An Open-Label, Parallel Study to Assess Tobacco-Related Biomarkers of Exposure, Biomarkers of Potential Harm, and Nicotine Uptake During a 56-Day Switch to myblu™ e-Cigarettes in Adult Smokers

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Study SAP – 05 March 2020

Statistical Analysis Plan

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Protocol No: CA22747
Final Protocol Date: 28 January 2019
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Product Names: *my*blu™ system with Tobacco Chill flavor Intense Liquidpod, 2.5% nicotine, *my*blu™ system with Tobacco Chill flavor Intense Liquidpod, 4.0% nicotine, *my*blu™ system with Honeymoon flavor Intense Liquidpod, 2.5% nicotine, *my*blu™ system with Honeymoon flavor Intense Liquidpod, 4.0% nicotine

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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 the 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 assess the change-from-baseline differences in the primary tobacco-related biomarkers of exposure (BoE) following a 28-day use period of *my*blu™ electronic cigarettes (e-cigarettes) relative to smoking usual brand combustible cigarettes (UBCC).

Secondary:

1. To assess the change-from-baseline differences in the primary tobacco-related BoE following a 56-day use period of *my*blu™ e-cigarettes relative to smoking usual brand combustible cigarettes.
2. To assess the change-from-baseline differences in the secondary tobacco-related BoE following 28-day and 56-day use periods of *my*blu™ e-cigarettes relative to smoking usual brand combustible cigarettes.
3. To characterize the change in the primary and secondary BoE and biomarkers of potential harm (BoPH) during a 56-day period of use of *my*blu™ e-cigarettes.
4. To assess the change-from-baseline differences in the primary and secondary tobacco-related BoE between Day 28 and Day 56 in subjects using *my*blu™ e-cigarettes.
5. To assess change-from-baseline differences in the (BoPH following 28-day and 56-day use periods of *my*blu™ e-cigarettes relative to smoking usual brand combustible cigarettes.
6. To assess change-from-baseline differences in physiologic endpoints following 28-day and 56-day use periods of *my*blu™ e-cigarettes relative to smoking usual brand combustible cigarettes.
7. To assess elements of abuse liability, subjective effects, and perceptions associated with use of *my*blu™ e-cigarettes.
8. To characterize use of four *my*blu™ e-liquids (Tobacco Chill and Honeymoon flavor Intense e-liquids, 2.5% and 4.0% nicotine) during a 56-day use period.

9. To characterize nicotine uptake from the *my*blu™ e-cigarettes relative to an e-cigarette comparator (JUUL® Virginia Tobacco 5% nicotine) and usual brand combustible cigarettes.
10. To confirm the safety of *my*blu™ e-cigarettes during a 56-day use period.

2.2 Endpoints

Hypothesis:

Switching from usual brand combustible cigarettes to a *my*blu™ e-cigarette will result in a significant decrease from baseline in the primary tobacco-related BoE following 28 days of use relative to the change associated with continuing to smoke combustible cigarettes. The hypothesis will be tested independently for each *my*blu™ e-liquid Product.

Primary Study Endpoints:

1. Biomarkers of Exposure

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

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

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. Physiological assessments
- Fractional concentration of exhaled nitric oxide (FeNO)
- Blood pressure
- Heart rate

4. Subjective measures
- Penn State [Electronic] Cigarette Dependence Index (PSCDI, PSECDI)
- Cough Questionnaire
- Questionnaire of Smoking Urges-Brief (QSU-Brief)
- Minnesota Tobacco Withdrawal Scale-Revised (MTWS-R)
- Product Evaluation Scale (PES)
- Product Liking Questionnaire
- Future Intent to Use Questionnaire
- Product and Health Effect Perceptions Questionnaire

5. Product Use

Daily in-clinic product use documented by the clinic staff:
- Number of cigarettes smoked
- Number of *my*blu™ and JUUL® pods started
- *my*blu™ pod weight change (for pods used during the 24 hour urine collections)
- Day 3 and Day 29 product preference selection

Daily product use endpoints documented by subjects (Day 3 through study discharge on Day 57):
- Number of cigarettes smoked

- Number of *my*blu™ pods started
- Number of puffs from the *my*blu™ product daily (< or ≥ 50 puffs)

6. Nicotine Pharmacokinetics Assessment

Product use during each product use session:
- Number of puffs taken
- *my*blu™ and JUUL® pod weight change

Pharmacokinetic (PK) parameters during each product use session:
- C_{max}
- AUC_{0-t}
- T_{max}

7. Urge to Smoke Parameters (during the *ad libitum* product use session)
- Maximum reduction from baseline score (E_{max_R})
- Time of the E_{max_R} (TE_{max})
- Area under the change from baseline "Urge to Smoke" visual analog scale (VAS) score versus time curve ($AUEC_{\_BL}$)

8. Other Compliance Assessments

Exhaled CO and urine cotinine measurements will be used to confirm smoking/nicotine use status prior to Day 1 and to assess subject compliance with product assignment requirements thereafter.

9. Safety Assessments

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

3. STUDY DESIGN

This will be an open-label, partially-randomized, parallel-arm, multi-site study in healthy adult smokers, consisting of two parts – the main study and a PK sub-study.

The main study will assess BoE, BoPH, physiologic effects, and subjective effects with use of *my*blu™ e-cigarettes relative to continuing to smoke combustible cigarettes. To account for potential attrition, up to 160 subjects are planned to be randomized into the *my*blu™ arm (with up to 40 subjects intended to be assigned to each *my*blu™ e-liquid) and up to 40 subjects will be randomized into the continue-smoking arm.

Baseline study assessments will be made during use of subjects' usual brand combustible cigarettes during the initial test visit through the morning of Day 1. All subjects in the *my*blu™ and continue-smoking arms will return to the clinic site for test visits scheduled to occur on Days 14, 28, 42, and 56 for post-baseline study assessments, compliance checks, and product dispensing and return. The subset of

subjects participating in the PK sub-study (described below) will also complete selected biomarker assessments (NNAL, NNN, 3-HPMA, CEMA, HMPMA, S-PMA, nicotine equivalents) on Days 3 and 4.

Subjects randomized to the *my*blu™ arm will participate in an in-clinic product acclimation period from Days 1 to 3. The acclimation period will afford the subjects the opportunity to try each of the four *my*blu™ e-liquids in order to become accustomed to their use and to determine those that they would be willing to use during the study. Initial product assignment for each subject will be based on preference as a method to enhance compliance. To further improve compliance through Day 56, at the end of Test Visit 3, subjects using a *my*blu™ product may be allowed to choose to switch to the alternate nicotine strength of their current flavor, to switch to the alternate flavor with the same nicotine strength as their initial choice, or to continue using the same e-liquid selected initially. This method for initial flavor assignment and the opportunity to re-select after 28 days of use is based on natural experimentation that consumers experience when choosing an e-cigarette flavor.

The PK sub-study will assess nicotine uptake and urge to smoke from the *my*blu™ products relative to combustible cigarettes and an e-cigarette comparator (JUUL®). A subset of up to 20 subjects assigned to each of the *my*blu™ e-liquids, 20 subjects from the continue-smoking arm, and all 20 subjects in the JUUL® arm will participate. Subjects in the JUUL® arm will begin using the product after check-in (Day -2) for Test Visit 1 and will continue to use the product through discharge on Day 1 from the study following the PK assessment (subjects in the JUUL® arm will only participate in the PK sub-study). PK assessments will be preceded by a minimum 10-hour abstention from product use and will take place on Day 1 for the JUUL® and continue-smoking arms, and on Day 5 for the *my*blu™ arm. Product use for the PK assessments will consist of two sessions: 1) a fixed/controlled puffing session in the morning consisting of 10 puffs taken at 30 second intervals, with puffs 3 seconds in duration, and 2) an *ad libitum* use session beginning 6 hours after the start of the morning session and consisting of unlimited use of the e-cigarette product for 5 minutes or one cigarette, with no limits on puff duration or inter-puff interval. No product use of any kind will be allowed between the sessions. E-cigarette pods used for each session will be weighed before and after use to measure the amount of e-liquid used.

All product use during confinement will be documented by the clinic staff. Subjects in the *my*blu™ and continue-smoking arms will be required to self-report product use from Day 3 through discharge from the study.

Exhaled CO and urine cotinine measurements will be used to confirm smoking/nicotine use status prior to Day 1 and to assess subject compliance with product assignment requirements thereafter.

The clinic staff will contact all subjects via a telephone call approximately 14 days after discharge from the study (either as scheduled or after early termination) for reporting of AEs and use of concomitant medications.

Screening of subjects will occur within 28 days prior to prior to check-in (Day -2) for Test Visit 1. Screening safety evaluations will include a physical examination, vital signs, ECG, clinical laboratory tests (clinical chemistry, hematology, urinalysis, and serology), lung function, urine drug tests, urine cotinine tests, and alcohol breath tests, FSH tests (post-menopausal females) and serum and urine pregnancy tests (females only).

