

**An Open-Label, Parallel-Group, Controlled Study to Evaluate Changes in Biomarkers of Cigarette Smoke Exposure and Biomarkers of Potential Harm in Adult Smokers Who Completely Switch to Using e-Vapor Products for 12 Weeks**

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## **Statistical Analysis Plan**

An Open-Label, Randomized, Parallel-Group, Controlled Study to Evaluate Changes in Biomarkers of Cigarette Smoke Exposure and Biomarkers of Potential Harm in Adult Smokers Who Completely Switch to Using e-Vapor Products for 12 Weeks

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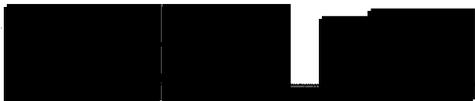
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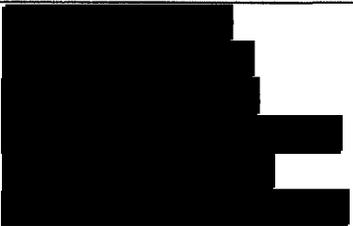
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## ABBREVIATIONS AND DEFINITIONS

AE	adverse event
ALCS	Altria Client Services LLC
ANCOVA	analysis of covariance
BLQ	below the limit of quantitation
BMI	body mass index
BOE	biomarker of exposure
BOPH	biomarker of potential harm
CI	confidence interval
CO	carbon monoxide
COHb	carboxyhemoglobin
CPD	cigarettes per day
CSP	clinical safety population
CSR	clinical study report
CV	coefficient of variation
ECG	electrocardiogram
eCO	exhaled carbon monoxide
EOS	end-of-study
EVP	e-vapor product
FVC	forced vital capacity
FEV <sub>1</sub>	forced expiratory volume in 1 second
GEE	generalized estimation equation
HDL-C	high-density lipoprotein cholesterol
ICF	informed consent form
ICH	International Conference on Harmonization
ITT	intent to treat
Kg	kilogram(s)
LC-MS	liquid chromatography–mass spectrometry
LLOQ	lower limit of quantitation
LLC	limited liability company
M	meter(s)
mCEQ	modified Cigarette Evaluation Questionnaire
MedDRA	Medical Dictionary for Regulatory Activities
Mg	milligram(s)
MITT	modified intent to treat
mL	milliliter(s)
MMRM	mixed model for repeated measures
N, n	sample size, number of observations
NBW	nicotine by weight
NE	nicotine Equivalents
Ng	Nanograms
NNAL	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol
NNN	N-nitrosornicotine
PFT	pulmonary function test
Pg	Pictogram
PMUSA	Phillip Morris USA
PP	per-protocol
Q1	first quartile

Q3	third quartile
QGEN	Generic Quality of Life scales
RBC	red blood cell
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
SEM	standard error of mean
sICAM-1	soluble intercellular adhesion molecule-1
SMS	short message service
TQOLIT	Tobacco-specific Quality of Life Impact Tool
WBC	white blood cell
WHO-DD	World Health Organization Drug Dictionary

## 1. INTRODUCTION

The following Statistical Analysis Plan (SAP) provides the framework for the summarization of the data from this study. The analysis plan may change due to unforeseen circumstances. Any changes made after locking of the database will be documented in the Clinical Study Report (CSR).

Any additional analyses not addressed within this SAP and/or driven by the data, or requested by Altria Client Services LLC, will be considered out of scope and must be approved, by Altria Client Services LLC, and must be described in the CSR.

## 2. OBJECTIVES AND ENDPOINTS

### 2.1 Objectives

#### 2.1.1 Primary Objective

The primary objective is to:

Compare absolute changes in selected biomarkers of exposure (BOEs) and biomarkers of potential harm (BOPHs) from Baseline to End of Study (Week 12) between adult smokers who continue to smoke conventional cigarettes (Control group) ad libitum and adult smokers who have completely<sup>b</sup> switched to ad libitum use of the test e-Vapor products (Test groups) for 12 weeks.

<sup>a</sup> Selected biomarkers include:

- o White Blood Cell Count (WBC Count)
- o High Density Lipoprotein Cholesterol (HDL-C)
- o Urinary 8-epi-prostaglandin F<sub>2α</sub>
- o Urinary 11-Dehydrothromboxane B<sub>2</sub>
- o Blood Soluble Intercellular Adhesion Molecule-1 (sICAM-1)
- o Urinary 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol and its glucuronides (total NNAL)
- o Carboxyhemoglobin (COHb)

<sup>b</sup> Subjects who exclusively use e-Vapor products and with eCO measurements < 8 ppm from Week 3 through Week 12

### 2.1.2 Secondary Objectives

The secondary objectives are to:

- Compare changes in selected biomarkers (same as those in the primary objective) from Day 1 to Week 6 between Test and Control groups
- Determine the number of cigarettes smoked (Test and Control groups) from Week 2 through Week 12
- Assess changes in the amount of test e-Vapor product use (Test groups only) from Week 2 through Week 12
- Assess adherence to protocol by comparing changes from Baseline to each post randomization measurement within the Test groups for exhaled CO (eCO) and urine N-nitrosornicotine (NNN)

### 2.1.3 Exploratory Objectives

The exploratory objectives are to:

- Assess differences in the BOPHs and BOEs (listed in the primary objective) between Baseline and Week 12 in the test groups that use different flavored e-Vapor products
- Assess changes in forced expiratory volume in the first second (FEV<sub>1</sub>), forced vital capacity (FVC) and FEV<sub>1</sub>/FVC ratios from Screening/Visit 2 to Week 12 between the Test and Control groups
- Assess changes in urine nicotine equivalents (NE) from Baseline to Week 6 and Week 12 between Test and Control groups
- Assess changes in the QGEN and TQOLIT questionnaires and the Cough Questionnaire responses from Baseline to Week 12 between the Test and Control groups
- Assess reasons for test product use/not-use at Week 12 and mCEQ questionnaires from Baseline to Week 12 for the Test groups
- Collect blood and urine samples for future assessment of BOE and or BOPH

## 2.2 Outcome Variables

### Primary

The primary outcome variables are the absolute change from Baseline (Day 1) to Week 12 for each of the following primary biomarkers:

- whole blood WBC Count
- serum HDL-C
- creatinine-adjusted urine 8-epi-prostaglandin F2 $\alpha$
- creatinine-adjusted urine 11-Dehydrothromboxane B2
- serum sICAM1
- creatinine-adjusted urine total NNAL
- blood COHb saturation

### **Secondary**

The secondary outcome variables are:

- The absolute change from Baseline to Week 6 for each of the primary biomarkers for each study group.
- The absolute change from Baseline to Week 12 for each of the primary biomarkers in the combined e-vapor use group (Test 1 + Test 2).
- Number of cigarettes smoked per day and test product used per day (number of new cartridges used and number of puffs taken, either 1-20 puffs or >20 puffs) during Week 2 through week 12
- Frequency and percentage of subjects with a reduction, no change, or increase in cigarettes used per day from Baseline to Week 12
- Frequency and percentage of subjects with a reduction, no change, or increase in e-vapor cartridges used per day from Baseline to Week 12
- Creatine-adjusted urine NNN determined at Baseline, Week 6, and Week 12
- eCO determined at Baseline, Week 3, Week 6, Week 9, and Week 12

### **Exploratory**

- The differences between Baseline and Week 12 for the primary biomarkers in the Test groups.
- Changes in FEV1, FCV, and FEV1/FVC from Screening (Visit 2) to Week 12 in the Test and Control Groups
- The creatinine-adjusted urine nicotine equivalent (NE) determined at Baseline, Week 6, and Week 12

- The absolute change in creatinine-adjusted urine NE from Baseline to Week 6 and from Baseline to Week 12
- Responses (Score) to the QGEN and TQOLIT questionnaires and the Cough Questionnaire recorded at Baseline, Week 6, and Week 12
- Responses to Reasons for Use and Not-use of Test Product at Week 12 and mCEQ questionnaires from Baseline to Week 12 (Test groups only)

#### **Clinical Safety**

- AEs and SAEs
- Blood pressure, ECG, vital signs, clinical chemistry, urinalysis, and hematology

### **3. STUDY DESIGN**

This is a randomized, parallel-group, open-label, controlled clinical study evaluating biomarkers of potential harm and exposure in adult smokers who continue to smoke conventional cigarettes or who completely switch to one of two different flavored e-Vapor products. Up to 450 adult male and female smokers (neither sex accounting for more than 60% of the population) were to be enrolled at multiple study sites.

Adult smokers (30 years of age to 65 years of age, inclusive) with  $\geq 10$  years of smoking and an average daily cigarette consumption of  $\geq 10$  cigarettes per day (CPD) will undergo initial screening procedures within 28 days prior to the start of the study at Visit 1 (Screening Part 1). Subjects who pass the initial screening at Visit 1 will be asked to return to the study site for a test product trial, completion of the Test e-Vapor Product Assessment questionnaire, and pulmonary function testing at Visit 2 (Screening Part 2). Subjects will continue to smoke their average CPD until returning to the study site for Visit 3 (Baseline, Day 1, Week 1).

Subjects who pass all eligibility requirements from Screening Parts 1 and 2 and are willing to replace all of their cigarettes with one of the test products will be asked to return to begin the study at Visit 3. At Visit 3, Subjects will be randomized (stratified by body mass index, sex, and age) in a 1:1:1 ratio to one of the following study groups:

- Test 1 group (n=150): Subjects who stop smoking during Week 1 and switch to ad libitum use of test e-Vapor Product XLCB, without use of any other type of tobacco/nicotine containing product, for the entire 12 weeks
- Test 2 group (n=150): Subjects who stop smoking during Week 1 and switch to ad libitum use of test e-Vapor Product XLMB, without use of any other type of tobacco/nicotine containing product, for the entire 12 weeks

- Control group (n=150): Subjects who continue smoking under ad libitum use of their own brand of conventional lit-end cigarettes, without use of any other type of tobacco/nicotine containing product, for the entire 12 weeks

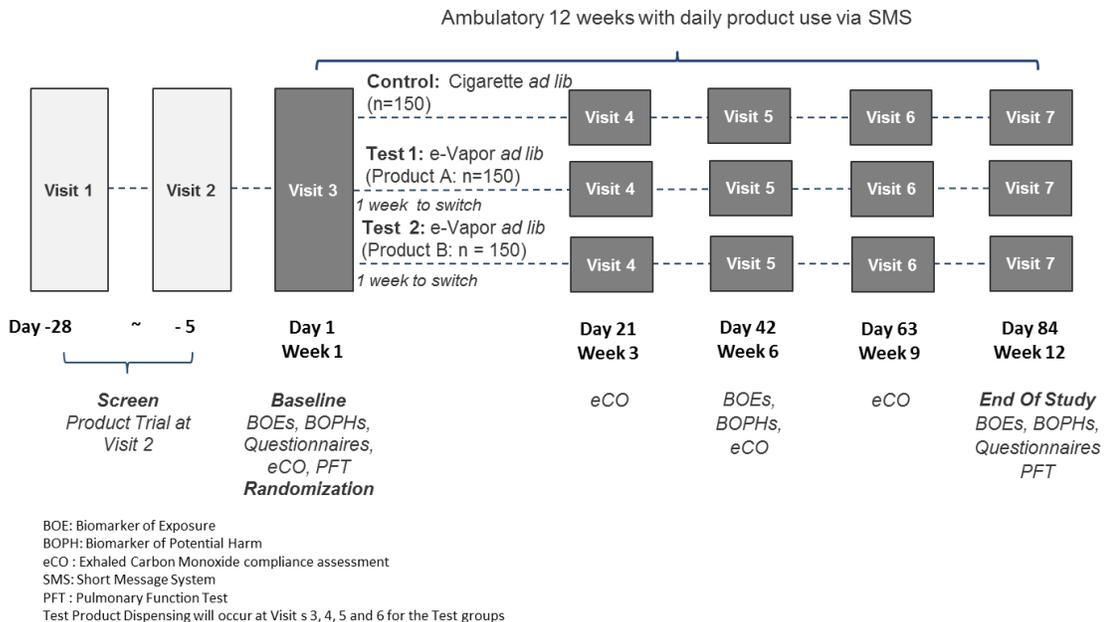
Subjects who drop out at the time of randomization will be replaced.

After screening, there will be 5 visits (Visits 3-7) to the study site at 3-week intervals over the 12-week study period. Subjects enrolled in the Test groups will receive a 3-week supply of test product at each visit except the end-of-study (EOS) visit, and will bring all used and unused cartridges to each visit to be counted.

All subjects will report their cigarettes per day (CPD) (Control and Test groups) and Test product use (Test groups only) daily using a Short Message Service (SMS), i.e., text message, based system (Med-Quest). The self-reported CPD, use of other tobacco products, and eCO measurements, taken during each of the five in-clinic visits after randomization will be used to monitor subject compliance.

At home on the morning of Visits 3, 5, and 7, subjects will obtain the first urine void of the day to be brought to the study site. At Visits 3, 5, and 7, blood and urine will be collected for assessment of biomarkers and biobanking, and questionnaires will be administered. At Visit 7, subjects will undergo pulmonary function testing and EOS procedures and be discharged from the study.

The overall design of the study is shown below.



#### 4. SAMPLE SIZE ESTIMATION

The study is designed to detect a statistically significant difference in change from baseline to the end of the study in 5 out of the 7 primary biomarkers between the Test

and the Control groups. Total NNAL, COHb, 11-Dehydrothromboxane B2, 8-epi-prostaglandin F2 $\alpha$  WBC and HDL values from a previous PMUSA longitudinal study (Study #: EHCJLI/02/02) for the Electronic Heating Cigarette Smoking System and S-ICAM values from another source (Scott DA et. al. 2000) were used for the sample size calculation. Assuming a two-sided test, 3.5 % Type I error rate (adjusted for multiplicity of detecting statistical significance in 5 out of the 7 biomarkers based on the Hailperion-Ruger approach), 80% power and a 1 to 1 ratio of the Test group over the Control group, a sample size of 120 subjects in the Test group and 120 in the Control group are needed. With a 15% dropout rate expected, 150 subjects are needed in each group. Because there are two test groups and one control group, a total of 450 subjects (300 in the Test and 150 in Control groups) are needed at the randomization.

## 5. ANALYSIS POPULATIONS

### **The Intent-to-Treat (ITT) Population:**

The Intent-to-Treat Population will include every subject who is randomized according to the randomization schedule.

### **The Modified Intent-to-Treat (mITT) Population:**

The Modified Intent-to-Treat Population will include those subjects in the ITT population for whom at least one use of study products (ie conventional cigarettes or test e-Vapor products) after randomization is recorded and for whom there is a baseline and at least one post-baseline biomarker measure.

### **The Clinical Safety Population (CSP):**

The Clinical Safety Population will consist of all subjects who are randomized and record at least one use of study products (ie conventional cigarettes or test e-Vapor products) after randomization. The subjects who only attend the product trial will also be included in the clinical safety population.

### **The Per-Protocol (PP) Population:**

The Per-Protocol Population will be a subset of the Modified Intent-to-Treat Population. The PP population will consist of subjects who completed the study without any major protocol violations. Major protocol violations are defined as:

- Control group: subjects who quit cigarette smoking (either by self report or NNN criteria of  $\geq 80\%$  reduction from baseline in NNN from baseline).
- Test groups: subjects who self-report use of  $> 10\%$  of baseline CPD over the course of the study, subjects with an eCO  $> 8$  ppm at Visits 4 – 7, subjects whose NNN levels are consistent with smoking cigarettes (ie,  $< 80\%$  reduction in NNN from baseline), and subjects who used  $\leq 2$  cartridges per week.

If it is determined that a subject was pregnant during the study, all of the pregnant subject's safety and biomarker data will be reported, but will be excluded from the biomarker summarization and statistical analyses.

## 6. STUDY GROUP AND PRODUCT DESCRIPTIONS

The following products will be tested in this study:

- Product A = Test EVP (currently marketed by Nu Mark LLC as MarkTen<sup>®</sup> XL Bold Classic [4.0% NBW]) [CVR2.6.8] Formula: 10381-44-B; Name: “Rosetta”; Label: B44 (Product XLCB)
- Product B = Test EVP (currently marketed by Nu Mark LLC as MarkTen<sup>®</sup> XL Bold Menthol [4.0% NBW]) [CVR2.6.8] Formula: 10381-40-E; Name: “Spencer”; Label: 40E (Product XLMB)

The following groups will be tested in this study:

- Test 1 Group = Exclusive ad libitum use of test e-Vapor Product XLCB for the entire 12 weeks
- Test 2 Group = Exclusive ad libitum use of test e-Vapor Product XLMB for the entire 12 weeks
- Test 1 + Test 2 Group = Combined e-vapor use group
- Control Group = Subjects who continued to smoke their own brand of lit-end conventional cigarettes ad libitum, without use of any other type of tobacco/nicotine containing product, for the entire 12 weeks

The following study group descriptions will be used in the footnotes for listings, tables, and figures.

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Test 1 + Test 2 Group = Combined e-Vapor Use Group

Control Group = Continue smoking lit-end conventional cigarette

Study groups will be referred to in the text as: Test 1 Group, Test 2 Group, Combined Test Group, and Control Group

## 7. BIOMARKER ASSESSMENT AND ANALYSIS

### 7.1 Biomarkers Sample Collection and Measurements

#### 7.1.1 Urine Biomarkers of Exposure and Biomarkers of Potential Harm

##### 7.1.1.1 Urine BOE and BOPH Sample Collection

The first urine void of the day will be collected by the subjects and brought to the study sites on Visit 3, Visit 5, and Visit 7. Aliquots will be taken for analysis of urine NE (nicotine, nicotine glucuronide, cotinine, cotinine glucuronide, trans-3'-hydroxycotinine, and trans-3'-hydroxycotinine glucuronide), total NNAL, NNN, 11-

dehydrothromboxane B<sub>2</sub>, and 8-epi-prostaglandin F<sub>2α</sub>, and creatinine. The remaining volume will be used for bio-banking.

#### 7.1.1.2 Bioanalytical Method

Urine aliquots for NE, total NNAL, NNN, 11-dehydrothromboxane B<sub>2</sub>, and 8-epi-prostaglandin F<sub>2α</sub> will be shipped to Celerion Bioanalytical Services for analysis. These samples will be analyzed using validated LC-MS/MS analytical methods.

Aliquots for creatinine will be shipped to the Celerion Clinical Laboratory for analysis.

Urine for bio-banking will be stored at Celerion until finalization of the CSR at which time they will be shipped to a long-term storage facility chosen by the Sponsor. The samples for future evaluation will be stored indefinitely and may be used to measure various biomarkers associated with tobacco use.

#### 7.1.1.3 Urine Biomarker Analysis Variables

- Creatinine-adjusted NE, total NNAL, NNN, 11-dehydrothromboxane B<sub>2</sub>, and 8-epi-prostaglandin F<sub>2α</sub> concentration
- Creatinine-adjusted absolute urine biomarker change from baseline (Visit 3)
- Creatinine-adjusted percent urine biomarker change from baseline (Visit 3)

Creatinine-adjusted concentrations will be calculated as shown in Section 6.1.1.3.2. Absolute and percent change from baseline will be calculated as shown in Section 6.1.1.3.3.

##### 7.1.1.3.1 Urine Nicotine Equivalents

Nicotine equivalents will be calculated as the molar sum of nicotine and 5 major nicotine metabolites. Values of individual components reported as below the limit of quantitation (BLQ) will be set to one-half of the limit of quantitation prior use in the calculation below. Missing urine data will not be imputed.

Nicotine equivalents (µg/mL) = (nicotine [ng/mL]/162.23 [mg/mmol] + nicotine-gluc [ng/mL]/338.36 [mg/mmol] + cotinine [ng/mL]/176.22 [mg/mmol] + cotinine-gluc [ng/mL]/352.34 [mg/mmol] + trans-3'-hydroxycotinine [ng/mL]/192.22 [mg/mmol] + trans-3'-hydroxycotinine-gluc [ng/mL]/368.34 [mg/mmol]) x 162.23 (mg/mmol) x 1 µg/1000 ng

##### 7.1.1.3.2 Urine Biomarkers Adjusted for Urine Creatinine

Urine creatinine concentration will also be measured in urine biomarker collection and will be used to adjust the concentration values of urine biomarkers as follows:

#### Nicotine Equivalents

Nicotine equivalents (mg/g creatinine) =  $\frac{\text{nicotine equivalents } (\mu\text{g/mL}) \times 100}{\text{creatinine (mg/dL)}}$

**NNAL, total NNAL, NNN, 11-dehydrothromboxane B2, and 8-epi-prostaglandin F2 $\alpha$**

$$\text{Urine biomarker (ng/g creatinine)} = \frac{\text{urine biomarker (pg/mL)} \times 100}{\text{creatinine (mg/dL)}}$$

**7.1.1.3.3 Urine Biomarker Change From Baseline**

Urine biomarker change from baseline will be calculated for creatinine-adjusted urinary NE, total NNAL, NNN, 11-dehydrothromboxane B2, and 8-epi-prostaglandin F2 $\alpha$  as follows, where Baseline = Visit 3:

$$\text{Absolute change from baseline} = \text{Post Product Use Value} - \text{Baseline Value}$$

$$\text{Percent change from baseline (\%)} = \frac{(\text{Post Product Use Value} - \text{Baseline Value})}{\text{Baseline Value}} \times 100 \%$$

**7.1.2 Blood Biomarkers of Exposure and Biomarkers of Potential harm**

**7.1.2.1 Blood BOE and BOPH Sample Collection**

Blood samples (approximately 4 mL each) will be collected via direct venipuncture for WBC count, sICAM-1 concentration, HDL-C concentration, and COHb saturation analysis at Visits 3, 5, and 7.

**7.1.2.2 Bioanalytical Method**

Blood samples for WBC count, HDL-C concentration, and COHb saturation will be shipped to the Celerion Clinical Laboratory for analysis. Whole blood COHb saturation will be determined using a validated spectrophotometric method at the Celerion Clinical Laboratory, Lincoln, Nebraska.

Blood samples for sICAM-1 concentration will be shipped to Celerion Bioanalytical Services for analysis. These samples will be analyzed using validated LC-MS/MS analytical methods.

**7.1.2.3 Blood Biomarker Analysis Variables**

The following variables will be determined for blood biomarkers:

- Blood WBC count, sICAM-1 concentration, HDL-C concentration, and COHb saturation
- Absolute blood biomarker change from baseline (Visit 3)
- Percent blood biomarker change from baseline (Visit 3)

Absolute and percent change from baseline will be calculated as shown in Section [6.1.1.3.3](#).

### **7.1.3 Product Use and Compliance Data Collection and Analysis Variables**

#### **7.1.3.1 Data Collection**

Product use (number conventional cigarettes used, number test e-vapor cartridges started, and number of puffs taken using the test products, either 1-20 or >20) will be reported daily (Day 1 through Day 84/Week 12) using a short message service. Exhaled CO (eCO) measurements will be performed by the clinic staff using the Micro+ basic™ Smokerlyzer® monitor (coVita) at Visits 3, 4, 5, 6, and 7. Use of other tobacco products will also be recorded at Visits 3, 4, 5, 6, and 7. Urine will be collected for determination of NNN at Visits 3, 5, and 7.

#### **7.1.3.2 Analysis Variables**

- Average number of cigarettes per day by week
- Average number of e-vapor cartridges started per day by week
- Frequency and percentage of subjects with a reduction, no change, or increase in cigarettes used per day from Baseline to Visit 7
- Frequency and percentage of subjects with a reduction, no change, or increase in e-vapor cartridges used per day from Baseline to Visit 7
- Measured eCO determined at Baseline, Visit 4, Visit 5, Visit 6, and Visit 7
- Use of Other tobacco products (yes/no)
- Creatinine-adjusted urine NNN determined at Baseline, Visit 5, and Visit 7 (calculated as described in Section 6.1.1.3.2)

### **7.1.4 Spirometry**

#### **7.1.4.1 Data Collection**

Pulmonary function testing will be performed at Screening Visit 2 (Baseline) and Visit 7 (Week 12).

#### **7.1.4.2 Analysis Variables**

The following pulmonary function parameters will be determined: measured FEV1, percent of predicted FEV1, measured FVC, percent of predicted FVC, measured FEV1/FVC, percent of predicted FEV1/FVC, FEV1% reversibility, and FEF25-75. Absolute change from baseline to Visit 7 will be determined for all parameters.

### **7.1.5 Questionnaires**

#### **7.1.5.1 Data Collection**

The QGEN, TQOLIT, and Cough questionnaires will be administered at Visits 3, 5, and 7 and the mCEQ Questionnaire will be administered at Visits 3 and 7. The Reasons of Use/Not-Use Test Product Questionnaire will be administered for the test groups only at Visit 7.

