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 24 Weeks

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Statistical Analysis Plan

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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_1	forced expiratory volume in 1 second
HDL-C	high-density lipoprotein cholesterol
ICF	informed consent form
ICH	International Conference on Harmonization
Kg	kilogram(s)
LC-MS	liquid chromatography–mass spectrometry
LLOQ	lower limit of quantitation
LLC	limited liability company
LOCF	Last observation carried forward
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-nitrosonornicotine
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 biomakers[a] from Baseline[b] to Week 24 (EOS) between adult smokers who continue to smoke conventional cigarettes (Control group) ad libitum and adult smokers who have completely[c] switched to ad libitum use of test e-vapor products (Test groups) for 24 weeks.

[a] Seleted biomarkers include:

- White Blood Cell Count (WBC Count)
- High Density Lipoprotein Cholesterol (HDL-C)
- Urinary 8-epi-prostaglandin $F_{2\alpha}$
- Urinary 11-Dehydrothromboxane B_2
- Blood Soluble Intercellular Adhesion Molecule-1 (sICAM-1)
- Urinary 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol and its glucuronides (total NNAL)
- Carboxyhemoglobin (COHb)

[b] Baseline of the 12-week ALCS-RA-16-06-EV study (CA20130), Week 1, will be used.

[c] Subjects who exclusively use e-vapor products and have exhaled carbon monoxide (eCO) measurements ≤ 8 ppm from Week 6 (of the 12-week ALCS-RA-16-06-EV study) through Week 24 (EOS) and urine N-nitrosonornicotine (NNN) levels from

Week 6 (of the 12-week ALCS-RA-16-06-EV study) through Week 24 (EOS) consistent with switching to an e-vapor product.

2.1.2 Secondary Objectives

The secondary objectives are to:

- Assess changes in forced expiratory volume in the first second (FEV_1), forced vital capacity (FVC) and FEV_1/FVC ratios from Screening/Visit 2 of the 12-week ALCS-RA-16-06-EV study (CA20130) to Week 18 and to Week 24 (EOS) between the Test and Control groups.

- Compare changes in selected biomarkers (same as those in the primary objective) from Baseline to Week 18 between Test and Control groups.

- Determine the number of cigarettes smoked (Test and Control groups) from Baseline through Week 24 (EOS).

- Assess changes in the amount of test e-vapor product use (Test groups only) from Baseline through Week 24 (EOS).

- Assess adherence to protocol by comparing changes from Baseline through Week 24 (EOS) within the Test groups for eCO and urinary NNN.

2.1.3 Exploratory Objectives

The exploratory objectives are to:

- Assess changes in biomarkers of potential harm (BOPHs) and biomarkers of exposure (BOEs) (same as in the primary objective) from Baseline through Week 24 (EOS) between the subgroups that used different flavored Test e-vapor products.

- Assess changes in urine nicotine equivalents (NE) from Baseline through Week 24 (EOS) **within** and **between** Test and Control groups.

- Assess changes in the QGEN and TQOLIT questionnaires and the Cough Questionnaire responses from Baseline through Week 24 (EOS) between the Test and Control groups.

- Assess reasons for test product use/not-use at EOS and modified Cigarette Evaluation Questionnaire (mCEQ) questionnaires from Baseline to Week 24 (EOS) 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* Week 1 (Day 1) to Week 24 for each of the following primary biomarkers:

- whole blood WBC Count
- serum HDL-C
- creatinine-adjusted urine 8-epi-prostaglandin $F_{2\alpha}$
- creatinine-adjusted urine 11-Dehydrothromboxane B_2
- serum sICAM1
- creatinine-adjusted urine total NNAL
- blood COHb saturation

*Baseline of the 12-week ALCS-RA-16-06-EV study (CA20130), Week 1, will be used.

Secondary

The secondary outcome variables are:

- Changes in FEV_1, FVC, and FEV_1/FVC ratios from Baseline to Week 18 and to Week 24 (EOS) in the Test and Control groups.
- The absolute change from Baseline to Week 18 for each of the primary biomarkers for each study group.
- The absolute change from Baseline to Week 24 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 ≤ 20 puffs or > 20 puffs) during Week 12 through week 24
- Frequency and percentage of subjects with a reduction, no change, or increase in cigarettes used per day from Baseline to Week 24
- Frequency and percentage of subjects with a reduction, no change, or increase in e-vapor cartridges used per day from Baseline to Week 24
- Creatine-adjusted urine NNN determined at Baseline, Week 18, and Week 24
- eCO determined at Baseline, Week 15, Week 18, Week 21, and Week 24

Exploratory

The exploratory outcome variables are:

- The differences between Baseline and Week 24 for the primary biomarkers in the Test groups.
- The creatinine-adjusted urine nicotine equivalent (NE) determined at Baseline, Week 18, and Week 24
- The absolute change in creatinine-adjusted urine NE from Baseline to Week 18 and from Baseline to Week 24
- Responses (Score) to the QGEN and TQOLIT questionnaires and the Cough Questionnaire recorded at Baseline, Week 18, and Week 24
- Reponses to Reasons for Use and Not-use of Test Product at Week 24 (Test groups only) and mCEQ questionnaires from Baseline to Week 24

Clinical Safety

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

3. STUDY DESIGN

This research study is an extension of the 12-week ALCS-RA-16-06-EV study (CA20130). A total of up to 250 subjects (up to 100 in each of the Test groups and 50 in the Control group) who were compliant with the requirements of the 12 week ALCS-RA-16-06-EV study and continued to satisfy all inclusion/exclusion criteria of that study were planned to be enrolled. The sample size of the extension study is much smaller and the statistical analysis is mostly exploratory in nature.

The study utilized a parallel-group, open-label, controlled design and was conducted at multiple study sites. A total of 150 adult male and female (neither gender should account for more than 60% of the population) smokers (30 to 65 years of age, inclusive, determined at Screening [Visit 1] of the 12-week ALCS-RA-16-06-EV study) who completed the 12-week ALCS-RA-16-06-EV study (CA20130), were compliant with the requirements of the 12-week study, and continued to satisfy all inclusion/exclusion criteria of that study, were invited to enroll into this study and remain in the group into which they were randomized in the 12-week ALCS-RA-16-06-EV study.

- Control Group (n=52): Continue smoking under ad libitum use of subjects' own brand of conventional lit-end cigarettes, without use of any other type of tobacco/nicotine containing product, for the entire additional 12 weeks.

- Test 1 Group (n=50): Continue ad libitum use of test e-vapor products (Product XLCB), without use of any other type of tobacco/nicotine containing product, for the entire additional 12 weeks.

- Test 2 Group (n=48): Continue ad libitum use of test e-vapor products (Product XLMB), without use of any other type of tobacco/nicotine containing product, for the entire additional 12 weeks.

Subjects in the Test groups will be provided a 3-week supply of the test product to which they were randomized in the 12-week ALCS-RA-16-06-EV study and will be given a return date for Visit 2 (Week 15).

At Visits 2 and 4 (Week 15 and Week 21, respectively), subjects will return to the study site with all of their used and unused cartridges, which will be counted. Vital signs will be taken and medical history and symptom-driven physical examination will be performed. Compliance with daily tobacco use reporting will be discussed and eCO will be measured; use of non-test product and/or eCO measurements > 5 ppm will prompt counceling by clinic staff on the tobacco and nicotine restrictions and, for measurements > 8 ppm, potential for removal from the study. Test Product for the following 3 weeks and a urine collection container will be dispensed. Subjects will receive reminder calls regarding their following clinic visits and need to collect the first void urine prior to returning to the study site (Visits 3 and 5).

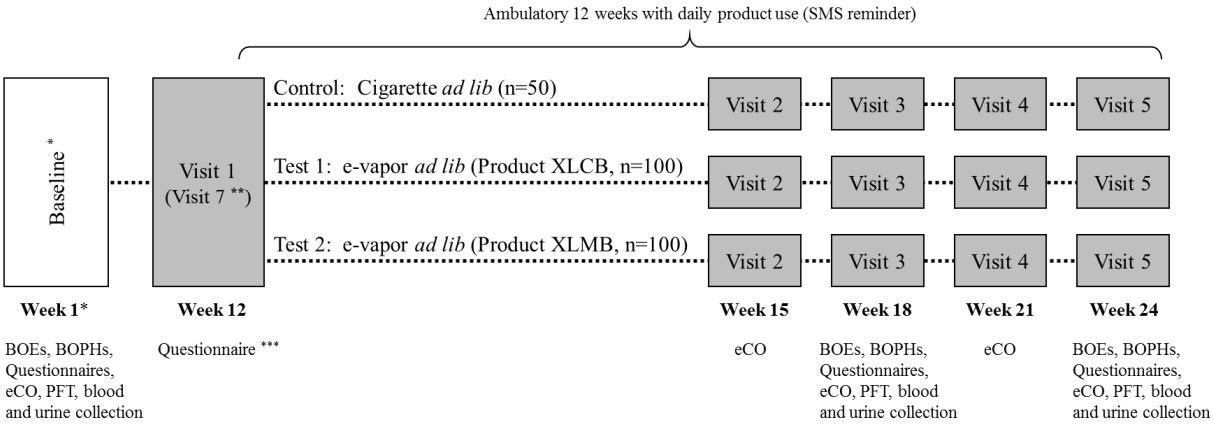
At Visit 3 (Week 18), procedures will be as described for Visits 2 and 4 (Weeks 15 and 21, respectively), with the addition of spirometry, questionnaires, and collection of urine and blood for Week 18 biomarkers and future biomarker assessments. A urine collection container will not be dispensed at Visit 3

At Visit 5 (Week 24), subjects will return to the study site with all of their used and unused cartridges (which will be counted), blood and urine samples will be collected for Week 24 biomarker assessments, questionnaires will be completed, and subjects will undergo EOS procedures and be discharged from the study.

All subjects will report their cigarettes per day (Control and Test groups) and Test product use (Test groups only) daily using a SMS, i.e., text message, based system (Med-Quest). The self-reported cigarettes per day (CPD), use of other tobacco products, and measurements of eCO and NNN taken during the in-clinic visits will be used to monitor subject compliance with exclusive use of the Test products. All subjects will return to the study sites for four visits at Weeks 15, 18, 21, and 24.

Throughout this SAP, Screening refers to Visit 1 and/or Visit 2 of the 12-week ALCS-RA-16-06-EV study (CA20130), and study weeks are relative to Week 1 (Visit 3) of the 12-week ALCS-RA-16-06-EV study. Baseline values reported on Day 1 (Week 1) or at Screening (for spirometry only) of the 12-week ALCS-RA-16-06-EV study (CA20130) will be used, except for product use. Baselines for product use will be defined in the product use sections.

The overall design of the study is shown below.



BOE: Biomarker of Exposure
BOPH: Biomarker of Potential Harm
eCO: Exhaled Carbon Monoxide compliance assessment
SMS: Short Message System
PFT: Pulmonary Function Test

* Baseline values reported on Day 1 (Week 1) or at Screening (for PFT only) of the 12-week ALCS-RA-16-06-EV study (CA20130) will be used.
** Visit 1 is the same as Visit 7 of the 12-week ALCS-RA-16-06-EV study (CA20130).
*** Changes in Your Health and Well-Being Questionnaire.

Test Products dispensing will occur at Visits 1, 2, 3, and 4 for the Test groups.

The expected duration of this study, from first subject, first visit (Visit 1, Week 12), through last subject, last visit will be approximately 12 weeks. The expected study duration from Screening (of the 12-week ALCS-RA-16-06-EV study) to End of Study for each individual subject is approximately 28 weeks.

Clinical safety evaluations will be performed to ensure that subjects meet the requirements of the study and to monitor subject safety. Visit 1 (Week 12, which is the same as Visit 7 of the 12-week ALCS-RA-16-06-EV study) safety evaluations will include the following: physical examination (symptom-driven); vital signs; body weight, BMI; 12-lead ECGs; clinical chemistry, hematology, and urinalysis; and pregnancy testing (all females). At Visits 2, 3, and 4, safety evaluations will include vital signs and physical examinations (symptom-driven). Visit 5/EOS (or early termination) safety evaluations will include a physical examination (symptom-driven); vital signs; body weight; BMI; 12-lead ECG; clinical chemistry, hematology, and urinalysis; and pregnancy testing (all females).

