure that approximately 30 complete the study.

8.1 Instructions: To participate in the study the subjects must agree to observe the following instructions:

- a. Abstain from the use of all antiperspirants for the entire conditioning and test periods.
- b. Use only the deodorant product issued by Hill Top Research, Inc. or nothing during the conditioning period.

HTR Study No.: 03-121791-112

Sponsor No.: 03-7331-069

Confidential

- c. All axillary washing will be confined to the laboratory during the test period.
- d. Abstain from shaving the axillae two days prior to and during the test period.

8.2 **Inclusion Criteria:** To participate in the test period of the study each subject must satisfy the following inclusion criteria:

- a. Age 18-65, in good general health
- b. Has had an annual medical screening, which qualifies them for antiperspirant testing
- c. Has participated in at least a 17-21-day conditioning period
- d. Has given signed informed consent (Exhibit A)
- e. Has participated in and satisfied the established requirements of a brief medical screening just prior to enrollment ( $\leq 100$  pulse,  $\leq 99.2^{\circ}\text{F}$  temperature,  $\leq 150$  systolic,  $\leq 90$  diastolic)
- f. Produces at least 100 mg of sweat/20 minutes/axilla during baseline sweat collection

8.3 **Exclusion Criteria:** A subject will be excluded from participation in the test period for any of the following exclusion criteria:

- a. Has axillary irritation
- b. Has a history of irritation or sensitivity to axillary antiperspirant, deodorant or soap products
- c. Has a recurring history of infections, boils, abscesses, or lymph node enlargement in the axilla
- d. Has active psoriasis, eczema, skin cancer or a dermatological condition that may interfere with the conduct of the study
- e. Has heart disease, uncontrolled hypertension, kidney disease, significant respiratory disease, epilepsy, heat intolerance
- f. Taking any medication or has a significant disease that may interfere with the study results or present the subject as unhealthy
- g. Insulin dependent diabetic
- h. Taken a systemic antibiotic or used a topical antibiotic medication in the axillary area within two weeks prior to the enrollment  
Pregnant or lactating

## 9.0 **SUBJECT WITHDRAWAL**

After admission to the study, the subject may withdraw at any time for any reason. The reason for withdrawal will be reported fairly and accurately.

## 10.0 PROCEDURE

10.1 **Conditioning Period:** Each subject will be provided with a deodorant product to use as needed for a period of at least 17-21 days prior to enrollment. To affect a washout (conditioning) of previously used axillary products, each subject will be instructed to discontinue using axillary antiperspirants during this period.

**Axillary Examinations:** Subjects will be screened for axillary irritation prior to being accepted on the study. A 100-watt blue incandescent light will be used for all examinations. Hill Top personnel will conduct axillary examinations daily according to the identified scoring procedure (Exhibit B).

**Baseline:** Baseline sweat volumes will be determined according to the procedures identified in 11.3. Baseline volumes will be used to compare differences between highest and lowest sweat volume among the subjects. If the difference between the highest and lowest rate does not exceed 600 milligrams of sweat/20 minutes/axilla the study will be discontinued. To be eligible for the treatment period, each subject must have a baseline perspiration level  $\geq 100$  milligrams of sweat/20 minutes/axilla.

Each Subject will be given a treatment assignment number after being accepted onto the treatment period.

**Supervised Washes:** Supervised washes will be conducted prior to each test article application according to the following procedure:

- 1 Wash right axilla for 10 seconds using a disposable towel saturated with a 2% aqueous solution of Camay soap.
2. Wet a fresh disposable towel under running water and rinse the axilla until all soap is removed.
3. Gently pat dry the axilla using a dry disposable towel.
- 4 Repeat for left axilla.

**Test Article Assignment/Application:** For each subject the determination of which axilla will receive which test article will be determined by the randomization schedule (Exhibit C). For replicate evaluations, treatment assignments to the right and left axillae of a specific subject will remain the same.

Each subject will receive eight (8) treatment applications to both axillae. The test articles will be applied to uniformly cover approximately a 4x6-inch area centered in the axillary vault. A qualified technician will make all applications.

Test articles A (509-003/A) antiperspirant roll-on and B (509-003/B) placebo roll-

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HTR Study No.: 03-121791-112  
Sponsor No.: 03-7331-069  
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on; will be applied at a rate of at least 0.400g per axilla/treatment. The amount of sample used will be determined by weighing each unit before and after each use.

Subjects will wait at the test facility for approximately twenty-minutes following each test article application to allow time for drying and absorption of test articles.

## 11.0 EVALUATIONS

**Sweat Collection Evaluation Intervals:** Evaluations will be conducted at baseline, one hour after no. 8, and 24 and 48-hours after application no. 8. A total of four collections, including baseline, will be conducted.

**Sweat Stimulation:** Sweating of the subjects is induced by having the subjects sit in a room maintained at  $100^{\circ}\text{F} \pm 2^{\circ}\text{F}$  and at a relative humidity of about 35%. The conditions in the room will be recorded.

**Sweat Collections:** During the first 40 minutes of the sweat stimulation period, the subject will hold unweighed pads of Webril (non-woven cotton padding fabric) in the axillae. This preliminary warm up period will be followed by two successive 20-minute collection periods, during which the subject will hold weighed Webril pads in the axillae.

The pads will be weighed in tightly capped polystyrene vials before and after use. The vials will be labeled with the subject's number, axilla and collection designation. To insure the correct assembly of the bottle, cap and pad after use, all three components of the right collection unit will be distinctively marked. The first collection made with weighed pads will be designated Collection B and the second Collection C. Hill Top personnel will insert and remove the weighed pads. The process will be conducted at approximately 15-second intervals between subjects.

During the collections with weighed pads, the subject will be required to sit in an erect position with both feet flat on the floor and with the arms at rest in a symmetrical manner. The subjects will be allowed to drink water as desired during the warm up period and between Collections B and C.

HTR Study No.: 03-121791-112  
 Sponsor No.: 03-7331-069  
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### TEST SCHEDULE

EVENT	DAY									
	1	2	3	4	5	6	7	8	9	10
Informed Consent	X									
Inclusion/Exclusion	X									
Axillary Evaluation	X	X	X	X	X	X	X	X	X	X
Supervised Wash	X	X	X	X	X	X	X	X		
Sweat Collection	X <sup>a</sup>							X <sup>b</sup>	X <sup>c</sup>	X <sup>c</sup>
Test Article Application	X	X	X	X	X	X	X	X		

<sup>a</sup> Day 1 sweat collection (baseline) will be conducted prior to the test article application.

<sup>b</sup> Day 8 sweat collection will be conducted ~ one-hour following test article application no. 8.

<sup>c</sup> Days 9 and 10 sweat collections will be conducted ~ 24-hours and 48-hours following test article application no. 8, respectively.

