STATISTICAL ANALYSIS PLAN

Randomized, Parallel Group, Assessor-Blind Study to Evaluate the Oral Mucosal Effects in Healthy Adult Smokers Associated with 3 Weeks of Use of Niconovum Nicotine Bitartrate 4 mg Mint Lozenge Relative to the GSK Nicorette® Nicotine Polacrilex 4 mg Mint Lozenge.

Sponsor Protocol Number: 2016-NBTL-S-005
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Clinical Research Organization:
Inflamax Research Limited
1310 Fewster Drive,
Mississauga, Ontario, L4W 1A4 CANADA

Sponsor:
Niconovum USA, Inc.
401 N. Main Street
Winston-Salem, NC 27101-2990, USA

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Abbreviations

Abbreviations	Term or Definition
AE	Adverse Event
BMI	Body Mass Index
°C	Centigrade
CS	Concomitant Smoker
DBP	Diastolic Blood Pressure
eCRF	Electronic Case Report Form
CO	Carbon Monoxide
ECG	Electrocardiogram
EOS	End of Study
ePDAT	Electronic Patient Data Acquisition Tablet
ET	Early Termination
GSK	GlaxoSmithKline
mITT	Modified Intent-to-Treat
HIV	Human Immunodeficiency Virus
HLU	Heavy Lozenge Use
ICF	Informed Consent Form
ICH	International Conference on Harmonization
mmol	Millimole
L	Liter
kg	Kilograms
mm	Millimeter
mmHg	Millimeters of Mercury
MedDRA	Medical Dictionary for Regulatory Activities
OMI	Oral Mucositis Index
PP	Per protocol
PT	Preferred Term
SAP	Statistical Analysis Plan
SAE	Serious Adverse Event
SAS	Statistical Analysis System
SBP	Systolic Blood Pressure
SD	Standard Deviation
SOC	System Organ Class

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1 INTRODUCTION TO THE STATISTICAL ANALYSIS PLAN

This Statistical Analysis Plan (SAP) provides a thorough description of statistical analysis methods and presentation of the study data from the clinical trial described in Study Protocol 2016-NBTL-S-005:

"**Randomized, Parallel Group, Assessor-Blind Study to Evaluate the Oral Mucosal Effects in Healthy Adult Smokers Associated with 3 Weeks of Use of Niconovum Nicotine Bitartrate 4 mg Mint Lozenge Relative to the GSK Nicorette® Nicotine Polacrilex 4 mg Mint Lozenge**".

This SAP is based on the final protocol dated 27 February 2017 (Final 1.0).

The SAP includes details of data handling procedures and statistical methodology. No interim analysis is planned for this study.

The final statistical analysis will proceed according to the SAP approved by Niconovum USA, Inc. as well as by Inflamax Research. There are no deviations of analysis methods from the protocol. Any deviations in final analysis from this SAP will be documented in the final Study Summary Report.

Tables and Listings are numbered following the International Conference on Harmonization (ICH) structure E3 "Structure and Content of Clinical Study Report". All summary tables and listings will be generated using SAS® Version 9.2 or higher. Tables, listings and graphs will be delivered to the Sponsor as .rtf files.

The following documents were reviewed in preparation of the SAP:

- Electronic Case Report Form (eCRF) Final Version 1.0 dated on 20MAR2017
- Data Management Plan Final Version 1.0 dated on 03APR2017
- eCRF Completion Guidelines Final Version 1.0 dated on 20MAR2017
- Codelist Details Final Version dated on 30MAR2017

2 INTRODUCTION TO THE STUDY

2.1 Overview of Study

This will be a single-center, ambulatory, randomized, parallel group, assessor-blind, 3-week, safety study in healthy adults motivated to quit smoking. Subjects will be instructed to quit smoking (starting Day 1) and use 9 - 20 lozenges per day for 3 weeks. Subjects will be randomized 1:1 to treatment with Nicotine Bitartrate 4 mg mint lozenge (test product) or Nicorette® [Nicotine Polacrilex] 4 mg mint lozenge (reference product). In each treatment group a minimum of 10% of the study population will be smokers of ≥ 30 cigarettes/day, and a minimum of 40% of the study population will be smokers of 20 - 29 cigarettes/day. Randomization will be stratified by smoking status so that the treatment assignment is balanced within smoking status.

2.2 Study Objectives

2.2.1 Primary

- To assess the oral mucosal health associated with 3 weeks of use of test product, Nicotine Bitartrate 4 mg mint lozenge (Niconovum), relative to a reference product, Nicorette® [Nicotine Polacrilex] 4 mg mint lozenge (GSK), in healthy adult smokers motivated to quit smoking.

2.2.2 Secondary

- To evaluate the safety and tolerability of Nicotine Bitartrate 4 mg mint lozenge and Nicorette® [Nicotine Polacrilex] 4 mg mint lozenge in this subject population.

2.3 Subject Selection

A total of 100 healthy males or females at the age of 18 years or up who have signed written informed consent and satisfy the study inclusion/exclusion criteria per protocol will be selected to participate in this study. The Day 0 visit reconfirms their eligibility.

2.4 Study procedures

There will be at least seven study visits, including the Screening Visit, as summarized in Table 1 'Schedule of Study Events'. At the Screening Visit, safety assessments, evaluation of oral health by a dental hygienist, carbon monoxide assessment and other procedures will be performed to determine eligibility of potential subjects to enroll in the study, and informed consent forms will be obtained prior to any screening procedures.

At the Test Visit Day 0 (baseline), eligibility will be reconfirmed and subjects will be enrolled. Evaluation of oral health will be conducted by a dental hygienist, and recorded as baseline

score. Subjects will receive a Study Kit consisting of individual Daily Packs each containing 20 lozenges on Day 0 and subsequent lozenge dispensing will occur on Days 7 and 14. Subjects will be informed that daily use is permitted to vary between 9 - 20 lozenges per day, and be instructed to use lozenges from only one Daily Pack per day. At baseline (Day 0), subjects will each receive Inflamax's ePDAT® (Electronic Patient Data Acquisition Tablet) system for the daily (at least once daily) recording of their daily lozenge usage. In addition, subjects will also be instructed to indicate on the ePDAT® system (once daily) if they have experienced any change in health and/or if any concomitant medication was taken or how many (if any) cigarettes were smoked. Furthermore, subjects will also be given a take-home journal on Day 0 of the study and will be instructed to record/describe, at their own discretion, further detail of any changes in health experienced and concomitant smoking/medication.

