An Open-Label, Randomized, Crossover Study to Assess Nicotine Uptake, Tobacco-Related Biomarkers of Exposure, Biomarkers of Potential Harm, and Puff Topography with Use of *my*bluTM Electronic Cigarettes in Adult Smokers

NCT# NCT04429932

Study SAP – 26 February 2020

Statistical Analysis Plan

An Open-Label, Randomized, Crossover Study to Assess Nicotine Uptake, Tobacco-Related Biomarkers of Exposure, Biomarkers of Potential Harm, and Puff Topography with Use of *my*blu™ Electronic Cigarettes in Adult Smokers

Protocol No: NER 01/003
Final Protocol Date: 4 November 2019
Amendment 1 Date: 4 December 2019

Product Names: *my*blu™ (freebase), Gold Leaf flavor, 2.4%; *my*blu™ (freebase), Polar Mint flavor, 2.4%; *my*blu™ (freebase), Cherry flavor, 2.4%; *my*blu™ (freebase), Vanilla flavor, 2.4%; *my*blu™ (freebase), Gold Leaf flavor, 1.2%; *my*blu™ (freebase), Polar Mint flavor, 1.2%; *my*blu™ (freebase), Menthol flavor, 2.4%; *my*blu™ Intense (nicotine salts), Fresh Mint flavor, 2.4%

[redacted] Project CA22736
Final Version 1.0
Date: 26 February 2020

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Statistical Analysis Plan Signature Page

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1. INTRODUCTION

The following statistical analysis plan (SAP) provides the framework for the summarization of the data from this study. The SAP may change due to unforeseen circumstances. Any changes made from the planned analysis within protocol, after the locking of the database will be documented in the clinical study report (CSR). The section referred to as Table Shells within this SAP describes the traceability of the tables, figures, and listings (TFLs) back to the data.

Any additional exploratory analyses not addressed within this SAP and/or driven by the data, or requested by Nerudia Ltd., will be considered out of scope and must be described in the CSR.

2. OBJECTIVES AND ENDPOINTS

2.1 Objectives

Primary:

1. To characterize nicotine uptake following controlled use of *my*blu™ electronic cigarettes (e-cigarettes)
2. To assess the change-from-baseline differences in the primary tobacco-related biomarkers of exposure (BoE) following a 9-day use period of *my*blu™ e-cigarettes.

Secondary:

1. To assess the change-from-baseline differences in the primary tobacco-related BoE following a 14-day use period of *my*blu™ e-cigarettes.
2. To assess the change-from-baseline differences in the secondary tobacco-related BoE following 9-day and 14-day use periods of *my*blu™ e-cigarettes.
3. To characterize the change in the primary and secondary tobacco-related BoE and biomarkers of potential harm (BoPH) during a 14-day period of use of *my*blu™ e-cigarettes and compare between exclusive e-cigarette use, exclusive combustible cigarette use and dual (combustible cigarette and e-cigarette) use.
4. To assess the change-from-baseline differences in the primary and secondary tobacco-related BoE between Day 9 and Day 14 in subjects using *my*blu™ e-cigarettes, both exclusively and alongside use of combustible cigarettes.
5. To assess change-from-baseline differences in BoPH following 9-day and 14-day use periods of *my*blu™ e-cigarettes.
6. To assess measures of subjective effects associated with use of *my*blu™ e-cigarettes.
7. To determine puffing topography parameters (puff count, puff duration, puff volume, peak puff flow rate, average puff flow rate, inter puff interval) following an 8-day use period of *my*blu™ e-cigarettes and assess change-from-baseline differences (if applicable).

8. To assess change-from-baseline differences in physiologic endpoints (i.e., blood pressure [BP], heart rate [HR], and spirometry) following 9-day and 14-day use periods of *my*blu™ e-cigarettes.
9. To characterize product use of *my*blu™ e-cigarettes under short-term controlled and *ad libitum* use conditions.
10. To assess the safety and tolerability of *my*blu™ e-cigarettes following short-term use.

2.2 Endpoints

Primary Study Endpoints:

1. Pharmacokinetics

   $AUC_{0\text{-}180}$, C_{max}, and T_{max} from each controlled product use session on Days 2, 4, 6, and 8.

2. Biomarkers of Exposure

   Concentration (blood BoE) or 24-hour mass excreted (Urine BoE) for the primary biomarkers of exposure listed below:

Biomarker	Matrix	Chemical Constituent
Carboxyhemoglobin (COHb)	Blood	Carbon monoxide (CO)
4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL)	Urine	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)
3-hydroxypropylmercapturic acid (3-HPMA)	Urine	Acrolein
S-phenyl mercapturic acid (S-PMA)	Urine	Benzene

Secondary Study Endpoints:

1. Biomarkers of Exposure

   24-hour mass excreted for the secondary biomarkers of exposure listed below:

Biomarker	Matrix	Chemical Constituent
N-nitrosonornicotine (NNN)	Urine	NNN
2-cyanoethyl-mercapturic acid (CEMA)	Urine	Acrylonitrile
Hydroxyethyl mercapturic acid (HEMA)	Urine	Ethylene oxide
3-hydroxy-1-methylpropylmercapturic acid (HMPMA)	Urine	Crotonaldehyde

Monohydroxybutenylmercapturic acid (MHBMA)	Urine	1,3-butadiene
Hydroxypyrene (1-OHP)	Urine	Pyrene
o-toluidine (o-tol)	Urine	Toluidine
3-hydroxybenzo[a]pyrene (3-OH B[a]P)	Urine	B[a]P
1-aminonaphthalene (1-AN)	Urine	Naphthalene
2-aminonaphthalene (2-AN)	Urine	Naphthalene
Nicotine equivalents	Urine	Nicotine

2. Biomarkers of Potential Harm

   Concentration (blood BoPH) or 24-hour mass excreted (urine BoPH) for the secondary biomarkers of exposure listed below:

Biomarker	**Matrix**	**Biological Effect**
Soluble intracellular adhesion molecule (sICAM)	Blood	Inflammation
White blood cells (WBCs)	Blood	Inflammation
High density lipoprotein cholesterol (HDL-C)	Blood	Inflammation
Monocyte chemoattractant protein 1 (MCP-1)	Blood	Inflammation
Type III isoprostane (8-epi-prostaglandin $F_{2\alpha}$)	Urine	Oxidative stress
11-dehydrothromboxane B_2	Urine	Platelet activation

3. Subjective measures

- Urge to Smoke (Part 1)
  - Maximum reduction from baseline score (E_{max_R})
  - Time of the $E_{max\ R}$ (TE_{max})
  - Area under the reduction from baseline "Urge to Smoke" visual analog scale (VAS) score versus time curve ($AUEC_{\_R}$)
- Product Liking Questionnaire VAS responses
- Product Evaluation Scale (PES) factor scores
- Future Intent to Use Questionnaire bipolar VAS scores
- Questionnaire of Smoking Urges-Brief (QSU-Brief) factor scores
- Minnesota Tobacco Withdrawal Scale-Revised (MTWS-R) total score
- Penn State [Electronic] Cigarette Dependence Index (PSCDI, PSECDI) total score

4. Puff Topography parameters: puff count, puff duration, puff volume, peak puff flow rate, average flow rate, inter-puff interval

5. Physiological Endpoints
- Blood Pressure and Heart Rate: Change from Baseline AUEC0-t, Emax, TEMax

- Pre-bronchodilator and change from pre to post-bronchodilator lung function variables: FEV1, FVC, FEV1:FVC ratio, FEF25-75%

6. Product Use Behavior

Days 1, 3, 5, 7, and 9

- Pod weight differences

Days 2, 4, 6, and 8

- Number of inhalations (first (controlled) product use session)
- Duration of each inhalation (first (controlled) product use session)
- Pod weight differences (first (controlled) and second (*ad libitum*) product use sessions)

Days 10-14

- Pod weight differences (Arm I and Arm K)
- Number of cigarettes smoked (Arm J and Arm K)

7. Safety Assessments

Safety endpoints will include physical examinations, vital signs, electrocardiograms (ECGs), clinical laboratory tests, AEs, and use of concomitant medications.

3. STUDY DESIGN

This will be an open-label, randomized, 2-part study in adult smokers. All subjects will participate in both study parts. Part 2 will begin immediately after Part 1.

Screening procedures will be performed within 28 days prior to study procedures on Day -2.

Subjects who successfully complete the screening procedures and meet the eligibility criteria will be eligible to check in to the clinical research unit (CRU) on Day -2 and will complete all subjective effects questionnaires for the purpose of familiarization with the questions, scales, and computerized tablet. Subjects will also participate in a brief trial on Day -2 (approximately 30 minutes) using the *my*blu™ device with a 0% nicotine e-liquid, to familiarize with the use of the device. Baseline study assessments, including BoE, BoPH, spirometry (Day -1 only), BP, HR, and puff topography (in a subset of 16 subjects [2 subjects from each sequence in Part 1] on Day -1 only) will be performed on Days -2 through -1, as appropriate. Subjects will continue to smoke their usual brand combustible cigarette from check-in through Day -1, but will abstain from use of any tobacco- or nicotine-containing products for at least 12 hours prior to the start of product use on Day 1. Subjects will be randomized to 1 of 8 sequences (Part 1) on Day -1. Sequences are shown in Figure 3.1

Part 1 (Days 1 to 9)

On Days 1, 3, 5, and 7, subjects will use the study product they are assigned to use the following day according to the randomization scheme. Subjects will use the assigned study product *ad libitum* until the start of the abstinence period (i.e., at least 12 hours prior to the start of the first product use session on the next day). A fully charged battery and a fresh pod will be provided on each day. Additional pods will be provided as needed. Pods will be weighed within 24 hours before the start and after completion of product use on each day. On Day 1, puff topography measurements will be performed in the same subset of 16 subjects (2 subjects from each sequence in Part 1) for 1 hour during *ab libitum* product use. Puff topography should be performed within ± 2 hours of the time of the baseline assessment on Day -1.

On Days 2, 4, 6, and 8, subjects will participate in two product use sessions on each day, using the assigned study product according to the randomization scheme. In the first (controlled) product use session, subjects will use the assigned study product under controlled conditions (i.e., 10 puffs taken at 30-second intervals, with puffs 3 seconds in duration). Blood samples for nicotine pharmacokinetic (PK) assessment will be collected prior to and for 3 hours following the start of the first product use session. Subjects will complete the Urge to Smoke questionnaire during and following the first product use session and the Product Liking, Product Evaluation Scale (PES), and Future Intent to Use questionnaires following the first product use session. Following collection of the last PK blood sample (180-minute time point) and completion of the subjective effects questionnaires, subjects will start the second (*ad libitum*) product use session, during which they will use the same assigned study product *ad libitum* (with no limits on puff duration or inter-puff interval) until approximately 23:00. Subjects will complete the Urge to Smoke, Product Liking, PES, and Future Intent to Use questionnaires at least 6 hours after the start of the second product use session. A fresh pod and fully charged device will be provided for each product use session. Pod weights will be measured before and after each product use session. On Day 8, puff topography measurements will be performed in the same subset of 16 subjects (2 subjects from each sequence in Part 1) for 1 hour during the second (ab libitum) product use session. Puff topography will be performed at least 4 hours after the start of the second (ab libitum) product use session and should be within ± 2 hours of the time of the baseline assessment on Day -1.

On Day 9, subjects may use all or any of the 4 study products (used previously on Days 1 to 8) *ad libitum* until approximately 23:00. For BoE and BoPH assessments, blood samples will be collected on Day 9 and urine samples will be collected over 24 hours (starting on Day 8 after completion of the second [*ab libitum*] product use session). BP and HR measurements will be taken throughout the period of *ad libitum* product use. Subjects will complete the Questionnaire on Smoking Urges-Brief (QSU-Brief), the Minnesota Tobacco Withdrawal Scale-Revised (MTWS-R), and the Penn State [Electronic] Cigarette Dependence Index (PSCDI/PSECDI) questionnaires at least 6 hours after the start of the *ad libitum* product use session on Day 9. Spirometry measurements will be conducted following completion of all subjective effects questionnaires on Day 9. Fresh pods and a fully charged device will be provided on Day 9 and pod weights will be measured.

Depending on the availability of topography equipment, puff topography may not be performed at all scheduled time points and may not be performed for some or all assigned subjects.

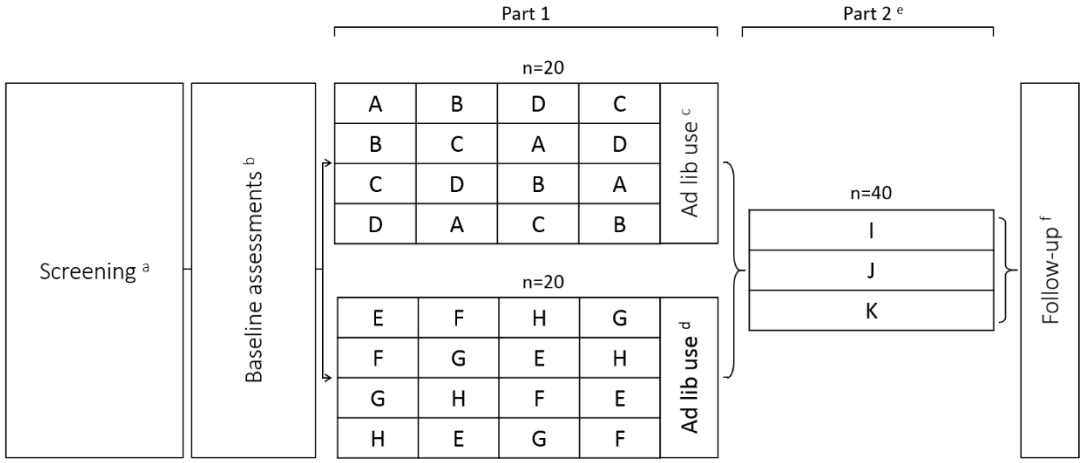
Part 2 (Days 10 to 14)

Subjects will be randomized to 1 of 3 study arms (Part 2) on Day 10. Subjects will use any or all of the 8 study products and/or smoke their usual brand combustible cigarettes *ad libitum* for 5 days (until approximately 23:00 on each day) according to the randomization scheme. For BoE and BoPH assessments, blood samples will be collected on Day 14 and urine samples will be collected over 24 hours (starting on Day 13 after the end of product use for that day). On Day 14, BP and HR measurements will be taken throughout the period of *ad libitum* product use/smoking. The QSU-Brief, MTWS-R, and PSCDI/PSECDI questionnaires will be completed at least 6 hours after the start of the *ad libitum* product use session on Day 14. Spirometry measurements will be conducted following completion of all subjective effects questionnaires on Day 14. Product use behavior will be assessed by documenting the number of cigarettes smoked, the flavor and strength of the *my*blu™ products, and pod weights, per day, as appropriate. On each study day, fresh pods and a fully charged device will be provided, as appropriate.

The CRU will attempt to contact all subjects who used at least one study product (including subjects who terminate the study early) using their standard procedures approximately 14 days after the last study product use to determine if any adverse event (AE) has occurred since the last study visit.

An overview of the study design is shown in the Figure 3.1.

Figure 3.1. Study Design Overview



Study Days	-2	-1	1 g	2	3 g	4	5 g	6	7 g	8	9	10	11	12	13	14
Randomization		X										X				
PK blood sampling				X		X		X		X						
BoE/BoPH	<-- X -->									<-- X -->					<-- X -->	
Subjective questionnaires	X h			X		X		X		X	X					X
Puff topography i		X	X							X						
Intensive BP and HR		X									X					X
Spirometry		X									X					X

a: To be performed within 28 days prior to study procedures on Day -2.

b: Baseline study assessments will be performed on Days -2 and -1 while subjects continue to smoke their usual brand combustible cigarette.

c: Subjects may use all or any of the 4 study products (i.e., A, B, C, and/or D) *ad libitum* (Ad lib) until approximately 23:00.

d: Subjects may use all or any of the 4 study products (i.e., E, F, G, and/or H) *ad libitum* (Ad lib) until approximately 23:00.

e: Subjects will be randomized to 1 of 3 study arms (Part 2) on Day 10 and will use any or all of the 8 study products (Products A to H) and/or smoke their usual brand combustible cigarettes *ad libitum* for 5 days according to the randomization scheme.

f: The CRU will attempt to contact all subjects who used at least one study product (including subjects who terminate the study early) using their standard procedures approximately 14 days after the last study product used.

g: Subjects will use *ad libitum* the study product they are assigned to use the following day according to the randomization scheme. Subjects will use the assigned study product *ad libitum* until the start of the abstinence period (i.e., at least 12 hours prior to the start of the first product use session on the next day).

h: Subjects will complete one set of questionnaires for the purpose of familiarization with subjective effects questions, appropriate use of the VAS, and use of the computerized tablet system.

i: A total of 16 subjects (2 subjects from each sequence in Part 1) will have puff topography evaluated for 1 hour during *ad libitum* product use.

4. ANALYSIS POPULATIONS

4.1 Analysis Populations

4.1.1 Safety Population

For Part 1, the Safety Population will include all subjects who used at least one study product from Day -2.

For Part 2, the Safety Population will include all subjects who completed Part 1 and were randomized in Part 2 on Day 10.

4.1.2 Outcomes Population

The Outcomes Population (Part 1) is a subset of the Part 1 safety population and will consist of subjects who used a study product and have evaluable Part 1 PK, biomarkers, subjective effects, or topography data. This population will be used in the summary and analysis of Part 1 PK, subjective effects, topography, biomarkers, and product use, and all available data will be included in the summary tables to the extent possible.

The Outcomes Population (Part 2) is a subset of the Part 2 safety population and will consist of subjects who completed Part 1 and have evaluable Part 2 biomarkers, subjective effects, BP, HR, or spirometry data. This population will be used in the summary and analysis of Part 2 biomarkers, subjective effects, BP, HR, spirometry, and product use, and all available data will be included in the summary tables to the extent possible.

4.2 Preliminary Data and Interim Analysis

[redacted] Biometrics will not perform interim analyses.

5. PRODUCT AND STUDY ARM DESCRIPTIONS

Subjects will be required to bring with them to the CRU a sufficient supply (i.e., 2-week supply [unopened packs]) of their usual brand combustible cigarettes for personal use throughout confinement (if applicable).