### ADVERSE EXPERIENCES

13.1 **Definitions:** An Adverse Event/Experience is any unexpected or undesirable experience occurring to a subject during a study, which may or may not be related to the test article. All adverse event/experiences will be recorded and reported according to Good Clinical Practice Regulations and the Standard Operating Procedures of Hill Top Research, Inc.

A **Serious Adverse Event/Experience** is any adverse experience that results in any of the following outcomes:

- \* death;
- \* a life-threatening adverse experience;
- \* inpatient hospitalization or prolongation of existing hospitalization;
- \* a persistent or significant disability/incapacity;
- \* a congenital anomaly/birth defect

Important medical event/experiences that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

An **Unexpected Adverse Event/Experience** is any adverse event/experience not listed in the current labeling for the test article, the current investigator's brochure or safety data. Where test article labeling, investigator's brochure, or safety data are not available, anticipated experience will be listed and explained in the protocol based on the pharmacological properties of the test article(s).

All adverse events, regardless of severity or the causal/effect relationship, are to be recorded. The severity of the effect will be noted as "Mild", "Moderate", or "Severe" according the following definitions:

Mild	Awareness of signs or symptom, but easily tolerated.
Moderate	Discomfort to a degree as to cause interference with normal daily life activities and /or requiring medication.
Severe	Incapacity with inability to work or do usual daily life activities and requiring medical attention/intervention.

**Causal Relationship of Adverse Event/Experience**

When determining the causal/effect relationship to the test article, the relationship will be described as "None," "Possible," "Probable," or "Definite."

The following definitions will be utilized

None	No association to the test article. Related to other etiologies such as concomitant medications or conditions or subject's known clinical state.
Possible	Uncertain association. Other etiologies are also possible.
Probable	Clear-cut association with improvement upon withdrawal of the test article. Not reasonably explained by the subject's known clinical state but not a anticipated event.
Definite	An adverse event with a clear-cut temporal relationship

- 13.2 **Follow-up:** If an adverse event/experience occurs, the subject under the direction of the Investigator (or designee), may be referred to Hill Top's consultant physician for treatment. Serious or Unexpected Event/Experience will be followed to resolution.
- 13.3 **Notification:** The sponsor will be notified of all adverse event/experiences. Any Serious or Unexpected Adverse Event/Experience which occurs during the study must be reported promptly by the investigator (or designee) to the sponsor and the reviewing IRB, where applicable, within 24 hours of the information being reported to Hill Top Research, Inc.
- 13.4 **Anticipated Reactions:** A reaction could be redness, rash, swelling, itching, burning sensation, cracking or peeling, or in rare cases, small blisters. Reactions usually occur only where the sample touches the skin. A detailed account of any adverse events will be documented on the appropriate case report form. The investigator will evaluate all adverse experiences as to severity and relatedness to the test material. If the event is considered significant to the study, whether or not it is considered related to the product treatment, Hill Top will notify the sponsor as soon as possible. For the purposes of this study, an adverse event is defined as an

HTR Study No.: 03-121791-112  
Sponsor No.: 03-7331-069  
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unexpected adverse experience that is not identified in nature or severity in the risk assessment section of the informed consent.

If an adverse event occurs, the subject, under the direction of the Investigator (or designee), may be referred to a consultant physician for treatment. All study related adverse events will be monitored by Hill Top staff until resolution. Hill Top will report all serious adverse events to the study sponsor within 24 hours. A serious adverse event is any experience that is fatal, life threatening, permanently disabling or requires hospitalization. Additionally, any event that involves cancer, a congenital anomaly or drug overdose is considered serious.

**14.0 STATISTICAL ANALYSIS**

Individual post-treatment sweat collections, in milligrams, will be shown. The amount of sample, in grams, used for each application to each panelist will be shown.

Antiperspirant activity is evaluated by determining shifts in ratios of the sweat output by the treated axilla to the output of the placebo treated axilla for each panelist. Estimates of percent reduction and 95% confidence intervals will be calculated.

The data will be analyzed using the Wilcoxon Signed Rank Test, which is recommended in the Guidelines for Effectiveness Testing of OTC Antiperspirant Drug Products, August

1982. The source data for this analysis are treated to control ratios adjusted for the ratio of right-to-left axillary sweating rates. These ratios are calculated using the post-treatment average B and C collections for each individual at each time period.

The adjusted treated to control ratios for this analysis will be calculated as follows:

$$Z = (PC \times T) / (PT \times C)$$

where Z is the adjusted ratio, PC is the pretreatment measure of moisture for the control axilla (placebo), PT is the pretreatment measure for the test axilla, T is the treated measure for the test axilla, and C is the corresponding quantity for the control axilla (placebo).

The study results are analyzed by comparing the adjusted ratio to 0.80, the ratio which corresponds to a 20 percent reduction in moisture due to treatment. The hypothesis that reduction in perspiration exceeds 20 percent is tested statistically by subtracting 0.80 from Z for all subjects and testing the resulting number with the Wilcoxon signed rank test.

The hypotheses tested in the signed rank test are stated below:

- H<sub>0</sub>: Median Z ≥ 0.80
- H<sub>a</sub>: Median Z < 0.80

03-121791-112  
II-11

HTR Study No.: 03-121791-112  
Sponsor No.: 03-7331-069  
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Hypothesis testing will be performed at the  $\alpha = 0.05$  level.

Rejection of the null hypothesis will justify the conclusion that at least 50 percent of the target population will obtain a sweat reduction of at least 20 percent.

**REPORT**

The final report will summarize the method, data and conclusions relative to the test articles, as well as any information regarding the subjects that would impact the study. Source data will be retained by the testing facility on microfilm. The original source data will be maintained according to the investigator's standard operating procedure. A copy of the source documents may be obtained upon request of the Study Sponsor. Copies of transcribed data will be incorporated in the report.

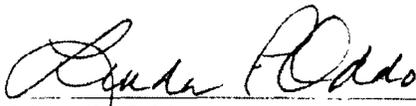
**NOTICE**

No amendments to the protocol will be permitted without approval from the Study Sponsor and Investigator and where applicable, the Institutional Review Board. Such changes will be documented in writing. Approval by the Board must be obtained prior to initiation of the amendment.

**17.0 PROTOCOL APPROVAL**

**HILL TOP RESEARCH, INC.**

Principal Investigator:

 10-27-03  
Linda P. Oddo Date  
Technical Director

**REVLON RESEARCH CENTER, INC.**

Monitor:  Representative to the sponsor

 June 30 2003  
Michael Dickens, Ph D. Date  
Director of Biological Sciences

03 791 112

II 12

Error in pagination

No missing data

Dr

7 22 03

Institution: Hill Top Research, Inc.  
Investigator: Linda P. Oddo  
Study Title: Antiperspirant Efficacy Study

HTR Study No. 03-121791-112

II 13  
Exhibit A

**CONSENT FORM**

**INTRODUCTION:** You are being asked to take part in a research study. Before you give your consent to be a subject, it is important that you take enough time to read and understand what your participation would involve. In preparing this consent form, it has been necessary to use some technical language. Please ask questions if there is anything you do not understand.