AEs will be monitored and recorded from the time of the test e-vapor product trial at Screening, Visit 2 of the 12-week ALCS-RA-16-06-EV study until Week 24/EOS (or upon early termination). Events occurring after the initial informed consent signing at Screening, Visit 1 of the 12-week ALCS-RA-16-06-EV study and before the test e-vapor product trial will be recorded and considered baseline signs and symptoms.

Any concomitant medications taken from 30 days prior to Screening, Visit 1 of the 12-week ALCS-RA-16-06-EV study through Week 24/EOS (or upon Early Termination) will also be recorded.

4. ANALYSIS POPULATIONS

The Clinical Safety Population (CSP):

The CSP will consist of all subjects who are enrolled into this study and record at least one use of study products (i.e., conventional cigarettes or test e-vapor products) after Week 12.

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

The mITT population includes those subjects in the CSP population for which there is a baseline for a primary biomarker and at least one post-baseline biomarker measure for the primary biomarker after Week 12.

The Per-Protocol (PP) Population:

The PP population will be a subset of the mITT Population, which is comprised of subjects who completed the study without any major protocol violations, which are defined as:

- Control group: subjects who quit cigarette smoking (either by self report or NNN criteria of ≥80% reduction in NNN from baseline at Visit 3 or 5).

- 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 any one visit in Visits 2 - 5, or subjects whose NNN levels are consistent with smoking cigarettes (ie, <80% reduction in NNN from baseline) at Visit 3 or 5, and subjects who used ≤ 2 cartridges per week during any given week from Weeks 13 to 24.

*Baseline is defined as the CPD reported at Screening (Visit 2) of the 12-week ALCS-RA-16-06-EV study (CA20130), and the course of the study (post baseline) is defined as the average number of cigarettes smoked from Day 1, Week 1 of ALCS-RA-16-06-EV through the end of Week 24.

The CSP and PP populations will be used for the analyses of subject demographics, baseline characteristics and tobacco product use.

The mITT and PP populations will be used for the analyses of the primary endpoint. All other endpoints (excluding demographics, baseline characteristics, and safety data) will be analyzed based on the mITT population concept defined for each endpoint that includes subjects who has a baseline value and at least one post-baseline value. A PP population will be applied to the spirometry dataset using the criteria listed above.

The CSP will be used for the analyses of AEs, vital signs, clinical laboratory findings and other study safety related variables.

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.

Deviations from the approved SAP will be reported in the final study report.

5. 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® 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® 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, without use of any other type of tobacco/nicotine containing product, for the entire additional 12 weeks

Test 2 Group: Exclusive ad libitum use of test e-Vapor Product XLMB, without use of any other type of tobacco/nicotine containing product, for the entire additional 12 weeks

Test 1 + Test 2 Group = Combined e-vapor use group

Control Group : Continue smoking under ad libitum use of subjects' own brand of conventional lit-end cigarettes, without use of any other type of tobacco/nicotine containing product, for the entire additional 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.

6. BIOMARKER, PRODUCT USE, PULMONARY FUNCTION, AND QUESTIONNAIREASSESSMENT AND ANALYSIS

6.1 Biomarkers Sample Collection and Measurements

6.1.1 Urine Biomarkers of Exposure and Biomarkers of Potential Harm

6.1.1.1 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 and Visit 5. 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_2, and 8-epi-prostaglandin $F2_{\alpha}$, and creatinine. The remaining volume will be used for bio-banking.

6.1.1.2 Bioanalytical Method

Urine aliquots for NE, total NNAL, NNN, 11-dehydrothromboxane B_2, and 8-epi-prostaglandin $F_{2\alpha}$ 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.

6.1.1.3 Urine Biomarker Analysis Variables

- Creatinine-adjusted NE, total NNAL, NNN, 11-dehydrothromboxane B_2, and 8-epi-prostaglandin $F_{2\alpha}$ concentration
- Creatinine-adjusted absolute urine biomarker change from Baseline*
- Creatinine-adjusted percent urine biomarker change from Baseline*

*Baseline values reported on Day 1 (Week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130) will be used.

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.

6.1.1.3.1 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

6.1.1.3.2 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

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

NNAL, total NNAL, NNN, 11-dehydrothromboxane B_2, and 8-epi-prostaglandin $F_{2\alpha}$

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

6.1.1.3.3 Urine Biomarker Change From Baseline

Urine biomarker change from Baseline will be calculated for creatinine-adjusted urinary NE, total NNAL, NNN, 11-dehydrothromboxane B_2, and 8-epi-prostaglandin $F_{2\alpha}$ as follows, where Baseline = values reported on Day 1 (Week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130):

Absolute change from Baseline = Post Product Use Value – Baseline Value

Percent change from Baseline (%) = (Post Product Use Value – Baseline Value) / Baseline Value x 100 %

6.1.2 Blood Biomarkers of Exposure and Biomarkers of Potential harm

6.1.2.1 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 and 5.

6.1.2.2 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.

6.1.2.3 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*
- Percent blood biomarker change from Baseline*

*Baseline values reported on Day 1 (Week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130) will be used.

Absolute and percent change from baseline will be calculated as shown in Section 6.1.1.3.3.

6.1.3 Product Use and Compliance Data Collection and Analysis Variables

6.1.3.1 Data Collection

Product use (number conventional cigarettes used, number test e-vapor cartridges started, and number of puffs taken using the test products, either ≤ 20 or > 20) will be reported daily 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, and 5. Use of other tobacco products will also be recorded at Visits 3, 4, and 5. Urine will be collected for determination of NNN at Visits 3 and 5.

6.1.3.2 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 (the cigarettes per day reported at Screening, Visit 2 of the 12-week ALCS-RA-16-06-EV study) to Visit 5 (Week 24)
- Frequency and percentage of subjects with a reduction, no change, or increase in e-vapor cartridges used per day from Baseline (the average e-vapor cartridges started per day during Week 1 of the 12-week ALCS-RA-16-06-EV study) to Visit 5 (Week 24)
- Measured eCO determined at Baseline, Visit 2, Visit 3, Visit 4, and Visit 5 (Week 24)
- Use of Other tobacco products (yes/no)
- Creatinine-adjusted urine NNN determined at Baseline*, Visit 3, and Visit 5 (Week 24) (calculated as described in Section 6.1.1.3.2)

*Baseline values reported on Day 1 (Week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130) will be used.

6.1.4 Spirometry

6.1.4.1 Data Collection

Pulmonary function testing will be performed at Screening (Visit 2 of the 12-week ALCS-RA-16-06-EV study [CA20130]), Visit 3 (Week 18), and Visit 5 (Week 24).

6.1.4.2 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, percent FEV1 reversibility, and FEF25-75. Absolute change from baseline (Screening Visit 2 of the 12-week ALCS-RA-16-06-EV study [CA20130]) to Visit 3 and Visit 5 will be determined for all parameters.

6.1.5 Questionnaires

6.1.5.1 Data Collection

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

6.1.5.2 Analysis Variables

- QGEN and TQOLIT questionnaires: responses, factor scores and the change in factor scores from Baseline* to Week 18 and Week 24
- Responses to each question on Cough Questionnaire at Baseline*, Visit 3 (Week 18) and Visit 5 (Week 24)
- Responses to Reasons for Use and Not-use of Test Product questionnaire at Visit 5 (Week 24) 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 24.

*Baseline values reported on Day 1 (Week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130) will be used.

6.2 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, absolute change and percent change from Baseline) will have two decimal points. For blood biomarkers, the absolute change from baseline will have the same precision as the original values.

- 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

6.2.1 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.

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

6.2.2 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.

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

6.2.3 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_2, and 8-epi-prostaglandin $F_{2\alpha}$. 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_2, and 8-epi-prostaglandin $F_{2\alpha}$ 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.

6.2.4 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 lower limit of quantitation (LLOQ). The descriptive statistics will be provided for both mITT and PP populations.

6.2.5 Product Use and Compliance

Product Use

The number of cigarettes smoked per day, number of new e-vapor cartridges started per day, and number of puffs taken using test products (≤ 20 puffs or > 20 puffs) will be listed by subject and study day. Continuous variables will be summarized by descriptive statistics while categorical data will be presented using frequency count table. The average number of cigarettes smoked per day and e-cartridges started per day will be summarized by group and Week (Weeks 12 through 24) 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 average for Weeks 12 through through 18 and 24 and Weeks 1 through 24 (CPD only for Weeks 1-24) will be presented. The percent change from Baseline to Week 18, Week 24, and Weeks 1-24 (CPD only for Weeks 1-24) will be calculated, where:

- Baseline for CPD is defined as the CPD reported at Screening, Visit 2 of the 12-week ALCS-RA-16-06-EV study;
- Baseline for the test products is defined as the average of Week 1 of the 12-week ALCS-RA-16-06-EV study;
- Week 18 is defined as the average of Week 18;
- Week 24 is defined as the average of Week 24;
- Weeks 1-24 is defined as the average of Weeks 1-24.

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 24 for each study group.

Compliance

ECO concentration, creatinine-adjusted NNN concentration, and absolute and percent change from baseline in creatinine-adjusted NNN concentration will be listed by

subject and study day. Frequency tables (n and %) will be used to summarize eCO (≤ 5, >5 to ≤ 8 and >8 ppm) and NNN (< 80% reduction from baseline or ≥ 80% reduction from baseline) for assessment of compliance and noncompliance for each study group.

Analysis of NNN will be performed on the mITT population. Other product use and compliance variables will be summarized using available data.

6.2.6 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[1] 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.

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 (Baseline*, Visits 3 and 5) and Reasons of Use/Not-Use Test Product Questionnaire (Visit 5) will be listed by subject and study

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

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.

The above questionnaire analyses will be conducted using the dataset of subjects with a baseline and at least one post-baseline response for each individual question, with the exception of Reasons of Use/Not-Use, which will be summarized using available data.

*Baseline values reported on Day 1 (Week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130) will be used.

6.3 Statistical Analyses

6.3.1 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 24 (Visit 5) 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^2 or greater or equal to 25 kg/m^2) are the fixed effect factors. The baseline value of the response biomarker, where baseline is defined as the value reported on Day 1 (Week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130), 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, first order autoregressive, first 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 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 24 value (primary endpoint) and Week 18 value (secondary endpoint). The above analysis will also output the residual diagnosis to check for normality and to identify outliers).

6.3.1.1 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.

6.3.2 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 24 between the combined e-vapor use group (Test 1 + Test 2) and the Control group.
- absolute change from Baseline to Week 24 between the two test groups (Test 1 vs Test 2).
- absolute change from Baseline to Week 18 between each Test group and the Control group.

The above analyses will be conducted on the mITT datasets.

The same statistical analysis model defined in the primary analysis Section 6.3.2 will also be used for assessment of:

- changes in percent of predicted FEV1, FVC, and FEV1/FVC ratios from Baseline [Screening (Visit 2) of the 12 week ALCS-RA-16-06-EV study (CA20130)] to Week 18 and Week 24 between each Test Group and the Control group.

The analysis of pulmonary function parameters will be conducted on the dataset of subjects with a valid baseline and at least one valid post baseline spirometry assessment. In addition, a PP dataset for pulmonary function parameters will be created from the subjects with valid baseline and post baseline spirometry data using the criteria for the PP population in Section 4, and the analysis will be conducted on this dataset.

6.3.3 Exploratory Endpoint Analysis

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:

- Absolute changes in urine nicotine equivalents (NE) from Baseline to Week 18 and Week 24 between the each Test Group and the Control group and between the combined e-vapor use group (Test 1 + Test 2) and the Control group (mITT population).

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 18 and Week 24 between the each Test Group and the Control group.

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 24 measurements, an ANCOVA model will be used for the exploratory analysis to evaluate:

- absolute changes in the mCEQ factor score from Baseline to Week 24 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 [Day 1 (Week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)] 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.

Questionnaire analyses will be conducted using the dataset of subjects with a baseline and at least one post-baseline response for each individual question.

6.3.4 Subgroup Analysis

Subgroup analysis will depend on subgroup sample sizes. Descriptive statistics will be provided for absolute change from Baseline* to Week 24 in all primary endpoints by study group, gender, age class (less than 45 years or greater or equal to 45 years and BMI class (less than 25 kg/m^2 or greater or equal to 25 kg/m^2). These analyses will be based on the mITT dataset.

