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BD

Indispensable to human health

August 25, 2003

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 75N-183H
Topical Antimicrobial Drug Products for Over-the-Counter Human Use;
Health-Care Antiseptic Drug Products; Reopening of the Administrative Record.

To Whom It May Concern:

Please accept these comments from Becton Dickinson and Company in response to the Food and Drug Administration's (FDA's) reopening of the administrative record regarding the Tentative Final Monograph (TFM) for Over-the-Counter (OTC) Health-Care Antiseptic Drug Products, 59 Fed. Reg. 31401 (June 17, 1994). These comments provide supportive clinical data of the 3% Chloroxylenol (PCMX) products that currently do not fall under the scope of the TFM.

Becton Dickinson has marketed several Chloroxylenol products since 1987. During this time there have not been any reported incidents regarding the safety of these products.

Becton Dickinson wishes to submit the following four reports:

1. Health Care Personal Handwash Study:
"Report for Determination of the Antimicrobial Efficacy of Three Test Products Using the Health Care Personnel Hand Wash Procedure". Report number 000813.
2. In-Vitro Time Kill Study:
"Report For Evaluation of Three Test Products for Their Antimicrobial Properties When Challenged with Various Microorganisms Strains Using An In-Vitro Time Kill Method". Report number 000302.

75N-183H C64

3. Minimum Inhibitory Concentration (MIC)
   "Report for Determination of the Minimum Inhibitory Concentration (MIC) of two products when challenged with Fifty Microorganisms Strains Using The Macro dilution Broth Method". Report number 000608.

4. Minimum Inhibitory Concentration (MIC)
   "Report for Minimum Inhibitory Concentration for 3% PCMX as Surgical Hand Scrub Solution" Report number 361-101.

The results of the submitted clinical studies demonstrate the effectiveness of Chloroxylenol (PCMX) formulated at a level of 2.5–3.75% (w/w) as a HealthCare Personnel Handwash and Surgical Hand Scrub. Becton Dickinson is specifically recommending that they be classified as Safe and Effective (Category I) for skin antisepsis.

Please do not hesitate to contact me at 801-565-2550 should you have any questions.

Sincerely,

Rand Pugmire, RAC
Manager, Regulatory Affairs

Minh Hoang
Manager, R&D Surgical Scrubs

Enclosures 4
cc: Charles J. Ganley, M.D. (HFD-560)
Debbie L. Lumpkins (HFD-560)
Albert T. Sheldon (HFD-560)

BIOSCIENCE
LABORATORIES•INC

3% PCMX foamer

December 1, 2000

FINAL REPORT #000813 - Product #2

DETERMINATION OF THE ANTIMICROBIAL EFFICACY OF THREE TEST PRODUCTS USING THE HEALTH CARE PERSONNEL HANDWASH PROCEDURE

Prepared for:

BECTON DICKINSON (SPONSOR)
9450 South State Street
Sandy, Utah 84070-3213

Prepared by:

BIOSCIENCE LABORATORIES, INC. (COMPANY)
P.O. Box 190
Bozeman, Montana 59771
(406) 587-5735

Copy # ____

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EXECUTIVE SUMMARY

The antimicrobial effectiveness of three (3) test products was determined using ten (10) consecutive hand contaminations/product applications. **This Final Report presents the results of testing Product #2; an individual Final Report was also prepared for Products 1 and 3.** Fifteen (15) human subjects utilized each test product (for a total of forty-five [45] subjects) over the course of ten (10) consecutive hand contaminations/product applications. Microbial samples were taken at baseline and after washes one (1), three (3), seven (7), and ten (10). All sampling of the hands was performed using the Glove Juice Sampling Procedure. *Serratia marcescens* (ATCC #14756) was the marker organism used for hand contaminations. The testing methods used were based on ASTM E 1174-94, *Standard Test Method for Evaluation of Healthcare Personnel Handwash Formulations.*

Test Product #2 demonstrated statistically significant ($p < 0.05$) $\log_{10}$ reductions in bacterial population from baseline population. Test Product 2 (3% PCMX Hand Foamer) demonstrated reductions of 3.14 after Wash 1 and 5.57 after Wash 10.

