Statistical Analysis Plan

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Protocol Title	A Randomized, Single-Center, Partially Blinded, Evaluation of the Time-Dependent Antimicrobial Effectiveness of Swabsticks Impregnated with 2% (w/v) Chlorhexidine Gluconate in 70% (v/v) Isopropyl Alcohol in Healthy Volunteers
SAP Date	August 2, 2019

Version History	Action
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Approval

Function	Name	Signature
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1 List of Abbreviations and Definitions

- **AC:** Active Control
- **AE:** Adverse Event
- **ANOVA:** Analysis of Variance
- **ASTM:** American Society for Testing and Materials
- **ATE:** Average Treatment Effect
- **BD:** Becton Dickinson and Company
- **CFU:** Colony Forming Units
- **CHG:** Chlorhexidine Gluconate
- **CI:** Confidence Interval
- **CRF:** Case Report/Record Form
- **EDC:** Electronic Data Capture
- **FDA:** Food and Drug Administration
- **GCD:** Global Clinical Development
- **HC:** Health Canada
- **IP:** Investigational Product
- **ITT:** Intent to Treat
- **MAR:** Missing at Random
- **mITT:** Modified Intent to Treat
- **NC:** Negative Control
- **PP:** Per-Protocol
- **RS:** Reference Standard
- **SAE:** Serious Adverse Event
- **SD:** Standard Deviation

2 Overall Study Description

2.1 Study Background

In this study, the antimicrobial activity of the investigational product (IP), a single Swabstick impregnated with 1.75 mL of 2% (w/v) chlorhexidine gluconate (CHG) in 70% (v/v) isopropyl alcohol, will be investigated according to established testing requirements described by Health Canada (HC) and the US FDA.

For evaluation of antimicrobial activity using the HC analysis criteria, immediate antimicrobial activity will be evaluated at 30 seconds and persistent antimicrobial activity will be evaluated at 6 hours post-product application on the abdomen and the groin for the IP. A reference standard, 60% v/v 1-Propanol, will be applied with a single Swabstick and will also be compared to the same log reduction standards as the IP.

For evaluation of antimicrobial activity using the FDA analysis criteria, the immediate antimicrobial activity will be evaluated at 10 minutes post-product application on the abdomen and the groin (primary objectives) and at 30 seconds post-product application on the abdomen only (secondary objectives). Persistent antimicrobial activity will be evaluated at 6 hours post-product application on the abdomen and the groin.

2.2 Objectives

2.2.1 Safety Objectives

To evaluate safety using skin irritation scores and the incidence of adverse events reported during the study for all study products.

2.2.2 HC Objectives

2.2.2.1 Primary Efficacy Objectives

To demonstrate the immediate and persistent antimicrobial activity of a single Swabstick impregnated with 2% (w/v) chlorhexidine gluconate in 70% (v/v) isopropyl alcohol at 30 seconds and 6 hours post-product application.

The reference standard of 60% v/v 1-propanol (RS) applied with a Swabstick, should meet the same efficacy standards described in Table 1 as the IP.

2.2.2.2 Exploratory Objective

- To evaluate the $\log_{10}$ CFU/cm^2 reductions from baseline for the IP and RS at each anatomical site, abdomen and groin, at 10 minutes post-product application.
- To determine if the 30-second, 10 minutes and 6 hour $\log_{10}$ CFU/cm^2 reductions on the abdomen and groin for the IP are not statistically worse than those for 60% v/v 1-propanol post-product application.

2.2.3 FDA Objectives

2.2.3.1 Primary Objectives

To demonstrate the immediate and persistent antimicrobial properties of a single Swabstick impregnated with 2% (w/v) chlorhexidine gluconate in 70% (v/v) isopropyl alcohol to ChloraPrep SEPP Clear Applicator AC and a NC of 0.9% normal saline at 10 minutes and 6 hours post product application.

- To demonstrate immediate antimicrobial efficacy at 10 minutes post-application (four co-primary objectives):
  - To demonstrate the non-inferiority of the average treatment effect (ATE) of the IP compared to the AC on the abdomen.
  - To demonstrate the non-inferiority of the average treatment effect (ATE) of the IP compared to the AC on the groin.
  - To demonstrate the superiority of the ATE of the IP compared to the NC on the abdomen.
  - To demonstrate the superiority of the ATE of the IP compared to the NC on the groin.
- To evaluate persistent antimicrobial efficacy at 6 hours post-product application. Log_{10} bacterial counts for each product application site will be converted to a binary (yes or no) success measure with success defined as having skin flora counts that are less than or equal to the baseline skin flora counts. Responder rates at 6 hours post-product application will be summarized descriptively for each product on each body site.

2.2.3.2 Secondary Objectives

To demonstrate antimicrobial efficacy at 30 seconds post-application (two secondary objectives):

- To demonstrate the non-inferiority of the average treatment effect (ATE) of the IP compared to the AC on the abdomen.
- To demonstrate the superiority of the ATE of the IP compared to the NC on the abdomen.

These two secondary objectives will be evaluated only when the four co-primary efficacy objectives pass both non-inferiority and superiority criteria. The secondary objectives will declare success when and only when all four primary and two secondary objectives pass both non-inferiority and superiority criteria.

2.2.3.3 Exploratory Objectives

- To evaluate the $\log_{10}$ CFU/cm^2 reductions from baseline for the IP, AC, and NC at each anatomical site at 30 seconds, 10 minutes and 6 hours.
- To calculate the product weight expression from product application [i.e., product weight prior to product application (g) - product weight post-product application (g)].

2.3 Study Design

This single site study is a randomized, controlled, partially blinded, design enrolling a minimum of 516 healthy volunteers, where each subject will receive two of the planned study products on the product application sites of the abdomen and/or groin. In this study, the antimicrobial activity of the investigational product (IP), a single Swabstick impregnated with 1.75 mL of 2% (w/v) chlorhexidine gluconate (CHG) in 70% (v/v) isopropyl alcohol, will be investigated according to established testing

requirements described by Health Canada (HC) and the US FDA. The study methods for this evaluation will be based on ASTM Standard Test Method E1173-15 [1].

Descriptions of study products are shown below.

- Investigational Product (IP): Single Swabstick impregnated with 2% (w/v) chlorhexidine gluconate (CHG) in 70% (v/v) isopropyl alcohol
- Reference Standard (RS): 60% (v/v) 1-propanol applied with a single Swabstick
- Active Control (AC): ChloraPrep SEPP - 2% chlorhexidine gluconate in 70% (v/v) isopropyl alcohol
- Negative Control (NC): 0.9% normal saline applied with a single Swabstick

A minimum of 516 evaluable subjects will be required to achieve a minimum of 192 evaluable product application sites for groin and abdominal regions for 60% (v/v) 1-propanol (RS) and 280 evaluable product application sites for groin and abdominal regions for each of the other three study product arms.

Due to the imbalance of the sample size between RS and other products, RS cannot be blinded and is coded as B and all the other three products will be blinded with assigned study product codes A, C, or D. More information about blinding and methods to reduce bias may be found in the protocol for this study.