The subgroup analysis using MMRM will be conducted for the difference in absolute change from Baseline* to Week 24 by gender, age class and BMI class if the subgroup factor (gender, age class, or BMI class) in the model is statistically significant and if the sample sizes are appropriate (n>=15 in each subgroup cell). The 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.

*Baseline values reported on Day 1 (Week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130) will be used.

6.3.5 Sensitivity Analysis

6.3.5.1 Analysis Variables for Sensitivity Analysis

The sensitivity analysis will be performed for primary endpoints (absolute change from baseline to Week 24 in whole blood WBC count, serum HDL-C concentration, creatinine-adjusted urine 8-epi-prostaglandin $F_{2\alpha}$, creatinine-adjusted urinary 11-dehydrothromboxane B_2, serum sICAM-1, creatinine-adjusted total NNAL, and whole blood COHb).

6.3.5.2 Handling of Missing Data

The last observation (Baseline value or Week 18 value) carried forward method will be applied to the mITT population to assess the effect of missing data.

6.3.5.3 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 24 in whole blood WBC count, serum HDL-C concentration, creatinine-adjusted urine 8-epi-prostaglandin $F_{2\alpha}$,

creatinine-adjusted urine 11-dehydrothromboxane B_2, 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 5 (Week 24) if any outliers are found using the above criteria.

6.3.5.4 Handling BLQ values

Values BLQ for nicotine and its metabolites, COHb, NNAL, NNN, 8-epi-prostaglandin $F_{2\alpha}$, 11-dehydrothromboxane B_2, 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 $F_{2\alpha}$, 11-dehydrothromboxane B_2, 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 F2α	25.0 pg/mL
sICAM-1	12.5 ng/mL
COHb	0.2%

7. 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 points 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.

7.1 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.

7.2 Adverse Events

Adverse events will be coded (to the lowest level term) with the Medical Dictionary for Regulatory Activities (MedDRA®) 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.

AEs will be monitored and recorded from the time of the test e-vapor product trial at Screening, Visit 2 of the 12-week ALCS-RA-16-06-EV study until Week 24/EOS (or upon early termination). 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.

7.3 Clinical Laboratory

Clinical laboratory evaluations (clinical chemistry, hematology, and urinalysis) will be performed Visit 1 and at End-of-Study or Early Termination.

Descriptive statistics will be reported for numeric clinical data by study group and time point. Normal ranges will be listed by site.

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

Urine pregnancy tests will be completed at each study visit, and the results will be listed as “Negative” or “Positive.”

7.4 Vital Signs

Vital signs (respiration rate, pulse rate, blood pressure, and oral temperature) will be measured at each study visit, and at the End-of-Study or upon Early Termination. At these study visits, vital signs will be taken in the sitting position after at least 5 minutes of rest and 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.

7.5 ECG

A 12-lead ECG will be obtained at Visit 1 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. ECG information will be listed by subject.

7.6 Concomitant Medications

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

7.7 Physical Examination

Physical examinations will be performed at Screening. A brief physical examination (symptom driven) may be performed at each study visit, and at 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.

8. 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® 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 (CSP, mITT, and PP population)

Table 14.1.2 Demographic Summary Overall and by Study Group (CSP, mITT, and PP population)

Table 14.1.3 Smoking History Overall and by Study Group (CSP, mITT, and PP population)

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

14.2.1 Biomarkers of Potential Harm and Exposure Tables

Primary and Secondary Biomarker endpoints (WBC count, HDL-C, urine 8-epi-prostaglandin $F_{2\alpha}$, urine 11-dehydrothromboxane B_2, sICAM-1, total NNAL, COHb)

Whole Blood WBC Count Tables

Table 14.2.1.1.1.1 Summary of Whole Blood WBC Count (x $10^3/\mu L$) by Study Group and Visit (mITT Population)

Table 14.2.1.1.1.2 Summary of Whole Blood WBC Count (x $10^3/\mu L$) 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 $10^3/\mu L$) 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 $10^3/\mu L$) 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 (x $10^3/\mu L$) 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 (x $10^3/\mu L$) 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 5 (x $10^3/\mu L$) by Study Group (PP Population)

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 5 (x $10^3/\mu L$) 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 5 (x $10^3/\mu L$) Study Groups (mITT Population with Imputation of Missing Data Using Last Observation Carried Forward Method)

Table 14.2.1.1.11.1 Summary of Whole Blood WBC Count Absolute Change From Baseline (x $10^3/\mu L$) by Study Group and Visit (mITT Population with Outliers Excluded)

Table 14.2.1.1.11.2 Statistical Summary of Whole Blood WBC Count Absolute Change From Baseline to Visit 5 (x $10^3/\mu L$) by Study Group (mITT Population with Outliers Excluded)

Table 14.2.1.1.11.3 Statistical Comparisons of Whole Blood WBC Count Absolute Change From Baseline to Visit 5 (x $10^3/\mu L$) Between Study Groups (mITT Population with Outliers Excluded)

Table 14.2.1.1.12.1 Statistical Summary of Whole Blood WBC Count Absolute Change From Baseline to Visit 5 (x $10^3/\mu L$) 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 14.2.1.1.12.2 Statistical Comparisons of Whole Blood WBC Count Absolute Change From Baseline to Visit 5 (x $10^3/\mu L$) 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.)

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)

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 5 (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 5 (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 5 (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 5 (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 5 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 5 (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 Summary of Serum HDL-C Absolute Change From Baseline (mg/dL) by Study Group and Visit (mITT Population with Outliers Excluded)

Table 14.2.1.2.11.2 Statistical Summary of Serum HDL-C Absolute Change From Baseline to Visit 5 (mg/dL) by Study Group (mITT Population with Outliers Excluded)

Table 14.2.1.2.11.3 Statistical Comparisons of Serum HDL-C Absolute Change From Baseline to Visit 5 (mg/dL) Between Study Groups (mITT Population with Outliers Excluded)

Table 14.2.1.2.12.1 Statistical Summary of Serum HDL-C Absolute Change From Baseline to Visit 5 (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 14.2.1.2.12.2 Statistical Comparisons of Serum HDL-C Absolute Change From Baseline to Visit 5 (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.)

Urine 8-epi-prostaglandin F2α Tables

Table 14.2.1.3.1.1 Summary of Urine 8-epi-prostaglandin F2α (ng/g Cr) by Study Group and Visit (mITT Population)

Table 14.2.1.3.1.2 Summary of Urine 8-epi-prostaglandin F2α (ng/g Cr) by Study Group and Visit (PP Population)

Table 14.2.1.3.2.1 Summary of Urine 8-epi-prostaglandin F2α 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 F2α 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 F2α Percent Change From Baseline (%) by Study Group and Visit (mITT Population)

Table 14.2.1.3.3.2 Summary of Urine 8-epi-prostaglandin F2α 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 F2α 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 F2α 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 F2α Absolute Change From Baseline to Visit 5 (ng/g Cr) by Study Group (PP Population)

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 F2α Absolute Change From Baseline to Visit 5 (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 F2α Absolute Change From Baseline to Visit 5 (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 Summary of Urine 8-epi-prostaglandin F2α Absolute Change From Baseline (ng/g Cr) by Study Group and Visit (mITT Population with Outliers Excluded)

Table 14.2.1.3.11.2 Statistical Summary of Urine 8-epi-prostaglandin F2α Absolute Change From Baseline to Visit 5 (ng/g Cr) by Study Group (mITT Population with Outliers Excluded)

Table 14.2.1.3.11.3 Statistical Comparisons of Urine 8-epi-prostaglandin F2α Absolute Change From Baseline to Visit 5 (ng/g Cr) Between Study Groups (mITT Population with Outliers Excluded)

Table 14.2.1.3.12.1 Statistical Summary of Urine 8-epi-prostaglandin F2α Absolute Change From Baseline to Visit 5 (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 14.2.1.3.12.2 Statistical Comparisons of Urine 8-epi-prostaglandin F2α Absolute Change From Baseline to Visit 5 (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.)

Urine 11-dehydrothromboxane B_2 Tables

Table 14.2.1.4.1.1 Summary of Urine 11-dehydrothromboxane B_2 (ng/g Cr) by Study Group and Visit (mITT Population)

Table 14.2.1.4.1.2 Summary of Urine 11-dehydrothromboxane B_2 (ng/g Cr) by Study Group and Visit (PP Population)

	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_2 Absolute Change From Baseline to Visit 5 (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_2 Absolute Change From Baseline to Visit 5 (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_2 Absolute Change From Baseline to Visit 5 (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_2 Absolute Change From Baseline to Visit 5 (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_2 Absolute Change From Baseline to Visit 5 (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_2 Absolute Change From Baseline to Visit 5 (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_2 Absolute Change From Baseline to Visit 5 (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 Summary of Urine 11-dehydrothromboxane B_2 Absolute Change From Baseline (ng/g Cr) by Study Group and Visit (mITT Population with Outliers Excluded)

Table 14.2.1.4.11.2 Statistical Summary of Urine 11-dehydrothromboxane B_2 Absolute Change From Baseline to Visit 5 (ng/g Cr) by Study Group (mITT Population with Outliers Excluded)

Table 14.2.1.4.11.3 Statistical Comparisons of Urine 11-dehydrothromboxane B_2 Absolute Change From Baseline to Visit 5 (ng/g Cr) Between Study Groups (mITT Population with Outliers Excluded)

Table 14.2.1.4.12.1 Statistical Summary of Urine 11-dehydrothromboxane B_2 Absolute Change From Baseline to Visit 5 (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 14.2.1.4.12.2 Statistical Comparisons of Urine 11-dehydrothromboxane B_2 Absolute Change From Baseline to Visit 5 (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.)

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 14.2.1.5.9.1	Statistical Summary of Serum sICAM-1 Absolute Change From Baseline to Visit 5 (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 5 (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 5 (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 5 (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	Summary of Serum sICAM-1 Absolute Change From Baseline (ng/mL) by Study Group and Visit (mITT Population with Outliers Excluded)
Table 14.2.1.5.11.2	Statistical Summary of Serum sICAM-1 Absolute Change From Baseline to Visit 5 (ng/mL) by Study Group (mITT Population with Outliers Excluded)
Table 14.2.1.5.11.3	Statistical Comparisons of Serum sICAM-1 Absolute Change From Baseline to Visit 5 (ng/mL) Between Study Groups (mITT Population with Outliers Excluded)
Table 14.2.1.5.12.1	Statistical Summary of Serum sICAM-1 Absolute Change From Baseline to Visit 5 (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 14.2.1.5.12.2	Statistical Comparisons of Serum sICAM-1 Absolute Change From Baseline to Visit 5 (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.)

Urine Total NNAL Tables

Table 14.2.1.6.7.1	Statistical Summary of Urine Total NNAL Absolute Change From Baseline to Visit 5 (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 5 (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 5 (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 5 (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 5 (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 5 (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 5 (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 5 (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 Summary of Urine Total NNAL Absolute Change From Baseline (ng/g Cr) by Study Group and Visit (mITT Population with Outliers Excluded)

Table 14.2.1.6.11.2 Statistical Summary of Urine Total NNAL Absolute Change From Baseline to Visit 5 (ng/g Cr) by Study Group and (mITT Population with Outliers Excluded)

Table 14.2.1.6.11.3 Statistical Comparisons of Urine Total NNAL Absolute Change From Baseline to Visit 5 (ng/g Cr) Between Study Groups (mITT Population with Outliers Excluded)

Table 14.2.1.6.12.1 Statistical Summary of Urine Total NNAL Absolute Change From Baseline to Visit 5 (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 14.2.1.6.12.2 Statistical Comparisons of Urine Total NNAL Absolute Change From Baseline to Visit 5 (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.)