You will be given a signed copy of this consent form and any other necessary written information prior to the start of the study.

**PURPOSE:** The purpose of this research study is to determine if the test article is an effective antiperspirant formulation. Approximately thirty (30) subjects' 18-65 years of age will participate in the study. You will be testing one antiperspirant formulation and a placebo. You will receive treatment under both underarms.

**TEST ARTICLES:** One test article is an antiperspirant roll-on, the second test article is a placebo roll-on (contains no active ingredient).

**STUDY PROCEDURES:** Approximately 17- 21 days ago you received a deodorant product to use at home. You were instructed to use this product exclusively or use nothing during this period. During the ten day study, you will come to Hill Top Research, Inc. each day. Product applications will be made on Days 1 through 8 of the study. During each product application visit, both underarms will be treated. You are expected to use only the test materials on your underarms throughout the study. Participation in the study will also require you, on Days 1, 8, 9 and 10 to spend about 80 minutes in a "hotroom" in which a temperature of approximately 100°F ± 2°F and a relative humidity of about 35% are maintained. The hotroom session will consist of a 40-minute warm-up period and two 20-minute sweat collections. Sweat collections will be conducted by placing absorbent pads in your underarms. You must remain seated with your feet flat on the floor throughout all sweat collections. You will be permitted to drink water during the 40-minute warm-up period and between the two 20-minute sweat collections. There will be a total of 10 visits to Hill Top Research.

Hill Top Research, Inc. personnel, will apply the test article. After these daily applications, you will be asked not to wash or otherwise wet your underarms or apply any deodorant/antiperspirant product until the following evening when you report to the laboratory.

Eligibility for participation in this study will be determined by the results of your annual medical screening as well as your present health state. This will be determined by a brief medical screening just prior to the start of the study.

**\*\*FEMALES OF CHILDBEARING POTENTIAL:** You may not participate in this study if you are pregnant, lactating, or planning a pregnancy. As part of giving your consent you must agree to have a urine pregnancy test at the start of the study.

Institution: Hill Top Research, Inc.  
Investigator: Linda P. Oddo  
Study Title: Antiperspirant Efficacy Study

HTR Study No. 03-121791-112  
14  
Exhibit A

**RISKS:** The test product contains ingredients available in marketed antiperspirant/deodorant formulations. No problems are expected; however, since the test is being done, in part, to see how the test article affect human skin, it is possible that you might have a "reaction". A reaction could be redness, rash, swelling, itching, cracking or peeling, or in rare cases, small blisters. Reactions usually occur only where the sample touches the skin.

A technician will examine your underarms daily to see if you are reacting. Such reactions may be due to skin irritation or allergy. However, the chance of an allergy is considered unlikely.

No risk to study participants, other than those described above as "reactions", is anticipated during the study.

**BENEFITS:** You will not benefit from the applications of test articles, but the study results may allow a new or improved product to be marketed.

**ALTERNATIVE PROCEDURES/TREATMENTS:** Because you are not being treated for a medical condition, alternative treatments do not apply to this study.

**CONFIDENTIALITY:** Information concerning you that is obtained in connection with this study will be kept confidential by Hill Top Research, except that the Company whose product is being tested will receive a copy of the study. In addition, the Food and Drug Administration and others in certain legal actions may inspect the records of the study. Information obtained in the study may be used for medical or scientific publication, but your identity will remain confidential.

**MEDICAL TREATMENT:** If in the course of this study you experience illness, discomfort or injury that appears to be a result of the study, Hill Top Research will provide you with medical care at no cost to you. Providing such medical care is not an admission of legal responsibility. If such illness, discomfort or injury does occur, ask any staff member to arrange a meeting for you with the appropriate personnel.

In certain cases of illness or injury resulting from this study, insurance benefits may be available.

**WHO TO CONTACT:** If you have any questions about this study or in case of an emergency, contact Dianna, Study Coordinator, at (480) 949-7766 during business hours (M-F, 8:00 A.M. - 4:00 P.M.) or JoAnne, Study Manager, at (602) 270-6697 after hours and on weekends. In addition, if you have any questions as to your rights as a research subject, contact Linda Oddo, Investigator, at (602) 270-6997.

**VOLUNTARY PARTICIPATION/WITHDRAWAL:** Your participation in this research study is strictly voluntary. If you fail to follow study instructions, your participation may be ended.

If you agree to participate in this study, you are also agreeing to provide Hill Top Research with accurate information and to follow study instructions as given to you. If you fail to comply with study procedures, your participation may be terminated.



II 16

## AUTHORIZATION FOR USE AND DISCLOSURE OF PERSONAL HEALTH INFORMATION

We are asking you to take part in a research study that was described in the informed consent. To do this research, the study staff will need to collect health information that identifies you.

Your personal health information includes, but is not limited to, information that was collected for your entry into the study and information collected during the study. The purpose of collecting this information is to allow *Hill Top Research, Inc.* study staff to conduct the study.

Study records that identify you will be kept confidential as required by law. Federal Privacy Regulations provide safeguards for privacy, security, and authorized access. Except when required by law, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside *Hill Top Research, Inc.* For records disclosed outside of *Hill Top Research, Inc.*, we will use your initials and assign a unique code number to the information that is sent to the sponsor.

You may decide not to give permission for the release of your personal health information for the study. In that case, you will not be able to participate in the study.

Your permission to share your personal health information for this study does not have an expiration date. If you no longer want to share your personal health information, you may cancel your permission at any time by writing *Hill Top Research, Inc.* at the address below.

Louise B. Aust  
Hill Top Research, Inc.  
3225 N. 75<sup>th</sup> St.  
Scottsdale, AZ 85251

If you cancel your permission after you have started the study, *Hill Top Research, Inc.* will stop collecting your personal health information. Although they will stop collecting new information about you, they will need to use the information already collected to evaluate the study results. If you start the study, then cancel your permission, you will not be able to continue to participate in the study.

The Sponsor and *Hill Top Research, Inc.* will make every reasonable effort to keep your personal health information private. Once the study staff shares your personal health information from the study, federal privacy laws may not keep the information private. There may be state laws or other federal laws that would protect the privacy of this information.

By signing this form, you authorize the use and disclosure of your personal health information for this research study. You will receive a copy of this form after you have signed it.

