A RANDOMIZED, CONTROLLED, OPEN-LABEL SHORT-TERM STUDY TO EVALUATE CHANGES IN EXPOSURE TO HARMFUL AND POTENTIALLY HARMFUL CONSTITUENTS IN ADULT SMOKERS WHO PARTIALLY OR COMPLETELY SWITCH TO VERVE® PRODUCTS (DISCS OR CHEWS) IN A CLINICAL SETTING

NCT03692078

06AUG2018

Statistical Analysis Plan

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Protocol No. ALCS-RDS-18-04-VRV
Celerion Project CA24563
Final Version 1.2
Date: 06 August 2018

Final Protocol Date: 30 March, 2018
Final Protocol Amendment 1 Date: 25 May 2018

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Statistical Analysis Plan Signature Page

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Issue Date: 06 August 2018

Signature: [redacted] Date: 06 AUG 2018

[redacted]

Signature: [redacted] Date: 09 AUG 2018

[redacted]

Signature: [redacted] Date: 06AUG2018

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ABBREVIATIONS AND DEFINITIONS

1-OHP	1-hydroxypyrene
1-OHPhe	1-OH-Phenanthrene
2-AN	2-aminonaphthalene
2-HPMA	2-hydroxypropyl-mercapturic acid
2-MHBMA	2-hydroxybutenyl-mercapturic acid
2-OHFle	2 OH-Fluorene
3-HMPMA	3-hydroxy-1-methylpropylmercapturic acid
3-HPMA	3-hydroxypropylmercapturic acid
4-ABP	4-aminobiphenyl
AAMA	N-acetyl-S-(2-carbamoylethyl)-l-cysteine
AE	adverse event
AIC	Akaike information criterion
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
CEMA	2-cyanoethylmercapturic acid
CI	confidence interval
CO	carbon monoxide
COHb	carboxyhemoglobin
CPD	cigarettes per day
CSR	clinical study report
CV	coefficient of variation
ECG	electrocardiogram
EOS	end-of-study
FTCD	Fagerström Test for Cigarette Dependence
GAMA	N-acetyl-S-(2-carbamoyl-2-hydroxyethyl)-l-cysteine
HEMA	2-hydroxyethyl mercapturic acid
HPHC	harmful and potentially harmful constituents
ICF	informed consent form
ICH	International Conference on Harmonization
ITT	intent to treat
kg	kilogram(s)
LC-MS	liquid chromatography–mass spectrometry
LLOQ	lower limit of quantitation
LLC	limited liability company
m	meter(s)
mCEQ	modified Cigarette Evaluation Questionnaire
MedDRA	Medical Dictionary for Regulatory Activities
mg	milligram(s)
mITT	modified intent to treat

mL	milliliter(s)
MMRM	mixed model for repeated measures
N, n	sample size, number of observations
NE	nicotine Equivalents
ng	nanograms
NNAL	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol
NNN	N-nitrosonornicotine
OB	own brand
OTDN	oral tobacco-derived nicotine
pg	pictogram
PP	per-protocol
Q1	first quartile
Q3	third quartile
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
SEM	standard error of the mean
S-PMA	S-phenyl mercapturic acid
µg	microgram
VPD	VERVE® product(s) per day
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. STUDY PURPOSE, HYPOTHESIS, OBJECTIVES AND ENDPOINTS

2.1 Study Purpose

The purpose of this study is to evaluate changes in exposure to selected harmful and potentially harmful constituents (HPHC) by measuring biomarkers in adult smokers who partially or completely switch from smoking to oral tobacco-derived nicotine (OTDN) products VERVE® Chews or VERVE® Discs use compared to those who continue exclusively smoking cigarettes or stop using all tobacco products.

2.2 Hypothesis:

Reducing daily cigarette consumption by at least 50% and using VERVE® products will result in a statistically significant reduction in 24-hour urinary total 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) on Day 7 compared to continued cigarette smoking.

2.3 Objectives

2.3.1 Primary Objective

The primary objective is to:

To compare 24-hour urinary total NNAL in adult smokers who reduce cigarette consumption by at least 50% with supplementary (dual) usage of VERVE® Chews or VERVE® Discs to those who continue to smoke cigarettes for 7 days.

2.3.2 Secondary Objectives

The secondary objectives are to:

1. To compare biomarkers of exposure (total N-nitrosonornicotine [NNN], nicotine equivalents [NE], 2-aminonaphthalene [2-AN], 4-aminobiphenyl [4-ABP], 2-hydroxyethyl mercapturic acid [HEMA], 2-cyanoethylmercapturic acid [CEMA], S-phenyl mercapturic acid [S-PMA], 3-hydroxy-1-methylpropylmercapturic acid [3-HMPMA], 3-hydroxypropylmercapturic acid [3-HPMA], 2-hydroxypropyl-mercapturic acid [2-HPMA], N-acetyl-S-(2-carbamoylethyl)-l-cysteine [AAMA], N-acetyl-S-(2-carbamoyl-2-hydroxyethyl)-l-cysteine [GAMA], 2-hydroxybutenyl-mercapturic acid [2-MHBMA], 2-OH-

Fluorene [2-OHFle], 2-Naphthol,1-OH-Phenanthrene [1-OHPhe], urine mutagenicity, 1-hydroxypyrene [1-OHP], and carboxyhemoglobin [COHb]) in adult smokers who reduce cigarette consumption by at least 50% with supplementary (dual) usage of VERVE® Chews or VERVE® Discs to those who continue to smoke cigarettes for 5 and 7 days.

2. To compare 24-hour urinary total NNAL in adult smokers who reduce cigarette consumption by at least 50% with supplementary (dual) usage of VERVE® Chews or VERVE® Discs to those who continue to smoke cigarettes for 5 days.
3. To compare biomarkers of exposure (total NNAL, total NNN, NE, 2-AN, 4-ABP, HEMA, CEMA, S-PMA, 3-HMPMA, 3-HPMA, 2-HPMA, AAMA, GAMA, 2-MHBMA, 2-OHFle, 2-Naphthol, 1-OHPhe, urine mutagenicity, 1-OHP and COHb) in adult smokers who reduce cigarette consumption by at least 50% with supplementary (dual) usage of VERVE® Chews or VERVE® Discs to those who cease from all tobacco use for 5 and 7 days.
4. To compare biomarkers of exposure (total NNAL, total NNN, NE, 2-AN, 4-ABP, HEMA, CEMA, S-PMA, 3-HMPMA, 3-HPMA, 2-HPMA, AAMA, GAMA, 2-MHBMA, 2-OHFle, 2-Naphthol, 1-OHPhe, urine mutagenicity, 1-OHP and COHb) in adult smokers who completely switch to VERVE® Chews or VERVE® Discs to those who continue to smoke cigarettes for 5 and 7 days.
5. To compare biomarkers of exposure (total NNAL, total NNN, NE, 2-AN, 4-ABP, HEMA, CEMA, S-PMA, 3-HMPMA, 3-HPMA, 2-HPMA, AAMA, GAMA, 2-MHBMA, 2-OHFle, 2-Naphthol, 1-OHPhe, urine mutagenicity, 1-OHP and COHb) in adult smokers who completely switch to VERVE® usage to those who cease from all tobacco use for 5 and 7 days.
6. To compare subjective effects (Questionnaire of Smoking Urges – Brief [QSU-Brief] total score, responses to modified cigarette evaluation questionnaire [mCEQ] and the Use the Product Again questionnaire) among subjects who continue to smoke cigarettes, subjects with dual usage of VERVE® Chews or VERVE® Discs and cigarettes, subjects with complete switch to VERVE® Chews or VERVE® Discs, and subjects who cease from all tobacco use for 1, 5 and 7 days.
7. To characterize product use behaviors (such as: number of cigarettes per day [CPD], number of VERVE® use per day [VPD], average and total duration of VERVE® use each day).

2.4 Outcome Variables

Primary

The primary outcome variable is:

- 24-hour total urinary NNAL (ng/24 hours) excreted on Day 7.

Secondary

The secondary outcome variables are:

- 24-hour urinary total total NNN, NE, 2-AN, 4-ABP, HEMA, CEMA, S-PMA, 3-HMPMA, 3-HPMA, 2-HPMA, AAMA, GAMA, 2-MHBMA, 2-OHFle, 2-Naphthol, 1-OHPhe, mutagenicity, and 1-OHP excreted on Day 5 and Day 7.
- 24-hour urinary total NNAL excreted on Day 5.
- COHb on Day 5 and Day 7.
- QSU-Brief responses and factor scores on Day 1, Day 5, and Day 7.
- Responses to the appropriate mCEQ on Day 1, Day 5, and Day 7.
- Responses to the appropriate Use the Product Again questionaire on Day 7.
- Product use behavior daily from Day 1 to Day 7 (i.e., CPD, VPD, and the average and total duration of VERVE® product use each day).

Clinical Safety

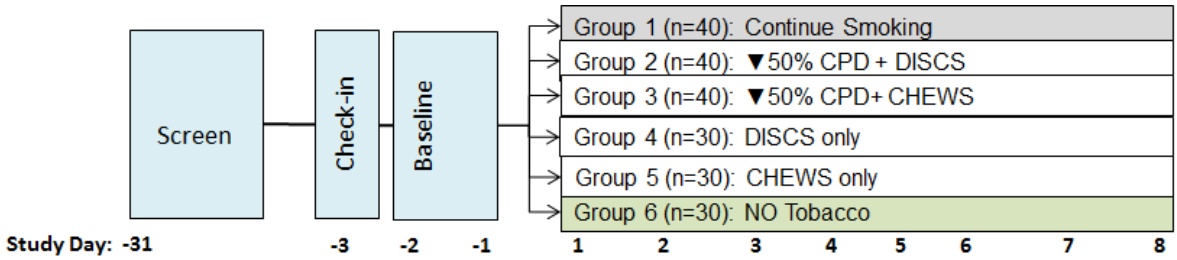
- AEs and SAEs
- ECG, vital signs, clinical chemistry, urinalysis, and hematology

3. STUDY DESIGN

This is an open label, randomized, 6 parallel-group clinical study evaluating changes in exposure to selected HPHCs, subjective effects, and product use behavior in adult smokers who are randomly assigned to continue smoking, partially or completely switch to VERVE® Chews or VERVE® Discs products, or stop using all tobacco products for 7 days.

The overall design of the study is shown in Figure 1.

Figure 1: Overall Study Design



Study Products:

Product A: Subject's own brand (OB) Cigarette (Reference Product)

Product B: Oral tobacco-derived nicotine chews marketed as VERVE® Discs Blue Mint (~1.5 mg nicotine/piece) (Test Product)

Product C: Oral tobacco-derived nicotine chews marketed as VERVE® Discs Green Mint (~1.5 mg nicotine/piece) (Test Product)

Product D: Oral tobacco-derived nicotine chews marketed as VERVE® Chews Blue Mint (~1.5 mg nicotine/piece) (Test Product)

Product E: Oral tobacco-derived nicotine chews marketed as VERVE® Chews Green Mint (~1.5 mg nicotine/piece) (Test Product)

Approximately 210 healthy adult male and female (no more than 60% of either gender) self-affirmed combustible cigarette smokers, 21 - 65 years of age, inclusive (determined at Screening), willing to abstain from smoking and use all four VERVE® products, and who fulfill all inclusion criteria and none of the exclusion criteria will be enrolled. All subjects must have an average daily consumption of at least 10 but no more than 30 factory manufactured combustible cigarettes for at least 12 months prior to Screening. Use of other types of tobacco- or nicotine-containing products will not be permitted within 1 week prior to Check-in.

Subjects, who meet all inclusion criteria and none of the exclusion criteria, will check-in to the clinic on Day -3 at a time determined by the clinic. After check-in, subjects will engage in a brief product trial with each flavor of VERVE® Chews (two flavors: blue mint and green mint) and VERVE® Discs (two flavors: blue mint and green mint). This trial period will involve *ad libitum* use for 10 minutes each to allow subjects to become accustomed to using the products. The trial of each flavor of VERVE® Chews or VERVE® Discs product will be separated by approximately 30 minutes (from the start of each product trial). Subjects who are unwilling to use and/or cannot tolerate all four VERVE® products will not continue in the study.

Following completion of the VERVE® product trial on Day -3, subjects will continue to smoke their OB cigarettes through 23:00 on Day -3 and from 07:00 to 23:00 on Days -2 and -1. Baseline cigarette consumption for each subject will be determined by the average number of cigarettes smoked (CPD) on Day -2 and Day -1 and will be used to calculate the CPD allowed for each subject in Group 2 or Group 3, according to their assigned randomization group, for the remainder of the study. Other baseline study events will include 24-hour urine collections for biomarkers of exposure (total NNAL, total NNN, NE, 2-AN, 4-ABP, HEMA, CEMA, S-PMA, 3-HMPMA, 3-HPMA, 2-HPMA, AAMA, GAMA, 2-MHBMA, 2-OHFle, 2-Naphthol, 1-OHPhe, mutagenicity, and 1-OHP), blood sampling for COHb, and administration of the QSU-Brief and the appropriate mCEQ questionnaire on Day -1.

On Day 1, subjects will be randomized into one of the following Groups:

- GROUP 1 (n = 40): Continue Smoking

Subjects will be asked to continue smoking their OB cigarettes *ad libitum* for 7 days.

- GROUP 2 (n = 40): VERVE® Discs Dual Use

Subjects will reduce their normal daily cigarette consumption by at least 50% of their baseline CPD and use at least 3 VERVE® Discs per day for 7 days.

- GROUP 3 (n = 40): VERVE® Chews Dual Use

Subjects will reduce their normal daily cigarette consumption by at least 50% of their baseline CPD and use at least 3 VERVE® Chews per day for 7 days.

- GROUP 4 (n = 30): VERVE® Discs Exclusive Use

Subjects will completely switch to exclusive use of VERVE® Discs, using at least 3 discs per day for 7 days.

- GROUP 5 (n = 30): VERVE® Chews Exclusive Use

Subjects will completely switch to exclusive use of VERVE® Chews, using at least 3 chews per day for 7 days.

- GROUP 6 (n = 30): Tobacco Cessation

Subjects will completely stop all tobacco product usage for 7 days.

Subjects will be randomized into each Group on Day 1 based on gender and CPD.

Subjects will begin using the assigned study products or completely stop using tobacco products on the morning of Day 1 and continue through discharge according to the randomization.

On each study day (Days 1 - 7), subjects in Group 1 will be allowed to smoke their OB cigarettes *ad libitum* (i.e., no restriction on the duration of use or the number of cigarettes per day) from 07:00 through 23:00. Subjects will be allowed to smoke upon request to the clinic staff but will only be allowed 1 cigarette at a time and will be instructed to return each cigarette butt upon completion.

On each study day (Days 1 - 7), subjects in Group 2 and Group 3 will smoke no more than 50% of their baseline CPD and will use the assigned VERVE® product *ad libitum* (i.e., no restrictions on the number of VERVE® products used at once, the number of VERVE® products used per day, or the duration of use) except for 3 specific VERVE® products use opportunities at approximately 11:00, 15:00, and 19:00 each day during which subjects will be asked to keep the assigned VERVE® product in their mouth for at least 10 minutes. Subjects will be allowed to smoke upon request to the clinic staff but will only be allowed 1 cigarette at a time and will be instructed to return each cigarette butt upon completion. Subjects will be allowed to use the VERVE® product upon request [more then 1 permitted at a time, but all returned before more are dispensed] and they will be instructed to return each used VERVE® product upon completion.