On all other visits (Days 3, 7, 14, 21 and Day 24 post-dosing), oral examinations by a blinded dental assessor (dental hygienist, dentist or dental surgeon) will be conducted using the Oral Mucositis Index (OMI-20) scale. In addition, the blinded assessor will identify any new areas of leukoplakia, erythroplakia or ulceration over 1 cm in diameter, or other oral lesions that cannot be diagnosed by clinical observation alone for potential biopsy. Vital signs, adverse events, and concomitant medications will be collected at each visit by the study staff to assess systemic health effects in addition to those on the oral mucosa. Clinical laboratory evaluations and electrocardiograms will be conducted at selected visits.

Subjects will be discharged from the study following completion of study procedures and all appropriate safety assessments, at the Investigator's discretion.

Table 1: Schedule of Study Events

Assessment	Screening Visit	Baseline	Treatment				Follow-up
	Day -21 to Day -1	Day 0	Day 3	Day 7	Day 14	Day 21	Day 24
Informed consent	X						
Inclusion/Exclusion criteria	X	X					
Demographics	X						
Height, weight and determine BMI	X						
Medical History	X	X					
Smoking History[1]	X						
Physical examination	X						
Oral Health Assessment[2]	X	X					
ePDAT® Instruction		X					
Pregnancy test(females)[3]	X	X					
Urine drug screen and alcohol breathalyzer test	X	X					
Urinalysis	X	X		X		X	
Vital signs[4]	X	X	X	X	X	X	X[11]
Electrocardiogram[5]	X			X		X	X[5]
Clinical laboratory evaluations[6]	X	X		X		X	X[11]
Concomitant medication[1]	X	X	X	X	X	X	X
Carbon monoxide assessment[7]		X	X	X	X	X	
Oral assessment (OMI-20)		X	X	X	X	X	X
Study drug dispensing		X[8]		X	X		
Recording of lozenge use[9]			X	X	X	X	
Adverse event monitoring[1]		X	X	X	X	X	X
Biopsy[10]			X	X	X	X	X

1 Changes in health (adverse events), any concomitant medication used and smoking history will be monitored through the ePDAT® system as per subject entries and take-home journals throughout the study duration.
2 A dentist or dental hygienist will evaluate the oral health of the subjects for exclusion criteria.
3 Serum pregnancy test at Screening; urine pregnancy test at Check-in of Day 0 Test Visit.
4 Vital sign measurements include systolic blood pressure, diastolic blood pressure, and heart rate.
5 ECG will be obtained after the subject has rested in the supine position for at least 5 minutes and either before obtaining blood samples or at least 30 minutes after venipuncture. ECG will be recorded for Day 24 if needed for safety follow-up of previously documented abnormalities.
6 Abnormal clinical lab results will be followed up if needed on subsequent visit days and post-study completion, if necessary.
7 Carbon monoxide measured by breath CO monitoring machine.
8 Subjects will be instructed to take their first lozenge the next morning (i.e., Quit day = Day 1).
9 Assessment of lozenge use will be collected through the ePDAT® system (once daily) and take-home journals.
10 Biopsy will only be performed in the case of suspicious lesions as determined by oral examinations through a second opinion by a dentist or dental surgeon. Each lesion will be biopsied once.
11 Clinically significant abnormalities at Study Day 21 will be re-evaluated at Day 24 for recovery.

3 Randomization and Blinding

3.1 Randomization

Subjects will be randomized in a 1:1 ratio to receive either Nicotine Bitartrate 4 mg mint lozenge (Test Product) or Nicorette® 4 mg mint lozenge (Reference Product). A total of 100 subjects (50 in each group) will be randomized in the study at a single study site. Randomization will be stratified by smoking status so that in each treatment group a minimum of 10% of the subjects will be smokers of ≥ 30 cigarettes/day, and a minimum of 40% of the subjects will be smokers of 20 - 29 cigarettes/day.

3.2 Blinding

The study staff conducting the oral assessment (dentist or dental hygienist) shall be blinded to the subject's treatment arm. These staff will not be present during distribution or use of lozenges. Subjects will be instructed not to show their investigational product to the oral assessors. In addition, subjects and blinded assessor will be instructed to not discuss the lozenge type (study arm) that the subject is using, and a separate study team member will manage all distribution and collection of study medication to assure assessor blinding is maintained. Furthermore, the blinded assessor will input OMI-20 scores using a separate eCRF which will not include subject lozenge use or type.

3.3 Sample Size Calculation

The primary purpose of this study is to assess the oral mucosal health associated with use of test product Nicotine Bitartrate 4 mg mint lozenge (Niconovum), relative to a reference product, Nicorette® [Nicotine Polacrilex] 4 mg mint lozenge (GSK). A total of 100 subjects, 50 in each test or reference treatment group, are considered reasonable for this purpose and no formal statistical analysis was performed in determining sample size.

4 DEFINITION OF ANALYSIS POPULATIONS

4.1 Randomized Population

The Randomized Population will consist of all subjects who are randomized to the Treatment.

4.2 Modified Intent-to-Treat (mITT) Population

The mITT population will include all subjects who were randomized and used at least 1 lozenge. This will be the main population for analysis.

4.3 Per-Protocol (PP) Population

The per-protocol population will be a subset of the mITT population and will consist of subjects who complete the study without any major protocol deviations, as determined by clinical review. Major protocol deviations include:

- CO levels exceeding 10 ppm at one or more study day visit (CO is expected to be > 10 ppm on Day 0)
- Use of < 9 or > 20 lozenges/day on more than 2 study days

4.4 Heavy Lozenge Use (HLU) Population

The heavy lozenge use population will be a subset of the mITT population and will consist of subjects who use on average 15 or more lozenges per day (irrespective of completion of the study).

4.5 Concomitant Smoker (CS) Population

The concomitant smoker population will be a subset of the mITT population and will consist of subjects who either admit smoking during the study or who have a CO > 10 ppm at any study day excluding Day 0 or Day 24 that cannot otherwise be explained.