December 1, 2000

FINAL REPORT #000813 - Product #2

1.0 TITLE: **DETERMINATION OF THE ANTIMICROBIAL EFFICACY OF THREE TEST PRODUCTS USING THE HEALTH CARE PERSONNEL HANDWASH PROCEDURE**

2.0 SPONSOR: **BECTON DICKINSON**
9450 South State Street
Sandy, Utah 84070-3213

3.0 COMPANY: **BIOSCIENCE LABORATORIES, INC.**
P.O. Box 190
Bozeman, Montana 59771

4.0 STUDY DIRECTORS:

Carol Riccardi - Principal Study Director
Christopher Beausoleil - Associate Study Director
Robert McCormack - Associate Study Director

5.0 PURPOSE:

This study evaluated the antimicrobial effectiveness of three (3) test products using the healthcare personnel handwash procedure. **This Final Report presents the results of testing Product #2; an individual Final Report was also prepared for Products 1 and 3.**

6.0 SCOPE:

The antimicrobial effectiveness of three (3) test products was determined using ten (10) consecutive hand contaminations/product applications. Fifteen (15) human subjects utilized each test product (for a total of forty-five [45] subjects) over the course of ten (10) consecutive hand contaminations/product applications. Microbial samples were taken at baseline and after washes one (1), three (3), seven (7), and ten (10). All sampling of the hands was performed using the Glove Juice Sampling Procedure. *Serratia marcescens* (ATCC #14756) was the marker organism used for hand contaminations. The testing methods used were based on ASTM E 1174-94, *Standard Test Method for Evaluation of Healthcare Personnel Handwash Formulations.*

7.0 TEST MATERIAL:

Samples of the test product used in this evaluation were supplied by Sponsor. Records of the lot number utilized were maintained by both Sponsor and Company. Responsibility for the identity, strength, purity, composition, and stability of the test product remained with Sponsor. The product evaluated was:

Test Product 2: 3% PCMX Hand Foamer (Becton Dickinson)
Lot Number: 000703X
Expiration Date: 06/2003

8.0 EQUIPMENT:

8.1 Steam Autoclaves: BSLI 91113 and BSLI 91127
8.2 Laminar Biological Flowhood (certified): BSLI 91119
8.3 Scrub Sink: BSLI 960101
8.4 Scrub Sink Thermometer: BSLI 000701
8.5 Continuously Adjustable Pipette, 20 µL - 200 µL Capacity: BSLI 981201
8.6 Continuously Adjustable Pipette, 100 µL - 1000 µL Capacity: BSLI 991001
8.7 Portable Pipetters: BSLI 971205, BSLI 980601, and BSLI 980901
8.8 Autoplate 4000 Spiral Plater: BSLI 980409
8.9 CASBA™4 Plate Counting System: BSLI 980410
8.10 Walk-in Environmental Chamber, 25° ± 2°C: BSLI 930812
8.11 Walk-in Environmental Chamber Thermometers: BSLI TI-960101, BSLI TI-960102, BSLI TI-960103, and BSLI TI-960105
8.12 Incubator, 55° - 60°C: BSLI 91059 (BIs Only)
8.13 Incubator Thermometer: BSLI TI-2064
8.14 Vortex Mixers: BSLI 980103 and BSLI 991201
8.15 Calibrated Minute/Second Timers: BSLI 941002, BSLI 961003, BSLI 961005, BSLI 961007, BSLI 961008, BSLI 961010, BSLI 980101, BSLI 980102, BSLI 980401, BSLI 980402, BSLI 980405, BSLI 000303, BSLI 000304, BSLI 000305, BSLI 000306, BSLI 000307, and BSLI 000308
8.16 Orion pH Meter Model 720: BSLI 931104
8.17 Mettler BB240 Balance: BSLI 930409
8.18 A & D Balance Model EK-2000G: BSLI 960801
8.19 Troemner Weights: BSLI 930408
8.20 Ohaus Weights: BSLI 961011
8.21 Hewlett-Packard HP-15C Hand Calculator
8.22 Texas Instruments TI-35X Hand Calculator
8.23 Texas Instruments TI-36X Hand Calculator
8.24 MiniTab® Statistical Software (PC Version, 10xtra and 13)