The effectiveness of the neutralizer system must be validated prior to the main treatment study start date to demonstrate that the antimicrobials are effectively neutralized and there is no effect on the growth of microorganisms. GCD statistics group will not perform any summary or analysis for the neutralization validation data so this statistical analysis plan (SAP) only applies to the main treatment study.

2.4 Endpoints

- Safety Endpoints: Skin reactions using the modified Berger Bowman irritation assessment scale and the incidence of AEs reported during the study.
- Efficacy Endpoints: Log_{10} CFU/cm^2 of resident microbes on skin before and after each product application at 30 seconds, 10 minutes and 6 hours on the abdomen and groin.
- Exploratory Endpoints: Product weight prior to product application (g) and post-product application (g) on the abdomen and groin.

2.5 Acceptance Criteria

To be included in the primary analysis [modified intent-to-treat (mITT) data set], a product application site must have a Product Application Day microbial baseline within the stated requirements. Table 1 summarizes the baseline criteria for the mITT data set for each anatomical site and the expected minimum efficacy country specific standards.

For HC primary objectives, it will declare success when and only when all four primary objectives pass HC analysis acceptance criteria.

For FDA primary objectives [10-minute (abdomen and groin) post-product application time point], it will declare success when and only when all four primary objectives pass FDA analysis acceptance criteria. For FDA secondary objectives [30-second (abdomen only) post-product application time point], a gatekeeping procedure will be applied: the efficacy analysis for two secondary objectives will be performed only when all four primary objectives [10-minute (abdomen and groin) post-product application time point] pass the acceptance criteria and it will declare success when and only when all four primary and two secondary objectives pass FDA analysis acceptance criteria.

For responder rate at 6 hours, no acceptance criteria are applied.

Table 1: mITT Data Set for Each Anatomical Site and Expected Minimum Efficacy Standards

Anatomical Product Application Site	**Product Application Day Baseline Criteria**	**HC Analysis Acceptance Criteria at 30 Seconds, Primary Objectives**	**HC Analysis Acceptance Criteria at 6 Hours, Primary Objectives**	**FDA Analysis Acceptance Criteria at 30 Seconds, Secondary Objectives**	**FDA Analysis Acceptance Criteria at 10 Minutes, Primary Objectives**
Abdomen	3.20 to 6.00 $\log_{10}$ CFU/cm^2	Immediate effectiveness for the IP is at least a 2-$\log_{10}$ CFU/cm^2 reduction from baseline skin flora counts at 30 seconds.	Persistence effectiveness for the IP is at least a 2-$\log_{10}$ CFU/cm^2 reduction from baseline skin. flora counts at 6 hours.	At 30 seconds the upper two-sided 95% confidence bound of the average treatment effect (ATE) of IP - AC should be less than 0.5 $\log_{10}$. At 30 seconds the lower two-sided 95% confidence bound of the ATE of NC - IP should be greater than 1.2 $\log_{10}$.	At 10 minutes the upper two-sided 95% confidence bound of the average treatment effect (ATE) of IP - AC should be less than 0.5 $\log_{10}$. At 10 minutes the lower two-sided 95% confidence bound of the ATE of NC - IP should be greater than 1.2 $\log_{10}$.
Groin	5.50 to 7.50 $\log_{10}$ CFU/cm^2	Immediate effectiveness for the IP is at least a 3-$\log_{10}$ CFU/cm^2 reduction from baseline skin flora counts at 30 seconds.	Persistence effectiveness for the IP is at least a 3-$\log_{10}$ CFU/cm^2 reduction from baseline skin. flora counts at 6 hours.	None	At 10 minutes the upper two-sided 95% confidence bound of the average treatment effect (ATE) of IP - AC should be less than 0.5 $\log_{10}$. At 10 minutes the lower two-sided 95% confidence bound of the ATE of NC - IP should be greater than 1.2 $\log_{10}$.

3 Sample Size

3.1 HC Analysis

To evaluate the primary efficacy objective for HC analysis a sample size of at least 192 evaluable sites per study product arm (IP or RS) per body site can achieve > 95% power to pass HC analysis acceptance criteria for all four objectives (IP only) using one-sample t-test (two-sided), with the following assumptions in Table 2.

Table 2: Parameters Used in Sample Size Calculations For HC Analysis

Two-sided test Type I error (α) : 0.05					
Time Point	Study Product	Standard Deviation for Log Reduction: Abdomen	Standard Deviation for Log Reduction: Groin	Log Reduction: Abdomen ($\log_{10}$)	Log Reduction: Groin ($\log_{10}$)
30 seconds	IP	1.14	1.43	3.47	3.38
6 hours	IP	1.22	1.24	3.43	3.50

3.2 FDA Analysis

To evaluate the primary and secondary objectives for the US FDA analysis a sample size of 280 evaluable sites per study product arm (IP, AC or NC) per body site can achieve > 95% power to demonstrate the non-inferiority of the Investigational Product (IP) as compared to the Active Control (AC) and the superiority of the IP as compared to the negative control (NC) in antimicrobial effect at 30-second (abdomen only) and 10-minute (abdomen and groin) post-product application time point for all six objectives, with the following assumptions in Table 3.

Table 3: Parameters Used in Sample Size Calculations For FDA Analysis

Two-sided test Type I error (α) : 0.05		
Average Treatment Effect	Abdomen ($\log_{10}$)	Groin ($\log_{10}$)
IP - AC	0.06	0.10
NC - IP	1.58	2.31
Standard deviation for each product on Abdomen: 1.05 $\log_{10}$		
Standard deviation for each product on Groin: 1.2 $\log_{10}$		

The overall power to pass both HC analysis and FDA analysis acceptance criteria is > 90%.

4 Intended Statistical Software

The analyses will be performed using R version 3.6.0 (2019-04-26) [2] or higher. R libraries and versions that are used for analyses will be listed.

5 Data

5.1 Database Information

Data will be captured by electronic case report forms (eCRFs) and provided to study statistician and statistical programmer by Data Management. More information on database management may be found in Data Management Plan for this study.

5.2 Data Sets Analyzed

- The full intent-to-treat (ITT) data set (all randomized subjects that received study product) will be used for the safety analysis.
- A modified intent-to-treat (mITT) data set will be used for efficacy analyses. Inclusion for the mITT data set is evaluated for each anatomical site (left and right for the groin and abdomen). For each anatomical site, product application day baseline criteria must be met (refer to Table 1 for product application day baseline criteria) in order to be included in the mITT data set.
- Analyses conducted on the mITT data set will also be conducted on the Per Protocol data set as supportive analyses when Per Protocol data are different from mITT data. The Per-Protocol data set will include evaluable product application sites from the mITT data set that adhere to defined assessments and procedures in the protocol central to patient enrollment, safety, rights or wellbeing, as well as the completeness, accuracy and reliability of study data.

5.3 Protocol Deviations and Use of Associated Data

Table 4 lists pre-defined potential protocol deviations and rules for use of associated data in analysis, which has been documented in a note-to-file "MPS-17IPVSS02_Guideline_Protoocl_Deviations_Data_Use.pdf". For any additional protocol deviations or issues that are not listed in Table 4, exclusion of the data from each population set will be reviewed and finalized on a case by case prior to the database lock.