5 ASSESSMENT AND STUDY ENDPOINTS

5.1 Oral Safety Assessment

Oral examinations will be conducted using a 20 Item Oral Mucositis Index (OMI-20), a validated scale developed to measure several indications of oral mucositis. Assessors will be licensed dental professionals (dental hygienists or dentists). These selected dental professionals will be trained in the assessment protocol and the OMI-20 by a board-certified oral medicine professional. Prior to initiation of study visits, the selected dental professionals will be trained onsite in the assessment protocol and the OMI-20 test. An assessment will be conducted to ensure consistent evaluation among the dental professionals that will partake in the study. All assessors will be blinded to the study treatment the subject has been randomized to receive. OMI-20 will be assessed on Days 0, 3, 7, 14, 21 and Day 24 (post dose) visits.

5.2 Primary Endpoint

OMI-20 Total score change from baseline (Day 0) at each study visit (Days 3, 7, 14 and 21) in the Modified-Intent-to-Treat (mITT) population.

5.3 Secondary Endpoints

- OMI-20 Total score change from baseline (Day 0) at each study visit (Days 3, 7, 14 and 21) in PP population, heavy lozenge use population and concomitant smoker population.
- OMI-20 Erythema subscore change from baseline at each study visit (Days 3, 7, 14 and 21) in all populations.
- OMI-20 Ulcer subscore change from baseline at each study visit (Days 3, 7, 14 and 21) in all populations.

5.4 Safety Endpoints

- Clinical laboratory assessments (clinical chemistry; hematology; serology; urinalysis)
- Vital signs
- 12-lead Electrocardiogram (ECG)
- Analysis of biopsied materials (if any) and adverse events

5.5 Other Safety Endpoints

- OMI-20 Total score Day 24 versus Day 21
- OMI-20 Erythema score Day 24 versus Day 21
- OMI-20 Ulcer score Day 24 versus Day 21
- Safety endpoints Day 24 versus Day 21

6 STATISTICAL METHODOLOGY

6.1 Summary Statistics

Subject disposition will be summarized for all the randomized subjects. The primary endpoints will be summarized for mITT population. The secondary endpoints will be summarized for mITT population, PP population, HLU population and CS population. The safety endpoints and baseline characteristics will be summarized only for the mITT population.

The standard summary statistics that will be calculated for quantitative and qualitative variables are:

Quantitative:	number of subjects, mean, median, standard deviation (SD), minimum and maximum of the raw data
Qualitative:	number of subjects, number of missing data (if not zero), absolute and relative frequencies per class

6.2 Reporting Precision

Summary statistics will be presented to the following degree of precision:

Statistics	Degree of Precision
Mean (of all kinds), Median,	One more decimal place than the raw data
Standard deviation	Two more decimal places than the raw data
Minimum, Maximum	The same number of decimal places as the raw data
Percent	One decimal place

6.3 Commonly Used Algorithms

6.3.1 Duration of Adverse Events

When adverse events (AEs) have incomplete start dates and times, no imputation will be performed. Duration will be calculated for AEs that resolve as the difference between the resolution date and time and onset date and time and will be expressed in days, hours and minutes. If either time is missing, duration will be expressed in days. Duration will only be calculated when both dates are complete.

6.4 Data Handling Rules

The following section describes the rules for handling data, including the definitions of derived variables and handling missing data.

6.4.1 Derived Variables

- Age is calculated in years after rounding down as follows:
  Year of age = (Date [in days format] informed consent signed - Date [in days format] of birth) / 365.25

6.4.2 Missing Data

Any missing values for the study endpoints will not be replaced and the observed data will be used for the endpoint analysis. No data interpolation or extrapolation will be carried out if there is missing data.

6.5 Level of Significance

No formal comparisons between groups will be conducted. No inferential statistics will be output. Therefore, no level of significance will be assigned.

6.6 Interim Analysis

No interim analysis is planned for this study.

7 STATISTICAL ANALYSES

7.1 Subject Disposition and Withdrawals

The following frequencies (number and percent) will be displayed by treatment group and overall for all the randomized subjects:

- Subjects in the Randomized Population (number only)
- Subjects in the Modified Intent-to-Treat Population (number only)
- Subjects in the Per-Protocol Population (number only)
- Subjects in the Heavy Lozenge Use Population (number only)
- Subjects in the Concomitant Smoker Population (number only)
- Subjects who completed the study (number and percent)
- Subjects who discontinued early, as well as reasons for subject discontinuation (number and percent)

The denominators for the percent calculations will be the number of subjects in the Randomized population per treatment or overall.

Subjects' completion/discontinuation status will be listed by treatment group and will include subject identifier, date of enrollment, date of completion/early discontinuation, date of last contact and, for those who discontinued early, the specific reason for discontinuation.

All deviations related to study inclusion or exclusion criteria, conduct of the trial, subject compliance or subject concomitant smoking will be listed. The justification of major/minor on protocol deviations may be determined among the Principal Investigator and Biostatistician from Inflamax Research, and the Sponsor.

7.2 Baseline Characteristics

Demographics (age, sex, race, ethnicity, weight, height and BMI) will be summarized using descriptive statistics (number of subjects, mean, standard deviation, minimum, median and maximum for quantitative variables, and number of subjects and percent of subjects for qualitative variables) by treatment group and overall for the mITT population. No formal statistical comparison between treatment groups will be performed. Together with the informed consent date, the above information will be listed by treatment groups for the randomized subjects.

Other baseline characteristics will be listed by treatment group for all subjects:

- Medical/medication history
- History of Tobacco/nicotine product use/consumption and smoking/vaping habits
- Pregnancies (female only)
- Urine drug screen and alcohol breathalyzer test

The history of tobacco/nicotine production use/consumption and smoking/vaping habits will be listed as treatment, subject, substance name, start date of use, end date of use, ongoing use, frequency of use, amount used (amount/unit/frequency).. A summary table will be produced by treatment for the duration of substance use and average amount. The summary statistics will also report the number of subjects who reported using the product at each frequency level (less than 20 cigarettes per day, 20 – 29 per day, and more than 30 per day) within treatment group and overall.

7.3 Concomitant Medication

The use of concomitant medications will be requested in the ePDAT® system, and subjects will be able to indicate whether any concomitant medication was used during the study. The full description of the concomitant medication usage will be recorded in the take-home journals provided to the subjects, indicating the following information (as possible): Name of drug, Reason for use, Frequency of use, Route of administration, Dose, and Start date and Stop date (where applicable). The above information will listed by treatment. No summary table will be output.