On each study day (Days 1 - 7), subjects in Group 4 and Group 5 will use the assigned VERVE® product *ad libitum* (i.e., no restrictions on the number of VERVE® products used at once, the number of VERVE® products used per day, or the duration of use) except for 3 specific VERVE® products use opportunities at approximately

11:00, 15:00, and 19:00 each day during which subjects will be asked to keep the assigned VERVE® product in their mouth for at least 10 minutes. Subjects will be allowed to use the VERVE® product upon request [more then 1 permitted at a time, but all returned before more are dispensed] and they will be instructed to return each used VERVE® product upon completion.

On each study day (Days 1 - 7), subjects in Group 6 will completely stop cigarette use and they will not be allowed to smoke or use VERVE® products.

All product use (CPD, VPD, and VERVE® product use duration, [i.e., time of VERVE® product placement in the subjects' mouth, and time it was removed from the subjects' mouth], as appropriate) will be determined to assess product use behavior.

Study events will include 24-hour urine collections for biomarkers of exposure (total NNAL, total NNN, NE, 2-AN, 4-ABP, HEMA, CEMA, S-PMA, 3-HMPMA, 3-HPMA, 2-HPMA, AAMA, GAMA, 2-MHBMA, 2-OHFle, 2-Naphthol, 1-OHPhe, mutagenicity, and 1-OHP) and blood sample collection for COHb assessment. Urine creatinine will be measured in each 24-hour collection and will be used to adjust the concentration values of urine biomarkers. Each 24-hour urine collection (Day -1, Day 5 and Day 7) will be from approximately (± 30 minutes) 07:00 on the scheduled day to approximately 07:00 the following day. The 24-hour urine collection begins on each scheduled day after the first morning void and any void prior to 07:00, and finishes the following morning with the last void collected at approximately 07:00 (including first morning void). Subjects will be specifically instructed to collect all urine voided, and any missed collection during the 24-hour interval will be documented as a deviation.

Subjects will also complete in the moment subjective effects questionnaires, which include QSU-Brief (Protocol Appendix 2), Modified Cigarette Evaluation Questionnaire (mCEQ-C & mCEQ-V; Protocol Appendix 3), and Use the Product Again questionnaire (UPA-C & UPA-V; Protocol Appendix 4). Details for subject effect data collection is in Section 7.1.4.1.

4. SAMPLE SIZE ESTIMATION

This study is designed to evaluate changes in exposure to selected HPHC when adult smokers partially or completely switch to oral tobacco-derived nicotine VERVE® Chews or VERVE® Discs compared to those who continue smoking cigarettes or stop using all tobacco products. Assuming a similar effect size for the new study as for the previous ALCS study (ToPP4ST_1011_07) between the continued cigarette smoking group and each of the two dual usage groups (≥50% CPD reduction with VERVE® DISCS or VERVE® CHEWS), a two-sided t test, 85% power and an α =0.025 Type I error rate to account for the multiplicity adjustment for the two comparisons, 35 subjects are needed to complete for the continue cigarette smoking group and the dual usage groups. We expect that the effect will be larger in the VERVE® only and smoking cessation groups, so 25 subjects are needed to complete in these groups.

5. ANALYSIS POPULATIONS

Safety Analysis Dataset:

All subjects who used any study products (including subjects randomized to Group 6).

Modified Intent-to-Treat (mITT) Dataset:

All randomized subjects who used at least one study product after randomization (except Group 6) and have a valid baseline and at least one post-baseline biomarker measure of any one biomarker.

Per-Protocol (PP) Dataset:

A subset of the mITT dataset and includes subjects who completed the study without important (or major) protocol deviations that are considered to impact data integrity (e.g., non adherence to study group assignment).

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

6. STUDY GROUP AND PRODUCT DESCRIPTIONS

The following products will be tested in this study:

Product A: Subject's OB Cigarette (Reference Product)

Product B: Oral tobacco-derived nicotine chews marketed as VERVE® Discs Blue Mint (~1.5 mg nicotine/piece) (Test Product)

Product C: Oral tobacco-derived nicotine chews marketed as VERVE® Discs Green Mint (~1.5 mg nicotine/piece) (Test Product)

Product D: Oral tobacco-derived nicotine chews marketed as VERVE® Chews Blue Mint (~1.5 mg nicotine/piece) (Test Product)

Product E: Oral tobacco-derived nicotine chews marketed as VERVE® Chews Green Mint (~1.5 mg nicotine/piece) (Test Product)

The following groups will be tested in this study and the group descriptions will be used in the footnotes for listings, tables, and figures:

GROUP 1: Continue Smoking

GROUP 2: VERVE® Discs Dual Use

GROUP 3: VERVE® Chews Dual Use

GROUP 4: VERVE® Discs Exclusive Use

GROUP 5: VERVE® Chews Exclusive Use

GROUP 6: Tobacco Cessation

Study groups will be referred to in the text as: Continue Smoking Group, VERVE® Discs Dual Use Group, VERVE® Chews Dual Use Group, VERVE® Discs Exclusive Use Group, VERVE® Chews Exclusive Use Group, and Tobacco Cessation Group.

7. BIOMARKER ASSESSMENT AND ANALYSIS

7.1 Biomarkers Sample Collection and Measurements

7.1.1 Urine Biomarkers of Exposure (BOE)

7.1.1.1 Urine BOE Sample Collection

24-hour urine collections for biomarkers of exposure (total NNAL, total NNN, NE, 2-AN, 4-ABP, HEMA, CEMA, S-PMA, 3-HMPMA, 3-HPMA, 2-HPMA, AAMA, GAMA, 2-MHBMA, 2-OHFle, 2-Naphthol, 1-OHPhe, mutagenicity, and 1-OHP) will be performed on Days -1, 5, and 7. Urine creatinine will be measured in each 24-hour collection and will be used to adjust the concentration values of urine biomarkers. Each 24-hour urine collection will be from approximately (± 30 minutes) 07:00 on the scheduled day to approximately 07:00 the following day. The 24-hour urine collection begins on each scheduled day after the first morning void and any void prior to 07:00, and finishes the following morning with the last void collected at approximately 07:00 (including first morning void). Subjects will be specifically instructed to collect all urine voided, and any missed collection during the 24-hour interval will be documented as a deviation.

7.1.1.2 Bioanalytical Method

Urine aliquots for NE 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 aliquots for NNAL, NNN, 2-AN, 4-ABP, HEMA, CEMA, S-PMA, 3-HMPMA, 3-HPMA, 2-HPMA, AAMA, GAMA, 2-MHBMA, 2-OHFle, 2-Naphthol, 1-OHPhe, and 1-OHP will be shipped to ABF for analysis.

Mutagenicity testing will be done by Labstat.

7.1.1.3 Urine Biomarker Analysis Variables

The following variables will be determined for each urine biomarker except mutagenicity testing.

- Measured concentration
- Total biomarker mass excreted per 24 hours (primary analysis variable)
- Total mass excreted per 24 hours absolute change from Baseline
- Total mass excreted per 24 hours percent change from Baseline
- Measured concentration adjusted for urine creatinine

Urine biomarker concentration values reported as below the limit of quantitation (BLQ) will be set to one-half of the limit of quantitation prior to calculating the 24-hour mass excreted. Total urine weight (g) will be collected during the study and converted to urine volume using the assumed density of 1 gram (g) equals 1 milliliter (mL).

Creatinine-adjusted concentrations will be calculated as shown in Section 7.1.1.3.2. Absolute and percent change from baseline will be calculated as shown in Section 7.1.1.3.3.

7.1.1.3.1 Urine Nicotine Equivalents

NE will be calculated as the molar sum of nicotine and 5 major nicotine metabolites excreted in urine over 24 hours. Values of individual components reported as below the limit of quantitation will be set to one-half of the limit of quantitation prior use in the calculation below.

The concentration of each metabolite will first be multiplied by the 24-hour urine volume to obtain the total amount excreted in 24 hours, then divided by the molecular weight of the metabolite to obtain the total amount of each in moles. The sum in moles will then be converted to mass of NE by multiplying by the molecular weight of nicotine.

Nicotine (mg/24h)	=	nicotine concentration [ng/mL] × 24h urine volume [mL] ÷ 1000 000
Nicotine-glucuronide (mg/24h)	=	nicotine glucuronide concentration [ng/mL] × 24h urine volume [mL] ÷ 1000 000
Cotinine (mg/24 hours)	=	cotinine concentration [ng/mL] × 24h urine volume [mL] ÷ 1000 000
Cotinine-glucuronide (mg/24h)	=	cotinine glucuronide concentration [ng/mL] × 24h urine volume [mL] ÷ 1000 000
Trans-3'-hydroxycotinine (mg/24h)	=	trans-3'-hydroxycotinine concentration [ng/mL] × 24h urine volume [mL] ÷ 1000 000
Trans-3'-hydroxycotinine-glucuronide (mg/24h)	=	trans-3'-hydroxycotinine glucuronide concentration [ng/mL] × 24h urine volume [mL] ÷ 1000 000

Nicotine equivalents (mg/24 hours)	=	(nicotine [mg/24h]/162.23 [mg/mmol] + nicotine-gluc [mg/24h]/338.36 [mg/mmol] + cotinine [mg/24h]/176.22 [mg/mmol] + cotinine-gluc [mg/24h]/352.34 [mg/mmol] + trans-3'-hydroxycotinine [mg/24h]/192.22 [mg/mmol] + trans-3'-hydroxycotinine-gluc [mg/24h]/368.34 [mg/mmol]) x 162.23 (mg/mmol)

7.1.1.3.2 Urine Biomarkers Adjusted for Urine Creatinine

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

Nicotine Equivalents

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

Other Urine Biomarkers

$$\text{Urine biomarker (unit2/g creatinine)} = \frac{\text{urine biomarker (unit1/mL)} \times 100}{\text{creatinine (mg/dL)}}$$

Where: if unit1 = pg, then unit2 = ng and if unit1 = ng, then unit2 = µg

7.1.1.3.3 Urine Biomarker Change From Baseline

Urine biomarker change from baseline will be calculated as follows, where Baseline = Day -1:

Absolute change from baseline = Post Randomization Value – Baseline Value

Percent change from baseline (%) = (Post Randomization Value – Baseline Value) / Baseline Value x 100 %

7.1.1.3.4 Urine Mutagenicity

Urine mutagenicity will be analyzed and reported by Labstat.

250 mL urine sample will be concentrated to 1 mL and used for urine mutagenicity testing. The measurement results will be reported as revertants/µL. The urine mutagenicity count in the 24 hour urine will be calculated as follow:

Urine mutagenicity (revertants/250 mL) = Urine mutagenicity (revertants/ µL) x 1000

Note: the coeffiecient 1000 is for 1 mL = 1000 µL. If the volume after concentration is X mL, the coefficient will be X*1000.

Urine mutagenicity (revertants/24 hour) = Urine mutagenicity (revertants/250 mL) x urine volume/250

Note: the coeffiecient 250 is the volume of urine sample used for mutagenicity test. If the sample volume is XXX mL, the coefficient will be XXX.

7.1.2 Blood Biomarkers of Exposure

7.1.2.1 Blood BOE Sample Collection

The blood sample for COHb will be collected 15 minutes to 45 minutes following the start of subject's in the moment subjective questionnaires (QSU-Brief, mCEQ, and Use Product Again, as appropriate) at 21:30 (±30 minutes) on Days -1, 5, and 7. Subjects will abstain from product use, as appropriate, for at least 15 minutes prior to blood draw for COHb.

7.1.2.2 Bioanalytical Method

Blood samples for COHb saturation will be shipped to the Celerion Clinical Laboratory for analysis. COHb saturation will be determined using a validated spectrophotometric method at the Celerion Clinical Laboratory, Lincoln, Nebraska.

7.1.2.3 Blood Biomarker Analysis Variables

The following variables will be determined for blood COHb.

- Measured saturation (%) (primary analysis variable)
- Measured saturation (%) absolute change from Baseline
- Measured saturation (%) percent change from Baseline

Values reported as below the limit of quantitation (BLQ) will be set to one-half of the limit of quantitation for summarization and statistical analysis.

Absolute and percent change from baseline will be calculated as shown in Section 7.1.1.3.3.

7.1.3 Product Use Data Collection and Analysis Variables

7.1.3.1 Data Collection

Subjects will use the assigned products or be abstinent, as per randomization. All subjects (except Group 6) will use the assigned study product *ad libitum* (except

during meals and study procedures, as appropriate) from 07:00 through 23:00. Subjects in Group 2 and Group 3 will smoke no more than 50% of their baseline CPD and will use assigned VERVE® product ad libitum except for 3 specific VERVE® product use opportunities at 11:00, 15:00, and 19:00 each day during which subjects will be asked to keep VERVE® product in their mouth for at least 10 minutes. Subjects in Group 4 and Group 5 will only use the assigned VERVE® product ad libitum except for 3 specific VERVE® product use opportunities at 11:00, 15:00, and 19:00 each day during which subjects will be asked to keep assigned VERVE® product in their mouth for at least 10 minutes. Subjects will abstain from any product use from the start of the subjective effects questionnaires administration scheduled for 21:30 (±30 minutes) until after the COHb sample has been collected on Days -1, 5, and 7.

The number of each product used per day (CPD and VPD, as appropriate) will be counted for each cigarette or VERVE® product used during each day in a product use period. The total duration of each VERVE® product will be the sum of product use durations during each day in a product use period. The average duration of each VERVE® product will be the average of product use durations used per use each day in a product use period.

7.1.3.2 Analysis Variables

- number of each product used per day (CPD and VPD, as appropriate)
- average duration of VERVE® product used per use each day
- total duration of VERVE® product used per day

7.1.4 Subjective Effect

7.1.4.1 Data Collection

Subjects will also complete in the moment subjective effects questionnaires, which include:

- QSU-Brief (Protocol Appendix 2) – All subjects will complete the QSU-Brief on Days -1, 1, 5, and 7 in the morning at 07:00 (± 30 minutes) before product use, as appropriate, and at 21:30 (± 30 minutes).
- Modified Cigarette Evaluation Questionnaire (mCEQ-C or mCEQ-V; Protocol Appendix 3) – the appropriate mCEQ will be administered at 21:30 (± 30 minutes). All subjects will complete the mCEQ-C on Day -1. Subjects in Group 1 will also complete the mCEQ-C on Days 1, 5, and 7. Subjects in Groups 2 and 3 will complete both of the mCEQ-C and mCEQ-V on Days 1, 5, and 7. Subjects in Groups 4 and 5 will complete mCEQ-V on Days 1, 5, and 7.
- Use the Product Again questionnaire (Protocol Appendix 4) – Subjects in Groups 1 - 5 will complete the Use the Product Again questionnaire at 21:30 (± 30 minutes) on Day 7. Subjects in Group 1 will complete Use the Product Again questionnaire for cigarettes. Subjects in Groups 2 and 3 will complete both Use the Product Again questionnaire for cigarettes and VERVE® products. Subjects

in Groups 4 and 5 will complete Use the Product Again questionnaire for VERVE® products.