9.0 SUPPLIES:

9.1 Sterile 5.0 mL Capacity Serological Pipettes: Kimble Lot Number N00080C and Sterilin Lot Number 950408
9.2 Sterile Dilution Tubes and Bottles
9.3 Sterile Polystyrene Petri Dishes
9.4 Sterile Powder-Free Surgical Gloves: Ansell Perry Lot Numbers 8608 and 790215
9.5 Non-Sterile Latex Gloves: Ultra Care Lot Numbers R8A14098 and R8B24059
9.6 Non-Sterile Nitrile Gloves: Safe Skin Lot Numbers 8225A-4V and 9184S-13V
9.7 Non-Sterile Vinyl Gloves: American Health & Safety Lot Numbers 0003INGEPF-62479 and 0004BAGEPF-200103
9.8 Sterile 1.0 and 0.1 mL Capacity Pipette Tips
9.9 Sterile 5 cc Syringes: Becton Dickinson Lot Number 0007120
9.10 70% Ethanol: BSLI Lot Numbers 70%EtOH001125A and 70%EtOH001225F
9.11 Bland Soap (Baby San®): Huntington Laboratories Lot Number L0630813, Expires 03/02
9.12 Antibacterial Soap (Hibiclens®): Zeneca Pharmaceuticals Lot Number 4723B, Expires 11/01
9.13 Polysporin: Lot Number 32320L, Expires 01/02

10.0 TEST SOLUTIONS AND MEDIA:

Sampling Solution

10.1 Sterile Stripping Fluid (SSF): SSF001124A, SSF001206B, SSF001213B, SSF001219A, SSF001220B, SSF001225D, and SSF001226E

Neutralizing/Diluting Fluid

10.2 Butterfield's Phosphate Buffer Solution with Product Neutralizers (BBP++): BBP++001124B, BBP++001212C, BBP++001220A, and BBP++010103H

10.3 Phosphate Buffered Saline (PBS) for Neutralization Assay Only: PBS001212B

Media

10.4 Tryptic Soy Agar with product neutralizers (TSA+): TSA+001219B, TSA+001221A, TSA+001221B, TSA+001222A, TSA+001222B, TSA+001225A, TSA+010102A, TSA+010102B, and TSA+010104A

10.5 Tryptic Soy Broth (TSB) for Neutralization Assay and Inoculum Preparation: TSB001118B, TSB001207B, and TSB001221C

10.6 Tryptic Soy Agar (TSA) for Neutralization Assay and Inoculum Preparation: TSA001131B and TSA001218A

11.0 NEUTRALIZATION ASSAY:

Prior to initiation of this study, *Serratia marcescens* (ATCC #14756) was used to confirm the adequacy of the antimicrobial product neutralizer in accordance with *Standard Practices for Evaluating Inactivators of Antimicrobial Agents Used in Disinfectant, Sanitizer, Antiseptic, or Preserved Products* (ASTM E 1054-91).

12.0 TEST METHODS:

Institutional Review Board

12.1 Informed Consent Forms and any other supportive material relevant to the safety of the subjects were supplied by principal investigators to the Gallatin Institutional Review Board (GIRB) for their review and approval. The primary purpose of the GIRB is the protection of the rights and welfare of the subjects involved (reference CFR 21, Parts 50 and 56). This study began only after GIRB approval was obtained.

Subjects

12.2 The study utilized forty-five (45) subjects using three (3) test products (fifteen [15] subjects per product) over the course of eleven (11) consecutive microbial contamination procedures, followed by ten (10) product application procedures.