\_\_\_\_\_  
Name of Subject or Subject's Representative

\_\_\_\_\_  
Signature of Subject or Subject's Representative

\_\_\_\_\_  
Date

\_\_\_\_\_  
If signed by Representative, explain authority to act for Subject

Exhibit B

**AXILLARY IRRITATION SCALE**

- 0 = No visible reaction
- 0.5 = Slight, confluent<sup>1</sup> or patchy erythema
- 1.0 = Mild erythema (pink)
- 2.0 = Moderate erythema (definite redness)
- 3.0 = Strong erythema (very intense redness)

<sup>1</sup>confluent - flowing or running together

Exhibit B

Axilla Examination and Axillary Irritation Scoring

The axillary area of all subjects will be examined by a qualified person, capable of detecting a problem under the supervision of the investigator, before the initial exposure to the hotroom, and before receiving each daily treatment application. The examination will consist of a visual inspection of the axillae for "Axillary Irritation" (edema, broken or abraded skin, erythema or abnormal physical appearance). The grading scale is attached. All scores will be documented in the study diary.

A subject exhibiting "Axillary Irritation" (score 0.5 or greater) before the study start will not be eligible for participation in the study. The presence of "Axillary Irritation" during the test period will not automatically necessitate withdrawal from the study. Should such a condition arise, the investigator will determine if the subject will continue in the study. The condition will be followed closely and documented until remission of the symptoms. If the investigator decides to drop the subject from the study, the decision will be recorded in the diary, identified by the subject's name and number, axilla involved, date and the reason for their termination. If the symptoms still exist at the end of the test, the investigator will establish a follow-up procedure.

If "Axillary Irritation" (score 2.0 or greater) appears, the subject will be withdrawn from the test and the investigator will establish a follow-up procedure which will continue until remission. All procedures and medication will be documented in the diary and a final report issued by the Investigator.

Subjective Observations

Any voluntary comments from the subjects (such as itching and burning) will also be noted in the diary. As noted in the informed consent, a subject is free to withdraw from the study at anytime for any reason.

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# 19

03-121791-112

STUDY RANDOMIZATION

EXHIBIT C

SUBJECT NUMBER	RIGHT	LEFT
1	A	B
2	A	B
3	B	A
4	B	A
5	A	B
6	A	B
7	A	B
8	B	A
9	A	B
10	B	A
11	A	B
12	A	B
13	B	A
14	B	A
15	B	A
16	A	B
17	A	B
18	B	A
19	A	B
20	B	A
21	B	A
22	B	A
23	B	A
24	A	B
25	A	B
26	A	B
27	B	A
28	B	A
29	A	B
30	B	A
31	B	A
32	A	B

# Randomization Report

03121791112  
Print Date - 7/8/2003 II-20  
7:44:48PM

Study ID 03-121791-112-01  
Sponsor Name revlon

Created By - DCHRISTE 7/8/2003  
Revised By -

Subject Number	Right	Left
1	A	B
2	A	B
3	B	A
4	B	A
5	A	B
6	A	B
7	A	B
8	B	A
9	A	B
10	B	A
	A	B
12	A	B
13	B	A
14	B	A
15	B	A
16	A	B
17	A	B
18	B	A
19	A	B
20	B	A

# Randomization Report

121791112  
Print Date - 7/8/2003 11-21  
7:44:48PM

Study ID 03-121791-112-01  
Sponsor Name revlon

Created By - DCHRISTE 7/8/2003  
Revised By -

Subject Number	Right	Left
21	B	A
22	B	A
23	B	A
24	A	B
25	A	B
26	A	B
27	B	A
28	B	A
29	A	B
30	B	A
31	B	A
32	A	B

## **APPENDIX II**

Total number of pages = 10

### **Statistical Tables**

Table 1AB	Presentation of the net milligrams for sweat collected at each evaluation and the averages of the B & C collection net milligrams of sweat
Table 2AB	Presentation of the baseline and adjusted post-treatment sweating ratios
Table 3AB	Summary statistics for post-treatment sweating ratios
Table 4AB	Wilcoxon signed rank test
Table 5AB	Summary of the results of the signed rank test
Table 6AB	Grams of test article used at each application

HTR No. 03-121791-112 Sponsor No : 03-7331-069 13:49 Monday, July 21, 2003 1  
 Table 1AB. Presentation of the net milligrams of sweat (final-initial weights) collected at each evaluation  
 and the averages of the B & C collection net milligrams of sweat.  
 509-003/A Antiperspirant roll-on (HTR Code A) vs 509-003/B Placebo roll-on (HTR Code B)

HTR Code A		BASELINE			APPLN 8-1 HOUR			APPLN 8-24 HOUR			APPLN 8-48 HOUR		
Collection		Collection			Collection			Collection			Collection		
B		C			average			B			C		
Subject		Axilla			B			C			average		
1	R	539	597	568.0	405	342	373.5	449	496	472.5	584	417	500.5
2	R	570	918	744.0	779	951	865.0	709	1161	935.0	1247	1278	1262.5
3	L	268	450	359.0	179	210	194.5	138	210	174.0	153	181	167.0
4	L	322	361	341.5	301	306	303.5	137	160	148.5	431	258	344.5
5	R	594	1186	890.0	349	464	406.5	369	435	402.0	305	438	371.5
6	R	270	408	339.0	156	187	171.5	134	155	144.5	143	185	164.0
7	R	285	866	575.5	160	240	200.0	497	251	374.0	307	358	332.5
8	L	971	1580	1275.5	121	216	168.5	272	396	334.0	465	855	660.0
9	R	543	598	570.5	209	280	244.5	169	209	189.0	324	371	347.5
10	L	551	695	623.0	166	296	231.0	128	153	140.5	247	296	271.5
11	R	397	472	434.5	187	197	192.0	174	238	206.0	167	239	203.0
12	R	488	539	513.5	152	190	171.0	170	220	195.0	172	201	186.5
13	L	506	742	624.0	170	230	200.0	212	219	215.5	315	284	299.5
14	L	606	605	605.5	179	243	211.0	214	205	209.5	215	266	240.5
15	L	1151	1140	1145.5	314	697	505.5	859	1011	935.0	734	953	843.5
16	R	495	456	475.5	208	223	215.5	140	192	166.0	273	265	269.0
17	R	385	324	354.5	ND	ND	ND	ND	ND	ND	ND	ND	ND
18	L	1305	885	1095.0	394	463	428.5	698	699	698.5	1075	858	966.5
19	R	543	693	618.0	248	386	317.0	179	311	245.0	262	376	319.0
20	L	886	1385	1135.5	249	252	250.5	235	281	258.0	585	478	531.5
21	L	1311	1746	1528.5	584	497	540.5	365	493	429.0	669	473	571.0
22	L	908	826	867.0	927	369	648.0	783	1355	1069.0	358	954	656.0
23	L	233	304	268.5	113	105	109.0	119	141	130.0	155	208	181.5
24	R	522	706	614.0	216	244	230.0	264	322	293.0	352	365	358.5
25	R	1336	1101	1218.5	766	825	795.5	881	1091	986.0	758	818	788.0
26	R	322	348	335.0	127	137	132.0	125	177	151.0	216	286	251.0
27	L	343	341	342.0	89	148	118.5	158	205	181.5	148	235	191.5
28	L	330	370	350.0	159	194	176.5	197	236	216.5	198	203	200.5
29	R	764	690	727.0	249	240	244.5	153	205	179.0	201	201	201.0
30	L	526	437	481.5	246	266	256.0	249	379	314.0	271	305	288.0
31	L	966	576	771.0	230	318	274.0	406	253	329.5	716	895	805.5
32	R	253	415	334.0	118	123	120.5	157	129	143.0	145	168	156.5
Mean		609.0	711.3	660.1	282.3	317.4	299.8	314.2	386.7	350.5	393.3	440.9	417.1

(Continued)

ND = No Data.  
 Subject 17 withdrew.