7.1.4.2 Analysis Variables

QSU-Brief

According to the literature[1], the factor scores for the QSU-Brief will be calculated as follows.

- Factor 1 (anticipation of pleasure from smoking): average of items 1, 3, 6, 7, and 10.
- Factor 2 (relief of nicotine withdrawal): average of items 2, 4, 5, 8, and 9.

The following variable will be determined for each factor score.

- Change from pre-product use score (07:00 ± 30 min) to post-product use score (21:30 ± 30 min), i.e. post-product use score minus pre-product use score, on each day

Modified Cigarette Evaluation Questionnaires

Responses on the 7-point scales for each mCEQ (mCEQ-V for days in which VERVE® products are used and mCEQ-C for days in which subject's OB cigarettes are used) will be treated as continuous variables and the following factor scores will be calculated according to the literature[2]:

- 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.

The following variable will be determined for each factor score.

- Actual score

Use Product Again Questionnaires

The analysis variable will be the response VAS score to the Use the Product Again questionnaire for each product. In addition, responses to Use the Product Again questionnaire will also be treated as bipolar variable and used as an analysis variable. The bipolar score is calculated by subtracting 50 from the original VAS score, then categorizing into three categories: -50 to <0, 0, and >0 to 50.

7.2 Data Summary and Presentation

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

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

- Number of observations (n)/number of missing values (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;
- Standard deviation/standard error of the mean (SD/SEM) with one more decimal/significant figure than mean/median.
- Coefficient of variation (CV%) with one decimal;
- Minimum/maximum in same precision as in the database
- 95% confidence intervals (CI) with one more decimal/significant figure than minimum/ maximum

7.2.1 Demographic Summary

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

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

7.2.2 Smoking History

CPD including Days -2 through -1 collected on site, years of smoking (calculated from Screening date), Fagerström Test for Cigarette Dependence scores (individual questions and total score), and usual brand, brand style, flavor, and cigarette size reported at Screening will be listed. Descriptive statistics will be summarized by study group and overall for continuous variables and frequency counts and percentage will be presented for categorical variables. Subjects only enrolled in the product trial period will be summarized separately as a group.

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

7.2.3 Urine BOE

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 day for all urine biomarkers. All BLQ values will be presented as "BLQ" in the listings.

Urine biomarker mass excreted per 24 hours, absolute change from baseline and percent change from baseline of total mass excreted per 24 hours, and creatinine-adjusted urine biomarker concentrations, will be summarized by group and study day for all urine biomarkers using descriptive statistics (n, n missing, mean, SD, CV%, SEM, minimum, median, maximum, and 95% CI). The descriptive statistics will be provided for both mITT and PP populations.

7.2.4 Blood BOE

Blood biomarker concentrations will be listed by subject and study visit for 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 day using descriptive statistics (n, n missing, mean, SD, CV%, SEM, minimum, median, maximum, and 95% CI). BLOQ COHb saturation will be treated as one-half the LLOQ. The descriptive statistics will be provided for both mITT and PP populations.

7.2.5 Product Use

Product Use

Number of CPD smoked per day (Groups 1, 2, and 3, only), number of VPD per day (Groups 2, 3, 4, and 5 only), average duration of VERVE® product used per use each day (Groups 2, 3, 4, and 5 only), and total duration of VERVE® product use per Day (Groups 2, 3, 4, and 5 only) will be listed by subject and study day and summarized by group and study day using descriptive statistics (n, n missing, mean, SD, CV%, SEM, minimum, Q1, median, Q3, maximum and 95% CI). The start time of VERVE producct use along time of the day (x-axis, 7:00 to 23:00) by group (y-axis, Group 2, 3, 4, 5) for Day 1, 5, 7 (one plot per day) will be plotted.

Product use analyses will be performed on the mITT dataset.

7.2.6 Questionnaires

The responses and the factor scores from the QSU-Brief will be listed by subject, study day and collection time. Factor scores (original scores, and change from pre-use scores) will be summarized by group, day and collection time using descriptive statistics (n, n missing, mean, SD, CV%, SEM, minimum, Q1, median, Q3, maximum, and 95% CI).

The mCEQ will be considered as a 7-point scale and treated as a continuous variable. The responses from mCEQ-C or mCEQ-V and factor scores will be listed by subject and study day. The factor scores will be summarized by group and study day using descriptive statistics (n, n missing, mean, SD, CV%, SEM, minimum, Q1, median, Q3, maximum and 95% CI).

Responses to Use the Product Again questionnaire recorded as VAS scores will be treated as bipolar variable and summarized by study group, study product and category using frequency count tables. The original response VAS score and bipolar score for the Use the Product Again questionnaire will be summarized using descriptive statistics (n, n missing, mean, SD, CV%, SEM, minimum, Q1, median, Q3, maximum and 95% CI).

These analyses will be performed on the mITT dataset.

7.3 Statistical Analyses

7.3.1 Primary Endpoint Analysis

A linear mixed model for repeated measures (MMRM) analysis will be used for comparing each test group (Groups 2-5) to the control group (Group 1 and Group 6) in the primary endpoint (24-hour total urinary NNAL (mg/24 hours) excreted on Day 7). In the model, study group, study day, and study group by study day interaction, and gender are the fixed effect factors. The baseline value of the response biomarker is the covariate. A restricted maximum likelihood estimation method will be applied and several covariance structures will be tried. Five candidate covariance structures will be considered: compound symmetry, 1st order autoregressive, 1st order autoregressive with a random subject effect, unstructured and Toeplitz. The most appropriate covariance structure will be determined based on the AIC criteria (the covariance structure with the smallest AIC will be chosen). The least-square mean, 95% confidence interval and p-value will be provided for the study groups. The least-square mean difference, 95% confidence interval and p-value will be provided for the study group comparisons. Pairwise comparisons (Group 2 vs. Group 1, Group 3 vs. Group 1, Group 4 vs. Group 1, Group 5 vs. Group 1, Group 2 vs. Group 6, Group 3 vs. Group 6, Group 4 vs. Group 6, and Group 5 vs. Group 6,) will be performed using a Dunnett's test at a 2-sided significance level of 0.05 to adjust for multiplicity. Group 1 & 6 will be considered as the control groups. The test is for each of the other groups to compare with the control groups. 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 day;
Model response = gender group day group*day baseline/ddfm=kr;
Repeated day/type=<type> subject=subject;
LSmeans group*day/CL alpha=0.05 pdiff dunnett ('1'*Day 7, '6'*Day 7);
```

Run;

Note: This model will include both the Day 7 value (primary endpoint) and interim time points (Day 5, secondary endpoint). The above analysis will also output the residual diagnosis to check for normality and to identify outliers).

7.3.1.1 Multiplicity adjustment

There is one primary analysis variable. No multiplicity adjustment will be done among biomarkers. For the test groups compared to the reference groups for each biomarker, Dunnett's method will be used for the adjustment of multiple comparisons.

7.3.1.2 Dealing with non-normality

A standard residual analysis using Proc Mixed procedure will be used to examine validity of normality assumptions for the primary endpoint. A natural logarithmic transformation might be applied to the endpoint in the linear mixed model with repeated measurements if the normality assumption does not hold. Square Root transformation will be used for urine mutagenicity statistical analysis.

7.3.2 Secondary Endpoint Analysis

The same statistical analysis model defined in the primary analysis Section 7.3.1 will also be used to make same comparisons as the primary endpoint (i.e. total NNAL on Day 7) for the secondary biomarker endpoints listed in Section 2.4.

These analyses will be conducted on the mITT and PP datasets.

7.3.3 Subjective Effects

Similar statistical comparison analysis (defined in 7.3.1) will be preformed on QSU-brief change from pre-use score and mCEQ original scores (mCEQ-C, among Group 1, 2, and 3; mCEQ-V, among Groups 2, 3, 4, and 5). The comparisons interested for QSU-brief will be the test groups (Groups 2-5) versus the continue smoking group (Group 1) and test groups (Groups 2-5) versus the tobacco cessation Group. The comparisons interested for mCEQ-C will be the dual use groups (Groups 2-3) versus the continue smoking group (Group 1). The comparisons interested for mCEQ-V will be the dual use groups (Groups 2-3) versus the exclusive use group (Groups 4 -5) [i.e. Group 2 vs Group 4 and Group 3 vs Group 5].

This analysis will be conducted on the mITT datasets. No multiple adjustment will be performed for subject effect scores.

7.3.4 Sensitivity Analysis

7.3.4.1 Analysis Variables for Sensitivity Analysis

The sensitivity analysis will be performed for primary endpoint (24-hour total urinary NNAL (ng/24 hours) excreted on Day 7).

7.3.4.2 Handling of Missing Data

Two methods (last observation carried forward and multiple imputation) will be tested for the handling of missing data for the primary endpoint if the percentage of missing data is larger than 5% in the mITT population. For all other analyses, data will not be imputed. Baseline is not expected to be missing for the mITT population.

Multiple imputation will be conducted to impute the missing data values for the primary endpoints (24-hour total urinary NNAL (ng/24 hours) excreted on Day 7). The imputation starts with using SAS procedure Proc MI to generate (n=m) completed data sets. Then each data set will be analyzed with SAS procedure Proc Mixed to generate m point estimates and standard errors for the model parameters. Finally, SAS procedure Proc Mianlyze will be used to combine the estimation results

The Following SAS codes will be used for imputation and analysis.
1) use PROC MI to impute the missing data;

```
proc mi data=… seed=… nimpute=200 out=miout noprint;
mcmc;
var  biomarker_baseline biomarker_Day5 biomarker_Day7 ;
run;
```

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

```
proc mixed data=miout order=internal ;
where day=7;
by _imputation_;
class  subject  gender group ;
model biomarker = gender group baseline/ddfm=kr;
lsmeans group / alpha=0.05 CL pdiff;
  ods output lsmeans=lsmnout;
  ods output diffs=diff;
run;
```

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

```
proc sort data=lsmnout;by group _imputation_;run;
proc mianalyze data=lsmnout alpha=0.05;
```

```
 by group ;
modeleffects  group;
  ods output ParameterEstimates=lsmnoutmi;
stderr stderr;
run;

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

7.3.4.3 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 endpoint (24-hour total urinary NNAL (ng/24 hours) excreted on Day 7). A sensitivity analysis by excluding outliers will be performed for the primary analysis variable if any outliers are found using the above criteria.

7.3.4.4 Handling BLQ values

Values below the limit of quantitation (BLQ) for nicotine and its metabolites, COHb, and other urine biomarkers 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 to use in the calculation of nicotine equivalents and data analysis of NE. Values BLQ for other urine biomarkers and COHb will be set to one-half of the LLOQ prior to data analysis. A sensitivity analysis of the primary endpoint (24-hour total urinary NNAL (ng/24 hours) excreted on Day 7) 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.

Approximate LLOQ values for each analyte are shown in the table below. LLOQs will be reported out to the most current validation data and included in the bioanalytical report.

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	0.500 pg/mL
NNAL	2.00 pg/mL
2-AN	1.7 pg/mL
HEMA	0.2 ng/mL
3-HMPMA	5 ng/mL
3-HPMA	25 ng/mL
CEMA	0.25 ng/mL
4-ABP	1.5 pg/mL
S-PMA	0.02 ng/mL
2-HPMA	2.5 ng/mL
AAMA	10 ng/mL
GAMA	1 ng/mL
2-MHBMA	0.129 ng/mL
2-OHFle	0.05 ng/mL
2-Naphthol	0.10 ng/mL
1-OHP	0.01 ng/mL
Creatinine	30 µg/mL
COHb	0.2%

8. SAFETY

No inferential statistics will be performed on the safety data.

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

Decimal point will be presented as follows:

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

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

8.1 Subject Disposition

The number of subjects enrolled, the number who completed the study, and the number who did not complete the study (overall and reasons for early withdrawal) will be tabulated by study group and overall. A listing of subjects who discontinued the study prematurely will also be presented. Screen failure subjects and subjects only enrolled in the product trial period will be summarized separately.

8.2 Adverse Events

Adverse events will be coded (to the lowest level term) with the Medical Dictionary for Regulatory Activities (MedDRA®) version 20.0.

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

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

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

8.3 Clinical Laboratory

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

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

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

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

8.4 Vital Signs

Vital signs (respiration rate, pulse rate, blood pressure, and oral temperature) will be measured at screening, at Check-in, and at the End-of-Study or upon Early Termination.

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

8.5 ECG

A 12-lead ECG will be obtained during screening and listed by subject.

8.6 Concomitant Medications

All concomitant medications recorded during the study will be coded using the WHO Drug Dictionary (WHODD) version 01MAR2018 and listed by subject.

8.7 Physical Examination

Physical examinations will be performed at Screening. A brief physical examination (symptom driven) may be performed at Check-in and End of Study (or Early Termination). Physical examinations will be listed by subject and time point of collection. Changes in physical examinations (if any) will be described in the text of the final report.

9. SUMMARY OF CHANGES FROM PROTOCOL-PLANNED ANALYSIS

The analyses described in this SAP are aligned with those analyses described in the protocol with the following changes for statistical analysis.

1. Mixed model with repeated measurement instead of mixed model will be used in the analysis for biomarker statistical analysis as there are two response values (Days 5 and 7) for each subject.

2. Emax for Use Product Again questionnaire was mentioned in the protocol. As the Use Product Again questionnaire will only be conducted at Day 7 and only one response value for each subject, no maximum value will be available. The analysis will be performed based on the original response.

3. The statistical analysis model for Use Product Again questionnaire was modified based on the study design and data collection.

10. 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 14.1.1.1 Summary of Disposition by Study Group and Overall
Table 14.1.1.2 Summary of Disposition for Screen Failures

Table 14.1.2 Demographic Summary by Study Group and Overall

Table 14.1.3 Smoking History by Study Group and Overall

14.2 Data Summary Tables and Figures for Biomarkers, Product Use, and Questionnaire Reponses

14.2.1 Urine and Blood Biomarkers Tables

Primary and Secondary Biomarker endpoints

Total Urine NNAL

Table 14.2.1.1.1.1 Summary of Total Urine NNAL 24-Hour Excreted (ng/24 hour) by Study Group and Study Day (mITT Population)

Table 14.2.1.1.1.2 Summary of Total Urine NNAL 24-Hour Excreted (ng/24 hour) by Study Group and Study Day (PP Population)

Table 14.2.1.1.2.1 Summary of Total Urine NNAL 24-Hour Excreted Absolute Change From Baseline (ng/24 hour) by Study Group and Study Day (mITT Population)

Table 14.2.1.1.2.2 Summary of Total Urine NNAL 24-Hour Excreted Absolute Change From Baseline (ng/24 hour) by Study Group and Study Day (PP Population)

Table 14.2.1.1.3.1 Summary of Total Urine NNAL 24-Hour Excreted Percent Change From Baseline (%) by Study Group and Study Day (mITT Population)

Table 14.2.1.1.3.2 Summary of Total Urine NNAL 24-Hour Excreted Percent Change From Baseline (%) by Study Group and Study Day (PP Population)

Table 14.2.1.1.4.1 Summary of Total Urine NNAL Adjusted for Urine Creatinine (ng/g creatinine) by Study Group and Study Day (mITT Population)

Table 14.2.1.1.4.2 Summary of Total Urine NNAL Adjusted for Urine Creatinine (ng/g creatinine) by Study Group and Study Day (PP Population)

Table 14.2.1.1.5.1 Statistical Summary of Total Urine NNAL 24-Hour Excreted (ng/24 hour) by Study Group and Study Day (mITT Population)

Table 14.2.1.1.5.2 Statistical Comparisons of Total Urine NNAL 24-Hour Excreted (ng/24 hour) Between Study Groups by Study Day (mITT Population)

	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 14.2.1.1.10.2	Statistical Comparisons of Total Urine NNAL 24-Hour Excreted (ng/24 hour) at Day 7 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.)