#### **7.1.5.2 Analysis Variables**

- QGEN and TQOLIT questionnaires: factor scores and the change in factor scores from Baseline to Week 6 and Week 12
- Responses to each question on Cough Questionnaire at Visits 3, 5, and 7 for test group only
- Responses to Reasons for Use and Not-use of Test Product questionnaire at Visit 7 for test group only
- mCEQ: Response scores for each question, the factor scores for Smoking satisfaction, Psychological reward, Aversion, Enjoyment of sensation, and Craving reduction, and the change in factor scores from Baseline to Week 12.

## 7.2 Data Summary and Presentation

The descriptive statistics tables for blood and urine biomarkers and products used per day will be generated with the following level of precision for the summary statistics:

The derived values (amount excreted in urine biomarkers, change and percent change from baseline) will have two decimal points.

- n, n missing without a decimal;
- Mean/median with one more decimal/significant figure than minimum/maximum;
- Q1 and Q3 with one more decimal/significant figure than minimum/ maximum;
- SD/SEM with one more decimal/significant figure than mean/median.
- CV% with one decimal;
- Minimum/maximum in same precision as in the database
- 95% CI with one more decimal/significant figure than minimum/ maximum

### 7.2.1 Demographic Summary

Descriptive statistics will be summarized for continuous demographics variables (e.g., age, weight, height, and BMI) and frequency counts will be tabulated for categorical demographics variables (e.g., gender, ethnicity, race, income level, and highest education grade level) by study group, and overall. The variable BMI is calculated from the weight and height collected at the Screening assessment and age is calculated from the date of the Screening visit. Subjects only enrolled in the product trial period (dropped prior to randomization) will be summarized separately.

The CSP, ITT and PP populations will be used for this summary.

### 7.2.2 Smoking History

CPD and years of smoking (calculated from Screening date reported at Screening will be listed. Descriptive statistics will be summarized by study group, age class, and gender for continuous variables and frequency counts will be tabulated for categorical variables. Subjects only enrolled in the product trial period will be summarized separately.

The CSP, ITT and PP populations will be used for this summary.

### **7.2.3 Urine BOE and BOPH**

Urine biomarker concentration (including each component of NE), urine creatinine concentration, and the creatinine-adjusted urine biomarker concentration will be listed by subject and study visit for urine NE, total NNAL, NNN, 11-dehydrothromboxane B<sub>2</sub>, and 8-epi-prostaglandin F<sub>2</sub> $\alpha$ . All BLQ values will be presented as “BLQ” in the listings.

Creatinine-adjusted urine biomarker concentration, absolute change from baseline creatinine-adjusted urine biomarker concentration, and percent change from baseline creatinine-adjusted urine biomarker concentration will be summarized by group and visit for each of the following biomarkers: urine NE, total NNAL, NNN 11-dehydrothromboxane B<sub>2</sub>, and 8-epi-prostaglandin F<sub>2</sub> $\alpha$  using descriptive statistics (number of observations [n], number of missing values [n missing], arithmetic mean (mean), standard deviation [SD], coefficient of variation [CV%], standard error of the mean (SEM), minimum, median, minimum, maximum, and 95% CI). The descriptive statistics will be provided for both mITT and PP populations.

### **7.2.4 Blood BOE and BOPH**

Blood biomarker concentrations will be listed by subject and study visit for WBC count, HDL-C, sICAM-1, and COHb. All BLQ values for COHb will be presented as “BLQ” in the listings.

Blood biomarker concentration, absolute change from baseline blood biomarker concentration, and percent change from baseline biomarker concentration will be summarized by group and study visit using descriptive statistics (number of observations[n], number of missing values [n missing], arithmetic mean [mean], standard deviation [SD], coefficient of variation [CV%], standard error of the mean [SEM], minimum, median, maximum, and 95% CI). BLOQ COHb saturation will be treated as one-half the LLOQ. The descriptive statistics will be provided for both mITT and PP populations.

### **7.2.5 Product Use and Compliance**

#### Product Use

Number of cigarettes smoked per day, number of new e-vapor cartridges started per day, and number of puffs taken using test products (1-20 puffs or >20 puffs) will be listed by subject and study day. The average number of cigarettes smoked per day and e-cartridges started per day will be summarized by group and Week (Weeks 1 through 12) using descriptive statistics (number of observations [n], number of missing values [n missing], arithmetic mean [mean], standard deviation [SD], coefficient of variation [CV%], standard error of the mean [SEM], minimum, Q1, median, Q3, maximum and 95% CI). The overall averages for Weeks 2 through 6 and

Weeks 7 through 12 will be presented. The percent change from baseline (Week 1) to Week 6 and Week 12 will be calculated. Frequency tables (n, %) will also be used to summarize the proportions of subjects in the following percent change categories: reduce, no change, or increase from Baseline to Week 12 for each study group.

#### Compliance

Use of other tobacco products (yes/no), eCO concentration, and creatinine-adjusted NNN concentration will be listed by subject and study day. Frequency tables (n and %) will be used to summarize use of other tobacco products (yes/no), eCO ( $\leq 5$ ,  $>5$  to  $\leq 8$  and  $>8$ ) ppm and NNN ( $< 80\%$  reduction from baseline or  $\geq 80\%$  reduction from baseline) for assessment of compliance and noncompliance for each study group.

Product use and compliance analyses will be performed on the mITT dataset.

### **7.2.6 Questionnaires**

The responses and the following factor scores from the QGEN and TQOLIT will be presented and listed by subject and study visit:

- QGEN Physical Health General Score
- QGEN Emotional Health General Score
- QGEN estimated Physical Component Summary
- QGEN estimated Mental Component Summary
- TQOLIT Physical Functioning Supplemental
- TQOLIT General Health-Confidence
- TQOLIT Smoking Symptoms
- TQOLIT Smoking or Vaping Impact

The mCEQ will be considered as a 7-point scale and treated as a continuous variable. The responses from mCEQ-C or mCEQ-E will be listed as individual responses and as following factor scores<sup>1</sup> by subject and study visit:

- Smoking satisfaction: average of the response scores from questions 1, 2, and 12;
- Psychological reward: average of the response scores from questions 4 to 8;
- Aversion: average of the response scores from questions 9 and 10;
- Enjoyment of sensation: response score from question 3;
- Craving Reduction: response score from question 11.

---

<sup>1</sup> Cappelleri et al. 2007. Confirmatory factor analysis and reliability of the modified cigarette evaluation questionnaire. Addictive Behaviors. (32)912-923

Descriptive statistics (n, n missing, mean, SD, CV%, SEM, minimum, Q1, median, Q3, maximum, and 95% CI) of each of the response score and factor score will be provided by study group and study visit.

The responses from Cough Questionnaire (Visits 3, 5, and 7) and Reasons of Use/Not-Use Test Product Questionnaire (Visit 7) will be listed by subject and study visit. The frequency (n, %) of responses to Questions I and III through X will be summarized by study group. The responses to Question II will be summarized by study group using the same descriptive statistics as for the above questionnaires.

These analyses will be performed on the mITT dataset.

### 7.3 Statistical Analyses

#### 7.3.1 Primary Endpoint Analysis

A linear mixed model for repeated measures (MMRM) analysis will be used for comparing each test group (Test 1 or 2) to the control group in the mean absolute change from Baseline to Week 12 (Visit 7) in each primary biomarker (WBCs, HDL-C, 8-epi-prostaglandin  $F_{2\alpha}$ , 11-dehydrothromboxane  $B_2$ , sICAM-1, total NNAL, and COHb). In the model, study group (each of the two test group vs control), visit, and study group by visit interaction, gender, age class (less than 45 years or greater or equal to 45 years), and BMI class (less than 25 kg/m<sup>2</sup> or greater or equal to 25 kg/m<sup>2</sup>) are the fixed effect factors. The baseline value of the response biomarker is the fixed effect covariate and subject is the random effect factor. A restricted maximum likelihood estimation method will be applied and several covariance structures will be tried. Five candidate covariance structures will be considered: compound symmetry, 1st order autoregressive, 1st order autoregressive with a random subject effect, unstructured and Toeplitz. The most appropriate covariance structure will be determined based on the AIC criteria (the covariance structure with the smallest AIC will be chosen). If the model cannot be converged, a robust sandwich estimator for the standard error of the fixed effects will be used. The least-square mean difference, 95% confidence interval and p-value will be provided for the group difference. Pairwise comparisons (Test 1 vs. control, and Test 2 vs. control) will be performed using a Dunnett's test at a 2-sided significance level of 0.05 to adjust for multiplicity. The analysis will be conducted on the mITT and PP datasets.

The following SAS codes will be used to perform the analysis.

```
Proc mixed data=< >;  
Class subject gender race group visit age bmi;  
Model response = gender group visit group*visit age bmi baseline/ddfm=kr;  
Repeated visit/type=<type> subject=subject;  
LSmeans group*visit/CL alpha=0.05 pdiff dunnett('CONTROL');  
Run;
```

Note: This model will include both the Week 12 value (primary endpoint) and interim time points (secondary endpoint). The above analysis will also output the residual diagnosis to check for normality and to identify outliers).

### **7.3.1.1 Multiplicity adjustment**

The study was designed to detect a statistically significant difference in change from Baseline to Week 12 (Visit 7) in 5 of 7 primary biomarkers using a two-sided test with a 3.5% Type I error rate (adjusted for multiplicity based on the Hailperin-Ruger approach). Multiplicity adjustments will be applied to the primary statistical analysis for the biomarker endpoints. Multiplicity adjustment will not be conducted for secondary and exploratory analyses. After the completion of the primary analysis for the seven primary biomarkers, a decision will be made with regard to the overall study endpoint. The overall study result will be considered as beneficial if the lsmean difference in biomarker level change between each of the test groups and the control group is statistically significant with a p value < 0.035 in at least 5 of the 7 biomarkers and with a favorable change (HDL level goes up and all other levels of all other biomarkers go down) in the mITT population.

### **7.3.1.2 Dealing with non-normality**

A standard residual analysis using Proc Mixed procedure will be used to examine validity of normality assumptions for the primary endpoints including WBCs, HDL-C, 8-epi-prostaglandin  $F_{2\alpha}$ , 11-dehydrothromboxane  $B_2$ , sICAM-1, total NNAL, and COHb. A natural logarithmic transformation will be applied to the endpoint in the linear mixed model if the normality assumption does not hold.

## **7.3.2 Secondary Endpoint Analysis**

The same statistical analysis model defined in the primary analysis Section 6.3.2 will also be used to make the following comparisons for the primary biomarkers (WBCs, HDL-C, 8-epi-prostaglandin  $F_{2\alpha}$ , 11-dehydrothromboxane  $B_2$ , sICAM-1, total NNAL, and COHb):

- absolute change from Baseline to Week 12 between the combined e-vapor use group (Test 1 + Test 2) and the Control group.
- absolute change from Baseline to Week 12 between the two test groups (Test 1 vs Test 2).
- absolute change from Baseline to Week 6 between each Test group and the Control group.

These analyses will be conducted on the mITT datasets.

Product use and compliance variables will be summarized using the mITT dataset as described in Section 7.2.5.

### 7.3.3 Exploratory Endpoint Analysis

A paired t-test will be used for the exploratory analysis to compare:

- each of the primary biomarkers between baseline and Week 12 within each test product group.

The following SAS codes will be used to perform the analysis:

```
proc ttest data=< >;  
by group;  
paired baseline*EOS;  
run;
```

*Note for programmer: The dataset need to be transposed to put the baseline and end-of-study value in the same row for the same subject prior to perform the analysis. The analysis will be performed for both test groups.*

The same statistical analysis model defined in the primary analysis Section 6.3.2 will also be used for the exploratory analysis to provide estimates for:

- changes in urine nicotine equivalents (NE) from Baseline to Week 6 and Week 12 between the Test and Control groups.

For the following endpoints, the same statistical analysis model defined in the primary analysis Section 6.3.2 but without the fixed effect of BMI will be used for the exploratory analysis to evaluate:

- Absolute changes in the QGEN and TQOLIT questionnaire responses from Baseline to Week 12 between the Test and Control groups.

The following SAS codes will be used to perform the analysis:

```
Proc mixed data=< >;  
Class subject gender group visit age;  
Model response = gender group visit group*visit age baseline/ddfm=kr;  
Repeated visit/type=<type> subject=subject;  
LSmeans group*visit/CL alpha=0.05 pdiff;  
Run;
```

For the endpoints with only Baseline and Week 12 measurements, an ANCOVA model will be used for the exploratory analysis to evaluate:

- Absolute changes in percent of predicted FEV1, FVC, and FEV1/FVC ratios from Baseline to Week 12 between the Test and Control groups

- Absolute changes in the mCEQ factor score from Baseline to Week 12 in the Test and Control groups

In the model, study group, gender, and age class (less than 45 years or greater or equal to 45 years) are the fixed effect factors. The baseline value of the measurement is the fixed effect covariate.

The following SAS codes will be used to perform the analysis:

```
proc mixed data=< >;  
class subject gender group age;  
model testname = gender group age baseline;  
lsmeans group/diff cl alpha=0.05;  
run;
```

Responses to the Reasons of Use/Not-Use Test Product questionnaire will be summarized using frequency count tables for each question.

These analyses will be conducted on the mITT datasets, except for spirometry data analyses, which will be conducted on mITT and PP datasets.

#### **7.3.4 Subgroup Analysis**

Descriptive statistics will be provided for absolute change from baseline to Week 12 (for primary endpoints) by gender and age class (less than 45 years or greater or equal to 45 years and BMI class (less than 25 kg/m<sup>2</sup> or greater or equal to 25 kg/m<sup>2</sup>). These analyses will be based on the mITT dataset.

Subgroup analysis will be conducted for the difference in absolute change from baseline to Week 12 by gender, age class and BMI class if the subgroup factor in the model is statistically significant. Subgroup analysis will be conducted on the mITT dataset.

The same statistical analysis model in the primary analysis will be used for subgroup analysis. An additional fixed effect, study group by subgroup interaction (gender, age class, or BMI class), will be included in the statistical analysis model. The subgroup analysis will only be performed when the main effect of the subgroup factor (gender, age class, or BMI class) is statistically significant in the primary analysis.

#### **7.3.5 Sensitivity Analysis**

##### **7.3.5.1 Analysis Variables for Sensitivity Analysis**

The sensitivity analysis will be performed for primary endpoints (whole blood WBC count, serum HDL-C concentration, creatinine-adjusted urine 8-epi-prostaglandin F<sub>2α</sub>, creatinine-adjusted urinary 11-dehydrothromboxane B<sub>2</sub>, serum sICAM-1, creatinine-adjusted total NNAL, and whole blood COHb).

### 7.3.5.2 Handling of Missing Data

Two methods will be tested for the handling of missing data, last observation carried forward and multiple imputation, using the mITT population. For all other analyses, data will not be imputed. Baseline is not expected to be missing for the mITT population.

Multiple imputation is needed as a sensitivity analysis for the primary endpoint analysis in case the data are missing not at random. Multiple imputation will be conducted to impute the missing data values for the primary endpoints (absolute change from baseline to Week 12 for whole blood WBC count, serum HDL-C concentration, creatinine-adjusted urine 8-epi-prostaglandin F<sub>2α</sub>, creatinine-adjusted urine 11-dehydrothromboxane B<sub>2</sub>, serum sICAM-1, creatinine-adjusted total NNAL, and whole blood COHb). The imputation starts with using SAS procedure Proc MI to generate (n=m) completed data sets. Then each data set will be analyzed with SAS procedure Proc Mixed to generate m point estimates and standard errors for the model parameters. Finally, SAS procedure Proc Mianalyze will be used to combine the estimation results

The Following SAS codes will be used for imputation and analysis.

1) use PROC MI to impute the missing data;

```
proc mi data=... seed=... nimpute=200 out=miout noprint;  
mcmc;  
var biomarker_baseline biomarker_Week6 biomarker_Week12 ;  
run;
```

2) use PROC MIXED to model the multiple imputed datasets:

```
proc mixed data=miout order=internal ;  
by _imputation_ ;  
class subject gender BMI age group ;  
model biomarker CFS= gender group age bmi baseline/ddfm=kr;  
lsmeans group / alpha=0.05 CL pdiff;  
ods output lsmeans=lsmnout;  
ods output diffs=diff;  
run;
```

3) use PROC MIANALYZE to generate the int (lsmnoutmi, diffmi) from the multiple estimates (lsmnout, diff).

```
proc sort data=lsmnout;by group _imputation_ ;run;  
proc mianalyze data=lsmnout alpha=0.05;  
by group ;  
modeleffects group;  
ods output ParameterEstimates=lsmnoutmi;
```

```

stderr stderr;
run;

proc sort data=diff;by group _imputation_;run;
proc mianalyze data=diff alpha=0.05;
  by group ;
modeleffects group;
  ods output ParameterEstimates=diffmi;
stderr stderr;
run;

```

### 7.3.5.3 Examining Influence of Outliers

Data outliers will be examined through Proc Mixed model residual diagnosis (+/- 4 studentized residuals). The outlier test results will be conducted for the primary endpoints (absolute change from baseline to Week 12 for whole blood WBC count, serum HDL-C concentration, creatinine-adjusted urine 8-epi-prostaglandin F<sub>2α</sub>, creatinine-adjusted urine 11-dehydrothromboxane B<sub>2</sub>, serum sICAM-1, creatinine-adjusted total NNAL, and whole blood COHb). A sensitivity analysis by excluding outliers will be performed for the primary analysis variables at Visit 7 (Week 12) if any outliers are found using the above criteria.

### 7.3.5.4 Handling BLQ values

Values below the limit of quantitation (BLQ) for nicotine and its metabolites, COHb, NNAL, NNN, 8-epi-prostaglandin F<sub>2α</sub>, 11-dehydrothromboxane B<sub>2</sub>, and sICAM-1 will be presented in the data listings as BLQ. Values BLQ for nicotine and metabolites will be set to one-half of the limit of quantitation prior use in the calculation of nicotine equivalents and data analysis of NE. Values BLQ for NNAL, NNN, 8-epi-prostaglandin F<sub>2α</sub>, 11-dehydrothromboxane B<sub>2</sub>, sICAM-1 and COHb will be set to one-half of the LLOQ prior to data analysis. A sensitivity analysis of the primary endpoint analysis will be conducted by setting the BLQ value to the LLOQ if the percentage of values that are BLQ is greater than 5% of observations. The sensitivity analysis for NE will be conducted if the percentage of observations that are BLQ is greater than 5% for any one of the NE components. LLOQ values for each analyte are shown in the table below.

Analyte	LLOQ
Nicotine	50.0 ng/mL
Cotinine	50.0 ng/mL
trans-3'-hydroxycotinine	50.0 ng/mL
nicotine glucuronide	50.0 ng/mL
cotinine glucuronide	200 ng/mL
trans-3'-hydroxycotinine glucuronide	200 ng/mL
NNN	0.200 pg/mL

NNAL	5.00 pg/mL
11-dehydrothromboxane B2	25.0 pg/mL
8-epi-prostaglandin F2 $\alpha$	25.0 pg/mL
sICAM-1	12.5 ng/mL
COHb	0.2%

## 8. SAFETY

No inferential statistics will be performed on the safety data.

All clinical safety data will be listed by subject. Continuous variables will be summarized using n, mean, SD, median, minimum, and maximum. Frequency counts will be reported for all categorical data.

Decimal point will be presented as follows:

- n will be presented without decimal;
- Minimum/maximum in same precision as in the database;
- Mean/median in one more decimal than minimum/maximum;
- SD in one more decimal than mean/median.

Where individual data points are missing because of dropouts or other reasons, the data will be summarized based on reduced denominators.

### 8.1 Subject Disposition

The number of subjects enrolled, the number who completed the study, and the number who did not complete the study (overall and reasons for early withdrawal) will be tabulated by study group and overall. A listing of subjects who discontinued the study prematurely will also be presented.

### 8.2 Adverse Events

Adverse events will be coded (to the lowest level term) with the Medical Dictionary for Regulatory Activities (MedDRA<sup>®</sup>) version 19.0.

A study product use-emergent AE is defined as an AE that is starting or worsening at the time of or after study product administration.

All events captured in the database will be listed in by-subject data listings. However, only study product use-emergent adverse events will be summarized.

Frequencies of subjects with study product use-emergent AEs, regardless of relationship to study product will be summarized by study group and sorted by system organ class. Frequencies of subjects with study product use-emergent serious adverse events will be likewise summarized. Frequencies of study product use-emergent adverse events will be summarized by severity and relationship to study group. Adverse events occurred during the product trial period will be summarized separately.

### **8.3 Clinical Laboratory**

Clinical laboratory evaluations (clinical chemistry, hematology, and urinalysis) will be performed at Screening and at End-of-Study or Early Termination.

Descriptive statistics will be reported for numeric clinical data by study group and time point. Rechecked values prior to randomization will be used in calculating summary statistics. Normal ranges will be listed by site. Subjects only enrolled in the product trial period will be summarized separately.

Out of normal range and clinically significant laboratory values will be listed by subject.

A urine cotinine test will be completed at Screening. Urine drug tests and alcohol breath tests will be completed at Screening. Serum pregnancy tests will be completed at Screening and urine pregnancy tests will be completed at each study visit. Results for these tests will be listed as “Negative” or “Positive.”

### **8.4 Vital Signs**

Vital signs (respiration rate, pulse rate, blood pressure, and oral temperature) will be measured at screening, at each study visit, and at the End-of-Study or upon Early Termination. At each study visit, vital signs will be taken at least 15 minutes after the last conventional cigarette smoked or test e-Vapor product used.

Descriptive statistics will be reported for vital sign measurements (blood pressure, pulse, respiration, and temperature) by study group and time point. Post randomization rechecks will not be used for calculation of descriptive statistics. Subjects only enrolled in the product trial period will be summarized separately.

### **8.5 ECG**

A 12-lead ECG will be obtained during screening and at End of Study or Early Termination.

Descriptive statistics will be reported for ECG measurements (HR, PR, QRS, QT, and QTcB intervals) by study group and time point. Rechecks prior to randomization will be used in determination of values. Subjects only enrolled in the product trial period will be summarized separately. ECG information will be listed by subject.

### **8.6 Concomitant Medications**

All concomitant medications recorded during the study will be coded using the WHO Drug Dictionary version 01SEP2016 and listed by subject.

### **8.7 Physical Examination**

Physical examinations will be performed at Screening. A brief physical examination (symptom driven) will be performed at Study Visit 3 (Week 1) and End of Study (or Early Termination). Physical examinations will be listed by subject and time point of

collection. Changes in physical examinations (if any) will be described in the text of the final report.

## 9. SUMMARY TABLES AND FIGURES

Summary tables and figures are numbered following the International Conference on Harmonization (ICH) structure. Please note that all summary tables and figures will be generated using SAS<sup>®</sup> Version 9.3 or higher.