HIR No. 03-121791-112 Sponsor No. 03-7331-069

13:49 Monday, July 21, 2003 2

Table 1AB. Presentation of the net milligrams of sweat (final-initial weights) collected at each evaluation and the averages of the B & C collection net milligrams of sweat.

509-003/A Antiperspirant roll-on (HIR Code A) vs 509-003/B Placebo roll-on (HIR Code B)

HIR Code A	BASELINE	APPLN 8-1 HOUR	APPLN 8-24 HOUR	APPLN 8-48 HOUR
	Collection	Collection	Collection	Collection
	B	C	average	B
	C	average	B	C
	average	B	C	average
Std	327.9	372.8	328.1	208.7
N	32	32	32.0	31
	31	31	31.0	31
	31	31	31.0	31
	31	31	31.0	31
	31	31	31.0	31

ND = No Data  
 Subject 17 withdrew.

HTR No. 03-121791-112 Sponsor No. 03-7331-069

13:49 Monday, July 21, 2003 3

Table 1AB Presentation of the net milligrams of sweat (final-initial weights) collected at each evaluation and the averages of the B & C collection net milligrams of sweat.  
 509-003/A Antiperspirant roll-on (HIR Code A) vs 509-003/B Placebo roll-on (HIR Code B)

HIR Code B		BASELINE		APPLN 8-1 HOUR		APPLN 8-24 HOUR		APPLN 8-48 HOUR					
		Collection		Collection		Collection		Collection					
		B C average		B C average		B C average		B C average					
Subject	Axilla												
,1	L	499	713	606.0	378	366	372.0	629	581	605.0	763	663	713.0
,2	L	623	977	800.0	706	1013	859.5	731	1192	961.5	1115	1193	1154.0
,3	R	333	514	423.5	256	406	331.0	221	547	384.0	317	391	354.0
,4	R	320	380	350.0	361	284	322.5	305	383	344.0	343	362	352.5
,5	L	394	789	591.5	472	465	468.5	390	437	413.5	343	399	371.0
,6	L	269	341	305.0	315	477	396.0	341	304	322.5	384	493	438.5
,7	L	302	794	548.0	331	374	352.5	816	369	592.5	416	557	486.5
,8	R	537	1075	806.0	161	410	285.5	448	539	493.5	604	791	697.5
,9	L	555	562	558.5	298	351	324.5	350	411	380.5	438	460	449.0
,10	R	471	643	557.0	297	483	390.0	421	576	498.5	510	724	617.0
,11	L	341	412	376.5	269	249	259.0	325	333	329.0	344	432	388.0
,12	L	395	482	438.5	268	381	324.5	343	395	369.0	379	450	414.5
,13	R	536	829	682.5	190	298	244.0	212	281	246.5	431	329	380.0
,14	R	506	652	579.0	263	384	323.5	215	374	294.5	280	388	334.0
,15	R	1342	1402	1372.0	491	1156	823.5	1208	1408	1308.0	1336	1443	1389.5
,16	L	465	447	456.0	353	370	361.5	472	446	459.0	561	658	609.5
,17	L	345	308	326.5	ND	ND	ND	ND	ND	ND	ND	ND	ND
,18	R	1526	1030	1278.0	643	569	606.0	1296	1466	1381.0	1498	1343	1420.5
,19	L	761	873	817.0	588	704	646.0	644	959	801.5	799	1014	906.5
,20	R	716	1104	910.0	441	427	434.0	540	523	531.5	821	741	781.0
,21	R	1349	1950	1649.5	781	627	704.0	481	737	609.0	948	734	841.0
,22	R	723	573	648.0	539	448	493.5	613	1052	832.5	400	904	652.0
,23	R	344	461	402.5	216	436	326.0	346	497	421.5	491	590	540.5
,24	L	415	480	447.5	476	553	514.5	436	498	467.0	588	617	602.5
,25	L	982	843	912.5	984	1053	1018.5	1516	1187	1351.5	1107	1422	1264.5
,26	L	342	326	334.0	248	281	264.5	269	296	282.5	391	463	427.0
,27	R	340	335	337.5	199	416	307.5	330	440	385.0	299	449	374.0
,28	R	443	606	524.5	461	493	477.0	530	724	627.0	467	474	470.5
,29	L	790	854	822.0	818	733	775.5	590	651	620.5	619	621	620.0
,30	R	458	426	442.0	267	309	288.0	350	557	453.5	414	428	421.0
,31	R	793	552	672.5	417	586	501.5	791	377	584.0	1468	992	1230.0
,32	L	253	305	279.0	160	334	247.0	318	222	270.0	212	242	227.0
,Mean		577.1	688.7	632.9	408.0	497.9	453.0	531.5	605.2	568.4	615.7	669.9	642.8

(Continued)

ND = No Data  
 Subject 17 withdrew

HTR No. 03-121791-112 Sponsor No. 03-7331-069

13:49 Monday, July 21, 2003 4

Table 1AB. Presentation of the net milligrams of sweat (final-initial weights) collected at each evaluation and the averages of the B & C collection net milligrams of sweat.  
 509-003/A Antiperspirant roll-on (HTR Code A) vs 509-003/B Placebo roll-on (HTR Code B)

HTR Code B	BASELINE	APPLN 8-1 HOUR	APPLN 8-24 HOUR	APPLN 8-48 HOUR
	Collection	Collection	Collection	Collection
	Collection	Collection	Collection	Collection
	B	C	average	B
	C	average	B	C
	average	B	C	average
Std	324.0	356.7	321.5	206.3
	225.6	202.1	316.5	334.4
	308.9	356.6	327.2	331.8
N	32	32	32.0	31
	31	31.0	31	31.0
	31	31.0	31	31.0

ND = No Data.  
 Subject 17 withdrew.

