STATISTICAL ANALYSIS PLAN

Brickell Biotech, Inc.

BBI-4000-CL-203

Protocol Title:	A Multicenter, Randomized, Double-Blinded, Vehicle-Controlled Study to Evaluate the Safety and the Efficacy of 5%, 10% and 15% Topically Applied BBI-4000 (Sofpironium Bromide) Gel in Subjects with Axillary Hyperhidrosis
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1 STATISTICAL ANALYSIS PLAN APPROVAL

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3 LIST OF ABBREVIATIONS

Table 1 List of Abbreviations

Abbreviation	Definition
AE	adverse event
AIC	Akaike information criterion
ANCOVA	analysis of covariance
ATC	Anatomical Therapeutic Chemical
BBI	Brickell Biotech, Inc.
BMI	body mass index
CRF	case report form
CS (CSH)	compound symmetry (heterogenous compound symmetry)
CSR	clinical study report
DLQI	Dermatology Life Quality Index
ECG	electrocardiogram
eCRF	electronic case report form
ET	Early Termination
FOCBP	female of childbearing potential
GLIMMIX	generalized linear mixed model
GSP	gravimetric sweat production
HDSS	Hyperhidrosis Disease Severity Scale
HDSM-Ax	Hyperhidrosis Disease Severity Measure-Axillary
ICH	International Conference on Harmonization
mITT	Modified Intent-to-Treat
LOCF	last observation carried forward
LS	least-square
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	mixed model for repeated measures
PP	Per-Protocol
PT	preferred term
SAE	serious adverse event
SAP	statistical analysis plan
SI	Système International
TEAE	treatment-emergent adverse event
TOEP (TOEPH)	Toeplitz (heterogenous Toeplitz)

Abbreviation	Definition
UPT	urine pregnancy test
WHO	World Health Organization

4 INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to provide comprehensive and detailed descriptions of the methods and presentation of data analyses proposed for Brickell Biotech, Inc. Protocol BBI-4000-CL-203 (A Multicenter, Randomized, Double-Blinded, Vehicle-Controlled Study to Evaluate the Safety and the Efficacy of 5%, 10% and 15% Topically Applied BBI-4000 (Sofpironium Bromide) Gel in Subjects with Axillary Hyperhidrosis). Descriptions of planned analyses are provided in order to avoid post hoc decisions that may affect the interpretation of the statistical analysis. The statistical methods applied in the design and planned analyses of this study are consistent with the International Conference on Harmonisation (ICH) guideline *Statistical Principals for Clinical Trials* (1998).

This SAP will be finalized prior to data analysis and before treatment unblinding and database lock to provide full details, including templates for tables, listings, and figures, to be presented in the clinical study report (CSR). Any changes between the statistical methods provided in the clinical study protocol and this SAP will be explained herein; any changes or deviations from this SAP relative to the final analysis will be fully documented in the CSR. Minor changes or deviations from the templates for tables, figures, and listings need not be documented in the CSR.

5 STUDY OBJECTIVES

5.1 Primary Study Objectives

The primary objectives of this study are to evaluate:

1. The effect of BBI-4000 5%, 10% and 15% gel on Hyperhidrosis Disease Severity Measure (HDSM-Ax) when applied topically in subjects with axillary hyperhidrosis

2. The safety and local tolerability of BBI-4000 5%, 10% and 15% gel when applied topically in subjects with axillary hyperhidrosis.

5.2 Secondary Study Objective

The secondary objective of this study is to evaluate:

The effect of BBI-4000 5%, 10% and 15% gel on hyperhidrosis disease severity as it relates to gravimetrically measured sweat production (GSP), patient reported Hyperhidrosis Disease Severity Score (HDSS) and Dermatology Quality of Life Index (DLQI) self-assessment.

6 INVESTIGATIONAL PLAN

6.1 Overall Study Design

This is a Phase 2 confirmatory, multicenter, randomized, double-blind, vehicle-controlled, parallel-group study comparing a new formulation of BBI-4000 5%, 10% and 15% gel with vehicle in subjects with axillary hyperhidrosis. A maximum of 220 subjects, at approximately 25 clinical sites, will be enrolled to obtain approximately 200 subjects that have completed dosing and critical assessments. Male or female subjects $\geq$ 18 years of age in good general health and with a diagnosis of primary axillary hyperhidrosis in the opinion of the Investigator are eligible for study admission. Subjects will be randomized to receive BBI-4000 5%, or 10%, or 15% gel, or vehicle gel (vehicle) in a balanced ratio of 1:1:1:1. Subjects will apply the investigational product (BBI-4000 5% or 10% or 15% gel or vehicle gel); once daily at bedtime, to both axilla for 42 consecutive days. BBI-4000 vehicle (vehicle) gel will be identical in appearance and constituents to BBI-4000 (sofpironium bromide) Gel but will not contain BBI-4000. The vehicle formulation is provided in the same plastic metered pump containers with the same applicators to provide matching kits. The vehicle pump container contains 45 mL vehicle product. Each vehicle pump container is sufficient for 21 days of dosing, as dispensed per protocol instructions. One pump actuation delivers ~ 0.67 mL of the vehicle formulation. The estimated maximum drug exposure for the subjects enrolled in this Phase 2 study will be approximately 2.5 mg/kg/day (i.e., 1.3 mL of 15% BBI-4000 gel/day in a 70-kg adult).

Gravimetric assessments and patient-reported outcomes HDSM-Ax, HDSS and DLQI will be recorded during the study at predefined time points. Vital signs, local tolerability assessments (including burning, itching, dryness, scaling and erythema assessed using standardized scales), and adverse events will be collected at each visit. A urine pregnancy test (UPT) for females of child-bearing potential and blood and urine samples will be collected and analyzed at the Screening Visit and at the End of Treatment Visit for routine hematology, chemistry, and urinalysis parameters.

A total of 14 scheduled visits will take place over approximately 12 to 16 weeks, depending on when the Baseline Visit (treatment) is scheduled after the four (4) screening period visits: initial screening, GSP1 and GSP2, and Rescreening GSP3. See Table 2 for an overview of study events and timing.

6.2 Schedule of Assessments

Table 2 Time and Events Table

Visit	1	2	3	4	5	6	7	8	9	10	11	12	13	14
PROCEDURE	Screening			Rescreening	Baseline								End of Treatment	Follow-up
Gravimetric Timepoint		GSP 1	GSP 2	GSP 3							GSP 4	GSP 5	GSP 6	
Day (allowable window)	*Up to 35 days prior to GSP1*	*Up to 14 days from GSP1 to GSP3*			Day 1 (within 7 days of Rescreening)	Day 8 (± 2)	Day 15 (± 2)	Day 22 (± 2)	Day 29 (± 2)	Day 36 (± 2)	Day 41 (±2)	Day 42 (± 2)	Day 43 (± 2)	Day 57 (± 3)
Informed Consent	X													
Medical History, demographics	X			X										
Physical Exam				X										
Vital Signs (blood pressure, heart rate, respiratory rate and temperature)				X	X	X	X	X	X	X			X	X
I/E Criteria	X			X										
Gravimetric Assessments [a, b]	X	X	X	X		X	X	X	X	X	X	X	X	X
HDSM-Ax, HDSS	X			X		X	X	X	X	X	X	X	X	X
DLQI				X									X	
Local Tolerability Assessments [c]					X	X	X	X	X	X			X	X
Adverse Events [c]		X	X	X	X	X	X	X	X	X	X	X	X	X
Randomization [d]				X										
Investigational Product [e] (IP) Dispensed / Returned					X[f]			X[f]					X	
IP Weight [g]					X			X					X	
Compliance Evaluation						X	X	X	X	X	X	X	X	
Safety Labs (hematology, chemistry, and urinalysis)	X												X	
UPT (females of childbearing potential only)[h]	X				X				X				X	
Concomitant Medication Review	X	X	X	X	X	X	X	X	X	X	X	X	X	X

a) Gravimetric assessments for all visits will be conducted from **7:00am-11:00am**.
b) One 5-minute gravimetric assessment will be conducted for each axilla.
c) Investigator assessments to be performed after the Subject assessments.
d) Randomization will take place only after the subject is qualified at the rescreening visit.
e) Order the investigational product only after the subject is qualified at the rescreening visit and randomized.
f) Pump 1 of 2 to be dispensed at Baseline (Visit 5). At Day 22 (Visit 8) Pump 2 of 2 to be primed and dispensed to patient. Written instructions for nightly dosing will be given to the subject. Subjects will apply their first dose of gel prior to bedtime the night of their Baseline visit. Instruct the subjects to return Pump 1 of 2 at Day 22 Visit 8 and Pump 2 of 2 at Day 43 (Visit 13, End of Treatment).
g) Pump container 1 of 2 will be weighed after priming at Baseline prior to dispensing to the subject and upon return at Day 22 (Visit 8). Pump container 2 of 2 will be weighed after priming at Day 22 (Visit 8) prior to dispensing to the subject and upon return at Day 43 (Visit 13, End of Treatment).
h) FOCBP for this study includes any female 18 years of age or older who has not undergone successful surgical sterilization (hysterectomy, bilateral tubal ligation [at least six months prior to baseline] or bilateral oophorectomy) or is not postmenopausal (defined as amenorrhea greater than 12 consecutive months in women 55 years or older).

6.3 Treatments

6.3.1 Treatments Administered

BBI-4000 (sofpironium bromide) Gel is a clear to slightly translucent colorless gel and is packaged in a white colored, metered pump container. Two pump containers are packaged in a carton with 4 applicators. The total gel volume in each container is 45 mL (~ 40 g). The gross weight of each full container at baseline is approximately 74 to 80 grams. BBI-4000 (sofpironium bromide) Gel is an anhydrous gel formulation containing the drug substance in a gel base comprising hydroxylpropyl cellulose NF, hexylene glycol NF, isopropyl myristate NF, citric acid anhydrous USP, and alcohol dehydrated USP. Each pump container is sufficient for 21 days of dosing, per protocol instructions. One pump actuation delivers ~ 0.67 mL (~ 0.56 g) of the gel formulation. BBI-4000 vehicle (vehicle) gel will be identical in appearance and constituents to BBI-4000 (sofpironium bromide) Gel, but will not contain the active ingredient, BBI-4000. Two vehicle pump containers are packaged in a carton with 4 applicators to match the active drug product kits. Subjects will apply the investigational product (BBI-4000 5% or 10% or 15% gel or vehicle gel); once daily at bedtime, to both axilla for 42 consecutive days. One full pump actuation delivers enough gel to apply to one axillae.

6.3.2 Method of Assigning Subjects to Treatment Groups

Subjects will be randomized to receive BBI-4000 5%, 10%, or 15% gel, or vehicle gel (vehicle) in a balanced ratio of 1:1:1:1. When subjects qualify for the study (determined by the investigator at the Rescreening Visit), they will be randomized to investigational product groups and will receive a randomization number. The kit carton and treatment plastic pumps have the randomization numbers displayed in their label.

The next eligible subject will be assigned the lowest available randomization number from the treatment kits available at the depot. In this manner, eligible subjects will be randomized to the investigational product sequence in accordance with the randomization schedule. The investigator will document the randomization/kit numbers in the source and on the case report form (CRF). The tear-off portion of the carton label from the outer carton (with blind-break panel) will be removed along the label perforation and placed into the study subject source file. In the event a subject is randomized at the Rescreening Visit but is not dispensed study medication (e.g. deemed ineligible at Baseline due to newly discovered ineligibility, withdraws consent, etc.) the randomization number will not be reassigned; the subject will be considered an early termination and the kit shall be placed in quarantine in the site's inventory.

6.4 Efficacy and Safety Variables

6.4.1 Efficacy Variables

The following assessment measures will be conducted to evaluate the efficacy of BBI-4000:

- HDSM-Ax as measured by the subject

- GSP by the investigator
- HDSS as measured by the subject
- DLQI as measured by the subject

6.4.1.1 Primary Efficacy Variables

The primary efficacy endpoint is improvement on the HDSM-Ax, defined as:

1. The proportion of subjects achieving at least a 1-point improvement in HDSM-Ax from baseline to end of therapy.
2. Change of HDSM-Ax from baseline to end of therapy as a continuous measure

6.4.1.2 Secondary Efficacy Variables

Secondary efficacy endpoints include the following:

1. The proportion of subjects achieving at least a 2-point improvement in HDSM-Ax from baseline to end of therapy.
2. The proportion of subjects achieving at least a 50% reduction in gravimetrically measured sweat production (both axilla combined) from baseline to end of therapy.
3. The absolute change from baseline in gravimetrically measured sweat production to end of therapy.
4. The percent change from baseline in gravimetrically measured sweat production to end of therapy.
5. The ranked change from baseline in gravimetrically measured sweat production to end of therapy.
6. The proportion of subjects achieving at least a 1-point improvement in the HDSM-Ax score and at least 50% reduction in gravimetrically measured sweat production from baseline to end of therapy.
7. The proportion of subjects achieving at least a 2-point improvement in the HDSM-Ax total score and at least 50% reduction in gravimetrically measured sweat production from baseline to end of therapy.
8. The proportion of subjects achieving at least a 2-point improvement in HDSS from baseline to end of therapy.

9. The proportion of subjects achieving at least a 1-point improvement in HDSS from baseline to end of therapy.

6.4.1.3 Other Efficacy Variables

Other efficacy endpoints are:

1. The proportion of subjects achieving at least a 1-point improvement in the HDSM-Ax score from baseline to Days 8, 15, 22, 29, 36, 41, 42, 43, and 57.

2. Change in HDSM-Ax from baseline to Days 8, 15, 22, 29, 36, 41, 42, 43, and 57 as a continuous measure

3. The proportion of subjects achieving at least a 2-point improvement in the HDSM-Ax score from baseline to Days 8, 15, 22, 29, 36, 41, 42, 43, and 57.

4. The proportion of subjects achieving at least a 50% reduction in gravimetrically measured sweat production (both axilla combined) from baseline to Days 8, 15, 22, 29, 36, 41, 42, 43, and 57.

5. Percent change from baseline in gravimetrically measured sweat production at Days 8, 15, 22, 29, 36, 41, 42, 43, and 57.

6. Absolute change from baseline in gravimetrically measured sweat production at Days 8, 15, 22, 29, 36, 41, 42, 43, and 57.

7. Ranked change from baseline in gravimetrically measured sweat production at Days 8, 15, 22, 29, 36, 41, 42, 43, and 57.

8. The proportion of subjects achieving at least a 1-point improvement in the HDSM-Ax score and at least 50% reduction in gravimetrically measured sweat production from baseline to Days 8, 15, 22, 29, 36, 41, 42, 43, and 57.

9. The proportion of subjects achieving at least a 2-point improvement in the HDSM-Ax total score and at least 50% reduction in gravimetrically measured sweat production from baseline to Days 8, 15, 22, 29, 36, 41, 42, 43, and 57.

10. The proportion of subjects achieving at least a 2-point improvement in HDSS from baseline to Days 8, 15, 22, 29, 36, 41, 42, 43, and 57.

11. The proportion of subjects achieving at least a 1-point improvement in the HDSS on Days 8, 15, 22, 29, 36, 41, 42, 43, and 57.

12. Change in the modified DLQI from baseline to Day 43 (end of therapy).

6.4.2 Description of Safety Variables

The following safety assessment measures will be conducted:

- Adverse events
- Local tolerability assessments including burning, itching, dryness, scaling and erythema
- Vital signs (blood pressure, pulse rate, respiratory rate, and temperature)
- Laboratory tests (hematology, chemistry, and urinalysis) and pregnancy testing in females of child bearing potential.

6.4.2.1 Adverse Events

An AE can be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not considered related to the medicinal (investigational) product. This definition includes the worsening of a pre-existing condition, the development of investigational product dependency, and suspected investigational product-drug interactions.

6.4.2.2 Local Tolerability Assessments

Local tolerability assessments will be evaluated through assessment of selected local signs and symptoms at the drug-application site. Burning, itching, dryness, scaling and erythema will be assessed using standardized 5-point scales (0-Absent to 4-Severe). These assessments are to be performed for both axillae individually. Subject assessments (burning and itching) will be made prior to the Investigator assessments (dryness, scaling and erythema).