The following is a list of table numbers and titles that will be included as summary tables:

### 14.1 Demographic Data Summary Tables

Table 14.1.1	Summary of Disposition Overall and by Study Group
Table 14.1.2	Demographic Summary Overall and by Study Group
Table 14.1.3	Smoking History Overall and by Study Group

### 14.2 Data Summary Tables and Figures for Biomarkers of Potential Harm and Exposure, Product Use, Spirometry, and Questionnaire Responses

#### 14.2.1 Biomarkers of Potential Harm and Exposure Tables

**Primary and Secondary Biomarker endpoints (WBC count, HDL-C, urine 8-epi-prostaglandin F2 $\alpha$ , urine 11-dehydrothromboxane B2, sICAM-1, total NNAL, COHb)**

***Whole Blood WBC Count Tables***

Table 14.2.1.1.1.1	Summary of Whole Blood WBC Count (x 10 <sup>3</sup> / $\mu$ L) by Study Group and Visit (mITT Population)
Table 14.2.1.1.1.2	Summary of Whole Blood WBC Count (x 10 <sup>3</sup> / $\mu$ L) by Study Group and Visit (PP Population)
Table 14.2.1.1.2.1	Summary of Whole Blood WBC Count Absolute Change From Baseline (x 10 <sup>3</sup> / $\mu$ L) by Study Group and Visit (mITT Population)
Table 14.2.1.1.2.2	Summary of Whole Blood WBC Count Absolute Change From Baseline (x 10 <sup>3</sup> / $\mu$ L) by Study Group and Visit (PP Population)
Table 14.2.1.1.3.1	Summary of Whole Blood WBC Count Percent Change From Baseline (%) by Study Group and Visit (mITT Population)

Table 14.2.1.1.3.2	Summary of Whole Blood WBC Count Percent Change From Baseline (%) by Study Group and Visit (PP Population)
Table 14.2.1.1.4.1	Statistical Summary of Whole Blood WBC Count Absolute Change From Baseline ( $\times 10^3/\mu\text{L}$ ) by Study Group and Visit (mITT Population)
Table 14.2.1.1.4.2	Statistical Comparisons of Whole Blood WBC Count Absolute Change From Baseline ( $\times 10^3/\mu\text{L}$ ) Between Study Groups by Visit (mITT Population)
Table 14.2.1.1.5.1	Statistical Summary of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) by Study Group (PP Population)
Table 14.2.1.1.5.2	Statistical Comparisons of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) Between Study Groups (PP Population)
Table 14.2.1.1.6.1	Summary of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) by Study Group and Gender (mITT Population)
Table 14.2.1.1.6.2	Summary of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) by Study Group and Age Class (mITT Population)
Table 14.2.1.1.6.3	Summary of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) by Study Group and BMI Class (mITT Population)
Table 14.2.1.1.7.1	Statistical Summary of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) by Study Group and Gender (mITT Population) (Note: This analysis will only be performed if gender term is statistically significant)
Table 14.2.1.1.7.2	Statistical Comparisons of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) Between Study Groups by Gender (mITT Population) (Note: This analysis will only be performed if gender is statistically significant)
Table 14.2.1.1.8.1	Statistical Summary of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) by Study Group and Age Class (mITT Population) (Note: This analysis will only be performed if Age Class is statistically significant)

- Table 14.2.1.1.8.2 Statistical Comparisons of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) Between Study Groups by Age Class (mITT Population) (Note: This analysis will only be performed if Age Class is statistically significant)
- Table 14.2.1.1.9.1 Statistical Summary of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) by Study Group and BMI Class (mITT Population) (Note: This analysis will only be performed if BMI Class is statistically significant)
- Table 14.2.1.1.9.2 Statistical Comparisons of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) Between Study Groups by BMI Class (mITT Population) (Note: This analysis will only be performed if BMI Class is statistically significant)
- Table 14.2.1.1.10.1 Statistical Summary of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) by Study Group (mITT Population with Imputation of Missing Data Using Last Observation Carried Forward Method)
- Table 14.2.1.1.10.2 Statistical Comparisons of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) Study Groups (mITT Population with Imputation of Missing Data Using Last Observation Carried Forward Method)
- Table 14.2.1.1.11.1 Statistical Summary of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) by Study Group (mITT Population with Imputation of Missing Data Using Multiple Imputation by SAS MI Procedure)
- Table 14.2.1.1.11.2 Statistical Comparisons of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) Between Study Groups (mITT Population with Imputation of Missing Data Using Multiple Imputation by SAS MI Procedure)
- Table 14.2.1.1.12.1 Summary of Whole Blood WBC Count Absolute Change From Baseline ( $\times 10^3/\mu\text{L}$ ) by Study Group and Visit (mITT Population with Outliers Excluded)
- Table 14.2.1.1.12.2 Statistical Summary of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) by Study Group (mITT Population with Outliers Excluded)

- Table 14.2.1.1.12.3 Statistical Comparisons of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) Between Study Groups (mITT Population with Outliers Excluded)
- Table 14.2.1.1.13.1 Statistical Summary of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) by Study Group (mITT Population with BLQ values set to the LLOQ) (Note: This analysis will only be performed if the percentage of values that are BLQ is greater than 5% of observations.)
- Table 14.2.1.1.13.2 Statistical Comparisons of Whole Blood WBC Count Absolute Change From Baseline to Visit 7 ( $\times 10^3/\mu\text{L}$ ) Between Study Groups (mITT Population with BLQ values set to the LLOQ) (Note: This analysis will only be performed if the percentage of values that are BLQ is greater than 5% of observations.)
- Table 14.2.1.1.14 Statistical Comparisons of Whole Blood WBC Count ( $\times 10^3/\mu\text{L}$ ) between Baseline and Visit 7 by Study Group (mITT Population) (Note: this analysis will be done for the two test groups.)

***Serum HDL-C Tables***

- Table 14.2.1.2.1.1 Summary of Serum HDL-C (mg/dL) by Study Group and Visit (mITT Population)
- Table 14.2.1.2.1.2 Summary of Serum HDL-C (mg/dL) by Study Group and Visit (PP Population)
- Table 14.2.1.2.2.1 Summary of Serum HDL-C Absolute Change From Baseline (mg/dL) by Study Group and Visit (mITT Population)
- Table 14.2.1.2.2.2 Summary of Serum HDL-C Absolute Change From Baseline (mg/dL) by Study Group and Visit (PP Population)
- Table 14.2.1.2.3.1 Summary of Serum HDL-C Percent Change From Baseline (%) by Study Group and Visit (mITT Population)
- Table 14.2.1.2.3.2 Summary of Serum HDL-C Percent Change From Baseline (%) by Study Group and Visit (PP Population)
- Table 14.2.1.2.4.1 Statistical Summary of Serum HDL-C Absolute Change From Baseline (mg/dL) by Study Group and Visit (mITT Population)

Table 14.2.1.2.4.2	Statistical Comparisons of Serum HDL-C Absolute Change From Baseline (mg/dL) Between Study Groups by Visit (mITT Population)
Table 14.2.1.2.5.1	Statistical Summary of Serum HDL-C Absolute Change From Baseline to Visit 7 (mg/dL) by Study Group (PP Population)
Table 14.2.1.2.5.2	Statistical Comparisons of Serum HDL-C Absolute Change From Baseline to Visit 7 (mg/dL) Between Study Groups (PP Population)
Table 14.2.1.2.6.1	Summary of Serum HDL-C Absolute Change From Baseline to Visit 7 (mg/dL) by Study Group and Gender (mITT Population)
Table 14.2.1.2.6.2	Summary of Serum HDL-C Absolute Change From Baseline to Visit 7 (mg/dL) by Study Group and Age Class (mITT Population)
Table 14.2.1.2.6.3	Summary of Serum HDL-C Absolute Change From Baseline to Visit 7 (mg/dL) by Study Group and BMI Class (mITT Population)
Table 14.2.1.2.7.1	Statistical Summary of Serum HDL-C Absolute Change From Baseline to Visit 7 (mg/dL) by Study Group and Gender (mITT Population) (Note: This analysis will only be performed if gender term is statistically significant)
Table 14.2.1.2.7.2	Statistical Comparisons of Serum HDL-C Absolute Change From Baseline to Visit 7 (mg/dL) Between Study Groups by Gender (mITT Population) (Note: This analysis will only be performed if the gender term is statistically significant)
Table 14.2.1.2.8.1	Statistical Summary of Serum HDL-C Absolute Change From Baseline to Visit 7 (mg/dL) by Study Group and Age Class (mITT Population) (Note: This analysis will only be performed if the Age class term is statistically significant)
Table 14.2.1.2.8.2	Statistical Comparisons of Serum HDL-C Absolute Change From Baseline to Visit 7 (mg/dL) Between Study Groups by Age Class (mITT Population) (Note: This analysis will only be performed if the Age Class interaction is statistically significant)
Table 14.2.1.2.9.1	Statistical Summary of Serum HDL-C Absolute Change From Baseline to Visit 7 (mg/dL) by Study Group and

	BMI Class (mITT Population) (Note: This analysis will only be performed if the BMI class term is statistically significant)
Table 14.2.1.2.9.2	Statistical Comparisons of Serum HDL-C Absolute Change From Baseline to Visit 7 (mg/dL) Between Study Groups by BMI Class (mITT Population) (Note: This analysis will only be performed if the BMI Class interaction is statistically significant)
Table 14.2.1.2.10.1	Statistical Summary of Serum HDL-C Absolute Change From Baseline (mg/dL) to Visit 7 by Study Group (mITT Population with Imputation of Missing Data Using Last Observation Carried Forward Method)
Table 14.2.1.2.10.2	Statistical Comparisons of Serum HDL-C Absolute Change From Baseline to Visit 7 (mg/dL) Between Study Groups (mITT Population with Imputation of Missing Data Using Last Observation Carried Forward Method)
Table 14.2.1.2.11.1	Statistical Summary of Serum HDL-C Absolute Change From Baseline to Visit 7 (mg/dL) by Study Group (mITT Population with Imputation of Missing Data Using Multiple Imputation by SAS MI Procedure)
Table 14.2.1.2.11.2	Statistical Comparisons of Serum HDL-C Absolute Change From Baseline to Visit 7 (mg/dL) Between Study Groups (mITT Population with Imputation of Missing Data Using Multiple Imputation by SAS MI Procedure)
Table 14.2.1.2.12.1	Summary of Serum HDL-C Absolute Change From Baseline (mg/dL) by Study Group and Visit (mITT Population with Outliers Excluded)
Table 14.2.1.2.12.2	Statistical Summary of Serum HDL-C Absolute Change From Baseline to Visit 7 (mg/dL) by Study Group (mITT Population with Outliers Excluded)
Table 14.2.1.2.12.3	Statistical Comparisons of Serum HDL-C Absolute Change From Baseline to Visit 7 (mg/dL) Between Study Groups (mITT Population with Outliers Excluded)
Table 14.2.1.2.13.1	Statistical Summary of Serum HDL-C Absolute Change From Baseline to Visit 7 (mg/dL) by Study Group (mITT Population with BLQ values set to the LLOQ) (Note: This analysis will only be performed if the

percentage of values that are BLQ is greater than 5% of observations.)

Table 14.2.1.2.13.2 Statistical Comparisons of Serum HDL-C Absolute Change From Baseline to Visit 7 (mg/dL) Between Study Groups (mITT Population with BLQ values set to the LLOQ) (Note: This analysis will only be performed if the percentage of values that are BLQ is greater than 5% of observations.)

Table 14.2.1.2.14 Statistical Comparisons of Serum HDL-C (mg/dL) between Baseline and Visit 7 by Study Group (mITT Population) (Note: this analysis will be done for the two test groups.)

***Urine 8-epi-prostaglandin F2 $\alpha$  Tables***

Table 14.2.1.3.1.1 Summary of Urine 8-epi-prostaglandin F2 $\alpha$  (ng/g Cr) by Study Group and Visit (mITT Population)

Table 14.2.1.3.1.2 Summary of Urine 8-epi-prostaglandin F2 $\alpha$  (ng/g Cr) by Study Group and Visit (PP Population)

Table 14.2.1.3.2.1 Summary of Urine 8-epi-prostaglandin F2 $\alpha$  Absolute Change From Baseline (ng/g Cr) by Study Group and Visit (mITT Population)

Table 14.2.1.3.2.2 Summary of Urine 8-epi-prostaglandin F2 $\alpha$  Absolute Change From Baseline (ng/g Cr) by Study Group and Visit (PP Population)

Table 14.2.1.3.3.1 Summary of Urine 8-epi-prostaglandin F2 $\alpha$  Percent Change From Baseline (%) by Study Group and Visit (mITT Population)

Table 14.2.1.3.3.2 Summary of Urine 8-epi-prostaglandin F2 $\alpha$  Percent Change From Baseline (%) by Study Group and Visit (PP Population)

Table 14.2.1.3.4.1 Statistical Summary of Urine 8-epi-prostaglandin F2 $\alpha$  Absolute Change From Baseline (ng/g Cr) by Study Group and Visit (mITT Population)

Table 14.2.1.3.4.2 Statistical Comparisons of Urine 8-epi-prostaglandin F2 $\alpha$  Absolute Change From Baseline (ng/g Cr) Between Study Groups by Visit (mITT Population)

Table 14.2.1.3.5.1 Statistical Summary of Urine 8-epi-prostaglandin F2 $\alpha$  Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group (PP Population)

Table 14.2.1.3.5.2	Statistical Comparisons of Urine 8-epi-prostaglandin F2 $\alpha$ Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups (PP Population)
Table 14.2.1.3.6.1	Summary of Urine 8-epi-prostaglandin F2 $\alpha$ Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and Gender (mITT Population)
Table 14.2.1.3.6.2	Summary of Urine 8-epi-prostaglandin F2 $\alpha$ Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and Age Class (mITT Population)
Table 14.2.1.3.6.3	Summary of Urine 8-epi-prostaglandin F2 $\alpha$ Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and BMI Class (mITT Population)
Table 14.2.1.3.7.1	Statistical Summary of Urine 8-epi-prostaglandin F2 $\alpha$ Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and Gender (mITT Population) (Note: This analysis will only be performed if gender term is statistically significant)
Table 14.2.1.3.7.2	Statistical Comparisons of Urine 8-epi-prostaglandin F2 $\alpha$ Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups by Gender (mITT Population) (Note: This analysis will only be performed if the gender term is statistically significant)
Table 14.2.1.3.8.1	Statistical Summary of Urine 8-epi-prostaglandin F2 $\alpha$ Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and Age Class (mITT Population) (Note: This analysis will only be performed if the Age class term is statistically significant)
Table 14.2.1.3.8.2	Statistical Comparisons of Urine 8-epi-prostaglandin F2 $\alpha$ Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups by Age Class (mITT Population) (Note: This analysis will only be performed if the Age class term is statistically significant)
Table 14.2.1.3.9.1	Statistical Summary of Urine 8-epi-prostaglandin F2 $\alpha$ Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and BMI Class (mITT Population) (Note: This analysis will only be performed if the BMI class term is statistically significant)
Table 14.2.1.3.9.2	Statistical Comparisons of Urine 8-epi-prostaglandin F2 $\alpha$ Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups by BMI Class (mITT

Population) (Note: This analysis will only be performed if the BMI class term is statistically significant)

- Table 14.2.1.3.10.1 Statistical Summary of Urine 8-epi-prostaglandin F2 $\alpha$  Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group (mITT Population with Imputation of Missing Data Using Last Observation Carried Forward Method)
- Table 14.2.1.3.10.2 Statistical Comparisons of Urine 8-epi-prostaglandin F2 $\alpha$  Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups (mITT Population with Imputation of Missing Data Using Last Observation Carried Forward Method)
- Table 14.2.1.3.11.1 Statistical Summary of Urine 8-epi-prostaglandin F2 $\alpha$  Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and Visit (mITT Population with Imputation of Missing Data Using Multiple Imputation by SAS MI Procedure)
- Table 14.2.1.3.11.2 Statistical Comparisons of Urine 8-epi-prostaglandin F2 $\alpha$  Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups (mITT Population with Imputation of Missing Data Using Multiple Imputation by SAS MI Procedure)
- Table 14.2.1.3.12.1 Summary of Urine 8-epi-prostaglandin F2 $\alpha$  Absolute Change From Baseline (ng/g Cr) by Study Group and Visit (mITT Population with Outliers Excluded)
- Table 14.2.1.3.12.2 Statistical Summary of Urine 8-epi-prostaglandin F2 $\alpha$  Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group (mITT Population with Outliers Excluded)
- Table 14.2.1.3.12.3 Statistical Comparisons of Urine 8-epi-prostaglandin F2 $\alpha$  Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups (mITT Population with Outliers Excluded)
- Table 14.2.1.3.13.1 Statistical Summary of Urine 8-epi-prostaglandin F2 $\alpha$  Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group (mITT Population with BLQ values set to the LLOQ) (Note: This analysis will only be performed if the percentage of values that are BLQ is greater than 5% of observations.)
- Table 14.2.1.3.13.2 Statistical Comparisons of Urine 8-epi-prostaglandin F2 $\alpha$  Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups (mITT Population with BLQ

values set to the LLOQ) (Note: This analysis will only be performed if the percentage of values that are BLQ is greater than 5% of observations.)

Table 14.2.1.3.14 Statistical Comparisons of Urine 8-epi-prostaglandin F2 $\alpha$  (ng/g Cr) between Baseline and Visit 7 by Study Group (mITT Population) (Note: this analysis will be done for the two test groups.)

***Urine 11-dehydrothromboxane B<sub>2</sub> Tables***

Table 14.2.1.4.1.1 Summary of Urine 11-dehydrothromboxane B<sub>2</sub> (ng/g Cr) by Study Group and Visit (mITT Population)

Table 14.2.1.4.1.2 Summary of Urine 11-dehydrothromboxane B<sub>2</sub> (ng/g Cr) by Study Group and Visit (PP Population)

Table 14.2.1.4.2.1 Summary of Urine 11-dehydrothromboxane B<sub>2</sub> Absolute Change From Baseline (ng/g Cr) by Study Group and Visit (mITT Population)

Table 14.2.1.4.2.2 Summary of Urine 11-dehydrothromboxane B<sub>2</sub> Absolute Change From Baseline (ng/g Cr) by Study Group and Visit (PP Population)

Table 14.2.1.4.3.1 Summary of Urine 11-dehydrothromboxane B<sub>2</sub> Percent Change From Baseline (%) by Study Group and Visit (mITT Population)

Table 14.2.1.4.3.2 Summary of Urine 11-dehydrothromboxane B<sub>2</sub> Percent Change From Baseline (%) by Study Group and Visit (PP Population)

Table 14.2.1.4.4.1 Statistical Summary of Urine 11-dehydrothromboxane B<sub>2</sub> Absolute Change From Baseline (ng/g Cr) by Study Group and Visit (mITT Population)

Table 14.2.1.4.4.2 Statistical Comparisons of Urine 11-dehydrothromboxane B<sub>2</sub> Absolute Change From Baseline (ng/g Cr) Between Study Groups by Visit (mITT Population)

Table 14.2.1.4.5.1 Statistical Summary of Urine 11-dehydrothromboxane B<sub>2</sub> Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group (PP Population)

Table 14.2.1.4.5.2 Statistical Comparisons of Urine 11-dehydrothromboxane B<sub>2</sub> Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups (PP Population)

Table 14.2.1.4.6.1	Summary of Urine 11-dehydrothromboxane B <sub>2</sub> Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and Gender (mITT Population)
Table 14.2.1.4.6.2	Summary of Urine 11-dehydrothromboxane B <sub>2</sub> Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and Age Class (mITT Population)
Table 14.2.1.4.6.3	Summary of Urine 11-dehydrothromboxane B <sub>2</sub> Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and BMI Class (mITT Population)
Table 14.2.1.4.7.1	Statistical Summary of Urine 11-dehydrothromboxane B <sub>2</sub> Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and Gender (mITT Population) (Note: This analysis will only be performed if gender term is statistically significant)
Table 14.2.1.4.7.2	Statistical Comparisons of Urine 11-dehydrothromboxane B <sub>2</sub> Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups by Gender (mITT Population) (Note: This analysis will only be performed if the gender term is statistically significant)
Table 14.2.1.4.8.1	Statistical Summary of Urine 11-dehydrothromboxane B <sub>2</sub> Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and Age Class (mITT Population) (Note: This analysis will only be performed if the Age class term is statistically significant)
Table 14.2.1.4.8.2	Statistical Comparisons of Urine 11-dehydrothromboxane B <sub>2</sub> Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups by Age Class (mITT Population) (Note: This analysis will only be performed if the Age class term is statistically significant)
Table 14.2.1.4.9.1	Statistical Summary of Urine 11-dehydrothromboxane B <sub>2</sub> Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and BMI Class (mITT Population) (Note: This analysis will only be performed if the BMI class term is statistically significant)
Table 14.2.1.4.9.2	Statistical Comparisons of Urine 11-dehydrothromboxane B <sub>2</sub> Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups by BMI Class (mITT Population) (Note: This analysis will

only be performed if the BMI class term is statistically significant)

- Table 14.2.1.4.10.1 Statistical Summary of Urine 11-dehydrothromboxane B<sub>2</sub> Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group (mITT Population with Imputation of Missing Data Using Last Observation Carried Forward Method)
- Table 14.2.1.4.10.2 Statistical Comparisons of Urine 11-dehydrothromboxane B<sub>2</sub> Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups (mITT Population with Imputation of Missing Data Using Last Observation Carried Forward Method)
- Table 14.2.1.4.11.1 Statistical Summary of Urine 11-dehydrothromboxane B<sub>2</sub> Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group (mITT Population with Imputation of Missing Data Using Multiple Imputation by SAS MI Procedure)
- Table 14.2.1.4.11.2 Statistical Comparisons of Urine 11-dehydrothromboxane B<sub>2</sub> Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups (mITT Population with Imputation of Missing Data Using Multiple Imputation by SAS MI Procedure)
- Table 14.2.1.4.12.1 Summary of Urine 11-dehydrothromboxane B<sub>2</sub> Absolute Change From Baseline (ng/g Cr) by Study Group and Visit (mITT Population with Outliers Excluded)
- Table 14.2.1.4.12.2 Statistical Summary of Urine 11-dehydrothromboxane B<sub>2</sub> Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group (mITT Population with Outliers Excluded)
- Table 14.2.1.4.12.3 Statistical Comparisons of Urine 11-dehydrothromboxane B<sub>2</sub> Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups (mITT Population with Outliers Excluded)
- Table 14.2.1.4.13.1 Statistical Summary of Urine 11-dehydrothromboxane B<sub>2</sub> Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group (mITT Population with BLQ values set to the LLOQ) (Note: This analysis will only be performed if the percentage of values that are BLQ is greater than 5% of observations.)
- Table 14.2.1.4.13.2 Statistical Comparisons of Urine 11-dehydrothromboxane B<sub>2</sub> Absolute Change From

Baseline to Visit 7 (ng/g Cr) Between Study Groups (mITT Population with BLQ values set to the LLOQ) (Note: This analysis will only be performed if the percentage of values that are BLQ is greater than 5% of observations.)

Table 14.2.1.4.14 Statistical Comparisons of Urine 11-dehydrothromboxane B<sub>2</sub> (ng/g Cr) between Baseline and Visit 7 by Study Group (mITT Population) (Note: this analysis will be done for the two test groups.)

***Serum sICAM-1 Tables***

Table 14.2.1.5.1.1 Summary of Serum sICAM-1 (ng/mL) by Study Group and Visit (mITT Population)

Table 14.2.1.5.1.2 Summary of Serum sICAM-1 (ng/mL) by Study Group and Visit (PP Population)

Table 14.2.1.5.2.1 Summary of Serum sICAM-1 Absolute Change From Baseline (ng/mL) by Study Group and Visit (mITT Population)

Table 14.2.1.5.2.2 Summary of Serum sICAM-1 Absolute Change From Baseline (ng/mL) by Study Group and Visit (PP Population)

Table 14.2.1.5.3.1 Summary of Serum sICAM-1 Percent Change From Baseline (%) by Study Group and Visit (mITT Population)

Table 14.2.1.5.3.2 Summary of Serum sICAM-1 Percent Change From Baseline (%) by Study Group and Visit (PP Population)

Table 14.2.1.5.4.1 Statistical Summary of Serum sICAM-1 Absolute Change From Baseline (ng/mL) by Study Group and Visit (mITT Population)

Table 14.2.1.5.4.2 Statistical Comparisons of Serum sICAM-1 Absolute Change From Baseline (ng/mL) Between Study Groups by Visit (mITT Population)

Table 14.2.1.5.5.1 Statistical Summary of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) by Study Group (PP Population)

Table 14.2.1.5.5.2 Statistical Comparisons of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) Between Study Groups (PP Population)

Table 14.2.1.5.6.1	Summary of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) by Study Group and Gender (mITT Population)
Table 14.2.1.5.6.2	Summary of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) by Study Group and Age Class (mITT Population)
Table 14.2.1.5.6.3	Summary of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) by Study Group and BMI Class (mITT Population)
Table 14.2.1.5.7.1	Statistical Summary of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) by Study Group and Gender (mITT Population) (Note: This analysis will only be performed if gender term is statistically significant)
Table 14.2.1.5.7.2	Statistical Comparisons of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) Between Study Groups by Gender (mITT Population) (Note: This analysis will only be performed if the gender term is statistically significant)
Table 14.2.1.5.8.1	Statistical Summary of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) by Study Group and Age Class (mITT Population) (Note: This analysis will only be performed if the Age class term is statistically significant)
Table 14.2.1.5.8.2	Statistical Comparisons of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) Between Study Groups by Age Class (mITT Population) (Note: This analysis will only be performed if the Age class term is statistically significant)
Table 14.2.1.5.9.1	Statistical Summary of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) by Study Group and BMI Class (mITT Population) (Note: This analysis will only be performed if the BMI class term is statistically significant)
Table 14.2.1.5.9.2	Statistical Comparisons of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) Between Study Groups by BMI Class (mITT Population) (Note: This analysis will only be performed if the BMI class term is statistically significant)
Table 14.2.1.5.10.1	Statistical Summary of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) by Study

	Group (mITT Population with Imputation of Missing Data Using Last Observation Carried Forward Method)
Table 14.2.1.5.10.2	Statistical Comparisons of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) Between Study Groups (mITT Population with Imputation of Missing Data Using Last Observation Carried Forward Method)
Table 14.2.1.5.11.1	Statistical Summary of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) by Study Group (mITT Population with Imputation of Missing Data Using Multiple Imputation by SAS MI Procedure)
Table 14.2.1.5.11.2	Statistical Comparisons of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) Between Study Groups (mITT Population with Imputation of Missing Data Using Multiple Imputation by SAS MI Procedure)
Table 14.2.1.5.12.1	Summary of Serum sICAM-1 Absolute Change From Baseline (ng/mL) by Study Group and Visit (mITT Population with Outliers Excluded)
Table 14.2.1.5.12.2	Statistical Summary of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) by Study Group (mITT Population with Outliers Excluded)
Table 14.2.1.5.12.3	Statistical Comparisons of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) Between Study Groups (mITT Population with Outliers Excluded)
Table 14.2.1.5.13.1	Statistical Summary of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) by Study Group (mITT Population with BLQ values set to the LLOQ) (Note: This analysis will only be performed if the percentage of values that are BLQ is greater than 5% of observations.)
Table 14.2.1.5.13.2	Statistical Comparisons of Serum sICAM-1 Absolute Change From Baseline to Visit 7 (ng/mL) Between Study Groups (mITT Population with BLQ values set to the LLOQ) (Note: This analysis will only be performed if the percentage of values that are BLQ is greater than 5% of observations.)
Table 14.2.1.5.14	Statistical Comparisons of Serum sICAM-1 (ng/mL) between Baseline and Visit 7 by Study Group (mITT

Population) (Note: this analysis will be done for the two test groups.)