HIR No. 03-121791-112 Sponsor No. 03-7331-069

13:49 Monday, July 21, 2003 5

Table 2AB. Presentation of the baseline and adjusted post-treatment sweating ratios.  
 509-003/A Antiperspirant roll-on (HIR Code A) vs 509-003/B Placebo roll-on (HIR Code B)

SUBJECT	BASELINE			APPLN 8-1 HOUR			APPLN 8-24 HOUR			APPLN 8-48 HOUR		
	Collection			Collection			Collection			Collection		
	B	C	Average	B	C	Average	B	C	Average	B	C	Average
	ratio	ratio	ratio	ratio	ratio	ratio	ratio	ratio	ratio	ratio	ratio	ratio
1	1.08	0.84	0.96	1.12	0.97	1.05	0.74	0.89	0.82	0.80	0.66	0.73
2	0.91	0.94	0.93	1.19	1.01	1.10	1.05	1.05	1.05	1.21	1.16	1.18
3	0.80	0.88	0.84	0.83	0.62	0.72	0.74	0.46	0.60	0.57	0.55	0.56
4	1.01	0.95	0.98	0.85	1.10	0.98	0.46	0.43	0.44	1.28	0.73	1.01
5	1.51	1.50	1.51	0.49	0.66	0.58	0.63	0.66	0.64	0.59	0.73	0.66
6	1.00	1.20	1.10	0.45	0.36	0.40	0.36	0.46	0.41	0.34	0.34	0.34
7	0.94	1.09	1.02	0.48	0.63	0.55	0.60	0.67	0.63	0.73	0.63	0.68
8	1.81	1.47	1.64	0.46	0.32	0.39	0.37	0.45	0.41	0.47	0.66	0.56
9	0.98	1.06	1.02	0.69	0.78	0.73	0.47	0.50	0.49	0.72	0.79	0.76
10	1.17	1.08	1.13	0.50	0.54	0.52	0.27	0.24	0.25	0.43	0.36	0.40
11	1.16	1.15	1.15	0.60	0.69	0.64	0.46	0.62	0.54	0.42	0.48	0.45
12	1.24	1.12	1.18	0.48	0.42	0.45	0.42	0.47	0.45	0.39	0.38	0.38
13	0.94	0.90	0.92	0.97	0.84	0.91	1.09	0.85	0.97	0.79	0.94	0.87
14	1.20	0.93	1.06	0.64	0.60	0.62	0.94	0.52	0.73	0.72	0.65	0.68
15	0.86	0.81	0.84	0.77	0.72	0.74	0.85	0.86	0.86	0.66	0.79	0.72
16	1.06	1.02	1.04	0.57	0.58	0.57	0.28	0.41	0.35	0.47	0.39	0.43
17	1.12	1.05	1.08	ND	ND	ND	ND	ND	ND	ND	ND	ND
18	0.86	0.86	0.86	0.71	0.95	0.83	0.63	0.56	0.59	0.84	0.75	0.79
19	0.71	0.79	0.75	0.56	0.73	0.64	0.37	0.43	0.40	0.44	0.49	0.46
20	1.24	1.25	1.25	0.45	0.47	0.46	0.35	0.43	0.39	0.57	0.52	0.54
21	0.97	0.90	0.93	0.80	0.85	0.82	0.81	0.72	0.76	0.76	0.69	0.72
22	1.26	1.44	1.35	1.28	0.61	0.94	0.95	0.96	0.95	0.66	0.78	0.72
23	0.68	0.66	0.67	0.78	0.36	0.57	0.51	0.42	0.47	0.47	0.53	0.50
24	1.26	1.47	1.36	0.33	0.32	0.33	0.44	0.47	0.46	0.44	0.43	0.44
25	1.36	1.31	1.33	0.58	0.59	0.59	0.44	0.69	0.56	0.51	0.43	0.47
26	0.94	1.07	1.00	0.51	0.49	0.50	0.46	0.60	0.53	0.55	0.61	0.58
27	1.01	1.02	1.01	0.44	0.35	0.40	0.47	0.46	0.47	0.49	0.52	0.50
28	0.74	0.61	0.68	0.51	0.58	0.54	0.55	0.48	0.51	0.63	0.63	0.63
29	0.97	0.81	0.89	0.34	0.37	0.36	0.29	0.35	0.32	0.37	0.36	0.37
30	1.15	1.03	1.09	0.85	0.79	0.82	0.65	0.63	0.64	0.60	0.66	0.63
31	1.22	1.04	1.13	0.49	0.48	0.48	0.45	0.59	0.52	0.43	0.80	0.61
32	1.00	1.36	1.18	0.62	0.31	0.47	0.42	0.49	0.46	0.58	0.59	0.58

(Continued)

ND = No Data  
 Subject 17 withdrew.

HTR No. 03-121791-112 Sponsor No.: 03-7331-069

13:49 Monday, July 21, 2003 6

Table 2AB Presentation of the baseline and adjusted post-treatment sweating ratios.  
 509-003/A Antiperspirant roll-on (HTR Code A) vs 509-003/B Placebo roll-on (HTR Code B)

	BASELINE			APPLN 8-1 HOUR			APPLN 8-24 HOUR			APPLN 8-48 HOUR		
	Collection			Collection			Collection			Collection		
	B	C	Average	B	C	Average	B	C	Average	B	C	Average
Mean	1.07	1.05	1.06	0.66	0.62	0.64	0.57	0.57	0.57	0.61	0.61	0.61
StdErr	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.03	0.04	0.04	0.03	0.03
N	32	32	32	31	31	31	31	31	31	31	31	31

ND = No Data.  
 Subject 17 withdrew.



HTR No. 03-121791-112 Sponsor No.: 03-7331-069  
 Table 4AB. Wilcoxon signed rank test.  
 509-003/A Antiperspirant roll-on (HTR Code A) vs 509-003/B Placebo roll-on (HTR Code B)