The e-cigarette products in Table 5.1 will be used in Part 1 of this study. In the CSR text and table headings, products will be referred to by the short descriptions. In the table footers, the 8 products will be referred to as Products A through H referenced to the long descriptions as shown in the following table:

Table 5.1. Product Description

Products	Short Description	Long Description
A	*my*blu™ Gold Leaf 2.4%	*my*blu™ (freebase), Gold Leaf flavor, 2.4%
B	*my*blu™ Polar Mint 2.4%	*my*blu™ (freebase), Polar Mint flavor, 2.4%
C	*my*blu™ Cherry 2.4%	*my*blu™ (freebase), Cherry flavor, 2.4%
D	*my*blu™ Vanilla 2.4%	*my*blu™ (freebase), Vanilla flavor, 2.4%
E	*my*blu™ Gold Leaf 1.2%	*my*blu™ (freebase), Gold Leaf flavor, 1.2%
F	*my*blu™ Polar Mint 1.2%	*my*blu™ (freebase), Polar Mint flavor, 1.2%
G	*my*blu™ Menthol 2.4%	*my*blu™ (freebase), Menthol flavor, 2.4%
H	*my*blu™ Intense Fresh Mint 2.4%	*my*blu™ Intense (nicotine salts), Fresh Mint flavor, 2.4%

Similarly, in Part 2, the following descriptions of study arms will be used:

Arm	Short Description	Long Description
I	*my*blu™	Exclusive use of *my*blu™ products *ad libitum*
J	Combustible Cigarette	Exclusive smoking of usual brand combustible cigarettes *ad libitum*
K	Dual Use	Smoking of usual brand combustible cigarettes (up to 50% of the subject's self-reported CPD) and use of *my*blu™ products *ad libitum*

6. ANALYSIS OF STUDY ENDPOINTS

6.1 Product Use Behavior

6.1.1 Product Use and Data Collection

Part 1
On Days -2 and -1, subjects will smoke their usual brand combustible cigarette *ad libitum*.

On Days 1, 3, 5, and 7, Subjects will use the assigned study product *ad libitum* until the start of the abstinence period.

On Days 2, 4, 6, and 8, subjects will participate in two product use sessions on each day, using the assigned study product according to the randomization scheme. In the first (controlled) product use session, subjects will use the assigned study product under controlled conditions (i.e., 10 puffs taken at 30-second intervals, with puffs 3 seconds in duration). In the second (*ad libitum*) product use session, they will use the same assigned study product *ad libitum* (with no limits on puff duration or inter-puff interval)

On Day 9, subjects may use all or any of the 4 study products (used previously on Days 1 to 8) *ad libitum.*

Pods will be weighed before the start and after completion of product use on each day for Days 1 through 9.

Part 2
On Days 10 to 14, subjects will use any or all of the 8 study products and/or smoke their usual brand combustible cigarettes *ad libitum*. The number of cigarettes smoked, the flavor and strength of the *my*blu™ products, and pod weights will be documented each day, as appropriate.

6.1.2 Product Use Data Summarization

The following product use variables will be determined:

Part 1
Days 1, 3, 5, 7, and 9

- Pod weight differences

Days 2, 4, 6, and 8

- Number of inhalations (first (controlled) product use session)
- Duration of each inhalation (first (controlled) product use session)

- Pod weight differences (first (controlled) and second (ad libitum) product use sessions)

Part 2
Days 10-14

- Pod weight differences (Arm I and Arm K)
- Number of cigarettes smoked (Arm J and Arm K)

Product use variables will be summarized by study product, product use session, and study day as applicable (Part 1) and by study arm and study day (Part 2) using descriptive statistics presented overall and by sex. When multiple pods are used, the pod weight differences will be calculated using the sums of the weights before and after product use.

The level of precision for each statistic will be presented as follows:

- minimum/maximum in same precision as the data,
- arithmetic mean/median in one more level of precision than minimum/maximum,
- SD in one more level of precision than mean/median,
- n will be presented as an integer,
- arithmetic CV% will be presented to 1 decimal point

6.2 Plasma Nicotine Pharmacokinetics (Part 1 only)

6.2.1 Measurements and Collection Schedule

On each of Days 2, 4, 6, and 8, a 4 mL blood sample for plasma nicotine analysis will be drawn into a plastic K2-EDTA (lavender top) vacutainer tube approximately 5 minutes prior to and at 3, 5, 7, 10, 12, 15, 20, 30, 60, 120 and 180 minutes following the start of the controlled product use episode.

6.2.2 Pharmacokinetic Concentrations

Plasma concentrations of nicotine as determined at the collection times described in Section 6.2.1 will be used for the calculation of the plasma nicotine PK parameters.

All concentration data will be included in the calculation of the individual PK parameters, the individual concentration-time plots (based on actual sample times), and in the mean concentration-time plots (based on nominal sample times). However, if there are any significant deviations from nominal sample times, some concentration data may be excluded from mean concentration-time plots and/or additional concentration-time plots of the mean data may be provided. All deviations and excluded data will be provided and discussed in the CSR.

6.2.3 Plasma Nicotine Pharmacokinetic Parameters

The appropriate noncompartmental PK parameters will be calculated for each controlled product use episode from the baseline adjusted plasma nicotine concentration-time data using Phoenix® WinNonlin® Version 7.0 or higher. Actual sample times will be used in the calculations of the PK parameters. The calculation of the actual time for nicotine will be in respect to the start of product use episodes. All PK parameters included in the protocol are listed in Table 6.1 below, and are defined as appropriate for study design.

Table 6.1. Noncompartmental Pharmacokinetic Parameters to be Calculated (Baseline Adjusted)

Label to be Used in the Text, Tables and Figures	Definition	Method of Determination
AUC0-t	Area under the nicotine concentration-time curve from time 0 (defined as the start of product use) to 180 minutes (or the last quantifiable concentration during the interval)	Calculated using the Linear Trapezoidal with Linear Interpolation Method
Cmax	Maximum measured plasma concentration over the duration of the measurement interval	Taken directly from bioanalytical data
Tmax	Time to reach the maximum measured plasma concentration over the duration of the measurement interval. If the maximum value occurs at more than one time point, Tmax is defined as the first time point with this value.	Taken from clinical database as the difference in the time of administration and the time of the blood draw which is associated with the Cmax.

Pharmacokinetic parameters will not be calculated for subjects with less than 3 consecutive post-product use time points with quantifiable concentrations. Subjects for whom there are insufficient data to calculate the PK parameters will be included in the concentration tables only and excluded from the descriptive statistics.

Plasma concentrations below the limit of quantitation will be set to one-half of the lower limit of quantitation for the calculation of descriptive statistics of unadjusted plasma nicotine concentrations and for the calculation of baseline-adjusted nicotine concentrations.

Baseline (pre-product use) adjustments will be performed for calculation of PK parameters. The values used for all pre-product use adjustments is the plasma nicotine concentration value obtained before the first product use on each study day.

Baseline-adjustment method: For each PK profile, the pre-product administration nicotine concentration value for each subject will be subtracted from each nicotine

concentration obtained after test product administration on that day using the following equation:

$C_t = C_{t\ uncorrected} - [C_0 \cdot e^{-Kel \cdot t1}]$

Where:

C_t = Corrected concentration.
$C_{t\ uncorrected}$ = the uncorrected concentration.
C_0 = the pre-product administration concentration.
$Kel = \frac{\ln(2)}{t½}$

Where t½ is 120 minutes for all subjects (estimated nicotine half-life)

t = actual sampling time since product administration.
t1 = actual sampling time since pre-product administration sampling.

After correction for pre-product administration values, some concentrations may be below the lower limit of quantitation and some may be negative values. Negative values will be assigned a value of zero in the analyses and all other values obtained will be reported as is even if these values are BLQ.

6.2.4 PK Data Summarization and Presentation

All nicotine PK concentrations and/or PK parameters descriptive statistics will be generated using SAS® version 9.4.

The plasma concentrations of nicotine will be listed and summarized by product and time point for all subjects in the Outcomes Population. Unadjusted and baseline adjusted plasma concentrations of nicotine will be presented with the same level of precision as received from the bioanalytical laboratory. Summary statistics, including number of observations (n), arithmetic mean (Mean), standard deviation (SD), coefficient of variation (CV%), minimum, median, maximum will be calculated for all nominal concentration time points. Excluded subjects will be included in the concentration listings, but will be excluded from the summary statistics and noted as such in the tables. All BLQ values will be presented as "BLQ" in the concentration listings and footnoted accordingly.

Mean and individual concentration-time profiles will be presented on linear and semi-log scales. Linear mean plots will be presented with and without SD.

Plasma nicotine PK parameters will be listed and summarized by product (overall and by sex) for all subjects in the Outcomes Population. Pharmacokinetic parameters will be reported to 3 significant figures for individual parameters, with the exception of Tmax, which will be presented with 2 decimal places. Summary statistics (n, arithmetic mean, geometric mean, SD, CV%, geometric CV% (Geom CV%), minimum, median, maximum), will be calculated for plasma nicotine PK parameters AUC0-t, Cmax, and Tmax. Excluded subjects will be listed in the PK parameter

tables, but will be excluded from the summary statistics and noted as such in the tables.

The level of precision for each concentration and PK parameter statistic will be presented as follows:

- minimum/maximum in same precision as in bioanalytical data and/or parameter output,
- mean/geometric mean/median in one more level of precision than minimum/maximum,
- SD in one more level of precision than mean/median,
- n will be presented as an integer, and
- CV% and Geom CV% will be presented to the nearest tenth.

Statistical analyses will be performed using SAS and are described in Section 6.7.

6.3 Biomarkers of Exposure and Potential Harm

6.3.1 Biomarker Sample Collection

Blood Biomarker Sample Collection

Blood samples for COHb (2 x 4 mL) in whole blood, sICAM in plasma (1 x 4 mL), WBCs (1 x 4 mL) in whole blood, and HDL-C in serum (1 x 3.5 mL), and MCP-1 in serum (1 x 3.5 mL) will be collected on Days -1, 9, and 14. Samples for COHb will be collected in the afternoon and samples for the other biomarkers will be collected following a fast of at least 8 hours.

Urine Biomarker Sample Collection

24-hour urine collections for biomarker measurements (NNAL, 3-HPMA, S-PMA, NNN, CEMA, HEMA, HMPMA, MHBMA, 1-OHP, (o-tol, 3-OH B[a]P, 1-AN, 2-AN, nicotine equivalents, 8-epi-prostaglandin $F_{2\alpha}$, and 11-dehydrothromboxane B_2) will take place on Day -2 to -1, Day 8 to 9, and Day 13-14. Each 24-hour urine collection will begin at the start of overnight abstinence.

Subjects will be instructed to attempt to void prior to the beginning and at the end of each interval. All urine must be collected during the entire 24-hour interval. The start and stop time of each 24-hour interval and the total weight of the collection will be documented. The weight of the 24-hour urine collection containers will be documented prior to the collection (tare weight) and following completion of the collection.

Collections for each subject will be pooled into one labeled container throughout the interval and the total weight (g) will be recorded at the end of the 24-hour interval. Any missed voids will be documented, including the reason for missing.

6.3.2 Biomarker Calculations

Calculation of Urine Nicotine Equivalents

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

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

Calculation of Total Mass Excreted

Urine biomarker concentrations will be converted into biomarker quantities excreted in 24 hours by multiplying the measured concentration by the total weight (i.e., 1 kilogram = 1 liter) of urine produced by the subject during the 24-hour period.

Creatinine Adjustments

Urine creatinine will be measured and used to adjust the values of the primary and secondary urine BoPH and BoE as follows.

$$\text{Biomarker (unit/g creatinine)} = \frac{\text{Biomarker (units)} \times 100}{\text{creatinine (mg/dL)}}$$

6.3.3 Biomarker Data Summarization

Biomarker concentrations reported as below the limit of quantitation will be reported as "BLQ" in the listings and set to one-half of the limit of quantitation for summarization and statistical analysis.

The following variables will be determined and summarized for each urine biomarker.

- Measured concentration
- Total biomarker mass excreted per 24 hours
- Creatinine-adjusted excretion level

Absolute and percent change-from-baseline will be determined for the mass excreted and creatinine-adjusted values. The total urine biomarker mass excreted per 24 hours change-from-baseline value will be used in the statistical analysis.

Data will be listed by subject, sequence, and study day and summarized by study day (Day -1 and Day 9) in Part 1, by study day (Day -1 and Day 14) in Part 2 for Arm I only, and by study arm and study day (Day 9 and Day 14) in Part 2. All summaries will be presented overall and by sex. Absolute and percent change-from-baseline values will also be listed and summarized.

Descriptive statistics (number of observations, mean, median, standard deviation, standard error of the mean, CV%, minimum, and maximum) will be presented using the level of precision details in section 6.1.2. Figures will be used to display the data graphically as applicable. All data summarizations and figures will be generated using the Outcomes Population. Data summarizations and statistical analyses will be performed using SAS procedures. Statistical analyses are described in Section 6.7.

6.4 Topography (Part 1 only)

6.4.1 Data Collection

Puff topography will be performed in a subset of 16 subjects (2 subjects from each sequence in Part 1). Subjects will engage in a 1-hour *ad libitum* product use with their usual brand combustible cigarette (Day -1) or the assigned study product (Days 1 and 8), using the topography device (SPA-M). The topography session should start at least 4 hours after the start of the *ad libitum* product use of that day.

6.4.2 Data Summarization

The following topography parameters will be assessed:

- Total Puff count
- Average Puff Duration
- Total Puff Duration
- Average Puff volume
- Total Puff Volume
- Average Peak flow rate
- Average flow rate
- Average Inter-puff interval

Topography parameters will be listed by subject and summarized by study day, overall and by sex. Other summaries by usual brand cigarette flavor (non-menthol or menthol), age, number of years smoking, or CPD may be done if the data permit.

Correlation analyses may be performed to determine the potential relationship between puff topography parameters and pod weight change.

6.5 Physiologic Assessments

6.5.1 Data Collection

On Days -1, 9, and 14, BP and HR will be measured within 2 hours prior to and at every hour after the start of *ad libitum* product use, and at 0, 3, and at least 30 minutes prior to the start of product use on the next day, to generate 24-hour profiles.

Spirometry assessments will be done on Days -1, 9, and 14.

6.5.2 Data Summarization

BP and HR

The following parameters will be calculated from the change-from-baseline BP and HR profiles for *my*blu™ exclusive use Arm I:

AUEC0-24 The area under the change from baseline versus time curve from time 0 to 24 hours, calculated using the linear trapezoidal method with linear interpolation using nominal sample times.

Emax The maximum change from baseline.

TEmax Time of the Emax. If the maximum value occurs at more than one time point, TEmax will be defined as the first time point with this value.

Change from baseline will be calculated by subtracting the time-matched post-baseline values from Day 9 and Day 14 from the baseline (Day -1) using nominal sample times. Original data, change from baseline data, and change from baseline parameters will be listed by subject and study day and summarized by study day. Parameters will be summarized by sex and overall.

Spirometry

The following pre- and post-bronchodilator lung function variables will be listed by subject and study arm (as applicable):

- Measured and percent of predicted FEV1
- Measured and percent of predicted FVC
- Measured and percent of predicted FEV1:FVC ratio
- Measured and percent of predicted FEF25-75%

The following pre- and post-bronchodilator lung function variables as well as change from baseline (Day -1) pre values and post-pre for each variable will be listed by subject and summarized by study day, for subjects in *my*blu™ exclusive use arm (Arm I) using descriptive statistics:

- percent of predicted FEV1
- percent of predicted FVC
- Percent of predicted FEV1:FVC ratio
- Percent of predicted FEF25-75%

Descriptive statistics (number of observations, mean, median, standard deviation, standard error of the mean, CV%, minimum, and maximum) will be used for summarizations. Summaries for the change variables will be by sex and overall.

Figures may be used to display the data graphically, as applicable. All data summarizations including figures will be generated using the Outcomes population. Data summarizations and statistical analyses will be performed using SAS procedures. Statistical analyses are described in Section 6.7.

6.6 Subjective Measures

The Urge to Smoke (VAS), Product Liking (VAS), PES (7-point scale), Future Intent to Use (VAS), QSU-Brief, MTWS-R, and PSCDI/PSECDI questionnaires will be completed using a computerized tablet device.

6.6.1 Data Collection

Days 2, 4, 6, and 8
Urge to smoke (UTS) will be assessed using a 100 mm VAS approximately 10 minutes prior to the start of the controlled product use session and within approximately 30 seconds prior to the scheduled blood draws at 5, 10, 15, 30, 60, and 120 minutes following the start of the controlled product use session.

PES, Product Liking, and Future Intent to Use questionnaires will be administered following the completion of the controlled product use session.

UTS, PES, Product Liking, and Future Intent to Use questionnaires will be administered at least 6 hours following the start of the *ad libitum* product use session.

Days 9 and 14

The Penn State [Electronic] Cigarette Dependence Index (PSCDI/PSECDI) questionnaires, the Minnesota Tobacco Withdrawal Scale-Revised (MTWS-R), and the Questionnaire on Smoking Urges-Brief (QSU-Brief) will be administered at least 6 hours after the start of the *ad libitum* product use session.

6.6.2 Data Summarization

Days 2, 4, 6, and 8 of Part 1

The following parameters and subscales will be calculated and summarized. UTS parameters will be calculated from urge to smoke assessments taken during the controlled product use sessions using Phoenix® WinNonlin® Version 7.0 or higher (model 202). For questionnaires without summary parameters (Product Liking Questionnaire, Future Intent to Use Questionnaire, and UTS after *ad libitum* session), each item on the subjective measures questionnaires will be summarized.

- UTS parameters calculated from the reduction from baseline (VASpreuse – VAS postuse) vs time profiles:
  - Emax_R The maximum reduction from baseline VAS score.
  - TEmax Time of the Emax_R. If the maximum value occurred at more than one time point, TEmax will be defined as the first time point with this value.
  - AUEC0-120_R The area under the reduction from baseline "Urge to Smoke" VAS score versus time curve from 0 to 120 minutes, calculated using the linear trapezoidal method with linear interpolation using actual sample times.
- PES subscales (controlled and ad libitum product use sessions):
  - Satisfaction - average of items 1, 2, 3, and 12
  - Psychological reward - average of items 4 through 8
  - Aversion - average of items 9, 10, 16, and 18
  - Relief - average of items 11, 13, 14, 15, and reversed for item 20
  - Items 17, 19, 21 will be summarized as individual item scores.

UTS, Product Liking, PES, and Future Intent to Use responses will be listed by subject, product, day, and product use session (and time point as applicable). UTS parameters, PES subscales, and Product Liking and Future Intent to Use responses will be summarized by product (and product use session as applicable). For Future Intent to Use, responses recorded as VAS scores will also be treated as bipolar categorical variables (-50 to <0, 0, >0 to 50) and summarized by study product using frequency count tables. The bipolar score for the Future Intent to Use questionnaire is calculated by subtracting 50 from the original VAS score. The bipolar scores will also be treated as continuous variables and summarized using descriptive statistics.

Days 9 and 14

The following total scores and factor scores will be calculated and summarized. Total scores, factor scores, and responses to individual questionnaire items will be listed.

- PSCDI/PSECDI total score

- MTWS-R total score

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

(QSU-Brief), the Minnesota Tobacco Withdrawal Scale-Revised (MTWS-R), and the Penn State [Electronic] Cigarette Dependence Index (PSCDI/PSECDI)

QSU-Brief, MTWS-R, PSCDI/PSECDI responses and factor/total scores will be listed by subject and day and study arm. Factor and total scores will be summarized by study day and study arm.

Descriptive statistics (number of observations, mean, median, standard deviation, standard error of the mean, CV%, minimum, and maximum) will be used for all questionnaire summarizations, and summaries will be presented overall and by sex.

Figures may be used to display the data graphically, as applicable. All data summarizations and figures will be generated using the Outcomes Population. Data summarizations and statistical analyses will be performed using SAS procedures. Statistical analyses are described in Section 6.7.