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 14.2.1.7.9.1 Statistical Summary of Whole Blood COHb Absolute Change From Baseline to Visit 5 (% 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 5 (% 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 5 (% 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 5 (% Saturation) Between Study Groups (mITT Population with Imputation of Missing Data Using Last Observation Carried Forward Method)

Table 14.2.1.7.11.1 Summary of Whole Blood COHb Absolute Change From Baseline (% Saturation) by Study Group and Visit (mITT Population with Outliers Excluded)

Table 14.2.1.7.11.2 Statistical Summary of Whole Blood COHb Absolute Change From Baseline to Visit 5 (% Saturation) by Study Group (mITT Population with Outliers Excluded)

Table 14.2.1.7.11.3 Statistical Comparisons of Whole Blood COHb Absolute Change From Baseline to Visit 5 (% Saturation) Between Study Groups (mITT Population with Outliers Excluded)

Table 14.2.1.7.12.1 Statistical Summary of Whole Blood COHb Absolute Change From Baseline to Visit 5 (% 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 14.2.1.7.12.2 Statistical Comparisons of Whole Blood COHb Absolute Change From Baseline to Visit 5 (% 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.)

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

Table 14.2.1.8.2 Summary of Urine Nicotine Equivalents Absolute Change From Baseline (mg/g Cr) by Study Group and Visit

Table 14.2.1.8.3 Summary of Urine Nicotine Equivalents Percent Change From Baseline (%) by Study Group and Visit

Table 14.2.1.8.4 Statistical Summary of Urine Nicotine Equivalents Absolute Change From Baseline (mg/g Cr) by Study Group and Visit

Table 14.2.1.8.5 Statistical Comparisons of Urine Nicotine Equivalents Absolute Change From Baseline (mg/g Cr) Between Study Groups by Visit

14.2.2 Product Use and Compliance Tables

Table 14.2.2.1.1 Summary of Average Number of Cigarettes Used Per Day by Study Group and Week (Week 12 through Week 18)

Table 14.2.2.1.2 Summary of Average Number of Cigarettes Used Per Day by Study Group and Week (Week 19 through Week 24)

Table 14.2.2.1.3 Summary of Change from Baseline Cigarettes Used Per Day by Study Group and Visit

Table 14.2.2.1.4 Summary of Average Number of e-Vapor Cartridges Started Per Day by Study Group and Week (Week 12 through Week 18)

Table 14.2.2.1.5 Summary of Average Number of e-Vapor Cartridges Started Per Day by Study Group and Week (Week 19 through Week 24)

Table 14.2.2.1.6 Summary of Change from Baseline e-Vapor Cartridges Started Per Day by Study Group and Visit

Table 14.2.2.2 Frequency of Reduction, No Change, or Increase in Cigarettes Per Day and e-Vapor Cartridges Started Per Day from Baseline to Week 12 by Study Group

Table 14.2.2.3.1 Frequency of Subject Days with ≤ 20 or > 20 Puffs per Day for e-Vapor Products by Study Group and Week (Week 12 through Week 18)

Table 14.2.2.3.2	Frequency of Subject Days with ≤ 20 or > 20 Puffs per Day for e-Vapor Products Study Group and Week (Week 19 through Week 24)
Table 14.2.2.4.1	Summary of eCO (ppm) by Study Group and Visit
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	Summary of urine NNN (ng/g Cr) absolute change from Baseline by Study Group and Visit (mITT population)
Table 14.2.2.4.4	Summary of urine NNN (ng/g Cr) percent change from Baseline by Study Group and Visit (mITT population)
Table 14.2.2.4.5	Frequency of eCO and Urine NNN by Study Group and Visit

14.2.3 Spirometry

Table 14.2.3.1.1	Summary of Pulmonary Function Parameters by Study Group and Visit (All Subjects*)
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 in Pulmonary Function Parameters by Study Group and Visit (All Subjects*)
Table 14.2.3.2.2	Summary of Absolute Change From Baseline Pulmonary Function Parameters by Study Group and Visit (PP Population)
Table 14.2.3.3.1	Statistical Summary of Absolute Change From Baseline in Pulmonary Function Parameters by Study Group and Visit (All Subjects*)
Table 14.2.3.3.2	Statistical Comparisons of Absolute Change From Baseline in Pulmonary Function Parameters Between Study Groups by Visit (All Subjects*)
Table 14.2.3.4.1	Statistical Summary of Absolute Change From Baseline in Pulmonary Function Parameters by Study Group and Visit (PP Population)
Table 14.2.3.4.2	Statistical Comparisons of Absolute Change From Baseline in Pulmonary Function Parameters Between Study Groups by Visit (PP Population)

*All subjects with a valid baseline and at least one valid post-basline spirometry session

14.2.4 Subject Questionnaires

QGEN Questionnaire

Table 14.2.4.1.1	Summary of QGEN Original Scores by Study Group and Visit
Table 14.2.4.1.2	Summary of QGEN Factor Scores by Study Group and Visit
Table 14.2.4.1.3	Summary of Absolute Change From Baseline in QGEN Factor Scores by Study Group and Visit
Table 14.2.4.1.4.1	Statistical Summary of Absolute Change From Baseline in QGEN Factor Scores by Study Group and Visit
Table 14.2.4.1.4.2	Statistical Comparisons of Absolute Change From Baseline QGEN Factor Scores Between Study Groups by Visit

TQOLIT Questionnaire

Table 14.2.4.2.1.1	Summary of TQOLIT Original Scores by Study Group and Visit (Question Set 1)
Table 14.2.4.2.1.2	Summary of TQOLIT Original Scores by Study Group and Visit (Question Set 2)
Table 14.2.4.2.1.3	Summary of TQOLIT Original Scores by Study Group and Visit (Question Set 3)
Table 14.2.4.2.1.4	Summary of TQOLIT Original Scores by Study Group and Visit (Question Set 4)
Table 14.2.4.2.1.5	Summary of TQOLIT Original Scores by Study Group and Visit (Question Set 5)
Table 14.2.4.2.1.6	Summary of TQOLIT Original Scores by Study Group and Visit (Question Set 6)
Table 14.2.4.2.1.7	Summary of TQOLIT Original Scores by Study Group and Visit (Question Set 7)
Table 14.2.4.2.2	Summary of TQOLIT Factor Scores by Study Group and Visit
Table 14.2.4.2.3	Summary of Absolute Change From Baseline in TQOLIT Factor Scores by Study Group and Visit
Table 14.2.4.2.4.1	Statistical Summary of Absolute Change From Baseline in TQOLIT Factor Scores by Study Group and Visit
Table 14.2.4.2.4.2	Statistical Comparisons of Absolute Change From Baseline in TQOLIT Factor Scores Between Study Groups by Visit

mCEQ

Table 14.2.4.3.1 Summary of mCEQ Original Scores by Study Group and Visit

Table 14.2.4.3.2 Summary of mCEQ Factor Scores by Study Group and Visit

Table 14.2.4.3.3 Summary of Absolute Change from Baseline to Visit 5 mCEQ Factor Scores by Study Group

Table 14.2.4.3.4.1 Statistical Summary of Absolute Change From Baseline to Visit 5 in mCEQ Factor Scores by Study Group

Table 14.2.4.3.4.2 Statistical Comparisons of Absolute Change From Baseline to Visit 5 in mCEQ Factor Scores Between Study Groups

Cough Questionnaire

Table 14.2.4.4.1 Summary of Cough Questionnaire Questions I and III through X by Study Group and Visit

Table 14.2.4.4.2 Summary of Cough Questionnaire Question II by Study Group and Visit

Reasons to Use/Not-Use Test Product Questionnaire

Table 14.2.4.5.1 Summary of Reasons of Use/Not-Use Test Product Questionnaire by Study Group at Week 24: Likelihood of Use

Table 14.2.4.5.2 Summary of Reasons of Use/Not-Use Test Product Questionnaire by Study Group at Week 24: Reasons to Use

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 Mean (SD) Whole Blood WBC Count Versus Visit (mITT Population)

Figure 14.2.5.1.2 Mean (SD) Whole Blood WBC Count Versus Visit (PP Population)

Figure 14.2.5.1.3 Box Plot of Whole Blood WBC Count at Baseline and Visit 5 by Study Group (mITT Population)

Figure 14.2.5.1.4 Box Plot of Whole Blood WBC Count at Baseline and Visit 5 by Study Group (PP Population)

Figure 14.2.5.1.5 Box Plot of Whole Blood WBC Count at Baseline and Visit 3 by Study Group (mITT Population)

Figure 14.2.5.1.6 Box Plot of Whole Blood WBC Count Absolute Change from Baseline to Visit 3 and Visit 5 by Study Group

Figure 14.2.5.6.6 Box Plot of Urine Total NNAL Absolute Change from Baseline to Visit 3 and Visit 5 by Study Group (mITT Population)

Figure 14.2.5.6.7 Box Plot of Urine Total NNAL Absolute Change from Baseline to Visit 5 by Study Group (PP Population)

Whole Blood COHb Figures

Figure 14.2.5.7.1 Mean (SD) Whole Blood COHb Versus Visit (mITT Population)

Figure 14.2.5.7.2 Mean (SD) Whole Blood COHb Versus Visit (PP Population)

Figure 14.2.5.7.3 Box Plot of Whole Blood COHb at Baseline and Visit 5 by Study Group (mITT Population)

Figure 14.2.5.7.4 Box Plot of Whole Blood COHb at Baseline and Visit 5 by Study Group (PP Population)

Figure 14.2.5.7.5 Box Plot of Whole Blood COHb at Baseline and Visit 3 by Study Group (mITT Population)

Figure 14.2.5.7.6 Box Plot of Whole Blood COHb Absolute Change from Baseline to Visit 3 and Visit 5 by Study Group (mITT Population)

Figure 14.2.5.7.7 Box Plot of Whole Blood COHb Absolute Change from Baseline to Visit 5 by Study Group (PP Population)

Note (applies to all the above figures): Figures 14.2.5.X.1 will contain Baseline and Visits 3 and 5 for Test 1, Test 2, Test 1 + Test 2, and Control groups. Figures 14.2.5.X.2 will contain Baseline and Visits 3 and 5 for Test 1, Test 2, and Control groups. Figures 14.2.1.X.3 will contain Test 1, Test 2, Test 1 + Test 2, and Control groups. Figures 14.2.5.X.4 and 14.2.5.X.5 will contain Test 1, Test 2, and Control group. Figures 14.2.5.X.6 will contain Test 1, Test 2, and Control groups for Visit 3 and Test 1, Test 2, Test 1 + Test 2, and Control groups for Visit 5. Figures 14.2.5.X.7 will contain Test 1, Test 2, and Control groups.

Urine Nicotine Equivalents Figures

Figure 14.2.5.8.1 Mean (SD) Nicotine Equivalents Versus Visit

Figure 14.2.5.8.3 Box Plot of Urine Nicotine Equivalents at Baseline and Visit 5 by Study Group

Figure 14.2.5.8.4 Box Plot of Urine Nicotine Equivalents at Baseline and Visit 3 by Study Group

Figure 14.2.5.8.5 Box Plot of Urine Nicotine Equivalents Absolute Change from Baseline to Visit 3 and Visit 5 by Study Group

Note: Figure 14.2.5.8.1 will contain Baseline and Visits 3 and 5 for Test 1,

Test 2, Test 1 + Test 2, and Control groups. Figure 14.2.5.8.2 will contain Test 1, Test 2, Test 1 + Test 2, and Control groups. Figure 14.2.5.8.3 will contain Test 1, Test 2, and Control group. Figure 14.2.5.8.4 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 5.