On-study safety evaluations will include a symptom-driven physical examinations, vital signs, ECG, clinical laboratory tests (clinical chemistry, hematology, and urinalysis), lung function, and urine pregnancy tests (females only).

AEs spontaneously reported by the subjects or observed by the Investigator or other study personnel will be documented and monitored from the time of first product use after successful completion of the check-in (Day -2) events for Test Visit 1 through the end of the Follow-up Period. Any prior and concomitant medications taken from 30 days prior to Screening through the Follow-up Period will also be recorded.

Product Use

Baseline and Product Use Period 1 (Days -2 to 29, Test Visits 1-3):
Subjects who meet study requirements following screening will be scheduled to check in to the clinic for Test Visit 1 on Day -2 (check-in for JUUL® arm will be as early in the day as possible to maximize the time to use the product) and will remain in the clinic until completion of all study events. Subjects who fail the check-in requirements will be considered a "screen failure" and will be excluded from participation. For the *my*blu™ and continue-smoking arms, the Baseline Period will consist of the time between check-in and first product use on Day 1.

Following discharge from Test Visit 1 (Day 5), subjects in the *my*blu™ and continue-smoking arms will follow the product use requirements of their randomization arm and will report product use daily. All subjects in the *my*blu™ and continue-smoking arms will be required to present to the clinic site on Day 14 and Day 28 (each ± 2 days) for Test Visits 2 and 3, respectively. Test Visit 2 will be ambulatory and primarily for the return and dispensing of test products for the *my*blu™ arm and for compliance and safety checks for both study arms. Test Visit 3 (Days 28 and 29) will be for these purposes in addition to completion of the endpoint assessments during confinement.

Product Use Period 2 (Days 30 to 57, Test Visits 4 and 5):
Following discharge from Test Visit 3, subjects in the *my*blu™ and continue-smoking arms will follow the product use requirements of their randomization arm and will report product use daily. All subjects in both arms will be required to present to the

clinic site on Day 42 and Day 56 (each ± 2 days) for Test Visits 4 and 5, respectively. Test Visit 4 will be ambulatory and primarily for the return and dispensing of test products for the *my*blu™ arm and for compliance and safety checks for both study arms. Test Visit 5 will be for these purposes in addition to completion of the endpoint assessments during confinement. Subjects will be discharged from the clinical portion of the study at the end of Test Visit 5.

4. ANALYSIS POPULATIONS

4.1 Analysis Populations

4.1.1 Safety Population

The safety population will include all subjects with at least one reported product use from Day -1.

4.1.2 Intent-to-Treat (ITT) Population

The ITT population will consist of randomized subjects in the main study with at least one documented product-use experience from Day 1, irrespective of their compliance of the product-use to which they were randomized.

4.1.3 Per-Protocol Population

The PP population (main study) is a subset of the ITT population who meet the requirements below. Separate populations for Product Use Period 1 (PP28/29) and Product Use Period 2 (**PP56/57**) will be established based on data collected during each of those periods.

The PP population will be used (in addition to the ITT population) only in the analysis of primary biomarkers of exposure (COHb in plasma and NNAL, 3-HPMA, and S-PMA in urine) and in the product use analysis.

***my*blu™ and continue-smoking arms**

- Have no protocol deviations significantly impacting the integrity of the analysis or interpretation of the individual endpoint under consideration (e.g., compromised urine samples, use of prohibited medications impacting the endpoint)
- Have a daily product use response rate of at least 70% during the product use period
- Have a positive urine cotinine test at each scheduled assessment.

***my*blu™ arm**

- Self-report reducing cigarette consumption by at least 90% of that reported at baseline

- Have exhaled CO values ≤ 8 ppm at each scheduled post-baseline assessment
- Have post-baseline urine NNAL values reduced by ≥ 75% from baseline.

4.1.4 Pharmacokinetic Population (for the PK Sub-Study Evaluations)

The PK population for each product use session will include subjects who used a product and have evaluable PK profiles. This population will include approximately half (up to 20 out of 40) of the subjects from each of the four *my*blu™ arms and from the Cigarette arm, plus all subjects (20) from the JUUL® arm. The sub-study will therefore include approximately 120 subjects, of which 100 subjects would also participate in the main study and 20 subjects (the JUUL® arm) exclusively in the sub-study.

4.2 Preliminary Data and Interim Analysis

Preliminary analyses may be performed, as judged applicable.

5. PRODUCT DESCRIPTIONS

All subjects will be required to provide a sufficient supply of their usual brand combustible cigarettes to the study site for use on Day 1.

Each subject's usual brand information, including Universal Product Code (UPC) number, will be documented.

The following investigational products will be used during the study:

- *my*blu™ system with Tobacco Chill flavor Intense Liquidpod, 2.5% nicotine
- *my*blu™ system with Tobacco Chill flavor Intense Liquidpod, 4.0% nicotine
- *my*blu™ system with Honeymoon flavor Intense Liquidpod, 2.5% nicotine
- *my*blu™ system with Honeymoon flavor Intense Liquidpod, 4.0% nicotine

Each blu e-liquid contains a mixture of glycerin, propylene glycol, nicotine, and a proprietary blend of flavors.

The following comparator products will be used during the study:

- Subject's usual brand combustible cigarette
- JUUL® system with Virginia Tobacco Flavor JUULpod, 5.0% nicotine

In the CSR text and table headings, product use will be referred to by the short descriptions; the 6 products referred to as Products A-F and table footers by the long description in the following table:

Table 5.1. Product Description

Arm	Products	Short Description	Format	Long Description
A	A	*my*blu™ Tobacco Chill 2.5%	e-cigarette	*my*blu™ closed system with CF Cosmic Fog Tobacco Chill flavor, nicotine salt liquid 2.5 %
	B	*my*blu™ Tobacco Chill 4.0%	e-cigarette	*my*blu™ closed system with CF Cosmic Fog Tobacco Chill flavor, nicotine salt liquid 4.0%
	C	*my*blu™ Honeymoon 2.5%	e-cigarette	*my*blu™ closed system with CF Cosmic Fog Honeymoon flavor, nicotine salt liquid 2.5 %
	D	*my*blu™ Honeymoon 4.0%	e-cigarette	*my*blu™ closed system with CF Cosmic Fog Honeymoon flavor, nicotine salt liquid 4.0%
B	E	Cigarette	combustible cigarette	Subject's usual brand combustible cigarette
C	F	JUUL®	e-cigarette	JUUL® system with Virginia Tobacco Flavor JUULpod, 5.0% nicotine

6. ANALYSIS OF STUDY ENDPOINTS

6.1 Product Use and Compliance

6.1.1 Product Use and Compliance Assessments

***my*blu™ Product Use**

Following product training on Day 1, subjects will use each of the four test products individually for approximately 2 hours each, with the order of use selected by the subject. Following the last 2-hour period, subjects may choose any of the e-liquids freely through 23:00 on Day 2. At 20:00 on Day 2, subjects will complete the *my*blu™ Product Preference Questionnaire. Initial product assignment for each subject will be made by the study statistician or designee. Beginning on the morning of Day 3, subjects will use the assigned e-liquid through Day 28 and will be given the opportunity at Visit 3 to switch to the alternate nicotine strength of their current flavor, to switch to the alternate flavor with the same nicotine strength as their initial choice, or to continue using the same e-liquid selected initially through Day 57 (Visit 5, last study day). Each day from Day 3 through discharge from the study on Day 57, subjects randomized to the *my*blu™ arm will self report their product use via a text message system (Medquest).

Subjects participating in the PK sub-study will continue to use the assigned product through the evening of Day 4. All pods used during the 24-hour urine collections will be weighed within 24 hours before and after use, with the weights documented. On Test Visit 3 (Day 28) and Test Visit 5 (Day 56) as well, all pods used during the 24-hour urine collections will be weighed within 24 hours before and after use, with the weights documented.

Usual Brand Cigarette Use

Subjects randomized to the continue-smoking arm will smoke their usual brand cigarettes at home and throughout each confinement visit, and will self-report the number of cigarettes smoked each day from Day 3 through discharge from the study via a text message system.

JUUL® Product Use

Subjects in the JUUL® arm will begin using the product following the demonstration and training on Day -2 and will continue to use the product through 23:00 on Day -1.

Product Use Compliance

Subject self-reported product use will be used as a measure of compliance. The clinic staff will monitor the frequency with which subjects complete the daily product use entries leading up to each Test Visits 2 through 5.

Biochemical verification of compliance will also be performed. Exhaled CO and urine cotinine will be used as methods of verifying compliance in real-time.

NNAL is a tobacco-specific nitrosamine with a longer half-life than CO, thus may provide an estimate of compliance over a long period of time by comparison of the post-baseline values to the baseline values. As this will be measured in a bioanalytical assay, real-time monitoring will not be possible and the verification will be completed at the end of the study.