For the following urine biomarkers, tables similar to those for Total Urine NNAL will be created as appropriate and numbered as specified:

Urine NNN Tables
Tables 14.2.1.2.1.1 through 14.2.1.2.6.2

Urine Nicotine Equivalents Tables
Tables 14.2.1.3.1.1 through 14.2.1.3.6.2

Urine 2-AN Tables
Tables 14.2.1.4.1.1 through 14.2.1.4.6.2

Urine 4-ABP Tables
Tables 14.2.1.5.1.1 through 14.2.1.5.6.2

Urine HEMA Tables
Tables 14.2.1.6.1.1 through 14.2.1.6.6.2

Urine CEMA Tables
Tables 14.2.1.7.1.1 through 14.2.1.7.6.2

Urine S-PMA Tables
Tables 14.2.1.8.1.1 through 14.2.1.8.6.2

Urine 3-HMPMA Tables
Tables 14.2.1.9.1.1 through 14.2.1.9.6.2

Urine 3-HPMA Tables
Tables 14.2.1.10.1.1 through 14.2.1.10.6.2

Urine 2-HPMA Tables

Tables 14.2.1.11.1.1 through 14.2.1.11.6.2

Urine AAMA Tables

Tables 14.2.1.12.1.1 through 14.2.1.12.6.2

Urine GAMA Tables

Tables 14.2.1.13.1.1 through 14.2.1.13.6.2

Urine 2-MHBMA Tables

Tables 14.2.1.14.1.1 through 14.2.1.14.6.2

Urine 2-OHFle Tables

Tables 14.2.1.15.1.1 through 14.2.1.15.6.2

Urine 2-Naphthol Tables

Tables 14.2.1.16.1.1 through 14.2.1.16.6.2

Urine 1-OHPhe Tables

Tables 14.2.1.17.1.1 through 14.2.1.17.6.2

Urine 1-OHP Tables

Tables 14.2.1.18.1.1 through 14.2.1.18.6.2

Urine Mutagenicity Tables

Tables 14.2.1.19.1.1 through 14.2.1.19.6.2

Blood COHb Tables

Table 14.2.1.20.1.1 Summary of Blood COHb (% Saturation) by Study Group and Study Day (mITT Population)

Table 14.2.1.20.1.2 Summary of Blood COHb (% Saturation) by Study Group and Study Day (PP Population)

Table 14.2.1.20.2.1 Summary of Blood COHb Absolute Change From Baseline (% Saturation) by Study Group and Study Day (mITT Population)

Table 14.2.1.20.2.2 Summary of Blood COHb Absolute Change From Baseline (% Saturation) by Study Group and Study Day (PP Population)

Table 14.2.1.20.3.1 Summary of Blood COHb Percent Change From Baseline (%) by Study Group and Study Day (mITT Population)

Table 14.2.1.20.3.2 Summary of Blood COHb Percent Change From Baseline (%) by Study Group and Study Day (PP Population)

Table 14.2.1.20.4.1 Statistical Summary of Blood COHb (% Saturation) by Study Group and Study Day (mITT Population)

Table 14.2.1.20.4.2 Statistical Comparisons of Blood COHb (% Saturation) Between Study Groups by Study Day (mITT Population)

Table 14.2.1.20.5.1 Statistical Summary of Blood COHb (% Saturation) by Study Group and Study Day (PP Population)

Table 14.2.1.20.5.2 Statistical Comparisons of Blood COHb (% Saturation) Between Study Groups by Study Day (PP Population)

14.2.2 Product Use

Table 14.2.2.1 Summary of Number of Cigarettes Smoked Per Day by Study Group and Study Day (mITT Population)

Table 14.2.2.2 Summary of VERVE Product Used Per Day by Study Group and Study Day (mITT Population)

Table 14.2.2.3 Summary of Average Duration of VERVE Product Used Per Use by Study Group and Study Day (mITT Population)

Table 14.2.2.4 Summary of Total Duration of VERVE Product Per Day by Study Group and Study Day (mITT Population)

14.2.3 Subjective Effect Questionnaires

QSU-Brief Questionnaire

Table 14.2.3.1.1 Summary of QSU-Brief Factor Scores and Change from Pre Product Use by Study Group and Study Day (mITT Population)

Table 14.2.3.1.2.1 Statistical Summary of QSU-Brief Factor Change from Pre Product Use Scores by Study Group and Study Day (mITT Population)

Table 14.2.3.1.2.2 Statistical Comparisons of QSU-Brief Factor Change from Pre Product Use Scores Between Study Groups by Study Day (mITT Population)

mCEQ

Table 14.2.3.2.1 Summary of mCEQ Factor Scores by Study Group and Study Day (mITT Population)

Table 14.2.3.2.2.1 Statistical Summary of mCEQ-C Factor Scores by Study Group and Study Day (mITT Population)

Table 14.2.3.2.2.2 Statistical Comparisons of mCEQ-C Factor Scores Between Study Groups by Study Day (mITT Population)

Table 14.2.3.2.3.1 Statistical Summary of mCEQ-V Factor Scores by Study Group and Study Day (mITT Population)

Table 14.2.3.2.3.2 Statistical Comparisons of mCEQ-V Factor Scores Between Study Groups by Study Day (mITT Population)

Use Product Again

Table 14.2.3.3.1 Frequency of Response to Use the Product Again VAS Scores by Study Group and Study Product (mITT Population)

Table 14.2.3.3.2 Summary of Response to Use the Product Again VAS Scores by Study Group and Study Product (mITT Population)

Table 14.2.3.3.3 Summary of Response to Use the Product Again Bipolar Scores by Category, Study Group and Study Product (mITT Population)

14.2.4 Biomarker Figures (mITT, PP Populations)

Total Urine NNAL Count Figures

Figure 14.2.4.1.1 Box Plot of Total Urine NNAL 24-Hour Excreted (ng/24 hour) at Baseline and Day 7 by Study Group (mITT Population)

Figure 14.2.4.1.2 Box Plot of Total Urine NNAL 24-Hour Excreted (ng/24 hour) at Baseline and Day 7 by Study Group (PP Population)

Figure 14.2.4.1.3 Box Plot of Total Urine NNAL 24-Hour Excreted (ng/24 hour) at Baseline and Day 5 by Study Group (mITT Population)

For the following urine biomarkers, figuress similar to those for Total Urine NNAL will be created as appropriate and numbered as specified:

Urine NNN Figures

Figures 14.2.4.2.1 through 14.2.4.2.3

Urine Nicotine Equivalents Figures

Figures 14.2.4.3.1 through 14.2.4.3.3

Urine 2-AN Figures
Figures 14.2.4.4.1 through 14.2.4.4.3

Urine 4-ABP Figures
Figures 14.2.4.5.1 through 14.2.4.5.3

Urine HEMA Figures
Figures 14.2.4.6.1 through 14.2.4.6.3

Urine CEMA Figures
Figures 14.2.4.7.1 through 14.2.4.7.3

Urine S-PMA Figures
Figures 14.2.4.8.1 through 14.2.4.8.3

Urine 3-HMPMA Figures
Figures 14.2.4.9.1 through 14.2.4.9.3

Urine 3-HPMA Figures
Figures 14.2.4.10.1 through 14.2.4.10.3

Urine 2-HPMA Figures
Figures 14.2.4.11.1 through 14.2.4.11.3

Urine AAMA Figures
Figures 14.2.4.12.1 through 14.2.4.12.3

Urine GAMA Figures
Figures 14.2.4.13.1 through 14.2.4.13.3

Urine 2-MHBMA Figures
Figures 14.2.4.14.1 through 14.2.4.14.3

Urine 2-OHFle Figures
Figures 14.2.4.15.1 through 14.2.4.15.3

Urine 2-Naphthol Figures
Figures 14.2.4.16.1 through 14.2.4.16.3

Urine 1-OHPhe Figures

Figures 14.2.4.17.1 through 14.2.4.17.3

Urine 1-OHP Figures

Figures 14.2.4.18.1 through 14.2.4.18.3

Urine Mutagenicity Figures

Figures 14.2.4.19.1 through 14.2.4.19.3

Whole Blood COHb Figures

Figure 14.2.4.20.1	Box Plot of Whole Blood COHb (% Saturation) at Baseline and Day 7 by Study Group (mITT Population)
Figure 14.2.4.20.2	Box Plot of Whole Blood COHb (% Saturation) at Baseline and Day 7 by Study Group (PP Population)
Figure 14.2.4.20.3	Box Plot of Whole Blood COHb (% Saturation) at Baseline and Day 5 by Study Group (mITT Population)

14.2.5 Product Use Figures (mITT Populations)

Figure 14.2.5.1	Start Time of VERVE Product Use Along Time of the Day by Study Group (Day 1) (mITT Population)
Figure 14.2.5.2	Start Time of VERVE Product Use Along Time of the Day by Study Group (Day 5) (mITT Population)
Figure 14.2.5.3	Start Time of VERVE Product Use Along Time of the Day by Study Group (Day 7) (mITT Population) (mITT Population)

Note: The x-axis will be the time of the day (from 7:00 to 23:00),the y-axis will have 4 ticks for the 4 groups (Groups 2 – 5). All the start times from all the subjects in the same group will form a single horizontal dotted line. The dotted line will be dense at certain timepoints when the subjects are using the VERVE product at the same time, otherwise the dotted line is loose.

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 or in Study Group)

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

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

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

14.3.2 Listings of Deaths, other Serious and Significant Adverse Events

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

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

14.3.4. Abnormal Laboratory Value Listing (each subject)

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

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

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

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

Table 14.3.5.1 Clinical Laboratory Summary – Serum Chemistry

Table 14.3.5.2 Clinical Laboratory Summary – Hematology

Table 14.3.5.3 Clinical Laboratory Summary – Urinalysis

Table 14.3.5.4 Vital Sign Summary

11. 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

16.2. Subject Data Listings

16.2.1. Subject Discontinuation

Appendix 16.2.1.1 Subject Disposition and Discontinuation (Randomized)
Appendix 16.2.1.2 Subject Disposition and Discontinuation (Product Trial)
Appendix 16.2.1.3 Subject Disposition and Discontinuation (Screen Failures)
Appendix 16.2.1.4 Subject Population information

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 Biomarker 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)
Appendix 16.2.4.5 Fagerstrom Test for Cigarette Depedence

16.2.5. Compliance Data

Appendix 16.2.5.1 Inclusion / Exclusion Criteria Not Met
Appendix 16.2.5.2.1 Product Trial
Appendix 16.2.5.2.2 In-Clinic Product Use
Appendix 16.2.5.2.3 Max CPD
Appendix 16.2.5.3.1 24-Hour Urine Collection
Appendix 16.2.5.3.2 Urine Samples

Appendix 16.2.5.4 Carboxyhemoglobin Blood Collection
Appendix 16.2.5.5 Prior and On-Study Concomitant Medications

16.2.6. Individual Response Data

Appendix 16.2.6.1 Total Urine NNAL
Appendix 16.2.6.2 Urine NNN
Appendix 16.2.6.3.1 Urine Nicotine and Metabolites Concentrations
Appendix 16.2.6.3.2 Urine Nicotine Equivalents
Appendix 16.2.6.4 Urine 2-AN
Appendix 16.2.6.5 Urine 4-ABP
Appendix 16.2.6.6 Urine HEMA
Appendix 16.2.6.7 Urine CEMA
Appendix 16.2.6.8 Urine S-PMA
Appendix 16.2.6.9 Urine 3-HMPMA
Appendix 16.2.6.10 Urine 3-HPMA
Appendix 16.2.6.11 Urine 2-HPMA
Appendix 16.2.6.12 Urine AAMA
Appendix 16.2.6.13 Urine GAMA
Appendix 16.2.6.14 Urine 2-MHBMA
Appendix 16.2.6.15 2-OHFle
Appendix 16.2.6.16 Urine 2-Naphthol
Appendix 16.2.6.17 Urine 1-OHPhe
Appendix 16.2.6.18 Urine 1-OHP
Appendix 16.2.6.19 Whole Blood COHb
Appendix 16.2.6.20.1 Cigarettes Used per Day
Appendix 16.2.6.20.2 VERVE Product Used per Day
Appendix 16.2.6.21.1 Average Duration of VERVE Product Used per Use
Appendix 16.2.6.21.2 Total Duration of VERVE Product Used per Day
Appendix 16.2.6.22 Original and Factor Score to QSU-Brief Questionnaire
Appendix 16.2.6.23.1 Original Score to MCEQ Questionnaire
Appendix 16.2.6.23.2 Factor Score to MCEQ Questionnaire
Appendix 16.2.6.24 Use the Product Again Questionnaire

16.2.7. Individual Adverse Event Listings

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

16.2.8. Individual Laboratory Measurements and Other Safety Observations

Appendix 16.2.8.1.1	Clinical Laboratory Report - Serum Chemistry
Appendix 16.2.8.1.2	Clinical Laboratory Report - Hematology
Appendix 16.2.8.1.3	Clinical Laboratory Report - Urinalysis
Appendix 16.2.8.1.4	Clinical Laboratory Report - Comments
Appendix 16.2.8.1.5	Alcohol Breath Tests
Appendix 16.2.8.1.6	Urine Drug Screens
Appendix 16.2.8.1.7	Pregnancy Tests
Appendix 16.2.8.1.8	FSH
Appendix 16.2.8.1.9	Contraception
Appendix 16.2.8.1.10	Urine Cotinine Screens
Appendix 16.2.8.1.11	Serology Sample Collection
Appendix 16.2.8.2	Vital Signs
Appendix 16.2.8.3	12-Lead Electrocardiogram
Appendix 16.2.8.4	Smoking Cessation Information

12. 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 14.1.1.1 Summary of Disposition by Study Group and Overall

			Group						
		Product							
Population	Category	Trial*	1	2	3	4	5	6	Overall#
Safety	Enrolled	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
	Completed	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
	Discontinued Early	XX	XX	XX	XX	XX	XX	XX	XX
	<Reason1>	XX	XX	XX	XX	XX	XX	XX	XX
	<Reason2>	XX	XX	XX	XX	XX	XX	XX	XX
	<Reason3>	XX	XX	XX	XX	XX	XX	XX	XX
mITT	Enrolled		XXX	XXX	XXX	XXX	XXX	XXX	XXX
	Completed		XXX	XXX	XXX	XXX	XXX	XXX	XXX
	Discontinued Early		XX	XX	XX	XX	XX	XX	XX
	<Reason1>		XX	XX	XX	XX	XX	XX	XX
	<Reason2>		XX	XX	XX	XX	XX	XX	XX
	<Reason3>		XX	XX	XX	XX	XX	XX	XX
PP	Enrolled		XXX	XXX	XXX	XXX	XXX	XXX	XXX
	Completed		XXX	XXX	XXX	XXX	XXX	XXX	XXX
	Discontinued Early		XX	XX	XX	XX	XX	XX	XX
	<Reason1>		XX	XX	XX	XX	XX	XX	XX
	<Reason2>		XX	XX	XX	XX	XX	XX	XX
	<Reason3>		XX	XX	XX	XX	XX	XX	XX

Note: * Only includes subjects that enrolled in the product trial period and dropped prior to randomization.
Subjects who only participated in the product trial period are excluded from the Overall summary.
Group X = <description of groups>
mITT = Modified Intent-to-treat, PP = Per protocol

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

Table 14.1.1.2 Summary of Disposition for Screen Failures

Population	Category	
Screen Failuers	Screened	XXX
	Discontinued Early	XX
	<Reason1>	XX
	<Reason2>	XX
	<Reason3>	XX

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

Table 14.1.2 Demographic Summary by Study Group and Overall

Population	Trait		Product Trial*	Group 1	Group 2	….	Group 6	Overall#
Safety	Gender	Male	X(XX.X%)	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%)	X(XX.X%)
	Race	XXXXXXXXXX	X(XX.X%)	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%)	X(XX.X%)
		XXXXX	X(XX.X%)	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%)	X(XX.X%)
		Not Hispanic or Latino	X(XX.X%)	X(XX.X%)	X(XX.X%)		X(XX.X%)	X(XX.X%)
	Age (yrs)	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: * Only includes subjects that enrolled in the product trial Period and dropped prior to randomization.
Subjects who only participated in the product trial period are excluded from the Overall summary.
Group X = <description of groups>
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. mITT and PP population will also be presented.