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) (CSP population)

Table 14.3.1.2 Adverse Event Frequency by Study Group – Number of Adverse Events (% of Total Adverse Events) (CSP population)

Table 14.3.1.3 Adverse Event Frequency by Study Group, Severity, and Relationship to Study Product – Number of Subjects Reporting Events (CSPS population)

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

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 (CSP population)

Table 14.3.4.2 Out-of-Range Values and Recheck Results – Hematology (CSP population)

Table 14.3.4.3 Out-of-Range Values and Recheck Results – Urinalysis (CSP population)

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 (CSP population)

Table 14.3.5.2 Clinical Laboratory Summary – Hematology (CSP population)
Table 14.3.5.3 Clinical Laboratory Summary – Urinalysis (CSP population)
Table 14.3.5.4 Vital Sign Summary (CSP population)
Table 14.3.5.5 12-Lead Electrocardiogram Summary (CSP population)

9. 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 Subject Disposition and Discontinuation

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 F2α, 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 Assessment Questionnaire
Appendix 16.2.5.2.2 Confirm Regular Cigarette Brand
Appendix 16.2.5.2.3 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 F2α
Appendix 16.2.6.4 Urine 11-dehydrothromboxane B2
Appendix 16.2.6.5 Serum sICAM-1
Appendix 16.2.6.6 Urine Total NNAL
Appendix 16.2.6.7 Whole Blood COHb
Appendix 16.2.6.8.1 Product Used per Day
Appendix 16.2.6.8.2 Test Product Used per Day
Appendix 16.2.6.8.3 Average Product Used per Day
Appendix 16.2.6.8.4 Product Used Per Day Change From Baseline
Appendix 16.2.6.9 Urine NNN
Appendix 16.2.6.10.1 Pulmonary Function Test (Spirometry) (I of II)
Appendix 16.2.6.10.2 Pulmonary Function Test (Spirometry) (II of II)
Appendix 16.2.6.10.3 Pulmonary Function Test (Spirometry) Absolute Change from Baseline to Week 24 (Visit 5)
Appendix 16.2.6.11.1 Urine Nicotine and Metabolites Concentrations
Appendix 16.2.6.11.2 Urine Nicotine Equivalents
Appendix 16.2.6.12.1.1 TQOLIT Questionnaire

Appendix 16.2.6.12.1.2 Factor Score TQOLIT Questionnaire
Appendix 16.2.6.12.2.1 QGEN Questionnaire
Appendix 16.2.6.12.2.2 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 16.2.6.12.6.1 End-of-Study Questionnaire (Test Groups)
Appendix 16.2.6.12.6.1 End-of-Study Questionnaire (Control Group)

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 Smoking Cessation Information
Appendix 16.2.8.13 Reminder Phone Call

10. 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 (CSP, mITT, and PP population)

		Group			
Population	Category	Test 1	Test 2	Control	Overall
CSP	Enrolled	XXX	XXX	XXX	XXX
	Completed	XXX	XXX	XXX	XXX
	Discontinued Early	XX	XX	XX	XX
	<Reason1>	XX	XX	XX	XX
	<Reason2>	XX	XX	XX	XX
	<Reason3>	XX	XX	XX	XX
mITT	Enrolled	XXX	XXX	XXX	XXX
	Completed	XXX	XXX	XXX	XXX
	Discontinued Early	XX	XX	XX	XX
	<Reason1>	XX	XX	XX	XX
	<Reason2>	XX	XX	XX	XX
	<Reason3>	XX	XX	XX	XX
PP	Enrolled	XXX	XXX	XXX	XXX
	Completed	XXX	XXX	XXX	XXX
	Discontinued Early	XX	XX	XX	XX
	<Reason1>	XX	XX	XX	XX
	<Reason2>	XX	XX	XX	XX
	<Reason3>	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

CSP = Clinical safety population, mITT = Modified Intent-to-treat, PP = Per protocol

Program: /CAXXXXX/sas_prg/stsas/PROGRAMNAME.SAS DDMMMYYYY HH:MM

Table 14.1.2 Demographic Summary Overall and by Study Group (CSP, mITT, and PP population)

Population	Trait		Group: Test 1	Group: Test 2	Group: Control	Overall
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%)
		XXXXX	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
		XXXXX	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: 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, mITT = Modified Intent-to-treat, PP = Per protocol

Program: /CAXXXXX/sas_prg/stsas/PROGRAMNAME.SAS DDMMMYYYY HH:MM

Programmer Note: Weight (kg), height (cm), BMI (kg/m^2) 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 (CSP, mITT, and PP population)

			Study Group			
Population	Trait		1	2	Control	Overall
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	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: 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, mITT = Modified Intent-to-treat, PP = Per protocol

Program: /CAXXXXX/sas_prg/stsas/PROGRAMNAME.SAS DDMMMYYYY HH:MM

Programmer Note: mITT and PP population will also be presented if sample size is appropriate. Subset by gender and age group [i.e CSP (Male), CSP(Female), CSP (<45 years old), CSP(≥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:

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

		Group			
Visit	Statistics	Test 1	Test 2	Test 1 + Test 2	Control
X	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
X	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

Note: Baseline = Day 1 (Week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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/pksas/PROGRAMNAME.SAS DDMMMYYYY 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, 14.2.1.1.11.1, 14.2.1.2.2.1, 14.2.1.2.2.2, 14.2.1.2.11.1, 14.2.1.3.2.1, 14.2.1.3.2.2, 14.2.1.3.11.1, 14.2.1.4.2.1, 14.2.1.4.2.2, 14.2.1.4.11.1, 14.2.1.5.2.1, 14.2.1.5.2.2, 14.2.1.5.11.1, 14.2.1.6.2.1, 14.2.1.6.2.2, 14.2.1.6.11.1, 14.2.1.7.2.1, 14.2.1.7.2.2, 14.2.1.7.11.1, 14.2.1.8.2, and 14.2.2.4.3 will have the following format:

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

		Group			
Visit	Statistics	Test 1	Test 2	Test 1 + Test 2	Control
X	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
X	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

Note: Baseline = Day 1 (Week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 3)

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 DDMMMYYYY HH:MM **Programmer Note: Table 14.2.2.4.3 will not contain Test 1 + Test 2 Group**

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, and 14.2.2.4.4 will have the following format:

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

		Group			
Visit	Statistics	Test 1	Test 2	Test 1 + Test 2	Control
X	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
X	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

Note: Baseline = Day 1 (Week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 3)

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 DDMMMYYYY HH:MM

Programmer Note: Table 14.2.2.4.4 will not contain Test 1 + Test 2 Group

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:

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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	3	XX	X.XX	XX.XX – XXX.XX	X.XXXX
	5	XX	X.XX	XX.XX – XXX.XX	X.XXXX
Test 2	3	XX	X.XX	XX.XX – XXX.XX	X.XXXX
	5	XX	X.XX	XX.XX – XXX.XX	X.XXXX
Test 1 + Test 2	3	XX	X.XX	XX.XX – XXX.XX	X.XXXX
	3	XX	X.XX	XX.XX – XXX.XX	X.XXXX
Control	5	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.
< > variance-covariance structure is used for the final model.
n = Number of observation used in the analysis
Least-squares means (LS Means) are calculated from the MMRM.

Baseline = Day 1 (Week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 3)

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

Program: /CAXXXXX/sas_prg/pksas PROGRAMNAME.SAS DDMMMYYYY HH:MM

Note: Statistical Summary Tables for PP population, mITT with imputation population, 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, 14.2.1.1.11.2, 14.2.1.1.12.1, 14.2.1.2.5.1, 14.2.1.2.10.1, 14.2.1.2.11.2, 14.2.1.2.12.1, 14.2.1.3.5.1, 14.2.1.3.10.1, 14.2.1.3.11.2, 14.2.1.3.12.1, 14.2.1.4.5.1, 14.2.1.4.10.1, 14.2.1.4.11.2, 14.2.1.4.12.1, 14.2.1.5.5.1, 14.2.1.5.10.1, 14.2.1.5.11.2, 14.2.1.5.12.1, 14.2.1.6.5.1, 14.2.1.6.10.1, 14.2.1.6.11.2, 14.2.1.6.12.1, 14.2.1.7.5.1, 14.2.1.7.10.1, 14.2.1.7.11.2, 14.2.1.7.12.1, will have the following format:

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Table 14.2.1.1.5.1 Statistical Summary of <Matrix> <Biomarker>) Absolute Change from Baseline to Visit 5 (<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.
< > variance-covariance structure is used for the final model.
n = Number of observation used in the analysis
Least-squares means (LS Means) are calculated from the MMRM.

Baseline = Day 1 (week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 5 = Week 24 (Day 168 ± 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/pksas PROGRAMNAME.SAS DDMMMYYYY HH:MM

Programmer Note: Tables 14.2.1.X.12.1 (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:

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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 Test (n)	LS Means Reference (n)	LS Mean Difference (Test – Reference)	XX% Confidence Interval	p-value
Test 1 vs Control	3	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Test 2 vs Control	3	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Test 1 + Test 2 vs Control	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Test 1 vs Test 2	5	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.
< > variance-covariance structure is used for the final model.
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 = Day 1 (week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 3)

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

Program: /CAXXXXX/sas_prg/pksas PROGRAMNAME.SAS DDMMMYYYY 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, 14.2.1.1.11.3, 14.2.1.1.12.2, 14.2.1.2.5.2, 14.2.1.2.10.2, 14.2.1.2.11.3, 14.2.1.2.12.2, 14.2.1.3.5.2, 14.2.1.3.10.2, 14.2.1.3.11.3, 14.2.1.3.12.2, 14.2.1.4.5.2, 14.2.1.4.10.2, 14.2.1.4.11.3, 14.2.1.4.12.2, 14.2.1.5.5.2, 14.2.1.5.10.2, 14.2.1.5.11.3, 14.2.1.5.12.2, 14.2.1.5.13.2, 14.2.1.7.12.2, will have the following format:

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Table 14.2.1.1.5.2 Statistical Comparisons of <Biomarker> Absolute Change From Baseline to Visit 5 (Units) Between Study Groups (<Population>)

Comparison	LS Means Test (n)	LS Means Reference (n)	LS Mean Difference (Test − Reference)	XX% Confidence Interval	p-value
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 = Day 1 (Week 1) of the 12 week ALCS RA 16 06 EV study (CA20130)
Visit 5 = Week 24 (Day 168 ± 3)

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

Program: /CAXXXXX/sas_prg/pksas PROGRAMNAME.SAS DDMMMYYYY HH:MM

Programmer Note: Tables 14.2.1.X.12.2 (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:

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Table 14.2.1.1.6.1 Summary of <Matrix> <Biomarker> Absolute Change from Baseline to Visit 5 (<units>) by Study Group and <Gender>* (<Population>)

		Group		
<Gender>*	Statistics	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

Note: Baseline = Day 1 (Week 1) of the 12 week ALCS RA 16 06 EV study (CA20130)
Visit 5 = Week 24 (Day 168 ± 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/pksas PROGRAMNAME.SAS DDMMMYYYY HH:MM

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

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 5 (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, study group by study visit 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 = Day 1 (Week 1) of the 12 week ALCS RA 16 06 EV study (CA20130)
Visit 5 = Week 24 (Day 168 ± 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/pksas PROGRAMNAME.SAS DDMMMYYYY HH:MM

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

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 5 (Units) Between Study Groups by <Subgroup>* (<Population>)

Comparison	<Subgroup>*	LS Means Test (n)	LS Means Reference (n)	LS Mean Difference (Test − Reference)	XX% Confidence Interval	p-value
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, study group by study visit by <subgroup>* interaction, age class, and BMI classas as fixed effects, 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 = Day 1 (Week 1) of the 12 week ALCS RA 16 06 EV study (CA20130)
Visit 5 = Week 24 (Day 168 ± 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/pksas PROGRAMNAME.SAS DDMMMYYYY HH:MM

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

Table 14.2.2.1.1 Summary of Average Number of Cigarettes Used Per Day by Study Group and Week (Week 12 Through Week 18)

Group		Baseline	Week 12	13	14	15	16	17	18	12-18
Test 1	n	X	X	X	X	X	X	X	X	X
	n missing	X	X	X	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Minimum	X	X	X	X	X	X	X	X	X
	Q1	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X	X	X	X	X	X	X	X	X
	Q3	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	X.X	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	X, X
Test 2	<same as above>									
Control	<same as above>									

Note: Baseline = Cigarettes per day at Screening (Visit 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)

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 DDMMMYYYY HH:MM

Table 14.2.2.1.2 Summary of Average Number of Cigarettes Used Per Day by Study Group and Week (Week 19 Through Week 24)

Group		Week 19	20	21	22	23	24	12-24	1-24
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	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Minimum	X	X	X	X	X	X	X	X
	Q1	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X	X	X	X	X	X	X	X
	Q3	X.X	X.X	X.X	X.X	X.X	X.X	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: 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 DDMMMYYYY HH:MM

Table 14.2.2.1.3 Summary of Change from Baseline Cigarettes Used Per Day by Study Group

Group		Baseline	--- Absolute Change from Baseline-- Week 18	Week 24	Weeks 1-24	--- Percent Change from Baseline-- Week 18	Week 24	Weeks 1-24
Test 1	n	X	X	X	X	X	X	X
	n missing	X	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Minimum	X	X	X	X	X	X	X
	Q1	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X	X	X	X	X	X	X
	Q3	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	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
Test 2	<same as above>							
Control	<same as above>							