***Urine Total NNAL Tables***

Table 14.2.1.6.1.1	Summary of Urine Total NNAL (ng/g Cr) by Study Group and Visit (mITT Population)
Table 14.2.1.6.1.2	Summary of Urine Total NNAL (ng/g Cr) by Study Group and Visit (PP Population)
Table 14.2.1.6.2.1	Summary of Urine Total NNAL Absolute Change From Baseline (ng/g Cr) by Study Group and Visit (mITT Population)
Table 14.2.1.6.2.2	Summary of Urine Total NNAL Absolute Change From Baseline (ng/g Cr) by Study Group and Visit (PP Population)
Table 14.2.1.6.3.1	Summary of Urine Total NNAL Percent Change From Baseline (%) by Study Group and Visit (mITT Population)
Table 14.2.1.6.3.2	Summary of Urine Total NNAL Percent Change From Baseline (%) by Study Group and Visit (PP Population)
Table 14.2.1.6.4.1	Statistical Summary of Urine Total NNAL Absolute Change From Baseline (ng/g Cr) by Study Group and Visit (mITT Population)
Table 14.2.1.6.4.2	Statistical Comparisons of Urine Total NNAL Absolute Change From Baseline (ng/g Cr) Between Study Groups by Visit (mITT Population)
Table 14.2.1.6.5.1	Statistical Summary of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group (PP Population)
Table 14.2.1.6.5.2	Statistical Comparisons of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups (PP Population)
Table 14.2.1.6.6.1	Summary of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and Gender (mITT Population)
Table 14.2.1.6.6.2	Summary of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and Age Class (mITT Population)

Table 14.2.1.6.6.3	Summary of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and BMI Class (mITT Population)
Table 14.2.1.6.7.1	Statistical Summary of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and Gender (mITT Population) (Note: This analysis will only be performed if gender term is statistically significant)
Table 14.2.1.6.7.2	Statistical Comparisons of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups by Gender (mITT Population) (Note: This analysis will only be performed if the gender term is statistically significant)
Table 14.2.1.6.8.1	Statistical Summary of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and Age Class (mITT Population) (Note: This analysis will only be performed if the Age class term is statistically significant)
Table 14.2.1.6.8.2	Statistical Comparisons of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups by Age Class (mITT Population) (Note: This analysis will only be performed if the Age class term is statistically significant)
Table 14.2.1.6.9.1	Statistical Summary of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and BMI Class (mITT Population) (Note: This analysis will only be performed if the BMI class term is statistically significant)
Table 14.2.1.6.9.2	Statistical Comparisons of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups by BMI Class (mITT Population) (Note: This analysis will only be performed if the BMI class term is statistically significant)
Table 14.2.1.6.10.1	Statistical Summary of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group (mITT Population with Imputation of Missing Data Using Last Observation Carried Forward Method)
Table 14.2.1.6.10.2	Statistical Comparisons of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups (mITT Population with Imputation of

Missing Data Using Last Observation Carried Forward Method)

- Table 14.2.1.6.11.1 Statistical Summary of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group (mITT Population with Imputation of Missing Data Using Multiple Imputation by SAS MI Procedure)
- Table 14.2.1.6.11.2 Statistical Comparisons of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups (mITT Population with Imputation of Missing Data Using Multiple Imputation by SAS MI Procedure)
- Table 14.2.1.6.12.1 Summary of Urine Total NNAL Absolute Change From Baseline (ng/g Cr) by Study Group and Visit (mITT Population with Outliers Excluded)
- Table 14.2.1.6.12.2 Statistical Summary of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group and (mITT Population with Outliers Excluded)
- Table 14.2.1.6.12.3 Statistical Comparisons of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups (mITT Population with Outliers Excluded)
- Table 14.2.1.6.13.1 Statistical Summary of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) by Study Group (mITT Population with BLQ values set to the LLOQ) (Note: This analysis will only be performed if the percentage of values that are BLQ is greater than 5% of observations.)
- Table 14.2.1.6.13.2 Statistical Comparisons of Urine Total NNAL Absolute Change From Baseline to Visit 7 (ng/g Cr) Between Study Groups (mITT Population with BLQ values set to the LLOQ) (Note: This analysis will only be performed if the percentage of values that are BLQ is greater than 5% of observations.)
- Table 14.2.1.6.14 Statistical Comparisons of Urine Total NNAL (ng/g Cr) between Baseline and Visit 7 by Study Group (mITT Population) (Note: this analysis will be done for the two test groups.)

***Whole Blood COHb Tables***

- Table 14.2.1.7.1.1 Summary of Whole Blood COHb (% Saturation) by Study Group and Visit (mITT Population)

Table 14.2.1.7.1.2	Summary of Whole Blood COHb (% Saturation) by Study Group and Visit (PP Population)
Table 14.2.1.7.2.1	Summary of Whole Blood COHb Absolute Change From Baseline (% Saturation) by Study Group and Visit (mITT Population)
Table 14.2.1.7.2.2	Summary of Whole Blood COHb Absolute Change From Baseline (% Saturation) by Study Group and Visit (PP Population)
Table 14.2.1.7.3.1	Summary of Whole Blood COHb Percent Change From Baseline (%) by Study Group and Visit (mITT Population)
Table 14.2.1.7.3.2	Summary of Whole Blood COHb Percent Change From Baseline (%) by Study Group and Visit (PP Population)
Table 14.2.1.7.4.1	Statistical Summary of Whole Blood COHb Absolute Change From Baseline (% Saturation) by Study Group and Visit (mITT Population)
Table 14.2.1.7.4.2	Statistical Comparisons of Whole Blood COHb Absolute Change From Baseline (% Saturation) Between Study Groups by Visit (mITT Population)
Table 14.2.1.7.5.1	Statistical Summary of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) by Study Group (PP Population)
Table 14.2.1.7.5.2	Statistical Comparisons of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) Between Study Groups (PP Population)
Table 14.2.1.7.6.1	Summary of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) by Study Group and Gender (mITT Population)
Table 14.2.1.7.6.2	Summary of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) by Study Group and Age Class (mITT Population)
Table 14.2.1.7.6.3	Summary of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) by Study Group and BMI Class (mITT Population)
Table 14.2.1.7.7.1	Statistical Summary of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) by Study Group and Gender (mITT Population) (Note: This analysis will only be performed if gender term is statistically significant)

- Table 14.2.1.7.7.2 Statistical Comparisons of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) Between Study Groups by Gender (mITT Population) (Note: This analysis will only be performed if the gender term is statistically significant)
- Table 14.2.1.7.8.1 Statistical Summary of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) by Study Group and Age Class (mITT Population) (Note: This analysis will only be performed if the Age class term is statistically significant)
- Table 14.2.1.7.8.2 Statistical Comparisons of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) Between Study Groups by Age Class (mITT Population) (Note: This analysis will only be performed if the Age class term is statistically significant)
- Table 14.2.1.7.9.1 Statistical Summary of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) by Study Group and BMI Class (mITT Population) (Note: This analysis will only be performed if the BMI class term is statistically significant)
- Table 14.2.1.7.9.2 Statistical Comparisons of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) Between Study Groups by BMI Class (mITT Population) (Note: This analysis will only be performed if the BMI class term is statistically significant)
- Table 14.2.1.7.10.1 Statistical Summary of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) by Study Group (mITT Population with Imputation of Missing Data Using Last Observation Carried Forward Method)
- Table 14.2.1.7.10.2 Statistical Comparisons of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) Between Study Groups (mITT Population with Imputation of Missing Data Using Last Observation Carried Forward Method)
- Table 14.2.1.7.11.1 Statistical Summary of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) by Study Group (mITT Population with Imputation of Missing Data Using Multiple Imputation by SAS MI Procedure)

- Table 14.2.1.7.11.2 Statistical Comparisons of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) Between Study Groups (mITT Population with Imputation of Missing Data Using Multiple Imputation by SAS MI Procedure)
- Table 14.2.1.7.12.1 Summary of Whole Blood COHb Absolute Change From Baseline (% Saturation) by Study Group and Visit (mITT Population with Outliers Excluded)
- Table 14.2.1.7.12.2 Statistical Summary of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) by Study Group (mITT Population with Outliers Excluded)
- Table 14.2.1.7.12.3 Statistical Comparisons of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) Between Study Groups (mITT Population with Outliers Excluded)
- Table 14.2.1.7.13.1 Statistical Summary of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) by Study Group (mITT Population with BLQ values set to the LLOQ) (Note: This analysis will only be performed if the percentage of values that are BLQ is greater than 5% of observations.)
- Table 14.2.1.7.13.2 Statistical Comparisons of Whole Blood COHb Absolute Change From Baseline to Visit 7 (% Saturation) Between Study Groups (mITT Population with BLQ values set to the LLOQ) (Note: This analysis will only be performed if the percentage of values that are BLQ is greater than 5% of observations.)
- Table 14.2.1.7.14 Statistical Comparisons of Whole Blood COHb (% Saturation) between Baseline and Visit 7 by Study Group (mITT Population) (Note: this analysis will be done for the two test groups.)

**Exploratory Biomarker**

***Urine Nicotine Equivalents Tables***

- Table 14.2.1.8.1 Summary of Urine Nicotine Equivalents (mg/g Cr) by Study Group and Visit (mITT Population)
- Table 14.2.1.8.2 Summary of Urine Nicotine Equivalents Absolute Change From Baseline (mg/g Cr) by Study Group and Visit (mITT Population)
- Table 14.2.1.8.3 Summary of Urine Nicotine Equivalents Percent Change From Baseline (%) by Study Group and Visit (mITT Population)

Table 14.2.1.8.4	Statistical Summary of Urine Nicotine Equivalents Absolute Change From Baseline (mg/g Cr) by Study Group and Visit (mITT Population)
Table 14.2.1.8.5	Statistical Comparisons of Urine Nicotine Equivalents Absolute Change From Baseline (mg/g Cr) Between Study Groups by Visit (mITT Population)

#### **14.2.2 Product Use and Compliance Tables**

Table 14.2.2.1.1	Summary of Average Number of Cigarettes or e-Vapor Cartridges Used Per Day by Study Group and Week (Week 1 through Week 6) (mITT Population)
Table 14.2.2.1.2	Summary of Average Number of Cigarettes or e-Vapor Cartridges Used Per Day by Study Group and Week (Week 7 through Week 12) (mITT Population)
Table 14.2.2.2	Summary of Reduction, No Change, or Increase in Cigarettes Per Day and e-Vapor Cartridges Used Per Day from Baseline to Week 12 (Visit 7) by Study Group (mITT Population)
Table 14.2.2.3.1	Frequency of Days with 1-20 or >20 Puffs per Day for e-Vapor Products by Study Group and Week (Week 1 through Week 6) (mITT Population)
Table 14.2.2.3.2	Frequency of Days with 1-20 or >20 Puffs per Day for e-Vapor Products Study Group and Week (Week 7 through Week 12) (mITT Population)
Table 14.2.2.4.1	Summary of eCO (ppm) by Study Group and Visit (mITT Population)
Table 14.2.2.4.2	Summary of urine NNN (ng/g Cr) by Study Group and Visit (mITT Population)
Table 14.2.2.4.3	Frequency of Use of Other Tobacco Products, eCO, and Urine NNN by Study Group and Visit (mITT Population)

#### **14.2.3 Spirometry**

Table 14.2.3.1.1	Summary of Pulmonary Function Parameters by Study Group and Visit (mITT Population)
Table 14.2.3.1.2	Summary of Pulmonary Function Parameters by Study Group and Visit (PP Population)

Table 14.2.3.2.1	Summary of Absolute Change From Baseline to Visit 7 in Pulmonary Function Parameters by Study Group (mITT Population)
Table 14.2.3.2.2	Summary of Pulmonary Function Parameters by Study Group and Visit (PP Population)
Table 14.2.3.3.1	Statistical Summary of Absolute Change From Baseline to Visit 7 in Pulmonary Function Parameters by Study Group (mITT Population)
Table 14.2.3.3.2	Statistical Comparisons of Absolute Change From Baseline to Visit 7 in Pulmonary Function Parameters Between Study Groups (mITT Population)
Table 14.2.3.4.1	Statistical Summary of Absolute Change From Baseline to Visit 7 in Pulmonary Function Parameters by Study Group (PP Population)
Table 14.2.3.4.2	Statistical Comparisons of Absolute Change From Baseline to Visit 7 in Pulmonary Function Parameters Between Study Groups (PP Population)

#### **14.2.4 Subject Questionnaires**

##### ***QGEN Questionnaire***

Table 14.2.4.1.1.1	Summary of QGEN Factor Scores by Study Group and Visit (mITT Population)
Table 14.2.4.1.2.1	Summary of Absolute Change From Baseline in QGEN Factor Scores by Study Group and Visit (mITT Population)
Table 14.2.4.1.3.1	Statistical Summary of Absolute Change From Baseline in QGEN Factor Scores by Study Group and Visit (mITT Population)
Table 14.2.4.1.3.2	Statistical Comparisons of Absolute Change From Baseline in QGEN Factor Scores Between Study Groups by Visit (mITT Population)

##### ***TQOLIT Questionnaire***

Table 14.2.4.2.1.1	Summary of TQOLIT Factor Scores by Study Group and Visit (mITT Population)
Table 14.2.4.2.2.1	Summary of Absolute Change From Baseline in TQOLIT Factor Scores by Study Group and Visit (mITT Population)
Table 14.2.4.2.3.1	Statistical Summary of Absolute Change From Baseline in TQOLIT Factor Scores by Study Group and Visit (mITT Population)

Table 14.2.4.2.3.2 Statistical Comparisons of Absolute Change From Baseline in TQOLIT Factor Scores Between Study Groups by Visit (mITT Population)

***mCEQ***

Table 14.2.4.3.1.1 Summary of mCEQ Original Scores by Study Group and Visit (mITT Population)

Table 14.2.4.3.2.1 Summary of mCEQ Factor Scores by Study Group and Visit (mITT Population)

Table 14.2.4.3.3.1 Summary of Absolute Change from Baseline mCEQ Factor Scores by Study Group and Visit (mITT Population)

Table 14.2.4.3.4.1 Statistical Summary of Absolute Change From Baseline in mCEQ Factor Scores by Study Group and Visit (mITT Population)

Table 14.2.4.3.4.2 Statistical Comparisons of Absolute Change From Baseline in mCEQ Factor Scores Between Study Groups by Visit (mITT Population)

***Cough Questionnaire***

Table 14.2.4.4.1.1 Summary of Cough Questionnaire Questions I and III through X (mITT Population)

Table 14.2.4.4.2.1 Summary of Cough Questionnaire Question II (mITT Population)

***Reasons to Use/Not-Use Test Product Questionnaire***

Table 14.2.4.5.1.1 Summary of Reasons of Use/Not-Use Test Product Questionnaire by Study Group at Week 12: Likelihood of Use (mITT Population)

Table 14.2.4.5.2.1 Summary of Reasons of Use/Not-Use Test Product Questionnaire by Study Group at Week 12: Reasons to Use (mITT Population)

**14.2.5 BOE and BOPH Figures (mITT, PP Populations)**

Subgroup Figures will be included if the subgroup term is significant in the model.

Whole Blood WBC Count Figures

Figure 14.2.5.1.1 Box Plot of Whole Blood WBC Count ( $\times 10^3/\mu\text{L}$ ) at Baseline and Visit 7 by Study Group (mITT Population)

Figure 14.2.5.1.2 Box Plot of Whole Blood WBC Count ( $\times 10^3/\mu\text{L}$ ) at Baseline and Visit 7 by Study Group (PP Population)

Figure 14.2.5.1.3 Box Plot of Whole Blood WBC Count ( $\times 10^3/\mu\text{L}$ ) at Baseline and Visit 5 by Study Group (mITT Population)

Figure 14.2.5.1.4 Box Plot of Whole Blood WBC Count Absolute Change from Baseline ( $\times 10^3/\mu\text{L}$ ) to Visit 5 and Visit 7 by Study Group (mITT Population)

Figure 14.2.5.1.5 Box Plot of Whole Blood WBC Count Absolute Change from Baseline ( $\times 10^3/\mu\text{L}$ ) to Visit 7 by Study Group (PP Population)

Serum HDL-C Figures

Figure 14.2.5.2.1 Box Plot of Serum HDL-C (mg/dL) at Baseline and Visit 7 by Study Group (mITT Population)

Figure 14.2.5.2.2 Box Plot of Serum HDL-C (mg/dL) at Baseline and Visit 7 by Study Group (PP Population)

Figure 14.2.5.2.3 Box Plot of Serum HDL-C (mg/dL) at Baseline and Visit 5 by Study Group (mITT Population)

Figure 14.2.5.2.4 Box Plot of Serum HDL-C Absolute Change from Baseline (mg/dL) to Visit 5 and Visit 7 by Study Group (mITT Population)

Figure 14.2.5.2.5 Box Plot of Whole Blood WBC Count Absolute Change from Baseline (mg/dL) to Visit 7 by Study Group (PP Population)

Urine 8-epi-prostaglandin F2 $\alpha$  Figures

Figure 14.2.5.3.1 Box Plot of Urine 8-epi-prostaglandin F2 $\alpha$  (ng/g Cr) at Baseline and Visit 7 by Study Group (mITT Population)

Figure 14.2.5.3.2 Box Plot of Urine 8-epi-prostaglandin F2 $\alpha$  (ng/g Cr) at Baseline and Visit 7 by Study Group (PP Population)

Figure 14.2.5.3.3 Box Plot of Urine 8-epi-prostaglandin F2 $\alpha$  (ng/g Cr) at Baseline and Visit 5 by Study Group (mITT Population)

Figure 14.2.5.3.4 Box Plot of Urine 8-epi-prostaglandin F2 $\alpha$  Absolute Change from Baseline (ng/g Cr) to Visit 5 and Visit 7 by Study Group (mITT Population)

Figure 14.2.5.3.5 Box Plot of Urine 8-epi-prostaglandin F2 $\alpha$  Absolute Change from Baseline (ng/g Cr) to Visit 7 by Study Group (PP Population)

Urine 11-Dehydrothromboxane B2 Figures

Figure 14.2.5.4.1 Box Plot of Urine 11-Dehydrothromboxane B2 (ng/g Cr) at Baseline and Visit 7 by Study Group (mITT Population)

Figure 14.2.5.4.2 Box Plot of Urine 11-Dehydrothromboxane B2 (ng/g Cr) at Baseline and Visit 7 by Study Group (PP Population)

Figure 14.2.5.4.3 Box Plot of Urine 11-Dehydrothromboxane B2 (ng/g Cr)

at Baseline and Visit 5 by Study Group (mITT Population)

Figure 14.2.5.4.4 Box Plot of Urine 11-Dehydrothromboxane B2 Absolute Change from Baseline (ng/g Cr) to Visit 5 and Visit 7 by Study Group (mITT Population)

Figure 14.2.5.4.5 Box Plot of Urine 11-Dehydrothromboxane B2 Absolute Change from Baseline (ng/g Cr) to Visit 7 by Study Group (PP Population)

#### Serum sICAM-1 Figures

Figure 14.2.5.5.1 Box Plot of Serum sICAM-1 (ng/mL) at Baseline and Visit 7 by Study Group (mITT Population)

Figure 14.2.5.5.2 Box Plot of Serum sICAM-1 (ng/mL) at Baseline and Visit 7 by Study Group (PP Population)

Figure 14.2.5.5.3 Box Plot of Serum sICAM-1 (ng/mL) at Baseline and Visit 5 by Study Group (mITT Population)

Figure 14.2.5.5.4 Box Plot of Serum sICAM-1 Absolute Change from Baseline (ng/mL) to Visit 5 and Visit 7 by Study Group (mITT Population)

Figure 14.2.5.5.5 Box Plot of Serum sICAM-1 Absolute Change from Baseline (ng/mL) to Visit 7 by Study Group (PP Population)

#### Urine Total NNAL Figures

Figure 14.2.5.6.1 Box Plot of Urine Total NNAL (ng/g Cr) at Baseline and Visit 7 by Study Group (mITT Population)

Figure 14.2.5.6.2 Box Plot of Urine Total NNAL (ng/g Cr) at Baseline and Visit 7 by Study Group (PP Population)

Figure 14.2.5.6.3 Box Plot of Urine Total NNAL (ng/g Cr) at Baseline and Visit 5 by Study Group (mITT Population)

Figure 14.2.5.6.4 Box Plot of Urine Total NNAL Absolute Change from Baseline (ng/g Cr) to Visit 5 and Visit 7 by Study Group (mITT Population)

Figure 14.2.5.6.5 Box Plot of Urine Total NNAL Absolute Change from Baseline (ng/g Cr) to Visit 7 by Study Group (PP Population)

#### Whole Blood COHb Figures

Figure 14.2.5.7.1 Box Plot of Whole Blood COHb (% Saturation) at Baseline and Visit 7 by Study Group (mITT Population)

- Figure 14.2.5.7.2 Box Plot of Whole Blood COHb (% Saturation) at Baseline and Visit 7 by Study Group (PP Population)
- Figure 14.2.5.7.3 Box Plot of Whole Blood COHb (% Saturation) at Baseline and Visit 5 by Study Group (mITT Population)
- Figure 14.2.5.7.4 Box Plot of Whole Blood COHb Absolute Change from Baseline (% Saturation) to Visit 5 and Visit 7 by Study Group (mITT Population)
- Figure 14.2.5.7.5 Box Plot of Whole Blood COHb Absolute Change from Baseline (% Saturation) to Visit 7 by Study Group (PP Population)

***Note (applies to all the above figures): Figures 14.2.1.X.1 will contain Test 1, Test 2, Test 1 + Test 2, and Control groups. Figures 14.2.5.X.2 and 14.2.5.X.3 will contain Test 1, Test 2, and Control group. Figures 14.2.5.X.4 will contain Test 1, Test 2, and Control groups for Visit 5 and Test 1, Test 2, Test 1 + Test 2, and Control groups for Visit 7. Figures 14.2.5.X.5 will contain Test 1, Test 2, and Control groups.***

#### Urine Nicotine Equivalents Figures

- Figure 14.2.5.8.1 Box Plot of Urine Nicotine Equivalents (mg/g Cr) at Baseline and Visit 7 by Study Group (mITT Population)
- Figure 14.2.5.8.2 Box Plot of Urine Nicotine Equivalents (mg/g Cr) at Baseline and Visit 5 by Study Group (mITT Population)
- Figure 14.2.5.8.3 Box Plot of Urine Nicotine Equivalents Absolute Change from Baseline (mg/g Cr) to Visit 5 and Visit 7 by Study Group (mITT Population)

***Note: Figure 14.2.5.8.1 will contain Test 1, Test 2, Test 1 + Test 2, and Control groups. Figure 14.2.5.8.2 will contain Test 1, Test 2, and Control group. Figure 14.2.5.8.3 will contain Test 1, Test 2, and Control groups for Visit 5 and Test 1, Test 2, Test 1 + Test 2, and Control groups for Visit 7.***

### **14.3 Safety Data Summary Tables**

#### **14.3.1 Displays of Adverse Events**

- Table 14.3.1.1 Adverse Event Frequency by Study Group – Number of Subjects Reporting the Event (% of Subjects Who Received Study Product)
- Table 14.3.1.2 Adverse Event Frequency by Study Group – Number of Adverse Events (% of Total Adverse Events)
- Table 14.3.1.3 Adverse Event Frequency by Study Group, Severity, and Relationship to Study Product – Number of Subjects Reporting Events

Table 14.3.1.4 Adverse Event Frequency by Study Group, Severity, and Relationship to Study Product – Number of Adverse Events

**14.3.2 Listings of Deaths, other Serious and Significant Adverse Events**

Table 14.3.2.1 Serious Adverse Events (if no serious adverse event occurred, a statement ‘No serious adverse event is reported’ will be in the table)

**14.3.3. Narratives of Deaths, other Serious and Certain other Significant Adverse Events**

**14.3.4. Abnormal Laboratory Value Listing (each subject)**

Table 14.3.4.1 Out-of-Range Values and Recheck Results – Serum Chemistry

Table 14.3.4.2 Out-of-Range Values and Recheck Results – Hematology

Table 14.3.4.3 Out-of-Range Values and Recheck Results – Urinalysis

**14.3.5. Displays of Other Laboratory, Vital Signs, Electrocardiogram, Physical Examination, and Other Safety Data**

Table 14.3.5.1 Clinical Laboratory Summary – Serum Chemistry

Table 14.3.5.2 Clinical Laboratory Summary – Hematology

Table 14.3.5.3 Clinical Laboratory Summary – Urinalysis

Table 14.3.5.4 Vital Sign Summary

Table 14.3.5.5 12-Lead Electrocardiogram Summary

**10. DATA LISTING TITLES AND NUMBERS**

Note: Hepatitis and HIV results that are provided by the clinical laboratory will not be presented in subject data listings and will not be included in any database transfer.