Subject Local Tolerability Assessments: Burning and itching for each axilla will be reviewed with the subject and assessed for the previous 24 hours using the standardized scales.

Investigator Local Tolerability Assessments: Dryness, scaling and erythema for each axilla will be assessed by the investigator using the standardized scales.

Local tolerability signs and symptoms that result in the subject's requiring a concomitant therapy, interruption of treatment, or discontinuation from the study, will be reported as an AE.

6.4.2.3 Vital Signs

Subjects should be seated for at least 2 minutes prior to measurements. Pulse rate (bpm) will be counted over 60 seconds. Blood pressure (mmHg) will be measured with a sphygmomanometer.

Vital sign measurements will include systolic and diastolic blood pressure, pulse rate, respiratory rate and temperature.

6.4.2.4 Laboratory Parameters

Hematology, clinical chemistry, urinalysis and additional parameters to be tested are listed in Table 3:

Table 3 Laboratory Tests

Hematology		
Platelet Count	*RBC Indices*:	*Automated WBC Differential:*
RBC Count	MCV	Neutrophils
WBC Count (absolute)	MCH	Lymphocytes
Reticulocyte Count	MCHC	Monocytes
Hemoglobin		Eosinophils
Hematocrit		Basophils
Clinical Chemistry		
BUN	Chloride	Alkaline phosphatase
Creatinine	AST (SGOT)	Total and direct bilirubin
Sodium	ALT (SGPT)	
Potassium	GGT	
Routine Urinalysis		
Specific gravity		
pH, glucose, protein, blood and ketones by dipstick		
Microscopic examination (if blood or protein is abnormal)		
Other screening tests		
Urine Pregnancy Test (females of childbearing potential* only, using UPT tests provided by the Sponsor.)		
* Females of childbearing potential for this study includes any female 18 years of age or older who has not undergone successful surgical sterilization (hysterectomy, bilateral tubal ligation at least six months prior to baseline or bilateral oophorectomy) or is not postmenopausal (defined as amenorrhea greater than 12 consecutive months in women 55 years or older).		

6.5 Data Quality Assurance

Report summaries will be generated using validated Base SAS® software, version 9.4 or higher, on a PC or server-based platform. Additional validated software may be used to generate analyses, as needed.

All SAS programs that create outputs or supporting analysis datasets will be validated by a second statistical programmer or biostatistician. At a minimum, validation of programs will consist of a review of the program log, review of output or dataset format and structure, and independent confirmatory programming to verify output results or dataset content. Additionally, all outputs will undergo a review by a senior level team member before finalization.

The content of the source data will be reviewed on an ongoing basis by project statistical programmers and statisticians. Data will be checked for missing values, invalid records, and extreme outliers through defensive programming applications, analysis-based edit checks, and

other programmatic testing procedures. All findings will be forwarded to the project data manager for appropriate action and resolution.

7 STATISTICAL METHODS

7.1 General Methodology

Data will be analyzed by Agility Clinical biostatistics personnel. Statistical analyses will be reported with tables, figures, and listings, presented in rich text format, and using recommended ICH numbering. Output specifications for all tables, figures, and listings will be in conformance with guidelines specified by the ICH in Appendix 7 of the *Electronic Common Technical Document Specification* (Apr 2003).

7.1.1 Reporting Conventions

Tables and figures will be summarized by treatment group. Tables summarizing demographics and other baseline characteristics will also include a column for all subjects combined. In general, all data collected and any derived data will be presented in subject data listings, for all enrolled subjects. Listings will be ordered by site, subject number, treatment group, and assessment or event date. The treatment group presented in listings will be based on the planned assignment, unless otherwise noted.

In general, continuous variables will be summarized to indicate the population sample size (N), number of subjects with available data (n), mean, SD, median, minimum, and maximum values. Categorical variables will be summarized by the population size (N), number of subjects with available data (n), number of subjects in each category, and the percentage of subjects in each category. Unless otherwise noted, the denominator to determine the percentage of subjects in each category will be based on the number of subjects with available data. Select ordinal data may be summarized using both descriptive statistics and counts and percentages of subjects in each category, as appropriate.

Non-zero percentages will be rounded to one decimal place. Rounding conventions for presentation of summary statistics will be based on the precision of the variable of summarization, as it is collected in its rawest form (i.e., on the electronic case report form [eCRF] or as provided within an external file) and are outlined as follows:

- The mean and median will be rounded to one more decimal place than the precision of the variable of summarization;
- Measures of variability (e.g., SD, SE) will be rounded to two more decimal places than the precision of the variable of summarization; and
- Minimum and maximum values will be presented using the same precision as the variable of summarization.

Other statistics (e.g., CIs) will be presented using the same general rules outlined above, or assessed for the most appropriate presentation based on the underlying data.

Statistical significance testing will be one-sided as described in Section 7.4.4.1, and performed using α=0.10. P-values will be reported for all statistical tests, rounded to four decimal places. P-values less than 0.0001 will be displayed as "<0.0001"; p-values greater than 0.9999 will be displayed as ">0.9999". Tests of interaction terms, if applicable, will be two-sided and performed using α=0.10.

7.1.2 Standard Calculations

Where appropriate, the calculated study day of each assessment or event will be presented with the assessment or event date on subject data listings, where study day will be determined as:

- The assessment/event date minus the date of first dose, if the assessment/event date is prior to the date of first dose; and

- The assessment/event date minus the date of first dose, plus one, if the assessment/event date is on or after the date of first dose.

Other variables requiring calculations will be derived using the following formulas:

- **Days:** A duration between two dates expressed in days will be calculated using the following conventions:

    - Later date – earlier date + 1, if the earlier date is on or after the date of first dose of study drug; or

    - Later date – earlier date, if the earlier date is prior to the date of first dose of study drug.

- **Change from Baseline:** Change from baseline will be calculated as the post-baseline value minus the baseline value;

- **Percentage Change from Baseline:** Percentage change from baseline will be calculated as the change from baseline divided by the baseline value, multiplied by 100.

- **Rank Transformation:** All raw data will be ranked together within time point without regard to treatment group, from smallest value to highest value. The smallest observation will be assigned the rank of 1, the second smallest the rank of 2, and so on. Average ranks will be used for tied observations.

Unless otherwise noted, values reported as greater than or less than some quantifiable limit (e.g., "< 1.0") will be summarized with the sign suppressed in summary tables and figures, using the numeric value reported. Data will display on subject listings to include the sign.

7.2 Analysis Populations

The analysis populations are defined as follows:

- Safety Population: Includes all subjects randomized in the study who received study drug at least once. Subjects will be included in the treatment group based on the lowest dose of active treatment they actually received (even if not the treatment group to which they were randomized). Thus, a subject randomized to 15% BBI-4000 but who actually received 10% and 5% would be included in the 5% BBI-4000 group. A subject randomized to vehicle but who actually received 5% and 10% would be included in the 5% BBI-4000 group.

- Modified Intent-to-Treat (mITT) Population: Includes all subjects who were randomized and dispensed study drug. Subjects will be included in the treatment group to which they were randomized, regardless of the treatment received.

- Per-Protocol (PP) Population: Includes all Safety Population subjects who meet the following criteria:

    1. Meets the inclusion/exclusion criteria

    2. Has not taken or applied any interfering concomitant medications.

    3. Completed the following visits:

        - Visit 2 GSP 1, and the required GSP data collection
        - Visit 3 GSP 2, and the required GSP data collection
        - Visit 4 GSP 3, and the required GSP data collection
        - Visit 11 GSP 4, and the required GSP data collection
        - Visit 12 GSP 5, and the required GSP data collection
        - Visit 13 GSP 6, and the required GSP data collection

    Subjects will be included in the treatment group based on the treatment actually received, as described above.

Data summaries to be presented on both the Safety Population and the mITT Population will only be produced on both analysis sets if there is a difference in the population groups (e.g., at least one subject receives a different treatment than they were originally assigned or some subjects never received any protocol treatment).

7.3 Study Subjects

7.3.1 Disposition of Subjects

Subject disposition will be summarized for all randomized subjects by treatment group and over all subjects combined. Summaries will include the number and percentage of subjects in each analysis population, completing the study, and discontinuing the study early by the primary reason for discontinuation. Subject disposition will also be summarized separately for each study center.

7.3.2 Protocol Deviations

Major protocol violations will be summarized by treatment group and over all subjects combined for the Safety Population. Major protocol violations may include, but will not be limited to the following:

- Violation of eligibility criteria;
- Randomization error;
- Non-compliance with study drug dosing;
- On-study administration of a prohibited medication;
- Unauthorized changes to protocol procedure that could potentially affect subject safety or are a flagrant deviation of protocol defined procedures

All major protocol violations will be determined and appropriately categorized prior to database lock and prior to breaking the blind of the treatment group assignments. The number and percentage of subjects with any major protocol violations as well as the number and percentage of subjects with violations within each category will presented. A per subject listing will be provided for all protocol violations. All protocol violations will be determined and appropriately categorized prior to database lock.

7.4 Efficacy

7.4.1 Datasets Analyzed

All efficacy summaries will be based on the mITT Population; select efficacy summaries will also be produced on the PP Population. A data listing of subjects excluded from the mITT or PP Population, to include the reason for exclusion, will be presented.

7.4.2 Demographic and Other Baseline Characteristics

Demographic variables including age, sex, ethnicity and race, will be summarized by treatment group and over all subjects combined for the Safety, mITT, and PP Populations.

Age will be summarized using descriptive statistics. Sex, ethnicity, and race will be summarized with the number and percentage of subjects in each parameter category.

Baseline characteristics include medical history, height, weight, time since onset of axillary hyperhidrosis symptoms and body mass index (BMI). BMI will be calculated as: weight (kg) / (height (cm) / 100)^2. Time since onset of axillary hyperhidrosis symptoms will be reported in months and calculated by dividing the duration in days by (365.25 / 12). Baseline characteristics will be summarized for the Safety Population by treatment group and for all subjects combined. Height, weight, and BMI at baseline will be summarized using descriptive statistics. Medical history events will be coded to system organ class using the Medical Dictionary for Regulatory Activities (MedDRA, version 19.1). Frequency counts and percentages to summarize subjects reporting abnormal medical history by system organ class as will be presented.

7.4.3 Measurements of Treatment Compliance

Study drug compliance will be calculated for each subject by taking into account whether a subject took all doses of study drug as instructed through dosing deviations collected on the CRF. Compliance to the study treatment regimen will be determined as the total number of doses received divided by the number of expected doses, multiplied by 100. As study drug is applied 1 time daily per axilla for 42 days, the expected number of doses will be the number of days between the date of last dose of study drug minus the date of first dose of study drug, plus one, times two. The number of doses received will be the number of days between the date of last dose of study drug minus the date of first dose of study drug, plus one, times 2 minus the number of missed doses recorded on the Dosing page of the CRF. Dosing compliance will be summarized using descriptive statistics based on the Safety Population, and separately based on the PP Population.

7.4.4 Primary Efficacy Endpoint Analysis Methods

The mean of the items in sections No. 1, 2, and 3 of the HDSM-Ax (11 sub-items in total) will be used for analysis. The mean will be derived by taking the total score and dividing by the number of questions answered. Subjects must answer at least 6 of the 11 sub-items to be evaluable for HDSM-Ax total score. Baseline and End of therapy values are defined as follows.

- Baseline value = average of two screening values, i.e., Visit 1 and Visit 4
- End of therapy value = average of Days 41, 42, and 43 measurements, i.e., Visit 11, Visit 12, and Visit 13, respectively.
- End of Therapy Imputed value = includes subjects missing all end of therapy values, where data is imputed by the last three available post-baseline visits.

7.4.4.1 Primary Efficacy ANCOVA

The primary efficacy endpoint is the change from baseline to the end of therapy in the mean HDSM-Ax score. The primary efficacy endpoint will be analyzed both as a continuous measure and as a binary outcome. As a continuous measure, the HDSM-Ax change scores will be compared between treatment groups in pairwise fashion by an ANCOVA model adjusting for the baseline HDSM-Ax score. The analysis will be performed with no imputation of missing data. As a binary measure, i.e. achieving a ≥ 1-point improvement or not from baseline to end of therapy, a binary logistic regression will be performed with treatment assignment and baseline HDSM-Ax score as independent variables in the model. Any subject without a definable 1-point improvement (e.g., missing data) between Baseline and End of Treatment will be considered a non-responder. P values will generally be regarded as descriptive and statistical significance will be assessed using a gate-keeping hierarchy as described in Section 7.4.6.5 for both the continuous measure and binary data analyses.

The null hypothesis to be tested for the continuous measure is as below:

$$H_0: \mu_A \geq \mu_P;$$

where μ_A and μ_P represent the true underlying mean change scores for Treatment A (active drug) and Treatment P (vehicle), respectively. The alternate hypothesis to be tested is that the true active treatment group mean change score is smaller than the true vehicle group mean change score:

$$H_1: \mu_A < \mu_P;$$

Tested in the logit scale, the null hypothesis for the dichotomous outcome is that the true proportion of subjects with a 1 point or more improvement is lower in the active treatment group:

$$H_0: P_A \leq P_P;$$

The alternate hypothesis to be tested is that the true proportion of subjects with a 1 point or more improvement is higher in the active treatment group:

$$H_1: P_A > P_P;$$

7.4.4.2 Sensitivity Analysis by Mixed Effects Models

As a method that is known to be robust to missing data, mixed model repeated measures (MMRM) analyses will also be performed for the primary efficacy endpoint using all available HDSM-Ax change from baseline data on study days 8, 15, 22, 29, 36, and end of therapy. As fixed effects, treatment (active treatment group or vehicle gel), baseline HDSM-Ax score and visit (included in the class statement as a class variable) and baseline*visit interactions will be

included in the model both without and with treatment*visit interaction terms. Subject will be analyzed as a random effect. Similarly, MMRMs will also be performed for the primary efficacy endpoint using HDSM-Ax dichotomized response data, and HDSM-Ax + GSP dichotomized response data. The models will be the same as the model for continuous data but the dependent variable of interest will be the response status with a logit link, using the SAS Proc GLIMMIX module. Both the heterogeneous CS (CSH) and TOEP (TOEPH) covariance structures will be considered and the structure with lower AIC will be used. The percentage of responders will also be summarized at each visit in the result table.

MMRM analysis as described above will also be performed for continuous GSP data (both Normal model and using rank transformed data) and binary GSP response (i.e. 50% reduction from baseline) data.

7.4.4.3 Additional Sensitivity Analysis

An additional sensitivity analysis will be performed as follows. For subjects missing all 3 end of therapy values, the data will be imputed by the last three available post-baseline (i.e., from Day 8 onward) assessment values. This analysis will be performed for both the continuous data analysis and the binary data analysis using the same ANCOVA models as described above.

7.4.5 Secondary and Other Efficacy Endpoint Analysis Methods

Baseline and End of Therapy values for HDSS and GSP are defined as follows.

HDSS:

- Baseline value = average of two screening values, i.e., Visit 1 and Visit 4
- End of Therapy value = average of Days 41, 42, and 43 measurements, i.e., Visit 11, Visit 12, and Visit 13, respectively.
- End of Therapy Imputed value = includes subjects missing all end of therapy values, where data is imputed by the last three available post-baseline visits.

Gravimetric Sweat Production (both axilla combined total):

- Baseline value = the median of GSP1, GSP2, and GSP3 measurements obtained on Visit 2, Visit 3, and Visit 4, respectively. The mean value of the same visits will also be used for analysis.
- End of Therapy value = the median of GSP4, GSP5, and GSP6 measurements obtained on Visit 11, Visit 12, and Visit 13, respectively. The mean value of the same visits will also be used for analysis.

- End of Therapy Imputed value = includes subjects missing all end of therapy values, where data is imputed by the last three available post-baseline visits.

- Where data from a single axilla is missing, data will be imputed by using the median of the last 3 available values for that axilla.