NNAL will be considered as an additional exploratory variable for compliance.

6.1.2 Product Use and Compliance Data Summarization

The following product use variables will be determined:

PK Sub-Study
- Number of puffs taken during each controlled and ad libitum product use session
- *my*blu™ and JUUL® pod weight change (only on Day 5 or Day 1, respectively)

In-clinic
- Number of cigarettes smoked
- Number of *my*blu™ pods started

- *my*blu™ pod weight change (for pods used during the 24 hour urine collections)
- Day 3 and Day 29 product preference selection (a listing)

Self report
- Number of cigarettes smoked (*my*blu™ and cigarette arms)
- Number of *my*blu™ pods started (*my*blu arm)
- > 50 puffs taken from of *my*blu™ product (Y/N) (*my*blu™ arm)

Compliance
- ≥ 90% reduction of cigarette use from baseline (*my*blu™ arm)
- ≥ 70% daily product use reporting (yes/no) – all cohorts
- Measured eCO (≤8 ppm) – all cohorts
- ≥ 75% reduction in post-baseline urine NNAL from baseline (*my*blu™ arm)
- Urine cotinine (yes/no) – all cohorts

All product use data (including the number of puffs and including the PK product use sessions) and compliance variables will be summarized by study product using descriptive statistics (by time point, day, and product use session as appropriate) but no statistical comparisons will be made. The difference in weight before and after use of each e-cigarette (Products A to D and Product F) will be summarized.

For the PK sub-study, the number of puffs and the difference in weight before and after use of each e-cigarette will also be summarized.

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, and

6.2 Biomarkers of Exposure and Potential Harm

6.2.1 Biomarker Sample Collection

Blood Biomarker Sample Collection

Blood samples for COHb in whole blood (2 x 4 mL), sICAM in plasma (1 x 4 mL), WBCs in whole blood (measured in hematology sample), HDL-C in serum (1 x 3.5 mL), MCP-1 in serum (1 x 3.5 mL), and serum for bio-banking (up to 17 mL) will be collected during Test Visit 1 (on Days -2, and -1), Test Visit 3 (Days 28 and 29), and Test Visit 5 (Days 56 and 57). Samples for COHb will be collected in the afternoon

and samples for the other biomarkers and bio-banking will be collected following an overnight ITTt 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, (-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, as applicable, during Test Visit 1 (on Days -2, -1, 3, and 4), Test Visit 3 (Days 28 and 29), and Test Visit 5 (Days 56 and 57). Each 24-hour urine collection will begin at a time following check-in and will end at the same time ± 30 minutes the following day.

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.

6.2.2 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.

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

6.2.3 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, product, and visit or day (and time point as applicable) and summarized by product and visit or day (and time point as necessary). Absolute and percent change-from-baseline values, and absolute and percent differences between Test Visits 3 and 5 (Days 28 and 56, respectively), will also be listed and summarized where indicated.

Descriptive statistics (number of observations, mean, median, standard deviation, standard error of the mean, CV%, minimum, and maximum) will be presented. Figures will be used to display the data graphically as applicable. All data summarizations and figures will be generated using the ITT population. In addition, PP population will also be used for the primary biomarkers only: COHb in plasma and NNAL, 3-HPMA, and S-PMA in urine. Data summarizations and statistical analyses will be performed using SAS procedures. Statistical analyses are described in Section 6.7.

6.3 Physiologic Assessments

6.3.1 Physiologic Assessments and Visits

Test Visit 1, 3, and 5 check-in blood pressure (systolic and diastolic) and heart rate measurements will be assessed for physiologic assessment purposes.

6.3.2 Data Summarization for Physiologic Assessments

Data will be listed by subject, product, and visit or day (and time point as applicable) and summarized by product and visit or day (and time point as necessary). Absolute and percent change-from-baseline values, and absolute and percent differences between Test Visits 3 and 5, will also be listed and summarized, as applicable.

Descriptive statistics (number of observations, mean, median, standard deviation, standard error of the mean, CV%, minimum, and maximum) will be used for continuous data variables and frequency counts (number of observations and percentage) for categorical data variables.

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

6.4 Subjective Measures

6.4.1 Subjective Effects Questionnaire

The PSCDI/PSECDI, Cough Questionnaire, QSU-Brief, MTWS-R, PES, Product Liking Questionnaire, Future Intent to Use Questionnaire, and Product and Health Effect Perceptions Questionnaire will be completed during Test Visit 1 (Day -2), Test Visit 3 (Day 28), and Test Visit 5 (Day 56), as applicable, using an electronic device. The QSU-Brief, MTWS-R, PES, and Product Liking Questionnaire will also be completed on Day 3 (Visit 1).

6.4.2 Subjective Effects Data Summarization

The following total scores, factor scores, and subscales will be calculated and summarized. For questionnaires without total scores, factor scores, or subscales (Cough Questionnaire, Product Liking Questionnaire, Future Intent to Use Questionnaire, and Product and Health Effect Perceptions Questionnaire), each item on the subjective measures questionnaires will be summarized.

- 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 (relief of nicotine withdrawal) - average of items 2, 4, 5, 8, and 9
- PES subscales:

- 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.

Data will be listed by subject, product, and visit or day (and time point as applicable) and summarized by product and visit or day (and time point as necessary). Absolute and percent change-from-baseline values, and absolute and percent differences between Test Visits 3 and 5, will also be listed and summarized, as applicable. Baseline is the last no-missing observation collected prior to Day 1 product use.

Descriptive statistics (number of observations, mean, median, standard deviation, standard error of the mean, CV%, minimum, and maximum) will be used for continuous data variables and frequency counts (number of observations and percentage) for categorical data variables.

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

6.5 Plasma Nicotine Pharmacokinetics

6.5.1 Measurements and Collection Schedule

PK assessments will take place on Day 1 for the JUUL® and continue-smoking arms, and on Day 5 for the *my*blu™ arm. 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 each product use episode (fixed/controlled and *ad libitum*).

6.5.2 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.

6.5.3 Plasma Nicotine Pharmacokinetic Parameters

The appropriate noncompartmental PK parameters will be calculated for each product use episode (controlled and *ad libitum*) 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 on Day 1 for the JUUL® and continue-smoking arms, and on Day 5 for the *my*blu™ arm. 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.

For the calculation of the PK parameters, plasma concentrations that are BLQ will be set to one-half of the LLOQ for the calculation of descriptive statistics of unadjusted plasma nicotine concentrations. Baseline adjustments (pre-product use) 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 Day 1 – 6 and the adjustment will be subject-specific.

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/episode 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.
$Kel = \frac{\ln(2)}{t1/2}$

Where t1/2 is 2.0 hours 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.

6.5.4 PK Data Summarization and Presentation

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

The plasma concentrations of nicotine will be listed and summarized by product, product use episode, and time point for all subjects in the PK 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, product use episode, and time point for all subjects in the PK 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.

6.6 Urge to Smoke

6.6.1 Urge to Smoke Parameters

Urge to smoke will be assessed using a 100 mm VAS approximately 10 minutes prior to 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 *ad libitum* product use session.

The following parameters will be calculated for the urge to smoke assessments performed during the PK assessments.

E_{max_R}	The maximum reduction from baseline VAS score (VASpre-use – VASpost-use).
TE_{max}	Time of the E_{max_R}. If the maximum value occurred at more than one time point, TE_{max} will be defined as the first time point with this value.
$AUEC_{0\text{-}120\_R}$	The area under the reduction from baseline "Urge to Smoke" VAS score (VASpre-use – VASpost-use) versus time curve from 0 to 120 minutes, calculated using the linear trapezoidal method with linear interpolation using actual sample times

6.6.2 Urge to Smoke Data Summarization

Data will be listed by subject, product, and day (and time point as applicable) and summarized by product and visit (and time point as applicable).

Descriptive statistics (number of observations, mean, median, standard deviation, minimum, and maximum) will be used for continuous data variables.

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

6.7 Statistical Analyses

6.7.1 Statistical Analyses of Primary Endpoints

Statistical Analyses of Primary BoE (Day 28 only) (*my*blu™ Products Versus the Continue-smoking Arm)

Comparisons of the Day 28 primary BoE (COHb, NNAL, 3-HPMA, and S-PMA) change-from-baseline values between the continue-smoking arm and each *my*blu™ e-liquid product selected at Day 2 will be made using a linear mixed model ANOVA.

The ITT population will be used as the primary analysis population and an analysis using the PP population will be used as a supportive analysis.

The ANOVA model will include product arm, study day, and product arm by study day interaction as fixed effect and subject as a random effect. Least square means (LSMs) will be provided for each product arm at each study day. LSM differences, 95% confidence intervals of LSM differences, and p-values will be provided for the product arm comparisons at each study day. The comparisons of interest will include each of the *my*blu™ product arms compared to continue-smoking arm. The above statistical analyses will be performed using the following SAS codes.