All protocol deviations for this study will be listed (cf. Listing B.1). Any data that are excluded from any analysis will be listed indicating from which population sets data are excluded (cf. Listings B.2 for HC analysis and B.3 for FDA analysis).

5.4 Analysis Population Set(s)

For subject disposition, refer to Table A.1.1. Subjects who did not complete the study will be listed along with the status at the end of study (cf. Listing B.4).

For each analysis (HC analysis and FDA analysis), the number of subjects evaluable for ITT (randomized and treated/study product received), mITT and per-protocol (PP) analyses for CFU count and product weight per body site/location will be tabulated (cf. Tables A.1.2 for HC analysis and A.1.3 for FDA analysis). Subjects who were randomized and treated but did not pass the product application day baseline criteria (not eligible for mITT or PP analysis) will be listed (cf. Listing B.5).

Table 4: Guideline on Use of Associated Data in Analysis for Potential Protocol Deviations

		Use of Associated Data in Analysis			
Category	**Description of Deviation (Examples)**	**mITT CFU count**	**PP CFU count**	**mITT weight**	**PP weight**
Randomization error	Incorrect product applied based on randomization schedule or Subject received application of one or more incorrect products (grouped based on product applied)	Yes	No	Yes	No
	Subject received correct product but product was applied to incorrect side of the body based on randomization schedule				
	Sample taken from incorrect sample site within the treatment area based on randomization schedule				
Deviation from defined procedure	Loss of partial sampling volume	Yes	No	Yes	No
	Samples not plated in the 30 minute timeframe from collection				
	Subject leaves the study site but returns for assessments				
	Product application time outside of 30 seconds $\pm$ 5 seconds on the abdomen or 2 minutes $\pm$ 5 seconds on the groin				
Clinical assessment not done	Plates not dosed or plates contamination	No	No	No	No
Clinical assessment outside of window	Sampling time outside specified windows	Yes	No	Yes	No
Other	Pooling of samples from different subjects or different time points from the same subject	No	No	No	No
	Product weight error (difference in weights between pre application and post application less than 0 or greater than 2 grams)	Yes	Yes	No	No

6 Statistical Analysis/Calculations

6.1 Derived Variables

6.1.1 Log_{10} CFU/cm^2 of skin

Raw colony counts from each dilution will be recorded on the appropriate eCRFs for each subject. The average number of microorganisms recovered will be calculated using the formula below to convert the bacterial counts into log_{10} CFU/cm^2 of skin:

$$R = log_{10}\left[\frac{F\left(\frac{\sum_{i=1}^{3} C_i}{n}\right) D}{A}\right] \quad (1)$$

Where:
R = the average CFU count in log_{10} scale per cm^2 of skin.
F = Total number of mL of stripping fluid added to the sampling cylinder (6 mL). Note: If sample solution is lost during the procedure for a certain time point, the F value for that time point will change from 6 mL to the "Volume Remaining (mL)" recorded in the Core Lab Procedure Overview eCRFs.

$\frac{\sum_{i=1}^{3} C_i}{n}$ = average of the triplicate colony counts used for each sample collected (n = 3).
D = Dilution factor of the plates counted. One of 10^0, 10^1, 10^2, 10^3, 10^4, or 10^5.
A = Inside area of the sampling cylinder in cm^2 (3.80 cm^2).

The average CFU/mL, CFU/cm^2, and log_{10} CFU/cm^2 will be calculated for samples from each product application site in the same manner.

In order to avoid potential calculation problems due to taking the logarithm of zero, values of less than 1 CFU/cm^2 will be treated as 1 CFU/cm^2, such that the log_{10} transformation is not less than zero.

If colonies on one of the plates are uncountable, the average count from the remaining plates will be used. If colonies on two of the plates are uncountable, the count from the remaining plate will be used. If colonies on three plates are all uncountable, the average count will be missing.

6.1.2 Log Reduction

Log_{10} CFU/cm^2 reductions from baseline will be calculated separately for each subject, each of the four sites (left and right for the abdomen and groin), and each post-product application sampling time by taking the baseline log_{10} CFU/cm^2 values and then subtracting the log_{10} CFU/cm^2 values for the samples taken after baseline. The mean log_{10} CFU/cm^2 changes from baseline will be calculated separately for each product, at each anatomical site (abdomen and groin), and at each post-product application sampling time point (30 seconds, 10 minutes and 6 hours).

6.1.3 Responder Rate

To evaluate the persistent antimicrobial properties of a single Swabstick impregnated with 2% (w/v) chlorhexidine gluconate in 70% (v/v) isopropyl alcohol, log_{10} bacterial counts at 6 hours post-product application for each product application site will be converted to a binary (yes or no) success measure with success defined as having skin flora counts that are less than or equal to the baseline skin flora counts.

6.1.4 Product Weight

The weight (grams) of product solutions applied to an anatomical area will be estimated as:

Product weight prior to product application (g) - product weight post-product application (g)

6.2 Analysis Methods

6.2.1 HC Analysis

6.2.1.1 Summary Statistics

The following descriptive statistics for $\log_{10}$ CFU/cm^2 at each time point (baseline, 30 seconds, 10 minutes and 6 hours) and $\log_{10}$ CFU/cm^2 reductions at each post application sampling time point (30 seconds, 10 minutes and 6 hours) will be computed for the IP and RS, grouped by anatomical site: mean, median, standard deviation, minimum, maximum, and count (cf. Tables A.2.1 and A.2.2).

6.2.1.2 Primary Analysis

The 95% confidence intervals (two-sided) will be calculated for the average log reductions for the IP and RS at each post application sampling time point on each anatomical area using one-sample t-test (two-sided). The 95% confidence lower bound for mean log reduction at 30 seconds and 6 hours will be compared to the acceptance criteria (cf. Table A.2.4).

- If the lower limit of the 95% confidence interval (two-sided) of mean log reduction at 30 seconds is greater than or equal to 2 on the abdomen, acceptance criteria are met on the abdomen at 30 seconds.
- If the lower limit of the 95% confidence interval (two-sided) of mean log reduction at 30 seconds is greater than or equal to 3 on the groin, acceptance criteria are met on the groin at 30 seconds.
- If the lower limit of the 95% confidence interval (two-sided) of mean log reduction at 6 hours is greater than or equal to 2 on the abdomen, acceptance criteria are met on the abdomen at 6 hours.
- If the lower limit of the 95% confidence interval (two-sided) of mean log reduction at 6 hours is greater than or equal to 3 on the groin, acceptance criteria are met on the groin at 6 hours.

The RS will be also compared to the acceptance criteria applied to the IP.

6.2.1.3 Exploratory Analysis

The same analysis as described in Section 6.2.1.2 will be performed for log reduction at the 10 minute time point on each anatomical area for the IP and RS using one-sample t-test (two-sided) (cf. Table A.2.5).

Log_{10} CFU/cm^2 reductions at 30 seconds, 10 minutes, and 6 hours on the abdomen and the groin for the IP will be compared to the RS using two-sample t-test (two-sided). Difference in log reduction along with 95% confidence interval (CI) at each post application sampling time point will be compared to zero. If 95% CI contains zero, the conclusion is no significant difference in log reduction between IP and RS. If 95% CI does not contain zero, the conclusion is significant difference in log reduction exists and the direction of the difference will be indicated (cf. Table A.2.6).