- Analyses of continuous data will be performed using both Normal model and rank-transformed data.

DLQI:

The DLQI total score is calculated by summing answers to questions 1 through 10, including both parts of Question 7. All questions must be answered at the first DLQI assessment. Subsequent DLQI assessments with a single missing answer will be scored 0 for that question and totaled. Subjects with more than one missing question will have the instrument dropped for that visit.

The DLQI's change from baseline at 43 days (Visit 13) will be compared between each BBI-4000 active arm and the vehicle arm using an ANCOVA model adjusting for the baseline DLQI score.

With the exception of DLQI, analysis for secondary and other efficacy endpoints will generally be similar to the HDSM-Ax analysis described in Section 7.4.4.1 and Section 7.4.4.3. For GSP results analyzed as continuous measures, analyses assuming Normality for the data distribution (i.e., comparing means) will be performed using ANCOVA as described in Section 7.4.4. In addition, continuous gravimetric change scores will also be analyzed with rank transformed data using the t test for ANCOVA models. For both Normal model and non-parametric ANCOVA, treatment and baseline value will be the independent variables and continuous gravimetric change scores or rank scores (of change values) will be the dependent variable as appropriate.

All non-primary analyses will be based on available data without missing data imputation unless otherwise specified.

A table by treatment arm and visit summarizing the number of subjects with non-missing data will be also provided for HDSM-Ax, HDSS, and GSP. Subjects with non-missing data will be summarized for Visits 1 and 4, combined, Visit 1, Visit 4, and missing data at both Visit 1 and Visit 4. The number of subjects with non-missing data at each of Visits 6 through Visit 14 will be summarized, and subjects with complete data at Visits 11, 12, and 13, combined, any 2 of the three (Visit 11, 12, or 13), any one of the three, and subjects missing data at all of Visits 11 through 13 will be summarized.

In parallel to the traditional statistical analysis, psychometric evaluation of the HDSM-Ax will be carried out to confirm the most appropriate HDSM-Ax scoring algorithm and to examine internal validity, construct validity (i.e., examinations of the magnitude of correlation between the HDSM-Ax total score (Items 1, 2, and 3) and key variables such as; items 4 and 5 of the HDSM-

Ax, HDSS and gravimetrically measured sweat production), stability, reliability, ability to detect change, and interpretability of clinical trial results. The psychometric evaluation is outside the scope of this SAP and will be described in a separate analysis plan.

7.4.6 Statistical/Analytical Issues

7.4.6.1 Adjustments for Covariates

The ANCOVA model and binary logistic regression model to compare treatment groups for the primary endpoint will include a covariate adjustment for the baseline value. Select secondary endpoints will be analyzed similarly.

7.4.6.2 Handling of Dropouts or Missing Data

Generally, no imputations will be performed on missing data; all analyses will be based on observed data unless otherwise specified.

7.4.6.3 Interim Analyses and Data Monitoring

There are no interim analyses planned, nor is there a plan to establish a data monitoring committee for this study.

7.4.6.4 Multicenter Studies

This is a multicenter study, with approximately 25 sites expected to participate. Data collected from all study centers will be pooled for data analysis. The effect of study center on the efficacy analysis results may be explored post-hoc, as needed.

7.4.6.5 Multiple Comparisons/Multiplicity

To limit the study-wide false positive rate to 0.10, a gate-keeping hierarchical testing algorithm will be employed to assess statistical significance regarding the primary analyses for the primary efficacy endpoint, i.e. ANCOVA analyses on change from baseline in HDSM-Ax score. The hierarchy is, the comparison between BBI-4000 15% group and vehicle group will be considered first, if the result is favorable with a 1-sided $p<0.10$, then the comparison between BBI-4000 10% group and vehicle will be considered. Similarly, if the BBI-4000 10% group is favorable with a 1-sided $p<0.10$, then comparison between BBI-4000 5% group and vehicle will be considered. The same gate keeping hierarchical testing algorithm will be employed for both the binary data analysis and the continuous measurement analysis.

The primary efficacy analysis will be performed on the mITT population; the PP population will be utilized for selected efficacy analyses. The PP population is described in Section 7.2.

7.4.6.6 Active-Control Studies Intended to Show Equivalence

This study does not include an active-control product and is not intended to demonstrate equivalence between any two drug products.

7.4.6.7 Examination of Subgroups

There are no planned analyses to assess efficacy results by subgroups.

7.5 Safety Analysis

Safety analysis will be carried out for the Safety Population, to include all subjects who receive at least one dose of study drug. Subjects who do not complete the study, for whatever reason, will have all available data up until the time of termination included in the analysis. For safety analysis presented by study visit, the baseline value will be defined as the last value reported prior to first study drug administration.

7.5.1 Extent of Exposure

Extent of exposure to study treatment will be summarized for the Safety Population by treatment group. The duration of exposure will be presented in days and calculated as the date of last dose of study drug minus the date of first dose of study drug, plus one. Duration of exposure will be summarized using descriptive statistics. Drug (pump) dispensation will be provided in a listing, to include total drug delivered per subject. Each pump will be primed, then weighed, prior to dispensing pumps to subjects. Each pump will be weighed upon return. Total drug delivered will be calculated as the total weight of all pumps dispensed minus the total weight of all returned pumps.

7.5.2 Adverse Events

Treatment-emergent adverse events (TEAEs) are defined as those adverse events (AEs) with onset after the first dose of study drug or existing events that worsened after the first dose during the study. Treatment-emergent AEs will be summarized by treatment group. Events reported with a partial onset date (e.g., month and year are reported but the day is missing) will be considered to be treatment-emergent if it cannot be confirmed that the event onset was prior to the first dose of study drug based on the available date entries.

Verbatim terms on case report forms will be mapped to preferred terms and system organ classes using MedDRA version 19.1.

Summaries that are displayed by system organ class and preferred terms will be ordered by descending incidence of system organ class in the combined BBI-4000 group and preferred term within each system organ class. Summaries displayed by preferred term only will be ordered by descending incidence of preferred term in the combined BBI-4000 group. Summaries of the following types will be presented:

- Overall summary of number of unique TEAEs and treatment-emergent serious adverse events (SAEs) and subject incidence of TEAEs meeting various criteria;
- Subject incidence of TEAEs by MedDRA system organ class and preferred term;
- Subject incidence of the most frequently-occurring TEAEs (i.e., TEAEs occurring in ≥ 10% of the Safety Population) by MedDRA system organ class and preferred term;
- Subject incidence of TEAEs related to study drug by MedDRA system organ class and preferred term;
- Subject incidence of TEAEs by severity grade, MedDRA system organ class, and preferred term;
- Subject incidence of TEAEs related to Study Drug by severity, MedDRA system organ class and preferred term; and,
- Subject incidence of SAEs by MedDRA system organ class and preferred term
- Subject incidence of SAEs related to study drug by MedDRA preferred term.

At each level of summarization (e.g., any AE, system organ class, and preferred term), subjects experiencing more than one TEAE will be counted only once. In the summaries of TEAEs by severity grade, subjects will be counted once at the highest severity reported at each level of summarization, and by each level of severity; in the summary of TEAEs by relationship, subjects will be counted once at the closest relationship to study drug.

Adverse event data will be presented in data listings by subject, treatment group, and event. Serious AEs and AEs leading to discontinuation of the study drug will be presented in separate data listings.

7.5.3 Local Tolerability Assessments

Subject and Investigator assessments will be included in separate tables and listings, with the count and percentage of subjects within each severity (maximum severity assessed at either axilla) and treatment group presented by parameter and visit.

7.5.4 Deaths, Other Serious Adverse Events, and Other Significant Adverse Events

All deaths during the study, including the post-treatment follow-up period, will be listed by subject, to include the primary cause of death and investigator narratives. Serious AEs and other significant AEs, including those that led to withdrawal, interruption, or dose reduction of the study drug, will be provided in separate subject data listings.

7.5.5 Clinical Laboratory Evaluation

All descriptive summaries of laboratory results will be based on data analyzed by the central laboratory and presented in Système International (SI) units, as suggested by the Center for Biologics Evaluation and Research and the Center for Drug Evaluation and Research *Position on Use of SI Units for Lab Tests* (Oct 2013). All data will be included in by-subject data listings. Laboratory measurements identified as abnormal (i.e., outside the normal range) will also be listed separately by subject, laboratory test, and unit.

Clinical laboratory measurements, including serum chemistry and hematology, will be summarized by treatment group. Descriptive statistics will be presented for observed values and changes from baseline at each visit where parameters were scheduled to be collected per the clinical study protocol.

Where applicable, laboratory results will be classified as "low," "normal," or "high" with respect to the parameter-specific reference ranges (i.e., below the lower limit of the normal range, within the normal range, or above the upper limit of the normal range). Three-by-three contingency tables will be presented for each laboratory parameter to summarize the shift from the baseline category to the worst post-baseline measurement, defined as the value numerically farthest outside of the normal range across all post-baseline visits through the end of the study.

Summary results will include the count and percentage of subjects within each shift category and treatment group.

7.5.6 Vital Signs, Physical Findings, and Other Observations Related to Safety

7.5.6.1 Vital Signs

Vital sign parameter measurements will be summarized by treatment group. Descriptive statistics will be presented for results and change from baseline at each visit where parameters were scheduled to be collected.

7.5.6.2 Physical Examination

Results of the physical examination will be presented in subject data listings by subject, study visit, and body system.

7.5.6.3 Prior and Concomitant Medications

Medications will be coded using the World Health Organization (WHO) drug dictionary, enhanced (version B2 March 1, 2016). Medications entered on the eCRF will be mapped to Anatomic Therapeutic Chemical (ATC) drug class (level 4) and drug name.

Prior and concomitant medications will be summarized separately and the study phase of each medication will be determined programmatically based on medication start and end dates. A

prior medication is defined as any medication administered prior to the date of the first dose of study drug. A concomitant medication is defined as any medication administered on or after the date of the first dose of study drug. A medication may be defined as both prior and concomitant. If it cannot be determined whether a medication was received prior to the start of study drug dosing due to partial or missing medication start and/or end dates, it will be considered a prior medication. Likewise, if it cannot be determined whether a medication was received after the start of study drug dosing, it will be considered concomitant.

For the summary of both prior medications and concomitant medications, the number and percentage of subjects receiving any medication will be summarized by treatment group, as will the number and percentage receiving any medication by ATC drug class and generic drug name. Subjects reporting use of more than one medication at each level of summarization (any medication received, ATC class, and generic drug name) will be counted only once. ATC class terms will be displayed by descending order of incidence, as will generic drug names within each ATC class. The study phase during which each medication was received (e.g., prior, concomitant, or both) will be presented on the listing of prior and concomitant medications.

7.5.6.4 Prior and Concomitant Therapies/Procedures

Therapies/Procedures will be coded using MedDRA version 19.1. Therapies entered on the eCRF will be mapped to SOC.

The study phase of each therapy/procedure will be determined programmatically based on start and end dates. A prior therapy/procedure is defined as any therapy/procedure occurring prior to the date of the first dose of study drug. A concomitant therapy/procedure is defined as any therapy/procedure occurring on or after the date of the first dose of study drug. A therapy/procedure may be defined as both prior and concomitant. If it cannot be determined whether a therapy/procedure occurred prior to the start of study drug dosing due to partial or missing, it will be considered a prior therapy/procedure. Likewise, if it cannot be determined whether a therapy/procedure occurred after the start of study drug dosing, it will be considered concomitant. Therapies and procedures will be reported in a subject listing, and identified as prior or concomitant, and as a therapy or a procedure.

7.6 Determination of Sample Size

For the binary version of the primary endpoint, i.e., proportion of subjects achieving at least a 1-point improvement in HDSM-Ax from baseline to end of therapy, the true response rates will be assumed to be 75% for each BBI-4000 arm and 50% for vehicle control (based on prior data). With 100 evaluable subjects at a 1:1 ratio for each pairwise comparison between a BBI-4000 arm and the vehicle arm, i.e., 50 evaluable subjects per arm, the power is approximately 0.87 for observing a response rate difference in favor of BBI-4000 at a 1-sided $p<0.10$ level.

For the continuous version of HDSM-Ax change from baseline to end of therapy, the true mean difference between each BBI-4000 arm and the vehicle arm will be assumed to be 0.18, with a common standard deviation of 0.36, i.e., an effect size (mean difference/standard deviation) of

0.50. With 100 evaluable subjects at a 1:1 ratio for each pairwise comparison between a BBI-4000 arm and the vehicle arm, the power is approximately 0.89 for observing a difference in favor of BBI-4000 at a 1-sided $p<0.10$ level.

Assuming an approximate 10% non-evaluable rate for the mITT primary efficacy analyses, 220 randomized subjects are targeted for enrollment.

7.7 Changes in the Conduct of the Study or Planned Analyses

Analysis of change in DLQI score between baseline and Day 57 removed as this data is not collected.

An explanation of how subjects receiving multiple doses will be assigned to dosage groups in the Safety Population was added.

ITT population was changed to mITT population.

The Per Protocol population definition was changed to a subset of the Safety population, as subjects must receive one dose of study drug.

An Imputed End of Therapy time point added to primary and secondary outcomes as a sensitivity analysis.

GSP data to be analyzed separately with baseline/EOT mean value and baseline/EOT median value.

MMRM sensitivity analysis expanded to include GSP continuous (raw and ranked) data, and a logit-linked, generalized MMRM analysis of HDSM-Ax, GSP, and HDSM-Ax+GSP binary outcomes.

7.8 Changes in SAP from Version 1.0 to Version 2.0

Table summaries of the MMRM sensitivity analysis expanded to include GSP continuous (Normal model and ranked) data, and a logit-linked, generalized MMRM analysis of GSP change from baseline binary outcomes.

8 REFERENCE LIST

International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use. Statistical principles for clinical trials (E9). International Conference on Harmonization; 1998.

M2 eCTD: Electronic Common Technical Document Specification Appendix 7, provided by the International Conference on Harmonization. Available from: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073240.pdf

Data Standards: Position on Use of SI Units for Lab Tests. U.S Food and Drug Administration; 25 October 2013. Available from:
http://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/ucm372553.htm

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APPENDIX B: TABLE LAYOUTS

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Subject Disposition
All Randomized Subjects

	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)	Total (N=)
All Randomized	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Study Medication not Dispensed	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Safety Population[1]	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
mITT Population[2]	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
PP Population[3]	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Completed Study[4]					
Yes	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
No	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Primary reason for Discontinuation					
Adverse Event	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Withdrawal by Subject	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Physician Decision	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Protocol Violation	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Lost to Follow-Up	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Death	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Pregnancy	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Worsening Condition	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Lack of Efficacy	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Study Terminated by Sponsor	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Other	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)

Abbreviations: GSP, gravimetrically measured sweat production; mITT, Intent-to-Treat; PP, Per-Protocol

[1] Safety Population includes all subjects randomized in the study who received study drug at least once. Treatment group assignment is based on the treatment actually received.
[2] mITT Population includes all subjects who were randomized and dispensed study drug. Treatment group assignment is based on the planned treatment assignment.
[3] PP Population includes all Safety subjects who meet all inclusion/exclusion criteria, have not taken/applied any interfering concomitant medications, and have full data collected for all GSP visits.
[3] Defined as a disposition term of "Normal Study Completion".