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

6.7.2 Statistical Analyses of Secondary Endpoints

Statistical Analyses of Primary BoE (Day 56 only), Secondary BoE, BoPH, Physiologic Endpoints, and Subjective Measure Endpoints (*my*blu™ Products Versus the Continue-smoking Arm)

An approach similar to that used for the primary endpoints will be used to make Day 28 and Day 56, as applicable, change-from-baseline comparisons between the *my*blu™ products and the continue-smoking arm for the applicable primary and secondary BoE, BoPH, physiologic endpoints, and subjective measure endpoints as described in the SAP. For the Day 56 analysis, the initial *my*blu™ flavor Product assignments for each subject will be maintained within the statistical model and a separate sensitivity analysis will be performed for subjects that do not switch flavors at Day 29.

The ITT population will be used for these analyses.

Statistical Analyses of Primary BoE (Day 56 only) and Secondary BoE (Within *my*blu™ Products)

Comparisons of the primary and secondary BoE change-from-baseline values at each time point within the *my*blu™ products will also be made using a linear mixed model ANOVA.

Statistical Analyses of Pharmacokinetics (*my*blu™ Products Versus the Continue-smoking arm or JUUL arm)

A linear mixed model ANOVA will be performed on the log-transformed nicotine PK parameters AUC and C_{max} from each product use session (PK population). The model will include product arm as a fixed effect. Geometric LSMs will be provided for the PK parameters of Cmax and AUC by product arm. Geometric LSM ratio, 95% confidence intervals of geometric LSM ratio, and p-values will be provided for the product arm comparisons for Cmax and AUC. The comparisons of interest will include each of the *my*blu™ product arms compared to continue-smoking arm or JUUL arm. The above statistical analyses will be performed using the following SAS codes.

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

Non-parametric analysis (Wilcoxon Rank Sum test) will be performed for the comparisons of T_{max} between test and reference products.

Similar methods will be used to compare the urge to smoke 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 arm and overall.

7.2 Demographics

Descriptive statistics will be calculated for continuous variables (age, weight, height, and body mass index) by randomized product arm and overall.

Frequency counts will be provided for categorical variables (race, ethnicity, and sex, and other characteristics) for each randomized product arm and overall.

7.3 Smoking History

Descriptive statistics will be calculated for continuous variables (cigarettes smoked per day [CPD] and number of years smoked) by randomized product arm and overall.

Frequency counts will be provided for subject's usual brand for each randomized product arm and overall.

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 21.0.

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, 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 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 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 and check-in (Day -2) for all product arms. For *my*blu™ and continue-smoking arms, the clinical laboratory tests will also be performed at the end of Period 1 (Day 29) and the discharge from the study (Day 57, Period 2) or upon early termination.

Descriptive statistics will be reported for numeric clinical data and change from baseline by product arm and time point. 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 and Check-in (Day -2) for all product arms. For *my*blu™ and continue-smoking arms, the urine cotinine test will also be performed on the first day of each Test Visit.

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

For females, serum pregnancy tests will be completed at Screening and urine pregnancy tests will be completed at Check-in for all product arms. For *my*blu™ and continue-smoking arms, the urine pregnancy tests will also be performed on the first day of each Test Visit. Results for these tests will be listed as “Negative” or “Positive.”

7.6 Vital Signs

Vital signs (pulse and blood pressure) will be measured at Screening and Check-in for all product arms. For *my*blu™ and continue-smoking arms, the vital signs will also be performed at Day 5 and at Day 28, 29 (Period 1), and in Period 2 on Day 56 and at

the discharge from the study (Day 57) or upon early termination. For JUUL arm, the vital sign will be performed at Day 1 or upon early termination.

Descriptive statistics will be reported for vital sign measurements by product arm 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 Screening for all product arms. For *my*blu™ and continue-smoking arms, the ECG will also be performed at the discharge from the study (Day 57) or upon early termination. For JUUL arm, the ECG will be performed at Day 1 and upon early termination.

Descriptive statistics will be reported for ECG parameters by product arm 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.

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 01MAR2018 and listed by subject.

7.9 Physical Examination

Full physical examinations will be performed at Screening. For *my*blu™ and continue-smoking arms, symptom driven physical examination will also be performed at Check-in (Day -2), Test Visit 1 discharge (Day 5) and at Day 28, 29 of Period 1, Day 56 of Period 2 and the discharge from the study (Day 57) or upon early termination. For JUUL arm, the symptom driven physical examination will be performed at Check-in (Day -2) and Day 1 or upon early termination.

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 and Check-in (Day -2) for all product arms. For *my*blu™ and continue-smoking arms, exhaled CO will also be performed at Test Visit 1 discharge (Day 5) and at Day 28, 29 of Period 1, Day 56 of Period 2.

Descriptive statistics will be reported for exhaled CO by product arm 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.

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 $(FEF)_{25-75\%}$). For *my*blu™ and continue-smoking arms, spirometry will also be performed at the discharge from the study (Day 57) or upon early termination.

Descriptive statistics will be reported for measured and percent of predicted spirometry parameters by product arm 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.

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 or higher.

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 Summary of Disposition (Safety, ITT, and PP Populations)
Table 14.1.2 Demographic Summary (Safety, ITT, and PP Populations)
Table 14.1.3 Smoking History Summary (Safety, ITT, and PP Populations)

Table 14.1.4 Summary of Disposition (PK Population)
Table 14.1.5 Demographic Summary (PK Population)
Table 14.1.6 Smoking History Summary (PK Population)

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

14.2.1 Product Use Tables

Table 14.2.1.1 Summary of In-Clinic Number of *my*blu™ Pods Started by Product and Day (ITT)

Table 14.2.1.2 Summary of In-Clinic Number of *my*blu™ Pods Started by Product and Day (PP 28/29)

Table 14.2.1.3 Summary of In-Clinic Number of *my*blu™ Pods Started by Product and Day (PP 56/57)

Table 14.2.1.4 Summary of In-Clinic Product Weight Changes by Product and Day (ITT)

Table 14.2.1.5 Summary of In-Clinic Product Weight Changes by Product and Day (PP 28/29)

Table 14.2.1.6 Summary of In-Clinic Product Weights Changes by Product and Day (PP 56/57)

Table 14.2.1.7 Summary of In-Clinic Number of Cigarettes Smoked by Product and Day (ITT)

Table 14.2.1.8 Summary of In-Clinic Number of Cigarettes Smoked Started by Product and Day (PP 28/29)

Table 14.2.1.9 Summary of In-Clinic Number of Cigarettes Smoked by Product and Day (PP 56/57)

Table 14.2.1.10 Summary of Self-Reported Number of *my*blu™ Pods Started by Product and Day (ITT)

Table 14.2.1.11 Summary of Self-Reported Number of *my*blu™ Pods Started by Product and Day (PP 28/29)

Table 14.2.1.12 Summary of Self-Reported Number of *my*blu™ Pods Started by Product and Day (PP 56/57)

Table 14.2.1.13 Frequency of Self-Reported Number of Puffs Taken From *my*blu™ product (>= 50) by Product and Day (ITT)

Table 14.2.1.14 Frequency of Self-Reported Number of Puffs Taken From *my*blu™ product (>= 50) by Product Day (PP 28/29)

Table 14.2.1.15 Frequency of Self-Reported Number of Puffs Taken From *my*blu™ product (>= 50) by Product and Day (PP 56/57)

14.2.2 Biomarker Tables

14.2.2.1 Blood COHb

14.2.2.2 Urine NNAL

Table 14.2.2.2.1.10	Summary of Urine NNAL Adjusted for Urine Creatinine by Study Product and Study Day (PP Population)
Table 14.2.2.2.1.11	Summary of Urine NNAL Adjusted for Urine Creatinine Change From Baseline by Study Product and Study Day (PP Population)
Table 14.2.2.2.1.12	Summary of Urine NNAL Adjusted for Urine Creatinine Percent Change From Baseline by Study Product and Study Day (PP Population)
Table 14.2.2.2.2.1	Statistical Comparison of Urine NNAL 24-hour Amount Excreted Change From Baseline Between *my*blu™ and Continuous Smoking by Study Day (ITT Population)
Table 14.2.2.2.2.2.2	Statistical Comparison of Urine NNAL 24-hour Amount Excreted Change From Baseline Between *my*blu™ and Continuous Smoking by Study Day (PP Day28/29 Population)
Table 14.2.2.2.2.2.3	Statistical Comparison of Urine NNAL 24-hour Amount Excreted Change From Baseline Between *my*blu™ and Continuous Smoking by Study Day (PP Day56/57 Population)
Table 14.2.2.2.2.2.4	Statistical Comparison of Urine NNAL 24-hour Amount Excreted Change From Baseline Between *my*blu™ and Continuous Smoking by Study Day (PP Day56/57 Population – Sensitivity Analysis)

14.2.2.3 Urine 3-HPMA

Tables 14.2.2.3.1.1 through 14.2.2.3.2.2.4 will be generated for Urine 3-HPMA similar to Urine NNAL.