6.7 Statistical Analyses

a. Pharmacokinetics (primary objective 1)

A linear mixed model for analysis of variance will be performed on the log-transformed PK parameters Cmax and AUC following the first product use session on each of Days 2, 4, 6, and 8. The two blocks of subjects (ABCD, EFGH) will be modeled separately. Each model will include sequence, study product, and day as fixed effects and subject-nested-within-sequence as a random effect. Sequence will be tested using subject-nested-within-sequence as the error term. Geometric least-squares means (LSM) and 95% confidence intervals (CIs) will be provided for the PK parameters of Cmax and AUC by study product. Geometric LSM ratio, 95% CIs of geometric LSM ratio, and p-values will be provided for the study product comparisons in Cmax and AUC. The comparisons of interest will include each of the study products compared to each other.

ABCD Block:
Product A versus Product B
Product A versus Product C
Product A versus Product D
Product B versus Product C
Product B versus Product D

Product C versus Product D

EFGH Block:
Product E versus Product F
Product E versus Product G
Product E versus Product H
Product F versus Product G
Product F versus Product H
Product G versus Product H

The above statistical analyses will be performed using the following SAS codes.

Proc MIXED data=< >;
Class subject sequence product day;
Model LN_dependent variable = sequence product day /DDFM=KR;
Random Subject(sequence);
LSMeans product/pdiff CL alpha=0.05;
Run;

Non-parametric analysis (Wilcoxon signed rank test) will be performed for the comparisons of T_{max} between each product.

b. <u>Primary and Secondary Biomarkers Day 9 for *my*blu™ (primary objective 2 and secondary objectives 2 and 5)</u>

Comparisons of the Day 9 and Day -1 primary and secondary BoE and BoPH values will be made using a linear mixed model analysis of variance (ANOVA).

The ANOVA model will include day as a fixed effect and subject as a random effect. Least square means (LSMs) will be provided for each day. LSM differences, 95% confidence intervals of LSM differences, and p-values will be provided for the day comparisons. The above statistical analyses will be performed using the following SAS codes.

Proc MIXED data=< >;
Class subject day;
Model dependent variable = day/DDFM=KR;
Random subject;
LSMeans day/pdiff CL alpha=0.05;
Run;

LSM differences, 95% confidence intervals of LSM differences, and p-values will be provided for the day comparisons.

c. <u>Primary and Secondary Biomarkers Day 14 for *my*blu™ (secondary objectives 1, 2, and 5)</u>

Comparisons of the Day 14 and Day -1 primary and secondary BoE and BoPH values in exclusive *my*blu™ arm will be made using the same linear mixed model ANOVA as for Day 9 above.

d. <u>Change-from-baseline differences (Day 14 – Day 9) in the primary and secondary tobacco-related BoE and BoPH between study arms (secondary objective 4)</u>

Comparisons of the change-from-baseline differences in the primary and secondary BoE and BoPH values among the study arms will be made using a linear mixed model analysis of variance (ANOVA).

The ANOVA model will include arm as fixed effects and subject as a random effect. Least square means (LSMs) will be provided for each arm. LSM differences, 95% confidence intervals of LSM differences, and p-values will be provided for the day comparisons. The above statistical analyses will be performed using the following SAS codes.

```
Proc MIXED data=< >;
Class arm;
Model dependent variable = arm/DDFM=KR;
LSMeans arm/pdiff CL alpha=0.05;
Run;
```

The comparisons of interest are:

*my*blu™ vs Combustible Cigarette
*my*blu™ vs Dual Use
Dual Use vs Combustible Cigarette

e. <u>Other Secondary Objectives:</u>

Changes in the primary and secondary tobacco-related BoE in the exclusive e-cigarette use, exclusive combustible cigarette use and dual use groups at Day 14 (Secondary objective 3) will be summarized descriptively.

Urge to smoke parameters from the controlled product use session will be analyzed using analysis a. Other questionnaire information will be summarized descriptively (Secondary objective 6).

Puff topography and product use (secondary objectives 7 and 9) will be summarized descriptively.

Analyses b and c will be used to assess in physiologic endpoints following 9-day and 14-day use periods of *my*blu™ e-cigarettes (secondary objective 8):

- change from baseline blood pressure [BP] and heart rate [HR] parameters

- change from baseline pre-bronchodilator values for percent of predicted parameters

- change from baseline in post-pre bronchodilator values for percent of predicted parameters

7. SAFETY

All case report form (CRF) data will be listed by subject and chronologically by assessment time points. This will include rechecks, unscheduled assessments, and early termination.

Applicable continuous variables will be summarized using n, arithmetic mean, SD, minimum, median, and maximum.

The level of precision will be presented as follows: minimum/maximum in the same precision as in the database, mean/median in one more precision level than minimum/maximum, SD in one more precision level than mean/median, and n will be presented as an integer.

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

7.1 Subject Discontinuation

Subjects will be summarized by number of subjects enrolled, randomized, completed, and discontinued the study with discontinuation reasons by randomized product sequence (Part 1) or study arm (Part 2) and overall for each study part.

7.2 Demographics

Descriptive statistics will be calculated for continuous variables (age, weight, height, and body mass index) by randomized product sequence (Part 1) or study arm (Part 2) and overall for each study part.

Frequency counts will be provided for categorical variables (race, ethnicity, and sex, and other characteristics) for each randomized product sequence (Part 1) or study arm (Part 2) and overall for each study part.

7.3 Smoking History

Descriptive statistics will be calculated for continuous variables (cigarettes smoked per day [CPD] and number of years smoked) by randomized randomized product sequence (Part 1) or study arm (Part 2) and overall for each study part.

Frequency counts will be provided for subject's usual brand for each randomized product sequence (Part 1) or study arm (Part 2) and overall for each study part.

7.4 Adverse Events

All adverse events (AEs) occurring during this clinical trial will be coded using the Medical Dictionary for Regulatory Activities (MedDRA®), Version 22.1.

All AEs captured in the database will be listed in by-subject data listings including verbatim term, coded term, product, severity, relationship to study product (Part 1) or study arm (Part 2), and action; however, only product use-emergent AEs (PUEAEs) will be summarized.

A PUEAE is defined as an AE that is starting or worsening at the time of or after the first randomized study product use. Each PUEAE will be attributed to a study product (Part 1) or study arm (Part 2) based on the onset date and time of the AE.

If the onset time of an AE is missing and the onset date is the same as the first study product use date, then the AE will be considered product use emergent in the study product. If onset time of an AE is missing and the onset date does not fall on a study product use date, then the AE will be considered product use emergent for the last study product administered. If the onset date of an AE is missing, then the AE will be considered product use emergent, unless the onset date is known to have occurred within or between specific product use days.

PUEAEs will be tabulated by System Organ Class (SOC) and Preferred Term. Summary tables will include number of subjects reporting the AE and as percent of number of subjects who used study product by product. The number of AEs will be tabulated in a similar manner. Tables which tabulate the number of PUEAEs by severity and relationship to study product will also be included.

In addition, adverse events occurred during baseline period on Day -2 and day -1 will be summarized separately.

Serious adverse events (SAEs), if present, will also be listed. Applicable narratives will be included in the CSR.

7.5 Clinical Laboratory Tests (Serum Chemistry, Hematology, and Urinalysis)

Serum Chemistry, hematology, and urinalysis samples will be collected at screening, check-in (Day -2), and prior to discharge or prior to early termination from the study.

Descriptive statistics will be reported for numeric clinical data and change from baseline for each assessment timepoint. Rechecked values prior to randomization will be used in calculating summary statistics. Baseline is the last non-missing value including recheck and unscheduled event before randomization (usually on Day -2 Check-in). Normal ranges will be listed.

Out of normal range and clinically significant laboratory values will be listed by subject. Results that are indicated as CS by the PI will be listed in the table.

A urine cotinine test will be completed at Screening.

Urine drug tests and alcohol breath tests will be completed at Screening and Check-in (Day -2).

For females, serum pregnancy tests will be completed at Screening and urine pregnancy tests will be completed at Check-in (Day -2).

Results for these tests will be listed as "Negative" or "Positive."

7.6 Vital Signs

Vital signs (pulse, blood pressure, respiration rate, and body temperature) will be measured at Screening and Check-in (Day -2). BP and HR will also be measured within 2 hours prior to and at every hour after the start of *ad libitum* product use and throughout the period of *ad libitum* product use. Following completion of *ad libitum* product use on that day, BP and HR will be measured at 00:00, 03:00, and at least 30 minutes prior to the start of product use on the next day on Days -1, Day 9, and Day 14 (for Day 14, the last measurement will be collected at approximately 06:00 on Day 15). Respiration rate and body temperature will also be measured prior to the start of the first product use session.

Descriptive statistics will be reported for vital sign measurements by product (Part 1) or study arm (Part 2) and time point. Unscheduled events or rechecks post randomization will not be included in summaries. Similarly early termination results will not be included in summaries.

7.7 Electrocardiogram

A single 12-lead electrocardiogram (ECG) will be recorded at collected at screening, check-in (Day -2), and prior to discharge or prior to early termination from the study.

Descriptive statistics will be reported for ECG parameters by time point. Unscheduled events or rechecks post randomization will not be included in summaries. Similarly early termination results will not be included in summaries.

ECG results will be listed by subject.

7.8 Concomitant Medications

All concomitant medications recorded during the study will be coded with the WHO Drug Dictionary Version 01SEP2019 b3 and listed by subject.

7.9 Physical Examination

Full physical examinations will be performed at Screening and prior to discharge or prior to early termination from the study.

Physical examinations will be listed by subject. Changes in physical examinations (if any) will be described in the text of the final report.

7.10 Exhaled CO

Exhaled CO will be collected at Screening.

Exhaled CO will be listed by subject.

7.11 Lung Function (Spirometry)

Subjects will undergo lung function testing at Screening to affirm eligibility (FEV_1, FEV_1:FVC ratio) and as a safety endpoint (FEV_1, FVC, FEV_1:FVC ratio, and forced expiratory flow $(FEF)_{25-75\%}$) at Day -1, Day 9, and Day 14.

Descriptive statistics will be reported for measured and percent of predicted spirometry parameters. Unscheduled events or rechecks post randomization will not be included in summaries. Similarly early termination results will not be included in summaries.

Spirometry results will be listed by subject.

8. SUMMARY OF CHANGES FROM PROTOCOL-PLANNED ANALYSIS

The analyses described in this SAP are aligned with those analyses described in the protocol.

9. SUMMARY TABLES AND FIGURES

Summary tables and figures are numbered following the International Conference on Harmonization (ICH) structure but may be renumbered as appropriate during the compilation of the tables and figures for the CSR. Note that all summary tables and figures will be generated using SAS® Version 9.4.

Section 14 Summary Tables and Figures

The following is a list of table and figure titles that will be included in Section 14 of the report. Tables and figures may be renumbered as appropriate during the compilation of the report.

14.1 Demographic Data Summary Tables

Table 14.1.1.1 Summary of Disposition - Part 1 (Safety Population)

14.2 Study Product Use, Pharmacokinetics, Biomarkers, Physiologic Assessments, Questionnaires, and Topography Data Summary Tables and Figures

14.2.1 Product Use Tables

14.2.2 Pharmacokinetics Tables

Table 14.2.2.4.1	Statistical Comparisons of Baseline-Adjusted Plasma Nicotine PK Parameters Among *my*blu™ Products A, B, C, and D Following Controlled Use (Outcomes Population)
Table 14.2.2.4.2	Statistical Comparisons of Baseline-Adjusted Plasma Nicotine PK Parameters Among *my*blu™ Products E, F, G, and H Following Controlled Use (Outcomes Population)
Table 14.2.2.4.3	Nonparametric Statistical Comparisons of Plasma Nicotine PK Parameter Tmax Among *my*blu™ Products A, B, C, and D following Controlled Use (Outcomes Population)
Table 14.2.2.4.4	Nonparametric Statistical Comparisons of Plasma Nicotine PK Parameter Tmax Among *my*blu™ Products A, B, C, and D following Controlled Use (Outcomes Population)

14.2.3 Biomarker Tables

14.2.3.1 Part 1

Table 14.2.3.1.1	Summary of Blood COHb (% saturation) by Study Day in Part 1: 9-Day Switch to Exclusive *my*blu™ Use (Outcomes Population)

Table 14.2.3.1.2 through 14.2.3.1.21 (one per biomarker) will be generated similarly:

Table 14.2.3.1.2	Urine NNAL
Table 14.2.3.1.3	Urine 3-HPMA
Table 14.2.3.1.4	Urine S-PMA
Table 14.2.3.1.5	Urine NNN
Table 14.2.3.1.6	Urine CEMA
Table 14.2.3.1.7	Urine HEMA
Table 14.2.3.1.8	Urine 3-HMPMA
Table 14.2.3.1.9	Urine MHBMA
Table 14.2.3.1.10	Urine 1-OHP
Table 14.2.3.1.11	Urine o-tol
Table 14.2.3.1.12	Urine 3-OH B[a]P
Table 14.2.3.1.13	Urine 1-AN
Table 14.2.3.1.14	Urine 2-AN
Table 14.2.3.1.15	Urine Nicotine Equivalents
Table 14.2.3.1.16	Plasma sICAM (ng/mL)
Table 14.2.3.1.17	WBCs ($x10^3/\mu L$)

Table 14.2.3.1.18 Serum HDL-C (mg/dL)
Table 14.2.3.1.19 Serum MCP-1 (units)
Table 14.2.3.1.20 Urine 8-epi-prostaglandin F2α
Table 14.2.3.1.21 Urine 11-dehydrothromboxane B2

Note: units are in the table header for urine biomarkers

Table 14.2.3.1.22 Statistical Comparisons of BoE and BoPH Between Study Days in Part 1: 9-Day Switch to Exclusive *my*blu™ Use (Outcomes Population)

14.2.3.2 Part 2 by Study Day

Table 14.2.3.2.1 Summary of Blood COHb (% Saturation) by Study Day in Part 2: Continue Exclusive *my*blu™ Use (Outcomes Population)

Table 14.2.3.2.2 through 14.2.3.2.21 (one per biomarker) will be generated similarly:

Table 14.2.3.2.2 Urine NNAL
Table 14.2.3.2.3 Urine 3-HPMA
Table 14.2.3.2.4 Urine S-PMA
Table 14.2.3.2.5 Urine NNN
Table 14.2.3.2.6 Urine CEMA
Table 14.2.3.2.7 Urine HEMA
Table 14.2.3.2.8 Urine 3-HMPMA
Table 14.2.3.2.9 Urine MHBMA
Table 14.2.3.2.10 Urine 1-OHP
Table 14.2.3.2.11 Urine o-tol
Table 14.2.3.2.12 Urine 3-OH B[a]P
Table 14.2.3.2.13 Urine 1-AN
Table 14.2.3.2.14 Urine 2-AN
Table 14.2.3.2.15 Urine Nicotine Equivalents
Table 14.2.3.2.16 Plasma sICAM (ng/mL)
Table 14.2.3.2.17 WBCs ($x10^3/\mu L$)
Table 14.2.3.2.18 Serum HDL-C (mg/dL)
Table 14.2.3.2.19 Serum MCP-1 (units)
Table 14.2.3.2.20 Urine 8-epi-prostaglandin F2α
Table 14.2.3.2.21 Urine 11-dehydrothromboxane B2

Note: units are in the table header for urine biomarkers

Table 14.2.3.2.22 Statistical Comparisons of BoE and BoPH Between Study Days in Part 2: Continue Exclusive *my*blu™ Use (Outcomes Population)

14.2.3.3 Part 2 by Study Arm

Table 14.2.3.3.1 Summary of Blood COHb (% Saturation) by Study Arm in Part 2 (Outcomes Population)

Tables 14.2.3.3.2 through 14.2.3.3.21 will be generated for each biomarker similarly:

Table 14.2.3.3.2 Urine NNAL
Table 14.2.3.3.3 Urine 3-HPMA
Table 14.2.3.3.4 Urine S-PMA
Table 14.2.3.3.5 Urine NNN
Table 14.2.3.3.6 Urine CEMA
Table 14.2.3.3.7 Urine HEMA
Table 14.2.3.3.8 Urine 3-HMPMA
Table 14.2.3.3.9 Urine MHBMA
Table 14.2.3.3.10 Urine 1-OHP
Table 14.2.3.3.11 Urine o-tol
Table 14.2.3.3.12 Urine 3-OH B[a]P
Table 14.2.3.3.13 Urine 1-AN
Table 14.2.3.3.14 Urine 2-AN
Table 14.2.3.3.15 Urine Nicotine Equivalents
Table 14.2.3.3.16 Plasma sICAM (ng/mL)
Table 14.2.3.3.17 WBCs (x103/µL)
Table 14.2.3.3.18 Serum HDL-C (mg/dL)
Table 14.2.3.3.19 Serum MCP-1 (units)
Table 14.2.3.3.20 Urine 8-epi-prostaglandin F2α
Table 14.2.3.3.21 Urine 11-dehydrothromboxane B2

Note: units are in the table header for urine biomarkers

Table 14.2.3.3.22 Statistical Comparisons of BoE and BoPH Differences From Baseline Among *my*blu™, Combustible Cigarette, and Dual Use Arms in Part 2 (Outcomes Population)

14.2.4 Physiologic Assessments Tables

14.2.4.1 SPB, DPB, and HR

14.2.4.2 Spirometry

14.2.5 Urge to Smoke Tables

14.2.6 Questionnaire Tables

14.2.6.1 PES Subscales

14.2.6.2 Product Liking VAS Score

14.2.6.3 Future Intent to Use VAS Score

Figures 14.2.9.1.2 through 14.2.9.1.19 (one per biomarker) will be generated similarly:

Figure 14.2.9.1.2 Urine NNAL
Figure 14.2.9.1.3 Urine 3-HPMA
Figure 14.2.9.1.4 Urine S-PMA
Figure 14.2.9.1.5 Urine NNN
Figure 14.2.9.1.6 Urine CEMA
Figure 14.2.9.1.7 Urine HEMA
Figure 14.2.9.1.8 Urine 3-HMPMA
Figure 14.2.9.1.9 Urine 1-OHP
Figure 14.2.9.1.10 Urine o-tol
Figure 14.2.9.1.11 Urine 3-OH B[a]P
Figure 14.2.9.1.12 Urine 1-AN
Figure 14.2.9.1.13 Urine 2-AN
Figure 14.2.9.1.14 Plasma sICAM
Figure 14.2.9.1.15 WBCs
Figure 14.2.9.1.16 Serum HDL-C
Figure 14.2.9.1.17 Serum MCP-1
Figure 14.2.9.1.18 Urine 8-epi-prostaglandin F2α
Figure 14.2.9.1.19 Urine 11-dehydrothromboxane B2

14.2.9.2 Part 2 by Study Day

Figure 14.2.9.2.1 Arithmetic Mean (SD) Blood COHb (% Saturation) by Study Day in Part 2: Continue Exclusive myblu™ Use (Outcomes Population)

Figures 14.2.9.2.2 through 14.2.9.2.19 (one per biomarker) will be generated similarly:

Figure 14.2.9.2.2 Urine NNAL
Figure 14.2.9.2.3 Urine 3-HPMA
Figure 14.2.9.2.4 Urine S-PMA
Figure 14.2.9.2.5 Urine NNN
Figure 14.2.9.2.6 Urine CEMA
Figure 14.2.9.2.7 Urine HEMA
Figure 14.2.9.2.8 Urine 3-HMPMA
Figure 14.2.9.2.9 Urine 1-OHP
Figure 14.2.9.2.10 Urine o-tol
Figure 14.2.9.2.11 Urine 3- 3-OH B[a]P
Figure 14.2.9.2.12 Urine 1-AN

Figure 14.2.9.2.13 Urine 2-AN
Figure 14.2.9.2.14 Plasma sICAM
Figure 14.2.9.2.15 WBCs
Figure 14.2.9.2.16 Serum HDL-C
Figure 14.2.9.2.17 Serum MCP-1
Figure 14.2.9.2.18 Urine 8-epi-prostaglandin F2α
Figure 14.2.9.2.19 Urine 11-dehydrothromboxane B2

14.2.9.3 Part 2 by Study Arm

Figure 14.2.9.3.1 Arithmetic Mean (SD) Blood COHb (% Saturation) by Study Day in Part 2 (Outcomes Population)

Figures 14.2.9.3.2 through 14.2.9.3.19 (one per biomarker) will be generated similarly:

Figure 14.2.9.3.2 Urine NNAL
Figure 14.2.9.3.3 Urine 3-HPMA
Figure 14.2.9.3.4 Urine S-PMA
Figure 14.2.9.3.5 Urine NNN
Figure 14.2.9.3.6 Urine CEMA
Figure 14.2.9.3.7 Urine HEMA
Figure 14.2.9.3.8 Urine 3-HMPMA
Figure 14.2.9.3.9 Urine 1-OHP
Figure 14.2.9.3.10 Urine o-tol
Figure 14.2.9.3.11 Urine 3- 3-OH B[a]P
Figure 14.2.9.3.12 Urine 1-AN
Figure 14.2.9.3.13 Urine 2-AN
Figure 14.2.9.3.14 Plasma sICAM
Figure 14.2.9.3.15 WBCs
Figure 14.2.9.3.16 Serum HDL-C
Figure 14.2.9.3.17 Serum MCP-1
Figure 14.2.9.3.18 Urine 8-epi-prostaglandin F2α
Figure 14.2.9.3.19 Urine 11-dehydrothromboxane B2

14.2.10 Physiologic Assessments Figures

14.2.10.1 SBP, DBP, HR

Figure 14.2.10.1.1 Change from Baseline Systolic Blood Pressure Versus Time (Arm I) (Outcomes Population)

The 24-hour change-from-baseline profiles for each endpoint, for Day 9 and Day 14, will be plotted, with y axis = Change from Baseline (unit) and x axis = time (hr)

14.2.10.2 Lung Function

14.2.11 Urge to Smoke Figures

14.2.12 Questionnaire Figures

14.2.12.1 PES Subscales

Figure 14.2.14.6.1 Frequency of Future Intent to Use (Not Likely to Buy Another E-Cigarette) by Study Product Following Controlled Product Use

Figure 14.2.14.7.2 Frequency of Future Intent to Use (Not Likely to Buy Another E-Cigarette) by Study Product Following Ad Libitum Product Use (Outcomes Population)

Note: Above figures will be bar graphs

14.2.15 PSCDI or PSECDI Total Score

Figure 14.2.15 Box plot of PSCDI or PSECDI Total Score by Study Arm and Study Day (Outcomes Population)

14.2.16 MTWS-R Total Score

Figure 14.2.16 Box Plot of MTWS-R Total Score by Study Arm and Study Day (Outcomes Population)

14.2.17 QSU-brief Factor Scores

Figure 14.2.17.1 Box Plot of QSU-brief Factor Scores (Factor 1) by Study Product and Study Day (Outcomes Population)

Figure 14.2.17.3 Box Plot of QSU-brief Factor Scores (Factor 2) by Study Product and Study Day (Outcomes Population)

14.3 Safety Data Summary Tables

14.3.1 Displays of Adverse Events

Table 14.3.1.1.1 Product Use-emergent Adverse Event Frequency by Study Product – Number of Subjects Reporting the Event (% of Subjects Who Used Study Product) - Part 1 (Safety Population)

Table 14.3.1.1.2 Product Use-emergent Adverse Event Frequency by Study Product – Number of Adverse Events (% of Total Adverse Events) – Part 1 (Safety Population)

Table 14.3.1.1.3 Product Use-emergent Adverse Event Frequency by Study Product, Severity, and Relationship to Study Product – Number of Subjects Reporting Events - Part 1 (Safety Population)

Table 14.3.1.2.1 Product Use-emergent Adverse Event Frequency by Study Arm – Number of Subjects Reporting the Event (% of Subjects Who Used Study Product) - Part 2 (Safety Population)

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 but may be renumbered as appropriate during the compilation of the TFLs for the CSR. The following is a list of appendix numbers and titles that will be included as data listings:

16.1 Study Information

Appendix 16.1.9 Statistical Methods

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 Discontinuation (Safety Population)

16.2.2 Protocol Deviations

Appendix 16.2.2 Protocol Deviations

16.2.3 Subjects Excluded from Analysis

Appendix 16.2.3 Subjects Excluded from Analysis

Note: Appendix 16.2.3 is generated in MS Word for inclusion in the study report.

16.2.4 Demographic Data

Appendix 16.2.4.1.1 Demographics (Safety Population)
Appendix 16.2.4.1.2 Reproductive Status (Safety Population)
Appendix 16.2.4.2 Physical Examination (Safety Population)
Appendix 16.2.4.3.1 Medical History (Safety Population)
Appendix 16.2.4.3.2 Allergy History (Safety Population)
Appendix 16.2.4.3.3 Surgical History (Safety Population)
Appendix 16.2.4.4 Smoking History (Safety Population)
Appendix 16.2.4.5 Caffeine, Alcohol, and Drug History (Safety Population)

16.2.5 Compliance and/or Concentration Data

Appendix 16.2.5.1.1 Inclusion Criteria
Appendix 16.2.5.1.2 Exclusion Criteria
Appendix 16.2.5.2 Subject Eligibility (Safety Population)
Appendix 16.2.5.3 Randomization (Safety Population)
Appendix 16.2.5.4.1 Usual Brand Cigarette (Safety Population)

Appendix 16.2.6.3.1 PES Questionnaire (Outcomes Population)
Appendix 16.2.6.3.2 PES Questionnaire Responses (Outcomes Population)
Appendix 16.2.6.3.3 PES Questionnaire Subscales (Outcomes Population)
Appendix 16.2.6.4 Product Liking Questionnaire Responses (Outcomes Population)
Appendix 16.2.6.5 Future Intent to Use Questionnaire Responses (Outcomes Population)
Appendix 16.2.6.6.1 PSCDI, PSECDI Questionnaire (Outcomes Population)
Appendix 16.2.6.6.2 PSCDI, PSECDI Questionnaire Responses (Outcomes Population
Appendix 16.2.6.7.1 MTWS-R Questionnaire (Outcomes Population)
Appendix 16.2.6.7.2 MTWS-R Questionnaire Responses (Outcomes Population)
Appendix 16.2.6.8.1 QSU-brief Questionnaire (Outcomes Population)
Appendix 16.2.6.8.2 QSU-brief Questionnaire Responses (Outcomes Population
Appendix 16.2.6.9 Individual Puff Topography Parameters (Outcomes Population)

16.2.7 Adverse Events Listings

Appendix 16.2.7.1.1 Adverse Events (I of II) (Safety Population)
Appendix 16.2.7.1.2 Adverse Events (II of II) (Safety Population)
Appendix 16.2.7.2 Adverse Event Non- Medication Therapy (Safety Population)
Appendix 16.2.7.3 Adverse Event Preferred Term Classification (Safety Population)

16.2.8 Listings of Individual Laboratory Measurements and Other Safety Observations

Appendix 16.2.8.1.1 Clinical Laboratory Report - Serum Chemistry (Safety Population)
Appendix 16.2.8.1.2 Clinical Laboratory Report - Hematology (Safety Population)
Appendix 16.2.8.1.3 Clinical Laboratory Report - Urinalysis (Safety Population)
Appendix 16.2.8.1.4 Clinical Laboratory Report - Urine Drug Screen (Safety Population)
Appendix 16.2.8.1.5 Clinical Laboratory Report - Comments (Safety Population)

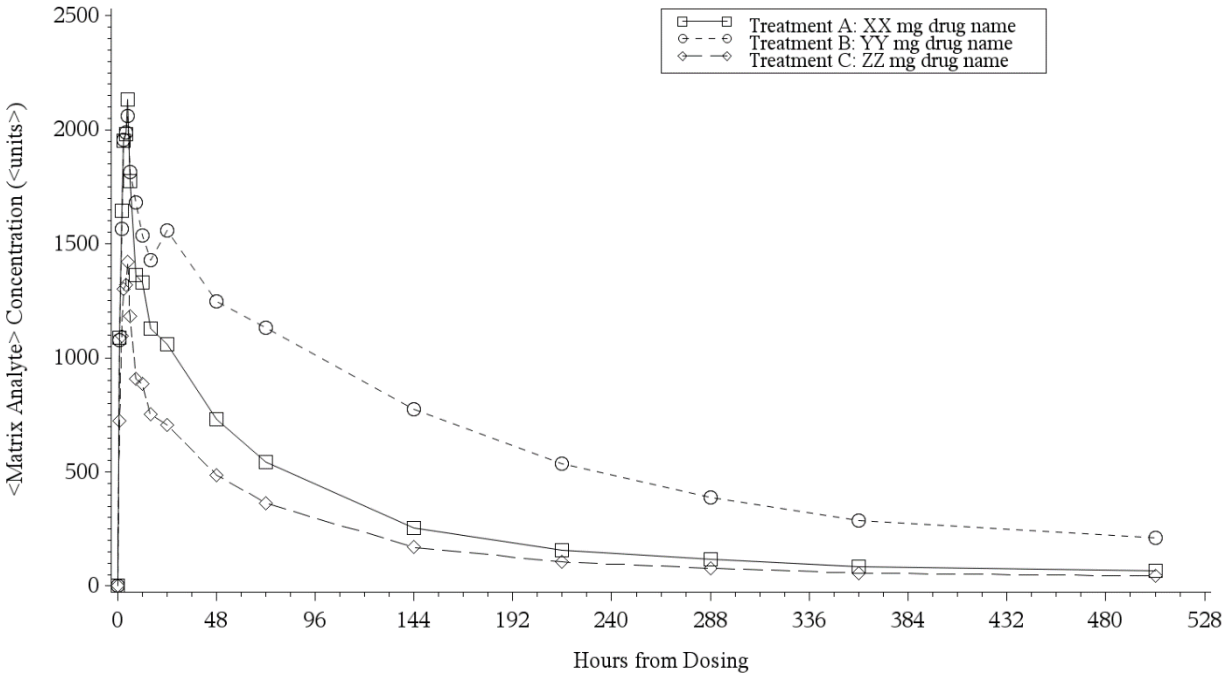
10. TABLE AND FIGURE SHELLS

The following table and figure 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 presented and included in the final report. Unless otherwise noted, all tables will be presented in Times New Roman font size 8. These tables will be generated off of the [redacted] ADaM Version 1.0.

10.1 Figures Shells

In-text and post-text PK Figures of mean plasma concentrations and UTS on linear scale will be in the following format: Figure 11-X, 14.X, and appendix 16.2.6.1:

Figure X.X Arithmetic Mean Baseline-Adjusted Plasma Nicotine Concentration-Time Profiles Following Controlled Product Use by Product (Linear Scale) (Outcomes Population)



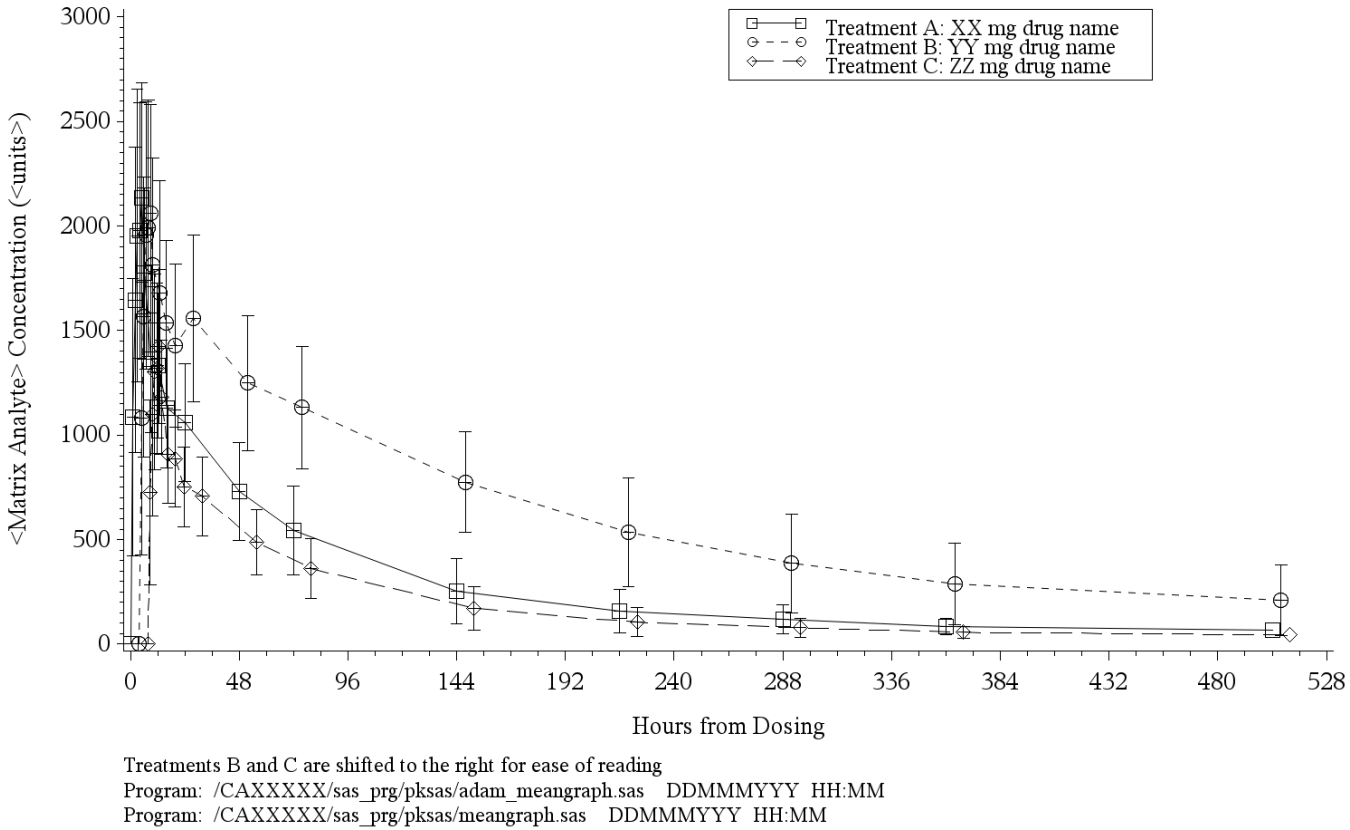
Notes for Generating the Actual Mean Figure:

I. Legend will use the short descriptions
II. Y axis label will be "Plasma Nicotine Concentration (ng/mL)" for PK figures and "Urge to Smoke" for UTS figure
III. X axis label will be "Minutes from Product Use" for all figures

Program: /CAXXXXX/sas_prg/pksas/meangraph.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_meangraph.sas DDMMMYYYY HH:MM

Post-text PK Figures of mean (SD) plasma concentrations and UTS on linear scale will be in the following format:

Figure 14.X: Arithmetic Mean (SD) Baseline-Adjusted Plasma Nicotine Concentration-Time Profiles Following Controlled Product Use by Product (Linear Scale) (Outcomes Population)



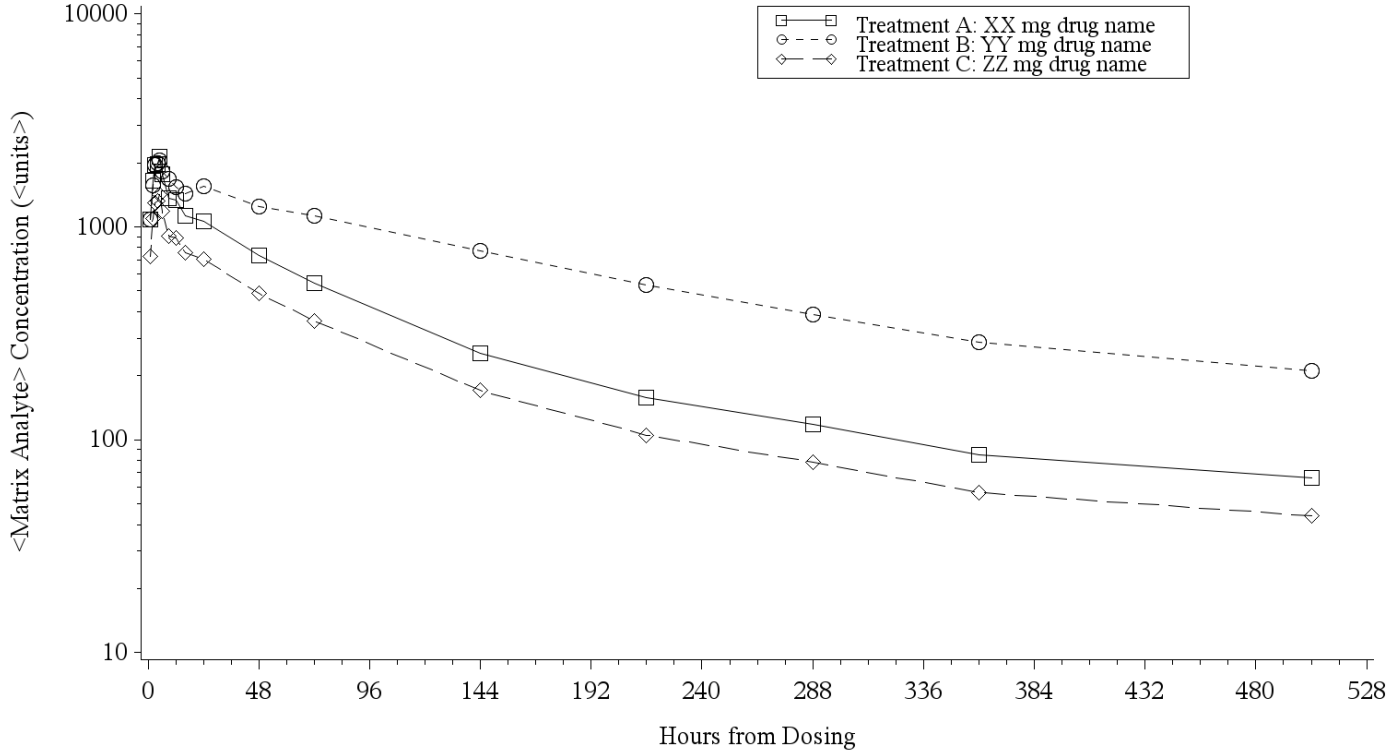
Notes for Generating the Actual Mean Figure:

IV. Legend will use the short descriptions
V. Y axis label will be "Plasma Nicotine Concentration (ng/mL)" for PK figures and "Urge to Smoke" for UTS figure
VI. X axis label will be "Minutes from Product Use" for all figures
VII. Please add the footnote for products that are shifted to the right for ease of reading

```
Program:  /CAXXXXX/sas_prg/pksas/meangraph.sas            DDMMMYYYY  HH:MM
Program:  /CAXXXXX/sas_prg/pksas/adam_meangraph.sas       DDMMMYYYY  HH:MM
```

Post-text PK Figures of mean plasma concentrations on semi-log scale (Figure 14.X, Appendix 16.2.6.1) will be in the following format:

Figure 14.X: Arithmetic Mean Baseline-Adjusted Plasma Nicotine Concentration-Time Profiles Following Controlled Product Use by Product (Semi-Log Scale) (Outcomes Population)



Notes for Generating the Actual Mean Figure:

I. Legend will use the short descriptions
II. Y axis label will be "Plasma Nicotine Concentration (ng/mL)" for all figures
III. X axis label will be "Minutes from Product Use" for all figures

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Program: /CAXXXXX/sas_prg/pksas/adam_meangraph.sas DDMMMYYYY HH:MM

Post-text Figure(s) for Total Scores will be in the following format:

Figure 14.X: Box Plot of PSCDI or PSECDI Total Score by Study Arm and Study Day (Outcomes Population)

Notes for Generating the Actual Mean Figure:

I. Note: this figure will be a boxplot figure
II. Please present each subjective measurement on different graphs but associated with Figure 14.2.9.1 or similar graphs. Present each question (or factor scale, subscale, or total score) in the title of each graph.
III. Y axis label will be "Subjective Measurement Score"
IV. X axis label will be labelled with "A, B, C, D, E, F, G, H" for each figure representing each product or Arm I, J, K as appropriate

10.2 Post-Text Summary Tables Shells

14.1 Demographic Tables

Tables 14.1.1.1 and 14.1.5.1 will have the following format.