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

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Table 14.1.1.2
Subject Disposition by Study Center
All Randomized Subjects

		Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)	Total (N=)
Site 1	All Randomized	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Study Medication not Dispensed	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Safety Population[1]	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	mITT Population[2]	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	PP Population[3]	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Completed Study					
	Yes	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	No	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Study Medication not Dispensed	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Primary reason for Discontinuation					
	Adverse Event	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Withdrawal by Subject	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Physician Decision	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Protocol Violation	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Lost to Follow-Up	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Death	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Pregnancy	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Worsening Condition	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Lack of Efficacy	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Study Terminated by Sponsor	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Other	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Site 2	…					

Abbreviations: mITT, Intent-to-Treat; PP, Per-Protocol

[1] Safety population includes all subjects randomized in the study who received study drug at least once. Treatment group assignment is based on the treatment actually received.
[2] mITT population includes all subjects who were randomized and dispensed study drug. Treatment group assignment is based on the planned treatment assignment.
[3] PP population includes all Safety subjects who meet all inclusion/exclusion criteria, have not taken/applied any interfering concomitant medications, and have full data collected for all GSP visits.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Table 14.1.2
Major Protocol Violations
Safety Population

	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)	Total (N=)
Any Major Protocol Violations	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Violation Category #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Violation Category #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
…					

Note: Subjects reporting more than one violation in a category are counted only once and subjects may be included in more than one category.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

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Table 14.1.3.1
Demographics
Safety Population

	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)	Total (N=)
Age					
n	n	n	n	n	n
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x	x	x	x	x
Min, Max	x, x	x, x	x, x	x, x	x, x
Sex					
Male	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Female	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Ethnicity					
Hispanic or Latino	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Not Hispanic or Latino	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Race[1]					
American Indian or Alaska Native	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Asian	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Black or African American	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Native Hawaiian or Other Pacific Islander	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
White	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Other	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)

[1] Subjects reporting more than one race are included in all relevant race categories. Percentages will add up to >100%.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Notes:

- *Repeat for the following:*
  Table 14.1.3.2 Demographics (mITT Population)
  Table 14.1.3.3 Demographics (PP Population);

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Table 14.1.4.1
Baseline Characteristics
Safety Population

	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)	Total (N=)
Height (cm)					
n	n	n	n	n	n
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x.x	x.x	x.x	x.x	x.x
Min, Max	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
Weight (kg)					
n	n	n	n	n	n
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x.x	x.x	x.x	x.x	x.x
Min, Max	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
BMI (kg/m^2)					
n	n	n	n	n	n
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x.x	x.x	x.x	x.x	x.x
Min, Max	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
Time Since Start of Axillary Hyperhidrosis Symptoms (Months)[1]					
n	n	n	n	n	n
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x.x	x.x	x.x	x.x	x.x
Min, Max	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x

Abbreviations: BMI, body mass index

[1] Time since start of axillary hyperhidrosis symptoms is calculated as date informed consent signed – start date of axillary hyperhidrosis symptoms.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Note: Repeat as Table 14.1.4.2 Baseline Characteristics, mITT Population

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Table 14.1.5
Medical History
Safety Population

System Organ Class[1]	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)	Total (N=)
Subjects Reporting any Medical History	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Body System #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Body System #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
…					

Note: Subjects reporting more than one medical history event for a given body system are counted only once.

[1] Medical history events are coded to system organ class using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

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Table 14.1.6
Prior Medications
Safety Population

ATC Class / Generic Drug Name	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)
Subjects Receiving any Prior Medications	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
ATC Class #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Generic Drug Name #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Generic Drug Name #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
.				
.				
ATC Class #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Generic Drug Name #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Generic Drug Name #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
.				
.				

Abbreviations: ATC, anatomic therapeutic chemical, WHO, World Health Organization

Notes:

- Prior medications are those medications received prior to the first dose of study drug.
- Medications are coded to ATC drug class (level 4) and generic drug names using the WHO Drug dictionary enhanced, version B2 March 1, 2016.
- At each level of summarization (any medication, ATC class, generic drug name), subjects reporting use of more than one medication are counted only once.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Notes:

- *Sort medications by descending order of ATC class incidence and by descending order of drug name incidence within ATC class, based on the overall incidence (i.e., sum over all treatment groups).*
- *When creating ATC level 4 drug class, utilize level 3 term if level 4 is missing in dataset and level 2 if both level 3 and level 4 are missing in the dataset*
- *Repeat as Table 14.1.7 Prior Therapy and Procedures*

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Table 14.2.1.1
HDSM-Ax Summary of First and Last Visits
mITT Population

Study Day/s with Non-Missing Data	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)
Subjects with Data:				
At Visit 1 and Visit 4	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
At Visit 1 Only	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
At Visit 4 Only	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Missing Visit 1 and Visit 4	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Last Study Visit Data at				
Day 8	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 15	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 22	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 29	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 36	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 41	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 42	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 43	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 57	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Subjects with Data:				
At Day 41 and Day 42 and Day 43	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
At Any 2 of Days 41, 42, or 43	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
At Any 1 of Days 41, 42, or 43	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Missing data at Days 41, 42, and 43	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)

Abbreviation: HDSM-Ax, Hyperhidrosis Disease Severity Measure-Axillary

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Note: Repeat for Table 14.2.1.2 HDSM-Ax Summary of First and Last Visits (PP Population)

Table 14.2.1.3
HDSM-Ax End of Therapy Change from Baseline ANCOVA
mITT Population

	Vehicle (N=)			BBI-4000 5% (N=)		
Time Point	Observed Value	Change from Baseline	% Change from Baseline	Observed Value	Change from Baseline	% Change from Baseline
Baseline[1]						
n	n			n		
Mean (SD)	x.x (x.xx)			x.x (x.xx)		
Median	x.x			x.x		
Min, Max	x.x, x.x			x.x, x.x		
End of Therapy[2]						
n	n	n	n	n	n	n
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x.x	x.x	x.x	x.x	x.x	x.x
Min, Max	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
LSM (SE)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
LSMD (active dose – vehicle) (SE)		xx.x (xx.xx)	xx.x (xx.xx)		xx.x (xx.xx)	xx.x (xx.xx)
95% CI of LSMD		xx.x, xx.x	xx.x, xx.x		xx.x, xx.x	xx.x, xx.x
ANCOVA p-value[4]					x.xxxx	x.xxxx
….						

Abbreviations: ANCOVA, analysis of covariance; HDSM-Ax, Hyperhidrosis Disease Severity Measure-Axillary; mITT, Intent-to-Treat; LSM, Least Square Mean; LSMD Least Square Mean Difference

[1] Baseline is defined as the average of any available Visit 1 (Screening) and Visit 4 (Rescreening) values.
[2] End of Therapy is defined as the average of any available Day 41, Day 42, and Day 43 values.
[3] End of Therapy Imputed includes subjects missing all end of therapy values, where data is imputed by the last three available post-baseline visits.
[4] P-values comparing active dose to vehicle are based on an ANCOVA model with covariate adjustment for the baseline value.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Notes: Continue for End of Therapy Imputed[3], and BBI -4000 Doses (10%, 15%). Repeat for Table 14.2.1.4 HDSM-Ax End of Therapy Change from Baseline ANCOVA (PP Population)

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Table 14.2.1.5
HDSM-Ax Change from Baseline MMRM and Change from Baseline by Visit ANCOVA
mITT Population

	Vehicle (N=)			BBI-4000 5% (N=)		
Time Point	Observed Value	Change from Baseline	% Change from Baseline	Observed Value	Change from Baseline	% Change from Baseline
Baseline[1]						
n	n			n		
Mean (SD)	x.x (x.xx)			x.x (x.xx)		
Median	x.x			x.x		
Min, Max	x.x, x.x			x.x, x.x		
Day 8						
….						
LSM (SE)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
LSMD (active dose – vehicle) (SE)		xx.x (xx.xx)	xx.x (xx.xx)		xx.x (xx.xx)	xx.x (xx.xx)
95% CI of LSMD		xx.x, xx.x	xx.x, xx.x		xx.x, xx.x	xx.x, xx.x
ANCOVA p-value[2]					x.xxxx	x.xxxx
….						
MMRM treatment p-value[3]					x.xxxx	x.xxxx
MMRM treatment*visit p-value[4]					x.xxxx	x.xxxx

Abbreviations: ANCOVA, analysis of covariance; HDSM-Ax, Hyperhidrosis Disease Severity Measure-Axillary; mITT, Intent-to-Treat; MMRM, mixed model for repeated measures; LSM, Least Square Mean; LSMD Least Square Mean Difference

[1] Baseline is defined as the average of any available Visit 1 (Screening) and Visit 4 (Rescreening) values.
[2] P-values comparing active dose to vehicle are based on an ANCOVA model with covariate adjustment for the baseline value.
[3] P-value comparing active dose to vehicle are based on an MMRM with subject as a random effect, treatment, protocol-specified visit, baseline, and baseline*visit interaction as fixed effects.
[4] P-value is for the collective treatment*visit interaction based on an MMRM with subject as a random effect, and treatment, protocol-specified visit, treatment*visit interaction, baseline, and baseline*visit interactions as fixed effects.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Notes: Table continues on next page.

- *Continue for Day 8 summary statistics (n, Mean (SD), Median, and Min, Max).*
- *Continue for Days 15, 22, 29, 36, and 57, each visit to include summary statistics.*
- *Continue for remaining BBI -4000 Doses (10%, 15%).*
- *For Days 8, 15, 22, 29, 36, 41-43, and 57 include ANCOVA p-value for each visit.*
- *For MMRM analyses, use data on Days 8, 15, 22, 29, 36 and End of Therapy.*
- *MMRM p-values are not associated with any visit Day. Show treatment and treatment*visit p-values once at bottom of each treatment group.*
- *Repeat for Table 14.2.1..6 HDSM-Ax Change from Baseline MMRM and Change from Baseline by Visit ANCOVA (PP Population)*

Table 14.2.1.7
HDSM-Ax Responder MMRM
mITT Population

		Vehicle (N=)	BBI-4000 5% (N=)	
HDSM-Ax Parameter	Time Point	n (%)	n (%)	P-value[1]
Reduction from Baseline[2] ≥1	Day 8	n (x.x%)	n (x.x%)	x.xxxx
	Day 15	n (x.x%)	n (x.x%)	x.xxxx
	Day 22	n (x.x%)	n (x.x%)	x.xxxx
	Day 29	n (x.x%)	n (x.x%)	x.xxxx
	Day 36	n (x.x%)	n (x.x%)	x.xxxx
	….			
	End of Therapy[3]	n (x.x%)	n (x.x%)	x.xxxx
	MMRM treatment p-value[4]			x.xxxx
	MMRM treatment*visit p-value[5]			x.xxxx
Reduction from Baseline[2] ≥2	…			

Abbreviations: HDSM-Ax, Hyperhidrosis Disease Severity Measure-Axillary; mITT, Intent-to-Treat; MMRM, mixed model for repeated measures

Note: Responder is defined as a subject who achieved the reduction in HDSM-Ax score specified in the HDSM-Ax Parameter column, between Baseline and End of Therapy. Subjects without a defined improvement in score are considered non-responders.

[1] P-values comparing active treatment to vehicle are based on a binary logistic regression model where treatment and baseline HDSM-Ax Score are predictors.
[2] Baseline is defined as the average of any available Visit 1 (Screening) and Visit 4 (Rescreening) values.
[3] End of Therapy is defined as the average of any available Day 41, Day 42, and Day 43 values.
[4] P-values comparing active dose to vehicle are based on an MMRM with subject as a random effect, treatment, protocol-specified visit, baseline, and baseline*visit interaction as fixed effects.
[5] P-value is for the collective treatment*visit interactions based on an MMRM with subject as a random effect, and treatment, protocol-specified visit, treatment*visit interaction, baseline, and baseline*visit interactions as fixed effects.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Notes: Continue for Days 41, 42, 43, 57, HDSM-Ax ≥2, and remaining BBI-4000 dose groups (10%, 15%). Repeat as Table 14.2.1.8 HDSM-Ax Responder MMRM (PP Population). MMRM = generalized linear mixed model for repeated measures, with logit linkage. For MMRM .analyses, use data on Days 8, 15, 22, 29, 36 and End of Therapy.

Table 14.2.2.1
HDSM-Ax and GSP Responder MMRM
mITT Population

HDSM-Ax and GSP Parameters	Time Point	Vehicle (N=) n (%)	BBI-4000 5% (N=) n (%)	P-value[1]
HDSM-Ax reduction from Baseline[2] ≥1 and GSP reduction from Baseline[2] ≥ 50%	Day 8	n (x.x%)	n (x.x%)	x.xxxx
	Day 15	n (x.x%)	n (x.x%)	x.xxxx
	Day 22	n (x.x%)	n (x.x%)	x.xxxx
	….			
	End of Therapy[3]	n (x.x%)	n (x.x%)	x.xxxx
	MMRM treatment p-value[4]			x.xxxx
	MMRM treatment*visit p-value[5]			x.xxxx
HDSM-Ax reduction from Baseline[2] ≥2 and GSP reduction from Baseline[2] ≥ 50%				
	….			

Abbreviations: GSP, gravimetrically measured sweat production; HDSM-Ax, Hyperhidrosis Disease Severity Measure-Axillary; mITT, Intent-to-Treat; MMRM, mixed model for repeated measures

Note: Responder is defined as a subject who achieved the reduction in HDSM-Ax score specified in the HDSM-Ax Parameter column, between Baseline and End of Therapy. Subjects without a defined improvement in score are considered non-responders.

[1] P-values comparing active treatment to vehicle are based on a binary logistic regression model where treatment and baseline HDSM-Ax Score are predictors.
[2] HDSM-Ax baseline is defined as the average of any available Visit 1 (Screening) and Visit 4 (Rescreening) values; GSP baseline is defined as the median of any available GSP measurements from Visit 2, Visit 3, and Visit 4.
[3] HDSM-Ax End of Therapy is defined as the average any available Day 41, Day 42, and Day 43 values; GSP End of Therapy is defined as the median of any available GSP measurements from Day 41, Day 42, and Day 43.
[4] P-values comparing active dose to vehicle are based on an MMRM with subject as a random effect, treatment, protocol-specified visit, baseline, and baseline*visit interaction as fixed effects.
[5] P-value is for the collective treatment*visit interactions based on an MMRM with subject as a random effect, and treatment, protocol-specified visit, treatment*visit interaction, baseline, and baseline*visit interactions as fixed effects.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Notes: Continue for Days 29, 36, 41, 42, 43, 57, HDSM-Ax ≥2, and remaining BBI-4000 dose groups (10%, 15%); Repeat as Table 14.2.2.2 HDSM-Ax and GSP Responder MMRM (PP Population). MMRM = generalized linear mixed model for repeated measures, with logit linkage. For MMRM analyses, use data on Days 8, 15, 22, 29, 36 and End of Therapy.

Brickell Biotech, Inc.
BBI-4000-CL-203

Table 14.2.3.1
GSP Summary of First and Last Visits
mITT Population

Study Day/s with Non-Missing Data	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)
Subjects with Data:				
At Visit 1 and Visit 4	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
At Visit 1 Only	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
At Visit 4 Only	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Missing Visit 1 and Visit 4	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Last Study Visit Data at				
Day 8	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 15	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 22	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 29	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 36	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 41	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 42	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 43	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 57	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Subjects with Data:				
At Day 41 and Day 42 and Day 43	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
At Any 2 of Days 41, 42, or 43	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
At Any 1 of Days 41, 42, or 43	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Missing data at Days 41, 42, and 43	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)

Abbreviations: GSP, gravimetrically measured sweat production; mITT, Intent-to-Treat

Reference: *Listing #(s)*
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Programming Note: Repeat as Table 14.2.3.2 GSP Summary of First and Last Visits (PP Population)

Table 14.2.3.3
Summary of Missing Singular Axilla GSP Measurements
mITT Population

Study Day/s with GSP data missing from a single axilla	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)
Subjects missing GSP data from a single axilla:				
At Any Visit	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
GSP 1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
GSP 2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
GSP 3	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 8	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 15	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 22	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 29	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 36	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 41	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 42	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 43	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 57	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)

Abbreviations: GSP, gravimetrically measured sweat production; mITT, Intent-to-Treat

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Note: Repeat as Table 14.2.3.4 Summary of Missing Singular Axilla GSP Measurements (PP Population)

Brickell Biotech, Inc.
BBI-4000-CL-203

Table 14.2.3.5
GSP End of Therapy Change from Baseline ANCOVA
mITT Population

		Vehicle (N=)			BBI-4000 5% (N=)		
Time Point	Type of Average[1]	Observed Value	Change from Baseline	% Change from Baseline	Observed Value	Change from Baseline	% Change from Baseline
Baseline[2]	Median						
n		n			n		
Mean (SD)		x.x (x.xx)			x.x (x.xx)		
Median		x.x			x.x		
Min, Max		x.x, x.x			x.x, x.x		
End of Therapy[3]							
n		n	n	n	n	n	n
Mean (SD)		x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median		x.x	x.x	x.x	x.x	x.x	x.x
Min, Max		x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
LSM (SE)		xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
LSMD (active dose – vehicle) (SE)			xx.x (xx.xx)	xx.x (xx.xx)		xx.x (xx.xx)	xx.x (xx.xx)
95% CI of LSMD			xx.x, xx.x	xx.x, xx.x		xx.x, xx.x	xx.x, xx.x
ANCOVA p-value[5]						x.xxxx	x.xxxx
….							