14.2.2.4 Urine S-PMA

Tables 14.2.2.4.1.1 through 14.2.2.4.2.2.4 will be generated for Urine S-PMA similar to Urine NNAL.

14.2.2.5 Urine NNN

Tables 14.2.2.5.1.1 through 14.2.2.5.2.2.2, as applicable (ITT population only), will be generated for Urine NNN similar to Urine NNAL.

14.2.2.6 Urine CEMA

Tables 14.2.2.6.1.1 through 14.2.2.6.2.2.2, as applicable (ITT population only), will be generated for Urine CEMA similar to Urine NNAL.

14.2.2.7 Urine HEMA

Tables 14.2.2.7.1.1 through 14.2.2.7.2.2.2, as applicable (ITT population only), will be generated for Urine HEMA similar to Urine NNAL.

14.2.2.8 Urine HMPMA

Tables 14.2.2.8.1.1 through 14.2.2.8.2.2.2, as applicable (ITT population only), will be generated for Urine HMPMA similar to Urine NNAL.

14.2.2.9 Urine MHBMA

Tables 14.2.2.9.1.1 through 14.2.2.9.2.2.2, as applicable (ITT population only), will be generated for Urine MHBMA similar to Urine NNAL.

14.2.2.10 Urine 1-OHP

Tables 14.2.2.10.1.1 through 14.2.2.10.2.2.2, as applicable (ITT population only), will be generated for Urine 1-OHP similar to Urine NNAL.

14.2.2.11 Urine o-tol

Tables 14.2.2.11.1.1 through 14.2.2.11.2.2.2, as applicable (ITT population only), will be generated for Urine o-tol similar to Urine NNAL.

14.2.2.12 Urine 3-OH B[a]P

Tables 14.2.2.12.1.1 through 14.2.2.12.2.2.2, as applicable (ITT population only), will be generated for Urine 3-OH B[a]P similar to Urine NNAL.

14.2.2.13 Urine 1-AN

Tables 14.2.2.13.1.1 through 14.2.2.13.2.2.2, as applicable (ITT population only), will be generated for Urine 1-AN similar to Urine NNAL.

14.2.2.14 Urine 2-AN

Tables 14.2.2.14.1.1 through 14.2.2.14.2.2.2, as applicable (ITT population only), will be generated for Urine 2-AN similar to Urine NNAL.

14.2.2.15 Urine Nicotine Equivalents

Tables 14.2.2.15.1.1 through 14.2.2.15.2.2.2, as applicable (ITT population only), will be generated for Urine Nicotine Equivalents similar to Urine NNAL.

14.2.2.16 Plasma sICAM

Tables 14.2.2.16.1.1 through 14.2.2.15.2.2.2, as applicable (ITT population only), will be generated for Plasma sICAM similar to Whole Blood COHb.

14.2.2.17 WBCs

Tables 14.2.2.17.1.1 through 14.2.2.17.2.2.2, as applicable (ITT population only), will be generated for Whole Blood WBCs similar to Whole Blood COHb.

14.2.2.18 Serum HDL-C

Tables 14.2.2.18.1.1 through 14.2.2.18.2.2.2, as applicable (ITT population only), will be generated for Serum HDL-C similar to Whole Blood COHb.

14.2.2.19 Serum MCP-1

Tables 14.2.2.19.1.1 through 14.2.2.19.2.2.2, as applicable (ITT population only), will be generated for Serum MCP-1 similar to Whole Blood COHb.

14.2.2.20 Urine Type III isoprostane (8-epi-prostaglandin F2α)

Tables 14.2.2.20.1.1 through 14.2.2.20.2.2.2, as applicable (ITT population only), will be generated for Urine Type III isoprostane (8-epi-prostaglandin F2α) similar to Urine NNAL.

14.2.2.21 Urine 11-dehydrothromboxane B2

Tables 14.2.2.21.1.1 through 14.2.2.21.2.2.2, as applicable (ITT population only), will be generated for Urine 11-dehydrothromboxane B2 similar to Urine NNAL.

14.2.3 Physiologic Assessments Tables

14.2.3.1 FeNO

Tables 14.2.3.1.1.1 through 14.2.3.1.2.2.2, as applicable (ITT population only), will be generated for FeNO similar to Whole Blood COHb.

14.2.3.2 Systolic Blood Pressure

Tables 14.2.3.2.1.1 through 14.2.3.2.2.2.2, as applicable (ITT population only), will be generated for Systolic Blood Pressure similar to Whole Blood COHb.

14.2.3.3 Diastolic Blood Pressure

Tables 14.2.3.3.1.1 through 14.2.3.3.2.2.2, as applicable (ITT population only), will be generated for Diastolic Blood Pressure similar to Whole Blood COHb.

14.2.3.4 Heart Rate

Tables 14.2.3.4.1.1 through 14.2.3.4.2.2.2, as applicable (ITT population only), will be generated for Heart Rate similar to Whole Blood COHb.

14.2.4 Pharmacokinetics Tables

Table 14.2.4.1.1.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following *myblu*™ Closed System With CF Cosmic Fog Tobacco Chill Flavor, Nicotine Salt Liquid 2.5 % Following Controlled Use (Product A) (PK Population)

Table 14.2.4.1.1.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following myblu™ Closed System With CF Cosmic Fog Tobacco Chill Flavor, Nicotine Salt Liquid 2.5 % Following Ad Libitum Use (Product A) (PK Population)

Table 14.2.4.1.2.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following myblu™ Closed System With CF Cosmic Fog Tobacco Chill Flavor, Nicotine Salt Liquid 4.0% Following Controlled Use (Product B) (PK Population)

Table 14.2.4.1.2.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following myblu™ Closed System With CF Cosmic Fog Tobacco Chill Flavor, Nicotine Salt Liquid 4.0% Following Ad Libitum Use (Product B) (PK Population)

Table 14.2.4.1.3.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following myblu™ Closed System With CF Cosmic Fog Honeymoon Flavor, Nicotine Salt Liquid 2.5 % Following Controlled Use (Product C) (PK Population)

Table 14.2.4.1.3.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following myblu™ Closed System With CF Cosmic Fog Honeymoon Flavor, Nicotine Salt Liquid 2.5 % Following Ad Libitum Use (Product C) (PK Population)

Table 14.2.4.1.4.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following myblu™ Closed System With CF Cosmic Fog Honeymoon Flavor, Nicotine Salt Liquid 4.0% Following Controlled Use (Product D) (PK Population)

Table 14.2.4.1.4.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following myblu™ Closed System With CF Cosmic Fog Honeymoon Flavor, Nicotine Salt Liquid 4.0% Following Ad Libitum Use (Product D) (PK Population)

14.2.6.6 Product Liking VAS Score

Table 14.2.6.6.1 Summary of Product Liking VAS Score by Study Product and Study Day (ITT Population)

14.2.6.7 Future Intent to Use VAS Score

Table 14.2.6.7.1 Summary of Future Intent to Use VAS Score by Study Product and Study Day (ITT Population)

14.2.6.8 Product and Health Effect Perceptions VAS Score

Table 14.2.6.8.1 Summary of Product and Health Effect Perceptions VAS Score by Study Product and Study Day (ITT Population)

14.2.7 Product Use Figures

Figure 14.2.7.1 Mean (+/- SD) Self-Reported Number of *my*blu™ Pods Started Versus Day (ITT)

Figure 14.2.7.2 Mean Self-Reported Number of *my*blu™ Pods Started Versus Day (ITT)

Figure 14.2.7.3 Mean (+/- SD) Self-Reported Number of *my*blu™ Pods Started Versus Day (PP 28/29)

Figure 14.2.7.4 Mean Self-Reported Number of *my*blu™ Pods Started Versus Day (PP 28/29)

Figure 14.2.7.5 Mean (+/- SD) Self-Reported Number of *my*blu™ Pods Started Versus Day (PP 56/57)

Figure 14.2.7.6 Mean Self-Reported Number of *my*blu™ Pods Started Versus Day (PP 56/57)

Figure 14.2.7.7 Mean (+/- SD) Self-Reported Number of Cigarettes Smoked Versus Day for *my*blu™ Products (ITT)

Figure 14.2.7.8 Mean Self-Reported Number of Cigarettes Smoked Versus Day for *my*blu™ Products (ITT)

Figure 14.2.7.9 Mean (+/- SD) Self-Reported Number of Cigarettes Smoked Versus Day for *my*blu™ Products (PP 28/29)

Figure 14.2.7.10 Mean Self-Reported Number of Cigarettes Smoked Versus Day for *my*blu™ Products (PP 28/29)

Figure 14.2.7.11 Mean (+/- SD) Self-Reported Number of Cigarettes Smoked Versus Day for *my*blu™ Products (PP 56/57)

Figure 14.2.7.12 Mean Self-Reported Number of Cigarettes Smoked Versus Day for *my*blu™ Products (PP 56/57)

14.2.8 Biomarker Figures

14.2.8.1 Whole Blood COHb

14.2.8.2 Urine NNAL

14.2.8.3 Urine 3-HPMA

Figures 14.2.8.3.1.1 through 14.2.8.3.6.2 will be generated for Urine 3-HPMA similar to Urine NNAL.