12.3 Seventy-two (72) overtly healthy subjects over the age of eighteen (18), but under the age of seventy (70) were admitted into the study. Forty-five (45) subjects completed the study. Of the forty-five (45) subjects who completed the study, twenty (20) were male, twenty-five (25) were female, two (2) were Hispanic-American, three (3) were Asian-American, and forty (40) were Caucasian. The median age of the forty-five (45) subjects who completed the study was twenty-five (25) years, with nineteen (19) being the youngest, and sixty-two (62) the oldest tested. All subjects' hands and forearms were free from clinically evident dermatoses, injuries, open wounds, hangnails, and/or any other disorders which could compromise the subject and the study. All subjects signed Informed Consent Forms and the Study Description (Addendum I, Appendix I) prior to participating in the study.

12.4 No subject was admitted into the study who was using any topical or systemic antimicrobial, steroids, or any other medications known to affect the normal microbial flora of the skin. Only subjects meeting the inclusion criteria (Addendum I, Sections 11.4 - 11.8) and none of the exclusion criteria (Addendum I, Sections 11.9 - 11.17) were admitted into the study.

Pre-Test Period

12.5 The seven (7) days prior to the test portion of the study constituted the pre-test period. During that time, subjects were instructed to avoid using medicated soaps, lotions, deodorants and shampoos, as well as skin contact with solvents, detergents, acids and bases, or any other products known to effect the normal microbial populations of the skin (Addendum I, Appendix II). Subjects were supplied a personal hygiene kit containing non-medicated soap, shampoo, deodorant, lotion, and rubber gloves to be worn when contact with antimicrobials, solvents, detergents, acids, or bases could not be avoided. Subjects were instructed to use the contents of this kit exclusively during their participation in the study and also, to avoid using UV tanning beds and swimming or bathing in biocide-treated pools or hot tubs.

12.6 A study description, personal hygiene kit, and the Informed Consent statement were provided to each subject prior to their beginning the study. Trained laboratory personnel explained the study to each participant and were available to answer any questions which arose.

Inoculum Preparation

12.7 *Serratia marcescens* (ATCC #14756) was used to challenge the efficacy of the test products.

12.8 Using aseptic technique, a 10 mL tube of Tryptic Soy Broth was inoculated with a cryobead of *Serratia marcescens*. The inoculated tubes of Tryptic Soy Broth were incubated at 25° ± 2°C for 21 - 22.5 hours. After incubation, a 1.0 mL aliquot of the 10 mL Broth culture was transferred aseptically to a 2-liter flask containing 1 liter of Tryptic Soy Broth. The flask was incubated at 25° ± 2°C for 18 - 20.25 hours. Prior to testing, the cultures were Gram-stained to assure culture purity. The cultures were assayed for the number of microorganisms/mL at the beginning and end of the use-period. Prior to any withdrawal of culture, whether for hand contamination or for numbers assay, the suspension was gently swirled. Each suspension was not used for more than eight (8) consecutive hours. Seven (7) inoculum flasks were used during the course of testing. The results of the initial and final population assays are listed in the table at the top of the next page.

Flask #	Initial Population (Just Prior to Use)	Final Population (Just After Use)
1	1.86×10^9	2.46×10^9
2	2.32×10^9	1.89×10^9
3	9.55×10^8	1.18×10^9
4	9.91×10^8	1.32×10^9
5	9.05×10^8	1.24×10^9
6	9.76×10^8	1.06×10^9
7	1.01×10^9	1.14×10^9

Test Period

12.9 Subjects were assigned randomly to one (1) of the three (3) test products. Each subject was utilized for two (2) to three (3) hours on a single day of the test period. Subjects clipped their fingernails to a free edge of ≤ 1 mm, if they had not already done so. All jewelry was removed from the hands and arms prior to washing.

12.10 Subjects performed a thirty (30) second handwash using a bland soap, followed by a thirty (30) second rinse, to remove dirt and oil from the hands and to familiarize the subjects with the Test Product wash procedure. The temperature of the water used for this, and all subsequent wash cycles was controlled at 40° ± 2°C.