Abbreviations: ANCOVA, analysis of covariance; GSP, gravimetrically measured sweat production; mITT, Intent-to-Treat; LSM, Least Square Mean; LSMD Least Square Mean Difference

[1] Method of calculating average for Baseline, End of Therapy, and End of Therapy Imputed.
[2] Baseline is defined as the median/mean of any available Visit 2, Visit 3, and Visit 4 values.
[3] End of Therapy is defined as the median/mean of any available Day 41, Day 42, and Day 43 values.
[4] End of Therapy Imputed includes subjects missing all end of therapy values, where data is imputed by the median/mean of the last three available post-baseline visits.
[5] P-values comparing active dose to vehicle are based on an ANCOVA model with covariate adjustment for the baseline value.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Notes: Table continues on next page.

- *Continue for End of Therapy Imputed*[4]*, BBI -4000 Doses (10%, 15%), and repeat using mean method for calculating Baseline, EoT and EoT Imputed.*
- *Repeat for Table 14.2.3.6 GSP End of Therapy Change from Baseline ANCOVA (PP Population)*
- *For ranked values, rank continuous data low-to-high within each visit, disregarding treatment.*
- *Repeat for Table 14.2.3.7 GSP End of Therapy Change from Baseline ANCOVA for Ranked Values (mITT Population)*
- *Repeat for Table 14.2.3.8 GSP End of Therapy Change from Baseline ANCOVA for Ranked Values (PP Population)*

Table 14.2.3.9
GSP Change from Baseline MMRM and Change from Baseline by Visit ANCOVA
mITT Population

		Vehicle (N=)			BBI-4000 5% (N=)		
Time Point	Type of Average[1]	Observed Value	Change from Baseline	% Change from Baseline	Observed Value	Change from Baseline	% Change from Baseline
Baseline[2]	Median						
n		n			n		
Mean (SD)		x.x (x.xx)			x.x (x.xx)		
Median		x.x			x.x		
Min, Max		x.x, x.x			x.x, x.x		
Day 8							
….							
LSM (SE)		xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
LSMD (active dose – vehicle) (SE)			xx.x (xx.xx)	xx.x (xx.xx)		xx.x (xx.xx)	xx.x (xx.xx)
95% CI of LSMD			xx.x, xx.x	xx.x, xx.x		xx.x, xx.x	xx.x, xx.x
ANCOVA p-value[3]						x.xxxx	x.xxxx
….							
MMRM treatment p-value[4]						x.xxxx	x.xxxx
MMRM treatment*visit p-value[5]						x.xxxx	x.xxxx

Abbreviations: ANCOVA, analysis of covariance; GSP, gravimetrically measured sweat production; mITT, Intent-to-Treat; MMRM, mixed model for repeated measures; LSM, Least Square Mean; LSMD Least Square Mean Difference

[1] Method of calculating average for Baseline and End of Therapy.
[2] Baseline is defined as the median/mean of any available Visit 2, Visit 3, and Visit 4 values.
[3] P-values comparing active dose to vehicle are based on an ANCOVA model with covariate adjustment for the baseline value.
[4] P-value comparing active dose to vehicle are based on an MMRM with subject as a random effect, treatment, protocol-specified visit, baseline, and baseline*visit interaction as fixed effects.
[5] P-value is for the collective treatment*visit interactions based on an MMRM with subject as a random effect, and treatment, protocol-specified visit, treatment*visit interaction, baseline, and baseline*visit interactions as fixed effects.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Notes: Table continues on next page.

- *Continue for Day 8 summary statistics (n, Mean (SD), Median, and Min, Max).*
- *Continue for Days 15, 22, 29, 36, and 57, each visit to include summary statistics.*
- *Continue for remaining BBI -4000 Doses (10%, 15%).*
- *For Days 8, 15, 22, 29, 36, 41-43, and 57 include ANCOVA p-value for each visit.*
- *For MMRM analyses, use data on Days 8, 15, 22, 29, 36 and End of Therapy.*
- *MMRM p-values are not associated with any visit Day. Show treatment and treatment*visit p-values once at bottom of page for each treatment group.*
- *Repeat analyses with mean method for calculating Baseline and EoT.*
- *Repeat for Table 14.2.3.10 GSP Change from Baseline MMRM and Change from Baseline by Visit ANCOVA (PP Population)*
- *Repeat tables with ranked values. Rank continuous data low-to-high within each visit, disregarding treatment, and use average for ties.*
- *Repeat for Table 14.2.3.11 GSP Change from Baseline MMRM and Change from Baseline by Visit ANCOVA for Ranked Values (mITT Population)*
- *Repeat for Table 14.2.3.12 GSP Change from Baseline MMRM and Change from Baseline by Visit ANCOVA for Ranked Values (PP Population*

Brickell Biotech, Inc.
BBI-4000-CL-203

Table 14.2.3.13
GSP Responder MMRM
mITT Population

Time Point	Type of Average[1]	Vehicle (N=) n (%)	BBI-4000 5% (N=) n (%)	BBI-4000 5% (N=) P-value[2]	BBI-4000 10% (N=) n (%)	BBI-4000 10% (N=) P-value[2]	BBI-4000 15% (N=) n (%)	BBI-4000 15% (N=) P-value[2]
Day 8	Median	n (x.x%)	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx
Day 15		n (x.x%)	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx
Day 22		n (x.x%)	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx
….								
End of Therapy[3]		n (x.x%)	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx
MMRM treatment p-value[4]				x.xxxx		x.xxxx		x.xxxx
MMRM treatment*visit p-value[5]				x.xxxx		x.xxxx		x.xxxx

Abbreviations: GSP, gravimetrically measured sweat production; mITT, Intent-to-Treat; MMRM, mixed model for repeated measures

Note: Responder is defined as a subject who achieved a reduction in GSP of at least 50% between Baseline and End of Therapy. Subjects without a defined improvement in score are considered non-responders.

[1] Method of calculating average for Baseline and End of Therapy.
[2] P-values comparing active treatment to vehicle are based on a binary logistic regression model where treatment and baseline GSP are predictors.
[3] End of Therapy is defined as the median/mean of any available Day 41, Day 42, and Day 43 values.
[4] P-values comparing active dose to vehicle are based on a logit-linked MMRM with subject as a random effect, treatment, protocol-specified visit, baseline, and baseline*visit interaction as fixed effects.
[5] P-value is for the collective treatment*visit interactions based on a logit-linked MMRM with subject as a random effect, and treatment, protocol-specified visit, treatment*visit interaction, baseline, and baseline*visit interactions as fixed effects.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Notes:

- *Continue for Days 29, 33, 41, 42, 43, 57. Repeat analysis with mean method for calculating Baseline and EoT.*
- *MMRM = generalized linear mixed model for repeated measures, with logit linkage.*
- *For MMRM analyses, use data on Days 8, 15, 22, 29, 36 and End of Therapy.*
- *Repeat as Table 14.2.3.14 GSP Responder MMRM (PP Population).*

Table 14.2.4.1
HDSS Summary of First and Last Visits
mITT Population

Study Day/s with Non-Missing Data	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)
Subjects with Data:				
At Visit 1 and Visit 4	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
At Visit 1 Only				
At Visit 4 Only	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Missing Visit 1 and Visit 4	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Last Study Visit Data at				
Day 8	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 15	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 22	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 29	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 36	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 41	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 42	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 43	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Day 57	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Subjects with Data:				
At Day 41 and Day 42 and Day 43	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
At Any 2 of Days 41, 42, or 43	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
At Any 1 of Days 41, 42, or 43	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Missing data at Days 41, 42, and 43	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)

Abbreviations: HDSS, Hyperhidrosis Disease Severity Scale; mITT, Intent-to-Treat

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Notes: Repeat as Table 14.2.4.2 HDSS Summary of First and Last Visits (PP Population)

Table 14.2.4.3
HDSS Responder Regression
mITT Population

		Vehicle (N=)		BBI-4000 5% (N=)		BBI-4000 10% (N=)		BBI-4000 15% (N=)	
HDSS Parameter	Time Point	n (%)	P-value[1]	n (%)	P-value[1]	n (%)	P-value[1]	n (%)	P-value[1]
Change from Baseline≥1									
	Day 8	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx
	Day 15	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx
	Day 22	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx
	Day 29	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx
	Day 36	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx
	Day 41	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx
	Day 42	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx
	Day 43	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx
	End of Therapy[3]	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx
	Day 57	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx	n (x.x%)	x.xxxx
Change from Baseline ≥2	…								

Abbreviations: HDSS, Hyperhidrosis Disease Severity Scale; mITT, Intent-to-Treat

Note: Responder is defined as a subject who achieved a reduction in HDSS score specified in the Parameter column, between Baseline and End of Therapy. Subjects without a defined improvement in score are considered non-responders.

[1] P-values comparing active treatment to vehicle are based on a binary logistic regression where treatment and baseline HDSS score are predictors.
[2] Baseline is defined as the average of any available Visit 1 (Screening) and Visit 4 (Rescreening) values.
[3] End of Therapy is defined as the average of any available Day 41, Day 42, and Day 43 values.

Reference: *Listing #(s)*
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Programming Notes: Continue for Change from Baseline ≥2. Repeat as Table 14.2.4.4 HDSS Responder Regression (PP Population)

Brickell Biotech, Inc.
BBI-4000-CL-203

Table 14.2.5.1
DLQI Change Score ANCOVA
mITT Population

	Vehicle (N=)		BBI-4000 5% (N=)		BBI-4000 10% (N=)		BBI-4000 15% (N=)	
Time Point	Observed Value	Change from Baseline	Observed Value	Change from Baseline	Observed Value	Change from Baseline	Observed Value	Change from Baseline
Baseline [1]								
n	n		n		n		n	
Mean (SD)	x.x (x.xx)		x.x (x.xx)		x.x (x.xx)		x.x (x.xx)	
Median	x.x		x.x		x.x		x.x	
Min, Max	x.x, x.x		x.x, x.x		x.x, x.x		x.x, x.x	
Day 43								
n	n	n	n	n	n	n	n	n
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
Min, Max	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
LSM (SE)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
LSMD (active dose – vehicle) (SE)		xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)
95% CI of LSMD		xx.x, xx.x		xx.x, xx.x		xx.x, xx.x		xx.x, xx.x
ANCOVA p-value[2]				x.xxxx		x.xxxx		x.xxxx

Abbreviations: ANCOVA, analysis of covariance; DLQI, Dermatology Life Quality Index; mITT, Intent-to-Treat; LSM, Least Square Mean; LSMD Least Square Mean Difference

[1] Baseline is defined as the last available measurement taken prior to the first dose of study drug.
[2] P-values comparing active dose to vehicle are based on an ANCOVA model for change scores, with covariate adjustment for the baseline value.

Reference: *Listing #(s)*
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Programming Notes: Repeat for Table 14.2.5.2 DLQI Change Score ANCOVA (PP Population)

Table 14.3.1.1
Overall Summary of Treatment-Emergent Adverse Events
Safety Population
Part 1 of 2

	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)
Total Number of TEAEs	xx	xx	xx	xx
Total Number of TESAEs	xx	xx	xx	xx
Number (%) of Subjects Reporting at Least One:				
TEAE	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
TEAE by Severity[1]				
Mild	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Moderate	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Severe	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
TEAE by Relationship[2]				
Not Related	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Related	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
TEAE Leading to Discontinuation of Study Drug	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
TEAE Requiring Dose Interruption of Study Drug	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
TEAE Requiring Dose Reduction of Study Drug	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
TEAE Leading to Premature Withdrawal from the Study	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
TEAE Causing Death	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Treatment Area				
TEAE in Treatment Area?	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)

Abbreviations: SAE, serious adverse event; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event

[1] Subjects reporting more than one adverse event are counted only once using the highest severity.
[2] Subjects reporting more than one adverse event are counted only once using the closest relationship to study drug. Not related events includes those reported as “Unlikely” or “Not Related” to study drug; related events include those reported as “Possibly Related,” “Probably Related,” or “Definitely Related” to study drug.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming note: Table continues on next page.

Table 14.3.1.1
Overall Summary of Treatment-Emergent Adverse Events
Safety Population
Part 2 of 2

	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)
TESAE	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
TESAE by Severity[1]				
Mild	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Moderate	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Severe	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
TESAE by Relationship[2]				
Not Related	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Related	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Treatment Area				
TESAE in Treatment Area?	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)

Abbreviations: SAE, serious adverse event; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event

[1] Subjects reporting more than one adverse event are counted only once using the highest severity.
[2] Subjects reporting more than one adverse event are counted only once using the closest relationship to study drug. Not related events includes those reported as "Unlikely" or "Not Related" to study drug; related events include those reported as "Possibly Related," "Probably Related," or "Definitely Related" to study drug.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Brickell Biotech, Inc.
BBI-4000-CL-203

Table 14.3.1.2
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class / Preferred Term[1]	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)
Subjects Reporting at Least One Adverse Event	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
System Organ Class #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
…				
System Organ Class #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
…				

Note: At each level of summarization (any event, system organ class, and preferred term), subjects reporting more than one adverse event are counted only once.

[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Note: Sort events by descending order of system organ class incidence and by descending order of preferred term incidence within system organ class, based on the overall incidence (i.e., sum over all treatment groups).

Brickell Biotech, Inc.
BBI-4000-CL-203

Table 14.3.1.3
Most Frequently-Occurring (≥ 10% Overall) Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class / Preferred Term[1]	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)
System Organ Class #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
…				
System Organ Class #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
…				

Note: Subjects reporting more than one adverse event are counted only once. Summary includes all events reported by ≥ 10% of subjects in the Safety Population.

[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Note: Sort events by descending order of SOC term incidence, preferred term incidence, based on the overall incidence (i.e., sum over all treatment groups).

Brickell Biotech, Inc.
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Table 14.3.1.4
Treatment-Emergent Adverse Events Related to Study Drug by Preferred Term
Safety Population

Preferred Term[1]	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)
Preferred Term #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #3	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
…				

Note: Subjects reporting more than one related adverse event are counted only once. Summary includes all related events (i.e., "Possibly Related," "Probably Related," or "Definitely Related" to study drug).

[1] Adverse events are coded to preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Note: Sort events by descending order of preferred term incidence, based on the overall incidence (i.e., sum over all treatment groups

Brickell Biotech, Inc.
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Table 14.3.1.5
Treatment-Emergent Adverse Events by Severity, System Organ Class, and Preferred Term
Safety Population

System Organ Class / Preferred Term[1]	Vehicle (N=)			BBI-4000 5% (N=)			BBI-4000 10% (N=)			BBI-4000 15% (N=)		
	Mild	Moderate	Severe	Mild	Moderate	Severe	Mild	Moderate	Severe	Mild	Moderate	Severe
Subjects Reporting at Least One Adverse Event	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
System Organ Class #1												
Preferred Term #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
…	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
System Organ Class #2												
Preferred Term #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
…	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)

Note: At each level of summarization (any event, system organ class, and preferred term), subjects reporting more than one adverse event are counted only once using the highest severity.

[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Note: Sort events by descending order of system organ class incidence, and preferred term incidence within system organ class, based on the overall incidence (ie, sum over all severity grades and treatment groups).