7.4 Medication Administration and Treatment Compliance

Subjects will be instructed to self-administer 9-20 lozenges per day and record lozenge use through Inflamax's ePDAT take-home tablet once daily. Number of used lozenges since last visit will be calculated as deduction of the dispensed lozenge number of last visit from the

returned lozenge number of this visit. Average number of lozenges used per day will be also calculated as dividing total number of used lozenges by total number of treatment days.

Treatment compliance will be determined by Breath Carbon Monoxide (CO) and average number of lozenges.

Breath carbon monoxide (CO) levels will be presented by subject for each visit and will be used to identify concurrent smokers. Based on level of CO, subjects will be divided as compliant subjects (CO<=10 ppm at all study day visits) and non-compliant subjects (CO>10 ppm at any study day visit). Breath carbon monoxide (CO) levels will be listed by treatment, together with visit and date. In the listing, non-compliance will be flagged. For those who comply with the requirements, CO level will be summarized with descriptive statistics (number, mean, SD, minimum, median and maximum) by treatment and visit. The number of subjects and percentage will be calculated based on whether the CO level is higher or lower than 10 ppm.

Number of lozenges will also be used to determine compliance. Lozenge use of less than 9 or more than 20 for more than 2 study days will be treated as a major violation of compliance and qualifies subjects as non-compliant.

The average number of used lozenges will be summarized with descriptive statistics (n, mean, SD, minimum, median and maximum) by treatment for the mITT population and subpopulations. The number of subjects and percentage will also be calculated based on compliance.

Compliance or non-compliance will be tabulated by treatment with frequency and percentage using the mITT population.

Medication administration will be listed by treatment, including subject number, visit, visit date, the number of dispensed lozenges, the number of returned lozenges, the number of used lozenges and average number of lozenges used per day. Non-compliance on specific day(s) will be flagged, and total number of non-compliant days will be listed.

7.5 Primary Analyses

The primary endpoint, change from baseline (Day 0) compared to each treatment study visit day (Days 3, 7, 14 and 21) in OMI-total score, will be summarized using descriptive statistics (number, mean, standard deviation, minimum, maximum, median) and presented by treatment group using mITT populations. No inferential statistical comparisons between groups will be conducted.

7.6 Secondary Analyses

The primary endpoint change from baseline (Day 0) compared to each treatment study visit day (Days 3, 7, 14 and 21) in OMI-total score will be summarized using descriptive statistics (number, mean, standard deviation, minimum, maximum, median) and presented by treatment group using the PP population, HLU population, and CS population.

The change from baseline in erythema and ulcer subscores for each treatment study visit day (Days 3, 7, 14 and 21) will be summarized using descriptive statistics (number, mean, standard deviation, minimum, maximum and median) and presented by treatment group using the mITT population, PP population, HLU population, and CS population.

No inferential statistical comparisons between groups will be conducted.

7.7 Safety Analyses

Safety data in this study are comprised of adverse events, physical examination, vital signs and clinical laboratory assessment. All safety data will be analyzed using the mITT Population.

The continuous type safety endpoints will be summarized by treatment using descriptive statistics (n, mean, SD, median, minimum, maximum) for mITT population. The categorical type safety endpoints will be summarized by treatment using frequency and percentage for mITT population. No formal inferential tests will be performed on safety data.

7.7.1 Adverse Events

Adverse events (AEs) will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) Coding Dictionary version 19.1. All subjects in the mITT population will be included in the adverse event analysis. All adverse events will be listed chronologically by treatment, subject and AE start date/time. This listing will include all data collected in the eCRF, along with the derived variable duration of AE and the coded variables system organ class (SOC) and preferred term (PT).

Displays of AEs will include:

- Overall Summary of AEs

  This table will include the number of events, number and percent of subjects who experienced AEs, serious AEs, severe AEs, related AEs and AEs leading to study discontinuation, summarized by treatment.

- Summary of AEs by SOC, PT and Treatment

  A summary of the number of events, number and percent of subjects who experienced at least one AE, as well as the number of events, number and percent of subjects who experienced each specific SOC, and PT will be presented by treatment. If a subject has more than one occurrence of the same PT then the PT will be counted only once for that subject under the SOC at which it was experienced.

7.7.2 Physical Examination

Subjects will take a complete physical examination including a review of all body systems at the Screening Visit. On Day 0 visit, an assessment of general oral health by a dental professional will be conducted to assure compliance with relevant inclusion and exclusion criteria. Any abnormal findings at baseline will be recorded as medical history, and findings after baseline will be recorded as adverse events. No separate listing will be produced.

7.7.3 Vital Signs

Systolic (SBP), diastolic (DBP) blood pressure and heart rate will be measured, for all scheduled study visit days (Days 0, 3, 7, 14, 21 and 24), including Screening, in a seated position after at least 5 minutes of rest. Subjects with a systolic blood pressure ≥ 150 mmHg or a diastolic blood pressure ≥ 95 mmHg on Day 0 may be excluded from the study, as judged by the Investigator. The vital signs will be summarized by treatment and visit using the standard summary statistics (n, mean, SD, minimum, median and maximum) for mITT population. All data will also be listed by treatment, subject, visit and vital sign parameters.

7.7.4 12-Lead Electrocardiogram

During the Screening Visit, a standard12-lead Electrocardiogram (ECG) will be obtained after the subject has rested in the supine position for at least 5 minutes. This assessment can be performed any time before blood sampling or at least 30 minutes after blood sampling, if applicable. Additionally, ECG will be measured on Day 7, Day 21 and Day 24 (if follow-up is required). ECG will be summarized by treatment and visit using the standard summary statistics (n, mean, SD, minimum, median and maximum) for the mITT population. All data will also be listed by treatment, subject, visit and ECG parameters. Overall assessment will be summarized using frequencies and percentage.

7.7.5 Clinical Laboratory

Serum chemistry, hematology and urinalysis will be measured in all subjects at Screening, Day 0 (baseline), Day 7 and Day 21. A drug screen will be conducted at Screening and Day 0. All clinical laboratory samples and urine samples for urinalysis will be analyzed at a central laboratory. The urine pregnancy test will be analyzed in the clinic. The Investigator will evaluate

the clinical significance of each laboratory value outside of the reference range.