12.11 On the designated test day and test phase, a 5.0 mL aliquot of a suspension containing approximately 1.0×10^8 CFU/mL of *Serratia marcescens* (ATCC #14756) was transferred into each subject's cupped hands in three (3) aliquots of approximately 1.5 mL, 1.5 mL, and 2.0 mL. The inoculum was then distributed evenly over both hands, and not reaching above the wrists, via gentle continuous massage for forty-five (45) seconds. After a timed two (2) minute air-dry, the Glove Juice Sampling Procedure was performed (Section 12.14). This first contamination cycle provided the baseline recovery levels and was followed with a thirty (30) second handwash using a non-medicated, bland soap.

12.12 The microbial inoculum was again evenly distributed over both hands, and not reaching above the wrists, via gentle continuous massage for forty-five (45) seconds. After a timed two (2) minute air-dry, the subjects utilized their assigned test product according to the directions below. This was followed by the Glove Juice Sampling Procedure (Section 12.14).

1. 2 pumps of Test Product were dispensed into the subject's cupped hands.

2. Subjects rubbed their hands together in a vigorous manner for fifteen (15) seconds, or until the product was completely absorbed by the skin and the hands were dry.

3. For washes that were followed by a sample, the hands were gloved dry.

12.13 Each subject completed this contamination/product application cycle a total of ten (10) consecutive times, with a minimum of five (5), and a maximum of fifteen (15) minutes between microbe/product applications. The hands were sampled for residual *Serratia marcescens* after contamination/product application cycles one (1), three (3), seven (7), and ten (10). All samples were taken using the Glove Juice Sampling Procedure (Section 12.14).

Glove Juice Sampling Procedure

12.14 Following the prescribed product application procedure (Section 12.12), powder-free, loose-fitting sterile latex gloves were donned. At the designated sampling time, seventy-five (75) mL of Sterile Stripping Fluid without product neutralizers were instilled into each glove. The wrists were secured, and attendants massaged the hands through the gloves in a uniform manner for sixty (60) seconds. A 5.0 mL aliquot of the glove juice was removed from each glove, diluted in 5.0 mL of Butterfield's Phosphate Buffer solution with product neutralizers (dilution 10^0), and then serially diluted in Butterfield's Phosphate Buffer solution with product neutralizers.

Subject Safety

12.15 Subjects were not allowed to leave the laboratory for any reason once the testing began. Additionally, subjects were required to wear protective garments and not touch their clothing, faces, or any other body parts with their hands during the test period. On completion of testing, subjects were required to perform a one (1) minute rinse with 70% ethanol, an air-dry, and a water-rinse followed by a supervised four (4) minute scrub of the hands and forearms with a 4% Chlorhexidine Gluconate solution. A topical antibiotic ointment (Polysporin) was applied to the hands following the decontamination procedure.

12.16 An antibiotic sensitivity profile for the *Serratia marcescens* (ATCC #14756) used in this study is retained on file at BSLI.

Plating

12.17 Triplicate spiral plates were prepared from appropriate dilutions using Tryptic Soy Agar with product neutralizers. The plates were incubated at 25° ± 2°C for approximately forty-eight (48) hours. *Serratia marcescens* produced red colonies, and only those colonies were counted.

Data Collection

12.18 The colonies on the plates were counted and the data recorded using the computerized CASBA™4 plate-counting system. If 10^0 plates gave an average count of zero (0), the average plate count was expressed as 1.00×10^1. The estimated number of viable microorganisms recovered was obtained from the formula, 75 x Dilution Factor x Mean Plate Count for the three (3) plates.

13.0 METHODS OF ANALYSIS:

13.1 The plate count data collected from this study were evaluated using MiniTab® statistical computer software.

13.2 The estimated $\log_{10}$ number of viable microorganisms recovered from each hand was designated the "R-value," the adjusted average $\log_{10}$ colony count measurement for each subject at each sampling time. Each R-value was determined using the following formula:

$$R = \log_{10} [75 \times C_i \times 10^{-D} \times 2]$$

Where:

75	=	the amount (mL) of stripping solution instilled into each glove
C_i	=	the arithmetic average colony count of the three (3) plate counts for each subject at a particular dilution level
D	=	the dilution factor
2	=	the neutralization-step dilution (10^0)

NOTE: A $\log_{10}$ transformation was performed on these data to convert them to a linear scale. A linear scale, more appropriately a $\log_{10}$ linear scale, is a requirement of the statistical models used.