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Table 14.3.1.6
Treatment-Emergent Adverse Events Related to Study Drug by Severity, System Organ Class, and Preferred Term
Safety Population

System Organ Class / Preferred Term[1]	Vehicle (N=)			BBI-4000 5% (N=)			BBI-4000 10% (N=)			BBI-4000 15% (N=)		
	Mild	Moderate	Severe	Mild	Moderate	Severe	Mild	Moderate	Severe	Mild	Moderate	Severe
Subject Reporting at Least One Adverse Event	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
System Organ Class #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
…												
System Organ Class #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
…												

Note: At each level of summarization (any event, system organ class, and preferred term), subjects reporting more than one related are counted only once using the highest severity. Related adverse events are those reported as "Possibly Related," "Probably Related," or "Definitely Related" to study drug.

[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Note: Sort events by descending order of system organ class incidence and by descending order of preferred term incidence within system organ class, based on the overall incidence (i.e., sum over all treatment groups).

Table 14.3.1.7
Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class / Preferred Term[1]	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)
Subject Reporting at Least One Serious Adverse Event	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
System Organ Class #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
…				
System Organ Class #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
…				

Note: At each level of summarization (any event, system organ class, and preferred term), subjects reporting more than one serious adverse event are counted only once.

[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Note: Sort events by descending order of system organ class incidence and by descending order of preferred term incidence within system organ class, based on the overall incidence (i.e., sum over all treatment groups).

Table 14.3.1.8
Treatment-Emergent Serious Adverse Events Related to Study Drug by Preferred Term
Safety Population

Preferred Term[1]	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)
Preferred Term #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Preferred Term #3	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
…				

Note: Subjects reporting more than one related adverse event are counted only once. Summary includes all related events (i.e., "Possibly Related," "Probably Related," or "Definitely Related" to study drug).

[1] Adverse events are coded to preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Note: Sort events by descending order of preferred term incidence, based on the overall incidence (i.e., sum over all treatment groups

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Table 14.3.1.9
Local Tolerability Assessments – Subject Assessments
Safety Population

		Vehicle (N=) Baseline Assessment[1]						BBI-4000 5% (N=) Baseline Assessment[1]					
Parameter	Visit	Absent	Minimal	Mild	Moderate	Severe	Missing	Absent	Minimal	Mild	Moderate	Severe	Missing
Itching	Day 8	(n=)						(n=)					
	Absent	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Mild	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Moderate	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Severe	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Missing	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	…												

Abbreviation: ET, early termination

Notes:
- Tolerability is assessed on a 5-point scale where 0= Absent, 1= Minimal, 2= Mild, 3= Moderate, 4= Severe.
- Subjects self-evaluate Itching and Burning for each axilla prior to the Investigator's evaluation.
- Maximum severity assessed for either axilla is reported.

[1] Baseline is defined as the last available measurement taken prior to the first dose of study drug.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Note: Continue for Days 15, 22, 29, 36, 43, and 57, parameter Burning, for all BBI-4000 doses (10%, 15%).

Table 14.3.1.10
Local Tolerability Assessments – Investigator Assessments
Safety Population

		Vehicle (N=)					BBI-4000 5% (N=)				
		Baseline Assessment[1]					Baseline Assessment[1]				
Parameter	Visit	Absent	Mild	Moderate	Severe	Missing	Absent	Mild	Moderate	Severe	Missing
Dryness	Day 8	(n=)					(n=)				
	Absent	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Mild	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Moderate	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Severe	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	Missing	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
	…										

Abbreviation: ET, early termination

Notes:
- Tolerability is assessed on a 5-point scale where 0= Absent, 1= Minimal, 2= Mild, 3= Moderate, 5= Severe.
- Investigators evaluate Dryness, Scaling, and Erythema for each axilla after the Subject's evaluation.
- Maximum severity assessed at either axilla is reported.

[1] Baseline is defined as the last available measurement taken prior to the first dose of study drug.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Note: Continue for Days 15, 22, 29, 36, 43, and 57, parameters Scaling and Erythema, and BBI-4000 doses (10%, 15%)

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Table 14.3.2.1
Listing of Deaths
Safety Population

Subject ID	Treatment Group	Date of Death (Study Day[1])	Cause of Death
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	ddMMMyyyy (xx)	*Adverse event or cause of death from the study exit form*
xxx-xxxx			
…			

[1] Time (days) relative to date of first dose of study drug

Path\filename.sas ddmmmyyyy hh:mm

Table 14.3.2.2
Listing of Serious Adverse Events
Safety Population

Subject ID	Treatment Group	System Organ Class[1] / Preferred Term[1] / Event Name	In the Treatment Area?	Start Date (Study Day[2])	End Date (Study Day[2])	Serious Criteria	Severity	Relationship to Study Drug	Action Taken with Study Treatment	Action Taken to Treat Event	Outcome
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	*System Organ Class / Preferred Term / Event Name*	Yes / No	ddMMMyyyy (xx)	ddMMMyyyy (xx) / Ongoing	Congenital Anomaly or Birth Defect / Persistent or significant Disability / Death / Inpatient or Prolonged Hospitalization / Life Threatening / Other Serious or Important Medical Event *Display all that are reported, separated by a comma*	Mild / Moderate / Severe	Not Related / Unlikely Related / Possibly Related / Related	None / Drug Interrupted / Drug Reduced / Drug Interrupted / Drug Withdrawn / Not Applicable / Unknown / *Display all that are reported, separated by a comma*	None / Medication / Procedure or Therapy / Hospitalization / Discontinued from Study / Other / Unknown *Display all that are reported, separated by a comma*	Fatal / Not Recovered/Not Resolved/ Recovered/Resolved/ Recovered/Resolved with Sequelae / Recovering/Resolving/ Unknown
		…									
xxx-xxxx											
…											

[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.
[2] Time (days) relative to date of first dose of study drug

Path\filename.sas ddmmmyyyy hh:mm

Table 14.3.2.3
Listing of Adverse Events Leading to Study Drug Discontinuation, Reduction or Interruption
Safety Population

Subject ID	Treatment Group	System Organ Class[1] / Preferred Term[1] / Event Name	In the Treatment Area?	Start Date (Study Day[2])	End Date (Study Day[2])	Serious	Severity	Relationship to Study Drug	Action Taken with Study Treatment	Action Taken to Treat Event	Outcome
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10%/ BBI-4000 15%	*System Organ Class / Preferred Term / Event Name*	Yes / No	ddMMMyyyy (xx)	ddMMMyyyy (xx) / Ongoing	Yes / No	Mild / Moderate / Severe	Not Related / Unlikely Related / Possibly Related / Related	None / Drug Interrupted / Drug Reduced / Drug Interrupted / Drug Withdrawn / Not Applicable / Unknown / *Display all that are reported, separated by a comma*	None / Medication / Procedure or Therapy / Hospitalization / Discontinued from Study / Other / Unknown *Display all that are reported, separated by a comma*	Fatal / Not Recovered/Not Resolved/ Recovered/Resolved // Recovered/Resolved with Sequelae / Recovering/Resolving/ Unknown
		…									
xxx-xxxx											
…											

Note: Summary includes all adverse events where action taken is reported as “dose reduced,” “drug interrupted,” or “drug withdrawn.”

[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.
[2] Time (days) relative to date of first dose of study drug

Path\filename.sas ddmmmyyyy hh:mm

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BBI-4000-CL-203

Table 14.3.4.1
Listing of Abnormal Hematology Values
Safety Population

Subject ID	Treatment Group	Visit	Collection Date (Study Day[1])	Test	Unit	Normal Range	Result	Alert	Clinically Significant
xxx-xxxx	Vehicle / BBI-4000 5%/ BBI-4000 10% / BBI-4000 15%	Screening	ddMMMyyyy (xx)	*Test #1*	*Unit*	xxx – xxx	xxx	Low / High	Yes / *null*
				Test #2					
				…					
		Day 43							
xxx-xxxx									
…									

[1] Time (days) relative to date of first dose of study drug

Path\filename.sas ddmmmyyyy hh:mm

Programming Notes:

- *Repeat as Table 14.3.4.2* *Listing of Abnormal Chemistry Values (Safety Population)*
- *Repeat as Table 14.3.4.3* *Listing of Abnormal Urinalysis Values (Safety Population)*

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Table 14.3.5.1
Extent of Exposure
Safety Population

	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)
Duration of Exposure (days)[1]				
n	n	n	n	n
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x	x	x	x
Min, Max	x, x	x, x	x, x	x, x

[1] Duration of exposure to study treatment is calculated as the date of last dose of study drug – the date of first dose of study drug + 1.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Table 14.3.5.2
Study Drug Compliance
Safety Population

Study Drug Compliance (%)[1]	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)
n	n	n	n	n
Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
Median	x	x	x	x
Min, Max	x, x	x, x	x, x	x, x
< 80% Compliant	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
≥ 80% Compliant	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)

[1] Study drug compliance is calculated as the number of doses received / the expected number of doses x 100.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

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Table 14.3.6.1
Hematology – Univariate Summary by Parameter and Visit
Safety Population

Parameter	Visit	Vehicle (N=) Observed Value	Vehicle (N=) Change from Baseline	BBI-4000 5% (N=) Observed Value	BBI-4000 5% (N=) Change from Baseline	BBI-4000 10% (N=) Observed Value	BBI-4000 10% (N=) Change from baseline	BBI-4000 15% (N=) Observed Value	BBI-4000 15% (N=) Change from Baseline
RBC Count (10^{12}/L)	Baseline[1]								
	n	n		n		n		n	
	Mean (SD)	x.x (x.xx)		x.x (x.xx)		x.x (x.xx)		x.x (x.xx)	
	Median	x		x		x		x	
	Min, Max	x, x		x, x		x, x		x, x	
	Day 43								
	n	n	n	n	n	n	n	n	n
	Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
	Median	x	x	x	x	x	x	x	x
	Min, Max	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x
	…								
Hematocrit (L/L)									
…									

Abbreviations: ET, early termination; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; RBC, red blood cell; WBC, white blood cell

[1] Baseline is defined as the last available measurement taken prior to the first dose of study drug.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Notes: Continue for regularly-collected hematology parameters: Hemoglobin (g/L), MCH (pg), MCHC (g/L), MCV (fL), Platelet Count (10^9/L), WBC Count (10^9/L), Reticulocyte Count (10^9/L) Neutrophils (%), Lymphocytes (%), Monocytes (%), Eosinophils (%), Basophils (%).

Table 14.3.6.2
Hematology – Shift from Baseline to Worst Post-Baseline Value by Parameter
Safety Population

Parameter Worst Post-Baseline Assessment[2]	Vehicle (N=) Baseline Assessment[1] Low	 Normal	 High	BBI-4000 5% (N=) Baseline Assessment[1] Low	 Normal	 High	BBI-4000 10% (N=) Baseline Assessment[1] Low	 Normal	 High	BBI-4000 15% (N=) Baseline Assessment[1] Low	 Normal	 High
RBC Count		(n=)			(n=)			(n=)			(n=)	
Low	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Normal	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
High	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Hematocrit		(n=)			(n=)			(n=)			(n=)	
Low	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Normal	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
High	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Hemoglobin												
…												

Abbreviations: MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; RBC, red blood cell; WBC, white blood cell

Note: Percentages are based on the number of subjects with a non-missing baseline value and at least one non-missing post-baseline value (n=).

[1] Baseline is defined as the last available measurement taken prior to the first dose of study drug.
[2] The worst post-baseline assessment is defined as the value numerically farthest outside the normal range across all post-baseline visits through the end of the study.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Note: Continue for regularly-collected hematology parameters: (MCH, MCHC, MCV, Platelet Count, WBC Count, Reticulocyte Count, Neutrophils, Lymphocytes Monocytes, Eosinophils, Basophils

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Table 14.3.6.3
Chemistry – Univariate Summary by Parameter and Visit
Safety Population

		Vehicle (N=)		BBI-4000 5% (N=)		BBI-4000 10% (N=)		BBI-4000 15% (N=)	
Parameter	Visit	Observed Value	Change from Baseline	Observed Value	Change from Baseline	Observed Value	Change from Baseline	Observed Value	Change from Baseline
AST (SGOT) (U/L)	Baseline[1]								
	n	n		n		n		n	
	Mean (SD)	x.x (x.xx)		x.x (x.xx)		x.x (x.xx)		x.x (x.xx)	
	Median	x		x		x		x	
	Min, Max	x, x		x, x		x, x		x, x	
	Day 43								
	n	n	n	n	n	n	n	n	n
	Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
	Median	x	x	x	x	x	x	x	x
	Min, Max	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x
ALT (SGPT) (U/L)									
…									

Abbreviations: ALT (SGPT), alanine aminotransferase; AST (SGOT), aspartate aminotransferase; BUN, blood urea nitrogen; GGT, gamma glutamyl transferase

[1] Baseline is defined as the last available measurement taken prior to the first dose of study drug.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Notes: Continue for regularly-collected chemistry parameters: Alkaline Phosphatase (U/L), Total Bilirubin (µmol/L), Direct Bilirubin (µmol/L), GGT (µmol/L), BUN (mmol/L), Creatinine (µmol/L), Sodium (mmol/L), Potassium (mmol/L), Chloride (mmol/L).

Table 14.3.6.4
Chemistry – Shift from Baseline to Worst Post-Baseline Value by Parameter
Safety Population

Parameter / Worst Post-Baseline Assessment[2]	Vehicle (N=) Baseline Assessment[1]			BBI-4000 5% (N=) Baseline Assessment[1]			BBI-4000 10% (N=) Baseline Assessment[1]			BBI-4000 15% (N=) Baseline Assessment[1]		
	Low	Normal	High	Low	Normal	High	Low	Normal	High	Low	Normal	High
AST (SGOT)												
Low	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Normal	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
High	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
ALT (SGPT)												
Low	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Normal	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
High	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Alkaline Phosphatase												
…												

Abbreviations: ALT (SGPT), alanine aminotransferase; AST (SGOT), aspartate aminotransferase; BUN, blood urea nitrogen; GGT, gamma glutamyl transferase

Note: Percentages are based on the number of subjects with a non-missing baseline value and at least one non-missing post-baseline value.

[1] Baseline is defined as the last available measurement taken prior to the first dose of study drug.
[2] The worst post-baseline assessment is defined as the value numerically farthest outside the normal range across all post-baseline visits through the end of the study.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Notes: Continue for regularly-collected chemistry parameters: Total Bilirubin, Direct Bilirubin, GGT, Albumin, Total Protein, BUN, Creatinine, Sodium, Potassium, Chloride

Table 14.3.7.1
Vital Signs – Univariate Summary by Parameter and Visit
Safety Population

		Vehicle (N=)		BBI-4000 5% (N=)		BBI-4000 10% (N=)		BBI-4000 15% (N=)	
Vital Sign	Visit	Observed Value	Change from Baseline	Observed Value	Change from Baseline	Observed Value	Change from Baseline	Observed Value	Change from Baseline
Systolic Blood Pressure (mmHg)	Baseline[1]								
	n	n		n		n		n	
	Mean (SD)	x.x (x.xx)		x.x (x.xx)		x.x (x.xx)		x.x (x.xx)	
	Median	x		x		x		x	
	Min, Max	x, x		x, x		x, x		x, x	
	Day 8								
	n	n	n	n	n	n	n	n	n
	Mean (SD)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)	x.x (x.xx)
	Median	x	x	x	x	x	x	x	x
	Min, Max	x, x	x, x	x, x	x, x	x, x	x, x	x, x	x, x
	Day 15								
	…								
Diastolic Blood Pressure (mmHg)									
…									

[1] Baseline is defined as the last available measurement taken prior to the first dose of study drug.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Notes:

- *Continue for remaining regularly-scheduled visits (Days 22, 29, 36, 43, and 57)*
- *Continue for regularly-collected vital signs : Heart Rate (beats/minute), Respiratory Rate (breaths/minute), and Temperature (C^o)*

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Table 14.3.7.2
Concomitant Medications
Safety Population

ATC Class / Generic Drug Name	Vehicle (N=)	BBI-4000 5% (N=)	BBI-4000 10% (N=)	BBI-4000 15% (N=)
Subjects Receiving any Concomitant Medications	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
ATC Class #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Generic Drug Name #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Generic Drug Name #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
…				
ATC Class #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Generic Drug Name #1	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
Generic Drug Name #2	n (x.x%)	n (x.x%)	n (x.x%)	n (x.x%)
…				

Abbreviations: ATC, anatomic therapeutic chemical, WHO, World Health Organization

Notes:
- Concomitant medications are those medications received on or after the first dose of study drug.
- Medications are coded to ATC drug class (level 4) and generic drug names using the WHO Drug dictionary enhanced, version B2 March 1, 2016.
- At each level of summarization (any medication, ATC class, generic drug name), subjects reporting use of more than one medication are counted only once.