14.2.8.4 Urine S-PMA

Figures 14.2.8.4.1.1 through 14.2.8.4.6.2 will be generated for Urine S-PMA similar to Urine NNAL.

14.2.8.5 Urine NNN

Figures 14.2.8.5.1.1 through 14.2.8.5.6.1, as applicable (ITT population only) will be generated for Urine NNN similar to Urine NNN.

14.2.8.6 Urine CEMA

Figures 14.2.8.6.1.1 through 14.2.8.6.6.1, as applicable (ITT population only) will be generated for Urine CEMA similar to Urine NNAL.

14.2.8.7 Urine HEMA

Figures 14.2.8.7.1.1 through 14.2.8.7.6.1, as applicable (ITT population only) will be generated for Urine HEMA similar to Urine NNAL.

14.2.8.8 Urine HMPMA

Figures 14.2.8.8.1.1 through 14.2.8.8.6.1, as applicable (ITT population only) will be generated for Urine HMPMA similar to Urine NNAL.

14.2.8.9 Urine MHBMA

Figures 14.2.8.9.1.1 through 14.2.8.9.6.1, as applicable (ITT population only) will be generated for Urine MHBMA similar to Urine NNAL.

14.2.8.10 Urine 1-OHP

Figures 14.2.8.10.1.1 through 14.2.8.10.6.1, as applicable (ITT population only) will be generated for Urine 1-OHP similar to Urine NNAL.

14.2.8.11 Urine o-tol

Figures 14.2.8.11.1.1 through 14.2.8.11.6.1, as applicable (ITT population only) will be generated for Urine o-tol similar to Urine NNAL.

14.2.8.12 Urine 3-OH B[a]P

Figures 14.2.8.12.1.1 through 14.2.8.12.6.1, as applicable (ITT population only) will be generated for Urine 3-OH B[a]P similar to Urine NNAL.

14.2.8.13 Urine 1-AN

Figures 14.2.8.13.1.1 through 14.2.8.13.6.1, as applicable (ITT population only) will be generated for Urine 1-AN similar to Urine NNAL.

14.2.8.14 Urine 2-AN

Figures 14.2.8.14.1.1 through 14.2.8.14.6.1, as applicable (ITT population only) will be generated for Urine 2-AN similar to Urine NNAL.

14.2.8.15 Urine Nicotine Equivalents

Figures 14.2.8.15.1.1 through 14.2.8.15.6.1, as applicable (ITT population only) will be generated for Urine Nicotine Equivalents similar to Urine NNAL.

14.2.8.16 Plasma sICAM

Figures 14.2.8.16.1.1 through 14.2.8.16.31, as applicable (ITT population only) will be generated for Plasma sICAM similar to Whole Blood COHb.

14.2.8.17 Whole Blood WBCs

Figures 14.2.8.17.1.1 through 14.2.8.17.3.1, as applicable (ITT population only) will be generated for Whole Blood WBCs similar to Whole Blood COHb.

14.2.8.18 Serum HDL-C

Figures 14.2.8.18.1.1 through 14.2.8.18.3.1, as applicable (ITT population only) will be generated for Serum HDL-C similar to Whole Blood COHb.

14.2.8.19 Serum MCP-1

Figures 14.2.8.19.1.1 through 14.2.8.19.3.1, as applicable (ITT population only) will be generated for Serum MCP-1 similar to Whole Blood COHb.

14.2.8.20 Urine Type III isoprostane (8-epi-prostaglandin F2α)

Figures 14.2.8.20.1.1 through 14.2.8.20.6.1, as applicable (ITT population only) will be generated for Urine Type III isoprostane (8-epi-prostaglandin F2α) similar to Urine NNAL.

14.2.8.21 Urine 11-dehydrothromboxane B2

Figures 14.2.8.21.1.1 through 14.2.8.21.6.1, as applicable (ITT population only) will be generated for Urine 11-dehydrothromboxane B2 similar to Urine NNAL.

14.2.9 Physiologic Assessments Figures

14.2.9.1 FeNO

Figures 14.2.8.22.1.1 through 14.2.8.22.3.1, as applicable (ITT population only) will be generated for FeNO similar to Whole Blood COHb.

14.2.9.2 Systolic Blood Pressure

Figures 14.2.9.2.1.1 through 14.2.9.2.3.1, as applicable (ITT population only) will be generated for Systolic Blood Pressure similar to Whole Blood COHb.

14.2.9.3 Diastolic Blood Pressure

Figures 14.2.9.3.1.1 through 14.2.9.3.3.1, as applicable (ITT population only) will be generated for Diastolic Blood Pressure similar to Whole Blood COHb.

14.2.9.4 Heart Rate

Figures 14.2.9.4.1.1 through 14.2.9.4.3.1, as applicable (ITT population only) will be generated for Heart Rate similar to Whole Blood COHb.

14.2.10 Pharmacokinetics Figures

Figure 14.2.10.1	Arithmetic Mean (SD) Unadjusted Plasma Nicotine Concentration Versus Time Profiles Following Controlled Use (Linear Scale) (PK Population)
Figure 14.2.10.2	Arithmetic Mean Plasma Unadjusted Nicotine Concentration Versus Time Profiles Following Controlled Use (Linear Scale) (PK Population)
Figure 14.2.10.3	Arithmetic Mean Plasma Unadjusted Nicotine Concentration Versus Time Profiles Following Controlled Use (Semi-log Scale) (PK Population)
Figure 14.2.10.4	Arithmetic Mean (SD) Baseline-adjusted Plasma Nicotine Concentration Versus Time Profiles Following Controlled Use (Linear Scale) (PK Population)
Figure 14.2.10.5	Arithmetic Mean Plasma Baseline-adjusted Nicotine Concentration Versus Time Profiles Following Controlled Use (Linear Scale) (PK Population)
Figure 14.2.10.6	Arithmetic Mean Plasma Baseline-adjusted Nicotine Concentration Versus Time Profiles Following Controlled Use (Semi-log Scale) (PK Population)
Figure 14.2.10.7	Arithmetic Mean (SD) Unadjusted Plasma Nicotine Concentration Versus Time Profiles Following Ad Libitum Use (Linear Scale) (PK Population)
Figure 14.2.10.8	Arithmetic Mean Plasma Unadjusted Nicotine Concentration Versus Time Profiles Following Ad Libitum Use (Linear Scale) (PK Population)

Note: Individual profiles will be presented in an appendix of the report.

14.2.11 Urge to Smoke Figures

14.2.12 Questionnaire Figures

14.2.12.1 PSCDI or PSECDI Total Score

14.2.12.2 MTWS-R Total Score

14.2.12.3 QSU-brief Factor Scores

14.2.12.4 PES Subscales

Table 14.3.1.2 Product Use-emergent Adverse Event Frequency by Study Product – Number of Adverse Events (% of Total Adverse Events) (Safety Population)

Table 14.3.1.3 Product Use-emergent Adverse Event Frequency by Study Product, Severity, and Relationship to Study Product – Number of Subjects Reporting Events (Safety Population)

14.3.2 Listings of Deaths, other Serious and Significant Adverse Events

Table 14.3.2.1 Serious Adverse Events (Safety Population) <if no serious adverse event occurred, a statement 'No serious adverse event is reported'>

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

14.3.4 Abnormal Laboratory Value Listing (each subject)

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

Table 14.3.4.2 Out-of-Range Values and Recheck Results – Hematology (Safety Population)

Table 14.3.4.3 Out-of-Range Values and Recheck Results – Urinalysis (Safety Population)

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

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

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

Table 14.3.5.2 Clinical Laboratory Summary – Hematology (Safety Population)

Table 14.3.5.3 Clinical Laboratory Summary – Urinalysis (Safety Population)

Table 14.3.5.4 Vital Sign Summary (Safety Population)

Table 14.3.5.5 12-Lead Electrocardiogram Summary (Safety Population)

Table 14.3.5.6 Spirometry Summary (Safety Population)

Section 16 Data Listings

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 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: Appendices 16.2.2 and 16.2.3 are generated in MS Word for inclusion in the study report.