Page 1 of X

Table 14.1.1.1 Summary of Disposition – Part 1 (Safety Population)

	Study Product Sequence								
Category	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	Overall
Enrolled	XX	XX	XX	XX	XX	XX	XX	XX	XX
Completed	XX	XX	XX	XX	XX	XX	XX	XX	XX
Discontinued Early	X	X	X	X	X	X	X	X	X
<Reason1>	X	X	X	X	X	X	X	X	X
<Reason2>	X	X	X	X	X	X	X	X	X
<Reason3>	X	X	X	X	X	X	X	X	X

Note: Product X = < >

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Tables 14.1.1.2 and 14.1.5.2 will have the following format.

Table 14.1.1.2 Summary of Disposition – Part 2 (Safety Population)

	Study Product Arm			
Category	X	X	X	Overall
Enrolled	XX	XX	XX	XX
Completed	XX	XX	XX	XX
Discontinued Early	X	X	X	X
<Reason1>	X	X	X	X
<Reason2>	X	X	X	X
<Reason3>	X	X	X	X

Note: Study Arm X = < >

Program: /CAXXXXX/ sas_prg/stsas/tab cdash_tbldisp1.sas DDMMMYYYY HH:MM

Table 14.1.2 will have the following format.

Table 14.1.2 Disposition of Subjects (Safety Population)

Subject Number	Product Sequence/Arm	Study Product Administration/ Completed					Study Completion	
		Period 1	Period 2	Period 3	Period 4	Part 2	Status	Date
X	XXXX/X	Yes/Yes	Yes/Yes	Yes/Yes	Yes/ No	Yes/ No	Terminated Study Prematurely	DDMMMYYYY
X	XXXX/X	Yes/Yes	Yes/Yes	Yes/Yes	Yes/Yes	Yes/Yes	Completed Study	DDMMMYYYY
X	XXXX/X	Yes/Yes	Yes/Yes	Yes/Yes	Yes/Yes	Yes/Yes	Completed Study	DDMMMYYYY
X	XXXX/X	Yes/Yes	Yes/Yes	Yes/Yes	Yes/Yes	Yes/Yes	Completed Study	DDMMMYYYY
		XX/XX	XX/XX	XX/XX	XX/XX	XX/XX		

Note: Product X = < >

Program: /CAXXXXX/sas_prg/stsas/tab cdash_tbldisp2.sas DDMMMYYYY HH:MM

Tables 14.1.3.1 and 14.1.6.1 will have the following format.

Page 1 of X

Table 14.1.3.1 Demographic Summary – Part 1 (Safety Population)

		Study Product Sequence								
Trait		XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	Overall
Sex	Male	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	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%)	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%)	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%)	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%)	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%)	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%)	X(XX.X%)	X(XX.X%	X(XX.X%)	X(XX.X%)
Age (yrs)	n	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
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.X	X.X	X.XX
	Minimum	XX	XX	XX	XX	XX	XX	X.XX	X.XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X	XX	XX	X.X
	Maximum	XX	XX	XX	XX	XX	XX	X.X	X.X	XX

Note: Product X = < >

Program: /CAXXXXX/sas_prg/stsas/tab cdash_demsum.sas DDMMMYYYY HH:MM

Programmer Note: Weight (kg), Height (cm), and BMI (kg/m^2) will also be included in the demographic summary table.

Tables 14.1.3.2 and 14.1.6.2 will have the following format.

Table 14.1.3.2 Demographic Summary – Part 2 (Safety Population)

		Study Product Arm			
Trait		X	X	X	Overall
Sex	Male	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
	Female	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
Race	XXXXXXXXXX	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
	XXXXX	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
	XXXXX	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
Ethnicity	Hispanic or Latino	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
	Not Hispanic or Latino	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
Age (yrs)	n	X	X	X	X
	Mean	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX

Note: Study Product Arm X = < >

Program: /CAXXXXX/sas_prg/stsas/tab cdash_demsum.sas DDMMMYYYY HH:MM

Programmer Note: Weight (kg), Height (cm), and BMI (kg/m^2) will also be included in the demographic summary table.

Tables 14.1.4.1 and 14.1.7.1 will have the following format.

Table 14.1.4.1 Smoking History Summary – Part 1 (Safety Population)

		Study Product Sequence								
Trait		XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	XXXX	Overall
Brand	XXXX	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
	XXXXXX	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
Flavor	XXXXXX	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	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%)	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
Number of Cigarettes Smoked per Day	n	X	X	X	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX	XX	XX	XX

Note: Product X = < >

Program: /CAXXXXX/sas_prg/stsas/tab cdash_demsum.sas DDMMMYYYY HH:MM

Programmer Note: Flavor and cigarette length will also be included in the smoking history summary table.

Tables 14.1.4.2 and 14.1.7.2 will have the following format.

Table 14.1.4.2 Smoking History Summary – Part 2 (Safety Population)

		Study Product Arm			
Trait		X	X	X	Overall
Brand	XXXX	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
	XXXXXX	X(XX.X%)	X(XX.X%)	X(XX.X%)	X(XX.X%)
Flavor	XXXXXX	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%)
Number of Cigarettes Smoked per Day	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: Study Product Arm X = < >

Program: /CAXXXXX/sas_prg/stsas/tab cdash_demsum.sas DDMMMYYYY HH:MM

Programmer Note: Flavor and cigarette length will also be included in the smoking history summary table.

14.2.1 Product Use Tables

Note: Summary Tables 14.2.1.1 through 14.2.1.4 will have the following format:

Table 14.2.1.1 Summary of Pod Weight Changes by Study Product and Study Day Following Controlled Use (Outcomes Population)

			Study Day			
	Product	Statistic	2	4	6	8
Overall	A	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		CV(%)	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
	B	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		CV(%)	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
	C	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		CV(%)	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
D,E,F,G,H		<Same as above>				
Female		<Same as above>				
Male		<Same as above>				

Note: Product < X >

Programming Note: Table 14.2.1.4 will present Days 1 through 8

Table 14.2.1.5 Summary of Pod Weight Changes by Study Product and Study Day Following Ad libitum Use on Day 9
(Outcomes Population)

Category	Statistic	Product A, B, C,or D	Product E, F, G,or H
Overall	n	X	X
	Mean	X.X	X.X
	SD	X.XX	X.XX
	CV(%)	XX.X	XX.X
	SEM	X.XX	X.XX
	Minimum	XX	XX
	Median	X.X	X.X
	Maximum	XX	XX
Female	<Same as above>		
Male	<Same as above>		

Note: Product: <X>

Table 14.2.1.6 Summary of Pod Weight Changes and Number of Cigarettes Smoked by Study Arm and Study Day (Outcomes Population)

			-----Weight Changes-----		--Number of Cigarettes--	
Category	Arm	Statistic	Day 9	Day 14	Day 9	Day 14
Overall	I	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		CV(%)	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
	J	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		CV(%)	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
	K	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		CV(%)	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
Female	<Same as above>					
Male	<Same as above>					

Note: Arm I: Exclusive use of myblu™ products ad libitum
Arm J: Exclusive smoking of usual brand combustible cigarettes ad libitum
Arm K: Smoking of usual brand combustible cigarettes (up to 50% of the subject's self-reported CPD) and use of myblu™ products ad libitum

Programming note: Arm I will have no data under number of cigarettes and Arm J will have no data under weight changes

14.2.2 Pharmacokinetic Tables and 14.2.5 Urge to Smoke Tables

Tables 14.2.2.1.1 through 14.2.2.1.8 for unadjusted and Tables 14.2.2.2.1 through 14.2.2.2.8 for baseline-adjusted concentration data and Tables 14.2.5.1.1 through 14.2.5.1.8 for UTS data will be in the following format:

Table 14.2.2.1.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Controlled Use of myblu™ (freebase), Gold Leaf flavor, 2.4% (Product A) (Outcomes Population)

Subject	Product Use			Sample Times (min)							
Number	Sequence	Product	Pre-use	XX	XX	XX	XX	XX	XX	XX	XX
X	XXX	X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
X	XXX	X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
X	XXX	X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
n			XX	XX	XX	XX	XX	XX	XX	XX	XX
Mean			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SD			XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
CV%			.	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM			XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Minimum			XX	XX	XX	XX	XX	XX	XX	XX	XX
Median			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Maximum			XX	XX	XX	XX	XX	XX	XX	XX	XX

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of <XX> are treated as 1/2 LLOQ.
. = Value missing or not reportable.

Notes for Generating the Actual Table:

Presentation of Data:
For baseline-adjusted table, Pre-use will be replaced with 0.
Concentrations will be presented to same precision as in bio data.
Summary statistics presentation with respect to the precision of the bio data: n = integer; Mean and Median +1; SD and SEM +2, Min and Max +0, CV% to 1 decimal

Programmer Note:
PK Time points are: pre-use and 3, 5, 7, 10, 12, 15, 20, 30, 60, 120 and 180 minutes following the start of product use
Please also present the geometric mean and geometric CV around the geometric mean for all concentration tables
UTS Time points are: pre-use and 5, 10, 15, 30, 60, and 120 minutes following the start of the fixed product use session and one value for 6 hours after ad libitum session (can be labelled "ad libitum*" with footnote *6 hours following the start of ad libitum product use session).
Please add column for Day

Program: /CAXXXXX/sas_prg/pksas/pk-conc-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/pk-conc-tables-sig.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_conc.sas DDMMMYYYY HH:MM

Tables 14.2.2.3.1 through 14.2.2.3.8 (PK) and Tables 14.2.5.2.1 through 14.2.5.2.8 (UTS) will be in the following format:

Table 14.2.2.3.1 Baseline-Adjusted Plasma Nicotine PK Parameters Following Controlled Use of myblu™ (freebase), Gold Leaf flavor, 2.4% (Product A) (Outcomes Population)

Subject Number	Product Use Sequence	Product	param1 (units)	param2 (units)	param3 (units)	param4 (units)	param5 (units)	param6 (units)
X	XXX	X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X	X.XX	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
n			XX	XX	XX	XX	XX	XX
Mean			XXX.X	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
SD			XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
CV%			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM			XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Minimum			XX.X	X.XX	XXX	XXX	XX.X	X.XXX
Median			XX.XX	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
Maximum			XXX	X.XX	XXX	XXX	XX.X	X.XXX
Geom Mean			XXX.X	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
Geom CV%			XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

. = Value missing or not reportable.

Notes for Generating the Actual Table:

Presentation of Data:

- PK Parameters will be presented in the following order and with following units: AUC0-t (ng*min/mL), Cmax (ng/mL), Tmax (min)
- UTS Parameters will be presented in the following order and with the following units: Emax_R, TEmax (min), AUEC0-120_R
- n will be presented as an integer (with no decimal);
- Parameter values for exposure based parameters (i.e. AUC0-t and Cmax) will be presented with, at maximum, the precision of the bio data, and, at minimum, 3 significant figures (to be determined by the PKist once bio data are received). Summary statistics for exposure parameters will be presented as: Mean, Median, and Geom Mean+1; SD and SEM +2, Min and Max +0.
- Values for time-based parameters (i.e. Tmax) will be presented with 2 decimals. Summary statistics for time-based parameters will be presented as: Mean, Median, and Geom Mean +1; SD +2, Min and Max +0 (omit Geom mean for UTS tables).
- CV% and Geom CV% for all parameters will be presented with 1 decimal (please omit Geom CV% for UTS tables)
- Summarize by overall, female, male
- Add column for Day

Program: /CAXXXXX/sas_prg/pksas/pk-tables.sas DDMMMYYYY HH:MM
Program: /CAXXXXX/sas_prg/pksas/adam_pkparam.sas DDMMMYYYY HH:MM

Tables 14.2.2.4.1 and 14.2.2.4.2 (PK) and Tables 14.2.5.3.1 and 14.2.5.3.2 (UTS) will be in the following format:

Table 14.2.2.4.1 Statistical Comparisons of Baseline-Adjusted Plasma Nicotine PK Parameters Among myblu™ Products A, B, C, and D Following Controlled Use (Outcomes Population)

Comparison	Parameter	Geometric LS Means Test (n)	Geometric LS Means Reference (n)	% Geometric LS Mean Ratio (Test/Reference)	Confidence Intervals (95% Confidence)	p-value
Product A vs Product B	AUC0-t	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXX
	Cmax	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXX
Product A vs Product C	AUC0-t	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXX
	Cmax	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXX
Product A vs Product D	AUC0-t	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXX
	Cmax	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXX
Product B vs Product C	AUC0-t	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXX
	Cmax	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXX
Product B vs Product D	AUC0-t	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXX
	Cmax	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXX
Product C vs Product D	AUC0-t	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXX
	Cmax	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXX

Test = The first product in the comparison; Reference = The second product in the comparison
n = Number of observations used in the analysis

Product A = < >
Product B = < >
Product C = < >
Product D = < >

Parameters are log-transformed prior to analysis. Geometric least-squares means (LS Means) are calculated by exponentiating the LS Means from the ANOVA.
% Geometric LS Mean Ratio = 100*(Test Product/Reference Product)

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

Analyst note: UTS table will based on untransformed data (ie LS means, differences, CIs and p-value)

Tables 14.2.2.4.3 and 14.2.2.4.4 will be in the following format:

Table 14.2.2.4.3 Nonparametric Statistical Comparisons of Plasma Nicotine PK Parameter Tmax Among myblu™ Products A, B, C, and D following Controlled Use (Outcomes Population)

	Product		Difference Test-Reference		
Comparison	Test (n)	Reference (n)	95% CI	Median	p-Value
Product A vs Product B	X.XX (X)	X.XX (X)	X.XX - X.XX	X.XX	X.XXXX
Product A vs Product C	X.XX (X)	X.XX (X)	X.XX - X.XX	X.XX	X.XXXX
Product A vs Product D	X.XX (X)	X.XX (X)	X.XX - X.XX	X.XX	X.XXXX
Product B vs Product C	X.XX (X)	X.XX (X)	X.XX - X.XX	X.XX	X.XXXX
Product B vs Product D	X.XX (X)	X.XX (X)	X.XX - X.XX	X.XX	X.XXXX
Product C vs Product D	X.XX (X)	X.XX (X)	X.XX - X.XX	X.XX	X.XXXX

Test = The first product in the comparison; Reference = The second product in the comparison
n = Number of observations used in the analysis

Product A = < >
Product B = < >
Product C = < >
Product D = < >

p-values are from Wilcoxon signed rank test.

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

14.3 Biomarker Tables

Summary tables for blood biomarkers (Part 1) will be in the following format:

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Table 14.2.3.1.1 Summary of Blood COHb (% saturation) by Study Day in Part 1: 9-Day Switch to Exclusive myblu™ Use (Outcomes Population)

			Change	Percent Change
Statistic	Day -1	Day 9		
n	X	X	X	X
Mean	X.X	X.X	X.X	X.X
SD	X.XX	X.XX	X.XX	X.XX
CV(%)	XX.X	XX.X	XX.X	XX.X
SEM	X.XX	X.XX	X.XX	X.XX
Minimum	XX	XX	XX	XX
Median	X.X	X.X	X.X	X.X
Maximum	XX	XX	XX	XX

Note: Change = Day 9 – Day -1; percent change = (Day 9 – Day -1)/Day -1*100

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

Programming Notes: Footnotes to include under the table, as appropriate: < . = Value missing or not reportable. > <For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of <XX> are treated as 1/2 LLOQ>. Summarize by Overall, female, male

Summary tables for urine biomarkers (Part 1) will be in the following format:

Table 14.2.3.1.2 Summary of Urine NNAL by Study Day in Part 1: 9-Day Switch to Exclusive myblu™ Use (Outcomes Population)

	Amount Excreted (xg/24 hours)			
Statistic	Day -1	Day 9	Change	Percent Change
n	X	X	X	X
Mean	X.X	X.X	X.X	X.X
SD	X.XX	X.XX	X.XX	X.XX
CV(%)	XX.X	XX.X	XX.X	XX.X
SEM	X.XX	X.XX	X.XX	X.XX
Minimum	XX	XX	XX	XX
Median	X.X	X.X	X.X	X.X
Maximum	XX	XX	XX	XX

Note: Change = Day 9 – Day -1; percent change = (Day 9 – Day -1)/Day -1*100

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

Programming Notes: Add four columns with the header "Creatinine-Adjusted (unit/g creatinine)" Footnotes to include under the table, as appropriate: < . = Value missing or not reportable. > <For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of <XX> are treated as 1/2 LLOQ>. Summarize by Overall, female, male.

Statistical comparison table for Part 1 will be in the following format:

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Table 14.2.3.1.22 Statistical Comparisons of BoE and BoPH Between Study Days in Part 1: 9-Day Switch to Exclusive myblu™ Use (Outcomes Population)

Biomarker (unit)	LS Means Day 9 (n)	LS Means Day -1 (n)	LS Mean Difference (Day 9 – Day -1)	95% Confidence Interval	p-value
Blood COHb (% Saturation)	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Urine NNAL (xg/24 hours)	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
<add remaining biomarkers>					

Note: n = Number of observation used in the analysis; Least-squares means (LS Means) are calculated from the ANOVA.