Table 14.1.3 Smoking History by Study Group and Overall

Population	Trait		Product Trial*	Group 1	2	…..	6	Overall#
Safety	CPD	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
	Years Smoked	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: * Only includes subjects that enrolled in the product trial Period and dropped prior to randomization.
# Subjects who only participated in the product trial period are excluded from the Overall summary.
CPD = Cigarettes per day
Group X = <description of groups>
mITT = Modified Intent-to-treat, PP = Per protocol

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

Programmer Note: Fagerstrom score will also be summarized in the table. mITT and PP population will also be presented.

Note: Summary Tables 14.2.1.1.1.1-2, 14.2.1.2.1.1-2, 14.2.1.3.1.1-2, 14.2.1.4.1.1-2, 14.2.1.5.1.1-2, 14.2.1.6.1.1-2, 14.2.1.7.1.1-2, 14.2.1.8.1.1-2, 14.2.1.9.1.1-2, 14.2.1.10.1.1-2, 14.2.1.11.1.1-2, 14.2.1.12.1.1-2, 14.2.1.13.1.1-2, 14.2.1.14.1.1-2, 14.2.1.15.1.1-2, 14.2.1.16.1.1-2, 14.2.1.17.1.1-2, 14.2.1.18.1.1-2, 14.2.1.19.1.1-2, and 14.2.1.20.1.1-2 will have the following format:

Page 1 of X

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

		Group					
Study Day	Statistics	1	2	3	4	5	6
-1	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	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
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
5	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	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
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
7	<same as above>						

Group X = <description of groups>

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

Note: Summary tables 14.2.1.1.2.1-2, 14.2.1.2.2.1-2, 14.2.1.3.2.1-2, 14.2.1.4.2.1-2, 14.2.1.5.2.1-2, 14.2.1.6.2.1-2, 14.2.1.7.2.1-2, 14.2.1.8.2.1-2, 14.2.1.9.2.1-2, 14.2.1.10.2.1-2, 14.2.1.11.2.1-2, 14.2.1.12.2.1-2, 14.2.1.13.2.1-2, 14.2.1.14.2.1-2, 14.2.1.15.2.1-2, 14.2.1.16.2.1-2, 14.2.1.17.2.1-2, 14.2.1.18.2.1-2, 14.2.1.19.2.1-2, and 14.2.1.20.2.1-2 will have the following format:

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

		Group					
Study Day	Statistics	1	2	3	4	5	6
5	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	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
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
7	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	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
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X

Baseline = Day -1
Group X = <description of groups>

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

Note: Summary tables 14.2.1.1.3.1-2, 14.2.1.2.3.1-2, 14.2.1.3.3.1-2, 14.2.1.4.3.1-2, 14.2.1.5.3.1-2, 14.2.1.6.3.1-2, 14.2.1.7.3.1-2, 14.2.1.8.3.1-2, 14.2.1.9.3.1-2, 14.2.1.10.3.1-2, 14.2.1.11.3.1-2, 14.2.1.12.3.1-2, 14.2.1.13.3.1-2, 14.2.1.14.3.1-2, 14.2.1.15.3.1-2, 14.2.1.16.3.1-2, 14.2.1.17.3.1-2, 14.2.1.18.3.1-2, 14.2.1.19.3.1-2, and 14.2.1.20.3.1-2 will have the following format:

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

		Group					
Study Day	Statistics	1	2	3	4	5	6
5	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	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
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
7	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	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
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X

Baseline = Day -1
Group X = <description of groups>

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

Note: Summary Tables 14.2.1.1.4.1-2, 14.2.1.2.4.1-2, 14.2.1.3.4.1-2, 14.2.1.4.4.1-2, 14.2.1.5.4.1-2, 14.2.1.6.4.1-2, 14.2.1.7.4.1-2, 14.2.1.8.4.1-2, 14.2.1.9.4.1-2, 14.2.1.10.4.1-2, 14.2.1.11.4.1-2, 14.2.1.12.4.1-2, 14.2.1.13.4.1-2, 14.2.1.14.4.1-2, 14.2.1.15.4.1-2, 14.2.1.16.4.1-2, 14.2.1.17.4.1-2, 14.2.1.18.4.1-2, and 14.2.1.19.4.1-2 will have the following format:

Page 1 of X

Table 14.2.1.1.4.1 Summary of <Matrix> <Biomarker> Adjusted for Urine Creatinine (<units>) by Study Group and Study Day (<Population>)

		Group					
Study Day	Statistics	1	2	3	4	5	6
-1	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	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
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
5	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	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
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
7	<same as above>						

Group X = <description of groups>

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

Note: Statistical summary tables 14.2.1.1.5-6.1, 14.2.1.2.5-6.1, 14.2.1.3.5-6.1, 14.2.1.4.5-6.1, 14.2.1.5.5-6.1, 14.2.1.6.5-6.1, 14.2.1.7.5-6.1, 14.2.1.8.5-6.1, 14.2.1.9.5-6.1, 14.2.1.10.5-6.1, 14.2.1.11.5-6.1, 14.2.1.12.5-6.1, 14.2.1.13.5-6.1, 14.2.1.14.5-6.1, 14.2.1.15.5-6.1, 14.2.1.16.5-6.1, 14.2.1.17.5-6.1, 14.2.1.18.5-6.1, 14.2.1.19.5-6.1, and 14.2.1.20.4-5.1 will have the following format:

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Table 14.2.1.1.5.1 Statistical Summary of <Matrix> <Biomarker>) (<Units>) by Study Group and Study Day (mITT Population)

Group	Study Day	n	-------- LS Mean ----------	XX% Confidence Interval	p-value
1	5	XX	X.XX	XX.XX – XXX.XX	X.XXXX
	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
2	5	XX	X.XX	XX.XX – XXX.XX	X.XXXX
	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
3	5	XX	X.XX	XX.XX – XXX.XX	X.XXXX
	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
4	5	XX	X.XX	XX.XX – XXX.XX	X.XXXX
	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
5	5	XX	X.XX	XX.XX – XXX.XX	X.XXXX
	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
6	5	XX	X.XX	XX.XX – XXX.XX	X.XXXX
	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX

Note: The mixed model for repeated measures includes study group, study day, study group by study visit interaction, and gender as fixed effects, baseline (Day -1)_ value as the covariate with a variance-covariance matrix based on the AIC value.
Final variance-covariance matrix is XXX.
n = Number of observation used in the analysis
Least-squares means (LS Means) are calculated from the MMRM.

Group X = <description of groups>

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

Note: Statistical Comparison tables 14.2.1.1.5-6.2, 14.2.1.2.5-6.2, 14.2.1.3.5-6.2, 14.2.1.4.5-6.2, 14.2.1.5.5-6.2, 14.2.1.6.5-6.2, 14.2.1.7.5-6.2, 14.2.1.8.5-6.2, 14.2.1.9.5-6.2, 14.2.1.10.5-6.2, 14.2.1.11.5-6.2, 14.2.1.12.5-6.2, 14.2.1.13.5-6.2, 14.2.1.14.5-6.2, 14.2.1.15.5-6.2, 14.2.1.16.5-6.2, 14.2.1.17.5-6.2, 14.2.1.18.5-6.2, 14.2.1.19.5-6.2, and 14.2.1.20.4-5.2 will have the following format:

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Table 14.2.1.1.5.2 Statistical Comparisons of <Biomarker> (Units) Between Study Groups by Study Day (mITT Population)

Comparison	Study Day	LS Means Test (n)	LS Means Reference (n)	LS Mean Difference (Test – Reference)	XX% Confidence Interval	p-value
Group 2 vs Group 1	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 3 vs Group 1	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 4 vs Group 1	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 5 vs Group 1	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 2 vs Group 6	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 3 vs Group 6	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 4 vs Group 6	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 5 vs Group 6	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX

Note: The mixed model for repeated measures includes study group, study day, study group by study visit interaction, and gender as fixed effects, baseline (Day -1) value as the covariate with a variance-covariance matrix based on the AIC value.
Final variance-covariance matrix is XXX.
Test = The first group in the comparison
Reference = The second group in the comparison
n = Number of observation used in the analysis
Dunnett-Hsu adjusted confidence interval and p-value are reported.

Group X = <description of groups>

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

Note: Statistical summary table 14.2.1.1.7.1 will have the following format:

Table 14.2.1.1.7.1 Statistical Summary of Total Urine NNAL 24-Hour Excreted (ng/24 hour) by Study Group (mITT Population with Imputation of Missing Data Using Last Observation Carried Forward Method)

Group	Study Day	n	-------- LS Mean ----------	XX% Confidence Interval	p-value
1	5	XX	X.XX	XX.XX – XXX.XX	X.XXXX
	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
2	5	XX	X.XX	XX.XX – XXX.XX	X.XXXX
	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
3	5	XX	X.XX	XX.XX – XXX.XX	X.XXXX
	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
4	5	XX	X.XX	XX.XX – XXX.XX	X.XXXX
	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
5	5	XX	X.XX	XX.XX – XXX.XX	X.XXXX
	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
6	5	XX	X.XX	XX.XX – XXX.XX	X.XXXX
	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX

Note: The mixed model for repeated measures includes study group, study day, study group by study visit interaction, and gender as fixed effects, baseline (Day -1) value as the covariate with a variance-covariance matrix based on the AIC value.
Final variance-covariance matrix is XXX.
n = Number of observation used in the analysis
Least-squares means (LS Means) are calculated from the MMRM.

Group X = <description of groups>

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

Note: Statistical Comparison table 14.2.1.1.7.2 will have the following format:

Table 14.2.1.1.7.2 Statistical Comparisons of Total Urine NNAL 24-Hour Excreted (ng/24 hour) Study Groups (mITT Population with Imputation of Missing Data Using Last Observation Carried Forward Method)

Comparison	Study Day	LS Means Test (n)	LS Means Reference (n)	LS Mean Difference (Test – Reference)	XX% Confidence Interval	p-value
Group 2 vs Group 1	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 3 vs Group 1	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 4 vs Group 1	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 5 vs Group 1	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 2 vs Group 6	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 3 vs Group 6	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 4 vs Group 6	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 5 vs Group 6	5	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX

Note: The mixed model for repeated measures includes study group, study day, study group by study visit interaction, and gender as fixed effects, baseline (Day -1) value as the covariate with a variance-covariance matrix based on the AIC value.
Final variance-covariance matrix is XXX.
Test = The first group in the comparison
Reference = The second group in the comparison
n = Number of observation used in the analysis
Dunnett-Hsu adjusted confidence interval and p-value are reported.

Group X = <description of groups>

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

Note: Statistical summary table 14.2.1.1.8.1 will have the following format:

Table 14.2.1.1.8.1 Statistical Summary of Total Urine NNAL 24-Hour Excreted (ng/24 hour) by Study Group (mITT Population with Imputation of Missing Data Using Multiple Imputation by SAS MI Procedure)

Group	Study Day	n	LS Mean	XX% Confidence Interval	p-value
1	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
2	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
3	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
4	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
5	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
6	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX

Note: The mixed model includes study group and gender as fixed effects, and baseline (Day -1) value as the covariate.
n = Number of observation used in the analysis
Least-squares means (LS Means) are calculated from the ANCOVA.

Group X = <description of groups>

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

Note: Statistical Comparison table 14.2.1.1.8.2 will have the following format:

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Table 14.2.1.1.8.2 Statistical Comparisons of Total Urine NNAL 24-Hour Excreted (ng/24 hour) Between Study Groups (mITT Population with Imputation of Missing Data Using Multiple Imputation by SAS MI Procedure)

Comparison	Study Day	LS Means Test (n)	LS Means Reference (n)	LS Mean Difference (Test – Reference)	XX% Confidence Interval	p-value
Group 2 vs Group 1	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 3 vs Group 1	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 4 vs Group 1	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 5 vs Group 1	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 2 vs Group 6	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 3 vs Group 6	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 4 vs Group 6	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 5 vs Group 6	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX

Note: The mixed model includes study group and gender as fixed effects, and baseline (Day -1) value as the covariate.
n = Number of observation used in the analysis
Least-squares means (LS Means) are calculated from the ANCOVA.
Test = The first group in the comparison
Reference = The second group in the comparison
n = Number of observation used in the analysis
Dunnett-Hsu adjusted confidence interval and p-value are reported.

Group X = <description of groups>

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

Note: Summary Table 14.2.1.1.9.1 will have the following format:

Table 14.2.1.1.9.1 Summary of <Matrix> <Biomarker> (<units>) by Study Group and Study Day (mITT Population with Outliers Excluded))

		Group					
Study Day	Statistics	1	2	3	4	5	6
-1	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	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
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
5	n	X	X	X	X	X	X
	n missing	X	X	X	X	X	X
	Mean	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
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
	95% CI	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
7	<same as above>						

Group X = <description of groups>

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

Note: Statistical summary tables 14.2.1.1.9.2 and 14.2.1.1.10.1 will have the following format:

Table 14.2.1.1.9.2 Statistical Summary of Total Urine NNAL 24-Hour Excreted (ng/24 hour) at Day 7 by Study Group (mITT Population with Outliers Excluded)

Group	Study Day	n	LS Mean	XX% Confidence Interval	p-value
1	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
2	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
3	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
4	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
5	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
6	7	XX	X.XX	XX.XX – XXX.XX	X.XXXX

Note: The mixed model for repeated measures includes study group, study day, study group by study visit interaction, and gender as fixed effects, baseline (Day -1) value as the covariate with a variance-covariance matrix based on the AIC value.
Final variance-covariance matrix is XXX.
n = Number of observation used in the analysis
Least-squares means (LS Means) are calculated from the MMRM.