16.2.4 Demographic Data

Appendix 16.2.4.1.1 Subject Information (Safety Population)
Appendix 16.2.4.1.2 Demographics (Safety Population)
Appendix 16.2.4.1.3 Additional Demographics Questionnaire (Safety Population)
Appendix 16.2.4.2.1 Physical Examination – Full (Safety Population)
Appendix 16.2.4.2.2 Physical Examination - Symptom-driven (Safety Population)
Appendix 16.2.4.3 Medical and Surgical History (Safety Population)
Appendix 16.2.4.4.1 Tobacco/Nicotine Product Use History Questionnaire (Safety Population)
Appendix 16.2.4.4.2 Smoking History (Safety Population)
Appendix 16.2.4.4.3 Usual Brand Documentation (Safety Population)

16.2.5 Compliance and/or Concentration Data

Appendix 16.2.5.1 Inclusion / Exclusion Criteria Not Met (Safety Population)

Appendix 16.2.5.2.1 *my*blu™ Product Preference Questionnaire (Safety Population)
Appendix 16.2.5.2.2 Product Selection (Safety Population)
Appendix 16.2.5.2.3 Staff-Recorded In-Clinic Product Use (Safety Population)
Appendix 16.2.5.2.4 Self-Reported Product Use (Safety Population)
Appendix 16.2.5.2.5 Product Use - Nicotine PK Assessment (Safety Population)
Appendix 16.2.5.3.1 Pharmacokinetics Blood Sampling (Safety Population)
Appendix 16.2.5.3.2 24-Hour Urine Collection (Safety Population)
Appendix 16.2.5.3.3 24-Hour Urine Collection - Pod Weight Documentation (Safety Population)
Appendix 16.2.5.3.4 Carboxyhemoglobin Blood Collection (Safety Population)
Appendix 16.2.5.3.5 Biomarkers and Bio-Banking Blood Collection (Safety Population)
Appendix 16.2.5.4 Concomitant Medications (Safety Population)

16.2.6 Individual, Biomarker, Pharmacokinetics and Subjective Effect Data

Appendix 16.2.6.2.1 Whole Blood COHb*

Appendix 16.2.6.2.2 Urine NNAL*

Appendix 16.2.6.2.3 Urine 3-HPMA*

Appendix 16.2.6.2.4 Urine S-PMA*

* Programmer note: Include population flags in these listings to show who was in ITT and PP population.

Appendix 16.2.6.2.5 Urine NNN (ITT Population)

Appendix 16.2.6.2.6 Urine CEMA (ITT Population)

Appendix 16.2.6.2.7 Urine HEMA (ITT Population)

Appendix 16.2.6.2.8 Urine HMPMA (ITT Population)

Appendix 16.2.6.2.9 Urine MHBMA (ITT Population)

Appendix 16.2.6.2.10 Urine 1-OHP (ITT Population)

Appendix 16.2.6.2.11 Urine o-tol (ITT Population)

Appendix 16.2.6.9 Future Intent to Use Questionnaire Responses (ITT Population)

Appendix 16.2.6.10 Product and Health Effect Perceptions Questionnaire Responses (ITT 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 Serology (Safety Population)
Appendix 16.2.8.1.5 Urine Drug Screen (Safety Population)
Appendix 16.2.8.1.6 Alcohol Breath Test (Safety Population)
Appendix 16.2.8.1.7 Urine Cotinine Screen (Safety Population)
Appendix 16.2.8.1.8 Pregnancy Test (Safety Population)
Appendix 16.2.8.1.9 Serum FSH (Safety Population)
Appendix 16.2.8.2 Vital Signs (Safety Population)
Appendix 16.2.8.3 12-Lead Electrocardiogram (Safety Population)
Appendix 16.2.8.4 Carbon Monoxide Breath Test (Safety Population)
Appendix 16.2.8.5 FeNO Measurement (Safety Population)
Appendix 16.2.8.6 Spirometry (Safety Population)

10. TABLE AND FIGURE SHELLS

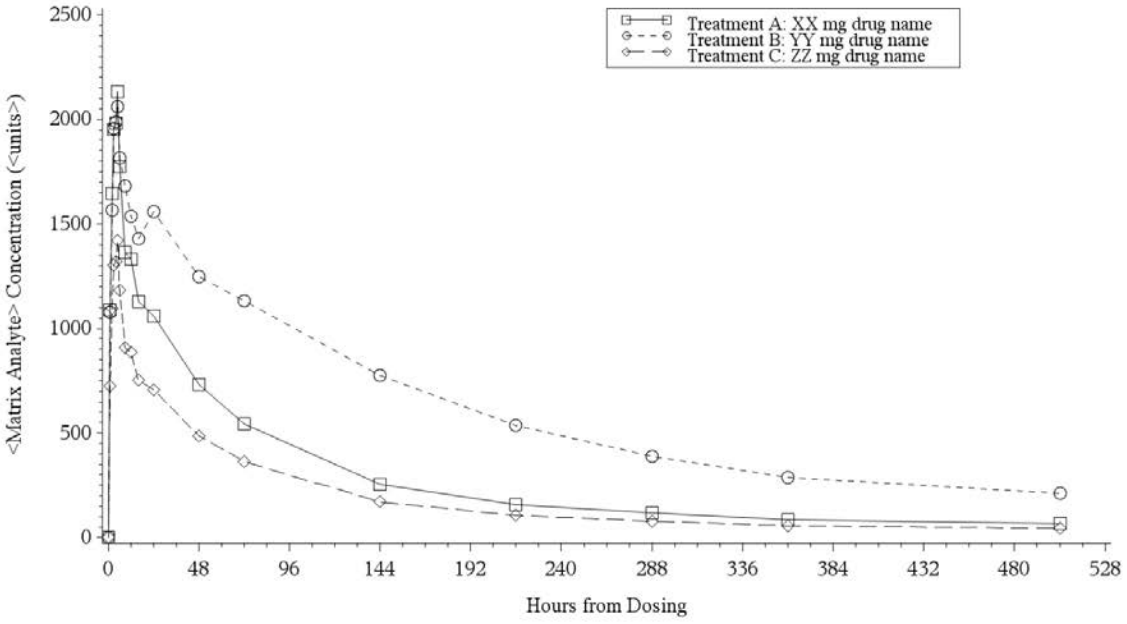
The following table shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the tables that will be presented and included 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 or Ad Libitum> Product Use by Product (Linear Scale) (PK Population)



Notes for Generating the Actual Mean Figure:

I. Legend will be the short description
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

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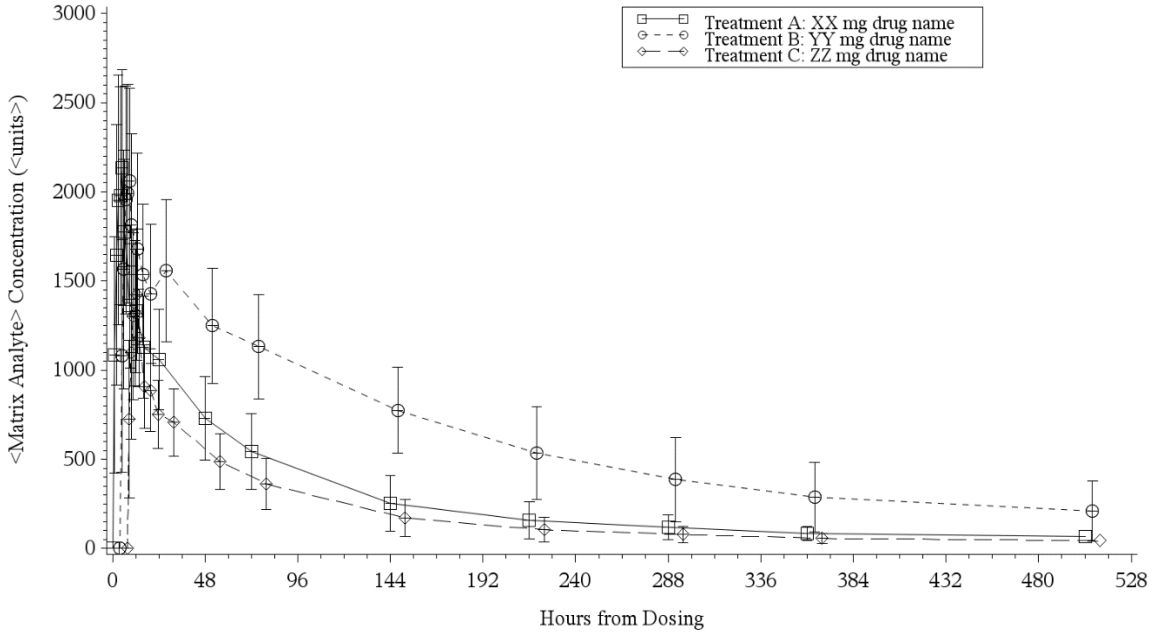
Program: /CAXXXXX/sas_prg/pksas/adam_meangraph.sas DDMMMYYYY HH:MM

Post-text PK Figures of mean (SD) plasma concentrations and UTS on linear scale will be in the following format: Figure 14.X:

Figure 14.X: Arithmetic Mean (SD) Baseline-Adjusted Plasma Nicotine Concentration-Time Profiles Following <Controlled or Ad Libitum> Product Use by Product (Linear Scale) (PK Population)