13:49 Monday, July 21, 2003 8

SUBJECT	APPLN. 8-1 HOUR							APPLN. 8-24 HOUR							APPLN. 8-48 HOUR						
	PC	PT	C	T	Z	Z-0.80		PC	PT	C	T	Z	Z-0.80		PC	PT	C	T	Z	Z-0.80	
1	606.0	568.0	372.0	373.5	1.07	0.27		606.0	568.0	605.0	472.5	0.83	0.03		606.0	568.0	713.0	500.5	0.75	-0.05	
2	800.0	744.0	859.5	865.0	1.08	0.28		800.0	744.0	961.5	935.0	1.05	0.25		800.0	744.0	1154.0	1262.5	1.18	0.38	
3	423.5	359.0	331.0	194.5	0.69	-0.11		423.5	359.0	384.0	174.0	0.53	-0.27		423.5	359.0	354.0	167.0	0.56	-0.24	
4	350.0	341.5	322.5	303.5	0.96	0.16		350.0	341.5	344.0	148.5	0.44	-0.36		350.0	341.5	352.5	344.5	1.00	0.20	
5	591.5	890.0	468.5	406.5	0.58	-0.22		591.5	890.0	413.5	402.0	0.65	-0.15		591.5	890.0	371.0	371.5	0.67	-0.13	
6	305.0	339.0	396.0	171.5	0.39	-0.41		305.0	339.0	322.5	144.5	0.40	-0.40		305.0	339.0	438.5	164.0	0.34	-0.46	
7	548.0	575.5	352.5	200.0	0.54	-0.26		548.0	575.5	592.5	374.0	0.60	-0.20		548.0	575.5	486.5	332.5	0.65	-0.15	
8	806.0	1275.5	285.5	168.5	0.37	-0.43		806.0	1275.5	493.5	334.0	0.43	-0.37		806.0	1275.5	697.5	660.0	0.60	-0.20	
9	558.5	570.5	324.5	244.5	0.74	-0.06		558.5	570.5	380.5	189.0	0.49	-0.31		558.5	570.5	449.0	347.5	0.76	-0.04	
10	557.0	623.0	390.0	231.0	0.53	-0.27		557.0	623.0	498.5	140.5	0.25	-0.55		557.0	623.0	617.0	271.5	0.39	-0.41	
11	376.5	434.5	259.0	192.0	0.64	-0.16		376.5	434.5	329.0	206.0	0.54	-0.26		376.5	434.5	388.0	203.0	0.45	-0.35	
12	438.5	513.5	324.5	171.0	0.45	-0.35		438.5	513.5	369.0	195.0	0.45	-0.35		438.5	513.5	414.5	186.5	0.38	-0.42	
13	682.5	624.0	244.0	200.0	0.90	0.10		682.5	624.0	246.5	215.5	0.96	0.16		682.5	624.0	380.0	299.5	0.86	0.06	
14	579.0	605.5	323.5	211.0	0.62	-0.18		579.0	605.5	294.5	209.5	0.68	-0.12		579.0	605.5	334.0	240.5	0.69	-0.11	
15	1372.0	1145.5	823.5	505.5	0.74	-0.06		1372.0	1145.5	1308.0	935.0	0.86	0.06		1372.0	1145.5	1389.5	843.5	0.73	-0.07	
16	456.0	475.5	361.5	215.5	0.57	-0.23		456.0	475.5	459.0	166.0	0.35	-0.45		456.0	475.5	609.5	269.0	0.42	-0.38	
17	326.5	354.5	ND	ND	ND	ND		326.5	354.5	ND	ND	ND	ND		326.5	354.5	ND	ND	ND	ND	
18	1278.0	1095.0	606.0	428.5	0.83	0.03		1278.0	1095.0	1381.0	698.5	0.59	-0.21		1278.0	1095.0	1420.5	966.5	0.79	-0.01	
19	817.0	618.0	646.0	317.0	0.65	-0.15		817.0	618.0	801.5	245.0	0.40	-0.40		817.0	618.0	906.5	319.0	0.47	-0.33	
20	910.0	1135.5	434.0	250.5	0.46	-0.34		910.0	1135.5	531.5	258.0	0.39	-0.41		910.0	1135.5	781.0	531.5	0.55	-0.25	
21	1649.5	1528.5	704.0	540.5	0.83	0.03		1649.5	1528.5	609.0	429.0	0.76	-0.04		1649.5	1528.5	841.0	571.0	0.73	-0.07	
22	648.0	867.0	493.5	648.0	0.98	0.18		648.0	867.0	832.5	1069.0	0.96	0.16		648.0	867.0	652.0	656.0	0.75	-0.05	
23	402.5	268.5	326.0	109.0	0.50	-0.30		402.5	268.5	421.5	130.0	0.46	-0.34		402.5	268.5	540.5	181.5	0.50	-0.30	
24	447.5	614.0	514.5	230.0	0.33	-0.47		447.5	614.0	467.0	293.0	0.46	-0.34		447.5	614.0	602.5	358.5	0.43	-0.37	
25	912.5	1218.5	1018.5	795.5	0.58	-0.22		912.5	1218.5	1351.5	986.0	0.55	-0.25		912.5	1218.5	1264.5	788.0	0.47	-0.33	
26	334.0	335.0	264.5	132.0	0.50	-0.30		334.0	335.0	282.5	151.0	0.53	-0.27		334.0	335.0	427.0	251.0	0.59	-0.21	
27	337.5	342.0	307.5	118.5	0.38	-0.42		337.5	342.0	385.0	181.5	0.47	-0.33		337.5	342.0	374.0	191.5	0.51	-0.29	
28	524.5	350.0	477.0	176.5	0.55	-0.25		524.5	350.0	627.0	216.5	0.52	-0.28		524.5	350.0	470.5	200.5	0.64	-0.16	
29	822.0	727.0	775.5	244.5	0.36	-0.44		822.0	727.0	620.5	179.0	0.33	-0.47		822.0	727.0	620.0	201.0	0.37	-0.43	
30	442.0	481.5	288.0	256.0	0.82	0.02		442.0	481.5	453.5	314.0	0.64	-0.16		442.0	481.5	421.0	288.0	0.63	-0.17	
31	672.5	771.0	501.5	274.0	0.48	-0.32		672.5	771.0	584.0	329.5	0.49	-0.31		672.5	771.0	1230.0	806.5	0.57	-0.23	
32	279.0	334.0	247.0	120.5	0.41	-0.39		279.0	334.0	270.0	143.0	0.44	-0.36		279.0	334.0	227.0	156.5	0.58	-0.22	