Reference: *Listing #(s)*
Path\filename.sas ddmmmyyyy hh:mm

Programming Note:
- *Sort medications by descending order of ATC class incidence and by descending order of drug name incidence within ATC class, based on the overall incidence (ie, sum over all treatment groups).*
- *When creating ATC level 4 drug class, utilize level 3 term if level 4 is missing in dataset and level 2 if both level 3 and level 4 are missing in the dataset*
- *Repeat as Table 14.3.7.3 Concomitant Therapies and Procedures, using (MedDRA), version 19.1 for SOC and PT.*

APPENDIX C: LISTING LAYOUTS

Listing 16.1.7
Randomization Scheme and Codes

Subject ID	Randomization Number	Treatment Group Code	Treatment Group	Treatment Group Description
xxx-xxxx	xxxx	A /	Vehicle /	Vehicle gel /
		B /	BBI-4000 5% /	5% BBI-4000 in vehicle gel /
		C /	BBI-4000 10% /	10% BBI-4000 in vehicle gel /
		D	BBI-4000 15%	15% BBI-4000 in vehicle gel
xxx-xxxx				
…				

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Listing 16.2.1
Subject Disposition

Subject ID	Treatment Group	Safety Population[1]	mITT Population[2]	PP Population[3]	Date of First Dose	Study Exit Date (Study Day[4])	Complete Treatment?	Reason Subject Did Not Complete Treatment	Complete Study?	Primary Reason for Early Termination
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Yes / No	Yes / No	Yes / No	ddMMMyyyy	ddMMMyyyy (xx)	Yes / No	Adverse Event / Withdrawal by Subject / Physician Decision / Protocol Violation / Lost to Follow-Up / Death / Pregnancy / Worsening Condition / Lack of Efficacy / Study Termination by Sponsor / Other	Yes / No	Normal Study Completion / Adverse Event / Withdrawal by Subject / Physician Decision / Protocol Violation / Lost to Follow-Up / Death / Pregnancy / Worsening Condition / Lack of Efficacy / Study Termination by Sponsor / Other
xxx-xxxx										
…										

Abbreviations: mITT, Intent-to-Treat; PP, Per-Protocol

[1] Safety population includes all subjects randomized in the study who received study drug at least once. Treatment group assignment is based on the treatment actually received.
[2] mITT population includes all subjects who were randomized and dispensed study drug. Treatment group assignment is based on the planned treatment assigned.
[3] PP population includes all Safety subjects who meet all inclusion/exclusion criteria, have not taken/applied prohibited concomitant medications, and have full data collected for all GSP visits.
[4] Time (days) relative to date of first dose of study drug

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Listing 16.2.2.1
Protocol Violations/Deviations

Subject ID	Treatment Group	Date of Deviation (Study Day[1])	Major Protocol Violation?	Deviation/Violation Category	Reason for Deviation/Violation	Date of Sponsor Approval
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	ddMMMyyyy (xx)	Yes / No	*Category*	*Deviation*	ddMMMyyyy
xxx-xxxx						
…						

[1] Time (days) relative to date of first dose of study drug

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Listing 16.2.2.2
Informed Consent and Eligibility Criteria

Subject ID	Treatment Group	Subject Sign Informed Consent?	Date Informed Consent Signed	Time Informed Consent Signed	Protocol Version	Does subject meet all eligibility criteria?	If No, Criterion Not Met	Inclusion/Exclusion Criteria Waivers: Was Waiver Granted?	Inclusion/Exclusion Criteria Waivers: Date of Waiver	Inclusion/Exclusion Criteria Waivers: Who Granted the Waiver?
xx-xxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Yes / No	ddMMMyyyy	hh:mm	Original November 22, 2016 / Version 1 22FEB2017	Yes / No	Inclusion # / Exclusion #	Yes / No	ddMMMyyyy	*Text*
							Inclusion # / Exclusion #	Yes / No	ddMMMyyyy	*Text*
							…			
xx-xxx										
…										

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Listing 16.2.3
Subjects Excluded from the Efficacy Analysis

Subject ID	Treatment Group	mITT Population[1]	PP Population[2]	Reason for Exclusion from the Efficacy Analysis
xx-xxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Yes / No	Yes / No	*Reason (e.g., screen failure, subject did not receive study drug, protocol violation, etc.), including any relevant specifications*
xx-xxx				
…				

Abbreviations: mITT, Intent-to-Treat; PP, Per-Protocol

[1] mITT population includes all subjects who were randomized and dispensed study drug. Treatment group assignment is based on the planned treatment assigned.
[2] PP population includes all Safety subjects who meet all inclusion/exclusion criteria, have not taken/applied prohibited concomitant medications, and have full data collected for all GSP visits.

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Listing 16.2.4.1
Demographics

Subject ID	Treatment Group	Date of Birth	Age (years)	Sex	If Female, is subject of childbearing potential?	Ethnicity	Race
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	ddMMMyyyy	xx	Male / Female	Yes / No	Hispanic or Latino / Not Hispanic or Latino	American Indian or Alaska Native / Asian / Black or African American / Native Hawaiian or Other Pacific Islander / White / Other
xxx-xxxx …							

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Programming Note: If multiple races are reported for a given subject, display all that are reported in the "Race" column, separated by a semicolon.

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Listing 16.2.4.2
Medical History

Subject ID	Treatment Group	System Organ Class[1]	Condition	Onset Date	Resolution Date
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	*Body System*	*Condition / Diagnosis / Surgery*	ddMMMyyyy	ddMMMyyyy / Ongoing
		Body System			
		…			
xxx-xxxx					
…					

[1] Medical history events are coded to system organ class using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.

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Programming Note: Sort conditions based on onset date. If partial onset dates are reported (e.g., month and year only), separate out the portions of the date to sort separately by year, then month, then day.

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Listing 16.2.5.1
Study Drug Dosing

Subject ID	Treatment Group	Start of Study Drug Administration	End of Study Drug Administration (Study Day[1])	Any Application Deviations?	Deviation Start Date (Study Day[1])	Deviation End Date (Study Day[1])	Deviation Type	Axilla	Reason for Deviation
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	ddMMMyyyy	ddMMMyyyy (xx)	Yes / No / Unknown	ddMMMyyyy (xx)	ddMMMyyyy (xx)	Missed / Other (*specify*)	Right / Left / Both	Adverse Event / Other *(specify)*
xxx-xxxx	…								

[1] Time (days) relative to date of first dose of study drug

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Listing 16.2.5.2
Study Drug Administration and Accountability

Subject ID	Treatment Group	Pump Container	Pump Dispensed?	If No, Specify	Date Dispensed (Study Day[1])	Kit #	Dispensed Weight (g)	Pump Returned?	If No, Specify	Date Returned (Study Day[1])	Returned Weight (g)
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	1	Yes / No	*text*	ddMMMyyyy (xx)	xxxx	xx.x	Yes / No	*text*	ddMMMyyyy (xx)	xx.x
		2									
xxx-xxxx	…										

[1] Time (days) relative to date of first dose of study drug

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Listing 16.2.5.3
Study Drug Exposure and Compliance

Subject ID	Treatment Group	Expected Number of Doses	Actual Number of Doses	Study Drug Compliance (%)[1]	Duration of Exposure (Days)[2]	Total Drug Delivered (g)[3]
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	xx	xx	xx.x	ddMMMyyyy (xx)	xxxx
xxx-xxxx	…					

[1] Study drug compliance is calculated as the number of doses received / the expected number of doses x 100
[2]Duration of exposure to study treatment is calculated as the date of last dose of study drug – the date of first dose of study drug + 1.
[3] Total drug delivered is calculated as total grams dispensed – total grams returned.

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Listing 16.2.6.1
Hyperhidrosis Disease Severity Measure-Axilla
Part 1 of 2

Question Number	Question Text	Responses
1a	Since you woke up yesterday, how often did you experience damp or wet clothing because of your underarm sweating while you were awake?	0-None of the time 1-Almost none of the time, 2-Some of the time, 3-Most of the time 4-All of the time
1b	Since you woke up yesterday, how often did you experience underarm sweating for no apparent reason while you were awake?	0-None of the time 1-Almost none of the time, 2-Some of the time, 3-Most of the time 4-All of the time
2a	Since you woke up yesterday, how severe was your experience with underarm sweating when you felt nervous, stressed or anxious?	0-I did not experience this 1-Mild 2-Moderate 3-Severe 4-Very severe
2b	Since you woke up yesterday, how severe was your experience with damp or wet clothing because of your underarm sweating?	0-I did not experience this 1-Mild 2-Moderate 3-Severe 4-Very severe

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Programming Note: Listing continues on next page

Listing 16.2.6.1
Hyperhidrosis Disease Severity Measure-Axilla
Part 1 of 2

Question Number	Question Text	Responses
2c	Since you woke up yesterday, how severe was your experience with underarm sweating after almost none or no physical exercise?	0-I did not experience this 1-Mild 2-Moderate 3-Severe 4-Very severe
2d	Since you woke up yesterday, how severe was your experience with underarm wetness?	0-I did not experience this 1-Mild 2-Moderate 3-Severe 4-Very severe
2e	Since you woke up yesterday, how severe was your experience with underarm sweating for no apparent reason?	0-I did not experience this 1-Mild 2-Moderate 3-Severe 4-Very severe
2f	Since you woke up yesterday, how severe was your experience with underarm sweating that was unmanageable?	0-I did not experience this 1-Mild 2-Moderate 3-Severe 4-Very severe

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Programming note: Listing continues on next page.

Listing 16.2.6.1
Hyperhidrosis Disease Severity Measure-Axilla
Part 1 of 2

Question Number	Question Text	Responses
2g	Since you woke up yesterday, how severe was your experience with underarm sweating when you were cool?	0-I did not experience this 1-Mild 2-Moderate 3-Severe 4-Very severe
3a	Since you woke up yesterday, describe your feeling the need to change clothes because of underarm sweating?	0-Not at all 1-Slight, 2-Moderate 3-Strong 4-Very strong
3b	Since you woke up yesterday, describe your feeling the need to wipe sweat from your underarms?	0-Not at all 1-Slight, 2-Moderate 3-Strong 4-Very strong

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Programming note: Listing continues on next page.

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Listing 16.2.6.1
Hyperhidrosis Disease Severity Measure-Axilla
Part 1 of 2

Question Number	Question Text	Responses
4	Since you woke up yesterday, how much of the time did you experience excessive underarm sweating while you were awake?	0-None of the time 1-Almost none of the time 2-Some of the time 3-Most of the time 4-All of the time
5	How severe was your underarm sweating at its worst since you woke up yesterday?	0-I did not have underarm sweating (completely dry) 1-I had underarm sweating but it was mild (moist) 2-I had underarm sweating and it was moderate (damp) 3-I had underarm sweating and it was severe (wet) 4-I had underarm sweating and it was very severe (soaking)
6	How normal was your level of physical exercise and stress since you woke up yesterday? choose all that apply:	It was a normal day in terms of physical exercise or stress. I experienced more physical exercise than usual. I experienced more nervousness, stress, or anxiety than usual. I experienced less physical exercise than usual. I experienced less nervousness, stress, or anxiety than usual.

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Listing 16.2.6.1
Hyperhidrosis Disease Severity Measure-Axilla
Part 2 of 2

Subject ID	Treatment Group	Visit	HDSM-Ax Completed?	Assessment Date (Study Day[1])	HDSM-Ax Scoring Questions														
					1a	1b	2a	2b	2c	2d	2e	2f	2g	3a	3b	Mean[2]	4	5	6
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Visit 1 (Screening)	Yes / No	ddMMMyyyy (xx)	0-4	0-4	0-4	0-4	0-4	0-4	0-4	0-4	0-4	0-4	0-4	0-4	0-4	0-4	*text*
		Visit 4 (Rescreening)																	
		…																	
xxx-xxxx																			

Abbreviation: HDSM-Ax, Hyperhidrosis Disease Severity Measure-Axilla

Note: Questions Q1a-Q5 specify one response per question; Q6 may respond with all that apply.

[1] Time (days) relative to date of first dose of study drug
[2] Mean is calculated as the total score for questions 1 through 3 (11 sub-items) divided by the number of questions answered. Subjects must answer at least 6 of 11 sub-items to be evaluable.
[3] Baseline is defined as the last available measurement taken prior to the first dose of study drug.

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Programming note: Continue for Baseline [3], Days 8, 15, 22, 29, 36, 41, 42, 43, 57

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Listing 16.2.6.2
Gravimetric Sweat Production Measurements

					Right Axilla				Left Axilla				
Subject ID	Treatment Group	Visit	Gravimetric Assessment Performed?	Assessment Date (Study Day[1])	Pre-test Weight	Start Time	End Time	Post-test Weight	Pre-test Weight	Start Time	End Time	Post-test Weight	Total Sweat Weight[2]
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Visit 1 (Screening)	Yes / No		xx.x	hh:mm	hh:mm	xx.x	xx.x	hh:mm	hh:mm	xx.x	xx.x
		Visit 2 (GSP1)	…										
xxx-xxxx													
…													

Abbreviation: GSP, gravimetrically measured sweat production

[1] Time (days) relative to date of first dose of study drug
[2] Total sweat weight is the sum of the post-test weights from the right axilla and left axilla.
[3] Baseline is defined as the last available measurement taken prior to the first dose of study drug.

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Programming note: Continue for Visits 3 and 4, Baseline[3], and Days 8, 15, 22, 29, 36, 41, 42, 43, 57

Listing 16.2.6.3
Hyperhidrosis Disease Severity Scale

Subject ID	Treatment Group	Visit	Date of Assessment (Study Day[1])	How would you rate the severity of your axillary hyperhidrosis?
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Visit 1 (Screening)	ddMMMyyyy (xx)	(1) My sweating is never noticeable and never interferes with my daily activities / (2) My sweating is tolerable but sometimes interferes with my daily activities / (3) My sweating is barely tolerable and frequently interferes with my daily activities / (4) My sweating is intolerable and always interferes with my daily activities
		Visit 4 (Rescreening)		
		…		
xxx-xxxx	…			

[1] Time (days) relative to date of first dose of study drug
[2] Baseline is defined as the last available measurement taken prior to the first dose of study drug.

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Programming note: Continue for Visits 3 and 4, Baseline[2], and Days 8, 15, 22, 29, 36, 41, 42, 43, 57

Listing 16.2.6.4
Dermatology Life Quality Index- Axilla
Part 1 of 2

Question Number	Question Text	Responses
1	Over the last week, how itchy, sore, painful or stinging has your underarm skin been?	Very much A lot Almost none Not at all
2	Over the last week, how embarrassed or self-conscious have you been because of your underarm sweating?	Very much A lot Almost none Not at all
3	Over the last week, how much has your underarm sweating interfered with you going shopping or looking after your home or garden?	Very much A lot Almost none Not at all
4	Over the last week, how much has your underarm sweating influenced the clothes you wear?	Very much A lot Almost none Not at all Not relevant

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Programming note: Listing continues on next page.