Data listings are numbered following the ICH structure. The following is a list of appendix numbers and titles that will be included as data listings:

**16.1. Study Information**

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges by Site

Appendix 16.1.10.2 Vital Signs Reference Ranges by Site

Appendix 16.1.10.3 12-Lead Electrocardiogram Reference Ranges by Site

**Note: Appendices 16.1.10.2 and 16.1.10.3 are generated in PDF files from the clinical sites for inclusion in the CSR.**

## **16.2. Subject Data Listings**

### **16.2.1. Subject Discontinuation**

Appendix 16.2.1.1 Subject Disposition and Discontinuation (Randomized)

Appendix 16.2.1.2 Subject Disposition and Discontinuation (Product Trial)

### **16.2.2. Protocol Deviations**

Appendix 16.2.2 Protocol Deviations

### **16.2.3. Subjects Excluded from Biomarker Analysis**

Appendix 16.2.3 Subjects Excluded from WBC Count, HDL-C, 8-epi-prostaglandin F2 $\alpha$ , 11-dehydrothromboxane B2, sICAM-1, total NNAL, and COHb Analysis

**Note: Appendices 16.2.2 and 16.2.3 are generated in Microsoft® Word® for inclusion in the CSR.**

### **16.2.4. Demographic Data**

Appendix 16.2.4.1.1 Demographics (I of II)

Appendix 16.2.4.1.2 Demographics (II of II)

Appendix 16.2.4.1.3 Subject Characteristics

Appendix 16.2.4.2.1 Physical Examination (I of II)

Appendix 16.2.4.2.2 Physical Examination (II of II)

Appendix 16.2.4.2.3 Physical Examination Descriptions

Appendix 16.2.4.3 Medical History

Appendix 16.2.4.4.1 Tobacco/Nicotine Product Use History (I of II)

Appendix 16.2.4.4.2 Tobacco/Nicotine Product Use History (II of II)

### **16.2.5. Compliance Data**

Appendix 16.2.5.1 Inclusion / Exclusion Criteria Not Met

Appendix 16.2.5.2.1 Test e-Vapor Product Trial

Appendix 16.2.5.2.2 Test e-Vapor Product Assessment Questionnaire

Appendix 16.2.5.2.3 Confirm Regular Cigarette Brand

Appendix 16.2.5.2.4 Test e-Vapor Product Accountability

Appendix 16.2.5.3 Urine Collection for BOEs and BOPHS

Appendix 16.2.5.4 Blood Sampling

Appendix 16.2.5.5 Exhaled CO Measurement

Appendix 16.2.5.6 Prior and On-Study Concomitant Medications

### **16.2.6. Individual Response Data**

Appendix 16.2.6.1 Whole Blood WBC Counts

- Appendix 16.2.6.2 Serum HDL-C
- Appendix 16.2.6.3 Urine 8-epi-prostaglandin F2 $\alpha$
- Appendix 16.2.6.4 Urine 11-dehydrothromboxane B2
- Appendix 16.2.6.5 Whole Blood sICAM-1
- Appendix 16.2.6.6 Urine Total NNAL
- Appendix 16.2.6.7 Blood COHb
- Appendix 16.2.6.8.1 Product Used per Day
- Appendix 16.2.6.8.2 Average Product Used per Day
- Appendix 16.2.6.8.3 Average Test Product Started/Cigarette Smoked Per Day % Change
- Appendix 16.2.6.9 Urine NNN
- Appendix 16.2.6.10.1 Spirometry
- Appendix 16.2.6.10.2 Spirometry Absolute Change from Baseline to Week 12 (Visit 7)
- Appendix 16.2.6.11.1 Urine Nicotine and Metabolites Concentrations
- Appendix 16.2.6.11.2 Urine Nicotine Equivalents
- Appendix 16.2.6.12.1 Factor Score to TQOLIT Questionnaire
- Appendix 16.2.6.12.2 Factor Score to QGEN Questionnaire
- Appendix 16.2.6.12.3.1 Modified Cigarette Evaluation Questionnaire
- Appendix 16.2.6.12.3.2 Factor Score to MCEQ Questionnaire
- Appendix 16.2.6.12.4.1 Cough Questionnaire
- Appendix 16.2.6.12.4.2 Cough Questionnaire Response
- Appendix 16.2.6.12.5.1 Reasons of Use/Not-Use Test Product Questionnaire (I of II)
- Appendix 16.2.6.12.5.2 Reasons of Use/Not-Use Test Product Questionnaire (II of II)
- Appendix 16.2.6.12.6 End of Study Questionnaire

**16.2.7. Individual Adverse Event Listings**

- Appendix 16.2.7.1 Adverse Events (I of II)
- Appendix 16.2.7.2 Adverse Events (II of II)
- Appendix 16.2.7.3 Adverse Event Preferred Term Classification

**16.2.8. Individual Laboratory Measurements and Other Safety Observations**

- Appendix 16.2.8.1 Clinical Laboratory Report - Serum Chemistry
- Appendix 16.2.8.2 Clinical Laboratory Report - Hematology
- Appendix 16.2.8.3 Clinical Laboratory Report - Urinalysis
- Appendix 16.2.8.4 Alcohol Breath Tests

Appendix 16.2.8.5	Urine Drug Screens
Appendix 16.2.8.6	Pregnancy Tests
Appendix 16.2.8.7	Urine Cotinine Screens
Appendix 16.2.8.8	Serology Sample Collection
Appendix 16.2.8.9	Clinical Laboratory Report - Comments
Appendix 16.2.8.10	Vital Signs
Appendix 16.2.8.11	12-Lead Electrocardiogram
Appendix 16.2.8.12.1	Pulmonary Function Test (Spirometry) (I of II)
Appendix 16.2.8.12.2	Pulmonary Function Test (Spirometry) (II of II)
Appendix 16.2.8.13	Smoking Cessation Information
Appendix 16.2.8.14	Reminder Phone Call

## 11. TABLE SHELLS

The following table shells provide 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 that will be included in the final report.

Table 14.1.1 Summary of Disposition Overall and by Study Group

Population	Category	Product Trial*	Group			Overall#
			Test 1	Test 2	Control	
CSP	Enrolled	XXX	XXX	XXX	XXX	XXX
	Completed	XXX	XXX	XXX	XXX	XXX
	Discontinued Early	XX	XX	XX	XX	XX
	<Reason1>	XX	XX	XX	XX	XX
	<Reason2>	XX	XX	XX	XX	XX
	<Reason3>	XX	XX	XX	XX	XX
ITT	Enrolled	XXX	XXX	XXX	XXX	XXX
	Completed	XXX	XXX	XXX	XXX	XXX
	Discontinued Early	XX	XX	XX	XX	XX
	<Reason1>	XX	XX	XX	XX	XX
	<Reason2>	XX	XX	XX	XX	XX
	<Reason3>	XX	XX	XX	XX	XX
PP	Enrolled	XXX	XXX	XXX	XXX	XXX
	Completed	XXX	XXX	XXX	XXX	XXX
	Discontinued Early	XX	XX	XX	XX	XX
	<Reason1>	XX	XX	XX	XX	XX
	<Reason2>	XX	XX	XX	XX	XX
	<Reason3>	XX	XX	XX	XX	XX

Note: \* Only includes subjects that enrolled in the product trial period and dropped prior to randomization.  
 # Subjects who only participated in the product trial period are excluded from the Overall summary.  
 Test 1 Group = e-Vapor Product XLCE  
 Test 2 Group = e-Vapor Product XLME  
 Control Group = Continue smoking lit-end conventional cigarette  
 CSP = Clinical safety population, ITT = Intent-to-treat, PP = Per protocol

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Table 14.1.2 Demographic Summary Overall and by Study Group

Population Trait		Product Trial*	Group			Overall#
			Test 1	Test 2	Control	
CSP	Gender	Male	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
		Female	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
	Race	XXXXXXXXXX	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
		XXXXXX	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
		XXXXXX	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
Ethnicity	Hispanic or Latino	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	
	Not Hispanic or Latino	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	
Age (yrs)	n	X	X	X	X	
	Mean	X.X	X.X	X.X	X.X	
	SD	X.XX	X.XX	X.XX	X.XX	
	Minimum	XX	XX	XX	XX	
	Median	X.X	X.X	X.X	X.X	
	Maximum	XX	XX	XX	XX	

Note: \* Only includes subjects that enrolled in the product trial Period and dropped prior to randomization.  
 # Subjects who only participated in the product trial period are excluded from the Overall summary.  
 Test 1 Group = e-Vapor Product XLCE  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette  
 CSP = Clinical safety population, ITT = Intent-to-treat, PP = Per protocol

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**Programmer Note: Weight (kg), height (cm), BMI (kg/m<sup>2</sup>) annual income and highest grade of school will also be included in the demographic summary table. ITT and PP population will also be presented.**

Table 14.1.3 Smoking History Overall and by Study Group

Population	Trait	Product Trial*	Study Group			Overall#
			1	2	Control	
CSP	CPD	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
		Years Smoked	n	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX

Note: \* Only includes subjects that enrolled in the product trial Period and dropped prior to randomization.  
 # Subjects who only participated in the product trial period are excluded from the Overall summary.  
 CPD = Cigarettes per day  
 Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette  
 CSP = Clinical safety population, ITT = Intent-to-treat, PP = Per protocol

Program: /CAXXXXXX/sas\_prg/stsas/PROGRAMNAME.SAS DDMMYYYY HH:MM

**Programmer Note: ITT and PP population will also be presented. Subset by gender and age group [i.e CSP (Male), CSP(Female), CSP (<45 years old), CPS(≥45 years old), etc.] will also be presented.**

**Note: Summary Tables 14.2.1.1.1.1, 14.2.1.1.1.2, 14.2.1.2.1.1, 14.2.1.2.1.2, 14.2.1.3.1.1, 14.2.1.3.1.2, 14.2.1.4.1.1, 14.2.1.4.1.2, 14.2.1.5.1.1, 14.2.1.5.1.2, 14.2.1.6.1.1, 14.2.1.6.1.2, 14.2.1.7.1.1, 14.2.1.7.1.2, 14.2.1.8.1. and 14.2.2.4.2 will have the following format:**

Table 14.2.1.1.1.1 Summary of <Matrix> <Biomarker> (<units>) by Study Group and Visit (<Population>)

Visit	Statistics	Group			
		Test 1	Test 2	Test 1 + Test 2	Control
3	n	X	X	X	X
	n missing	X	X	X	X
	Mean	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
5	n	X	X	X	X
	n missing	X	X	X	X
	Mean	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
7	<same as above>				

Visit 3 = Baseline (Day 1, Week 1)  
 Visit 5 = Week 6  
 Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Test1 + Test 2 Group = Combined e-Vapor Use Group  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas prg/pksas/PROGRAMNAME.SAS DDMMYYYY HH:MM

**Programmer Note: Table 14.2.2.4.2 will not contain Test 1 + Test 2 Group**

**Note: Summary tables 14.2.1.1.2.1, 14.2.1.1.2.2, 14.2.1.1.12.1, 14.2.1.2.2.1, 14.2.1.2.2.2, 14.2.1.2.12.1, 14.2.1.3.2.1, 14.2.1.3.2.2, 14.2.1.3.12.1, 14.2.1.4.2.1, 14.2.1.4.2.2, 14.2.1.4.12.1, 14.2.1.5.2.1, 14.2.1.5.2.2, 14.2.1.5.12.1, 14.2.1.6.2.1, 14.2.1.6.2.2, 14.2.1.6.12.1, 14.2.1.7.2.1, 14.2.1.7.2.2, 14.2.1.7.12.1, 14.2.1.8.2 will have the following format:**

Table 14.2.1.1.2.1 Summary of <Matrix> <Biomarker> Absolute Change from Baseline (<units>) by Study Group and Visit (<Population>)

Visit	Statistics	Group			
		Test 1	Test 2	Test 1 + Test 2	Control
5	n	X	X	X	X
	n missing	X	X	X	X
	Mean	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
7	n	X	X	X	X
	n missing	X	X	X	X
	Mean	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X

Baseline = Visit 3 (Day 1, Week 1)  
 Visit 5 = Week 6  
 Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCEB  
 Test 2 Group = e-Vapor Product XLMB  
 Test1 + Test 2 Group = Combined e-Vapor Use Group  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/pksas/PROGRAMNAME.SAS DDMMYYYY HH:MM

**Note: Summary tables 14.2.1.1.3.1, 14.2.1.1.3.2, 14.2.1.2.3.1, 14.2.1.2.3.2, 14.2.1.3.3.1, 14.2.1.3.3.2, 14.2.1.4.3.1, 14.2.1.4.3.2, 14.2.1.5.3.1, 14.2.1.5.3.2, 14.2.1.6.3.1, 14.2.1.6.3.2, 14.2.1.7.3.1, 14.2.1.7.3.2, 14.2.1.8.3 will have the following format:**

Table 14.2.1.1.3.1 Summary of <Matrix> <Biomarker> Percent Change from Baseline (%) by Study Group and Visit (<Population>)

Visit	Statistics	Group			
		Test 1	Test 2	Test 1 + Test 2	Control
5	n	X	X	X	X
	n missing	X	X	X	X
	Mean	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
7	n	X	X	X	X
	n missing	X	X	X	X
	Mean	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X

-----  
 Baseline = Visit 3 (Day 1, Week 1)  
 Visit 5 = Week 6  
 Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Test1 + Test 2 Group = Combined e-Vapor Use Group  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/pksas/PROGRAMNAME.SAS DDMMYYYY HH:MM

**Note: Statistical summary tables 14.2.1.1.4.1, 14.2.1.2.4.1, 14.2.1.3.4.1, 14.2.1.4.4.1, 14.2.1.5.4.1, 14.2.1.6.4.1, 14.2.1.7.4.1, 14.2.1.8.4 will have the following format:**

Table 14.2.1.1.4.1 Statistical Summary of <Matrix> <Biomarker> Absolute Change from Baseline (<Units>) by Study Group and Visit (mITT Population)

Group	Visit	n	----- LS Mean -----	XX% Confidence Interval	p-value
Test 1	5	XX	X.XX	XX.XX - XXX.XX	X.XXXX
	7	XX	X.XX	XX.XX - XXX.XX	X.XXXX
Test 2	5	XX	X.XX	XX.XX - XXX.XX	X.XXXX
	7	XX	X.XX	XX.XX - XXX.XX	X.XXXX
Test 1 + Test 2	7	XX	X.XX	XX.XX - XXX.XX	X.XXXX
Control	5	XX	X.XX	XX.XX - XXX.XX	X.XXXX
	7	XX	X.XX	XX.XX - XXX.XX	X.XXXX

Note: The mixed model for repeated measures includes study group, study visit, study group by study visit interaction, gender, age class, BMI class, baseline value as the covariate, and subject as the random effect, with a variance-covariance matrix based on the AIC value.

n = Number of observation used in the analysis

Least-squares means (LS Means) are calculated from the MMRM.

Baseline = Visit 3 (Day 1, Week 1)

Visit 5 = Week 6

Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Test1 + Test 2 Group = Combined e-Vapor Use Group

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/pksas PROGRAMNAME.SAS DDMMYYYY HH:MM

**Note: Statistical Summary Tables for PP population, mITT with imputation populations, mITT population with outliers excluded, and mITT Population with BLQ values set to the LLOQ: 14.2.1.1.5.1, 14.2.1.1.10.1, 14.2.1.1.11.1, 14.2.1.1.12.2, 14.2.1.1.13.1, 14.2.1.2.5.1, 14.2.1.2.10.1, 14.2.1.2.11.1, 14.2.1.2.12.2, 14.2.1.2.13.1, 14.2.1.3.5.1, 14.2.1.3.10.1, 14.2.1.3.11.1, 14.2.1.3.12.2, 14.2.1.3.13.1, 14.2.1.4.5.1, 14.2.1.4.10.1, 14.2.1.4.11.1, 14.2.1.4.12.2, 14.2.1.4.13.1, 14.2.1.5.5.1, 14.2.1.5.10.1, 14.2.1.5.11.1, 14.2.1.5.12.2, 14.2.1.5.13.1, 14.2.1.6.5.1, 14.2.1.6.10.1, 14.2.1.6.11.1, 14.2.1.6.12.2, 14.2.1.6.13.1, 14.2.1.7.5.1, 14.2.1.7.10.1, 14.2.1.7.11.1, 14.2.1.7.12.2, 14.2.1.7.13.1, will have the following format:**

Table 14.2.1.1.5.1 Statistical Summary of <Matrix> <Biomarker> Absolute Change from Baseline to Visit 7 (<Units>) by Study Group (<Population>)

Group	n	----- LS Mean -----	XX% Confidence Interval	p-value
Test 1	XX	X.XX	XX.XX - XXX.XX	X.XXXX
Test 2	XX	X.XX	XX.XX - XXX.XX	X.XXXX
Control	XX	X.XX	XX.XX - XXX.XX	X.XXXX

Note: The mixed model for repeated measures includes study group, study visit, study group by study visit interaction, gender, age class, BMI class, baseline value as the covariate, and subject as the random effect, with a variance-covariance matrix based on the AIC value.

n = Number of observation used in the analysis

Least-squares means (LS Means) are calculated from the MMRM.

Baseline = Visit 3 (Day 1, Week 1)

Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/pksas PROGRAMNAME.SAS DDMMYYYY HH:MM

**Programmer Note: Tables 14.2.1.X.13.1 (mITT Population with BLQ values set to the LLOQ) will only be presented if the percentage of values that are BLQ is greater than 5% of observations.**

**Note: Statistical comparison Tables 14.2.1.1.4.2, 14.2.1.2.4.2, 14.2.1.3.4.2, 14.2.1.4.4.2, 14.2.1.5.4.2, 14.2.1.6.4.2, 14.2.1.7.4.2, 14.2.1.8.5 will have the following format:**

Table 14.2.1.1.4.2 Statistical Comparisons of <Biomarker> Absolute Change From Baseline (Units) Between Study Groups by Visit (mITT Population)

Comparison	Visit	----- LS Means -----		LS Mean Difference (Test - Reference)	XX% Confidence Interval	p-value
		Test (n)	Reference (n)			
Test 1 vs Control	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
Test 2 vs Control	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
Test 1 + Test 2 vs Control	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
Test 1 vs Test 2	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX

Note: The mixed model for repeated measures includes study group, study visit, study group by study visit interaction, gender, age class, BMI class, baseline value as the covariate, and subject as the random effect, with a variance-covariance matrix based on the AIC value.

Least-squares means (LS Means) are calculated from the MMRM.

Test = First group in the comparison

Reference = Second group in the comparison

n = Number of observation used in the analysis

Baseline = Visit 3 (Day 1, Week 1)

Visit 5 = Week 6

Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Test1 + Test 2 Group = Combined e-Vapor Use Group

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/pksas PROGRAMNAME.SAS DDMMYYYY HH:MM

**Note: Statistical comparison tables for PP population, mITT with imputation populations, and mITT population with outliers excluded, and mITT Population with BLQ values set to the LLOQ: 14.2.1.1.5.2, 14.2.1.1.10.2, 14.2.1.1.11.2, 14.2.1.1.12.3, 14.2.1.1.13.2, 14.2.1.2.5.2, 14.2.1.2.10.2, 14.2.1.2.11.2, 14.2.1.2.12.3, 14.2.1.2.13.2, 14.2.1.3.5.2, 14.2.1.3.10.2, 14.2.1.3.11.2, 14.2.1.3.12.3, 14.2.1.3.13.2, 14.2.1.4.5.2, 14.2.1.4.10.2, 14.2.1.4.11.2, 14.2.1.4.12.3, 14.2.1.4.13.2, 14.2.1.5.5.2, 14.2.1.5.10.2, 14.2.1.5.11.2, 14.2.1.5.12.3, 14.2.1.5.13.2, 14.2.1.6.5.2, 14.2.1.6.10.2, 14.2.1.6.11.2, 14.2.1.6.12.3, 14.2.1.6.13.2, 14.2.1.7.5.2, 14.2.1.7.10.2, 14.2.1.7.11.2, 14.2.1.7.12.3, 14.2.1.7.13.2, will have the following format:**

Table 14.2.1.1.5.2 Statistical Comparisons of <Biomarker> Absolute Change From Baseline to Visit 7 (Units) Between Study Groups (<Population>)

Comparison	----- LS Means -----		LS Mean Difference (Test - Reference)	XX% Confidence Interval	p-value
	Test (n)	Reference (n)			
Test 1 vs Control	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
Test 2 vs Control	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX

Note: The mixed model for repeated measures includes study group, study visit, study group by study visit interaction, gender, age class, BMI class, baseline value as the covariate, and subject as the random effect, with a variance-covariance matrix based on the AIC value.

Least-squares means (LS Means) are calculated from the MMRM.

Test = First group in the comparison

Reference = Second group in the comparison

n = Number of observation used in the analysis

Baseline = Visit 3 (Day 1, Week 1)

Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Program: /CAXXXXX/sas\_prg/pksas PROGRAMNAME.SAS DDMMYYYY HH:MM

**Programmer Note: Tables 14.2.1.X.13.2 (mITT Population with BLQ values set to the LLOQ) will only be presented if the percentage of values that are BLQ is greater than 5% of observations.**

**Note: Summary tables for subgroups Tables 14.2.1.1.6.1, 14.2.1.1.6.2, 14.2.1.1.6.3, 14.2.1.2.6.1, 14.2.1.2.6.2, 14.2.1.2.6.3, 14.2.1.3.6.1, 14.2.1.3.6.2, 14.2.1.3.6.3, 14.2.1.4.6.1, 14.2.1.4.6.2, 14.2.1.4.6.3, 14.2.1.5.6.1, 14.2.1.5.6.2, 14.2.1.5.6.3, 14.2.1.6.6.1, 14.2.1.6.6.2, 14.2.1.6.6.3, 14.2.1.7.6.1, 14.2.1.7.6.2, 14.2.1.7.6.3 will have the following format:**

Table 14.2.1.1.6.1 Summary of <Matrix> <Biomarker> Absolute Change from Baseline to Visit 7 (<units>) by Study Group and <Gender>\* (<Population>)

<Gender>*	Statistics	Group		
		Test 1	Test 2	Control
Female	n	X	X	X
	n missing	X	X	X
	Mean	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX
	Median	X.X	X.X	X.X
	Maximum	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Male	n	X	X	X
	n missing	X	X	X
	Mean	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX
	Median	X.X	X.X	X.X
	Maximum	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X

-----  
 Baseline = Visit 3 (Day 1, Week 1)  
 Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/pksas PROGRAMNAME.SAS DMMMYYYY HH:MM

\*Subgroups are Gender (Male, Female), Age Class (<45, ≥45), and BMI Class (<25 kg/m<sup>2</sup>, ≥ 25 kg/m<sup>2</sup>)

**Note: Statistical Summary Tables for Subgroups Comparisons (if subgroup term is significant), Tables 14.2.1.1.7.1, 14.2.1.1.8.1, 14.2.1.1.9.1, 14.2.1.2.7.1, 14.2.1.2.8.1, 14.2.1.2.9.1, 14.2.1.3.7.1, 14.2.1.3.8.1, 14.2.1.3.9.1, 14.2.1.4.7.1, 14.2.1.4.8.1, 14.2.1.4.9.1, 14.2.1.5.7.1, 14.2.1.5.8.1, 14.2.1.5.9.1, 14.2.1.6.7.1, 14.2.1.6.8.1, 14.2.1.6.9.1, 14.2.1.7.7.1, 14.2.1.7.8.1, 14.2.1.7.9.1 will have the following format:**

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Table 14.2.1.1.7.1 Statistical Summary of <Matrix> <Biomarker> Absolute Change From Baseline to Visit 7 (Units) by Study Group and <Subgroup>\* (<Population>)

Group	<Subgroup>*	n	----- LS Mean -----	XX% Confidence Interval	p-value
Test 1	XXXXXX	XX	X.XX	XX.XX - XXX.XX	X.XXXX
	XXXX	XX	X.XX	XX.XX - XXX.XX	X.XXXX
Test 2	XXXXXX	XX	X.XX	XX.XX - XXX.XX	X.XXXX
	XXXX	XX	X.XX	XX.XX - XXX.XX	X.XXXX
Control	XXXXXX	XX	X.XX	XX.XX - XXX.XX	X.XXXX
	XXXX	XX	X.XX	XX.XX - XXX.XX	X.XXXX

Note: The mixed model for repeated measures includes study group, study visit, study group by study visit interaction, gender, study group by subgroup\* interaction, age class, and BMI class as fixed effects, baseline value as the covariate, and subject as the random effect, with a variance-covariance matrix based on the AIC value.

n = Number of observation used in the analysis

Least-squares means (LS Means) are calculated from the MMRM.