ND = No Data  
 Subject 17 withdrew





HTR Study No. 03-121791-112  
Sponsor No. 03-7331-069

Final Report

## **APPENDIX III**

Total number of pages = 4

### **Temperature and Humidity Charts**



PROJECT NO.: 03121791112

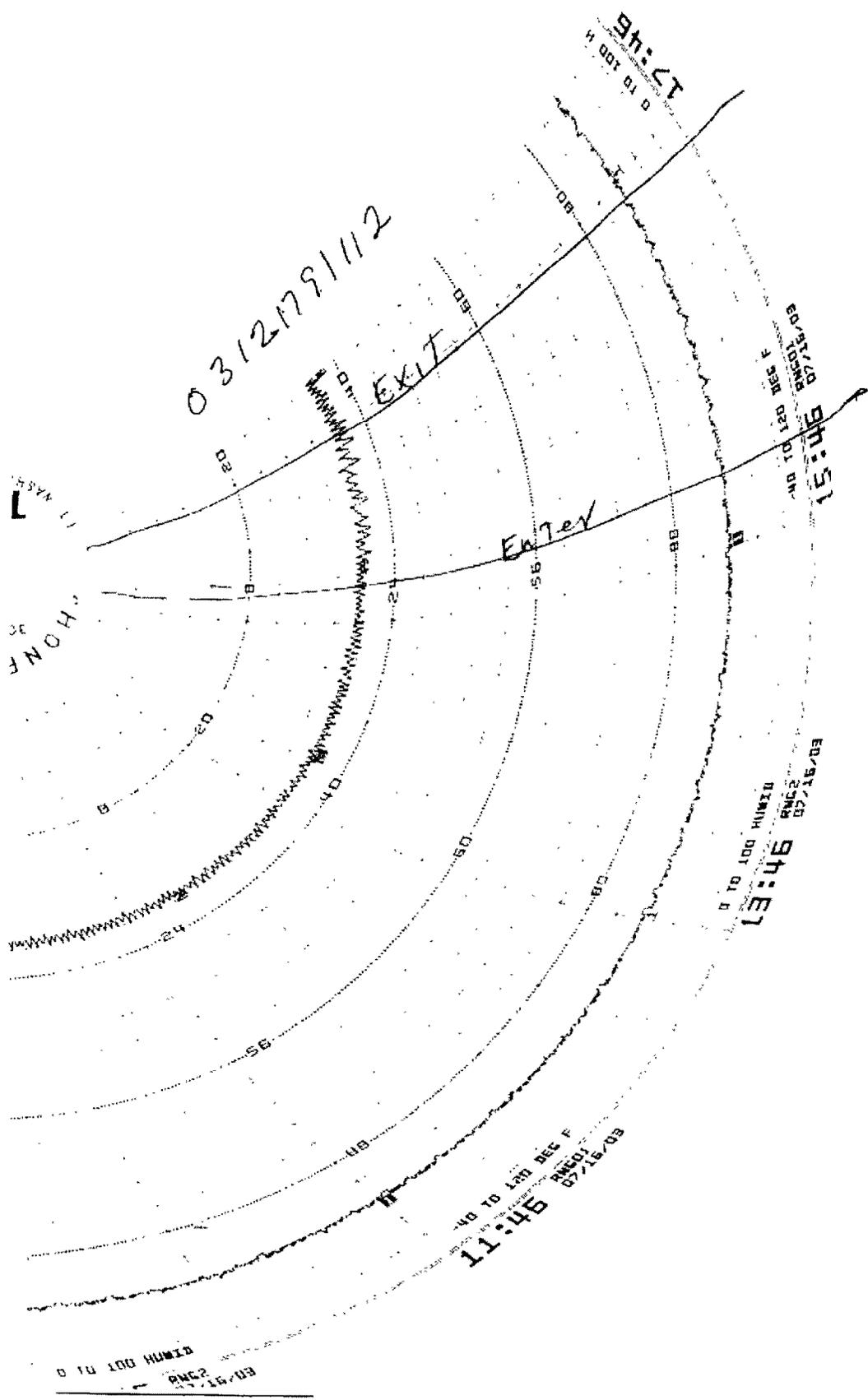
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40 minute warm-up period

Two 20 minute collections

INITIALS JS

DATE 7-16-03





PROJECT NO. U01010111

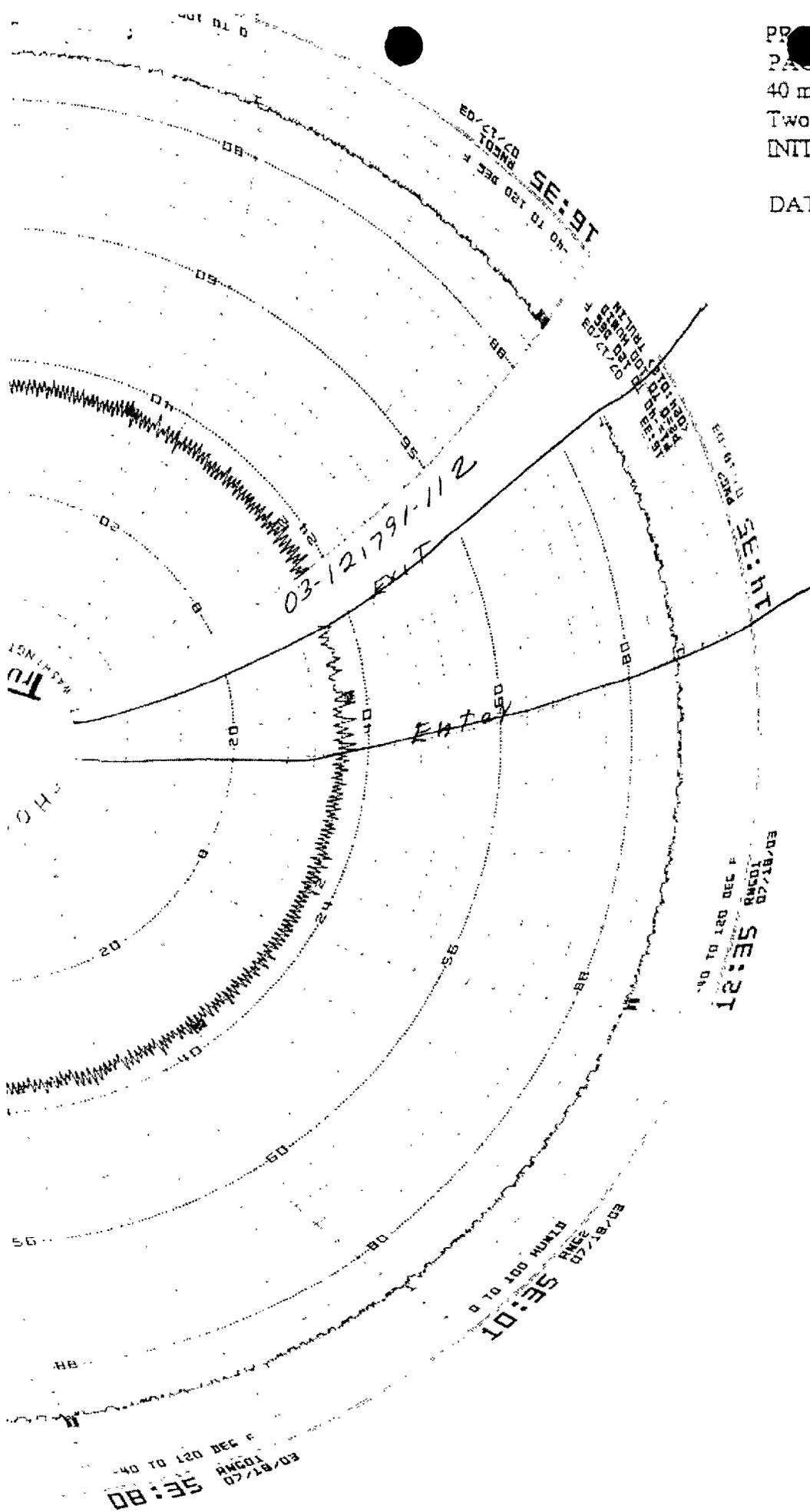
PAGE NO. VI-86

40 minute warm-up period

Two 20 minute collections

INITIALS P

DATE 7-18-03



HTR Study No. 03-121791-112  
Sponsor No. 03-7331-069

Final Report

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