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

Programming Notes: List biomarkers in the same order as section 2.2

Summary tables for blood biomarkers by Study Day (Part 2) will be in the following format:

Table 14.2.3.2.1 Summary of Blood COHb (% Saturation) by Study Day in Part 2: Continue Exclusive myblu™ Use (Outcomes Population)

Statistic	Day -1	Day 14	Change	Percent Change
n	X	X	X	X
Mean	X.X	X.X	X.X	X.X
SD	X.XX	X.XX	X.XX	X.XX
CV(%)	XX.X	XX.X	XX.X	XX.X
SEM	X.XX	X.XX	X.XX	X.XX
Minimum	XX	XX	XX	XX
Median	X.X	X.X	X.X	X.X
Maximum	XX	XX	XX	XX

Note: Change = Day 14 – Day -1; percent change = (Day 14 – Day -1)/Day -1*100

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

Programming Notes: Add four columns for with the header "Creatinine-Adjusted unit/g creatinine" Footnotes to include under the table, as appropriate: < . = Value missing or not reportable. > <For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of <XX> are treated as 1/2 LLOQ>. Summarize by Overall, female, male

Summary tables for urine biomarkers by Study Day (Part 2) will be in the following format:

Table 14.2.3.2.2 Summary of Urine NNAL by Study Day in Part 2: Continue Exclusive myblu™ Use (Outcomes Population)

	Amount Excreted (xg/24 hours)			
Statistic	Day -1	Day 14	Change	Percent Change
n	X	X	X	X
Mean	X.X	X.X	X.X	X.X
SD	X.XX	X.XX	X.XX	X.XX
CV(%)	XX.X	XX.X	XX.X	XX.X
SEM	X.XX	X.XX	X.XX	X.XX
Minimum	XX	XX	XX	XX
Median	X.X	X.X	X.X	X.X
Maximum	XX	XX	XX	XX

Note: Change = Day 14 – Day -1; percent change = (Day 14 – Day -1)/Day -1*100

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

Programming Notes: Add four columns for with the header "Creatinine-Adjusted unit/g creatinine" Footnotes to include under the table, as appropriate: < . = Value missing or not reportable. > <For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of <XX> are treated as 1/2 LLOQ>. Summarize by Overall, female, male

Statistical comparison table of biomarkers between study days for Part 2 will be in the following format:

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Table 14.2.3.2.22 Statistical Comparison of BoE and BoPH Between Study Days in Part 2: Continue Exclusive myblu™ Use (Outcomes Population)

Biomarker (unit)	LS Means Day 14 (n)	LS Means Day -1 (n)	LS Mean Difference (Day 14 – Day -1)	95% Confidence Interval	p-value
Blood COHb (% Saturation)	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Urine NNAL (xg/24 hours)	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
<add remaining biomarkers>					

Note: n = Number of observation used in the analysis; Least-squares means (LS Means) are calculated from the ANOVA.

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

Programming Notes: List biomarkers in the same order as section 2.2

Summary tables for blood biomarkers by Study Arm and Study Day (Part 2) will be in the following format:

Table 14.2.3.3.1 Summary of Blood COHb (% Saturation) by Study Arm in Part 2 (Outcomes Population)

	Arm	Statistic	Day 9	Day 14	Change	Percent Change
Overall	I	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		CV(%)	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
	J	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		CV(%)	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
	K	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		CV(%)	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
Female	<Same as above>					
Male	<Same as above>					

Note: Change = Day 14 – Day 9; percent change = (Day 14 – Day 9)/Day 9*100
Arm I: Exclusive use of myblu™ products ad libitum
Arm J: Exclusive smoking of usual brand combustible cigarettes ad libitum
Arm K: Smoking of usual brand combustible cigarettes (up to 50% of the subject's self-reported CPD) and use of myblu™ products ad libitum

Programming Notes: Footnotes to include under the table, as appropriate: < . = Value missing or not reportable. > <For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of <XX> are treated as 1/2 LLOQ>.

Summary tables for urine biomarkers by Study Arm and Study Day (Part 2) will be in the following format:

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Table 14.2.3.3.2 Summary of Urine NNAL by Study Arm in Part 2: (Outcomes Population)

			Amount Excreted (xg/24 hours)			
	Arm	Statistic	Day 9	Day 14	Change	Percent Change
Overall	I	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		CV(%)	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
	J	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		CV(%)	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
	K	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		CV(%)	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
Female	<Same as above>					
Male	<Same as above>					

Note: Change = Day 14 – Day 9; percent change = (Day 14 – Day 9)/Day 9*100
Arm I: Exclusive use of myblu™ products ad libitum
Arm J: Exclusive smoking of usual brand combustible cigarettes ad libitum
Arm K: Smoking of usual brand combustible cigarettes (up to 50% of the subject's self-reported CPD) and use of myblu™ products ad libitum

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

Programming Notes: Add four columns for with the header "Creatinine-Adjusted unit/g creatinine" Footnotes to include under the table, as appropriate: < . = Value missing or not reportable. > <For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of <XX> are treated as 1/2 LLOQ>.

Statistical comparison tables of biomarkers among study arms for Part 2 will be in the following format:

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Table 14.2.3.3.22 Statistical Comparisons of BoE and BoPH Differences From Baseline Among myblu™, Combustible Cigarette, and Dual Use Arms in Part 2 (Outcomes Population) (Outcomes Population)

Biomarker (unit)	Comparison	LS Means Day 14 (n)	LS Means Day 9(n)	LS Mean Difference (Day 14 – Day 9)	95% Confidence Interval	p-value
Blood COHb (% Saturation)	Arm I vs Arm J	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Arm I vs Arm K	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Arm K vs Arm J	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
Urine NNAL (xg/24 hours)	<same as above for the remaining biomarkers					

Note: n = Number of observation used in the analysis; Least-squares means (LS Means) are calculated from the ANOVA.

Arm I: Exclusive use of myblu™ products ad libitum
Arm J: Exclusive smoking of usual brand combustible cigarettes ad libitum
Arm K: Smoking of usual brand combustible cigarettes (up to 50% of the subject's self-reported CPD) and use of myblu™ products ad libitum

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

Programming Notes: List biomarkers in the same order as section 2.2

4.2.4 Physiologic Assessments Tables

Tables 14.2.4.1.1, 14.2.4.1.2, 14.2.4.1.4, 14.2.4.1.5, 14.2.4.1.7, 14.2.4.1.8 will be in the following format:

Table 14.2.4.1.1 Summary of Systolic Blood Pressure (mm Hg) by Time Point in Exclusive myblu™ Use (Arm I) (Outcomes Population)

		Sample Times (hr)								
Day		Pre-use	XX	XX	XX	XX	XX	XX	XX	XX
-1	n	XX	XX	XX	XX	XX	XX	XX	XX	XX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	CV%	.	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Minimum	XX	XX	XX	XX	XX	XX	XX	XX	XX
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Maximum	XX	XX	XX	XX	XX	XX	XX	XX	XX

Repeat for Days 9 and 14

. = Value missing or not reportable.

Programmer note: For change from baseline tables, present values for Day 9 – Day -1 and Day 14 – Day -1

Tables 14.2.4.1.3, 14.2.4.1.6, and 14.2.4.1.9 will be in the following format:

Table 14.2.4.1.3 Summary of Systolic Blood Pressure Change from Baseline Parameters in Exclusive myblu™ Use (Arm I) (Outcomes Population)

Day	Statistic	param1 (units)	param2 (units)	param3 (units)	param4 (units)	param5 (units)	param6 (units)
9	n	XX	XX	XX	XX	XX	XX
	Mean	XXX.X	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Minimum	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
	Median	XX.XX	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
	Maximum	XXX	X.XX	XXX	XXX	XX.X	X.XXX
14 (same as above)							

. = Value missing or not reportable.

Notes for Generating the Actual Table:

Presentation of Data:

- Parameters will be presented in the following order and with following units: AUEC0-24 (mm Hg * hr), Emax (mm hg), TEmax (min)
- n will be presented as an integer (with no decimal);
- Parameter values for exposure-based parameters (i.e. AUC0-t and Cmax) will be presented with, at maximum, the precision of the bio data, and, at minimum, 3 significant figures (to be determined by the PKist once bio data are received). Summary statistics for exposure parameters will be presented as: Mean, Median, +1; SD and SEM +2, Min and Max +0.
- Values for time-based parameters (i.e. TEmax) will be presented with 2 decimals. Summary statistics for time-based parameters will be presented as: Mean, Median, SD +2, Min and Max +0.
- Summarize by overall, female, male

Program: /CAXXXXX/sas_prg/pksas/pk-tables.sas DDMMMYYYY HH:MM

Table 14.2.4.1.10 Statistical Comparisons of Change From Baseline Systolic Blood Pressure, Diastolic Blood Pressure, and Heart Rate Heart Rate Parameters in Exclusive myblu™ Use (Arm I)

Vital Sign	Parameter (unit)	LS Means Day 14 (n)	LS Means Day 9(n)	LS Mean Difference (Day 14 – Day 9)	95% Confidence Interval	p-value
Systolic BP	AUEC (mmHg * hr)	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Emax (mmHg)	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	TEmax (min)	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX

<Repeat for other vital signs>

Note: n = Number of observation used in the analysis; Least-squares means (LS Means) are calculated from the ANOVA.

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

Table 14.2.4.2.1 Summary of Lung Function Parameters by Time Point in Exclusive myblu™ Use (Arm I) (Outcomes Population)

Parameter:	Statistics	Day -1	Day 9	Day -1	Day 14
FEV1 (pre) (%)	n	X	X	X	X
	Mean	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X
	Minimum	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX
FEV1 (post)	n	X	X	X	X
	Mean	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X
	Minimum	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX
FEV1 (Post - Pre)					

<Continue with remaining parameters>

Note: *Parameters values are are the percent of predicted
. = Value missing or not reportable.

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

Programmer note: Parameters are pre-, post-, and pre-post bronchodilator values for percent of predicted FEV1, FVC, FEV1:FVC ratio, and FEF25-25%

Table 14.2.4.2.2 Summary of Lung Function Variables Changes by Time Point in Exclusive myblu™ Use (Arm I) (Outcomes Population)

		--------- Pre-Broncodilator ----------	
Parameter:	Statistics	Day 9 – Day -1	Day 14 – Day -1
FEV1 (%)	n	X	X
	Mean	X.X	X.X
	SD	X.XX	X.XX
	CV(%)	XX.X	XX.X
	Minimum	XX	XX
	Median	X.X	X.X
	Maximum	XX	XX
FVC	n	X	X
	Mean	X.X	X.X
	SD	X.XX	X.XX
	CV(%)	XX.X	XX.X
	Minimum	XX	XX
	Median	X.X	X.X
	Maximum	XX	XX
<Continue with remaining parameters>			

Note: *Parameters values are are the percent of predicted
. = Value missing or not reportable.

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

Programmer note: Parameters percent of predicted FEV1, FVC, FEV1:FVC, and FEF25-25%. Add the same two columns for "Post Bronchodilator – Pre-Bronchodilator". Present results for Overall, Female, Male

Table 14.2.4.2.3 Statistical Comparisons of Change From Baseline Lung Function Parameters in Exclusive myblu™ Use (Arm I)

Parameter* (unit)	------ LS Means ------ Day 14 (n)	Day 9(n)	LS Mean Difference (Day 14 – Day 9)	95% Confidence Interval	p-value
Pre-Bronchodilator					
FEV1 (%)	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
FVC (%)	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
FEV1:FVC	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
FEF25-75%					
Post-Bronchodilator – Pre-Bronchodilator					
FEV1 (%)	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
FVC (%)	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
FEV1:FVC	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
FEF25-75%					

Note: *Parmeters are percent of predicted
n = Number of observation used in the analysis; Least-squares means (LS Means) are calculated from the ANOVA.

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

14.2.6 Questionnaires Tables

Tables 14.2.6.1.X and 14.2.6.2.X will be in the following format:

Page 1 of X

Table 14.2.6.1 Summary of < PES Subscales> by Study Product for Controlled Product Use Session (Outcomes Population)

			Product					
< Subscale or Question>		Statistic	A	B	C	D	E	F
Satisfaction	Overall	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.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
	Female	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.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
	Male	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.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

```
 Psychological Reward        < Continue with remaining subscales and individual items>
 ---------------------------------------------------------------------------------------

Product X =
Scale: 1 = not at all, 2 = very little, 3 = a little, 4 = moderately, 5 = a lot, 6 = quite a lot, 7 = extremely

Program:  /AAXXXXX/ECR/sas_prg/stsas/tab programname.sas  DDMMMYYYY  HH:MM
```

Programmer note: Add columns for Products G, and H.

Tables 14.2.6.3.1 and 14.2.6.3.2 will be in the following format:

Table 14.2.6.3.1 Frequency of Responses to Use the Product Again Questionnaire in Each Category After the Ad Libitum Product Use Episode by Product (Outcome Population)

Question	Product	Category	Statistics	Use the Product Again Response Category: -50 to <0	0	>0 to 50
1	A	Overall	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		Female	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		Male	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
	B	Overall	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		Female	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		Male	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
	C	Overall	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		Female	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		Male	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
	D	Overall	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		Female	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		Male	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
	E	Overall	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		Female	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		Male	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
	F	Overall	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		Female	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		Male	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
	G	Overall	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		Female	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		Male	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
	H	Overall	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		Female	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
		Male	n (%)	XX(XX%)	XX(XX%)	XX(XX%)
2	<repeat for questions 2 and 3>					

Question 1: How likely are you to continue to smoke after you complete this study?
Question 2: If available, how likely are you to buy your assigned study product in the future?
Question 3: How likely are you to buy an e-cigarette other than your assigned product in the future?

```
          Product A = <>
          Product B = <>
          Product C = <>
          Product D = <>
          Product E = <>
          Product F = <>
          Product G = <>
          Product H = <>

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

Programming Note: The percentage (%) is the row percentage.

Tables 14.2.6.3.3 and 14.2.6.3.4 will be in the following format:

Table 14.2.6.3.3 Summary of Future Intent to Use VAS Score in Each Category by Study Product for Ad Libitum Product Use Session (Outcomes Population)

Question	Product	Category	Statistics	Use the Product Again Response Category: -50 to <0	Use the Product Again Response Category: >0 to 50
1	A	Overall	n	X	X
			Mean	X.X	X.X
			SD	X.XX	X.XX
			CV(%)	XX.X	XX.X
			SEM	X.XX	X.XX
			Minimum	XX	XX
			Median	X.X	X.X
			Maximum	XX	XX
		Female	n	X	X
			Mean	X.X	X.X
			SD	X.XX	X.XX
			CV(%)	XX.X	XX.X
			SEM	X.XX	X.XX
			Minimum	XX	XX
			Median	X.X	X.X
			Maximum	XX	XX
		Male	n	X	X
			Mean	X.X	X.X
			SD	X.XX	X.XX
			CV(%)	XX.X	XX.X
			SEM	X.XX	X.XX
			Minimum	XX	XX
			Median	X.X	X.X
			Maximum	XX	XX

Question 1: How likely are you to continue to smoke after you complete this study?
Question 2: If available, how likely are you to buy your assigned study product in the future?
Question 3: How likely are you to buy an e-cigarette other than your assigned product in the future?

Product A = <>
Product B = <>
Product C = <>
Product D = <>
Product E = <>
Product F = <>
Product G = <>
Product H = <>

Programming Note: Summary for Products B, C, D, E, F, G, and H will also be included in the table. Include category 0 in the table if there sufficient data.

Tables 14.2.6.3.5 and 14.2.6.3.6 will be in the following format:

Table 14.2.6.3.5 Summary of Future Intent to Use VAS Raw Scores by Study Product for Ad Libitum Product Use Session (Outcomes Population)

		Product			
Category	Statistics	A	B	C	D
Overall	n	X	X	X	X
	Mean	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X
	SEM	XX.X	XX.X	XX.X	XX.X
	Minimum	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.
	Maximum	XX	XX	XX	XX
Female	n	X	X	X	X
	Mean	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X
	SEM	XX.X	XX.X	XX.X	XX.X
	Minimum	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.
	Maximum	XX	XX	XX	XX

Question 1: How likely are you to continue to smoke after you complete this study?
Question 2: If available, how likely are you to buy your assigned study product in the future?
Question 3: How likely are you to buy an e-cigarette other than your assigned product in the future?

Product A = <>
Product B = <>
Product C = <>
Product D = <>
Product E = <>
Product F = <>
Product G = <>
Product H = <>

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

Programmer Note: Summary for Male and Products E, F, G, H will be included in the table. Add a column to the left for "Question"

Tables 14.2.6.4, 14.2.6.5, and 14.2.6.6 will be in the following format:

Table 14.2.6.6 Summary of QSU-brief Factor Scores by Study Arm and Study Day (Outcomes Population)

			Day 9		
			Arm I	Arm J	Arm K
Subscale		Statistic			
Factor 1	Overall	n	X	X	X
		Mean	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX
		CV%	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX
		Median	X.X	X.X	X.X
		Maximum	XX	XX	XX
	Female	n	X	X	X
		Mean	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX
		CV%	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX
		Median	X.X	X.X	X.X
		Maximum	XX	XX	XX
	Male	n	X	X	X
		Mean	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX
		CV%	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX
		Median	X.X	X.X	X.X
		Maximum	XX	XX	XX
< Repeat for Factor 2>					

```
Arm I =
Factor 1 = Anticipation of pleasure from smoking
Factor 2 = Anticipation of Relief of nicotine withdrawal
Scale: 1 = Strongly disagree; 7 = Strongly agree

Program:  /AAXXXXX/ECR/sas_prg/stsas/tab programname.sas  DDMMMYYYY  HH:MM
```

Programmer note: Add columns for Day 14. Tables 14.2.6.4 and 14.2.6.5 will have no subscale column.