Note: Baseline = Cigarettes per day (CPD) at Screening (Visit 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Week 18 = Average CPD during Week 18
Week 24 = Average CPD during Week 24
Weeks 1-24 = Average CPD during Weeks 12-24

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 DDMMMYYYY HH:MM

Table 14.2.2.1.4 Summary of Average Number of e-Vapor Cartridges Started Per Day by Study Group and Week (Week 12 Through Week 18)

			Week							
Group		Baseline	12	13	14	15	16	17	18	12-18
Test 1	n	X	X	X	X	X	X	X	X	X
	n missing	X	X	X	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Minimum	X	X	X	X	X	X	X	X	X
	Q1	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X	X	X	X	X	X	X	X	X
	Q3	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	X.X	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	X, X
Test 2	<same as above>									
Control	<same as above>									

Note: Baseline = Average e-Vapor cartridges started per day during Week 1 of the 12-week ALCS-RA-16-06-EV study (CA20130)
Test 1 Group = e-Vapor Product XLCB
Test 2 Group = e-Vapor Product XLMB

Program: /CAXXXXX/ECR/sas_prg/pksas/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.2.1.5 Summary of Average Number of e-Vapor Cartridges Started Per Day by Study Group and Week (Week 19 Through Week 24)

		Week						
Group		19	20	21	22	23	24	12-24
Test 1	n	X	X	X	X	X	X	X
	n missing	X	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Minimum	X	X	X	X	X	X	X
	Q1	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Median	X	X	X	X	X	X	X
	Q3	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	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
Test 2	<same as above>							

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

Program: /CAXXXXX/ECR/sas_prg/pksas/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.2.1.6 Summary of Change from Baseline e-Vapor Cartridges Started Per Day by Study Group by Study Group

Group		Baseline	--- Absolute Change from Baseline-- Week 18	Week 24	--- Percent Change from Baseline-- Week 18	Week 24
Test 1	n	X	X	X	X	X
	n missing	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
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.X	X.X	X.X	X.X	X.X
	Minimum	X	X	X	X	X
	Q1	X.X	X.X	X.X	X.X	X.X
	Median	X	X	X	X	X
	Q3	X.X	X.X	X.X	X.X	X.X
	Maximum	X.X	X.X	X.X	X.X	X.X
	95% CI	X, X	X, X	X, X	X, X	X, X
Test 2	<same as above>					

Note: Baseline = Average e-Vapor cartridges started per day during Week 1 of the 12-week ALCS-RA-16-06-EV study (CA20130)
Week 18 = Average e-Vapor cartridges started per day during Week 18
Week 24 = Average e-Vapor cartridges started per day during Week 24

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

Program: /CAXXXXX/ECR/sas_prg/pksas/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.2.2 Frequency of Reduction, No Change, or Increase in Cigarettes Per Day and e-Vapor Cartridges Started Per Day from Baseline to Week 24 by Study Group

		Cigarettes per Day			e-Vapor Cartridges Per Day	
Category	statistic	Test 1	Test 2	Control	Test 1	Test 2
Reduction	n (%)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
No Change		XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
Increase		XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)

Note: Baseline = Cigarettes per day (CPD) at Screening (Visit 1) or average e-Vapor cartridges started per day during Week 1 of the 12-week ALCS-RA-16-06-EV study (CA20130)
Week 24 = Average CPD or e-Vapor cartridges started per day during Week 24

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 DDMMMYYYY HH:MM

Table 14.2.2.3.1 Frequency of Subject Days with ≤ 20 or > 20 Puffs per Day for e-Vapor Products by Study Group and Week (Week 12 through Week 18)

		Test 1		Test 2	
Week	Statistic	≤ 20 puffs	> 20 puffs	≤ 20 puffs	> 20 puffs
12	n (%)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
13		XX (XX)	XX (XX)	XX (XX)	XX (XX)
14		XX (XX)	XX (XX)	XX (XX)	XX (XX)
15		XX (XX)	XX (XX)	XX (XX)	XX (XX)
16		XX (XX)	XX (XX)	XX (XX)	XX (XX)
17		XX (XX)	XX (XX)	XX (XX)	XX (XX)
18		XX (XX)	XX (XX)	XX (XX)	XX (XX)
12-18*		XX (XX)	XX (XX)	XX (XX)	XX (XX)

Note: *For Weeks 12 through 18, values represent the average frequency per week.

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

Program: /CAXXXXX/ECR/sas_prg/pksas/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.2.3.2 Frequency of Subject Days with ≤ 20 or > 20 Puffs per Day for e-Vapor Products Study Group and Week (Week 19 through Week 24)

		Test 1		Test 2	
Week	Statistic	≤ 20 puffs	> 20 puffs	≤ 20 puffs	> 20 puffs
19	n (%)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
20		XX (XX)	XX (XX)	XX (XX)	XX (XX)
21		XX (XX)	XX (XX)	XX (XX)	XX (XX)
22		XX (XX)	XX (XX)	XX (XX)	XX (XX)
23		XX (XX)	XX (XX)	XX (XX)	XX (XX)
24		XX (XX)	XX (XX)	XX (XX)	XX (XX)
12-24*		XX (XX)	XX (XX)	XX (XX)	XX (XX)

Note: *For Weeks 12 through 24, values represent the average frequency per week.

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

Program: /CAXXXXX/ECR/sas_prg/pksas/PROGRAMNAME.sas DDMMMYYYY HH:MM

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

		Visit			
Group	Statistics	2	3	4	5
Test 1	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
Test 2	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
Control	<same as above>				

Note: Visit 2 = Week 15 (Day 105 ± 3)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 4 = Week 21 (Day 147 ± 3)
Visit 5 = Week 24 (Day 168 ± 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/pksas/PROGRAMNAME.SAS DDMMMYYYY HH:MM

Note: Tables 14.2.2.4.2, 14.2.2.4.3, and 14.2.2.4.3, (Creatinine-adjusted NNN, absolute change from baseline in creatinine-adjusted NNN, and percent change from baseline in creatinine adjusted NNN) have a similar format as Tables 14.2.1.1.1.1, 14.2.1.1.2.1, and 14.2.1.1.3.1 above.

Table 14.2.2.4.3 Frequency of eCO and Urine NNN by Study Group and Visit

			eCO (ppm)			Urine NNN % reduction*	
			≤ 5	5-8	>8	<80%	≥80%
Group	Visit	N	n (%)	n (%)	n (%)	n (%)	n (%)
Test 1	Baseline	XX	XX (XX)	XX (XX)	XX (XX)	ND	ND
	2	XX	XX (XX)	XX (XX)	XX (XX)	ND	ND
	3	XX	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	4	XX	XX (XX)	XX (XX)	XX (XX)	ND	ND
	5	XX	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
Test 2	Baseline	XX	XX (XX)	XX (XX)	XX (XX)	ND	ND
	2	XX	XX (XX)	XX (XX)	XX (XX)	ND	ND
	3	XX	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	4	XX	XX (XX)	XX (XX)	XX (XX)	ND	ND
	5	XX	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
Control	Baseline	XX	XX (XX)	XX (XX)	XX (XX)	ND	ND
	2	XX	XX (XX)	XX (XX)	XX (XX)	ND	ND
	3	XX	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
	4	XX	XX (XX)	XX (XX)	XX (XX)	ND	ND
	5	XX	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)

Note: *Reduction from Baseline
ND = Not done

Baseline = Day 1 (Week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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/ECR/sas_prg/pksas/PROGRAMNAME.sas DDMMMYYYY 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 (All Subjects*)

			Group		
Parameter	Visit		Test 1	Test 2	Control
Measured FEV1 (L)	Baseline	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
	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
		Median	X.X	X.X	X.X
		Maximum	XX	XX	XX
		95% CI	X, X	X, X	X, X
	5	<same as above>			

Note: *All subjects with a valid baseline and at least one post-baseline post-bronchodilator spirometry session

Baseline = Screening (Visit 2) of the 12 week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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/ECR/sas_prg/pksas/PROGRAMNAME.sas DDMMMYYYY 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 (%), FEV1 reversibility (mL), percent FEV1 reversibility (%), and FEF25-75 (L).

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 in Pulmonary Function Parameters by Study Group and Visit (All Subjects*)

Parameter	Visit		Group: Test 1	Test 2	Control
Measured FEV1 (L)	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
		Median	X.X	X.X	X.X
		Maximum	XX	XX	XX
		95% CI	X, X	X, X	X, X
	5	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: *All subjects with a valid baseline and at least one post-baseline post-bronchodilator spirometry session

Baseline = Screening (Visit 2) of the 12 week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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/ECR/sas_prg/pksas/PROGRAMNAME.sas  DDMMMYYYY  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 (%), FEV1 reversibility (mL), percent FEV1 reversibility (%), and FEF25-75 (L).

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 in Pulmonary Function Parameters by Study Group and Visit (<Population>)

Parameter	Group	Visit	n	-------- LS Mean ----------	XX% Confidence Intervals	p-Value
Percent of Predicted FEV1 (L)	Test 1	3	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
	Test 1	5	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 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 = Screening (Visit 2) of the 12 week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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/ECR/sas_prg/pksas/PROGRAMNAME.sas DDMMMYYYY HH:MM

Note: parameters to be included are: percent of predicted FEV1, percent of predicted FVC, and percent of predicted FEV1/FVC. Please add footnote for all subjects table:*All subjects with a valid baseline and at least one post-baseline post-bronchodilator spirometry session

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 in Pulmonary Function Parameters Between Study Groupsby Visit (<Population>)

Parameter	Comparison	Visit	LS Means Test (n)	LS Means Reference (n)	LS Mean Difference (Test - Reference)	XX% Confidence Intervals	p-Value
Percent of Predicted FEV1 (%)	Test 1 vs Control	3	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
	Test 1 vs Control	5	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 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 = Screening (Visit 2) of the 12 week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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/ECR/sas_prg/pksas/PROGRAMNAME.sas DDMMMYYYY HH:MM

Note: parameters to be included are: percent of predicted FEV1, percent of predicted FVC, and percent of predicted FEV1/FVC. Please add footnote for all subjects table:*All subjects with a valid baseline and at least one post-baseline post-bronchodilator spirometry session.

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:

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Table 14.2.4.1.1 Summary of <QGEN> <Factor Scores> by Study Group and Visit

<Question or Subscale>	Visit		Group: Test 1	Group: Test 2	Group: Control
XXXXX	Baseline	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
	3	<Same as above>			
	5	<Same as above>			
XXXXX <same for remaining questions or subscales>					

Note: Baseline = Day 1 (week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 3)
1 = < >; 2 = < > … X = < >

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 DDMMMYYYY HH:MM

Programmer note: For mCEQ, Visit 3 will not be shown. For mCEQ factor tables, the factors will be shown in a footnote:

Smoking Satisfaction: average of the responses from Questions 1, 2, and 12
Psychological Reward: average of the responses from Questions 4 to 8
Aversion: average of the responses from Questions 9 and 10
Enjoyment of Sensation: response to Question 9
Craving Reduction: response to Question 11

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:

Page 1 of X

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

Subscale	Visit	Group	n	LS Mean	XX% Confidence Intervals	p-Value
XXXXXXXX	3	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
	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
<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.
n = Number of observation used in the analysis
Least-squares means (LS Means) are calculated from the MMRM.

Baseline = Day 1 (week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3
Visit 5 = Week 24 (Day 168 ± 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/ECR/sas_prg/pksas/PROGRAMNAME.sas DDMMMYYYY HH:MM

Programmer note: For mCEQ, only the Visit 5 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:

Page 1 of X

Table 14.2.4.1.3.2 Statistical Comparisons of Absolute Change From Baseline in <QGEN> Factor Scores Between Study Groups by Visit

Subscale	Visit	Comparison	LS Means Test (n)	LS Means Reference (n)	LS Mean Difference (Test - Reference)	XX% Confidence Intervals	p-Value
XXXXXXXXX	3	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
	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

<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.
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 = Day 1 (week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3
Visit 5 = Week 24 (Day 168 ± 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/ECR/sas_prg/pksas/PROGRAMNAME.sas DDMMMYYYY HH:MM

Programmer note: For mCEQ, the model footnote will be "The mixed model includes study group, gender, and age class as fixed effects, and baseline score as the covariate. Least-squares means (LS Means) are calculated from the ANCOVA."