Each abnormal test will be evaluated as clinically significant or not clinically significant. All clinically significant abnormal laboratory values that represent an unexpected change from Baseline will be assessed as adverse events (AEs), and an AE eCRF must be completed.

Data in each of the three categories of hematology, chemistry and urinalysis will be listed by treatment, subject and parameter.

7.7.6 Recovery

Recovery will be assessed by comparing OMI-20 total score, erythema subscore, and ulcer subscore at Day 24 with those at Day 21. Other safety endpoints with clinically significant abnormal values at Day 21 will be re-evaluated on Day 24 to assess recovery from Day 21.

Difference between Day 21 and Day 24 in OMI-total score, erythema subscore and ulcer subscore will be summarized using descriptive statistics (mean, standard deviation, minimum, maximum, and median) and presented by treatment group using the mITT population and subpopulations. No inferential statistical comparisons between groups will be conducted.

7.8 Analysis Prior to Study Completion

An early statistical analysis of data of administrative type is planned for this study following completion of the 60th randomized subject and prior to the completion of full study with 100 randomized subjects and hard lock of the clinical database. This statistical analysis provides with only descriptive summaries and without any confirmatory type of analysis using statistical significance. This will provide an initial evaluation of selected study results and an assessment of adequacy of the result outputs for the final study report.

The study is blinded only to the extent that the dental hygienist evaluating the oral health of subjects does not know to which treatment group the subjects have been assigned. Otherwise the study could be considered an open label study as the subjects, investigators, and study staff are not blinded to the treatment. The individual dental hygienist evaluating the oral health of subjects will not be informed of the results of this pre-planned analysis prior to the completion of the full study analysis. The study will continue to recruit and randomize beyond 60 subjects until the protocol specified 100 randomized subjects are evaluated. Also, the results of the completed study will be presented in the final report, only descriptively.

8 TABLES, LISTINGS AND GRAPHS (TLGs) SHELLS

The following TL shells are provided as a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study but are intended to show the general layout of the Tables and Listings that will be included in the final report. Table headers, variables names and footnotes will be modified as needed following data analyses.

Table 14.1.1 Disposition of Subjects and Analysis Sets

	Nicotine Polacrilex n (%)	Nicotine Bitartrate n (%)	Overall n (%)
Number of Subjects in Randomized Population	xx	xx	xx
Number of Subjects in Modified Intent-to-Treat Population	xx	xx	xx
Number of Subjects in Per Protocol Population	xx	xx	xx
Number of Subjects in Heavy Lozenge Use Population	xx	xx	xx
Number of Subjects in Concomitant Smoker Population	xx	xx	xx
Number (%) of Subjects who Completed the Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number (%) of Subjects who Discontinued Early	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reasons for Early Discontinuation			
Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Physician Decision	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sponsor’s Decision	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subject Non-compliance	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Withdrawal by Subject	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: Percentages are calculated based on the number of subjects in the Randomized Population per treatment and overall.
Data Source: Listing 16.2.1

Table 14.1.2 Demographics and Baseline Characteristics
Modified Intent-to-Treat Population

	Nicotine Polacrilex (N=xx)	Nicotine Bitartrate (N=xx)	Overall (N=xx)
Age (years)*			
n	xx	xx	xx
Mean	xx.x	xx.x	xx.x
SD	xx.xx	xx.xx	xx.xx
Minimum	xx	xx	xx
Median	xx	xx	xx
Maximum	xx	xx	xx
Sex, n (%)			
n	xx	xx	xx
Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…			

Note: *Age at Informed Consent

Percentages are calculated based on the number of subjects in the ITT Population per treatment and overall.

Data Source: Listing 16.2.4.1, Listing 16.2.4.2

Programming Note: Table will also include race, ethnicity, height (cm), weight (kg), BMI (kg/m^2)

Table 14.1.3 Summary of Tobacco Use History
Modified Intent-to-Treat Population

Product	Categories	Nicotine Polacrilex (N=xx)	Nicotine Bitartrate (N=xx)	Overall (N=xx)
Cigarettes	Duration (Years)			
	n	xx	xx	xx
	Mean	xx.xxx	xx.xxx	xx.xxx
	SD	xx.xxxx	xx.xxxx	xx.xxxx
	Minimum	xx.xx	xx.xx	xx.xx
	Median	xx.xxx	xx.xxx	xx.xxx
	Maximum	xx.xx	xx.xx	xx.xx
	Cigarettes (Per Day)			
	n	xx	xx	xx
	Mean	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx
	Minimum	xx	xx	xx
	Median	xx.x	xx.x	xx.x
	Maximum	xx	xx	xx
	Frequency			
	≥ 30 cigarettes/day	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	20 - 29 cigarettes/day	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	< 20 cigarettes/day	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Data Source: Listing 16.2.4.9

Table 14.2.2.1 Summary of Change from Baseline in OMI-20 Total Score
Modified Intent-to-Treat Population

		Treatment	
	Statistics	Nicotine Polacrilex	Nicotine Bitartrate
Baseline	n	xx	xx
	Mean ± SD	xx.x ± x.xx	xx.x ± x.xx
	Median	xx.x	xx.x
	Min, Max	xx, xx	xx, xx
Day 3	n	xx	xx
	Mean ± SD	xx.x ± x.xx	xx.x ± x.xx
	Median	xx.x	xx.x
	Min, Max	xx, xx	xx, xx
Change from baseline to Day 3	n	xx	xx
	Mean ± SD	xx.x ± x.xx	xx.x ± x.xx
	Median	xx.x	xx.x
	Min, Max	xx, xx	xx, xx
Day 7	n	xx	xx
	Mean ± SD	xx.x ± x.xx	xx.x ± x.xx
	Median	xx.x	xx.x
	Min, Max	xx, xx	xx, xx
Change from baseline to Day 7	n	xx	xx
	Mean ± SD	xx.x ± x.xx	xx.x ± x.xx
	Median	xx.x	xx.x
	Min, Max	xx, xx	xx, xx

Note: OMI – Oral Mucositis Index
Data Source: Listing 16.2.6.1
<Programming Note: continue for Day 14 and Day 21.>

Similar tables as 14.2.2.1 will be generated for:

Table 14.2.2.2 Summary of Change from Baseline in OMI-20 Total Score Per-Protocol Population

Table 14.2.2.3 Summary of Change from Baseline in OMI-20 Total Score Heavy Lozenge Use Population

Table 14.2.2.4 Summary of Change from Baseline in OMI-20 Total Score Concomitant Smoker Population

Table 14.2.3.1 Summary of Change from Baseline in OMI Erythema Score Modified Intent-to-Treat Population

Table 14.2.3.2 Summary of Change from Baseline in OMI Erythema Score Per-Protocol Population

Table 14.2.3.3 Summary of Change from Baseline in OMI Erythema Score Heavy Lozenge Use Population

Table 14.2.3.4 Summary of Change from Baseline in OMI Erythema Score Concomitant Smoker Population

Table 14.2.4.1 Summary of Change from Baseline in OMI Ulcer Score Modified Intent-to-Treat Population

Table 14.2.4.2 Summary of Change from Baseline in OMI Ulcer Score Per-Protocol Population

Table 14.2.4.3 Summary of Change from Baseline in OMI Ulcer Score Heavy Lozenge Use Population

Table 14.2.4.4 Summary of Change from Baseline in OMI Ulcer Score Concomitant Smoker Population

Table 14.3.1.1 Overall Summary of Treatment Emergent Adverse Events (TEAEs)
Modified Intent-to-Treat Population

	All Adverse Events	
	Nicotine Polacrilex (N=xx)	Nicotine Bitartrate (N=xx)
Number (%) of Subjects with TEAE	xx (xx.x%) [xx]	xx (xx.x%) [xx]
Number (%) of Subjects with Serious TEAE	xx (xx.x%) [xx]	xx (xx.x%) [xx]
Number (%) of Subjects with Severe TEAE	xx (xx.x%) [xx]	xx (xx.x%) [xx]
Number (%) of Subjects with Related TEAE	xx (xx.x%) [xx]	xx (xx.x%) [xx]
Number (%) of Subjects with Study Discontinued Due to TEAE	xx (xx.x%) [xx]	xx (xx.x%) [xx]

Note: An AE is considered to be related if it is possibly or probably related to study processes.
Summaries are presented as: number of subjects, (percentage of subjects), and [number of events].
Data Source: Listing 16.2.7

Table 14.3.1.2 Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Modified Intent-to-Treat Population

System Organ Class/ Preferred Term	All Adverse Events	
	Nicotine Polacrilex (N=xx)	Nicotine Bitartrate (N=xx)
Any System Organ Class		
Any Event	xx (xx.x%) [xx]	xx (xx.x%) [xx]
Cardiac Disorders	xx (xx.x%) [xx]	xx (xx.x%) [xx]
Any Event	xx (xx.x%) [xx]	xx (xx.x%) [xx]
Bradycardia	xx (xx.x%) [xx]	xx (xx.x%) [xx]
…		

Note: All adverse events recorded throughout the study are summarized by treatment and MedDRA System Organ Class and Preferred Term.

Summaries are presented as: number of subjects, (percentage of subjects), and [number of events]. If multiple events occur in a category, it will be counted only once for calculation of frequencies at subject level.

Data Source: Listing 16.2.7

Table 14.3.1.3 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Maximum Relationship (Modified Intent-to-Treat Population)

System Organ Class/ Preferred Term	Maximum Relationship	All Adverse Events	
		Nicotine Polacrilex (N=xx)	Nicotine Bitartrate (N=xx)
Any System Organ Class			
Any Event	Unlikely	xx (xx.x%) [xx]	xx (xx.x%) [xx]
	Possible	xx (xx.x%) [xx]	xx (xx.x%) [xx]
	Probably	xx (xx.x%) [xx]	xx (xx.x%) [xx]
Cardiac Disorders			
Any Event	Unlikely	xx (xx.x%) [xx]	xx (xx.x%) [xx]
	Possible	xx (xx.x%) [xx]	xx (xx.x%) [xx]
	Probably	xx (xx.x%) [xx]	xx (xx.x%) [xx]

Note: All adverse events recorded throughout the study are summarized by treatment and MedDRA System Organ Class and Preferred Term.

Summaries are presented as: number of subjects, (percentage of subjects), and [number of events]. If multiple events occur in a category, it will be counted only once for calculation of frequencies at subject level.

Data Source: Listing 16.2.7

Table 14.3.4 Summary of Vital Signs
Modified Intent-to-Treat Population

Parameter (Unit)	Visit	Statistic	Nicotine Polacrilex (N=xx)	Nicotine Bitartrate (N=xx)
Systolic Blood Pressure (mmHg)	Screening			
		n	xx	xx
		Mean	xx.x	xx.x
		SD	xx.xx	xx.xx
		Minimum	xx	xx
		Median	xx.x	xx.x
		Maximum	xx	xx
	Day 0 Baseline	…		
	Day 3	…		
…..				

Note: EOS=End of Study, ET=Early Termination
Data Source: Listing 16.2.9
Programming Note: Parameter also includes Diastolic Blood Pressure (mmHg), Pulse Rate (bpm), Programming will continue for Day 7, 14, 21 and EOS.

Table 14.3.5.1 Summary of Overall ECG Interpretation
Modified Intent-to-Treat Population

Visit		Nicotine Polacrilex (N=xx)	Nicotine Bitartrate (N=xx)
Baseline			
	n	xx	xx
	Normal, n (%)	xx (xx.x%)	xx (xx.x%)
	Abnormal, Not Clinically Significant, n (%)	xx (xx.x%)	xx (xx.x%)
	Abnormal, Clinically Significant, n (%)	xx (xx.x%)	xx (xx.x%)
	…		
Day 7			
	n	xx	xx
	Normal, n (%)	xx (xx.x%)	xx (xx.x%)
	Abnormal, Not Clinically Significant, n (%)	xx (xx.x%)	xx (xx.x%)
	Abnormal, Clinically Significant, n (%)	xx (xx.x%)	xx (xx.x%)

Note: EOS=End of Study

Data Source: Listing 16.2.10
Programming Note: Programming will continue for Day 14, 21 and EOS/ET.