A graph for the log reduction at each post application sampling time point with 95% confidence interval will be provided (cf. Figure C.1.1 created based on the simulated data).

6.2.2 FDA Analysis

6.2.2.1 Summary Statistics

The following descriptive statistics for $\log_{10}$ CFU/cm^2 at each time point (baseline, 30 seconds, 10 minutes and 6 hours) and $\log_{10}$ CFU/cm^2 reductions at each post application sampling time point (30 seconds, 10 minutes and 6 hours) will be computed for the IP, AC and NC, grouped by anatomical site: mean, median, standard deviation, minimum, maximum, and count (cf. Tables A.3.1 and A.3.2).

Responder rates at 6 hours post-product application will be summarized descriptively for each product (IP, AC and NC) on each body site. No inferential analysis will be performed on the responder rates at 6 hours post-product application (cf. Table A.3.3).

The following descriptive statistics for product weight will be computed for the IP, AC and NC, grouped by anatomical site: mean, median, standard deviation, minimum, maximum, and count (cf. Table A.3.4).

6.2.2.2 Primary Analysis

A linear regression model for each body site (abdomen or groin) will be used for primary analysis of efficacy at 10 minutes. In the model, the response is the post-product application bacterial counts at 10 minutes and predictors are the study products (IP, AC or NC) as a fixed effect and the pre-product application bacterial loads as a covariate. The average treatment effect (ATE) corrected for pre-product application bacterial loads will be estimated from the model and compared to both non-inferiority and superiority criteria (cf. Table A.3.5).

For assessment of the four primary objectives (i.e., immediate activity at 10 minutes post application on the abdomen and groin for non-inferiority and superiority):

- A non-inferiority criterion with a 0.5 $\log_{10}$ margin will be implemented for ATE of the IP compared to the AC (i.e., if the upper two-sided 95% confidence bound of the post-product application bacterial load corrected for pre-product application bacterial load of the IP-AC is less than 0.5 $\log_{10}$, the non-inferiority criterion is met).
- A 1.2 $\log_{10}$ superiority criterion will be implemented for the ATE of the IP compared to the NC (i.e., if the lower two-sided 95% confidence bound of the post-product application bacterial load corrected for pre-product application bacterial load of the NC-IP is greater than 1.2 $\log_{10}$, the superiority criterion is met).

A graph showing the ATE with 95% confidence intervals for post-product log CFU at 10 minutes correcting for pre-product application will be provided for each contrast (cf. Figure C.2.1 created based on the simulated data).

6.2.2.3 Secondary Analysis

A gatekeeping procedure will be applied: the efficacy analysis for two secondary objectives [30-second (abdomen only) post-product application time point] will be performed only when all four primary

objectives [10-minute (abdomen and groin) post-product application time point] pass the acceptance criteria.

A linear regression model for abdomen only will be used for secondary analysis of efficacy at 30 seconds. In the model, the response is the post-product application bacterial counts at 30 seconds and predictors are the study products (IP, AC or NC) as a fixed effect and the pre-product application bacterial loads as a covariate. The average treatment effect (ATE) corrected for pre-product application bacterial loads will be estimated from the model and compared to both non-inferiority and superiority criteria (cf. Table A.3.6).

For assessment of the two secondary objectives (i.e., immediate activity at 30 seconds post application on the abdomen for non-inferiority and superiority):

- A non-inferiority criterion with a 0.5 $\log_{10}$ margin will be implemented for ATE of the IP compared to the AC (i.e., if the upper two-sided 95% confidence bound of the post-product application bacterial load corrected for pre-product application bacterial load of the IP-AC is less than 0.5 $\log_{10}$, the non-inferiority criterion is met).
- A 1.2 $\log_{10}$ superiority criterion will be implemented for the ATE of the IP compared to the NC (i.e., if the lower two-sided 95% confidence bound of the post-product application bacterial load corrected for pre-product application bacterial load of the NC-IP is greater than 1.2 $\log_{10}$, the superiority criterion is met).

A graph showing the ATE with 95% confidence intervals for post-product log CFU at 30 seconds correcting for pre-product application will be provided for each contrast if acceptance criteria are met for all four co-primary objectives (cf. Figure C.2.1 created based on the simulated data). If acceptance criteria are not met for any of four co-primary objectives, the plot for 30 seconds will be removed from the graph as no analysis for 30 seconds is performed.

6.2.3 Safety Analysis

Skin irritation scores for each product at each post application sampling time per body location will be tabulated with frequency and percentage (cf. Table A.4.1) for ITT population set (all randomized subjects that received study product).

The statistical significance of differences in skin irritation between the study products at each post application sampling time will be evaluated by Fisher's exact test on skin irritation data summarized for safety analysis as follows: any reaction above a zero (no reaction) on the skin irritation rating scale for any category (erythema, edema, rash, and dryness) will be considered a positive signal for that substance (cf. Table A.4.3). If Fisher's exact test shows statistically significant skin irritation between the study products, follow-up analyses (e.g., Fisher's exact test for subgroup analysis) may be conducted to determine how the reactions differ (cf. Table A.4.4).

Adverse events (AEs) will be listed for all enrolled subjects (cf. Listing B.6). Whether subjects are in ITT population set (randomized subjects that received study product) will be indicated. A summary showing number and percentage of subjects with AE(s) observed will be provided for ITT population set (cf. Table A.4.2). No inferential analysis will be performed on the incidence of AEs. If any serious adverse events (SAEs) happen, more details for SAEs will be listed (cf. Listing B.7).

6.3 Adjustments for Multiple Objectives

An overall significance level of 0.05 ($\alpha = 0.05$) is used.

This study has two sets of objectives, one for Health Canada (HC) analysis and the other for US FDA analysis. These two sets of objectives are considered independently of each other and no multiplicity adjustment between two sets of objectives is performed.

Within the HC analysis primary objectives, since the study HC efficacy analysis will declare success when and only when all four primary objectives pass HC analysis acceptance criteria, no multiplicity adjustment is required [3].

Within the FDA efficacy analysis, a gatekeeping procedure will be applied: the efficacy analysis for two secondary objectives [30-second (abdomen only) post-product application time point] will be performed only when all four primary objectives [10-minute (abdomen and groin) post-product application time point] pass the acceptance criteria. No multiplicity adjustment between primary and secondary objectives is performed. For primary objectives [10-minute (abdomen and groin) post-product application time point], since it will declare success when and only when all four primary objectives pass FDA analysis acceptance criteria, no multiplicity adjustment for the four primary objectives is required [3]. For secondary objectives [30-second (abdomen only) post-product application time point], since it will declare success when and only when all four primary and two secondary objectives pass FDA analysis acceptance criteria, no multiplicity adjustment for the two secondary objectives is required [3].