```
Footnote for Table 14.2.6.4: Total scoring: 0 - 3 = not dependent, 4 - 8 = low dependence, 9 - 12 = medium dependence,
13+ = high dependence
```

Table 14.2.7 Summary of Puff Topography Parameters by Study Day (Outcomes Population)

Parameter (Units)	Category	Statistics	Day -1	Day 1	Day 8
Total Puff Count	Overall	n	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	XX.X	XX.X	XX.X
		Minimum	XX	XX	XX
		Median	X.X	X.X	X.X
		Maximum	XX	XX	XX
	Female	n	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	XX.X	XX.X	XX.X
		Minimum	XX	XX	XX
		Median	X.X	X.X	X.X
		Maximum	XX	XX	XX

Programming note: Parameters are:

- Total Puff count
- Average Puff Duration (sec)
- Total Puff Duration sec)
- Average Puff volume (mL)
- Total Puff Volume (mL)
- Average Peak flow rate (mL/sec)
- Average flow rate (mL/sec)
- Average Inter-puff interval (sec)

Adverse event summary table (Tables 14.3.1.1.1 and 14.3.1.2.1) will be in the following format.

Page 1 of X

Table 14.3.1.1.1 Product Use-emergent Adverse Event Frequency by Study Product – Number of Subjects Reporting the Event (% of Subjects Who Used Study Product) - Part 1 (Safety Population)

	Product							
Adverse Event*	A	B	C	D	E	F	G	Overall
Number of Subjects Who Received Study Product	XX(100%)	XX(100%)	XX(100%)	XX(100%)	XX(100%)	XX(100%)	XX(100%)	XX(100%)
Number of Subjects With Adverse Events	X(X%)	X(XX%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Number of Subjects Without Adverse Events	XX(XX%)	XX(XX%)	XX(XX%)	XX(XX%)	XX(XXX%)	XX(XXX%)	XX(XXX%)	XX(XXX%)
Eye disorders	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Vision blurred	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Gastrointestinal disorders	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Dyspepsia	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Nausea	X(X%)	X(X%)	X(X%)	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%)	X(X%)	X(X%)	X(X%)
Back pain	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Muscle cramps	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Musculoskeletal pain	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Nervous system disorders	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Headache NOS	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)

Note: * Adverse events are classified according to MedDRA Version 22.0.
Product X = < >

Program: /CAXXXXX/sas_prg/stsas/tab cdash_tblae1a_auto.sas DDMMMYYYY HH:MM

Programmer Note: Product H will also be presented in the table. Table 14.3.1.2.1 will have three columns for the three study arms and an overall column.

Adverse event summary table (Tables 14.3.1.1.2 and 14.3.1.2.2) will be in the following format.

Page 1 of X

Table 14.3.1.1.2 Product Use-emergent Adverse Event Frequency by Study Product – Number of Adverse Events (% of Total Adverse Events) – Part 1 (Safety Population)

	Product							
Adverse Event*	A	B	C	D	E	F	G	Overall
Number of Adverse Events	XX(100%)	XX(100%)	XX(100%)	XX(100%)	XX(100%)	XX(100%)	XX(100%)	XX(100%)
Eye disorders	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Vision blurred	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Gastrointestinal disorders	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Dyspepsia	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Nausea	X(X%)	X(X%)	X(X%)	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%)	X(X%)	X(X%)	X(X%)
Back pain	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Muscle cramps	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Musculoskeletal pain	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Nervous system disorders	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
Headache NOS	X(X%)	X(X%)	X(X%)	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%)	X(X%)	X(X%)	X(X%)
Vaginal discharge	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)

Note: * Adverse events are classified according to MedDRA Version 22.0.
Product X = < >

Program: /CAXXXXX/sas_prg/stsas/tab cdash_tblae1a_auto.sas DDMMMYYYY HH:MM

Programmer Note: Product H will also be presented in the table. Table 14.3.1.2.2 will have three columns for the three study arms and an overall column.

Adverse event summary table (Tables 14.3.1.1.3 and 14.3.1.2.3) will be in the following format.

Page 1 of X

Product Use-emergent Adverse Event Frequency by Study Product, Severity, and Relationship to Study Product
– Number of Subjects Reporting Events - Part 1 (Safety Population)

Adverse Event*	Study Product	Number of Subjects with Adverse Events	Intensity			Relationship to Study Product				
			Mild	Moderate	Severe	Not Related	Unlikely	Probably	Likely	Related
Abdominal pain	X	X	X	X	X	X	X	X	X	X
Constipation	X	X	X	X	X	X	X	X	X	X
Dry throat	X	X	X	X	X	X	X	X	X	X
Headache	X	X	X	X	X	X	X	X	X	X
	X	X	X	X	X	X	X	X	X	X
Study Product A		X	X	X	X	X	X	X	X	X
Study Product B		X	X	X	X	X	X	X	X	X
Study Product C		X	X	X	X	X	X	X	X	X
Study Product D		X	X	X	X	X	X	X	X	X
Study Product E		X	X	X	X	X	X	X	X	X
Study Product F		X	X	X	X	X	X	X	X	X
Study Product G		X	X	X	X	X	X	X	X	X
Study Product H		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 22.0.
When a subject experienced the same AE at more than one level of intensity during a product use period, only the most severe one was counted.
When a subject experienced the same AE at more than one level of product relationship during a product use period, only the one most closely related to study product was counted.
Product X = < >

Program: /CAXXXXX/sas_prg/stsas/tab cdash_tblae3a_auto.sas DDMMMYYYY HH:MM

Programmer Note: Table 14.3.1.2.3 will have three rows for the three study arms and an overall row. The column header will be study product arm.

Serious adverse event table (Table 14.3.2.1) will be in the following format.

Page 1 of X

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

Post-text Tables 14.3.4.1, 14.3.4.2, and 14.3.4.3 will be in the following format:

Table 14.3.4.1 Out-of-Range Values and Recheck Results - Serum Chemistry (Safety Population)

Subject Number	Age#/ Sex	Study Period	Day	Hour	Date	Time	Parameter1 <Range> (Unit)	Parameter2 <Range> (Unit)	Parameter3 <Range> (Unit)	Parameter4 <Range> (Unit)	Parameter5 <Range> (Unit)
X	XX/X	Screen			DDMMMYYYY	HH:MM:SS				XX LY	XX HY
		X	-X	-X.XX	DDMMMYYYY	HH:MM:SS	XX HY				XX HY
		X	X	-X.XX	DDMMMYYYY	HH:MM:SS		XX LY	XX LY		
			X	X.XX	DDMMMYYYY	HH:MM:SS			XX HY		

Programmer Note: Table 14.3.4.2 (Hematology) and Table 14.3.4.3 (Urinalysis) will resemble Table 14.3.4.1. Replace Parameter1, 2 etc. with actual lab tests in the study. Sort unscheduled assessment and early termination chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for.

Note: # Age is calculated from the date of informed consent. F = Female, M = Male
H = Above Reference Range, L = Below Reference Range
PI Interpretation: N = Not Clinically Significant, Y = Clinically Significant
Study Part 1 is up to Day 9 and Study Part 2 is from Day 10 onward.

Program: /CAXXXXX/sas_prg/stsas/tab/programname.sas DDMMMYYYY HH:MM

Post-text Table 14.3.4.4 will be in the following format:

Table 14.3.4.4 Clinically Significant Values and Recheck Results (Safety Population)

Subject Number	Age#/ Sex	Study Period	Day	Hour	Date	Time	Department	Test	Result		Reference Range	Unit
X	XX/X	X	X	-X.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	XXXXXXXX	XXX		X - X	mg/dL
				X.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	XXXXXXXX	XXX	HYR+	X - X	mg/dL
				X.XX	DDMMMYYYY	HH:MM:SS	Serum Chemistry	XXXXXXXX	XXX	HY+	X - X	mg/dL

Programmer note: All time points for a subject/test with at least one value deemed as CS by the PI will be presented in this table. If no event meets this criteria then include a statement as follows: 'There were no clinical laboratory results documented as clinically significant by the Principal Investigator.'

Note: # Age is calculated from the date of informed consent. F = Female, M = Male
H = Above Reference Range
Computer: Y = Clinically Significant
PI Interpretation: R = Recheck Requested, + = Clinically Significant
Study Part 1 is up to Day 9 and Study Part 2 is from Day 10 and afterwards.

Program: /CAXXXXX/sas_prg/stsas/tab/programname.sas DDMMMYYYY HH:MM

Serum chemistry, hematology, and urinalysis summary tables (Table 14.3.5.1. Table 14.3.5.2, and 14.3.5.3) will be in the following format.

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Table 14.3.5.1 Clinical Laboratory Summary – Serum Chemistry (Safety Population)

Laboratory Test (units)	Reference Range	Statistic	Time Point		
			Screening	Check-in	End-of-Study
Testname (unit)	XX - XX #	n	X	X	X
		Mean	X.X*	X.X	X.X
		SD	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX
		Median	X.X	X.X	X.X
		Maximum	XX	XX	XX
Testname (unit)	XX - XX	n	X	X	X
		Mean	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX
		Median	X.X	X.X	X.X
		Maximum	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.
* Above Reference Range, ^ Below Reference Range

Program: /CAXXXXX/sas_prg/stsas/tab/programname.sas DDMMMYYYY HH:MM

Vital sign summary table (Table 14.3.5.4) will be in the following format.

Table 14.3.5.4 Vital Sign Summary (Safety Population)

Vital Sign (units)	Time Point	Statistic	
Testname (unit)	Screening	n	X
		Mean	X.X
		SD	X.XX
		Minimum	XX
		Median	X.X
		Maximum	XX
	Check-in	n	X
		Mean	X.X
		SD	X.XX
		Minimum	XX
		Median	X.X
		Maximum	XX

Note: Study Part 1 is up to Day 9 and Study Part 2 is from Day 10 and afterwards.

Program: /CAXXXXX/sas_prg/stsas/tab cdash_vitsummary.sas DDMMMYYYY HH:MM

ECG summary tables (Table 14.3.5.5) will be in the following format.

Table 14.3.5.5 12-Lead Electrocardiogram Summary (Safety Population) (Safety Population)

		Time Point		
Parameter (units)	Statistic	Screening	Check-in	End-of-Study
Testname (unit)	n	X	X	X
	Mean	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX
	Median	X.X	X.X	X.X
	Maximum	XX	XX	XX
Testname (unit)	n	X	X	X
	Mean	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX
	Median	X.X	X.X	X.X
	Maximum	XX	XX	XX

Program: /CAXXXXX/sas_prg/stsas/tab/programname.sas DDMMMYYYY HH:MM

Spirometry summary tables (Table 14.3.5.6) will be in the following format.

Table 14.3.5.6 Spirometry Summary (Safety Population) (Safety Population)

		Pre Bronchodilator			Post Bronchodilator		
Parameter (units)	Statistic	Screening	Day 9	Day 14	Screening	Day 9	Day 14
Testname (unit)	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
	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
Testname (unit)	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
	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

Note: Study Part 1 is up to Day 9 and Study Part 2 is from Day 10 and afterwards.

Program: /CAXXXXX/sas_prg/stsas/tab/programname.sas DDMMMYYYY HH:MM

11. LISTING SHELLS

The following listing shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the listings that will be presented and included in the final report. These listings will be generated off of the [redacted] SDTM Version 1.4. All listings will be presented in Courier New size font 9.

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges

Laboratory Group	Test Name	Sex	Age Category	Reference Range	Unit
Serum Chemistry	Test Name	XXXXXX	XX-XX	XX-XX	units
	Test Name	XXXXXX	XX-XX	XX-XX	units
	Test Name	XXXXXX	XX-XX	XX-XX	units
	Test Name	XXXXXX	XX-XX	XX-XX	units
Hematology	Test Name	XXXXXX	XX-XX	XX-XX	units
	Test Name	XXXXXX	XX-XX	XX-XX	units
	Test Name	XXXXXX	XX-XX	XX-XX	units
	Test Name	XXXXXX	XX-XX	XX-XX	units
Urinalysis	Test Name	XXXXXX	XX-XX	XX-XX	units
	Test Name	XXXXXX	XX-XX	XX-XX	units
	Test Name	XXXXXX	XX-XX	XX-XX	units
	Test Name	XXXXXX	XX-XX	XX-XX	units

<similar for remaining Laboratory Groups and Test Names>

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.1 Subject Discontinuation (Safety Population)

Subject Number	Study Period	Randomized Sequence/Arm Part 1	Randomized Sequence/Arm Part 2	Date	Completed Study?	Primary Discontinuation Reason	Specify
X	XXXX	XXXX	X	DDMMMYYYY	YES		
X	XXXX	XXXX	X	DDMMMYYYY	NO	Adverse Event	XXXXXXXXXX

Note: Product X: < >

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.2 Protocol Deviation

Subject Number	Any Deviation	Study Period	Study Product	Deviation Category	Deviation Type	Other, Specify	Deviation Date	Deviation Term
X	YES	XXX	X	XXXX	XXXX		DDMMMYYYY	XXXXXXXXXX

Note: Product X: < >

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.4.1.1 Demographics (Safety Population)

Subject Number	Randomized Sequence/Arm		Date of Birth	Age* (yrs)	Sex	Race	Ethnicity	Height (cm)	Weight (kg)	Body Mass Index (kg/m²)	Informed Consent Date
	Part 1	Part 2									
X	XXXX	X	DDMMMYYYY	XX	XXXXXX	XXXXXX	XXXXXX	XXX	XX.XX	XX.XX	DDMMMYYYY
X	XXXX	X	DDMMMYYYY	XX	XXXXXX	XXXXXX	XXXXXX	XXX	XX.XX	XX.XX	DDMMMYYYY
X	XXXX	X	DDMMMYYYY	XX	XXXXXX	XXXXXX	XXXXXX	XXX	XX.XX	XX.XX	DDMMMYYYY

Note: * Age is calculated from the date of first study product use.

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.4.1.2 Reproductive Status (Safety Population)

Subject Number	A Woman of Childbearing Potential?	Last Menstrual Period	Last Pregnancy	Outcome	Date of Outcome	Lactating, Pregnant, or Plan to Become Pregnant?	Reproductive Status	Method of Contraception	Agree to Use Double Barrier
X	XXXXXX	DDMMMYYYY	XXXXXXX	XXXXXX	DDMMMYYYY	XXXXXX	XXXXXXX	XXXXXXX	XXX

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.4.2 Physical Examination (Safety Population)

Subject Number	Study Period	Time Point	Date	Body System or Organ Class	Reason for Not Done	Finding	Clinically Significant?	Comment
X	Screen	XXXXXX	DDMMMYYYY	XXXXXXXX		XXXXXX	XXXXXX	

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.4.3.1 Medical History (Safety Population)

Subject Number	Study Period	Time Point	Medical History Present	Start Date	Start Time	End Date	End Time	Reported Term for the Medical History	Clinically Significant
X	Screen	XXXXXXX	XXX	DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	XXXXXXXXXXX	XXX

Programmer Note: Date can be YYYY, MMMYYYY, or DDMMMYYYY based on individual subject data.

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.4.3.1 Allergy History (Safety Population)

Subject Number	Study Period	Time Point	Allergy Present	Category of Allergy	State Date	End Date	Clinical Significance	Investigator Judgement
X	Screen	XXXXXXX	XXX	XXXXXXXXXX	DDMMMYYYY	DDMMMYYYY	XXXXX	XXXXXXXX

Programmer Note: Date can be YYYY, MMMYYYY, or DDMMMYYYY based on individual subject data.

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.4.3.2 Surgical History (Safety Population)

Subject Number	Study Period	Time Point	Surgical History Present	Date of Surgical Event	Surgery Comment	Clinically Significant
X	Screen	XXXXXXX	XXX	DDMMMYYYY		

Programmer Note: Date can be YYYY, MMMYYYY, or DDMMMYYYY based on individual subject data.

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.4.4 Smoking History (Safety Population)

Subject Number	Study Period	Cigarettes Per Day	Start Date	Type of Cigarette	Cigarette Brand	Cigarette Style	Cigarette Flavor	Cigarette Length	Question* 1	2	3	4
X	Screen	XX	DDMMMYYYY	Menthol	XXXXXXXX	XXXXXX	XXXXXX	XXXXXX	XXX	XX	XX	XXX

Programmer Note: Date can be YYYY, MMMYYYY, or DDMMMYYYY based on individual subject data.

Note: Question 1 = Has the subject used any other nicotine-containing products other than manufactured combustible cigarettes (e.g., e-cigarettes, roll-your-own cigarettes, bidis, snuff, nicotine inhaler, pipe, cigar, chewing tobacco, nicotine patch, nicotine spray, nicotine lozenge, or nicotine gum) within the last 14 days ?
Question 2 = Has the subject used any prescription smoking cessation treatments, including, but not limited to, varenicline (Chantix®) or bupropion (Zyban®) within the last 3 months?
Question 3 = Is the subject a self-reported puffer (i.e., adult smoker who draws smoke from the cigarette into the mouth and throat but does not inhale)?
Question 4 = Is the subject planning to quit smoking during the study or postponing a quit attempt in order to participate in the study?

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.4.5 Caffeine, Alcohol, and Drug History (Safety Population)

Subject Number	Alcohol					Caffeine				Drug				
	Consumption?	Abuse?	Type	Amount	Frequency	Consumption?	Type	Amount	Frequency	Abuse?	End Date	Used	Amount	Frequency
X	XX	XXX	XXX	XXX	XXXXX	XX	XXX	XXX	XXXXX	XX	DDMMMYYYY	XXX	XXX	XXXXX

Programmer Note: Date can be YYYY, MMMYYYY, or DDMMMYYYY based on individual subject data.

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.5.1.1 Inclusion Criteria

1. < >
2. < >
3. < >
4. < >
5. < >
etc.

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.5.1.2 Exclusion Criteria

1. < >
2. < >
3. < >
4. < >
5. < >
etc.

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.5.2 Subject Eligibility (Safety Population)

Subject Number	Study Period	Time Point	Date	Time	Did Subject meet all eligibility criteria?	Criterion Not Met*	Comment
X	Screen	XXXX	DDMMMYYYY	HH:MM	YES		
X	Screen	XXXX	DDMMMYYYY	HH:MM	NO	EXCLUSION X	XXXXXXXXXXXXXXXXX
X	Screen	XXXX	DDMMMYYYY	HH:MM	YES		
X	Screen	XXXX	DDMMMYYYY	HH:MM	NO	INCLUSION X	XXXXXXXXXXXXXXXXX

Note: * Please refer to Appendix 16.2.5.1.1 and Appendix 16.2.5.1.2 for specific inclusion and exclusion criteria.

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.5.3 Randomization (Safety Population)

Subject Number	Study Period	Time Point	Date	Time	Randomization Performed	Randomized Sequence	Randomized Arm
X	X	XXXXXX	DDMMMYYYY	HH:MM	XXX	XXXX	X

Note: Product X: < >
Arm X: < >

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.5.4.1 Usual Brand Cigarette (Safety Population)

Subject Number	Study Period	Time Point	Date	Time	Number of Cigarettes per Pack	Number of Unopened Packs from Subject	Comment
X	X	XXXXXX	DDMMMYYYY	HH:MM	XX	XXX	

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.5.4.2 Test Product Administration (Safety Population)

Subject Number	Study Period	Product	Time Point	Start Date	Start Time	End Time	Total Number of Inhalations	3 Seconds Per Puff?	Comment for Duration	Missed Puff?	Comment for Missed Puff