Statistical Analysis

13.3 A pre-post experimental design was utilized to evaluate the antimicrobial effectiveness of the test products.

Pre-Product Application	Post-Product Application
$R(1)\ O_{BL}$	$A(1)_1O_1\ \ A(1)_3O_3\ \ A(1)_7O_7\ \ A(1)_{10}O_{10}$
$R(2)\ O_{BL}$	$A(2)_1O_1\ \ A(2)_3O_3\ \ A(2)_7O_7\ \ A(2)_{10}O_{10}$
$R(3)\ O_{BL}$	$A(3)_1O_1\ \ A(3)_3O_3\ \ A(3)_7O_7\ \ A(3)_{10}O_{10}$

Where:

$R(I)$ = Subjects randomly assigned to one (1) of three (3) products
- I = 1, if test product 1
- 2, if test product 2
- 3, if test product 3

$A(I)_j$ = Independent variables - Test Products
- j = 1, if product application #1
- 3, if product application #3
- 7, if product application #7
- 10, if product application #10

O_k = Dependant variables - Microbial Counts
- k = BL, if baseline
- 1, if post-product application #1
- 3, if post-product application #3
- 7, if post-product application #7
- 10, if post-product application #10

13.4 Prior to performing a statistical analysis, Exploratory Data Analysis was performed on the data. Stem-Leaf Ordering, Letter Value Displays, and Box Plots were generated which assured that the data collected approximated the normal distribution. Any outlier values based on the Box Plots were noted. A two-sample Student's *t* test was conducted comparing the baseline $\log_{10}$ values from the right and left hand. The baseline $\log_{10}$ values were compared to $\log_{10}$ values recovered at Washes 1 and 10 using the two-sample Student's *t* test. All statistical tests were conducted using the 0.05 level of significance for Type I (α) error.

14.0 ADVERSE EVENTS:

No adverse events occurred following use of Test Product #2.

15.0 RESULTS:

15.1 A two-sample Student's *t* test ($\alpha = 0.05$) was used to assure that baseline values for the left and right hands were statistically equivalent before combining the data. The left hand baseline values and right hand baseline values were found to be equivalent (p value = 0.63). A statistical summary of the baseline values is presented in Table I.

Table I: Summary of Baseline Values for Left and Right Hands

Baseline	Sample Size	Mean	Standard Deviation
Left Hand	45	9.09	0.27
Right Hand	45	9.06	0.24

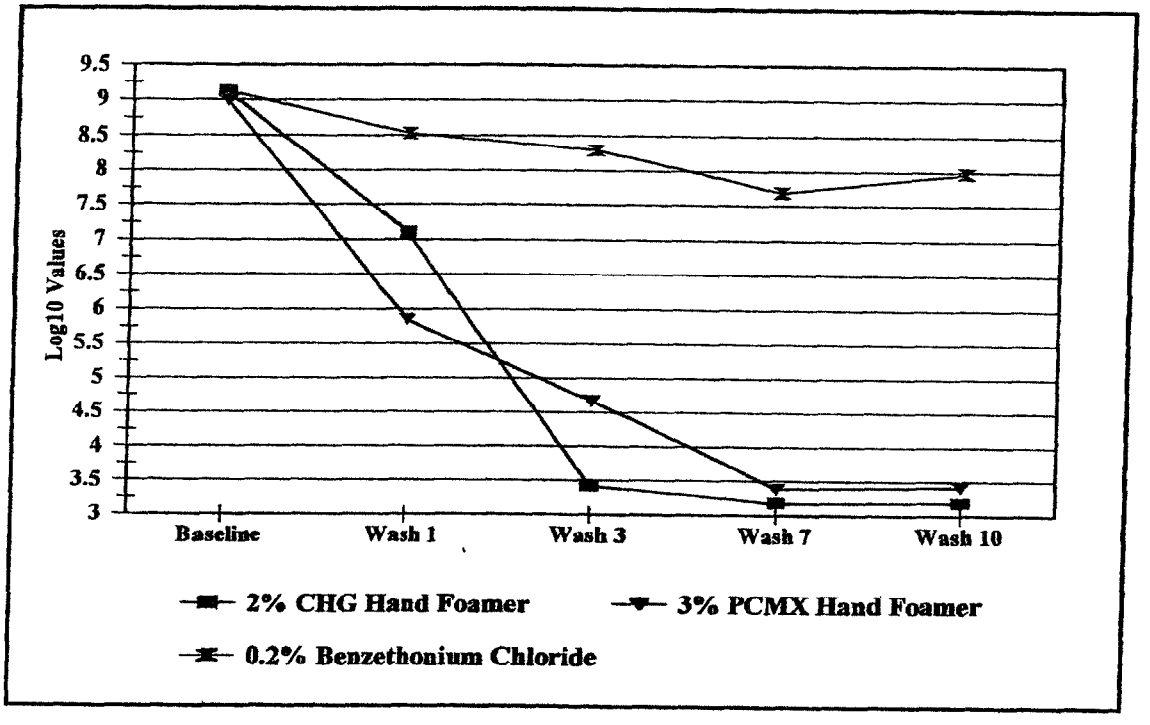
15.2 The wash values for the product were significantly different from Baseline ($p < 0.05$). Table II presents the results of analyses performed on data resulting from use of Test Product 2 (3% PCMX Hand Foamer).