6.4 Handling of Missing Data and Sensitivity Analysis

Missing $\log_{10}$ CFU/cm^2 determinations at 30 seconds, 10 minutes, or 6 hours, such as due to laboratory error or subject lost to follow up, will be reported as missing and will not be imputed for main analyses (log reduction, ATE and responder rate) as described in Section 6.2. Missing product weight will be also reported as missing and will not be imputed. Details of any missing data and rationale for inclusion/exclusion in the mITT or PP data set will be described in the statistical or study report.

Sensitivity analysis will be performed to evaluate the impact of missing data, if any, for primary and secondary objectives (refer to Section 6.4.1 for details).

- For HC analysis (log reduction), if acceptance criteria are met for primary objectives, sensitivity analysis will be performed for primary objectives based on the mITT population sets. No sensitivity analysis will be performed if acceptance criteria are not met for primary objectives.
- For FDA analysis (ATE), if acceptance criteria are met for both primary and secondary objectives, sensitivity analysis will be performed separately for primary and secondary objectives based on the mITT population sets. If acceptance criteria are met for primary objectives but not for secondary objectives, sensitivity analysis will be only performed for primary objectives based on the mITT population sets and no sensitivity analysis will be performed for secondary objectives. No sensitivity analysis will be performed if acceptance criteria are not met for primary objectives.
- No sensitivity analysis will be performed for exploratory objectives.

6.4.1 Sensitivity Analysis

For $\log_{10}$ CFU/cm^2 determinations, multiple imputation under the assumption that data are missing at random (MAR) will be performed to impute a series of $\log_{10}$ CFU values relative to the baseline $\log_{10}$ CFU values for all missing data points.

- For HC objectives, the multiple imputation will be performed separately for each of the four primary objectives (IP only).
- For FDA objectives, the multiple imputation will be performed separately for each of the four primary and two secondary objectives.

If results based on imputed data meet the acceptance criteria, a tipping-point sensitivity analysis will be performed by shifting the imputed values to assess how severe departures from missing at random (MAR) must be in order to find the tipping point at which the acceptance criteria would not be met.

Multiple imputation and tipping point approaches for either HC objectives or FDA objectives include the following steps:

1. The missing data are filled in 25 times to generate 25 complete data sets using Predictive Mean Matching (PPM) method provided in R package "MICE".
2. Each of the 25 complete data sets are analyzed by using routine analysis method applied for log reduction analysis (HC objectives) or for ATE analysis (FDA objectives).
3. The results from the 25 complete data sets are combined/pooled for the inference and compared to the acceptance criteria (cf. Tables A.5.1 for HC objectives and A.5.2 for FDA objectives).
4. If results based on imputed data meet the acceptance criteria, repeat Step 1 to generate multiple imputed data sets, with a specified shift parameter that shifts the imputed values (shift parameter will be applied to the IP group only).
    - For log reduction, the shift parameter will start from -0.1 to smaller (more stringent) numbers (i.e., -0.1, -0.2, ...).
    - For ATE of IP-AC or NC-IP, the shift parameter will start from 0.1 to larger (more stringent) numbers (i.e., 0.1, 0.2, ...);
5. Repeat Step 2 for the imputed data sets with shift parameter applied.
6. Repeat Step 3 to obtain the estimate and 95% confidence limits to see if acceptance criteria are met.
7. Repeat Steps 4-6 with more stringent shift parameters applied until acceptance criteria are not met.

The tipping point for the shift parameter that reverses the conclusion ("Met Criteria" changes from "Yes" to "No") will be listed (cf. Tables A.5.3 for HC objectives and A.5.4 for FDA objectives).

For responder rate at 6 hours (FDA objectives), subjects with missing $\log_{10}$ CFU/cm^2 determinations at 6 hours will not be excluded from sensitivity analysis. Missing data will be imputed by increasing the assumed number of failures sequentially from 0/M to M/M, where M is the number of missing data points at 6 hours. This sensitivity analysis will be performed for all products (IP, AC and NC) on each anatomical site and will provide information on the possible effect of missing data on study results (cf. Table A.5.5).

6.5 Demographics/Other Descriptive Information

Demographics: Table A.6.1 shows demographics information for subjects in ITT population sets.

Procedure Overview: Any sampling fluid from sampling site that extended to other remaining sites at a certain time point will be listed for each body location (cf. Listing B.8). Any dressing application that was placed on the application site at the 10-minute time point and dressing integrity was compromised any time prior to the 6-hour time point will be listed for each body location (cf. Listing B.9). This will be based on data from ITT population sets.

Core Lab Overview: Any sampling solution that was lost at any time during the procedure will be listed with time points affected (cf. Listing B.10). This will be based on data from ITT population sets.

Product Failures/Lab Accidents/User Errors: Any product failures/lab accidents/user errors will be listed for all study products used (cf. Listing B.11).

7 References

[1] ASTM E1173-15. *Standard Test Method for Evaluation of Preoperative, Precatheterization, or Preinjection Skin Preparations*. ASTM International, West Conshohocken, PA, 2015.

[2] R Core Team. *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing, Vienna, Austria, 2016. URL https://www.R-project.org/.

[3] Frank Bretz. Alex Dmitrienko, Ajit C.Tamhane. *Multiple Testing Problems in Pharmaceutical Statistics*. Chapman and Hall/CRC, 2009.

8 Appendix

A Tables

A.1 Analysis Population Set(s)

Table A.1.1: Overall Subject Disposition

Subject Information	Number of Subjects	Comments
Subjects Screened	n	
Subjects who Passed I/E Criteria	n	
Subjects Enrolled	n	
Subjects Randomized	n	
Subjects Randomized and Treated (ITT)	n	
Subjects who Completed the Study	n	

Table A.1.2: Number of Evaluable Subjects for HC Analysis

Body Location	Population Sets	IP	RS	Overall
Abdomen/Groin	ITT Safety	n	n	n
	mITT CFU Count 30 Seconds	n	n	n
	PP CFU Count 30 Seconds	n	n	n
	mITT CFU Count 10 Minutes	n	n	n
	PP CFU Count 10 Minutes	n	n	n
	mITT CFU Count 6 Hours	n	n	n
	PP CFU Count 6 Hours	n	n	n
	mITT Product Weight	n	n	n
	PP Product Weight	n	n	n

Table A.1.3: Number of Evaluable Subjects for FDA Analysis

Body Location	Population Sets	IP	AC	NC	Overall
Abdomen/Groin	ITT Safety	n	n	n	n
	mITT CFU Count 30 Seconds	n	n	n	n
	PP CFU Count 30 Seconds	n	n	n	n
	mITT CFU Count 10 Minutes	n	n	n	n
	PP CFU Count 10 Minutes	n	n	n	n
	mITT Responder Rate 6 Hours	n	n	n	n
	PP Responder Rate 6 Hours	n	n	n	n
	mITT Product Weight	n	n	n	n
	PP Product Weight	n	n	n	n

A.2 HC Analysis

Table A.2.1: mITT/PP - Summary Statistics for HC Analysis - Log CFU

Body Location	Product	Time Point	Count	Mean	Median	SD	Range (Min-Max)
Abdomen/Groin	IP/RS	Baseline	n	x.xx	x.xx	x.xx	x.xx - x.xx
		30 Seconds	n	x.xx	x.xx	x.xx	x.xx - x.xx
		10 Minutes	n	x.xx	x.xx	x.xx	x.xx - x.xx
		6 Hours	n	x.xx	x.xx	x.xx	x.xx - x.xx