X	X	X	XXXXXX	DDMMMYYYY	HH:MM	HH:MM	XXX	XXX		XXX	

Note: Product X: < >

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.5.4.3 Ad Libitum Product Use (Safety Population)

Subject Number	Study Period	Product	Time Point	Start Date	Start Time	Stop Date	Stop Time	No. of Pods Dispensed	No. of Pods Used
X	X	X	XXXXXX	DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	XXX	XXX

Note: Product X: < >

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.5.4.4 Product Use Behavior – Pod Weight (Safety Population)

Subject Number	Study Period	Product	Time Point	Pre Weight (g)	Post Weight (g)	Comment
X	X	X	HH:MM	X.XXXX	X.XXXX	

Note: Product X: < >

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.5.5.1 Blood Draw Times (Safety Population)

Subject Number	Study Period	Product	Time Point	Date	Actual Time	Comments
X	X	X	XXXXXXXXX	DDMMMYYYY	HH:MM:SS	
			XXXXXXXXX	DDMMMYYYY	HH:MM:SS	
			XXXXXXXXX	DDMMMYYYY	HH:MM:SS	

Note: Product X: < >

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.5.5.2 Urine Collection (Safety Population)

Subject Number	Study Period	Product	Time Point	Start /Stop Date / Time	Void/Container Storage Date / Time	Tare Weight (g)	Total Weight (g)	Urine Weight (g)	Comment
X	X	X	XXXXXXXXX	DDMMMYYYY/HH:MM:SS	DDMMMYYYY/HH:MM:SS	XXXX	XXXX	XXXX	
				DDMMMYYYY/HH:MM:SS	DDMMMYYYY/HH:MM:SS	XXXX	XXXX	XXXX	

Note: Product X: < >

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.5.6 Meal Times (Safety Population)

Subject Number	Study Period	Product	Time Point	Category of Meal	Received and Consumed the Meal	Start Date	Start Time	Comments
X	X	X	XXXXXX	XXXXXXX	XXXX	DDMMMYYYY	HH:MM:SS	

Note: Product X: < >

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Appendix 16.2.5.7 Prior and Concomitant Medications (Safety Population)

Subject Number	Any Medications?	Product	Medication (WHO DD*)	Dosage	Route	Start Date	Start Time	Stop Date	Stop Time	Frequency	Indication	Continuing?	^Prior to Use
X	NO		None										
X	NO		None										
X	YES		XXXXXXXX	X MG	XXXXX	DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	XXXXXXX	XXXXXXXX	XXX	YES
		X	XXXXXXXX	X MG	XXXXX	DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	XXXXXXX	XXXXXXXX	XXX	NO

Note: * Concomitant medications are coded with WHO Drug Dictionary Version 01Sep2019-b3.
WHO DD = World Health Organization Drug Dictionary
^ is derived based on the first study product use.
Product X: < >

Program: /CAXXXXX/sas_prg/stsas/lis/programname.sas DDMMMYYYY HH:MM

Programmer Note: Other dose unit, route, frequency may presented if applicable.

Appendices for blood biomarkers will have the following format:

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Appendix 16.2.6.2.1 Blood COHb Saturation (Outcomes Population)

Subject Number	Sequence	Study Day	Blood COHb % Saturation	Day 9 – Day 1 Change	Day 9 – Day 1 % Change	Day 14 – Day -1 Change	Day 14 – Day -1 % Change	Day 14 – Day 9 Change	Day 14 – Day 9 % Change
XXXXX	X	-1	XXX	XXX	XXX	XXX	XXX	XXX	XXX
		9	XXX	XXX	XXX	XXX	XXX	XXX	XXX
		14	XXX	XXX	XXX	XXX	XXX	XXX	XXX

Note: Arm I: myblu™
Arm J: Combustible Cigarette
Arm K: Dual Use

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

Programming Notes: Day 14 - Day -1 is only presented for Arm I

Appendices for urine biomarkers except nicotine and metabs will have the following format:

Appendix 16.2.6.2.2 Urine NNAL (Outcomes Population)

Subject Number	Study Arm	Study Day	NNAL (xg/mL)	NNAL (xg/24 hours)	NNAL xg/g cr	Day 9 – Day 1 Change	Day 9 – Day 1 % Change	Day 14 – Day -1 Change	Day 14 – Day -1 % Change	Day 14 – Day 9 Change	Day 14 – Day 9 % Change
XXXXX	X	-1	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
		9	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX
		14	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX

Note: cr = creatinine
Arm I: myblu™
Arm J: Combustible Cigarette
Arm K: Dual Use

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

Programming Notes: Day 14 - Day -1 is only presented for Arm I

Appendix 16.2.6.2.15.1 Urine Nicotine and Metabolites (Outcomes Population)

Subject Number	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	-1	XXX	XXX	XXX	XXX	XXX	XXX
	9	XXX	XXX	XXX	XXX	XXX	XXX
	14	XXX	XXX	XXX	XXX	XXX	XXX

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

Appendix 16.2.6.3.1 PES Questionnaire (Outcomes Population)

1. Was it satisfying?
2. Did it taste good?
3. Did you enjoy the sensations in your mouth?
4. Did it calm you down?
5. Did it make you feel more awake?
6. Did it make you feel less irritable?
7. Did it help you concentrate?
8. Did it reduce your hunger for food?
9. Did it make you dizzy?
10. Did it make you nauseous?
11. Did it immediately relieve your craving for a cigarette?
12. Did you enjoy it?
13. Did it relieve withdrawal symptoms?
14. Did it relieve the urge to smoke?
15. Was it enough nicotine?
16. Was it too much nicotine?
17. Was it easy to use?
18. Were there bothersome side effects?
19. Were you comfortable using the product in public?
20. Did you still have a craving for a cigarette after using the product?
21. Are you concerned that you would become dependent on this product?

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

Appendix 16.2.6.3.2 PES Questionnaire Responses (Outcomes Population)

Subject Number	Product	Study Day	Session	Question 1	2	3	4	5	6	7	8	9	10	…….	21
XXXXXX	X	X	Controlled	X	X	X	X	X	X	X	X	X	X	X	X
			Ad libitum	X	X	X	X	X	X	X	X	X	X	X	X

Note: Product X: < >
Scale: 1 = not at all, 2 = very little, 3 = a little, 4 = moderately, 5 = a lot, 6 = quite a lot, 7 = extremely
Refer to Appendix 16.2.6.3.1 for the description of questions.

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

Appendix 16.2.6.3.3 PES Questionnaire Subscales (Outcomes Population)

Subject Number	Product	Study Day	Session	Subscale: Satisfaction	Subscale: Psychological Reward	Subscale: Aversion	Subscale: Relief
XXXXXX	X	XXXX	Controlled	X	X	X	X
XXXXXX	X	XXXX	Ad libitum	X	X	X	X

Note: Product X: < >
"Satisfaction" (Average of items 1, 2, 3, and 12);
"Psychological Reward" (Average of items 4 through 8);
"Aversion" (Average of 9, 10, 16, and 18);
"Relief" (Average of items 11, 13, 14, 15, and reversed for item 20)

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

Appendix 16.2.6.4 Product Liking Questionnaire Responses (Outcomes Population)

Subject Number	Product	Study Day	Session	How much do you like the test e-cigarette you are using? (VAS Score)
XXXXXX	X	X	Controlled	XX
			Ad libitum	XX

Note: Product X: < >

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

Appendix 16.2.6.5 Future Intent to Use Questionnaire Responses (Outcomes Population)

Subject Number	Product	Study Day	Session	VAS Scores: Question 1	Question 2	Question 3
XXXXXX	X	X	Controlled	XX	XX	XX
			Ad libitum	XX	XX	XX

Note: Question 1: How likely are you to continue to smoke after you complete this study?
Question 2: If available, how likely are you to buy your assigned study product in the future?
Question 3: How likely are you to buy an e-cigarette other than your assigned product in the future?
Product X: < >

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

Appendix 16.2.6.6.1 PSCDI, PSECDI Questionnaire (Outcomes Population)

1. How many cigarettes [times] per day do you usually smoke [use your electronic cigarette]? ([assume that one "time" consists of around 15 puffs or lasts around 10 minutes]) (Scoring: 0–4 times/day = 0, 5–9 = 1, 10–14 = 2, 15–19 = 3, 20–29 = 4, 30+ = 5)
2. On days that you can smoke [use your electronic cigarette] freely, how soon after you wake up do you smoke your first cigarette of the day [first use your electronic cigarette]? (Scoring: 0–5 mins = 5, 6–15 = 4, 16–30 = 3, 31–60 = 2, 61–120 = 1, 121+ = 0)
3. Do you sometimes awaken at night to have a cigarette [use your electronic cigarette]? (Scoring: Yes = 1, No = 0)
4. If yes, how many nights per week do you typically awaken to smoke [use your electronic cigarette]? (Scoring: 0–1 nights = 0, 2–3 nights = 1, 4+ nights = 2)
5. Do you smoke [use an electronic cigarette] now because it is really hard to quit? (Scoring: Yes = 1, No = 0)
6. Do you ever have strong cravings to smoke [use an electronic cigarette]? (Scoring: Yes = 1, No = 0)
7. Over the past week, how strong have the urges to smoke [use an electronic cigarette] been? (Scoring: None/Slight = 0, Moderate/Strong= 1, Very Strong/Extremely Strong = 2)
8. Is it hard to keep from smoking [using an electronic cigarette] in places where you are not supposed to? (Scoring: Yes = 1, No = 0)

When you haven't used tobacco [an electronic cigarette] for a while or when you tried to stop smoking [using]…

9. Did you feel more irritable because you couldn't smoke [use an electronic cigarette]? (Scoring: Yes = 1, No = 0)
10. Did you feel nervous, restless, or anxious because you couldn't smoke [use an electronic cigarette]? (Scoring: Yes = 1, No = 0)
11. Total scoring: 0 - 3 = not dependent, 4 - 8 = low dependence, 9 - 12 = medium dependence, 13+ = high dependence.

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

Appendix 16.2.6.6.2 PSCDI, PSECDI Questionnaire Responses (Outcomes Population)

Subject Number	Study Arm	Study Day	Question 1	2	3	4	5	6	7	8	9	10	Total Score
XXXXXX	X	X	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
		X	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX

Note: Arm I: myblu™
Arm J: Combustible Cigarette
Arm K: Dual Use

Refer to Appendix 16.2.6.6.1 for the description of questions.

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

Appendix 16.2.6.7.1 MTWS-R Questionnaire (Outcomes Population)

Please rate yourself for the period of the last 24 hours.

1. Angry, irritable, frustrated
2. Anxious, nervous
3. Depressed mood, sad
4. Difficulty concentrating
5. Increased appetite, hungry, weight gain
6. Insomnia, sleep problems, awakening at night
7. Restless
8. Desire or craving to smoke

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

Appendix 16.2.6.7.2 MTWS-R Questionnaire Responses (Outcomes Population)

Subject Number	Study Arm	Study Day	Question 1	2	3	4	5	6	7	8	Total Score
XXXXXX	X	X	X	X	X	X	X	X	X	X	XX
		X	X	X	X	X	X	X	X	X	XX

Note: Arm I: myblu™
Arm J: Combustible Cigarette
Arm K: Dual Use

Scale: 0 = none, 1 = slight, 2 = mild, 3 = moderate, 4 = severe
Refer to Appendix 16.2.6.7.1 for the description of questions.

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

Appendix 16.2.6.8.1 QSU-brief Questionnaire (Outcomes Population)

1. < >
2. < >
3. < >
4. < >
5. < >
6. < >
7. < >
8. < >
9. < >
10. < >

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

Appendix 16.2.6.8.2 QSU-Brief Questionnaire Responses (Outcomes Population)

Subject Number	Study Arm	Study Day	Question 1	2	3	4	5	6	7	8	9	10	Factor Score 1	2
XXXXXX	X	X	X	X	X	X	X	X	X	X	X	X	X	X
XXXXXX	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Note: Arm I: myblu™
Arm J: Combustible Cigarette
Arm K: Dual Use

Scale: 1 = Strongly disagree, 7 = Strongly agree
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.
Refer to Appendix 16.2.6.8.1 for the description of questions.

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

Appendix 16.2.6.9 Individual Puff Topography Parameters (Outcomes Population)

Subject Number	Study Day	Product	Date	Time	Did Subject Smoke?	Cigarette Number/ ENDS Number	Puff Number	Puff Duration (sec)	Puff Volume (mL)	Peak Flow (mL/sec)	Average Flow (mL/sec)	Inter-Puff Interval (sec)
1	-1	N/A	XXXXXXXXX	X:XX:XX	Yes	X	X	X.XX	XX	XX	XX	XX

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Appendix 16.2.7.1.1 Adverse Events (I of II) (Safety Population)

Subject Number	Study Period	Study Product	UE?^	Adverse Event*	Preferred Term	Onset Date	Onset Time	Resolved Date	Resolved Time	Duration (DD:HH:MM)
1	X	X	Yes	XXXXXXXXXXXX	XXXXXXXXX XXXXXXX	DDMMMYYYY	X:XX	DDMMMYYYY	X:XX	XX:XX:XX

Note: & = Abbreviation for study product use-emergent (UE),
* = Adverse events are classified according to the MedDRA Version XX.X.
Product X: < >

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

Appendix 16.2.7.1.2 Adverse Events (II of II) (Safety Population)

Subject Number	Study Period	Study Product	Adverse Event	Onset Date	Onset Time	Freq	Severity	Ser*	Outcome	Relationship to Study Product	Action	Unexpected Adverse Event	Comment
1	XXX	X	XXXXXXXXXXXXXXXXX	DDMMMYYYY	X:XX	Inter.	Mild	XXX	Resolved	XXXXXXXX	None	XXX	

Note: Ser* represents Serious event.
Freq represents Frequency: SI = Single Episode, Inter. = Intermittent, Cont. = Continuous
Product X: < >

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

Appendix 16.2.7.2 Adverse Event Non- Medication Therapy (Safety Population)

Subject Number	Study Period	Study Product	Adverse Event	Onset Date	Onset Time	Procedure Indication Given?	Procedure Start Date	Procedure Start Time	Procedure End Date	Procedure End Time	Procedure	Procedure Dosing Frequency
1	XXX	X	XXXXXXXXX	DDMMMYYYY	X:XX	XXXX Yes	DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	XXXXXXXXXXX	

Note: Product X: < >

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

Appendix 16.2.7.3 Adverse Event Preferred Term Classification (Safety Population)

Subject Number	Study Period	Study Product	Adverse Event	Preferred Term	Body System	Onset Date	Onset Time
1	X	X	XXXXXXX XXXXX XXXX XXXXXX	XXXXXXXXXX XXXXXXX	XXXXXXXXXXXXXXXXXXXX	DDMMMYYYY	X:XX

Note: * = Adverse events are classified according to the MedDRA Version XX.X.
Product X: < >

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

Appendices 16.2.8.1.2 to 16.2.8.1.4 will have the following format.

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Appendix 16.2.8.1.1 Clinical Laboratory Report - Serum Chemistry (Safety Population)

Subject Number	Age/ Sex	Study Period	Day	Date	Parameter1 < Range> (Unit)	Parameter2 < Range> (Unit)	Parameter3 < Range> (Unit)	Parameter4 < Range> (Unit)	Parameter5 < Range> (Unit)	Parameter6 < Range> (Unit)
X	XX	Screening	.	DDMMMYYYY	XX HN	XX	XX	XX	XX HN	XX
		XXXXXX	-X	DDMMMYYYY	XX HN	XX	XX	XX	XX HN	XX
		XXXXXX	X	DDMMMYYYY	XX HN	XX	XX	XX	XX HN	XX

Note: H = Above Reference Range, L = Below Reference Range
PI flag: Y = Clinically significant, N = not clinically significant

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

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

Appendix 16.2.8.1.5 Clinical Laboratory Report - Comments (Safety Population)

Subject Number	Age/ Sex	Study Period	Day	Date	Department	Test	Result	Unit	Comment
X	XX	Screening	.	DDMMMYYYY	XXXXXX	XXXXXXXXXXXXX	XX	XXXXXX	XXXXXXXXXXXXX

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

Appendix 16.2.8.1.6 Alcohol Breath Testing (Safety Population)

Subject Number	Study Period	Alcohol Breath Testing			
		Time Point	Date	Time	Result
X	XX	XXX	DDMMMYYYY	HH:MM	XXXX

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

Appendix 16.2.8.2 Vital Signs (Safety Population)

Subject Number	Study Visit	Product	Time Point	Date	Time	Blood Pressure (mmHg) Test	Systolic/Diastolic	Pulse (bpm)	Respiration (rpm)	Temperature (°C)	Weight (kg)	Comment
X	Screening		XXXXXXXXXX	DDMMMYYYY	X:XX	SIT5	XXX/ XX	XX	XX	XX.X	XXX.X	
	X	X	XXXXXXXXXX	DDMMMYYYY	XX:XX	SIT5	XXX/ XX	XX	XX	XX.X		

Note: Product X: < >

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

Appendix 16.2.8.3 12-Lead Electrocardiogram (Safety Population)

Subject Number	Study Period	Time Point	Date	Time	Overall Interpretation	Heart Rate (bpm)	PR (msec)	QRS (msec)	QT (msec)	QTcF* (msec)	Specify
1	Screen		DDMONYYYY	X:XX:XX	ANCS	XX	XXX	XX	XXX	XXX	EARLY REPOLARIZATION; LEFT AXIS DEVIATION
	XXXXX	XXXXXXXX	DDMONYYYY	XX:XX:XX	ANCS	XX	XXX	XX	XXX	XXX	LEFT AXIS DEVIATION
	XXXXX	XXXXXXXX	DDMONYYYY	XX:XX:XX	< >	XX	XXX	XX	XXX	XXX	

Note: ANCS = Abnormal, Not Clinically Significant
QTcF* = QT corrected for heart rate using Fridericia's correction.
= QTc > 450, @ = QTc change from baseline greater than 30 msec

Program: /CAXXXXX/sas_prg/stsas/standardlis/cdash_lis_ecg.sas 27NOV2015 18:35

Appendix 16.2.8.4 Carbon Monoxide Breath Test (Safety Population)

Subject Number	Study Period	Date	Time	Result (ppm)	Comment
X	Screen	DDMMMYYYY	HH:MM	XXX	

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

Appendix 16.2.8.5 Administration of Albuterol (Safety Population)

Subject Number	Study Period	Time Point		Date	Time
X	XXXXX	XXXXXXXX	Time of 1st Albuterol puff administered:	DDMMMYYYY	HH:MM
			Time of 2nd Albuterol puff administered:	DDMMMYYYY	HH:MM
			Time of 3rd Albuterol puff administered:	DDMMMYYYY	HH:MM
			Time of last Albuterol puff administered:	DDMMMYYYY	HH:MM
	XXXXX	XXXXXXXX	Time of 1st Albuterol puff administered:	DDMMMYYYY	HH:MM
			Time of 2nd Albuterol puff administered:	DDMMMYYYY	HH:MM
			Time of 3rd Albuterol puff administered:	DDMMMYYYY	HH:MM
			Time of last Albuterol puff administered:	DDMMMYYYY	HH:MM

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

Appendix 16.2.8.6 Spirometry (Safety Population)

Subject Number	Study Period	Time Point	Event*	Date	Time	FVC (L)	FVC %Predicted	FEV1 (L)	FEV1 %predicted	FVC:FEV1 Ratio	FVC:FEV1 Ratio %Predicted	FEF 25-75%	FEF 25-75% %Predicted	FEV1 Change	FVC Change
X	Screen	XXX	Pre	DDMMMYYYY	HH:MM	XX	XX	XX	XX	XX	XX	XX	XX		
			Post	DDMMMYYYY	HH:MM	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
	XXXX	XXX	Pre	DDMMMYYYY	HH:MM	XX	XX	XX	XX	XX	XX	XX	XX		
			Post	DDMMMYYYY	HH:MM	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX

Note: * pre = pre-bronchodilator, post = post-bronchodilator

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

Appendix 16.2.8.6 Tobacco Cessation Information (Safety Population)

Subject Number	Study Period	Date	Time	Question 1	Question 2	Comment
X	XXXXXX	DDMMMYYYY	HH:MM	XXX	XXX	
X	XXXXXX	DDMMMYYYY	HH:MM	XXX	XXX	

Note: Question 1 = Has the subject been advised that in order to reduce the health effects of smoking and using smokeless tobacco products, the best thing to do is to quit?
Question 2 = Has the subject been provided the Quit Assist card and referred to the Quit Assist website?

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