Group X = <description of groups>

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

Note: Statistical Comparison tables 14.2.1.1.9.3 and 14.2.1.1.10.2 will have the following format:

Table 14.2.1.1.9.3 Statistical Comparisons of Total Urine NNAL 24-Hour Excreted (ng/24 hour) at Day 7 Between Study Groups (mITT Population with Outliers Excluded)

Comparison	Study Day	LS Means Test (n)	LS Means Reference (n)	LS Mean Difference (Test – Reference)	XX% Confidence Interval	p-value
Group 2 vs Group 1	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 3 vs Group 1	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 4 vs Group 1	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 5 vs Group 1	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 2 vs Group 6	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 3 vs Group 6	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 4 vs Group 6	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Group 5 vs Group 6	7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX

Note: The mixed model for repeated measures includes study group, study day, study group by study visit interaction, and gender as fixed effects, baseline (Day -1) value as the covariate with a variance-covariance matrix based on the AIC value.
Final variance-covariance matrix is XXX.
Least-squares means (LS Means) are calculated from the MMRM.
Test = The first group in the comparison
Reference = The second group in the comparison
n = Number of observation used in the analysis
Dunnett-Hsu adjusted confidence interval and p-value are reported.

Group X = <description of groups>

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

Note: Summary table 14.2.2.1 will have the following format:

Table 14.2.2.1 Summary of Number of Cigarettes Smoked Per Day by Study Group and Study Day (mITT Population)

Group		Study Day -2	-1	Baseline	1	2	3	4	5	6	7
1	n	X	X	X	X	X	X	X	X	X	X
	n missing	X	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	X.X
	SD	X.XX	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	XX.X
	SEM	X.X	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	X
	Q1	X.X	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	X
	Q3	X.X	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	X.X
	95% CI	X, X	X, X	X, X	X, X	X, X	X, X	X, X	X, X	X, X	X, X
2	<same as above>										

Note: Baseline = Average of Days -2 and -1.

Group X = <description of groups>

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

Programmer Note: Groups 2 through 6 will also be presented in the table. For groups 1, 2, and 3, there will be data for all study days (from Day -2 to Day 7). For Groups 4, 5, and 6, there will only have data for Days -2, -1, and baseline.

Note: Summary tables 14.2.2.2, 14.2.2.3, and 14.2.2.4 will have the following format:

Table 14.2.2.2 Summary of VERVE Product Used Per Day by Study Group and Study Day (mITT Population)

Group		Study Day 1	2	3	4	5	6	7
2	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
3	<same as above>							

Note: Group X = <description of groups>

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

Programmer Note: Groups 3, 4, and 5 will also be presented in the table.

QSU-Brief Questionnaire Summary Table 14.2.3.1.1 will have the following format:

Table 14.2.3.1.1 Summary of QSU-Brief Factor Scores and Change from Pre Product Use by Study Group and Study Day (mITT Population)

<Question or Subscale>	Study Day	Time Point	Statistics	Group 1	2	3	4	5	6
XXXXX	-1	Morning	n	X	X	X	X	X	X
			n missing	X	X	X	X	X	X
			Mean	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
			CV(%)	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
			Minimum	X	X	X	X	X	X
			Q1	X.X	X.X	X.X	X.X	X.X	X.X
			Median	X.X	X.X	X.X	X.X	X.X	X.X
			Q3	X.X	X.X	X.X	X.X	X.X	X.X
			Maximum	XX	XX	XX	XX	XX	XX
			95% CI	X, X	X, X	X, X	X, X	X, X	X, X
		Evening	<Same as above>						
		Change	<Same as above>						
XXXXX <same for remaining questions or subscales>									

Note: Group X = <description of groups>
Change = Evening score – Morning score

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

Programmer note: There are two factor score for QSU-Brief and the time points are Day -1 (morning and Evening), Day 1 (morning and Evening), Day 5 (morning and Evening), and Day 7 (morning and Evening).

Note: Statistical summary table 14.2.3.1.2.1 will have the following format:

Table 14.2.3.1.2.1 Statistical Summary of QSU-Brief Factor Change from Pre Product Use Scores by Study Group and Study Day (mITT Population)

Factor	Group	Study Day	n	LS Mean	XX% Confidence Interval	p-value
1	1	1	XX	X.XX	XX.XX – XXX.XX	X.XXXX
		5	XX	X.XX	XX.XX – XXX.XX	X.XXXX
		7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
	2	1	XX	X.XX	XX.XX – XXX.XX	X.XXXX
		5	XX	X.XX	XX.XX – XXX.XX	X.XXXX
		7	XX	X.XX	XX.XX – XXX.XX	X.XXXX
	3	1	XX	X.XX	XX.XX – XXX.XX	X.XXXX
		5	XX	X.XX	XX.XX – XXX.XX	X.XXXX
		7	XX	X.XX	XX.XX – XXX.XX	X.XXXX

Note: The mixed model for repeated measures includes study group, study day, study group by study visit interaction, and gender as fixed effects, baseline (Day -1) value as the covariate with a variance-covariance matrix based on the AIC value.
Final variance-covariance matrix is XXX.
n = Number of observation used in the analysis
Least-squares means (LS Means) are calculated from the MMRM.

Group X = <description of groups>

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

Programmer note: Groups 4-6 and Factor 2 will also be presented in the table.

Note: Statistical Comparison table 14.2.3.1.2.2 will have the following format:

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Table 14.2.3.1.2.2 Statistical Comparisons of QSU-Brief Factor Change from Pre Product Use Scores Between Study Groups by Study Day (mITT Population)

Factor	Comparison	Study Day	LS Means Test (n)	LS Means Reference (n)	LS Mean Difference (Test – Reference)	XX% Confidence Interval	p-value
1	Group 2 vs Group 1	1	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
		7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Group 3 vs Group 1	1	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
		7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Group 4 vs Group 1	1	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
		7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Group 5 vs Group 1	1	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
		7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX

Note: The mixed model for repeated measures includes study group, study day, study group by study visit interaction, and gender as fixed effects, baseline (Day -1_) value as the covariate with a variance-covariance matrix based on the AIC value.
Final variance-covariance matrix is XXX.
Test = The first group in the comparison
Reference = The second group in the comparison
n = Number of observation used in the analysis

Group X = <description of groups>

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

Programmer note: Comparisons for Groups 2-5 versus Group 6 and Factor 2 will also be presented in the table.

mCEQ Questionnaire Summary Table 14.2.3.1.1 will have the following format:

Table 14.2.3.2.1 Summary of mCEQ Factor Scores by Study Group and Study Day (mITT Population)

<Question or Subscale>	Study Day	Questionnaire	Statistics	Group 1	2	3	4	5	6
XXXXX	-1	mCEQ-C	n	X	X	X	X	X	X
			n missing	X	X	X	X	X	X
			Mean	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
			CV(%)	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
			Minimum	X	X	X	X	X	X
			Q1	X.X	X.X	X.X	X.X	X.X	X.X
			Median	X.X	X.X	X.X	X.X	X.X	X.X
			Q3	X.X	X.X	X.X	X.X	X.X	X.X
			Maximum	XX	XX	XX	XX	XX	XX
			95% CI	X, X	X, X	X, X	X, X	X, X	X, X
	1	mCEQ-C	<Same as above>						
XXXXX <same for remaining questions or subscales>									

Note: Group X = <description of groups>

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

Programmer note: There are five factor scores for mCEQ and the time points are Day -1, Day 1, Day 5, and Day 7. On Day -1, all groups have the values for mCEQ-C. For Group 1, mCEQ-C will be used for Days 1, 5, and 7. For Groups 2 and 3, both mCEQ-C and mCEQ-V will be used for Days 1, 5, and 7. For Groups 4 and 5, mCEQ-V will be used for Days 1, 5, and 7. No mCEQ for Group 6 after Day 1.

Note: Statistical summary table 14.2.3.2.2.1 will have the following format:

Page 1 of X

Table 14.2.3.2.2.1 Statistical Summary of Statistical Summary of mCEQ-C Factor Scores by Study Group and Study Day (mITT Population)

Factor	Group	Study Day	n	LS Mean	XX% Confidence Interval	p-value
XXX	1	1	XX	X.XX	XX.XX - XXX.XX	X.XXXX
		5	XX	X.XX	XX.XX - XXX.XX	X.XXXX
		7	XX	X.XX	XX.XX - XXX.XX	X.XXXX
	2	1	XX	X.XX	XX.XX - XXX.XX	X.XXXX
		5	XX	X.XX	XX.XX - XXX.XX	X.XXXX
		7	XX	X.XX	XX.XX - XXX.XX	X.XXXX
	3	1	XX	X.XX	XX.XX - XXX.XX	X.XXXX
		5	XX	X.XX	XX.XX - XXX.XX	X.XXXX
		7	XX	X.XX	XX.XX - XXX.XX	X.XXXX

Note: The mixed model for repeated measures includes study group, study day, study group by study visit interaction, and gender as fixed effects, baseline (Day -1) value as the covariate with a variance-covariance matrix based on the AIC value.
Final variance-covariance matrix is XXX.
n = Number of observation used in the analysis
Least-squares means (LS Means) are calculated from the MMRM.

Group X = <description of groups>

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

Programmer note: All factor scores will be presented in the table. This analysis only contains data from Groups 1-3.

Note: Statistical Comparison table 14.2.3.2.2.2 will have the following format:

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Table 14.2.3.2.2.2 Statistical Comparisons of mCEQ-C Factor Scores Between Study Groups by Study Day (mITT Population)

Factor	Comparison	Study Day	LS Means Test (n)	LS Means Reference (n)	LS Mean Difference (Test − Reference)	XX% Confidence Interval	p-value
XXX	Group 2 vs Group 1	1	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
		7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Group 3 vs Group 1	1	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
		7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX

Note: The mixed model for repeated measures includes study group, study day, study group by study visit interaction, and gender as fixed effects, baseline (Day -1) value as the covariate with a variance-covariance matrix based on the AIC value.
Final variance-covariance matrix is XXX.
Test = The first group in the comparison
Reference = The second group in the comparison
n = Number of observation used in the analysis

Group X = <description of groups>

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

Programmer note: Comparisons for all factor scores will also be presented in the table. This analysis only contains data from Groups 1-3.

Note: Statistical summary table 14.2.3.2.3.1 will have the following format:

Page 1 of X

Table 14.2.3.2.3.1 Statistical Summary of Statistical Summary of mCEQ-V Factor Scores by Study Group and Study Day
(mITT Population)

Factor	Group	Study Day	n	LS Mean	XX% Confidence Interval	p-value
XXX	2	1	XX	X.XX	XX.XX - XXX.XX	X.XXXX
		5	XX	X.XX	XX.XX - XXX.XX	X.XXXX
		7	XX	X.XX	XX.XX - XXX.XX	X.XXXX
	3	1	XX	X.XX	XX.XX - XXX.XX	X.XXXX
		5	XX	X.XX	XX.XX - XXX.XX	X.XXXX
		7	XX	X.XX	XX.XX - XXX.XX	X.XXXX
	4	1	XX	X.XX	XX.XX - XXX.XX	X.XXXX
		5	XX	X.XX	XX.XX - XXX.XX	X.XXXX
		7	XX	X.XX	XX.XX - XXX.XX	X.XXXX
	5	1	XX	X.XX	XX.XX - XXX.XX	X.XXXX
		5	XX	X.XX	XX.XX - XXX.XX	X.XXXX
		7	XX	X.XX	XX.XX - XXX.XX	X.XXXX

Note: The mixed model for repeated measures includes study group, study day, study group by study visit interaction, and gender as fixed effects, baseline (Day -1) value as the covariate with a variance-covariance matrix based on the AIC value.
Final variance-covariance matrix is XXX.
n = Number of observation used in the analysis
Least-squares means (LS Means) are calculated from the MMRM.

Group X = <description of groups>

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

Programmer note: All factor scores will be presented in the table. This analysis only contains data from Groups 2-5.

Note: Statistical Comparison table 14.2.3.2.2.2 will have the following format:

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Table 14.2.3.2.2.2 Statistical Comparisons of mCEQ-C Factor Scores Between Study Groups by Study Day (mITT Population)

Factor	Comparison	Study Day	LS Means Test (n)	LS Means Reference (n)	LS Mean Difference (Test – Reference)	XX% Confidence Interval	p-value
XXX	Group 2 vs Group 4	1	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
		7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Group 3 vs Group 5	1	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
		7	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX

Note: The mixed model for repeated measures includes study group, study day, study group by study visit interaction, and gender as fixed effects, baseline (Day -1) value as the covariate with a variance-covariance matrix based on the AIC value.
Final variance-covariance matrix is XXX.
Test = The first group in the comparison
Reference = The second group in the comparison
n = Number of observation used in the analysis

Group X = <description of groups>

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

Programmer note: Comparisons for all factor scores will also be presented in the table. This analysis only contains data from Groups 2-5.

Use Product Again Questionnaire Frequency Count Table 14.2.3.3.1 will have the following format:

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Table 14.2.3.3.1 Frequency of Response to Use the Product Again VAS Scores by Study Group and Study Product (mITT Population)

Question	Group	Statistics	-50 to <0	0	>0 to 50
Use Cigarette Again	1	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		n (%)	XX(XX%)	XX(XX%)	XX(XX%)
	2	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		n (%)	XX(XX%)	XX(XX%)	XX(XX%)
	3	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		n (%)	XX(XX%)	XX(XX%)	XX(XX%)
Use VERVE Again	2	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		n (%)	XX(XX%)	XX(XX%)	XX(XX%)
	3	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		n (%)	XX(XX%)	XX(XX%)	XX(XX%)
	4	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		n (%)	XX(XX%)	XX(XX%)	XX(XX%)
	5	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		n (%)	XX(XX%)	XX(XX%)	XX(XX%)

Note: Group X = <description of groups>

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

Programmer note: Use product again for cigarettes will be presented for Groups 1 – 3. Use product again for VERVE will be presented for Groups 2, 3, 4 and 5. The questionnaire will not be conducted for Group 6.

Use Product Again Questionnaire Summary Table 14.2.3.3.2 will have the following format:

Table 14.2.3.3.2 Summary of Use Product Again Scores by Study Group and Study Product (mITT Population)

		Group				
Product	Statistics	1	2	3	4	5
Cigarette	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		
VERVE	<Same as above>					

Note: Group X = <description of groups>

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

Programmer note: Use product again for cigarettes will be presented for Groups 1 – 3. Use product again for VERVE will be presented for Groups 2, 3, 4 and 5. The questionnaire will not be conducted for Group 6.