Table A.2.2: mITT/PP - Summary Statistics for HC Analysis - Log Reduction

Body Location	Product	Time Point	Count	Mean	Median	SD	Range (Min-Max)
Abdomen/Groin	IP/RS	30 Seconds	n	x.xx	x.xx	x.xx	x.xx - x.xx
		10 Minutes	n	x.xx	x.xx	x.xx	x.xx - x.xx
		6 Hours	n	x.xx	x.xx	x.xx	x.xx - x.xx

Table A.2.3: mITT/PP - Summary Statistics for HC Analysis - Product Weight

Body Location	Product	Count	Mean	Median	SD	Range (Min-Max)
Abdomen/Groin	IP/RS	n	x.xx	x.xx	x.xx	x.xx - x.xx

Table A.2.4: mITT/PP - Analysis Results for HC Analysis - Log Reduction at 30 Seconds and 6 Hours

Body Location	Product	Time Point	Count	Mean Log Reduction (95% CI)	Met Criteria
Abdomen/Groin	IP/RS	30 Seconds	n	x.xx (x.xx, x.xx)	Yes/No
		6 Hours	n	x.xx (x.xx, x.xx)	Yes/No

Table A.2.5: mITT/PP - Analysis Results for for HC Analysis - Log Reduction at 10 Minutes

Body Location	Product	Time Point	Count	Mean Log Reduction (95% CI)
Abdomen/Groin	IP/RS	10 Minutes	n	x.xx (x.xx, x.xx)

Table A.2.6: mITT/PP - Analysis Results for for HC Analysis - Difference in Log Reduction

Body Location	Contrast	Time Point	Difference in Log Reduction (95% CI)	Conclusion
Abdomen/Groin	IP-RS	30 Seconds	x.xx (x.xx, x.xx)	Sign. Diff/No Sign. Diff
Abdomen/Groin	IP-RS	10 Minutes	x.xx (x.xx, x.xx)	Sign. Diff/No Sign. Diff
Abdomen/Groin	IP-RS	6 Hours	x.xx (x.xx, x.xx)	Sign. Diff/No Sign. Diff

A.3 FDA Analysis

Table A.3.1: mITT/PP - Summary Statistics for FDA Analysis - Log CFU

Body Location	Product	Time Point	Count	Mean	Median	SD	Range (Min-Max)
Abdomen/Groin	IP/AC/NC	Baseline	n	x.xx	x.xx	x.xx	x.xx - x.xx
		30 Seconds	n	x.xx	x.xx	x.xx	x.xx - x.xx
		10 Minutes	n	x.xx	x.xx	x.xx	x.xx - x.xx
		6 Hours	n	x.xx	x.xx	x.xx	x.xx - x.xx

Table A.3.2: mITT/PP - Summary Statistics for FDA Analysis - Log Reduction

Body Location	Product	Time Point	Count	Mean	Median	SD	Range (Min-Max)
Abdomen/Groin	IP/AC/NC	30 Seconds	n	x.xx	x.xx	x.xx	x.xx - x.xx
		10 Minutes	n	x.xx	x.xx	x.xx	x.xx - x.xx
		6 Hours	n	x.xx	x.xx	x.xx	x.xx - x.xx

Table A.3.3: mITT/PP - Summary Statistics for FDA Analysis - Responder Rate at 6 Hours

Body Location	Product	Responder Rate
Abdomen/Groin	IP/AC/NC	n/N (%)

Note: n is number of responders and N is total number of evaluable subjects.

Table A.3.4: mITT/PP - Summary Statistics for FDA Analysis - Product Weight

Body Location	Product	Count	Mean	Median	SD	Range (Min-Max)
Abdomen/Groin	IP/AC/NC	n	x.xx	x.xx	x.xx	x.xx - x.xx

Table A.3.5: mITT/PP - Analysis Results for FDA Analysis - ATE at 10 Minutes

Body Location	Contrast	Time Point	ATE (95% CI)	Met Criteria
Abdomen/Groin	IP-AC	10 Minutes	x.xx (x.xx, x.xx)	Yes/No
Abdomen/Groin	NC-IP	10 Minutes	x.xx (x.xx, x.xx)	Yes/No

Table A.3.6: mITT/PP - Analysis Results for for FDA Analysis - ATE at 30 Seconds

Body Location	Contrast	Time Point	ATE (95% CI)	Met Criteria
Abdomen	IP-AC	30 Seconds	x.xx (x.xx, x.xx)	Yes/No
Abdomen	NC-IP	30 Seconds	x.xx (x.xx, x.xx)	Yes/No

A.4 Safety Analysis

Table A.4.1: ITT - Summary Statistics for Irritation Scores for Abdomen/Groin at Baseline/30 Seconds/10 Minutes/6 Hours

Characteristic	IP	RS	AC	NC	Overall
Erythema					
0-No reaction	n (%)	n (%)	n (%)	n (%)	n (%)
1-Mild and/or transient redness	n (%)	n (%)	n (%)	n (%)	n (%)
2-Moderate redness	n (%)	n (%)	n (%)	n (%)	n (%)
3-Severe redness	n (%)	n (%)	n (%)	n (%)	n (%)
Edema					
0-No reaction	n (%)	n (%)	n (%)	n (%)	n (%)
1-Mild and/or transient swelling	n (%)	n (%)	n (%)	n (%)	n (%)
2-Moderate swelling	n (%)	n (%)	n (%)	n (%)	n (%)
3-Severe swelling	n (%)	n (%)	n (%)	n (%)	n (%)
Rash					
0-No reaction	n (%)	n (%)	n (%)	n (%)	n (%)
1-Mild and/or transient rash	n (%)	n (%)	n (%)	n (%)	n (%)
2-Moderate rash	n (%)	n (%)	n (%)	n (%)	n (%)
3-Severe rash	n (%)	n (%)	n (%)	n (%)	n (%)
Dryness					
0-No reaction	n (%)	n (%)	n (%)	n (%)	n (%)
1-Mild and/or transient dryness	n (%)	n (%)	n (%)	n (%)	n (%)
2-Moderate dryness	n (%)	n (%)	n (%)	n (%)	n (%)
3-Severe dryness	n (%)	n (%)	n (%)	n (%)	n (%)

Table A.4.2: ITT - Adverse Events Summary

Characteristic	IP	RS	AC	NC	Overall
Adverse Events					
No	n (%)	n (%)	n (%)	n (%)	n (%)
Yes	n (%)	n (%)	n (%)	n (%)	n (%)

Note: Overall column is calculated based on overall unique subjects included in ITT.

Table A.4.3: ITT - Safety Analysis - Overall Comparisons for Erythema/Edema/Rash/Dryness

Body Location	Time Point	p-value	Conclusion
Abdomen/Groin	30 Seconds	0.xxx	Sign. Diff/No Sign. Diff
Abdomen/Groin	10 Minutes	0.xxx	Sign. Diff/No Sign. Diff
Abdomen/Groin	6 Hours	0.xxx	Sign. Diff/No Sign. Diff

Note: If analysis is not applicable, p-value will be shown as "N/A".