Listing 16.2.6.4
Dermatology Life Quality Index- Axilla
Part 1 of 2

Question Number	Question Text	Responses
5	Over the last affected any social or leisure week, how much has your underarm sweating activities?	Very much A lot Almost none Not at all Not relevant
6	Over the last week, how much has your underarm sweating made it difficult for you to do any sport?	Very much A lot Almost none Not at all Not relevant
7	Over the last week, has your underarm sweating prevented you from working or studying?	Very much A lot Almost none Not at all Not relevant
	If "No", over the last week how much has your underarm sweating been a problem at work or studying?	A lot Almost none Not at all
8	Over the last week, how much has your underarm sweating created problems with your partner or any of your close friends or relatives?	Very much A lot Almost none Not at all Not relevant

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Programming note: Listing continues on next page.

Listing 16.2.6.4
Dermatology Life Quality Index- Axilla
Part 1 of 2

Question Number	Question Text	Responses
9	Over the last week, how much has your underarm sweating caused any sexual difficulties?	Very much A lot Almost none Not at all Not relevant
10	Over the last week, how much of a problem has the treatment for your underarm sweating been, for example by making your home messy, or by taking up time?	Very much A lot Almost none Not at all Not relevant

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Listing 16.2.6.4
Dermatology Life Quality Index
Part 2 of 2

Subject ID	Treatment Group	Visit	DLQI Completed?	Assessment Date (Study Day[1])	Question Number 1	2	3	4	5	6	7	8	9	10	Total Score
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Visit 4 (Rescreening) Day 43	Yes / No	ddMMMyyyy (xx)	0-3	0-3	0-3	0-3	0-3	0-3	0-3	0-3	0-3	0-3	0-30
		…													
xxx-xxxx															

Abbreviation: DLQI, Dermatology Life Quality Index-Axilla

Note: DLQI Total Score is calculated by summing the replies to Questions 1 through 10.

[1] Time (days) relative to date of first dose of study drug

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Listing 16.2.7.1
Adverse Events

Subject ID	Treatment Group	System Organ Class[1] / Preferred Term[1] / Event Name	In the Treatment Area?	Start Date (Study Day[2])	End Date (Study Day[2])	Serious	Severity	Relationship to Study Drug	Action Taken with Study Treatment	Action Taken to Treat Event	Outcome
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	*System Organ Class / Preferred Term / Event Name*	Yes / No	ddMMMyyyy (xx)	ddMMMyyyy (xx) / Ongoing	Yes / No	Mild / Moderate / Severe	Not Related / Unlikely Related / Possibly Related / Related	None / Drug Interrupted / Drug Reduced / Drug Interrupted / Drug Withdrawn / Not Applicable / Unknown / *Display all that are reported, separated by a comma*	None / Medication / Procedure or Therapy / Hospitalization / Discontinued from Study / Other / Unknown *Display all that are reported, separated by a comma*	Fatal / Not Recovered/Not Resolved/ Recovered/Resolved / Recovered/Resolved with Sequelae / Recovering/Resolving/ Unknown
		…									
xxx-xxxx …											

[1] Adverse events are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.
[2] Time (days) relative to date of first dose of study drug

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Brickell Biotech, Inc.
BBI-4000-CL-203

Listing 16.2.7.2
Local Tolerability Assessments – Subject Assessments

Subject ID	Treatment Group	Visit	Assessment Performed?	Visit Date (Study Day[1])	Right Axilla		Left Axilla	
					Itching	Burning	Itching	Burning
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-400 15%	Baseline [2]	Yes / No	ddMMMyyyy (xx)	0-4	0-4	0-4	0-4
		Day 8						
		Day 15						
		Day 22						
		Day 29						
		Day 36						
		Day 43						
		Day 57						
		Day 8						
xxx-xxxx		…						

Note: Subjects self-evaluate Itching and Burning for each axilla prior to the Investigator's evaluation.

[1] Time (days) relative to date of first dose of study drug
[2] Baseline is defined as the last available measurement taken prior to the first dose of study drug.

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Brickell Biotech, Inc.
BBI-4000-CL-203

Listing 16.2.7.3
Local Tolerability Assessments – Investigator Assessments

Subject ID	Treatment Group	Visit	Assessment Performed?	Visit Date (Study Day[1])	Right Axilla			Left Axilla		
					Dryness	Scaling	Erythema	Dryness	Scaling	Erythema
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Baseline [2]	Yes / No	ddMMMyyyy (xx)	0-4	0-4	0-4	0-4	0-4	0-4
		Day 8								
		Day 15								
		Day 22								
		Day 29								
		Day 36								
		Day 43								
		Day 57								
xxx-xxxx		…								

Note: Investigator evaluates Dryness, Scaling, and Erythema for each axilla after subject's evaluation.

[1] Time (days) relative to date of first dose of study drug
[2] Baseline is defined as the last available measurement taken prior to the first dose of study drug.

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Brickell Biotech, Inc.
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Listing 16.2.8.1
Hematology
Part 1 of 3

Subject ID	Treatment Group	Visit	Collection Date (Study Day[1])	Collection Time	RBC Count (10^{12}/L)	Hematocrit (L/L)	Hemoglobin (g/L)	MCH (pg)	MCHC (g/L)	MCV (fL)	Platelet Count (10^{9}/L)
xxx-xxxx	Vehicle / BBI-4000 5%/ BBI-4000 10% / BBI-4000 15%	Screening	ddMMMyyyy (xx)	HH:MM	x.x *CS, H/L*	x.x *CS, H/L*	x.x *CS, H/L*	x.x *CS, H/L*	x.x *CS, H/L*	x.x *CS, H/L*	x.x *CS, H/L*
		Day 43									
xxx-xxxx											
…											

Abbreviations: CS, clinically significant; H, high; L, low; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; RBC, red blood cell

Note: H = high; L = low is displayed if result is outside the reference range.

[1] Time (days) relative to date of first dose of study drug

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Brickell Biotech, Inc.
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Listing 16.2.8.1
Hematology
Part 2 of 3

Subject ID	Treatment Group	Visit	Collection Date (Study Day[1])	Collection Time	WBC Count (10^9/L)	Reticulocyte Count (10^9/L)	Neutrophils (%)	Lymphocytes (%)	Monocytes (%)	Eosinophils (%)	Basophils (%)
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Screening	ddMMMyyyy (xx)	HH:MM	x.x *CS, H/L*	x.x *CS, H/L*	x.x *CS, H/L*	x.x *CS, H/L*	x.x *CS, H/L*	x.x *CS, H/L*	x.x *CS, H/L*
		Day 43									
xxx-xxxx											
…											

Abbreviations: CS, clinically significant; H, high; L, low; WBC, white blood cell

Note: H = high; L = low is displayed if result is outside the reference range.

[1] Time (days) relative to date of first dose of study drug

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Brickell Biotech, Inc.
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Listing 16.2.8.1
Hematology
Part 3 of 3

Subject ID	Treatment Group	Visit	Collection Date (Study Day[1])	Collection Time	Test	Unit	Result	Alert	Clinically Significant
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Screening	ddMMMyyyy (xx)	HH:MM	*Test Name #1*	Unit	xxx	High / Low	Yes / *null*
		Day 43			*Test Name #2* *Test Name #3* …				
xxx-xxxx …									

[1] Time (days) relative to date of first dose of study drug

Path\filename.sas ddmmmyyyy hh:mm

Programming Note: Only those tests that are collected as part of the hematology panel but not presented in Parts 1 and 2 should appear in this part.

Brickell Biotech, Inc.
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Listing 16.2.8.2
Chemistry
Part 1 of 3

Subject ID	Treatment Group	Visit	Collection Date (Study Day[1])	Collection Time	AST (SGOT) (U/L)	ALT (SGPT) (U/L)	Alkaline Phosphatase (U/L)	Total Bilirubin (µmol/L)	Direct Bilirubin (µmol/L)	Albumin (g/L)
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Screening	ddMMMyyyy (xx)	HH:MM	x.x *CS, H/L*	x.x *CS, H/L*	x.x *CS, H/L*	x.x *CS, H/L*	x.x *CS, H/L*	x.x *CS, H/L*
		Day 43								
xxx-xxxx										
…										

Abbreviations: AST (SGOT), aspartate aminotransferase; ALT (SGPT), alanine aminotransferase; BUN, blood urea nitrogen; CS, clinically significant; H, high; L, low

Note: H = high; L = low is displayed if result is outside the reference range.

[1] Time (days) relative to date of first dose of study drug

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Brickell Biotech, Inc.
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Listing 16.2.8.2
Serum Chemistry
Part 2 of 3

Subject ID	Treatment Group	Visit	Collection Date (Study Day[1])	Collection Time	Total Protein (g/L)	BUN (mmol/L)	Creatinine (µmol/L)	Sodium (mmol/L)	Potassium (mmol/L)	Chloride (mmol/L)
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Screening	ddMMMyyyy (xx)	HH:MM	x.x *CS, H/L*	x.x *CS, H/L*	x.x *CS, H/L*	x.x *CS, H/L*	x.x *CS, H/L*	x.x *CS, H/L*
		Day 43								
xxx-xxxx										
…										

Abbreviations: CO_2, Carbon Dioxide; CS, clinically significant; H, high; L, low

Note: H = high; L = low is displayed if result is outside the reference range.

[1] Time (days) relative to date of first dose of study drug

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Listing 16.2.8.2
Serum Chemistry
Part 3 of 3

Subject ID	Treatment Group	Visit	Collection Date (Study Day[1])	Collection Time	Test	Unit	Result	Alert	Clinically Significant
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Screening	ddMMMyyyy (xx)	HH:MM	*Test Name #1*	Unit	xxx	High / Low	Yes / *null*
		Day 43			*Test Name #2*				
					Test Name #3				
					…				
xxx-xxxx									
…									

[1] Time (days) relative to date of first dose of study drug

Path\filename.sas ddmmmyyyy hh:mm

Programming Note: Only those tests that are collected as part of the chemistry panel but not presented in Parts 1 and 2 should appear in this part.

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Listing 16.2.8.3
Urinalysis
Part 1 of 2

Subject ID	Treatment Group	Visit	Collection Date (Study Day[1])	Collection Time	Appearance	Bilirubin (mg/dL)	Color	Glucose (mg/dL)	Ketones	Nitrite	pH	Protein	Occult Blood	Specific Gravity
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Screening	ddMMMyyyy (xx)	HH:MM	*Result*	*Result*	*Result*	*Result*	*Result*	*Result*	x.x *CS, H/L*	*Result*	*Result*	x.x *CS, H/L*
		Day 43	….											
xxx-xxxx														
…														

Abbreviations: CS, clinically significant; H, high; L, low

Note: H = high; L = low is displayed if result is outside the reference range.

[1] Time (days) relative to date of first dose of study drug

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Brickell Biotech, Inc.
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Listing 16.2.8.3
Urinalysis
Part 2 of 2

Subject ID	Treatment Group	Visit	Collection Date (Study Day[1])	Collection Time	Test	Unit	Result	Alert	Clinically Significant
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Screening	ddMMMyyyy (xx)	HH:MM	*Test Name #1*	Unit	xxx	High / Low	Yes / *null*
		Day 43			*Test Name #2* *Test Name #3* …				
xxx-xxxx …									

[1] Time (days) relative to date of first dose of study drug

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Programming Note: Only those tests that are collected as part of the urinalysis panel but not presented in Part 1 should appear in this part.

Listing 16.2.8.4
Urine Pregnancy Test

Subject ID	Treatment Group	Visit	Was a Pregnancy Test performed?	Collection Date (Study Day[1])	Result
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Screening	Yes / No	ddMMMyyyy (xx)	Positive / Negative / N/A
		Baseline[2]			
		…			
xxx-xxxx					
…					

Abbreviations: N/A, not applicable

[1] Time (days) relative to date of first dose of study drug
[2] Baseline is defined as the last available measurement taken prior to the first dose of study drug.

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Programming Note: Continue for Days 29 and 43

Brickell Biotech, Inc.
BBI-4000-CL-203

Listing 16.2.9.1
Vital Signs

Subject ID	Treatment Group	Visit	Visit Date (Study Day[1])	Height[2] (cm)	Weight[2] (kg)	BMI[3] (kg/m^2)	Blood Pressure (mmHg)	Heart Rate (bpm)	Respiratory Rate (breaths/min)	Temperature (°C)
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Visit 4 /(Rescreening)	ddMMMyyyy (xx)	xx.x	xx.x	xx.x	xxx – xxx	xxx	xxx	xx.x
		Baseline[4]					xxx – xxx	xxx	xxx	xx.x
		…								
xxx-xxxx										
…										

Abbreviations: BMI, body mass index

[1] Time (days) relative to date of first dose of study drug
[2] Height, weight, and BMI are collected at the Visit 4 only.
[3] BMI is calculated as weight (kg) / [height (cm) / 100]^2.
[4] Baseline is defined as the last available measurement taken prior to the first dose of study drug.

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Programming Note: Continue for Days 8, 15, 22, 29, 36, 43, and 57

Brickell Biotech, Inc.
BBI-4000-CL-203

Listing 16.2.9.2
Physical Examination

Subject ID	Treatment Group	Visit	Was a Physical Examination performed?	Assessment Date (Study Day[1])	Were there any abnormal findings on the physical examination?
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Visit 4 (Rescreening)	Yes / No	ddMMMyyyy (xx) / Not Done	Yes / No
		Unscheduled Visit	…		
		…			
xxx-xxxx					
…					

[1] Time (days) relative to date of first dose of study drug

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Brickell Biotech, Inc.
BBI-4000-CL-203

Listing 16.2.9.3
Prior and Concomitant Medications

Subject ID	Treatment Group	Any Medications to Report?	ATC Class[1] / Generic Drug Name[1] / Medication Name	In the Treatment Area?	Phase[2]	Start Date (Study Day[3])	End Date (Study Day[3])	Dose	Unit	Route	Frequency	Indication
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Yes / No	ATC Class / Generic Drug Name / *Medication Name*	Yes / No	P / C / P, C	ddMMMyyyy (xx)	ddMMMyyyy (xx) / Ongoing	*Dose*	*Unit*	*Route*	*Frequency*	Medical History: *specify* / Adverse Event: *specify* / Hyperhidrosis / Other: *Specify*
			…									
xxx-xxxx												
…												

Abbreviations: ATC, anatomic therapeutic chemical; WHO, World Health Organization

Note: Concomitant medications are those medications received after the first dose of study drug.

[1] Medications are coded to ATC class (level 4) and drug names using the WHO Drug dictionary enhanced, version B2 March 1, 2016.
[2] The study phase during which each medication was received. P = prior (i.e., received prior to the first dose of study drug); C = concomitant (i.e., received on or after the first dose of study drug); P, C = both prior and concomitant
[3] Time (days) relative to date of first dose of study drug

Path\filename.sas ddmmmyyyy hh:mm

Programming Note:

- *If specifications for indications are reported as an AE or MH #, merge with AE/MH data to present the actual reported event as the specification.*
- *When creating ATC level 4 drug class, utilize level 3 term if level 4 is missing in dataset and level 2 if both level 3 and level 4 are missing in the dataset*

Listing 16.2.9.4
Prior and Concomitant Therapy and Procedures

Subject ID	Treatment Group	Any Concomitant Therapies/Procedures?	System Organ Class[1] / Preferred Term[1]/ Therapy/Procedure Name	Phase[2]	Start Date (Study Day[3])	End Date (Study Day[3])	In the Treatment Area?	If Yes, Specify Axilla	Frequency	Indication
xxx-xxxx	Vehicle / BBI-4000 5% / BBI-4000 10% / BBI-4000 15%	Yes / No	*Body System* / *Preferred Term* / *Therapy/Procedure Name*	P / C / P, C	ddMMMyyyy (xx)	ddMMMyyyy (xx) / Ongoing	Yes / No	Right/ Left/ Both	*Frequency*	Medical History: *specify* / Adverse Event: *specify* / Hyperhidrosis / Other: *Specify*
			…							
xxx-xxxx										
…										

Note: Concomitant therapies/procedures are those therapies/procedures received after the first dose of study drug.

[1] Therapies/Procedures are coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA), version 19.1.
[2] The study phase during which each medication was received. P = prior (i.e., received prior to the first dose of study drug); C = concomitant (i.e., received on or after the first dose of study drug); P, C = both prior and concomitant
[3] Time (days) relative to date of first dose of study drug

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