Baseline = Visit 3 (Day 1, Week 1)  
 Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/pksas PROGRAMNAME.SAS DDMMYYYY HH:MM

\*Subgroups are Gender (Female, Male), Age Class (<45, ≥45), and BMI Class (<25 kg/m<sup>2</sup>, ≥ 25 kg/m<sup>2</sup>)

**Note: Statistical Comparisons Tables for Subgroups Comparisons (if subgroup term is significant), Tables 14.2.1.1.7.2, 14.2.1.1.8.2, 14.2.1.1.9.2, 14.2.1.2.7.2, 14.2.1.2.8.2, 14.2.1.2.9.2, 14.2.1.3.7.2, 14.2.1.3.8.2, 14.2.1.3.9.2, 14.2.1.4.7.2, 14.2.1.4.8.2, 14.2.1.4.9.2, 14.2.1.5.7.2, 14.2.1.5.8.2, 14.2.1.5.9.2, 14.2.1.6.7.2, 14.2.1.6.8.2, 14.2.1.6.9.2, 14.2.1.7.7.2, 14.2.1.7.8.2, 14.2.1.7.9.2 will have the following format:**

Table 14.2.1.1.7.2 Statistical Comparisons of <Matrix> <Biomarker> Absolute Change From Baseline to Visit 7 (Units) Between Study Groups by <Subgroup>\* (<Population>)

Comparison	<Subgroup>*	----- LS Means -----		LS Mean Difference (Test - Reference)	XX% Confidence Interval	p-value
		Test (n)	Reference (n)			
Test 1 vs Control	XXXXXX	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	XXXX	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
Test 2 vs Control	XXXXXX	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	XXXX	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX

Note: The mixed model for repeated measures includes study group, study visit, study group by study visit interaction, gender, study group by <subgroup>\* interaction, age class, and BMI classes as fixed effects, baseline value as the covariate, and subject as the random effect, with a variance-covariance matrix based on the AIC value.

Test = First group in the comparison

Reference = Second group in the comparison

n = Number of observation used in the analysis

Baseline = Visit 3 (Day 1, Week 1)

Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XIMB

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/pksas PROGRAMNAME.SAS DDMMYYYY HH:MM

\*Subgroups are Gender (Female, Male), Age Class (<45, ≥45), and BMI Class (<25 kg/m2, ≥ 25 kg/m2)

**Note: Paired Comparisons Tables (Baseline vs Visit 7) 14.2.1.1.14, 14.2.1.2.14, 14.2.1.3.14, 14.2.1.4.14, 14.2.1.5.14, 14.2.1.6.14, and 14.2.1.7.14 will have the following format:**

Table 14.2.1.1.14 Statistical Comparisons of <Matrix> <Biomarker> (<units>) Between Baseline and Visit 7 by Study Group (mITT Population)

Group	Mean Values		Difference			
	Baseline	Visit 7	Difference	DF	95% Confidence Interval	p-value
Test 1	X.XX	X.XX	XXX.XX	XX	XX.XX - XXX.XX	X.XXXX
Test 2	X.XX	X.XX	XXX.XX	XX	XX.XX - XXX.XX	X.XXXX

Note: Paired t-test is used to perform the analysis.

DF = Degrees of Freedom  
 Baseline = Visit 3 (Day 1, Week 1)  
 Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB

Program: /CAXXXXX/sas\_prg/pksas PROGRAMNAME.SAS DDMMYYYY HH:MM

Altria Client Services LLC  
 Study No. ALCS-RA-16-06-EV  
 Celerion Project CA20130

Table 14.2.2.1.1 Summary of Average Number of Cigarettes or e-Vapor Cartridges Used Per Day by Study Group and Week  
 (Week 1 Through Week 6) (mITT Population)

Group		Week						Weeks 2-6	% Change
		1	2	3	4	5	6		
Test 1	n	X	X	X	X	X	X	X	X
	n missing	X	X	X	X	X	X	X	X
	Mean	X.X	X.X						
	SD	X.XX	X.XX						
	CV(%)	XX.X	XX.X						
	SEM	X.X	X.X						
	Minimum	X	X	X	X	X	X	X	X
	Q1	X.X	X.X						
	Median	X	X	X	X	X	X	X	X
	Q3	X.X	X.X						
	Maximum	X.X	X.X						
95% CI	X, X	X, X	X, X	X, X	X, X	X, X	X, X	X, X	
Test 2	<same as above>								
Control	<same as above>								

Note: % Change = % Change from Baseline to Week 6  
 Data for e-Vapor products is number of new cartridges started per day.

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXX/ECR/sas\_prg/pksas/PROGRAMNAME.sas DDMMYYYY HH:MM

Altria Client Services LLC  
 Study No. ALCS-RA-16-06-EV  
 Celerion Project CA20130

Table 14.2.2.1.2 Summary of Average Number of Cigarettes or e-Vapor Cartridges Used Per Day by Study Group and Week (Week 7 Through Week 12) (mITT Population)

Group		Week						Weeks 7-12	% Change
		7	8	9	10	11	12		
Test 1	n	X	X	X	X	X	X	X	X
	n missing	X	X	X	X	X	X	X	X
	Mean	X.X	X.X						
	SD	X.XX	X.XX						
	CV(%)	XX.X	XX.X						
	SEM	X.X	X.X						
	Minimum	X	X	X	X	X	X	X	X
	Q1	X.X	X.X						
	Median	X	X	X	X	X	X	X	X
	Q3	X.X	X.X						
Maximum	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X	
95% CI	X, X	X, X	X, X	X, X	X, X	X, X	X, X	X, X	
Test 2	<same as above>								
Control	<same as above>								

Note: % Change = % Change from Baseline to Week 12  
 Data for e-Vapor products is number of new cartridges started per day.

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/ECR/sas\_prg/pksas/PROGRAMNAME.sas DDMMYYYY HH:MM

Table 14.2.2.2 Frequency of Reduction, No Change, or Increase in Cigarettes Per Day and e-Vapor Cartridges Used Per Day from Baseline to Week 12 (Visit 7) by Study Group (mITT Population)

Group	Reduction n %	No Change n (%)	Increase n (%)
Test 1	XX (XX)	XX (XX)	XX (XX)
Test 2	XX (XX)	XX (XX)	XX (XX)
Control	XX (XX)	XX (XX)	XX (XX)

Note: Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Altria Client Services LLC  
 Study No. ALCS-RA-16-06-EV  
 Celerion Project CA20130

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Table 14.2.2.3.1 Frequency of Days with 1-20 or >20 Puffs per Day for e-Vapor Products by Study Group and Week (Week 1 through Week 6) (mITT Population)

Week	Statistic	----- Test 1 -----		----- Test 2 -----		----- Control -----	
		1-20 puffs	>20 puffs	1-20 puffs	>20 puffs	1-20 puffs	>20 puffs
1	n (%)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
2		XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
3		XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
4		XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
5		XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
6		XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
2-6		XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)

Note: Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/ECR/sas\_prg/pksas/PROGRAMNAME.sas DDMMYYYY HH:MM

Table 14.2.2.3.2 Frequency of Days with 1-20 or >20 Puffs per Day for e-Vapor Products  
 Study Group and Week (Week 1 through Week 6) (mITT Population)

Week	Statistic	----- Test 1 -----		----- Test 2 -----		----- Control -----	
		1-20 puffs	>20 puffs	1-20 puffs	>20 puffs	1-20 puffs	>20 puffs
7	n (%)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
8		XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
9		XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
10		XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
11		XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
12		XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
7-12		XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)

Note: Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/ECR/sas\_prg/pksas/PROGRAMNAME.sas DDMMYYYY HH:MM

Table 14.2.2.4.1 Summary of eCO (ppm) by Study Group and Visit (mITT Population)

Group	Statistics	Visit		
		3	4	5
Test 1	n	X	X	X
	n missing	X	X	X
	Mean	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX
	Median	X.X	X.X	X.X
	Maximum	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Test 2	n	X	X	X
	n missing	X	X	X
	Mean	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX
	Median	X.X	X.X	X.X
	Maximum	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
Control	<same as above>			

Visit 3 = Baseline (Day 1, Week 1)  
 Visit 4 = Week 3  
 Visit 5 = Week 6  
 Visit 6 = Week 9  
 Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/pksas/PROGRAMNAME.SAS DDMMYYYY HH:MM

**Programmer Note: add columns for Visits 6 and 7**

**Note: Table 14.2.2.4.2 Summary of Creatinine-adjusted NNN by Study Group and Visit (mITT Population) has a similar format as Table 14.2.1.1.1.1 above**

Table 14.2.2.4.3 Frequency of Use of Other Tobacco Products, eCO, and Urine NNN by Study Group and Visit (mITT Population)

Group	Visit	N	Use of Other Tobacco Products n (%)	----- eCO (ppm)-----			----- Urine NNN % reduction-----	
				≤ 5 n (%)	5-8 n (%)	>8 n (%)	<80% n (%)	≥80% n (%)
Test 1	3	XX	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	5	XX	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	6	XX	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	7	XX	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
Test 2	3	XX	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	5	XX	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	6	XX	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	7	XX	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
Control	3	XX	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	5	XX	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	6	XX	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	7	XX	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)

Note: Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/ECR/sas\_prg/pksas/PROGRAMNAME.sas DMMYYYY HH:MM

**Note: Tables 14.2.3.1.1 and 14.2.3.1.2 will be in the following format:**

Table 14.2.3.1.1 Summary of Pulmonary Function Parameters by Study Group and Visit (<Population>)

Parameter	Visit		----- Group -----				
			Test 1	Test 2	Control		
Measured FEV1 (L)	2	n	X	X	X		
		n missing	X	X	X		
		Mean	X.X	X.X	X.X		
		SD	X.XX	X.XX	X.XX		
		CV (%)	XX.X	XX.X	XX.X		
		SEM	X.X	X.X	X.X		
		Minimum	X	X	X		
		Median	X.X	X.X	X.X		
		Maximum	XX	XX	XX		
		95% CI	X, X	X, X	X, X		
			7	n	X	X	X
				n missing	X	X	X
				Mean	X.X	X.X	X.X
				SD	X.XX	X.XX	X.XX
	CV (%)	XX.X		XX.X	XX.X		
	SEM	X.X		X.X	X.X		
	Minimum	X		X	X		

XXXXX <same for remaining parameters>

Note: Visit 2 = Baseline  
 Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/ECR/sas\_prg/pksas/PROGRAMNAME.sas DDMMYYYY HH:MM

**Note: parameters to be included are: measured FEV1 (L), percent of predicted FEV1 (%), measured FVC (L), percent of predicted FVC (%), measured FEV1/FVC, percent of predicted FEV1/FVC (%), and FEF25-75.**

**Note: Tables 14.2.3.2.1 and 14.2.3.2.2 will be in the following format:**

Table 14.2.3.2.1 Summary of Absolute Change From Baseline to Visit 7 in Pulmonary Function Parameters by Study Group (<Population>)

Parameter	Visit		----- Group -----		
			Test 1	Test 2	Control
Measured FEV1 (L)	7	n	X	X	X
		n missing	X	X	X
		Mean	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX
		CV(%)	XX.X	XX.X	XX.X
		SEM	X.X	X.X	X.X
		Minimum	X	X	X
		Median	X.X	X.X	X.X
		Maximum	XX	XX	XX
		95% CI	X, X	X, X	X, X
XXXXX		<same for remaining parameters>			

Note: Baseline = Visit 2  
 Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/ECR/sas\_prg/pksas/PROGRAMNAME.sas DDMMYYYY HH:MM

**Note: parameters to be included are: measured FEV1 (L), percent of predicted FEV1 (%), measured FVC (L), percent of predicted FVC (%), measured FEV1/FVC, percent of predicted FEV1/FVC (%), and FEF25-75.**

**Note: Tables 14.2.3.3.1 and 14.2.3.3.2 will be in the following format:**

Table 14.2.3.3.1 Statistical Summary of Absolute Change From Baseline to Visit 7 in Pulmonary Function Parameters by Study Group (<population>)

Parameter	Group	n	----- LS Mean -----	XX% Confidence Intervals	p-Value
Percent of Predicted FEV1 (L)	Test 1	X	X.XX	XX.XX - XXX.XX	X.XXXX
	Test 2	X	X.XX	XX.XX - XXX.XX	X.XXXX
	Control	X	X.XX	XX.XX - XXX.XX	X.XXXX

<Same for the remaining parameters>

Note: The model includes study group, gender, and age class as fixed effects, and baseline value as the covariate.  
 n = Number of observation used in the analysis  
 Least-squares means (LS Means) are calculated from the ANCOVA.

Baseline = Visit 2  
 Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/ECR/sas\_prg/pksas/PROGRAMNAME.sas DDMMYYYY HH:MM

**Note: parameters to be included are: percent of predicted FEV1, percent of predicted FVC, and percent of predicted FEV1/FVC.**

**Note: Tables 14.2.3.4.1 and 14.2.3.4.2 will be in the following format:**

Table 14.2.3.4.1 Statistical Comparisons of Absolute Change From Baseline to Visit 7 in Pulmonary Function Parameters Between Study Groups (<Population>)

Parameter	Comparison	----- LS Means ----- Test (n)	Reference (n)	LS Mean Difference (Test - Reference)	XX% Confidence Intervals	p-Value
Percent of Predicted FEV1 (%)	Test 1 vs Control	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	Test 2 vs Control	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
<Same for the remaining parameters>						

Note: The model includes study group, gender, and age class as fixed effects, and baseline value as the covariate.

Test = First group in the comparison

Reference = Second group in the comparison

n = Number of observation used in the analysis

Baseline = Visit 2

Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XIMB

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/ECR/sas\_prg/pksas/PROGRAMNAME.sas DDMMYYYY HH:MM

**Note: parameters to be included are: percent of predicted FEV1, percent of predicted FVC, and percent of predicted FEV1/FVC.**

**QGEN, TQOLIT and mCEQ Questionnaire Summary Tables 14.2.4.1.1 – 14.2.4.1.2, 14.2.4.2.1 – 14.2.4.2.2, and 14.2.4.3.1 – 14.2.4.3.3 will have the following format:**

Table 14.2.4.1.1.1 Summary of <QGEN> <Factor Scores> by Study Group and Visit (<Population>)

<Question or Subscale>	Visit	----- Group -----			
		Test 1	Test 2	Control	
XXXXX	3	n	X	X	X
		n missing	X	X	X
		Mean	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX
		CV(%)	XX.X	XX.X	XX.X
		SEM	X.X	X.X	X.X
		Minimum	X	X	X
		Q1	X.X	X.X	X.X
		Median	X.X	X.X	X.X
		Q3	X.X	X.X	X.X
		Maximum	XX	XX	XX
		95% CI	X, X	X, X	X, X
			5	<Same as above>	
	7	<Same as above>			

XXXXX <same for remaining questions or subscales>

Note: Visit 3 = Baseline (Day 1, Week 1)  
 Visit 5 = Week 6  
 Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/ECR/sas\_prg/pksas/PROGRAMNAME.sas DDMMYYYY HH:MM

**Programmer note: For mCEQ, only Visits 3 and 7 will be shown.**

**QGEN, TQOLIT and mCEQ Questionnaire Statistical Summary Tables 14.2.4.1.3.1, 14.2.4.2.3.1, and 14.2.4.3.4.1 will have the following format:**

Table 14.2.4.1.3.1 Statistical Summary of Absolute Change From Baseline in <QGEN> <Factor> Scores by Study Group and Visit (<Population>)

Subscale	Visit	Group	n	----- LS Mean -----	XX% Confidence Intervals	p-Value
XXXXXXXX	5	Test 1	X	X.XX	XX.XX - XXX.XX	X.XXXX
		Test 2	X	X.XX	XX.XX - XXX.XX	X.XXXX
		Control	X	X.XX	XX.XX - XXX.XX	X.XXXX
	7	Test 1	X	X.XX	XX.XX - XXX.XX	X.XXXX
		Test 2	X	X.XX	XX.XX - XXX.XX	X.XXXX
		Control	X	X.XX	XX.XX - XXX.XX	X.XXXX

<Same for the remaining subscales>

Note: The mixed model for repeated measures includes study group, study visit, study group by study visit interaction, gender, age class, and BMI class as fixed effects, baseline score as the covariate, and subject as the random effect, with an < XX > variance-covariance matrix.  
 n = Number of observation used in the analysis  
 Least-squares means (LS Means) are calculated from the ANCOVA.

Visit 3 = Baseline (Day 1, Week 1)  
 Visit 5 = Week 6  
 Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/ECR/sas\_prg/pksas/PROGRAMNAME.sas DDMMYYYY HH:MM

**Programmer note: For mCEQ, only the Visit 7 comparison will be shown. The first footnote will be “The mixed model includes study group, gender, and age class as fixed effects, and baseline score as the covariate”.**

**QGEN, TQOLIT and mCEQ Questionnaire Statistical Comparison Tables 14.2.4.1.3.2, 14.2.4.2.3.2, and 14.2.4.3.4.2 will have the following format:**

Table 14.2.4.1.3.2 Statistical Comparisons of Absolute Change From Baseline in <QGEN> Factor Scores Between Study Groups (<Population>)

Subscale	Visit	Comparison	----- LS Means -----		LS Mean Difference (Test - Reference)	XX% Confidence Intervals	p-Value
			Test (n)	Reference (n)			
XXXXXXXXXX	5	Test 1 vs Control	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
		Test 2 vs Control	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
	7	Test 1 vs Control	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX
		Test 2 vs Control	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX	X.XXXX

<Same for the remaining subscales>

Note: The mixed model for repeated measures includes study group, study visit, study group by study visit interaction, gender, and age class as fixed effects, baseline score as the covariate, and subject as the random effect, with an < XX > variance-covariance matrix.

Test = First group in the comparison

Reference = Second group in the comparison

n = Number of observation used in the analysis

Visit 3 = Baseline (Day 1, Week 1)

Visit 5 = Week 6

Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/ECR/sas\_prg/pksas/PROGRAMNAME.sas DDMMYYYY HH:MM

**Programmer note: For mCEQ, only the Visit 7 comparison will be shown. The first footnote will be “The mixed model includes study group, gender, and age class as fixed effects, and baseline score as the covariate”.**

Table 14.2.4.4.1 Summary of Cough Questionnaire Questions I and III through X (< > Population)

Question	Response	----- Visit 3 -----		----- Visit 5 -----		----- Visit 7 -----	
		Test 1 n (%)	Test 2 n (%)	Test 1 n (%)	Test 2 n (%)	Test 1 n (%)	Test 2 n (%)
I. Did you have a cough in the past 30 days?	Yes	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	No	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
III. When does the cough occur? (choose one)	Middle of the Night	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	Daytime	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	Anytime	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
IV. Do you have a cough that comes mainly from your chest and not your throat?	Yes	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	No	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
V. Do you ever cough up phlegm?	Never	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	Seldom	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	Sometimes	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	Often	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	Always	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)

<similar for remaining questions (VI, VII, VIII, IX, X) and responses>

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Note: Visit 3 = Baseline (Day 1, Week 1)  
 Visit 5 = Week 6  
 Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/ECR/sas\_prg/pksas/PROGRAMNAME.sas DDMMYYYY HH:MM

Table 14.2.4.4.2 Summary of Cough Questionnaire Question II (< > Population)

Question	Visit	Statistic	Group		
			Test 1	Test 2	Control
II. How long have you had the cough? (Days)	3	n	XX	XX	XX
		n missing	X	X	X
		Mean	XX	XX	XX
		SD	XX	XX	XX
		CV%	XX	XX	XX
		SEM	XX	XX	XX
		Minimum	XX	XX	XX
		Q1	XX	XX	XX
		Median	XX	XX	XX
		Q3	XX	XX	XX
		Maximum	XX	XX	XX
95% CI	X, X	X, X	X, X		

<Data will be presented similarly for Visits 5 and 7)

Note: Visit 3 = Baseline (Day 1, Week 1)  
 Visit 5 = Week 6  
 Visit 7 = Week 12

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/ECR/sas\_prg/pksas/PROGRAMNAME.sas DDMMYYYY HH:MM

Table 14.2.4.5.1 Summary of Reasons of Use/Not-Use Test Product Questionnaire by Study Group at Week 12: Likelihood of Use (mITT Population)

Question	Group	Statistics	-----Choice of Response-----					
			1	2	3	4	5	6
How Likely...	Test 1	n (%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Test 2	n (%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
How Likely...	Test 1	n (%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
	Test 2	n (%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)

Note: 1 = Strongly Likely; 2 = Quite Likely, 3 = Somewhat Likely Neutral/Neither, 4 = Strongly Unlikely, 5 = Quite Unlikely, 6 = Somewhat Unlikely

Week 12 = Visit 7

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB

Program: /CAXXXXX/ECR/sas\_prg/pksas/PROGRAMNAME.sas DDMMYYYY HH:MM

Table 14.2.4.5.2 Summary of Reasons of Use/Not-Use Test Product Questionnaire by Study Group at Week 12: Reasons to Use (< > Population)

Why Would You Use the Test Product Now?	Test 1 n (%)	Test 2 n (%)
-----		
Smoking/Other Tobacco-Related Reasons		
To satisfy..	XX (XX%)	XX (XX%)
To help...	XX (XX%)	XX (XX%)
<similar for remaining reasons>		
General Reasons		
Curiosity	XX (XX%)	XX (XX%)
Offered/given/used...	XX (XX%)	XX (XX%)
<similar for remaining reasons>		
-----		

Note: Week 12 = Visit 7

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB

Program: /CAXXXXX/ECR/sas\_prg/pksas/PROGRAMNAME.sas DDMMYYYY HH:MM

Table 14.3.1.1 Adverse Event Frequency by Study Group -  
 Number of Subjects Reporting the Event (% of Subjects Who Received Study Product)

Adverse Event*	Product Trial§	Group			Overall#
		Test 1	Test 2	Control	
Number of Subjects Who Received Study Product	XX(100%)	XX(100%)	XX(100%)	XX(100%)	XX(100%)
Number of Subjects With Adverse Events	X( X%)	X( X%)	X( XX%)	X( X%)	X( X%)
Number of Subjects Without Adverse Events	XX(XXX%)	XX( XX%)	XX( XX%)	XX( XX%)	XX(XXX%)
Eye disorders	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Vision blurred	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Gastrointestinal disorders	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Dyspepsia	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Nausea	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Musculoskeletal and connective tissue disorders	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Back pain	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Muscle cramps	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Musculoskeletal pain	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Nervous system disorders	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Headache NOS	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Reproductive system and breast disorders	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Vaginal discharge	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Respiratory, thoracic and mediastinal disorders	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Epistaxis	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)

Note: \* Adverse events are classified according to MedDRA Version 19.0.  
 § Only includes adverse events that occurred during the product trial period.  
 # Adverse events that occurred during the product trial period are excluded from the Overall summary.