Table A.4.4: ITT - Safety Analysis - Subgroup Comparisons for Irritation Scores

Body Location	Characteristic	Time Point	Comparison	Odds Ratio (95% CI)	Conclusion
Abdomen/Groin				x.xx (x.xx, x.xx)	Sign. Diff/No Sign. Diff

A.5 Sensitivity Analysis

Table A.5.1: Pooled Analysis Results Based on Imputated Datasets for HC Objectives - Log Reduction

Body Location	Product	Time Point	Log Reduction (95% CI)	Met Criteria
Abdomen/Groin	IP	30 Seconds	x.xx (x.xx, x.xx)	Yes/No
	IP	6 Hours	x.xx (x.xx, x.xx)	Yes/No

Table A.5.2: Pooled Analysis Results Based on Imputated Datasets for FDA Objectives - ATE

Body Location	Time Point	Contrast	ATE (95% CI)	Met Criteria
Abdomen/Groin	10 Minutes	IP-AC	x.xx (x.xx, x.xx)	Yes/No
	10 Minutes	NC-IP	x.xx (x.xx, x.xx)	Yes/No
Abdomen	30 Seconds	IP-AC	x.xx (x.xx, x.xx)	Yes/No
	30 Seconds	NC-IP	x.xx (x.xx, x.xx)	Yes/No

Table A.5.3: Tipping Point Analysis for HC Objectives - Log Reduction

Body Location	Product	Time Point	Shift Parameter	Log Reduction (95% CI)	Met Criteria
Abdomen/Groin	IP	30 Seconds	-x.x	x.xx (x.xx, x.xx)	Yes
	IP	30 Seconds	-x.x	x.xx (x.xx, x.xx)	Yes
	IP	30 Seconds	-x.x	x.xx (x.xx, x.xx)	No
	IP	6 Hours	-x.x	x.xx (x.xx, x.xx)	Yes
	IP	6 Hours	-x.x	x.xx (x.xx, x.xx)	Yes
	IP	6 Hours	-x.x	x.xx (x.xx, x.xx)	No

Table A.5.4: Tipping Point Analysis for FDA Objectives - ATE

Body Location	Time Point	Contrast	Shift Parameter	ATE (95% CI)	Met Criteria
Abdomen/Groin	10 Minutes	IP-AC	x.x	x.xx (x.xx, x.xx)	Yes
	10 Minutes	IP-AC	x.x	x.xx (x.xx, x.xx)	Yes
	10 Minutes	IP-AC	x.x	x.xx (x.xx, x.xx)	No
	10 Minutes	NC-IP	x.x	x.xx (x.xx, x.xx)	Yes
	10 Minutes	NC-IP	x.x	x.xx (x.xx, x.xx)	Yes
	10 Minutes	NC-IP	x.x	x.xx (x.xx, x.xx)	No
Abdomen	30 Seconds	IP-AC	x.x	x.xx (x.xx, x.xx)	Yes
	30 Seconds	IP-AC	x.x	x.xx (x.xx, x.xx)	Yes
	30 Seconds	IP-AC	x.x	x.xx (x.xx, x.xx)	No
	30 Seconds	NC-IP	x.x	x.xx (x.xx, x.xx)	Yes
	30 Seconds	NC-IP	x.x	x.xx (x.xx, x.xx)	Yes
	30 Seconds	NC-IP	x.x	x.xx (x.xx, x.xx)	No

Table A.5.5: Sensitivity Analysis for FDA Objectives - Responder Rate at 6 Hours

Body Location	Product	Subjects Imputed to Non-responders	Responder Rate
Abdomen/Groin	IP/AC/NC	+0	n/N (%)
		+1	n/N (%)
		+2	n/N (%)
		...	n/N (%)
		+M	n/N (%)

Note: Subjects imputated to non-responders are added to the denominator (N) for the responder rate.

A.6 Demographics

Table A.6.1: ITT - Demographics

Characteristic	IP	RS	AC	NC	Overall
Age at Time of Informed Consent (Years)					
Mean	x.x	x.x	x.x	x.x	x.x
Median	x.x	x.x	x.x	x.x	x.x
SD	x.x	x.x	x.x	x.x	x.x
Min, Max	x.x	x.x	x.x	x.x	x.x
Total Count	n	n	n	n	n
Gender					
Male	n (%)	n (%)	n (%)	n (%)	n (%)
Female	n (%)	n (%)	n (%)	n (%)	n (%)
Ethnicity					
Hispanic or Latino	n (%)	n (%)	n (%)	n (%)	n (%)
Not Hispanic or Latino	n (%)	n (%)	n (%)	n (%)	n (%)
Race					
American Indian or Alaska Native	n (%)	n (%)	n (%)	n (%)	n (%)
Asian	n (%)	n (%)	n (%)	n (%)	n (%)
Black or African American	n (%)	n (%)	n (%)	n (%)	n (%)
Native Hawaiian or Other Pacific Islander	n (%)	n (%)	n (%)	n (%)	n (%)
White	n (%)	n (%)	n (%)	n (%)	n (%)
Other	n (%)	n (%)	n (%)	n (%)	n (%)

Note: Overall column is calculated based on overall unique subjects included in ITT.

B Listings

Table B.1: Protocol Deviations

RandID	Nature of Deviation	Additional Details
Rxxxx		
Rxxxx		
Rxxxx		
Rxxxx		

Table B.2: Subjects with Excluded Data for HC Analysis

RandID	Body Location	Product	Time Point	Included in mITT CFU Count	Included in PP CFU Count
Rxxxx				Yes/No	Yes/No
Rxxxx				Yes/No	Yes/No
Rxxxx				Yes/No	Yes/No
Rxxxx				Yes/No	Yes/No

Table B.3: Subjects with Excluded Data for FDA Analysis

RandID	Body Location	Product	Time Point	Included in mITT CFU Count	Included in PP CFU Count	Included in mITT Responder Rate	Included in PP Responder Rate	Included in mITT Product Weight	Included in PP Product Weight
Rxxxx				Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
Rxxxx				Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
Rxxxx				Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No
Rxxxx				Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	Yes/No

Table B.4: Subjects who Did Not Complete the Study

RandID	Subject's Status	Comments
Rxxxx	Screen Failure	
Rxxxx		
Rxxxx		
Rxxxx		

Table B.5: Subjects Not Passing Treatment-day Baseline Criteria

RandID	Body Location	Product	Time Point	Result (log_{10})
Rxxxx				x.xx
Rxxxx				x.xx
Rxxxx				x.xx
Rxxxx				x.xx

Table B.6: Adverse Events

RandID	AE Term	Start Date	End Date	AE Outcome	Severity	Relationship to Device	Relationship to Procedure	SAE	Additional Details	Included in ITT
Rxxxx								Yes/No		Yes/No
Rxxxx								Yes/No		Yes/No
Rxxxx								Yes/No		Yes/No
Rxxxx								Yes/No		Yes/No