Table 14.3.5.2 Summary of ECG Continuous Data
Safety Population

ECG Parameters (unit)	Visit	Statistics	Nicotine Polacrilex (N=xx)	Nicotine Bitartrate (N=xx)
Ventricular Rate (bpm)	Baseline*			
		n	xx	xx
		Mean	xx.x	xx.x
		SD	xx.xx	xx.xx
		Minimum	xx	xx
		Median	xx.x	xx.x
		Maximum	xx	xx
	Day 7			
		n	xx	xx
		mean	xx.x	xx.x
		..	xx.x	xx.x
		xx	xx	xx
	…			

Note: *Baseline is defined as the last observation prior to the dose.
<ECG Parameter (unit)> = Ventricular Rate (bpm), PR Interval (msec), QRS Duration (msec), QT Interval (msec), QTcB Interval (msec)
Programming Note: Table also includes Day 14, 21 and EOS/ET.

Table 14.3.6.1 Summary of Breath carbon monoxide (CO) levels (mITT Population)

Visit		Statistics	Treatment	
			Nicotine Polacrilex	Nicotine Bitartrate
Day 3	Average CO level (Compliant)	n	xx	xx
		Mean ± SD	xx.x ± x.xx	xx.x ± x.xx
		Median	xx.x	xx.x
		Min, Max	xx, xx	xx, xx
	CO level <=10pmm or not?	n (%)		
	Yes		xx (xx.x%)	xx (xx.x%)
	No		xx (xx.x%)	xx (xx.x%)
Day 7				
Day 14				
Day 21				

Data Source: Listing 16.2.5.1

Table 14.3.6.2 Summary of Study Drug Administration

			Treatment	
Population		Statistics	Nicotine Polacrilex	Nicotine Bitartrate
mITT	mITT Average number of used lozenges per day	n	xx	xx
		Mean ± SD	xx.x ± x.xx	xx.x ± x.xx
		Median	xx.x	xx.x
		Min, Max	xx, xx	xx, xx
	Number of non-compliance days>2 or not	n (%)		
	Yes		xx (xx.x%)	xx (xx.x%)
	No		xx (xx.x%)	xx (xx.x%)
PP				
HLU				

Data Source: Listing 16.2.5.2

Table 14.3.6.3 Summary of Medication Compliance (mITT Population)

Compliance	Treatment	
	Nicotine Polacrilex n (%)	Nicotine Bitartrate n (%)
Yes	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)

Data Source: Listing 16.2.5.1 & Listing 16.2.5.2

Table 14.3.7.1 Summary of difference in OMI-20 Total Score Between Day 21 and Day 24

			Treatment	
Population		Statistics	Nicotine Polacrilex	Nicotine Bitartrate
mITT	Day 21	n	xx	xx
		Mean ± SD	xx.x ± x.xx	xx.x ± x.xx
		Median	xx.x	xx.x
		Min, Max	xx, xx	xx, xx
	Day 24	n	xx	xx
		Mean ± SD	xx.x ± x.xx	xx.x ± x.xx
		Median	xx.x	xx.x
		Min, Max	xx, xx	xx, xx
	Difference between Day 21	n	xx	xx
		Mean ± SD	xx.x ± x.xx	xx.x ± x.xx
		Median	xx.x	xx.x
		Min, Max	xx, xx	xx, xx
PP				
HLU				

Note: OMI – Oral Mucositis Index
Data Source: Listing 16.2.6.1

Similar tables as 14.3.7.1 will be generated for:

Table 14.3.7.2 Summary of difference in OMI Erythema Score Between Day 21 and Day 24
Modified Intent-to-Treat Population

Table 14.3.7.3 Summary of difference in OMI Ulcer Score Between Day 21 and Day 24
Modified Intent-to-Treat Population

Listing 16.1.7 Randomization Scheme

Subject	Treatment	Age* (years)	Gender	Date of Informed Consent	Date of Enrollment	Smoking category
xxxxx	Nicotine Polacrilex	xx	Male	DDMONYYYY	DDMONYYYY	Type 1
……						

Note: *Age at informed consent.
Type 1: # of smoked cigarette per day < 20; Type 2: 20-29; Type 3: >=30.

Listing 16.2.1 Subject Disposition and Completion/Early Termination

Treatment	Subject	Date of Study Completion or Early Discontinuation	Date of Last Contact	Completed Study	Reason for Study Discontinuation*
Nicotine Polacrilex	xxxx	DDMONYYYY	DDMONYYYY	No	xxxxxxxxxxx
	……				
……					

Note: *A corresponding AE number will be displayed if Reason for Discontinuation or Reason for Study Discontinuation is “Adverse Event”.

Listing 16.2.2 Protocol Deviations

Treatment	Subject	Deviation Start Date	Visit	Protocol Deviation Type	Description of Protocol Deviation
Nicotine Polacrilex	xxxx	DDMONYYYY	xxxx	Xxxxx	Xxxxxxx
	……				
….					

Listing 16.2.4.1 Demographic Data

Treatment	Subject	Informed Consent Date	Gender	Date of Birth	Age* (years)	Race	Ethnicity	Height (cm)	Weight (kg)	BMI (kg/m^2)
Nicotine Polacrilex	xxxx	DDMONYYYY	x	DDMONYYYY	xx	xxxxx	xxxxx	xxx	xx	xx
	……									
…										

Note: *Age at Informed Consent.

Listing 16.2.4.2 Urine Drug Screen and Alcohol Breath Test

Treatment	Subject	Visit	Collection Date	Ampheta -mines	Barbitur -ates	Benzodia -zepines	Canna -binoids	Cocaine	Opiates	Alcohol
Nicotine Polacrilex	xxxx	Screen	DDMONYYYY	Negative	Negative	Negative	Negative	Negative	Negative	Negative
		Day 0	….							
	…..									
……										

Listing 16.2.4.3 Medical History

Treatment	Subject	MH #	Medical History Category	Medical History Term	Start Date and Time	End Date and Time
Nicotine Polacrilex	xxxx	x		Xxxxxx	DDMONYYYY	DDMONYYYY
		x		Xxxxxx	DDMONYYYY	Ongoing
	……					
……						

Note: MH=Medical History (including relevant medical [within last 5 years]).