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Table 14.2.4.4.1 Summary of Cough Questionnaire Questions I and III through X by Study Group and Visit

Question	Response	--- Baseline --- Test 1 n (%)	--- Baseline --- Test 2 n (%)	--- Visit 3 --- Test 1 n (%)	--- Visit 3 --- Test 2 n (%)	--- Visit 5 --- Test 1 n (%)	--- Visit 5 --- 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>

Note: Baseline = Day 1 (week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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/ECR/sas_prg/pksas/PROGRAMNAME.sas DDMMMYYYY HH:MM

Programmer note: A third column labelled “Control” will be added to each Visit.

Table 14.2.4.4.2 Summary of Cough Questionnaire Question II by Study Group and Visit

Question	Visit	Statistic	Group: Test 1	Test 2	Control
II. How long have you had the cough? (Days)	Baseline	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 3 and 5)					

Note: Baseline = Day 1 (week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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/ECR/sas_prg/pksas/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.4.5.1 Summary of Reasons of Use/Not-Use Test Product Questionnaire by Study Group at Week 24: Likelihood of Use

			Choice of Response					
Question	Group	Statistics	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 24 = Visit 5 (Day 168 ± 3)

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

Program: /CAXXXXX/ECR/sas_prg/pksas/PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.2.4.5.2 Summary of Reasons of Use/Not-Use Test Product Questionnaire by Study Group at Week 24: Reasons to Use

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 24 = Visit 5 (Day 168 ± 3)

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

Program: /CAXXXXX/ECR/sas_prg/pksas/PROGRAMNAME.sas DDMMMYYYY 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) (CSP population)

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

Note: * Adverse events are classified according to 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/tab cdash_tblae1a_auto.sas DDMMMYYYY HH:MM

Table 14.3.1.2 Adverse Event Frequency by Study Group –
Number of Adverse Events (% of Total Adverse Events) (CSP population)

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

Note: * Adverse events are classified according to 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/tab cdash_tblae1a_auto.sas DDMMMYYYY HH:MM

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

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	X	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.
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 DDMMMYYYY HH:MM

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

			Severity			Relationship to Study Product				
Adverse Event*	Group	Number of Adverse Events	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	X	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.

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_tblae4a_auto.sas DDMMMYYYY 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 DDMMMYYYY HH:MM

Table 14.3.4.1 Out-of-Range Values and Recheck Results – Serum Chemistry (CSP population)

Subject Number	Age/ Gender	Study Visit Name	Study Visit Date	Group	Parameter1	Parameter2	Parameter3	Parameter4	Parameter5
XXXXXX	XX/X	Screening	DDMMMYYYY		XX HN	XX LN	XX	XX	XX HN
		XXX	DDMMMYYYY	X	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 DDMMMYYYY 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 (CSP population)

Laboratory Test (units)	Normal Range	Time Point	Statistic	Product Trial$	Group: Test 1	Group: Test 2	Group: Control	Overall*
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 DDMMMYYYY 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 (CSP population)

				Group			
			Product				
Vital Sign (units)	Time Point	Statistic	Trial$	Test 1	Test 2	Control	Overall*
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
	XXXXXXX	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: /CAXXXXX/sas_prg/stsas/tab cdash_vitsummary.sas DDMMMYYYY 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 (CSP population)

ECG Parameter(units)	Time Point	Statistic	Product Trial$	Group: Test 1	Group: Test 2	Group: Control	Overall*
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
	XXXXXXXXX	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 DDMMMYYYY HH:MM

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

11. 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 = XXXXXXXXXXXXX

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

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

Appendix 16.2.1 Subject Disposition and Discontinuation

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

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.2 Protocol Deviations

	Deviation								
Any Protocol Deviation?	Start Date	End Date	ID	Category	Classification	Description of Deviation	Date of Deviation	Date of Discovery	Action Taken
Yes	DDMMMYYYY	DDMMMYYYY	XX	Minor	Inclusion Criteria	XXXXXXXXXXXXX	DDMMMYYYY	DDMMMYYYY	Approved to Continue

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY 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^2)
XXX	XXXXXX	X	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX
	XXXXXX	X	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX
	XXXXXX	X	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX
	XXXXXX	X	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX
	XXXXXX	X	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX
	XXXXXX	X	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	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 = XXXXXXXXXXXXXXXXX

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY 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	DDMMMYYYY	DDMMMYYYY	XXXXXXX
	XXXXXX	X	DDMMMYYYY	DDMMMYYYY	XXXXXXX
	XXXXXX	X	DDMMMYYYY	DDMMMYYYY	XXXXXXX
	XXXXXX	X	DDMMMYYYY	DDMMMYYYY	XXXXXXX
	XXXXXX	X	DDMMMYYYY	DDMMMYYYY	XXXXXXX
	XXXXXX	X	DDMMMYYYY	DDMMMYYYY	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 = XXXXXXXXXXXXXXXX

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY 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	DDMMMYYYY	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX
	XXXXXX	X	XXX	DDMMMYYYY	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX
	XXXXXX	X	XXX	DDMMMYYYY	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX
	XXXXXX	X	XXX	DDMMMYYYY	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX
	XXXXXX	X	XXX	DDMMMYYYY	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX
	XXXXXX	X	XXX	DDMMMYYYY	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	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 = XXXXXXXXXXXXXXXXX

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.2.1 Physical Examination (I of II)

Subject Number	Visit Name	Date	Day	Study Group	Product	Was PE Done?	Reason for Not Done	System1	System2	System3	System4	System5
XXXXXX	Screening	DDMMMYYYY		X		XXX		XXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX
	XXXXXXX	DDMMMYYYY	-X		X	XXX		XXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX	XXXXXXX
	End of Study	DDMMMYYYY	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 XLCB
Test 2 Group = e-Vapor Product XLMB
Control Group = Continue smoking lit-end conventional cigarette

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.2.2 Physical Examination (II of II)

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

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: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.2.3 Physical Examination Descriptions

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

Note: NCS = 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

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.4.3 Medical History

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

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

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

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

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 DDMMMYYYY HH:MM

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

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

Note: 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/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.1 Inclusion / Exclusion Criteria Not Met

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

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 DDMMMYYYY HH:MM

Appendix 16.2.5.2.1 Test e-Vapor Product Assessment Questionnaire

Subject Number	Visit	Study Group	Questionnaire Completed?	Date	Replace All?*
XXXXXX	XXXXX	X	XXX	DDMMMYYY	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 DDMMMYYYY HH:MM

Appendix 16.2.5.2.2 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 DDMMMYYYY HH:MM

Appendix 16.2.5.2.3 Test e-Vapor Product Accountability

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

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 DDMMMYYYY HH:MM

Programmer Note: Subjects may have multiple dispensing.

Appendix 16.2.5.3 Urine Collection for BOEs and BOPHs

Subject	Visit			Study	Study	Was Collection	Collection		Urine Volume	Ice Pack
Number	Name	Date	Day	Group	Product	Performed?	Date	Time	(mL)	Status
XXXXXX	XXXXX	DDMMMYYYY	XX	X	X	XXX	DDMMMYYYY	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: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.4 Blood Sampling

Subject	Visit			Study	Blood for BOPH			Blood for COHb			Blood for BioBanking		
Number	Name	Date	Day	Group	Collected?	Date	Time	Collected?	Date	Time	Collected?	Date	Time
XXXXXX	XXXXX	DDMMMYYYY	X	X	XXX	DDMMMYYYY	HH:MM	XXX	DDMMMYYYY	HH:MM	XXX	DDMMMYYYY	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: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.5 Exhaled CO Measurement

Subject Number	Visit Name	Visit Date	Visit Day	Study Group	Exhaled CO Measurement Performed?	Exhaled CO Measurement Date	Exhaled CO Measurement Result (ppm)	Exhaled CO Measurement Category*
XXXXXX	XXXXX	DDMMMYYYY	X	X	XXX	DDMMMYYYY	XX	≤ 5 5-8 >8

Note: Test 1 Group = e-Vapor Product XLCB
Test 2 Group = e-Vapor Product XLMB
Control Group = Continue smoking lit-end conventional cigarette
*Category: exhaled CO results fall in one of <=5 parts per million (ppm), 5-8 (ppm), and > 8(ppm).

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.5.6 Prior and Concomitant Medications

Subject Number	Study Group	Study Product	Any Med?	Medication/ 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	DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	Once	Toothache	No	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 DDMMMYYYY HH:MM

Appendix 16.2.6.1 Whole Blood WBC Counts

Subject Number	Study Group	Study Visit	Concentration ($x\ 10^3/\mu L$)	Absolute Change From Baseline ($x\ 10^3/\mu L$)	% Change From Baseline
XXXXX	XXXXXX	Baseline	XXX	XXX	NA
		3	XXX	XXX	XXX
		5	XXX	XXX	XXX

Note: Baseline = Day 1 (Week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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 DDMMMYYYY 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	Baseline	XXX	XXX	NA
		3	XXX	XXX	XXX
		5	XXX	XXX	XXX

Note: Baseline = Day 1 (week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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 DDMMMYYYY HH:MM

Appendix 16.2.6.3 Urine 8-epi-prostaglandin F2α

Subject Number	Study Group	Study Visit	Creatinine (mg/dL)	epi-prostaglandin F2α (pg/mL)	epi-prostaglandin F2α (ng/g Cr)	Absolute Change From Baseline (ng/g Cr)	% Change From Baseline
XXXXXX	XXXXXX	Baseline	XXX	XXX	XXX	NA	NA
		3	XXX	XXX	XXX	XXX	XXX
		5	XXX	XXX	XXX	XXX	XXX

Note: Baseline = Day 1 (week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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 DDMMMYYYY 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	Baseline	XXX	XXX	XXX	NA	NA
		3	XXX	XXX	XXX	XXXX	XXX
		5	XXX	XXX	XXX	XXXX	XXX

Note: Baseline = Day 1 (week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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 DDMMMYYYY 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	Baseline	XXX	XXX	NA
		3	XXX	XXX	XXX
		5	XXX	XXX	XXX

Note: Baseline = Day 1 (week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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 DDMMMYYYY HH:MM

Appendix 16.2.6.6 Urine Total NNAL

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

Note: Baseline = Day 1 (week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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 DDMMMYYYY 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	Baseline	XXX	XXX	NA
		3	XXX	XXX	XXX
		5	XXX	XXX	XXX

Note: Baseline = Day 1 (week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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 DDMMMYYYY HH:MM

Appendix 16.2.6.8.1 Product Used Per Day

Subject Number	Study Group	Study Day	Date	Number of Cigarettes Smoked	Use of other Tobacco Products
XXXXXX	XXXXX	X	DDMMMYYY	XX	Yes
					No

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 DDMMMYYYY HH:MM

Programmer Note: Please include Baseline CPD (Screening value from ALCS-RA-16-06-EV study CA20130)

Appendix 16.2.6.8.2 Test Product Used Per Day

Subject Number	Study Group	Study Day	Date	Number of New Test Products Started	Puffs Per Day
XXXXXX	XXXXX	X	DDMMMYYY	XX	≤20
XXXXXX	XXXXX	X	DDMMMYYY	XX	>20

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

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

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Appendix 16.2.6.8.3 Average Product Used 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 DDMMMYYYY HH:MM

Programmer note: Use NA for control group for test product columns.

Appendix 16.2.6.8.4 Product Used Per Day Change from Baseline

Subject Number	Study Group	Week	Number of Test Products Started: Absolute Change From Baseline	Number of Test Products Started: % Change From Baseline	Number of Test Products Started: Change Category	Number of Cigarettes Smoked: Absolute Change From Baseline	Number of Cigarettes Smoked: % Change From Baseline	Number of Cigarettes Smoked: Change Category
XXXXX	XXXXXX	18	XXX	XXX	Reduction	XXXX	XXX	Reduction
XXXXX	XXXXXX	24	XXX	XXX	No Change	XXXX	XXX	No Change
XXXXX	XXXXXX	1-24	NA	NA	NA	XXXX	XXX	Increase

Note: Baseline is cigarettes per day at Screening (Visit 1) or average e-Vapor cartridges started per day during Week 1 of the 12-week ALCS-RA-16-06-EV study (CA20130).