Use Product Again Questionnaire Summary Table 14.2.3.3.3 will have the following format:

Table 14.2.3.3.3 Summary of Response to Use the Product Again Bipolar Scores by Category, Study Group and Study Product (mITT Population)

Product	Statistics	Group 1		Group 2		Group 3		Group 4	Group 5
		-50 to <0	>0 to 50	-50 to <0	>0 to 50	-50 to <0	>0 to 50		
Cigarette	n	X	X	X	X	X	X		
	Mean	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		
	CV(%)	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		
	Minimum	X	X	X	X	X	X		
	Q1	X.X	X.X	X.X	X.X	X.X	X.X		
	Median	X.X	X.X	X.X	X.X	X.X	X.X		
	Q3	X.X	X.X	X.X	X.X	X.X	X.X		
	Maximum	XX	XX	XX	XX	XX	XX		
	95% CI	X, X	X, X	X, X	X, X	X, X	X, X		
VERVE	<Same as above>								

Note: Group X = <description of groups>

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

Programmer note: Use product again for cigarettes will be presented for Groups 1 – 3. Use product again for VERVE will be presented for Groups 2, 3, 4 and 5. The questionnaire will not be conducted for Group 6.

Table 14.3.1.1 Adverse Event Frequency by Study Group –
Number of Subjects Reporting the Event (% of Subjects Who Received Study Product Or in a Study group)

Adverse Event*	Product Trial$	Group 1	2	…..	6	Overall#
Number of Subjects Who Received Study Product Or in a Study Group	XX(100%)	XX(100%)	XX(100%)		XX(100%)	XX(100%)
Number of Subjects With Adverse Events	X(X%)	X(X%)	X(XX%)		X(X%)	X(X%)
Number of Subjects Without Adverse Events	XX(XXX%)	XX(XX%)	XX(XX%)		XX(XX%)	XX(XXX%)
Eye disorders	X(X%)	X(X%)	X(X%)		X(X%)	X(X%)
Vision blurred	X(X%)	X(X%)	X(X%)		X(X%)	X(X%)
Gastrointestinal disorders	X(X%)	X(X%)	X(X%)		X(X%)	X(X%)
Dyspepsia	X(X%)	X(X%)	X(X%)		X(X%)	X(X%)
Nausea	X(X%)	X(X%)	X(X%)		X(X%)	X(X%)
Musculoskeletal and connective tissue disorders	X(X%)	X(X%)	X(X%)		X(X%)	X(X%)
Back pain	X(X%)	X(X%)	X(X%)		X(X%)	X(X%)
Muscle cramps	X(X%)	X(X%)	X(X%)		X(X%)	X(X%)
Musculoskeletal pain	X(X%)	X(X%)	X(X%)		X(X%)	X(X%)
Nervous system disorders	X(X%)	X(X%)	X(X%)		X(X%)	X(X%)
Headache NOS	X(X%)	X(X%)	X(X%)		X(X%)	X(X%)
Reproductive system and breast disorders	X(X%)	X(X%)	X(X%)		X(X%)	X(X%)
Vaginal discharge	X(X%)	X(X%)	X(X%)		X(X%)	X(X%)
Respiratory, thoracic and mediastinal disorders	X(X%)	X(X%)	X(X%)		X(X%)	X(X%)
Epistaxis	X(X%)	X(X%)	X(X%)		X(X%)	X(X%)

Note: * Adverse events are classified according to MedDRA Version 20.0.
$ Only includes adverse events that occurred during the product trial period.
# Adverse events that occurred during the product trial period are excluded from the Overall summary.

Group X = <description of groups>

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)

		Group			
Adverse Event*	Product Trial$	1	2 …..	6	Overall#
Number of Adverse Events	XX(100%)	XX(100%)	XX(100%)	XX(100%)	XX(100%)
Eye disorders	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Vision blurred	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Gastrointestinal disorders	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Dyspepsia	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Nausea	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Musculoskeletal and connective tissue disorders	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Back pain	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Muscle cramps	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Musculoskeletal pain	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Nervous system disorders	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Headache NOS	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Reproductive system and breast disorders	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Vaginal discharge	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Respiratory, thoracic and mediastinal disorders	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Epistaxis	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)

Note: * Adverse events are classified according to MedDRA Version 20.0.
$ Only includes adverse events that occurred during the product trial period.
# Adverse events that occurred during the product trial period are excluded from the Overall summary.

Group X = <description of groups>

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

Adverse Event*	Group	Number of Subjects with Adverse Events	Severity			Relationship to Study Product				
			Mild	Moderate	Severe	Not Related	Unlikely	Possibly	Likely	Definitely
Abdominal pain	X	X	X	X	X	X	X	X	X	X
Constipation	X	X	X	X	X	X	X	X	X	X
Dry throat	Product Trial	X	X	X	X	X	X	X	X	X
Headache	X	X	X	X	X	X	X	X	X	X
Product trial$		X	X	X	X	X	X	X	X	X
Group 1		X	X	X	X	X	X	X	X	X
Group 2		X	X	X	X	X	X	X	X	X
Group 3		X	X	X	X	X	X	X	X	X
Group 4		X	X	X	X	X	X	X	X	X
Group 5		X	X	X	X	X	X	X	X	X
Group 6		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 20.0.
$ Only includes adverse events that occurred during the product trial period.
# Adverse events that occurred during the product trial period are excluded from the Overall summary.
When a subject experienced the same AE at more than one level of severity during a product use period, only the most severe occurrence was counted.
When a subject experienced the same AE at more than one level of product relationship during a product use period, only the occurrence most closely related to study product was counted.

Group X = <description of groups>

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

			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	Product trial	X	X	X	X	X	X	X	X	X
Headache	X	X	X	X	X	X	X	X	X	X
Product trial$		X	X	X	X	X	X	X	X	X
Group 1		X	X	X	X	X	X	X	X	X
Group 2		X	X	X	X	X	X	X	X	X
Group 3		X	X	X	X	X	X	X	X	X
Group 4		X	X	X	X	X	X	X	X	X
Group 5		X	X	X	X	X	X	X	X	X
Group 6		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 20.0.
$ Only includes adverse events that occurred during the product trial period.
# Adverse events that occurred during the product trial period are excluded from the Overall summary.

Group X = <description of groups>

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

Site	Subject Number	Age/ Gender	Study Visit Name	Study Visit Date	Group	Parameter1	Parameter2	Parameter3	Parameter4	Parameter5
XXX	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: Refer to Appendix 16.1.10.1 for the reference ranges of clinical laboratory tests.
H = Above Reference Range, L = Below Reference Range
PI Interpretation: N = Not Clinically Significant

Group X = <description of groups>

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

Laboratory Test (units)	Normal Range	Time Point	Statistic	Product Trial$	Group 1	2	….	6	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
		End-of-Study	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.

Group X = <description of groups>

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

Vital Sign (units)	Time Point	Statistic	Product	Group			
			Trial$	1	2 …..	6	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.

Group X = <description of groups>

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 Screening, Check-in, and End-of-Study.

13. 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 = <description of sites>

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

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

Appendix 16.2.1.1 Subject Disposition and Discontinuation (Randomized)

Site	Subject Number	Randomization Number	Study Group	Product Assignment	Date	Completed Study?	Day	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: Group X = <description of groups>

Product A = Subject's OB Cigarette (Reference Product)
Product B = Oral tobacco-derived nicotine chews marketed as VERVE® Discs Blue Mint (~1.5 mg nicotine/piece) (Test Product)
Product C = Oral tobacco-derived nicotine chews marketed as VERVE® Discs Green Mint (~1.5 mg nicotine/piece) (Test Product)
Product D = Oral tobacco-derived nicotine chews marketed as VERVE® Chews Blue Mint (~1.5 mg nicotine/piece) (Test Product)
Product E = Oral tobacco-derived nicotine chews marketed as VERVE® Chews Green Mint (~1.5 mg nicotine/piece) (Test Product)

Site XXX = <description of sites>

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

Appendix 16.2.1.2 Subject Disposition and Discontinuation (Product Trial)

Site	Subject Number	Discontinuation Date	Day	Completed Study?	Reason for Discontinuation	Specify
XXX	XXXXXX	DDMMMYYYY	X	No	XXXXXXXXXXXX	
	XXXXXX	DDMMMYYYY	X	No	XXXXXXXXXX	
	XXXXXX	DDMMMYYYY	X	No	XXXXXXXXX	
	XXXXXX	DDMMMYYYY	X	No	XXXXXXXXXXXX	
	XXXXXX	DDMMMYYYY	X	No	XXXXXXXXX	

Note: Site XXX = <description of sites>

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

Appendix 16.2.1.3 Subject Disposition and Discontinuation (Screen Failures)

Site	Subject Number	Discontinuation Date	Completed Study?	Reason for Discontinuation	Specify
XXX	XXXXXX	DDMMMYYYY	No	XXXXXXXXXXXXX	
	XXXXXX	DDMMMYYYY	No	XXXXXXXXXXX	
	XXXXXX	DDMMMYYYY	No	XXXXXXXXXX	
	XXXXXX	DDMMMYYYY	No	XXXXXXXXXXXXX	
	XXXXXX	DDMMMYYYY	No	XXXXXXXXXX	

Note: Site XXX = <description of sites>

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	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

Group X = <description of groups>

Site XXX = <description of sites>

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: Group X = <description of groups>

Site XXX = <description of sites>

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
XXX	XXXXXX	X	XXX	DDMMMYYYY	XXXXXXXXX	XXXXXXXXXXX
	XXXXXX	X	XXX	DDMMMYYYY	XXXXXXXXX	XXXXXXXXXXX
	XXXXXX	X	XXX	DDMMMYYYY	XXXXXXXXX	XXXXXXXXXXX
	XXXXXX	X	XXX	DDMMMYYYY	XXXXXXXXX	XXXXXXXXXXX
	XXXXXX	X	XXX	DDMMMYYYY	XXXXXXXXX	XXXXXXXXXXX
	XXXXXX	X	XXX	DDMMMYYYY	XXXXXXXXX	XXXXXXXXXXX

Note: Group = <description of groups>

Site XXX = <description of sites>

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.

Group X = <description of groups>

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.

Group X = <description of groups>

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	Study 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

Group X = <description of groups>

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

Appendix 16.2.4.3 Medical History

Subject Number	Any History?	Visit		History Number	Report Term		Date		Ongoing?	Were any comcomitant medications taken?
		Name	Date				Start	End		
XXXXXX	XXX	Screening	DDMMMYYYY	1	XXXXXX	XXXXX	MMYYYY		YES	XXX
				2	XXXXXX	XXXXX	MMYYYY	MMYYYY	NO	XXX
XXXXXX	XXX	Screening	DDMMMYYYY	1	XXXXXX	XXXXX	MMYYYY		YES	XXX

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	Visit		Study	Not	Reason for	Nicotine	Cigarette Smoked							
Number	Name	Date	Group	Done?	Not Done	Replacement?	Quit?	Duration	Unit	CPD	Brand	Brand Style	Flavor	Length (mm)
XXXXXX	Screening	DDMMMYYYY	X			XX	XXXX	XX	XXXX	XXX	XXXX	XXXX	XXXX	XX
XXXXXX	Screening	DDMMMYYYY	X			XX	XXXX	XX	XXXX	XXX	XXXX	XXXX	XXXX	XX
XXXXXX	Screening	DDMMMYYYY	X			XX	XXXX	XX	XXXX	XXX	XXXX	XXXX	XXXX	XX
XXXXXX	Screening	DDMMMYYYY	X			XX	XXXX	XX	XXXX	XXX	XXXX	XXXX	XXXX	XX
XXXXXX	Screening	DDMMMYYYY	X			XX	XXXX	XX	XXXX	XXX	XXXX	XXXX	XXXX	XX
XXXXXX	Screening	DDMMMYYYY	X			XX	XXXX	XX	XXXX	XXX	XXXX	XXXX	XXXX	XX

Note: Group X = <description of groups>

Nicotine Replacement = Are you currently using a nicotine replacement therapy patch, gum, inhaler, nasal spray or lozenge?
Quit? = Do you plan to quit smoking in the next 30 days?
Duration = How long have you smoked cigarettes?
CPD = How many cigarettes do you typically smoke per day?

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: Group X = <description of groups>

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

Appendix 16.2.4.5 Fagerström Test for Cigarette Dependence

Subject Number	Visit Name	Visit Date	Study Group	Not Done?	Answer Question 1	Answer Question 2	Answer Question 3	Answer Question 4	Answer Question 5	Answer Question 6	FTCD Score
XXXXXX	Screening	DDMMMYYYY	X		XXXXXXXXX	XXX	XXXXXXXXXXXX	XXXXXXXXXX	XXX	XXX	X
XXXXXX	Screening	DDMMMYYYY	X		XXXXXXXXX	XXX	XXXXXXXXXXXX	XXXXXXXXXX	XXX	XXX	X
XXXXXX	Screening	DDMMMYYYY	X		XXXXXXXXX	XXX	XXXXXXXXXXXX	XXXXXXXXXX	XXX	XXX	X
XXXXXX	Screening	DDMMMYYYY	X		XXXXXXXXX	XXX	XXXXXXXXXXXX	XXXXXXXXXX	XXX	XXX	X
XXXXXX	Screening	DDMMMYYYY	X		XXXXXXXXX	XXX	XXXXXXXXXXXX	XXXXXXXXXX	XXX	XXX	X
XXXXXX	Screening	DDMMMYYYY	X		XXXXXXXXX	XXX	XXXXXXXXXXXX	XXXXXXXXXX	XXX	XXX	X

Note: Question 1 = How soon after you wake up do you smoke your first cigarette?
Question 2 = Do you find it difficult to refrain from smoking in places where it is forbidden, e.g., in church, at the library, cinema, etc?
Question 3 = Which cigarette would you hate most to give up?
Question 4 = How many cigarettes/day do you smoke?
Question 5 = Do you smoke more frequently during the first hours of waking than during the rest of the day?
Question 6 = Do you smoke if you are so ill that you are in bed most of the day?