Listing 16.2.4.4 Concomitant Medications

Treatment	Subject	MH #	Medication Name	Dose/Unit/Frequency /Route	Start Date/Stop Date	Indication/ Administered for AE or MH?
Nicotine Polacrilex	xxxx	x	xxxxxxxxx	20/ mg/ Once/ Oral	DDMONYYYY HH:MM / DDMONYYYY HH:MM	Headache/ Yes (AE # 4)
		x	xxxxxxxxx	xxx/ xxx/ xxxx/xxxx	DDMONYYYY HH:MM / Ongoing	xxxxx/ No
	……					
……						

Listing 16.2.4.5 Serology Screen

Treatment	Subject	Collection Date and Time	Hepatitis B Surface Antigen	Hepatitis C Virus Antibody	HIV Antibody
Nicotine Polacrilex	xxxx	DDMONYYYY HH:MM	Negative	Negative	Non-Reactive
	……				
……					

Listing 16.2.4.6 Pregnancy Tests

Treatment	Subject	Visit	Collection Date and Time	Results
Nicotine Polacrilex	xxxx	Screening	DDMONYYYY HH:MM	Negative
		Day 0	DDMONYYYY HH:MM	Negative
	……			
……				

Note: Serum pregnancy test at Screening; urine pregnancy test at Check-in of Day 0 Test Visit.

Listing 16.2.4.7 Tobacco Product Use History

Treatment	Subject	Substance	Start Date of Substance Used	End Date of Substance Used	Substance Use Ongoing?	Frequency of Use	Amount/ Unit/ Frequency	Typically Used Brand Style
Nicotine Polacrilex	xxxx	Cigarettes	20JAN1990		Yes	Daily	10/Cigarette/Per Day	xxxx
	……							
	xxxx	Cigarettes	01JUL2005	01AUG2015	No	Daily	15/Cigarette/Per Day	xxxx
	……							
……								

Listing 16.2.5.1 Study Drug Administration

Treatment	Subject	Visit	Dispense/ Administration Date	Number of Dispensed	Number of Returned	Number of Daily Use	Compliance Flag*	Number of Non-Compliance Days
Nicotine Polacrilex	xxxx	Day 0	DDMONYYYY	xx				
		Day 1	DDMONYYYY			xx	Yes	
		Day 7	DDMONYYYY	xx	xx	xx	No	
		….						
		Day 21	DDMONYYYY			xx	Yes	
		Day 24	DDMONYYYY		xx			xx
	xxxx	Day 0						
		….						
		….						

Note: Drug dispense happens on Day 0, 7 and 14; Drug return happens on Day 7, 14 and 24.
*Compliance will be flagged ‘No’ for daily lozenge use fewer than 9 or more than 20.

Listing 16.2.5.2 Carbon Monoxide Breath Test

Treatment	Subject	Visit	Collection Date	CO Level (ppm)	Compliance Flag	Total Number of Non-Compliance Days
Nicotine Polacrilex	xxxx	Day 0	DDMONYYYY	xxx		
		Day 3				
	……	Day 7				
……		Day 21				xx

Note: CO = Carbon Monoxide; CO levels exceeding 10 ppm during treatment will be flagged as 'No';
CO level should be higher than 10 ppm on Day 0. CO level will be measured on Day 0, 3, 7, 14 and 21.

Listing 16.2.6.1 Oral Mucositis Index (OMI-20)

Treatment	Subject	Visit	Collection Date	Organ	Location	Atrophy	Erythema	Edema	Ulcer /Pseudomembrane
Nicotine Polacrilex	xxxx		DDMONYYYY	Labial Mucosa	Lower		xx		xx
					Upper		xx		xx
	xxxx		DDMONYYYY	Buccal Mucosa	Right		xx		xx
					Left		xx		xx
	……			Tongue	Dorsal	xx	xx		xx
					Lateral		xx	xx	xx
					Ventral		xx		xx
				Mouth Floor			xx		xx
				Soft Palate			xx		xx

……

Listing 16.2.7.1 Adverse Events

Treat -ment	Subje ct	Visit	AE #	Treatment Emergent?	System Organ Class/ Preferred Term/ Verbatim Term	Start Date and Time/ Stop Date and Time/	Duration (DD:HH:M M)*	Severity/ Serious/ Relationship to study	Outcome	Action Taken/ Other Action	Caused Study Discontin -uation
Nicotin e Polacril ex	xxxx	Day 1	x	Yes	Nervous system disorders/ Headache/ Headache	DDMONYYYY HH:MM/ / Ongoing		Mild/ Yes (Death)/ Unrelated/	Recovered/ Resolved	None/None	No
			x	Yes	Gastrointestinal disorders/ Vomiting/ Vomiting	DDMONYYYY HH:MM/ DDMONYYYY HH:MM	DD:HH:MM	Moderate/ No/ Related /	Recovered/ Resolved	None/None	No
	……										
……											

Note: *DD: HH: MM = Days: Hours: Minutes.

Programming Note: 1) if the status of the adverse event is ongoing at the end of the study (i.e. AEONGO=”Y” and AEENDTC is missing), the “Stop Date and Time” will be presented as “Ongoing”; 2) if any serious adverse event (SAE) occurs, a similar listing will be produced for SAEs separately.

Listing 16.2.8.X Laboratory Measurements: <Laboratory Panel>
Full Analysis Set Population

Treatment	Subject	Test Performed?	Date of Sample Collection	Lab Test (Unit)	Value	Reference Range Indicator	Normal Range	Clinically Significant?
	xxxx	Yes	DDMONYYYY	xxxxxx(xxxx)	xx	High	xx - xxx	No
				xxxxx (xxxx)	xx	Abnormal	Negative	
				……				
	xxxx	No						
	……							
……								

Programming Note: < Laboratory Panel> = Hematology, Chemistry, Urinalysis. X will be assigned as 1, 2, and 3 for each laboratory panel, and each listing will continue for all parameters (unit) in that panel.

Listing 16.2.9 Vital Signs
Full Analysis Set Population

Treatment	Subject	Visit	Collection Date and Time	Position	SBP (mmHg)	DBP (mmHg)	HR (bpm)
	xxxx	Screening	DDMONYYYY HH::MM	Sitting	xxx	xx	xx
		Day 0	DDMONYYYY		xxx	xx	xx
	……						
……							

Note: SBP=Systolic Blood Pressure, DBP=Diastolic Blood Pressure, HR=Heart Rate.
EOS = End of Study, ET = Early Termination.

Programming Note: The table will continue on Day 3, 7, 14, 21 and EOS.