Table II: Statistical Summary of Sample Data for 3% PCMX Hand Foamer (Test Product 2)

Sample	Sample Size	Mean of $\log_{10}$ Values	Standard Deviation	95% Confidence Intervals	Reduction from Baseline ($\log_{10}$)	Percent Reduction
Baseline	30	8.99	0.21	8.91 to 9.07	N/A	N/A
Wash 1	30	5.85	0.47	5.67 to 6.02	3.14	99.93%
Wash 3	30	4.66	0.76	4.38 to 4.95	4.33	> 99.99%
Wash 7	30	3.39	0.42	3.23 to 3.55	5.60	> 99.99%
Wash 10	30	3.42	0.41	3.27 to 3.57	5.57	> 99.99%

15.3 Figure 1 graphically presents the data resulting from use of the three (3) Test Products.

Figure 1: Graphical Presentation of the log_{10} data for all 3 Test Products



16.0 CONCLUSION:

Test Product #2 demonstrated statistically significant ($p < 0.05$) log_{10} reductions in bacterial population from baseline population. Test Product 2 (3% PCMX Hand Foamer) demonstrated reductions of 3.14 after Wash 1 and 5.57 after Wash 10.

17.0 **ACCEPTANCE:**

BIOSCIENCE LABORATORIES, INC.
P.O. Box 190
Bozeman, Montana 59771

President and CEO: _____ 12-1-00
Daryl S. Paulson, Ph.D. Date

Executive Director of Operations/ Principal Study Director: NA JM 12/01/00 NA JM 12/01/00
Carol Riccardi Date
No longer in the employ of BioScience Laboratories, Inc.

Manager of Clinical Laboratory/ Associate Study Director: _____ 12/1/00
Christopher Beausoleil Date

Associate Study Director: Robert R. McCormack 12/1/00
Robert McCormack Date

QUALITY ASSURANCE STATEMENT:
This study was inspected by the Quality Assurance Unit, and reports were submitted to the Study Director and Management in accordance with Standard Operating Procedures, as follows:

Phase	Date
Neutralization Assay	09/22/00
Product Testing	09/26/00
Data Audit	11/16/00
Draft Report Review	11/16/00
Final Report Review	12/01/00
Reports to Study Director and Management	09/22/00, 09/26/00 & 11/16/00

This study was conducted in compliance with Good Laboratory Practices standards, as described by the FDA (21 CFR Part 58), with the following exception: test article preparations were not analyzed at BioScience Laboratories, Inc., to confirm concentration, stability, or homogeneity.

Director of Quality Assurance: _____ 12/01/00
John A. Mitchell, Ph.D. Date