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/tab cdash\_tbla\_ela\_auto.sas DDMMYYYY HH:MM

Table 14.3.1.2 Adverse Event Frequency by Study Group -  
 Number of Adverse Events (% of Total Adverse Events)

Adverse Event*	Product Trial\$	Group			Overall#
		Test 1	Test 2	Control	
Number of Adverse Events	XX(100%)	XX(100%)	XX(100%)	XX(100%)	XX(100%)
Eye disorders	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Vision blurred	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Gastrointestinal disorders	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Dyspepsia	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Nausea	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Musculoskeletal and connective tissue disorders	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Back pain	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Muscle cramps	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Musculoskeletal pain	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Nervous system disorders	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Headache NOS	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Reproductive system and breast disorders	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Vaginal discharge	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Respiratory, thoracic and mediastinal disorders	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)
Epistaxis	X( X%)	X( X%)	X( X%)	X( X%)	X( X%)

Note: \* Adverse events are classified according to MedDRA Version 19.0.  
 \$ Only includes adverse events that occurred during the product trial period.  
 # Adverse events that occurred during the product trial period are excluded from the Overall summary.

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/tab cdash\_tbla\_1a\_auto.sas DDMMYYYY HH:MM

Table 14.3.1.3 Adverse Event Frequency by Study Product, Severity, and Relationship to Study Group  
 - Number of Subjects Reporting Events

Adverse Event*	Group	Number of Subjects with Adverse Events	Severity			Relationship to Study Product				
			Mild	Moderate	Severe	Not Related	Unlikely	Possibly	Likely	Definitely
Abdominal pain	X	X	X	X	X	X	X	X	X	X
Constipation	X	X	X	X	X	X	X	X	X	X
Dry throat	Product Trial	X	X	X	X	X	X	X	X	X
Headache	X	X	X	X	X	X	X	X	X	X
Product trial§		X	X	X	X	X	X	X	X	X
Test 1 Group		X	X	X	X	X	X	X	X	X
Test 2 Group		X	X	X	X	X	X	X	X	X
Control Group		X	X	X	X	X	X	X	X	X
Overall#		X	X	X	X	X	X	X	X	X

Note: \* Adverse events are classified according to MedDRA Version 19.0.  
 § Only includes adverse events that occurred during the product trial period.  
 # Adverse events that occurred during the product trial period are excluded from the Overall summary.  
 When a subject experienced the same AE at more than one level of severity during a product use period, only the most severe occurrence was counted.  
 When a subject experienced the same AE at more than one level of product relationship during a product use period, only the occurrence most closely related to study product was counted.

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/tab cdash\_tblae3a\_auto.sas DDMMYYYY HH:MM

Table 14.3.1.4 Adverse Event Frequency by Study Product, Severity, and Relationship to Study Group  
 - Number of Adverse Events

Adverse Event*	Group	Number of Adverse Events	Severity			Relationship to Study Product				
			Mild	Moderate	Severe	Not Related	Unlikely	Possibly	Likely	Definitely
Abdominal pain	X	X	X	X	X	X	X	X	X	X
Constipation	X	X	X	X	X	X	X	X	X	X
Dry throat	Product trial	X	X	X	X	X	X	X	X	X
Headache	X	X	X	X	X	X	X	X	X	X
Product trial\$		X	X	X	X	X	X	X	X	X
Test 1 Group		X	X	X	X	X	X	X	X	X
Test 2 Group		X	X	X	X	X	X	X	X	X
Control Group		X	X	X	X	X	X	X	X	X
Overall#		X	X	X	X	X	X	X	X	X

Note: \* Adverse events are classified according to MedDRA Version 19.0.  
 \$ Only includes adverse events that occurred during the product trial period.  
 # Adverse events that occurred during the product trial period are excluded from the Overall summary.

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/tab cdash\_tbla4a\_auto.sas DDMMYYYY HH:MM

Table 14.3.2.1 Serious Adverse Events

-----  
There were no serious adverse events recorded during the study

Program: /CAXXXXX/sas\_prg/stsas/tab cdash\_tblae\_ser.sas DDMMYYYY HH:MM

Table 14.3.4.1 Out-of-Range Values and Recheck Results - Serum Chemistry

Subject Number	Age/ Gender	Study Visit		Group	Parameter1	Parameter2	Parameter3	Parameter4	Parameter5
		Name	Date						
XXXXXX	XX/X	Screening	DDMMYYYY	X	XX HN	XX LN	XX	XX	XX HN
		XXX	DDMMYYYY		XX HN	XX LN	XX	XX	XX HN

Note: H = Above Reference Range, L = Below Reference Range  
 PI Interpretation: N = Not Clinically Significant  
 See Appendix 16.1.10.1 for lab units and reference ranges.

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

**Programmer Note: In the shell above, replace Parameter1, 2 etc. with actual lab tests in the study. Table 14.3.4.2 (hematology) and Table 14.3.4.3 (Urinalysis) will resemble Table 14.3.4.1.**

Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry

Laboratory Test (units)	Normal Range	Time Point	Statistic	Product Trial\$	Group			Overall*
					Test 1	Test 2	Control	
Testname (unit)	< - >	Screening	n	X	X	X	X	X
			Mean	X.X	X.X	X.X	X.X	X.X
			SD	X.XX	X.XX	X.XX	X.XX	X.XX
			Minimum	XX	XX	XX	XX	XX
			Median	X.X	X.X	X.X	X.X	X.X
			Maximum	XX	XX	XX	XX	XX

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.

\$ Includes subjects only attended the product trial period.

\* Subjects only attended the product trial period are excluded from overall summarization.

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/tab cdash\_labsummary.sas DDMMYYYY HH:MM

**Programmer Note: Tables 14.3.5.2 (hematology summary), 14.3.5.3 (urinalysis summary) will resemble 14.3.5.1.**

Table 14.3.5.4 Vital Sign Summary

Vital Sign (units)	Time Point	Statistic	Product Trial\$	Group			Overall*
				Test 1	Test 2	Control	
Testname (unit)	Screening	n	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX
	XXXXX	n	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX
	XXXXXXXX	n		X	X	X	X
		Mean		X.X	X.X	X.X	X.X
		SD		X.XX	X.XX	X.XX	X.XX
		Minimum		XX	XX	XX	XX
		Median		X.X	X.X	X.X	X.X
		Maximum		XX	XX	XX	XX

Note: \$ Includes subjects only attended the product trial period.  
 \* Subjects only attended the product trial period are excluded from overall summarization.

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXXX/sas\_prg/stsas/tab cdash\_vitsummary.sas DDMMYYYY HH:MM

**Programmer Note: In the shell above, replace Testname with actual variables in the study. Data will also be reported for Day -1 through 14 and End-of-Study.**

Table 14.3.5.5 12-Lead Electrocardiogram Summary

ECG Parameter(units)	Time Point	Statistic	Product Trial\$	Group			Overall*
				Test 1	Test 2	Control	
Testname (unit)	Screening	n	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX
	XXXXXXXXXX	n	X	X	X	X	X
		Mean	XX.XX	X.X	X.X	X.X	XX.XX
		SD	X.XXX	X.XX	X.XX	X.XX	X.XXX
		Minimum	XX.X	XX	XX	XX	XX.X
		Median	XX.XX	X.X	X.X	X.X	XX.XX
		Maximum	XX.X	XX	XX	XX	XX.X

Note: \$ Includes subjects only attended the product trial period.  
 \* Subjects only attended the product trial period are excluded from overall summarization.

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/tab cdash\_ecgsummary.sas DDMMYYYY HH:MM

**Programmer Note: In the shell above, replace Testname with actual variables in the study.**

## **12. LISTING SHELLS**

The following listing shells provide 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 listings that will be included in the final report.

Note: Subjects only enrolled in the product trial period will show the study group as product trial in the listings when applicable.

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges by Site

Site	Laboratory Group	Test Name	Gender	Age Category	Normal Range	Unit
XXX	Serum Chemistry	Test Name	<>	<>	XX - XX	units
		Test Name	<>	<>	XX - XX	units
		Test Name	<>	<>	XX - XX	units
		Test Name	<>	<>	XX - XX	units
		Test Name	<>	<>	XX - XX	units
		Test Name	<>	<>	XX - XX	units
	Hematology	Test Name	<>	<>	XX - XX	units
		Test Name	<>	<>	XX - XX	units
		Test Name	<>	<>	XX - XX	units
		Test Name	<>	<>	XX - XX	units
		Test Name	<>	<>	XX - XX	units

Note: Site XXX = XXXXXXXXXXXXXXXX

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

**Programmer Note: Similar for remaining Laboratory Groups and Test Names.**

Appendix 16.2.1.1 Subject Disposition and Discontinuation (Randomized)

Site	Subject Number	Randomization Number	Study Group	Product Assignment	Discontinuation Date	Completed Study?	Visit	Reason for Discontinuation	Specify
XXX	XXXXXX	XXX	X	X	DDMMYYYY	Yes			
	XXXXXX	XXX	X	X	DDMMYYYY	Yes			
	XXXXXX	XXX	X	X	DDMMYYYY	Yes			
	XXXXXX	XXX	X	X	DDMMYYYY	Yes			
	XXXXXX	XXX	X	X	DDMMYYYY	No	XXX	Personal Reason	
	XXXXXX	XXX	X	X	DDMMYYYY	Yes			
	XXXXXX	XXX	X	X	DDMMYYYY	Yes			
	XXXXXX	XXX	X	X	DDMMYYYY	Yes			
	XXXXXX	XXX	X	X	DDMMYYYY	Yes			

Note: Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Product A = Test EVP (currently marketed by Nu Mark LLC as MarkTen® XL Bold Menthol [4.0% NBW]) [CVR2.6.8] Formula: 10381-40-E; Name: "Spencer"; Label: 40E (Product XLMB)  
 Product B = Test EVP (currently marketed by Nu Mark LLC as MarkTen® XL Bold Classic [4.0% NBW]) [CVR2.6.8] Formula: 10381-44-B; Name: "Rosetta"; Label: B44 (Product XLCB)

Site XXX = XXXXXXXXXXXXXXXX

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.1.2 Subject Disposition and Discontinuation (Product Trial)

Site	Subject Number	Discontinuation Date	Completed Study?	Reason for Discontinuation	Specify
XXX	XXXXXX	DDMMYYYY	No	XXXXXXXXXXXXXX	
	XXXXXX	DDMMYYYY	No	XXXXXXXXXXXXXX	
	XXXXXX	DDMMYYYY	No	XXXXXXXXXXXXXX	
	XXXXXX	DDMMYYYY	No	XXXXXXXXXXXXXX	
	XXXXXX	DDMMYYYY	No	XXXXXXXXXXXXXX	

Note: Site XXX = XXXXXXXXXXXXXXXXXXXX

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.4.1.1 Demographics (I of II)

Site	Subject Number	Study Group	Age (yrs)	Gender	Race	Ethnicity	Birth and Reproductive Status	Height (cm)	Weight (kg)	BMI (kg/m <sup>2</sup> )
XXX	XXXXXX	X	XX	XXXX	XXXXXXXXXX	XXXXXXXXXXXX	XXXXXXXXXXXX	XX.X	XXX.X	XX.XX
	XXXXXX	X	XX	XXXX	XXXXXXXXXX	XXXXXXXXXXXX	XXXXXXXXXXXX	XX.X	XXX.X	XX.XX
	XXXXXX	X	XX	XXXX	XXXXXXXXXX	XXXXXXXXXXXX	XXXXXXXXXXXX	XX.X	XXX.X	XX.XX
	XXXXXX	X	XX	XXXX	XXXXXXXXXX	XXXXXXXXXXXX	XXXXXXXXXXXX	XX.X	XXX.X	XX.XX
	XXXXXX	X	XX	XXXX	XXXXXXXXXX	XXXXXXXXXXXX	XXXXXXXXXXXX	XX.X	XXX.X	XX.XX

Note: BMI = Body Mass Index

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Control Group = Continue smoking lit-end conventional cigarette

Site XXX = XXXXXXXXXXXXXXXXXXXX

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.4.1.2 Demographics (II of II)

Site	Subject Number	Study Group	Informed Consent Date	Informed Re-Consent Date	Protocol Version
XXX	XXXXXX	X	DDMMYYYY	DDMMYYYY	XXXXXXX
	XXXXXX	X	DDMMYYYY	DDMMYYYY	XXXXXXX
	XXXXXX	X	DDMMYYYY	DDMMYYYY	XXXXXXX
	XXXXXX	X	DDMMYYYY	DDMMYYYY	XXXXXXX
	XXXXXX	X	DDMMYYYY	DDMMYYYY	XXXXXXX
	XXXXXX	X	DDMMYYYY	DDMMYYYY	XXXXXXX

Note: Test 1 Group = e-Vapor Product XLCE  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Site XXX = XXXXXXXXXXXXXXXXXXXX

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.4.1.3 Subject Characteristics

Site	Subject Number	Study Group	Was Subject Characteristics Collected?	Date of Collection	Annual Household Income	Highest Grade or Year of School Completed	Current Employment	Military Duty	Marital Status	Self-defined Gender
XXX	XXXXXX	X	XXX	DDMMYYYY	XXXXXXXXXX	XXXXXXXXXXXX	XXXXXXXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX
	XXXXXX	X	XXX	DDMMYYYY	XXXXXXXXXX	XXXXXXXXXXXX	XXXXXXXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX
	XXXXXX	X	XXX	DDMMYYYY	XXXXXXXXXX	XXXXXXXXXXXX	XXXXXXXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX
	XXXXXX	X	XXX	DDMMYYYY	XXXXXXXXXX	XXXXXXXXXXXX	XXXXXXXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX
	XXXXXX	X	XXX	DDMMYYYY	XXXXXXXXXX	XXXXXXXXXXXX	XXXXXXXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX
	XXXXXX	X	XXX	DDMMYYYY	XXXXXXXXXX	XXXXXXXXXXXX	XXXXXXXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX

Note: Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Site XXX = XXXXXXXXXXXXXXXXXXXX

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.4.2.1 Physical Examination (I of II)

Subject Number	Visit			Study Group	Product	Was PE Done?	Reason for Not Done	System1	System2	System3	System4	System5
	Name	Date	Day									
XXXXXX	Screening	DDMMYYYY		X		XXX		XXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX
	XXXXXXX	DDMMYYYY	-X		X	XXX		XXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX
	End of Study	DDMMYYYY	XX		X	XXX		XXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX

Note: See Appendix 16.2.4.2.3 for physical examination abnormality descriptions.

Test 1 Group = e-Vapor Product XLCE

Test 2 Group = e-Vapor Product XLME

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.4.2.2 Physical Examination (II of II)

Subject Number	Visit			Study Group	Product	System6	System7	System8	System9	System10	etc.
	Name	Date	Day								
XXXXXX	Screening	DDMMYYYY		X		XXXXXX	XXXXXX	XXXXXX	XXXXXX	XXXXXX	XXXXXX
	XXXXXXXX	DDMMYYYY	-X		X	XXXXXX	XXXXXX	XXXXXX	XXXXXX	XXXXXX	XXXXXX
	End of Study	DDMMYYYY	XX		X	XXXXXX	XXXXXX	XXXXXX	XXXXXX	XXXXXX	XXXXXX

Note: See Appendix 16.2.4.2.3 for physical examination abnormality descriptions.

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.4.2.3 Physical Examination Descriptions

Subject Number	Visit			Group	Study Product	Result	System	Specify if Abnormal or Not Done	Clinically Significant?
	Name	Date	Day						
XXXXXX	Screening	DDMMYYYY		X		ABNORMAL	Skin	RIGHT CHEST SCAR	NCS
XXXXXX	XXXXXX	DDMMYYYY	XX	X	X	ABNORMAL	Skin	ABDOMINAL SCAR	NCS
XXXXXX	Screening	DDMMYYYY		X		ABNORMAL	Skin	ABDOMINAL SCAR	NCS

Note: NCS = Not clinically significant

Test 1 Group = e-Vapor Product XLCE

Test 2 Group = e-Vapor Product XLMB

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.4.3 Medical History

Subject Number	Any History?	Visit		Description	Date		Ongoing?
		Name	Date		Start	End	
XXXXXX	XXX	Screening	DDMMYYYY	XXXXXX XXXXX	MMYYYY		YES
				XXXXXX XXXXX	MMYYYY	MMYYYY	NO
XXXXXX	XXX	Screening	DDMMYYYY	XXXXXX XXXXX	MMYYYY	MMYYYY	YES

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.4.4.1 Tobacco/Nicotine Product Use History (I of II)

Subject Number	Visit		Study Group	Cigarette Smoked								Other Products?	
	Name	Date		Duration	Unit	Smoke Everyday?	CPD	First Cigarette?	Stop?	Quit?	Photocopied?		
XXXXXX	Screening	DDMMYYYY	X	XX	XXXX	XXX	XX	XXXX	XXXX	XXXX	XXXX	XXXX	XXX
XXXXXX	Screening	DDMMYYYY	X	XX	XXXX	XXX	XX	XXXX	XXXX	XXXX	XXXX	XXXX	XXX
XXXXXX	Screening	DDMMYYYY	X	XX	XXXX	XXX	XX	XXXX	XXXX	XXXX	XXXX	XXXX	XXX
XXXXXX	Screening	DDMMYYYY	X	XX	XXXX	XXX	XX	XXXX	XXXX	XXXX	XXXX	XXXX	XXX
XXXXXX	Screening	DDMMYYYY	X	XX	XXXX	XXX	XX	XXXX	XXXX	XXXX	XXXX	XXXX	XXX

Note: Test 1 Group = e-Vapor Product XLCE  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Duration = How long have you smoked cigarettes on a CONSISTENT BASIS?  
 Smoke Everyday = During the past 12 months did you smoke cigarettes every day, some days, rarely, or not at all?  
 CPD = During the past 12 months, how many cigarettes did you smoke per day, on average?  
 First Cigarette? = How soon after you wake up do you smoke your first cigarette?  
 Stop? = During the PAST 12 MONTHS, have you stopped smoking for more than one day BECAUSE YOU WERE TRYING TO QUIT SMOKING?  
 Quit? = Are you planning to quit smoking cigarettes in the next 30 days?  
 Photocopied? = Was Cigarette Pack Photocopied?  
 Other Products? = Have you used a nicotine patch, gum, inhaler, nasal spray or lozenge in the past 30 days?

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.4.4.2 Tobacco/Nicotine Product Use History (II of II)

Subject Number	Visit		Study Group	Tobacco Product	EVER Used Even Once?	Used in the Past 30 days?
	Name	Date				
XXXXXX	Screening	DDMMYYYY	X	XXXXXXXXXXXXXX	XXX	XX
				XXXXXXXXXXXXXX	XXX	XX
				XXXXXXXXXXXXXX	XXX	XX

Note: Test 1 Group = e-Vapor Product XLCE  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.1 Inclusion / Exclusion Criteria Not Met

Subject Number	Visit		Study Group	Met All Eligibility Criteria?	Inclusion/ Exclusion Category	Criterion	
	Name	Date				Identifier	Criterion
X	Screening	DDMMYYYY	X	Yes			
X	Screening	DDMMYYYY	X	No	XX	XXXX	XXXXXXXXXXXXXXXXXXXX

Note: Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.2.1 Test e-Vapor Product Trial

Subject Number	Visit	Study Group	e-Vapor Episode	Product Code	Dispensed Date	Start Time	Stop Time
XXXXXX	XXXXX	X	X	XXXXXXX	DDMMYY	HH:MM	HH:MM

Note: Test 1 Group = e-Vapor Product XLCE  
Test 2 Group = e-Vapor Product XLME  
Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.2.2 Test e-Vapor Product Assessment Questionnaire

Subject Number	Visit	Study Group	Questionnaire Completed?	Date	Replace All?*
XXXXXX	XXXXX	X	XXX	DDMMYY	XXX

Note: Test 1 Group = e-Vapor Product XLCB  
Test 2 Group = e-Vapor Product XLMB  
Control Group = Continue smoking lit-end conventional cigarette

\*Replace All? = Now that you have tried the e-vapor products, how likely are you to be willing and able to use this product to replace all of your conventional cigarettes for 3 months during the study?

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.2.3 Confirm Regular Cigarette Brand

Subject Number	Visit	Study Group	Has the Subject's Regular Brand of Cigarettes (Control group) Changed?	If Changed, Was New Cigarette Pack Photocopied?
XXXXXX	XXXXX	X	XXX	XXX

Note: Test 1 Group = e-Vapor Product XLCB  
Test 2 Group = e-Vapor Product XLMB  
Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.2.4 Test e-Vapor Product Accountability

Subject Number	Visit	Study Group	Study Product	Flavor Code	Dispensed		Returned		Number of Batteries		Number of Cartridges		
					Date	Time	Date	Time	Dispensed	Returned	Dispensed	Returned Used	Returned Unused
XXXXXX	XXXXX	X	X	XXX	DDMMYYYY	HH:MM	DDMMYYYY	HH:MM	XX	XX	XX	X	X

Note: Test 1 Group = e-Vapor Product XLCE  
 Test 2 Group = e-Vapor Product XLME  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

**Programmer Note: Subjects may have multiple dispensing.**

Appendix 16.2.5.3 Urine Collection for BOEs and BOPHS

Subject Number	Visit			Study Group	Study Product	Was Collection Performed?	Collection		Urine Volume (mL)	Ice Pack Status
	Name	Date	Day				Date	Time		
XXXXXX	XXXXX	DDMMYYYY	XX	X	X	XXX	DDMMYYYY	HH:MM	XXXX	XXX

Note: Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.4 Blood Sampling

Subject Number	Visit			Study Group	Blood for BOPH			Blood for COHb			Blood for BioBanking		
	Name	Date	Day		Collected?	Date	Time	Collected?	Date	Time	Collected?	Date	Time
XXXXXX	XXXXX	DDMMYYYY	X	X	XXX	DDMMYYYY	HH:MM	XXX	DDMMYYYY	HH:MM	XXX	DDMMYYYY	HH:MM

Note: Test 1 Group = e-Vapor Product XLCE  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.5 Exhaled CO Measurement

Subject Number	Visit			Study Group	Exhaled CO Measurement			Was Exhaled CO Result Greater Than 5 Parts Per Million (ppm)?
	Name	Date	Day		Performed?	Date	Result (ppm)	
XXXXXX	XXXXX	DDMMYYYY	X	X	XXX	DDMMYYYY	XX	XXX

Note: Test 1 Group = e-Vapor Product XLCE  
 Test 2 Group = e-Vapor Product XLME  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.6 Prior and Concomitant Medications

Subject Number	Study Group	Study Product	Any Medication/ Med? Therapy	Prior to Study?	Dosage	Route	Start Date	Start Time	Stop Date	Stop Time	Frequency	Indication	Continuing?	AE#
XXXXXX	X	X	XXX ACETAMINOPHEN	XX	620 mg	ORAL	DDMMYYYY	HH:MM	DDMMYYYY	HH:MM	Once	Toothache	No	XXX

Note: Test 1 Group = e-Vapor Product XLCE  
 Test 2 Group = e-Vapor Product XLME  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.1 Whole Blood WBC Counts

Subject Number	Study Group	Study Visit	Concentration (x 10 <sup>3</sup> /μL)	Absolute Change From Baseline (x 10 <sup>3</sup> /μL)	% Change From Baseline
XXXXX	XXXXXX	3	XXX	XXX	NA
		5	XXX	XXX	XXX
		7	XXX	XXX	XXX

Note: Baseline = Visit 3

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.2 Serum HDL-C

Subject Number	Study Group	Study Visit	Concentration (mg/dL)	Absolute Change From Baseline (mg/dL)	% Change From Baseline
XXXXX	XXXXXX	3	XXX	XXX	NA
		5	XXX	XXX	XXX
		7	XXX	XXX	XXX

Note: Baseline = Visit 3

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.3 Urine 8-epi-prostaglandin F2 $\alpha$

Subject Number	Study Group	Study Visit	Creatinine (mg/dL)	epi-prostaglandin F2 $\alpha$ (pg/mL)	epi-prostaglandin F2 $\alpha$ (ng/g Cr)	Absolute Change From Baseline (ng/g Cr)	% Change From Baseline
XXXXXX	XXXXXX	3	XXX	XXX	XXX	NA	NA
		5	XXX	XXX	XXX	XXX	XXX
		7	XXX	XXX	XXX	XXX	XXX

Note: Baseline = Visit 3

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.5 Urine 11-dehydrothromboxane B2

Subject Number	Study Group	Study Visit	Creatinine (mg/dL)	11-dehydrothromboxane B2 (pg/mL)	11-dehydrothromboxane B2 (ng/g Cr)	Absolute Change From Baseline (ng/g Cr)	% Change From Baseline
XXXXX	XXXXXX	3	XXX	XXX	XXX	NA	NA
		5	XXX	XXX	XXX	XXXX	XXX
		7	XXX	XXX	XXX	XXXX	XXX