Table B.7: Serious Adverse Events

RandID	AE Term	Start Date	End Date	Serious Criteria	Hospital Admission Date	Hospital Discharge Date	Was SAE Unexpected/Unanticipated	Included in ITT
Rxxxx							Yes/No	Yes/No
Rxxxx							Yes/No	Yes/No
Rxxxx							Yes/No	Yes/No
Rxxxx							Yes/No	Yes/No

Table B.8: Procedure Overview - Sampling Fluid

RandID	Body Location	Product	Did Sampling Fluid from Sampling Site Extend to Other Remaining Sites at Any Time Point	Time Points Affected
Rxxxx			Yes	30 Seconds
Rxxxx			Yes	
Rxxxx			Yes	
Rxxxx			Yes	

Table B.9: Procedure Overview - Dressing Application

RandID	Body Location	Product	Was Dressing Application Placed on the Application Site at the 10 Minute Time Point	Was Dressing Integrity Compromised at Any Time Prior to the 6 Hour Time Point	Details
Rxxxx			Yes	Yes	Subject Confirmed Dressing was Adjusted and/or Touched
Rxxxx			Yes	Yes	
Rxxxx			Yes	Yes	
Rxxxx			Yes	Yes	

Table B.10: Core Lab Procedure Overview - Sample Solution

RandID	Body Location	Product	Was Any Sampling Solution Lost at Any Time During the Procedure	Time Point Affected	Volume Remaining (mL)
Rxxxx			Yes	Baseline	
Rxxxx			Yes		
Rxxxx			Yes		
Rxxxx			Yes		

Table B.11: Product Failures/Lab Accidents/User Errors

RandID	Are There Any Product Failures/Lab Accidents/User Errors to Report	Date of Incident	Product Affected	Time of Incident	Incident Code	Details	Was Product Used on Study Subject	Was an AE Associated with the Incident
Rxxxx	Yes			During Product Exposure	Product Handling Issue			
Rxxxx	Yes							
Rxxxx	Yes							
Rxxxx	Yes							

C Figures

C.1 HC Analysis

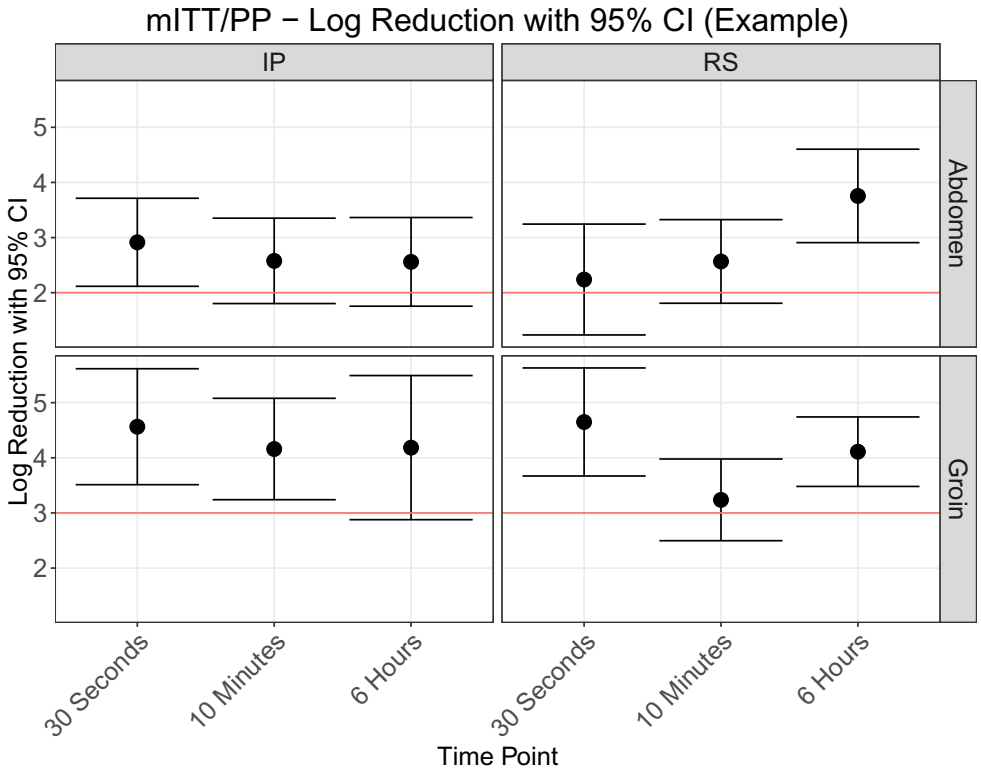

Figure C.1.1: mITT/PP - Log Reduction with 95% CI (Example Data Only)

C.2 FDA Analysis

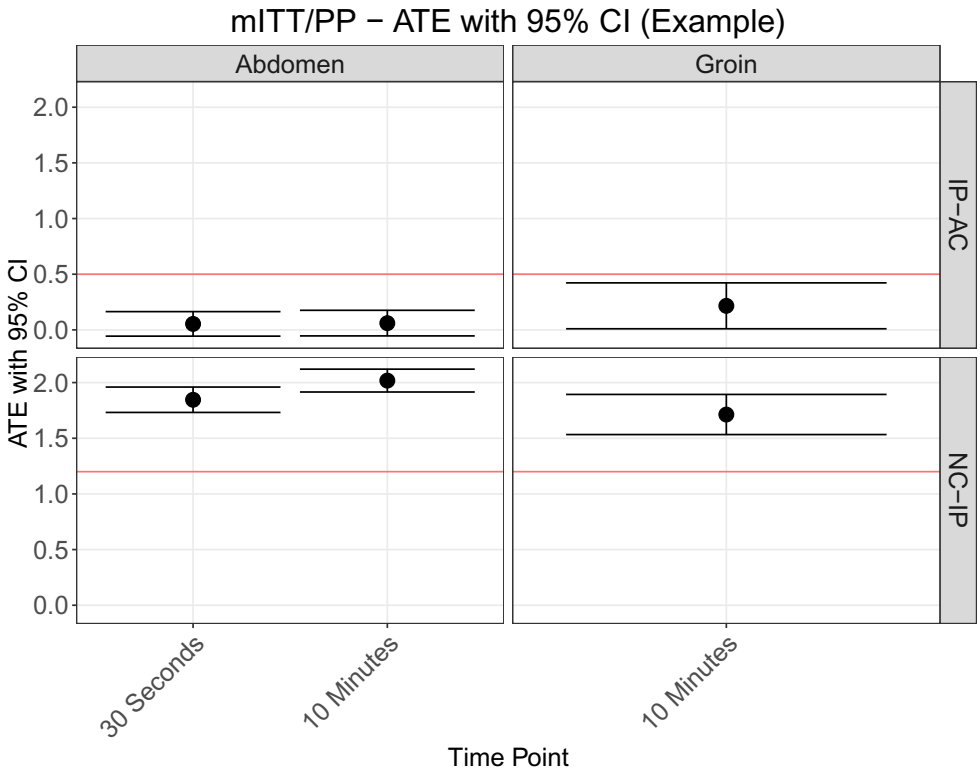

Figure C.2.1: mITT/PP - ATE with 95% CI (Example Data Only)