Group X = <description of groups>

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	XXXXXXXXXXXXXXXX

Note: Group X = <description of groups>

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

Appendix 16.2.5.2.1 Product Trial

Subject Number	Visit	Study Group	Was the Subject Willing to use the Verve products?	VERVE Product	Date	Start Time	Stop Time
XXXXXX	XXXXX	X	X	XXX	XXXXXXXXXX	DDMMMYYY	HH:MM	HH:MM

Note: Group X = <description of groups>

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

Appendix 16.2.5.2.2 In-Clinic Product Use

Subject Number	Study Day	Study Group	Episode #	Product Dispense	Dispense Date	Dispense Time	Product Returned?	Return Date	Returned Time	Comment
XXXXXX	XXXXX	X	1	XXX	DDMMMYYY	HH:MM	XXX	DDMMMYYY	HH:MM	

Note: Group X = <description of groups>

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

Appendix 16.2.5.2.3 Max CPD

Subject Number	Visit	Study Group	Max CPD Not Done	Reason for Not Done	Maximum CPD Allowed
XXXXXX	XXXXX	X	XX	XXX	XX

Note: Group X = <description of groups>

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

Appendix 16.2.5.3.1 24-Hour Urine Collection

Subject Number	Study Group	Study Product	Planned Timepoint	Was Collection Performed?	Reason for Not Done	Collection Start		Collection Stop		Urine Weight (g)	Number of Void	Incomplete, lost or discarded	Number of Incomplete, lost or discarded	Specify
						Date	Time	Date	Time					
XXXXXX	X	X	XXXXX	XXX		DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	XXXX	XX	XXX	XXX	

Note: Group X = <description of groups>

Product X = <description of products>

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

Appendix 16.2.5.3.2 Urine Samples

Subject Number	Study Group	Study Product	Planned Timepoint	Nicotine Equivalents- Samples Collected (2 aliquots of 5mL each	Creatinine- Samples Collected (2 aliquots of 5mL each)	Biomarkers of Exposure (2 aliquots of 40mL each)	Mutagenicity (2 aliquots of 250mL each)	Biobanking (2 aliquots of 40mL each)
XXXXXX	X	X	XXXXX	X	X	X	X	X

Note: Group X = <description of groups>

Product X = <description of products>

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

Appendix 16.2.5.4 Carboxyhemoglobin Blood Collection

Subject Number	Study Group	Study Product	Planned Timepoint	Was Blood Sample for COHb collected?	Collection Date	Collection Time	How Many COHb Samples Were Collected?
XXXXXX	X	X	XXXXX	XXX	DDMMMYYYY	HH:MM	X

Note: Group X = <description of groups>

Product X = <description of products>

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

Appendix 16.2.5.5 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: Group X = <description of groups>

Product X = <description of products>

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

Appendices 16.2.6.1 through 16.2.6.18 will have the following format:

Page 1 of X

Appendix 16.2.6.1 Total Urine NNAL

Subject Number	Study Group	Study Product	Study Day	Conc. (unit)	Urine Weight (g)	Total Mass (unit)	Absolute Change From Baseline (unit)	% Change From Baseline	Creatinine Conc. (mg/dL)	Adjusted for Urine Creatinine (mass/g Cr)
XXXXX	X	X	-1	XXX	XXX	XXX	NA	NA	XXX	XXX
			5	XXX	XXX	XXX	XXX	XXX	XXX	XXX
			7	XXX	XXX	XXX	XXX	XXX	XXX	XXX

Note: Baseline = Day -1, Conc. = Concentration

Group X = <description of groups>

Product X = <description of products>

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

Appendix 16.2.6.3.1 Urine Nicotine and Metabolites Concentrations

Subject Number	Study Group	Study product	Study Day	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	X	X	-1	XXX	XXX	XXX	XXXX	XXX	XXX
			5	XXX	XXX	XXX	XXXX	XXX	XXX
			7	XXX	XXX	XXX	XXXX	XXX	XXX

Note: Group X = <description of groups>

Product X = <description of products>

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

Appendix 16.2.6.19 Blood COHb

Subject Number	Study Group	Study Product	Study Day	Conc. (unit)	Absolute Change From Baseline (unit)	% Change From Baseline
XXXXX	X	X	-1	XXX	NA	NA
			5	XXX	XXX	XXX
			7	XXX	XXX	XXX

Note: Baseline = Day -1, Conc. = Concentration

Group X = <description of groups>

Product X = <description of products>

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

Appendix 16.2.6.20.1 Cigarettes Used per Day

Subject Number	Study Group	Study Product	Study Day	Cigarettes Per Day
XXXXX	X	X	-2	XX
			-1	XX
			Baseline	XX
			1	XX
			2	XX
			3	XX
			4	XX
			5	XX
			6	XX
			7	XX

Note: Baseline = Average of Days -2 and -1.

Group X = <description of groups>

Product X = <description of products>

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

Appendix 16.2.6.20.2 VERVE Product Used per Day

Subject Number	Study Group	Study Product	Study Day	VERVE Product Used per Day
XXXXX	X	X	1	XX
			2	XX
			3	XX
			4	XX
			5	XX
			6	XX
			7	XX

Note: Group X = <description of groups>

Product X = <description of products>

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

Appendix 16.2.6.21.1 Duration of VERVE Product Used per Use

Subject Number	Study Group	Study Product	Study Day	Episode Number	Duration (min)
XXXXX	X	X	1	1	XX.X
				2	XX.X
				3	XX.X

Note: Group X = <description of groups>

Product X = <description of products>

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

Appendix 16.2.6.21.2 Total Duration of VERVE Product Used per Day

Subject Number	Study Group	Study Product	Study Day	Total Duration (min)
XXXXX	X	X	1	XX.X
			2	XX.X
			3	XX.X
			4	XX.X
			5	XX.X
			6	XX.X
			7	XX.X

Note: Group X = <description of groups>

Product X = <description of products>

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

Appendix 16.2.6.22 Original and Factor Score to QSU-Brief Questionnaire

Subject Number	Study Group	Study Product	Study Day	Time Point	Date	Time	QSU-Brief 1	2	3	4	5	6	7	8	9	10	Factor Score 1	2
XXXXX	X	X	-1	Morning	DDMMMYYYY	HH:MM:SS	X	X	X	X	X	X	X	X	X	X	X	X
				Evening	DDMMMYYYY	HH:MM:SS	X	X	X	X	X	X	X	X	X	X	X	X
				Change	DDMMMYYYY		X	X	X	X	X	X	X	X	X	X	X	X

Note: 1. I have a desire for a cigarette right now. 2. Nothing would be better than smoking a cigarette right now.
3. If it were possible, I would probably smoke right now.
4. I could control things better right now if I could smoke.
5. All I want right now is a cigarette. 6. I have an urge for a cigarette.
7. A cigarette would taste good right now. 8. I would do almost anything for a cigarette right now.
9. Smoking would make me less depressed. 10. I am going to smoke as soon as possible.
Factor Score 1 (anticipation of pleasure from smoking) = Average of items 1, 3, 6, 7, and 10
Facore Score 2 (relief of nicotine withdrawal) = Average of items 2, 4, 5, 8, and 9.
Change = Evening score – Morning score

Group X = <description of groups>

Product X = <description of products>

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

Appendix 16.2.6.23.1 Original Score to MCEQ Questionnaire

Subject Number	Study Group	Study Product	Study Day	Questionnaire	Date	Time	mCEQ 1	2	3	4	5	6	7	8	9	10	11	12
XXXXX	X	X	-1	mCEQ-C	DDMMMYYYY	HH:MM:SS	X	X	X	X	X	X	X	X	X	X	X	X
			1	mCEQ-C	DDMMMYYYY	HH:MM:SS	X	X	X	X	X	X	X	X	X	X	X	X
				mCEQ-V	DDMMMYYYY	HH:MM:SS	X	X	X	X	X	X	X	X	X	X	X	X
			5	mCEQ-C	DDMMMYYYY	HH:MM:SS	X	X	X	X	X	X	X	X	X	X	X	X
				mCEQ-V	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?

Group X = <description of groups>

Product X = <description of products>

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

Appendix 16.2.6.23.2 Factor Score to MCEQ Questionnaire

Subject Number	Study Group	Study Product	Study Day	Questionnaire	Date	Time	Smoking Satisfaction	Psychological Reward	Aversion	Enjoyment of Sensation	Craving Reduction
XXXXX	X	X	-1	mCEQ-C	DDMMMYYYY	HH:MM:SS	X	X	X	X	X
			1	mCEQ-C	DDMMMYYYY	HH:MM:SS	X	X	X	X	X
				mCEQ-V	DDMMMYYYY	HH:MM:SS	X	X	X	X	X
			5	mCEQ-C	DDMMMYYYY	HH:MM:SS	X	X	X	X	X
				mCEQ-V	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

Group X = <description of groups>

Product X = <description of products>

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

Appendix 16.2.6.24 Use the Product Again Questionnaire

Subject Number	Study Group	Study Product	Study Day	Date	Time	If Given the Opportunity, I Would Want to Use the Cigarette Again (mm)	Category	Bipolar score
XXXXX	X	X	7	DDMMMYYYY	HH:MM:SS	XX	-50 to <0	-XX
		X	7	DDMMMYYYY	HH:MM:SS	XX	>0 to 50	XX

Note: Group X = <description of groups>

Product X = <description of products>

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 20.0.

Group X = <description of groups>

Product X = <description of products>

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: Group X = <description of groups>

Product X = <description of products>

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 20.0.

Group X = <description of groups>

Product X = <description of products>

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

Appendices 16.2.8.1.2 to 16.2.8.1.3 will have the following format.

Page 1 of X

Appendix 16.2.8.1.1 Clinical Laboratory Report - Serum Chemistry

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

Note: Refer to Appendix 16.1.10.1 for the reference ranges of clinical laboratory tests.
H = Above Reference Range, L = Below Reference Range
PI Interpretation: N = Not Clinically Significant

Group X = <description of groups>

Product X = <description of products>

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 16.2.8.1.4 Clinical Laboratory Report – Comments

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

Note: Group X = <description of groups>

Product X = <description of products>

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

Appendix 16.2.8.1.5 Alcohol Breath Tests

Subject Number	Study Group	Visit		Was an Alcohol Breath Test Performed?	Test	
		Name	Date		Date	Result
XXXXXX	X	Screening	DDMMMYYYY	XXX	DDMMMYYYY	XXXXXX
		Check-in	DDMMMYYYY	XXX	DDMMMYYYY	XXXXXX

Note: Group X = <description of groups>

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

Appendix 16.2.8.1.6 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: Group X = <description of groups>

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

Appendix 16.2.8.1.7 Pregnancy Tests

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

Note: Group X = <description of groups>

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

Appendix 16.2.8.1.8 Serum FSH

Subject Number	Study Group	Visit Name	Visit Date	Was Serum FSH Done?	Reason for Not Done	Was Postmenopausal Status confirmed?	Collection Date
XXXXXX	X	Screening	DDMMMYYYY	XXX		XXX	DDMMMYYYY

Note: Group X = <description of groups>

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

Appendix 16.2.8.1.9 Contraception

Subject Number	Study Group	Visit Name	Visit Date	Contraception?	Hormonal	Double Barrier?	Intrauterine Device?	Vasectomized Partner?	Other	Specify
XXXXXX	X	Screening	DDMMMYYYY	XXX	XXX	XXX	XXX	XXX		
		XXXXXXXXX	DDMMMYYYY	XXX	XXX	XXX	XXX	XXX		

Note: Group X = <description of groups>

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

Appendix 16.2.8.1.10 Urine Cotinine Screens

Subject Number	Study Group	Visit		Was the Urine Cotinine Sample Collected?	Date of Collection	Result (ng/mL)
		Name	Date			
XXXXXX	X	Screening	DDMMMYYYY	XXX	DDMMMYYYY	XXX

Note: Group X = <description of groups>

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

Appendix 16.2.8.1.11 Serology Sample Collection

Subject Number	Study Group	Visit		Was the Sample Collected?	Collection
		Name	Date		Date
XXXXXX	X	Screening	DDMMMYYYY	XXX	DDMMMYYYY

Note: Group X = <description of groups>

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

Appendix 16.2.8.2 Vital Signs

Subject Number	Name	Study Group	Study Product	Date	Time	Not Done?	Reason 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
	Check-in		X	DDMMMYYYY	HH:MM			XXX/ XX NCS	XX	XX	XX.X
	End-of-Study			DDMMMYYYY	HH:MM			XXX/ XX	XX CS	XX	XX.X

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

Group X = <description of groups>

Product X = <description of products>

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

Appendix 16.2.8.3 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		

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

Group X = <description of groups>

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

Appendix 16.2.8.4 Smoking Cessation Information

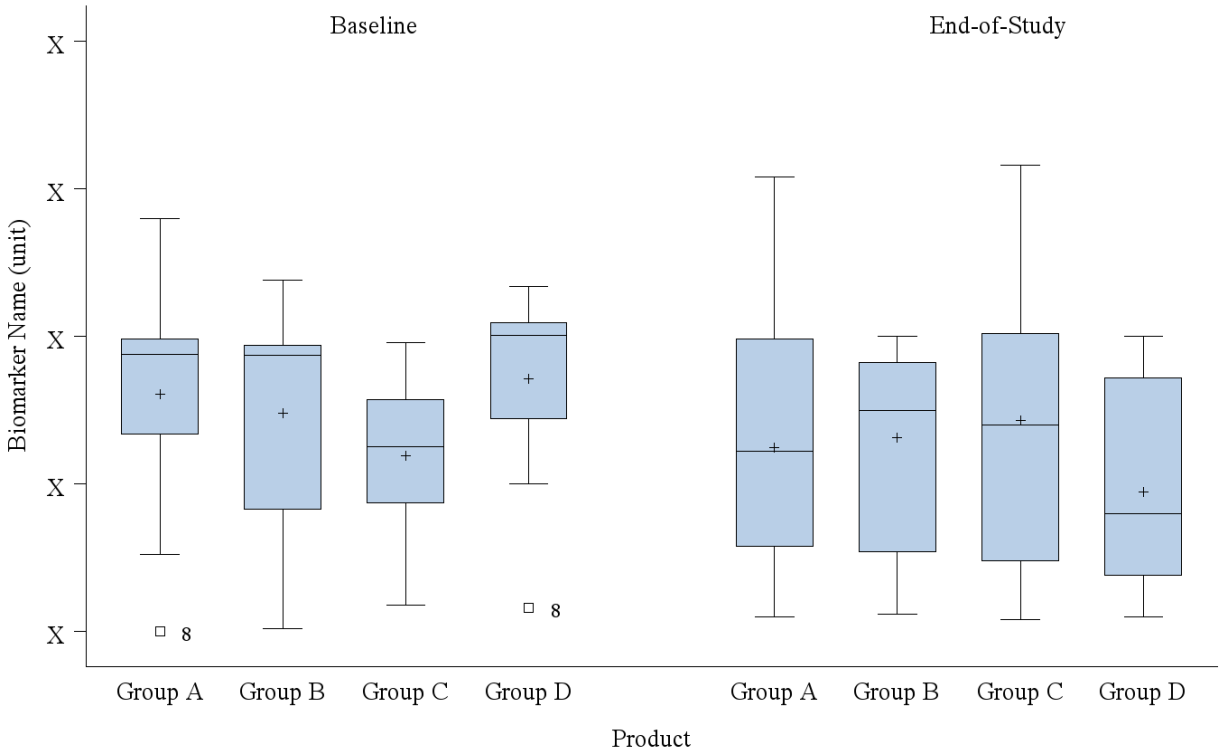
Subject Number	Visit	Was Smoking Cessation Information Offered?	Date Information Offered
XXXXXX	Screening	XXX	DDMMMYYYY
	End of Study	XXX	DDMMMYYYY

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

14. FIGURE SHELLS

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

Figure 14.2.4.1.1
Box Plot of Total Urine NNAL at Baseline and Day 7 by Study Group (mITT Population)



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

15. REFERENCES

1. Sanderson L et al. 2001. Evaluation of the brief questionnaire of smoking urges (QSU-brief) in laboratory and clinical settings. Nicotine and Tobacco Research. (3)7-16
2. Cappelleri et al. 2007. Confirmatory factor analysis and reliability of the modified cigarette evaluation questionnaire. Additive Behaviors. (32)912-923.