Note: Baseline = Visit 3

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.5 Whole Blood sICAM-1

Subject Number	Study Group	Study Visit	Concentration (ng/mL)	Absolute Change From Baseline (ng/mL)	% Change From Baseline
XXXXX	XXXXXX	3	XXX	XXX	NA
		5	XXX	XXX	XXX
		7	XXX	XXX	XXX

Note: Baseline = Visit 3

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.6 Urine Total NNAL

Subject Number	Study Group	Study Visit	Creatinine (mg/dL)	---- Total NNAL ---- (pg/mL)	---- (ng/g Cr)	Absolute Change From Baseline (ng/g Cr)	% Change From Baseline
XXXXX	XXXXXX	3	XXX	XXX	XXX	NA	NA
		5	XXX	XXX	XXX	XXXX	XXX
		7	XXX	XXX	XXX	XXXX	XXX

Note: Baseline = Visit 3

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.7 Whole Blood COHb

Subject Number	Study Group	Study Visit	Concentration (% Saturation)	Absolute Change From Baseline (% Saturation)	% Change From Baseline
XXXXX	XXXXXX	3	XXX	XXX	NA
		5	XXX	XXX	XXX
		7	XXX	XXX	XXX

Note: Baseline = Visit 3

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.8.1 Product Use Per Day

Subject Number	Study Group	Study Day	Date	Number of New Test Products Started	Number of Cigarettes Smoked
XXXXXX	XXXXX	X	DDMMYYYY	XX	XX

Note: Test 1 Group = e-Vapor Product XLCB  
Test 2 Group = e-Vapor Product XLMB  
Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.8.2 Average Product Use Per Day

Subject Number	Study Group	Study Week	Average Number of Test Products Started	Average Number of Cigarettes Smoked
XXXXXX	XXXXX	X	XX	XX

Note: Test 1 Group = e-Vapor Product XLCB  
Test 2 Group = e-Vapor Product XLMB  
Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.8.3 Average Test Product Started/Cigarette Smoked Per Day Change from Baseline

Subject Number	Study Group	Average Number of Test Products Started		Average Number of Cigarettes Smoked	
		Absolute Change from Week 1 to Week 6	Absolute Change from Week 1 to Week 12	% Change from Week 1 to Week 6	% Change from Week 1 to Week 12
XXXXXX	XXXXX	XX	XX	XX	XX

Note: Test 1 Group = e-Vapor Product XLCE  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.9 Urine NNN

Subject Number	Study Group	Study Visit	Creatinine (mg/dL)	----- NNN (pg/mL)	----- (ng/g Cr)	Absolute Change From Baseline (ng/g Cr)	% Change From Baseline
XXXXX	XXXXXX	3	XXX	XXX	XXX	NA	NA
		5	XXX	XXX	XXX	XXXX	XXX
		7	XXX	XXX	XXX	XXXX	XXX

Note: Baseline = Visit 3

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.10.1 Spirometry

Subject Number	Study Group	Study Visit	Parm1	Parm2	Parm3	Parm4	Parm5	Parm6	Parm7	Parm8	Parm9
XXXXXX	XXXXXX	2	XX								
		7	XX								

Note: Test 1 Group = e-Vapor Product XLCE  
 Test 2 Group = e-Vapor Product XLME  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Parameters are:  
 FEV1 (L)  
 Predicted FEV1 (L)  
 % of Predicted FEV1  
 FVC (L)  
 Predicted FVC  
 % of Predicted FVC  
 FEV1/FVC  
 % of Predicted FEV1/FVC  
 FEF 25-75%

Appendix 16.2.6.10.2 Spirometry Absolute Change from Baseline to Week 12 (Visit 7)

Subject Number	Study Group	Percent of Predicted FEV1	Percent of Predicted FVC	Percent of Predicted FEV1/FVC
XXXXXX	XXXXXX	XX XX	XX XX	XX XX

Note: Baseline = Visit 2

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.11.1 Urine Nicotine and Metabolites Concentrations

Subject Number	Study Group	Study Visit	Nicotine (ng/mL)	Nicotine Glucuronide (ng/mL)	Cotinine (ng/mL)	Cotinine Glucuronide (ng/mL)	Trans-3-hydroxy Cotinine (ng/mL)	Trans-3-hydroxy Cotinine Glucuronide (ng/mL)
XXXXXX	XXXXXX	3	XXX	XXX	XXX	XXXX	XXX	XXX
		5	XXX	XXX	XXX	XXXX	XXX	XXX
		7	XXX	XXX	XXX	XXXX	XXX	XXX

Note: Baseline = Visit 3

Test 1 Group = e-Vapor Product XLCE

Test 2 Group = e-Vapor Product XLMB

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.11.2 Urine Nicotine Equivalents

Subject Number	Study Group	Study Visit	Creatinine (mg/dL)	Nicotine (µg/mL)	Nicotine Equivalents (mg/g Cr)	Absolute Change From Baseline (mg/g Cr)	% Change From Baseline
XXXXX	XXXXXX	3	XXX	XXX	XXX	NA	NA
		5	XXX	XXX	XXX	XXXX	XXX
		7	XXX	XXX	XXX	XXXX	XXX

Note: Baseline = Visit 3

Test 1 Group = e-Vapor Product XLCE

Test 2 Group = e-Vapor Product XLME

Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

**Programmer Note: See section 6.1.1.3.1 for calculation of nicotine equivalents.**

Altria Client Services LLC  
 Study No. ALCS-RA-16-06-EV  
 Celerion Project CA20130

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Appendix 16.2.6.12.3.1 Modified Cigarette Evaluation Questionnaire

Subject Number	Study Group	Study Visit	Date	Time	mCEQ												
					1	2	3	4	5	6	7	8	9	10	11	12	
XXXXX	XXXXXX	X	DDMMYYYY	HH:MM:SS	X	X	X	X	X	X	X	X	X	X	X	X	X

- Note: 1. Was using the product satisfying? 2. Did the product taste good?  
 3. Did you enjoy the sensations in your throat and chest? 4. Did using the product calm you down?  
 5. Did using the product make you feel more awake? 6. Did using the product make you feel less irritable?  
 7. Did using the product help you concentrate? 8. Did using the product reduce your hunger for food?  
 9. Did using the product make you dizzy? 10. Did using the product make you nauseous?  
 11. Did using the product immediately relieve your craving for a cigarette? 12. Did you enjoy using the product?

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/ECR/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.12.3.2 Factor Score to Modified Cigarette Evaluation Questionnaire

Subject Number	Study Visit	Date	Time	Smoking Satisfaction	Psychological Reward	Aversion	Enjoyment of Sensation	Craving Reduction
X	X	XXXXXXXXXX	DDMMYYYY	HH:MM:SS	X	X	X	X
		XXXXXXXXXX	DDMMYYYY	HH:MM:SS	X	X	X	X
		XXXXXXXXXX	DDMMYYYY	HH:MM:SS	X	X	X	X
		XXXXXXXXXX	DDMMYYYY	HH:MM:SS	X	X	X	X

Note: Smoking satisfaction: average of 1,2,12;  
 Psychological reward: average of 4 to 8;  
 Aversion: average of 9,10;  
 Enjoyment of sensation: 3;  
 Craving Reduction: 11

Test 1 Group = e-Vapor Product XLCE  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/ECR/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

**Programmer Note: Add footnotes for descriptions of each question.**

Appendix 16.2.6.12.4.1 Cough Questionnaire

- I. Did you have a cough in the past 30 days? (1 = Yes, 2 = No)
- II. How long have you had the cough?
- III. When does the cough occur? (1 = Middle of the night, 2 = Daytime, 3 = Anytime)
- IV. Do you have a cough that comes mainly from your chest and NOT from your throat (1 = Yes, 2 = No)
- V. Do you cough up phlegm? (1 = never, 2 = seldom, 3 = Sometimes, 4 = Often, 5 = Always)
- VI. Do you cough more than the average person? (1 = Yes, 2 = No)
- VII. Have you taken medications for your cough? (1 = Yes, 2 = No)
- VIII. Have you sought the help of a health care provider to treat your cough? (1 = Yes, 2 = No)
- IX. In the last 24-hours, has your cough disturbed your sleep? (1 = All of the time, 2 = Most of the time, 3 = A good bit of the time, 4 = Some of the time, 5 = A little of the time, 6 = Hardly any of the time, 7 = None of the time)
- X. In the last 24-hours, how many times have you had coughing bouts? (1 = All the time, 2 = Most times during the day, 3 = Several times during the day, 4 = Some times during the day, 5 = Occasionally through the day, 6 = Rarely, 7 = none)

Program: /CAXXXXX/ECR/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.12.4.2 Cough Questionnaire Response

Subject Number	Study Group	Study Visit	Date	Time	Cough Questionnaire*										
					I	II	III	IV	V	VI	VII	VIII	IX	X	
XXXXX	XXXXXX	X	DDMMYYYY	HH:MM:SS	X	X	XXXXX	X	X	X	X	X	X	X	X

Note: \* Refer to Appendix 16.2.6.12.4.1 for the questions in the Cough Questionnaire.

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/ECR/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.12.5.1 Reasons of Use/Not-Use Test Product Questionnaire (I of II)

Subject Number	Study Group	Study Visit	Date	Time	Likelihood of Use	
					E-cigarette question	Test Product Question
XXXXX	XXXXXX	X	DDMMYYYY	HH:MM:SS	X	X

Note: E-cigarette question = How likely are you to use e-cigarettes exclusively in the next 30 days?  
 Test Product question = How likely would you be to use the test product exclusively in the next 30 days?

1 = Strongly Likely, 2 = Quite Likely, 3 = Somewhat Likely Neutral/Neigher, 4 = Strongly Likely,  
 5 = Quite Unlikely, 6 = Somewhat Unlikely

Test 1 Group = e-Vapor Product XLCE  
 Test 2 Group = e-Vapor Product XLME

Program: /CAXXXXX/ECR/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM



Appendix 16.2.6.12.6 End of Study Questionnaire

Subject Number	Study Group	Study Visit	Date	Time	Reasons of Use/Not-Use		
					1	2	3
XXXXX	XXXXXX	X	DDMMYYYY	HH:MM:SS	XXX	XXX X X	XXXXXXXXXX

- Note:
1. When you collected your 1st void of the day urine collections, were you able to always collect the first void of the day at least 4 hours after the prior void?
  2. Have you smoked cigarettes since you were instructed to completely replace your cigarettes with the test e-Vapor product?
  3. Did you use the test e-Vapor product..

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/ECR/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.7.1 Adverse Events (I of II)

Subject Number	Study Group	Study Product	UE?^	AE Number	Adverse Event*	Preferred Term	Time from Last Product Use	Onset		Resolved		Duration
							(DD:HH:MM)	Date	Time	Date	Time	(DD:HH:MM)
XXXXXX	X	X	XXX	XX	XXXXXXXXXXXXXXXX	XXXXXXXXXX XXXXXXXX	XX:XX:XX	DDMMYYYY	HH:MM	DDMMYYYY	HH:MM	XX:XX:XX
XXXXXX	X	X	XXX	XX	XXXXXXXXXXXXXXXX	XXXXXXXXXX XXXXXXXX	XX:XX:XX	DDMMYYYY	HH:MM	DDMMYYYY	HH:MM	XX:XX:XX
XXXXXX	X	X	XXX	XX	XXXXXXXXXXXXXXXX	XXXXXXXXXX XXXXXXXX	XX:XX:XX	DDMMYYYY	HH:MM	DDMMYYYY	HH:MM	XX:XX:XX
XXXXXX	X	X	XXX	XX	XXXXXXXXXXXXXXXX	XXXXXXXXXX XXXXXXXX	XX:XX:XX	DDMMYYYY	HH:MM	DDMMYYYY	HH:MM	XX:XX:XX

Note: ^ UE = study product use-emergent  
 \* = Adverse events are classified according to the MedDRA Version 19.0.

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.7.2 Adverse Events (II of II)

Subject Number	Study Group	Study Product	AE Number	Adverse Event	Onset		Frequency	Severity	Serious	Outcome	Relationship to Study Product	Action
					Date	Time						
XXXXXX	X	X	XX	XXXXXXXXXX	DDMMYYYY	HH:MM	XXXXXXXX	XXXXX	XXXX	XXXXXX	XXXXXXXXXX	XXXXX
XXXXXX	X	X	XX	XXXXXXXXXX	DDMMYYYY	HH:MM	XXXXXXXX	XXXXX	XXXX	XXXXXX	XXXXXXXXXX	XXXXX
XXXXXX	X	X	XX	XXXXXXXXXX	DDMMYYYY	HH:MM	XXXXXXXX	XXXXX	XXXX	XXXXXX	XXXXXXXXXX	XXXXX
XXXXXX	X	X	XX	XXXXXXXXXX	DDMMYYYY	HH:MM	XXXXXXXX	XXXXX	XXXX	XXXXXX	XXXXXXXXXX	XXXXX

Note: Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.7.3 Adverse Event Preferred Term Classification

Subject Number	Study Group	Study Product	AE Number	Adverse Event	Preferred Term	Body System	Onset	
							Date	Time
XXXXXX	X	X	XX	XXXXXXXX XXXX XXXX XXXXXX	XXXXXXXXXXXX XXXXXXXX	XXXXXXXXXXXXXXXXXXXXXXXXXXXX	DDMMYYYY	HH:MM
XXXXXX	X	X	XX	XXXXXXXX XXXX XXXX XXXXXX	XXXXXXXXXXXX XXXXXXXX	XXXXXXXXXXXXXXXXXXXXXXXXXXXX	DDMMYYYY	HH:MM
XXXXXX	X	X	XX	XXXXXXXX XXXX XXXX XXXXXX	XXXXXXXXXXXX XXXXXXXX	XXXXXXXXXXXXXXXXXXXXXXXXXXXX	DDMMYYYY	HH:MM
XXXXXX	X	X	XX	XXXXXXXX XXXX XXXX XXXXXX	XXXXXXXXXXXX XXXXXXXX	XXXXXXXXXXXXXXXXXXXXXXXXXXXX	DDMMYYYY	HH:MM

Note: \* = Adverse events are classified according to the MedDRA Version 19.0.

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendices 16.2.8.2 to 16.2.8.3 will have the following format.

Appendix 16.2.8.1 Clinical Laboratory Report - Serum Chemistry

Subject Number	Age/ Gender	Study Group	Visit			Parameter1	Parameter2	Parameter3	Parameter4	Parameter5	Parameter6
			Name	Date	Date						
XXXXXX	XX/X	X	Screening	DDMMYYYY	DDMMYYYY	XX HN	XX	XX	XX	XX HN	XX
			XXXXXX	DDMMYYYY	DDMMYYYY	XX HN	XX	XX	XX	XX HN	XX
			XXXXXX	DDMMYYYY	DDMMYYYY	XX HN	XX	XX	XX	XX HN	XX

Note: H = Above Reference Range, L = Below Reference Range  
 PI Interpretation: N = Not Clinically Significant  
 See Appendix 16.1.10.1 for lab units and reference ranges.

Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

**Programmer Note: Replace Parameter1, 2 etc. with actual lab tests in the study.**

Appendix 16.2.8.4 Alcohol Breath Tests

Subject Number	Study Group	Visit		Was an Alcohol Breath Test Performed?	Test		Result
		Name	Date		Date	Time	
XXXXXX	X	Screening	DDMMYYYY	XXX	DDMMYYYY	HH:MM	XXXXXX
		Check-in	DDMMYYYY	XXX	DDMMYYYY	HH:MM	XXXXXX

Note: Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.5 Urine Drug Screens

Subject Number	Study Group	Visit		Was the Urine Sample Collected?	Date of Collection	Test Name	Result
		Name	Date				
XXXXXX	X	Screening	DDMMYYYY	XXX	DDMMYYYY	XXXXXXXXXXXXXX XXXXXXXXXXXXXX	XXXXXX XXXXXX

Note: Test 1 Group = e-Vapor Product XLCE  
 Test 2 Group = e-Vapor Product XLME  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.6 Pregnancy Tests

Subject Number	Study Group	Visit		Was the Pregnancy Test Done?	Reason for Not Done	Collection		Category	Test Name	Test Result	Test Code
		Name	Date			Date	Time				
XXXXXX	X	Screening XXXXXXXXXX	DDMMYYYY DDMMYYYY	XXX XXX		DDMMYYYY DDMMYYYY	HH:MM HH:MM	XXXXXX XXXXXX	XXXX XXXX	XXX XXX	XXXX XXXX

Note: Test 1 Group = e-Vapor Product XLCE  
 Test 2 Group = e-Vapor Product XLME  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.7 Urine Cotinine Screens

Subject Number	Study Group	Visit		Was the Urine Cotinine Sample Collected?	Date of Collection	Is Result Greater Than or Equal to 500 ng/mL?
		Name	Date			
XXXXXX	X	Screening	DDMMYYYY	XXX	DDMMYYYY	XXX

Note: Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.8 Serology Sample Collection

Subject Number	Study Group	Visit		Was the Sample Collected?	Collection	
		Name	Date		Date	Time
XXXXXX	X	Screening	DDMMYYYY	XXX	DDMMYYYY	HH:MM

Note: Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.9 Clinical Laboratory Report - Comments

Subject Number	Study Group	Visit		Date	Department	Test	Result	Unit	Comment
		Name	Date						
XXXXXX	X	Screening	DDMMYYYY	DDMMYYYY	Other Tests	XXXXXXXX	XXX	mg/dL	Not significant in the context of this study.

Note: Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.10 Vital Signs

Subject Number	Visit		Study Group	Study Product	Date	Time	Not Done?	Blood Pressure (mmHg)		Pulse (bpm)	Respiration (rpm)	Temperature (°F)
	Name	Day						Systolic/Diastolic				
XXXXXX	Screening		X		DDMMYYYY	HH:MM		XXX/ XX		XX	XX	XX.X
	XXXXXX			1	DDMMYYYY	HH:MM		XXX/ XX NCS		XX	XX	XX.X
	XXXXXX	X			DDMMYYYY	HH:MM		XXX/ XX		XX CS	XX	XX.X
	XXXX	X			DDMMYYYY	HH:MM		XXX/ XX		XX	XX	XX.X

Note: NCS = Not clinically significant, CS = Clinically significant

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Control Group = Continue smoking lit-end conventional cigarette

See Appendix 16.1.10.2 for vital sign reference ranges.

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.11 12-Lead Electrocardiogram

Subject Number	Visit	Study Group	Date	Time	Result	Heart Rate (bpm)	PR (ms)	QRS (ms)	QT (ms)	QTcB* (ms)	If Abnormal	
											Specify	Action Taken
XXXXXX	Screening	X	DDMMYYYY	HH:MM	Normal	XX	XXX	XX	XXX	XXX		
	XXXXXX		DDMMYYYY	HH:MM	Normal	XX	XXX	XX	XXX	XXX		
	XXXXXX		DDMMYYYY	HH:MM	ANCS	XX	XXX	XX	XXX	XXX	XXXX	

Note: QTcB\* = QTc corrected using Bazett's correction, ANCS = Abnormal, Not Clinically Significant

Test 1 Group = e-Vapor Product XLCB

Test 2 Group = e-Vapor Product XLMB

Control Group = Continue smoking lit-end conventional cigarette

See Appendix 16.1.10.3 for ECG reference ranges.

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

**Programmer Note: Please add reference range footnote based on Appendix 16.1.10.3.**

Appendix 16.2.8.12.1 Pulmonary Function Test (Spirometry) (I of II)

Subject Number	Visit		Study Group	Test Performed?	Assessment		FVC (L)			FEV1 (L)		
	Visit	Date			Date	Time	Actual	Predicted	%Predicted	Actual	Predicted	%Predicted
XXXXXX	Screening	DDMMYYYY	X	XXX	DDMMYYYY	HH:MM	XX	XX	XX	XX	XX	XX
	XXXX	DDMMYYYY		XXX	DDMMYYYY	HH:MM	XX	XX	XX	XX	XX	XX

Note: Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.12.2 Pulmonary Function Test (Spirometry) (II of II) Page 1 of X

Subject Number	Visit		Study Group	Assessment		FEV1/FVC (L)			Auto Calculated	
	Visit	Date		Date	Time	Actual	Predicted	%Predicted	FEV1/FVC	Percent (%)
XXXXXX	Screening	DDMMYYYY	X	DDMMYYYY	HH:MM	XX	XX	XX		XX
	XXXX	DDMMYYYY		DDMMYYYY	HH:MM	XX	XX	XX		XX

Note: Test 1 Group = e-Vapor Product XLCB  
 Test 2 Group = e-Vapor Product XLMB  
 Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.13 Smoking Cessation Information

Subject Number	Visit	Was Smoking Cessation Information Offered?	Date Information Offered
XXXXXX	Screening End of Study	XXX XXX	DDMMYYYY DDMMYYYY

Program: /CAXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.14 Reminder Phone Call

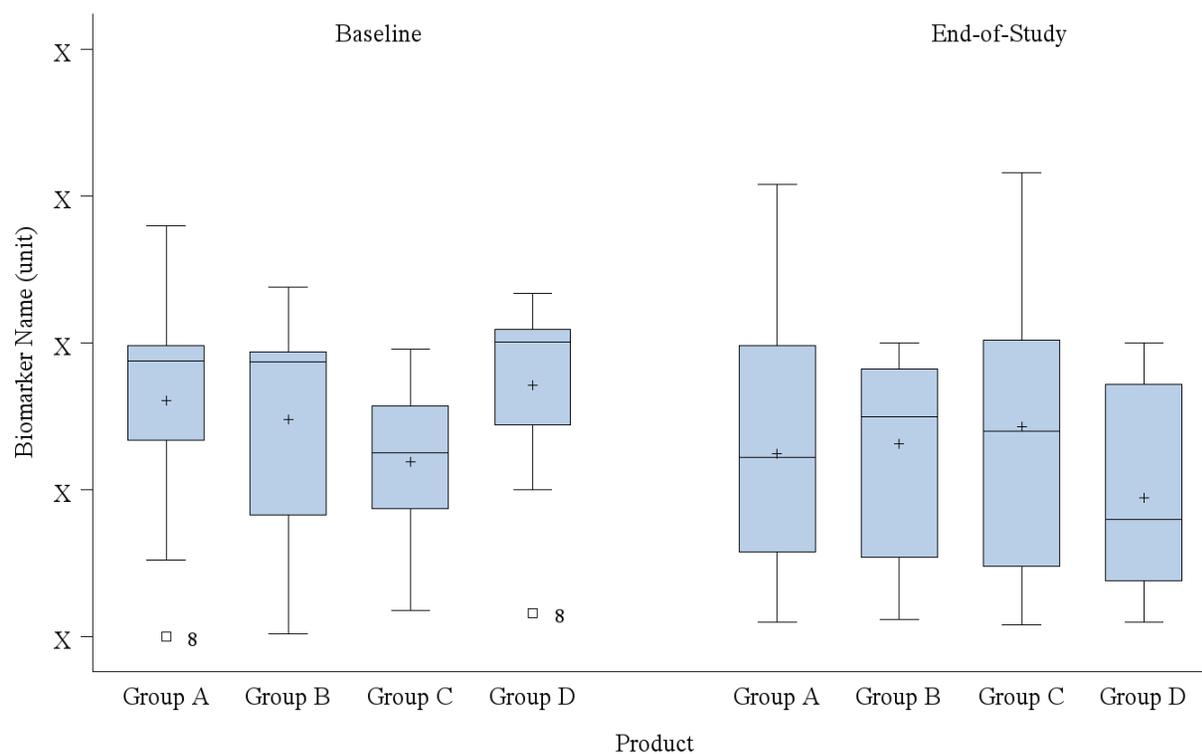
Subject Number	Visit ----- Visit	Was a Reminder Call Performed Within 24-48 Hours of This Visit?	Date
XXXXXX	Screening	XXX	DDMMYYYY
	End of Study	XXX	DDMMYYYY

Program: /CAXXXXX/sas\_prg/stsas/lis\_PROGRAMNAME.sas DDMMYYYY HH:MM

### **13. FIGURE SHELLS**

Box plots will be presented as in the figure below, with the headings of Baseline, Visit 5 or Visit 7:

Figure 14.2.5.1.1  
 Box Plot of Whole Blood WBC Count ( $\times 10^3/\mu\text{L}$ ) at Baseline and Visit 7 by Study Group (mITT Population)



The upper and lower whiskers of the boxplot represent, respectively, the largest and smallest observed values within  $1.5 \times$  the interquartile range (IQR) from the upper and lower quartiles (Q3 and Q1). Values greater or smaller than the bounds represented by these whiskers are identified as extreme values with the corresponding subject number.

Program: CAXXXXX/XXX/XXX PROGRAMNAME.SAS DDMMYYYY HH:MM