Week 18 = Average of Week 18 (Day 126 ± 3)
Week 24 = Average of Week 24 (Day 168 ± 3)
Week 1-24 = Average of Weeks 1-24

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 DDMMMYYYY HH:MM

Programmer note: Please include baseline columns (one for test products started and one for cigarettes smoked).

Appendix 16.2.6.9 Urine NNN

Subject Number	Study Group	Study Visit	Creatinine (mg/dL)	NNN (pg/mL)	NNN (ng/g Cr)	Absolute Change From Baseline (ng/g Cr)	% Change From Baseline	Change Category
XXXXX	XXXXXX	Baseline	XXX	XXX	XXX	NA	NA	NA
		3	XXX	XXX	XXX	XXXX	XXX	<80%
		5	XXX	XXX	XXX	XXXX	XXX	≥80%

Note: Baseline = Day 1 (Week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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 DDMMMYYYY HH:MM

Appendix 16.2.6.10.1 Pulmonary Function Test (Spirometry) (I of II)

Subject	Visit		Study	Assessment		FVC (L)			FEV1 (L)		
Number	Visit	Date	Group	Date	Time	Actual	Predicted	%Predicted	Actual	Predicted	%Predicted
XXXXXX	XXXX	DDMMMYYYY	X	DDMMMYYYY	HH:MM	XX	XX	XX	XX	XX	XX
	XXXX	DDMMMYYYY		DDMMMYYYY	HH:MM	XX	XX	XX	XX	XX	XX

Note: Baseline = Screening (Visit 2) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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 DDMMMYYYY HH:MM

Parameters for Appendices 16.2.6.10.1 and 16.2.6.10.2 are:
FEV1 (L)
Predicted FEV1 (L)
% of Predicted FEV1
FVC (L)
Predicted FVC (L)
% of Predicted FVC
FEV1/FVC
% of Predicted FEV1/FVC
FEV1 reversibility (mL)
% FEV1 reversibility
FEF25-75 (L)

Appendix 16.2.6.10.3 Pulmonary Function Test (Spirometry) Absolute Change from Baseline

Subject Number	Visit	Study Group	Percent of Predicted FEV1	Percent of Predicted FVC	Percent of Predicted FEV1/FVC
XXXX	X	XXXXXX	XXXX	XXXX	XXXX
XXXX	X	XXXXXX	XXXX	XXXX	XXXX

Note: Baseline = Screening (Visit 2) of the 12-week ALCS-RA-16-06-EV study (CA20130)

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 DDMMMYYYY HH:MM

Parameters are:
FEV1 (L)
Predicted FEV1 (L)
% of Predicted FEV1
FVC (L)
Predicted FVC (L)
% of Predicted FVC
FEV1/FVC
% of Predicted FEV1/FVC
FEV1 reversibility (mL)
% of Predicted FEV1 reversibility
FEF25-75

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	Baseline	XXX	XXX	XXX	XXXX	XXX	XXX
		3	XXX	XXX	XXX	XXXX	XXX	XXX
		5	XXX	XXX	XXX	XXXX	XXX	XXX

Note: Baseline = Day 1 (week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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 DDMMMYYYY HH:MM

Appendix 16.2.6.11.2 Urine Nicotine Equivalents

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

Note: Baseline = Day 1 (week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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 DDMMMYYYY HH:MM

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

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	DDMMMYYYY	HH:MM:SS	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?

Baseline = Day 1 (week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 5 = Week 24 (Day 168 ± 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/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY 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	XXXXXXXXX	DDMMMYYYY	HH:MM:SS	X	X	X	X	X
		XXXXXXXXX	DDMMMYYYY	HH:MM:SS	X	X	X	X	X
		XXXXXXXXX	DDMMMYYYY	HH:MM:SS	X	X	X	X	X
		XXXXXXXXX	DDMMMYYYY	HH:MM:SS	X	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

Baseline = Day 1 (week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 5 = Week 24 (Day 168 ± 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/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY 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 DDMMMYYYY 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	DDMMMYYYY	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.

Baseline = Day 1 (week 1) of the 12-week ALCS-RA-16-06-EV study (CA20130)
Visit 3 = Week 18 (Day 126 ± 3)
Visit 5 = Week 24 (Day 168 ± 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/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY 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	DDMMMYYYY	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

Visit 5 = Week 24 (Day 168 ± 3)

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

Program: /CAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.6.12.5.2 Reasons of Use/Not-Use Test Product Questionnaire (II of II)

Subject Number	Study Group	Study Visit	Date	Time	Reason(s) to Use: Smoking/Other Tobacco-Related Reasons	Reason(s) to Use: General Reasons
XXXXX	XXXXXX	X	DDMMMYYYY	HH:MM:SS	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXX

Note: Visit 5 = Week 24 (Day 168 ± 3)

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

Program: /CAXXXXX/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.6.12.6 End-of-Study Questionnaire

Subject Number	Study Group	Study Visit	Date	Time	End-of-study question 1	2	3
XXXXX	XXXXXX	X	DDMMMYYYY	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…

Visit 5 = Week 24 (Day 168 ± 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/ECR/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY 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 (DD:HH:MM)	Onset Date	Onset Time	Resolved Date	Resolved Time	Duration (DD:HH:MM)
XXXXXX	X	X	XXX	XX	XXXXXXXXXXXXX	XXXXXXXXXX XXXXXXX	XX:XX:XX	DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	XX:XX:XX
XXXXXX	X	X	XXX	XX	XXXXXXXXXXXXX	XXXXXXXXXX XXXXXXX	XX:XX:XX	DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	XX:XX:XX
XXXXXX	X	X	XXX	XX	XXXXXXXXXXXXX	XXXXXXXXXX XXXXXXX	XX:XX:XX	DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	XX:XX:XX
XXXXXX	X	X	XXX	XX	XXXXXXXXXXXXX	XXXXXXXXXX XXXXXXX	XX:XX:XX	DDMMMYYYY	HH:MM	DDMMMYYYY	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 DDMMMYYYY HH:MM

Appendix 16.2.7.2 Adverse Events (II of II)

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

Appendices 16.2.8.2 to 16.2.8.3 will have the following format.

Page 1 of X

Appendix 16.2.8.1 Clinical Laboratory Report - Serum Chemistry

Subject Number	Age/ Gender	Study Group	Visit Name	Visit Date	Collection Date	Collection Time	Parameter1	Parameter2	Parameter3	Parameter4	Parameter5	Parameter6
XXXXXX	XX/X	X	Screening	DDMMMYYYY	DDMMMYYYY	HH:MM	XX HN	XX	XX	XX	XX HN	XX
			XXXXXX	DDMMMYYYY	DDMMMYYYY	HH:MM	XX HN	XX	XX	XX	XX HN	XX
			XXXXXX	DDMMMYYYY	DDMMMYYYY	HH:MM	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 DDMMMYYYY 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		
		Name	Date		Date	Time	Result
XXXXXX	X	Screening	DDMMMYYYY	XXX	DDMMMYYYY	HH:MM	XXXXXX
		Check-in	DDMMMYYYY	XXX	DDMMMYYYY	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 DDMMMYYYY HH:MM

Appendix 16.2.8.5 Urine Drug Screens

Subject Number	Study Group	Visit Name	Visit Date	Was the Urine Sample Collected?	Date of Collection	Test Name	Result
XXXXXX	X	Screening	DDMMMYYYY	XXX	DDMMMYYYY	XXXXXXXXXXXXX	XXXXXX
						XXXXXXXXXXXXX	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 DDMMMYYYY HH:MM

Appendix 16.2.8.6 Pregnancy Tests

Subject Number	Study Group	Visit Name	Visit Date	Was the Pregnancy Test Done?	Reason for Not Done	Collection Date	Category	Test Name	Test Result	Test Code
XXXXXX	X	Screening	DDMMMYYYY	XXX		DDMMMYYYY	XXXXXX	XXXX	XXX	XXXX
		XXXXXXXXX	DDMMMYYYY	XXX		DDMMMYYYY	XXXXXX	XXXX	XXX	XXXX

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 DDMMMYYYY 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	DDMMMYYYY	XXX	DDMMMYYYY	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 DDMMMYYYY 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	DDMMMYYYY	XXX	DDMMMYYYY	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: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.9 Clinical Laboratory Report – Comments

Subject Number	Study Group	Visit Name	Visit Date	Date	Department	Test	Result	Unit	Comment
XXXXXX	X	Screening	DDMMMYYYY	DDMMMYYYY	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: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.10 Vital Signs

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

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

Appendix 16.2.8.12 Smoking Cessation Information

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

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:MM

Appendix 16.2.8.13 Reminder Phone Call

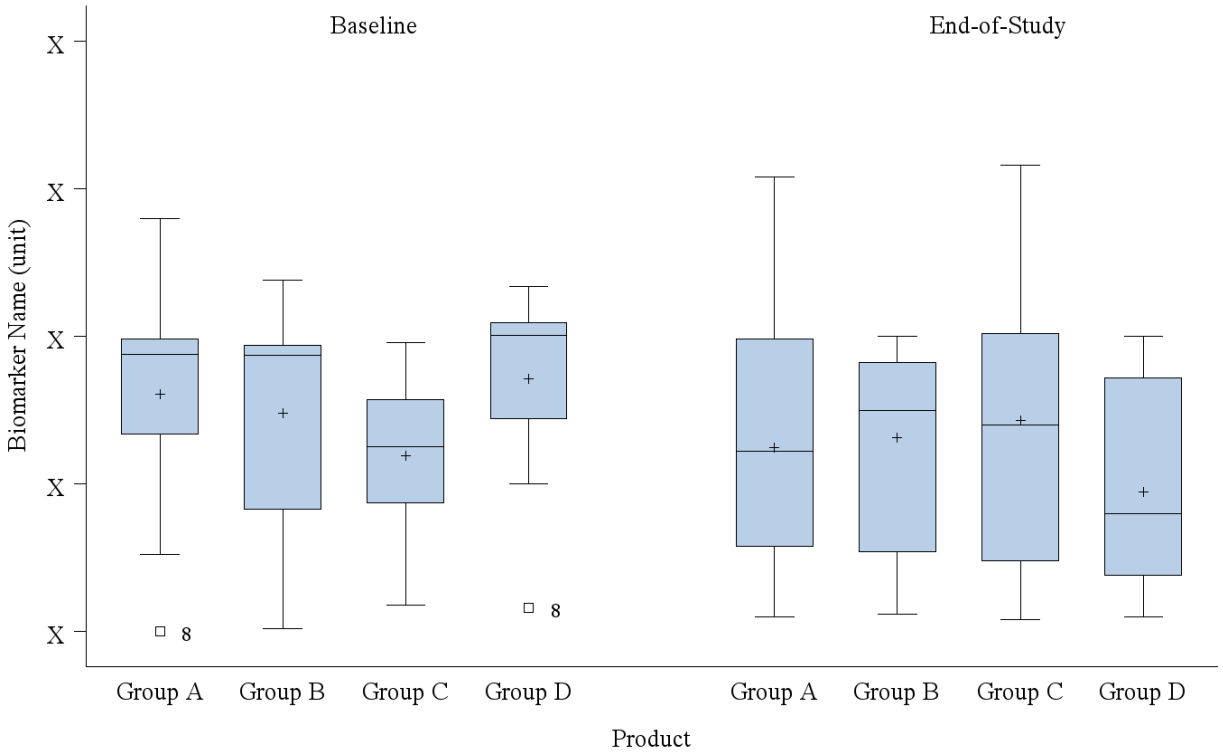
Subject Number	Visit	Was a Reminder Call Performed Within 24-48 Hours of This Visit?	Date
XXXXXX	Screening	XXX	DDMMMYYYY
	End of Study	XXX	DDMMMYYYY

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMMYYYY HH:M

12. FIGURE SHELLS

Box plots will be presented as in the figure below, with the headings of Baseline, Visit 3 or Visit 5 and X axis label of Study Group:

Figure 14.2.5.1.1
Box Plot of Whole Blood WBC Count (x 10^3/µL) at Baseline and Visit 5 by Study Group (mITT Population)



The upper and lower whiskers of the boxplot represent, respectively, the largest and smallest observed values within 1.5 × 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 DDMMMYYYY HH:MM