Notes for Generating the Actual Mean Figure:

IV. Legend will be the short description
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

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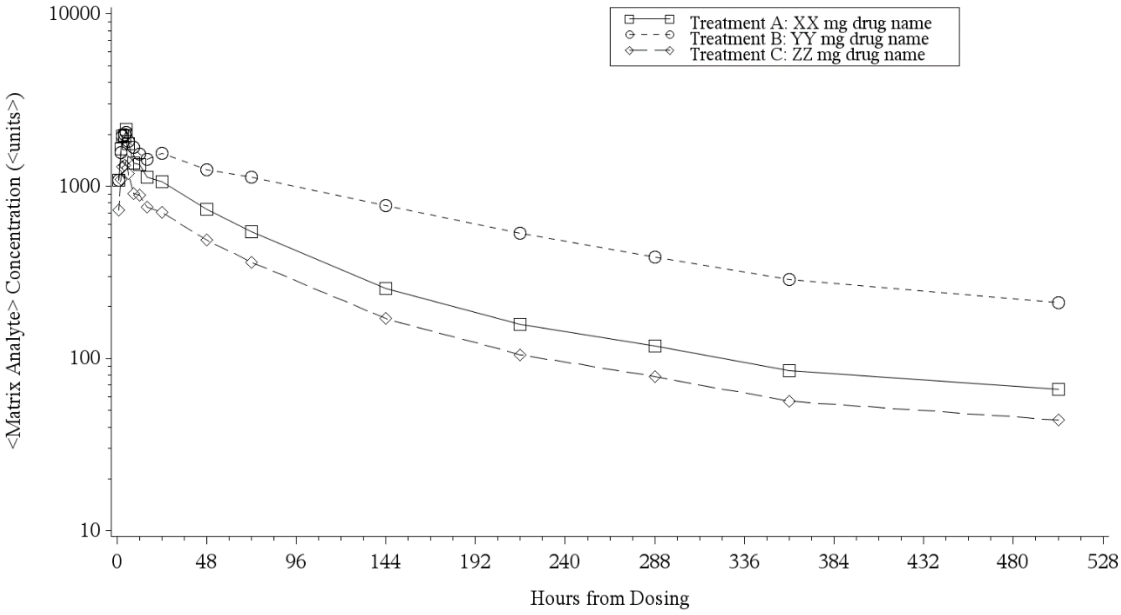
Post-text PK Figures of mean plasma concentrations on semi-log scale will be in the following format: 14.X, and appendix 16.2.6.1:

Figure 14.X: Arithmetic Mean Baseline-Adjusted Plasma Nicotine Concentration-Time Profiles Following <Controlled or Ad Libitum> Product Use by Product (Semi-Log Scale) (PK Population)



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Program: /CAXXXXX/sas_prg/pksas/meangraph.sas DDMMMYYY HH:MM

Notes for Generating the Actual Mean Figure:

VIII. Legend will be the short descriptions
IX. Y axis label will be "Plasma Nicotine Concentration (ng/mL)" for all figures
X. 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 Figure(s) for Total Scores will be in the following format:

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

*****Please note this will be a boxplot figure*****

Notes for Generating the Actual Mean Figure:

XI. Note: this figure will be a boxplot figure
XII. 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.
XIII. Y axis label will be "Subjective Measurement Score"
XIV. X axis label will be labelled with "A, B, C, D, E, F" for each figure representing each product

10.2 Post-Text Summary Tables Shells

14.1 Demographic Tables

Table 14.1.1 Summary of Disposition (Safety, ITT, and PP Populations)

Population	Category	Product A	B	C	D	E	F	Overall
Safety	Enrolled							XX
	Randomized	XX	XX	XX	XX	XX	XX	XX
	Completed	XX	XX	XX	XX	XX	XX	XX
	Discontinued Early	X	X	X	X	X	X	X
	<Reason>	X	X	X	X	X	X	X
ITT	Enrolled							XX
	Randomized	XX	XX	XX	XX	XX	XX	XX
	Completed	XX	XX	XX	XX	XX	XX	XX
	Discontinued Early	X	X	X	X	X	X	X
	<Reason>	X	X	X	X	X	X	X
PP	Enrolled							XX
	Randomized	XX	XX	XX	XX	XX	XX	XX
	Completed	XX	XX	XX	XX	XX	XX	XX
	Discontinued Early	X	X	X	X	X	X	X
	<Reason>	X	X	X	X	X	X	X

Note: Product X: < >

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Table 14.1.2 Demographic Summary (Safety, ITT, and PP Populations)

Population	Trait		Product A	Product B	Product C	Product D	Product E	Product F	Overall
Safety	Sex	Male	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%)
	Race	American Indian	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%	X (XX.X%))	X (XX.X%)
		Asian	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%	X (XX.X%))	X (XX.X%)
		Black	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
		Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX	XX	XX
	Weight(kg)	n	X	X	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX	XX	XX

<Continued with other measures – Body Mass Index (kg/m²) and ITT and PP populations.>

Note: Product X: < >
Age is derived from birth date to date of informed consent.

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Table 14.1.3 Smoking History Summary (Safety, ITT, and PP Populations)

			Product						
Population	Trait		A	B	C	D	E	F	Overall
Safety	CPD	n	X	X	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX	XX	XX
	Number of Years Smoked	n	X	X	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX	XX	XX
	Usual Brand Cigarette Flavor	Menthol	X(XX%)	X(XX%)	X(XX%)	X(XX%)	X(XX%)	X(XX%)	X(XX%)
		Regular	X(XX%)	X(XX%)	X(XX%)	X(XX%)	X(XX%)	X(XX%)	X(XX%)

<Continued with ITT and PP populations.>

Note: Product X: < >

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14.2.1 Main Study Product Use Tables

Note: Product Use (In-Clinic) Tables will have the following format:

Page 1 of X

Table 14.2.1.1 Summary of In-Clinic Number of myblu™ Pods Started by Product and Day (ITT)

		Day				
Product	Statistic	-2	-1	1	2	etc.
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	

Note: Product X: < >
NA: Not applicable

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

Programmer Note: Days 1 through 3, 28, 29, 56, and 57 will be presented in Tables 14.2.1.1 through 14.2.1.3. Product E will not be presented in Tables 14.2.1.1 through 14.2.1.6. Only Days 3, 28, 29, 56, and 57 will be presented in Tables 14.2.1.4 through 14.2.1.6. Days -2 through 3 (Days 2 and 3 will be NA for the combustible cigarette group), 28, 29, 56, and 57 will be presented in Tables 14.2.1.7 through 14.2.1.9.

Note: Product Use (Self-Reported) Tables will have the following format:

Table 14.2.1.10 Summary of Self-Reported Number of myblu™ Pods Started by Product and Day (ITT)

Product	Statistic	Day 3	Day 4	Day 5	Day 6
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

Note: Product X: < >

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

Programmer Note: Days 3 through 57 and Products C and D will be presented. Product E also be presented in Tables 14.2.1.16 through 14.2.1.18. Frequency counts (n,%) will be presented as the statistics in Tables 14.2.1.13 through 14.2.1.15.

Note: Summary Tables 14.2.1.19 through 14.2.1.21 will have the following format:

Table 14.2.1.19 Summary of Self-Reported Product Use by Product and Product Use Period (ITT)

Variable	Product Use Period	Statistic	Product A	Product B	Product C	Product D
Number of Cigarettes	1	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
	2	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: Product X: < >
NA: Not applicable

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

Programmer Note: Other variables presented will be Number of myblu™ started and >=50 Puffs Taken From myblu™. Frequency counts (n, %) will be presented for >= 50 Puffs Taken From myblu™. Product E will also be presented (NA for all variables except number of cigarettes)

14.2 Biomarker Tables

Tables 14.2.2.1.1.1, 14.2.2.1.1.2, 14.2.2.1.1.3 and other summary tables for ITT population will be in the following format:

Page 1 of X

Table 14.2.2.1.1.1 Summary of Whole Blood COHb by Study Product and Study Day (ITT Population)

		Product					
Day	Statistic	A	B	C	D	E	F
XXXXX	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

Note: Product X: < >

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

Programmer Notes: Footnotes to include under the table, as appropriate: < . = Value missing or not reportable. >
The Days will be Day -2 (for some endpoints this may be Day -1), Day 28, and Day 56. For Change from baseline and percent change from baseline, Day -2 will not be presented in the table.

A table should also be presented for PK population for the following biomarkers: NNAL, NNN, 3-HPMA, CEMA, HMPMA, S-PMA; this table shall include Day 3.

Tables 14.2.2.1.1.4, 14.2.2.1.1.5, 14.2.2.1.1.6 and other summary tables for PP population (only for primary biomarkers) will be in the following format:

Page 1 of X

Table 14.2.2.1.1.4 Summary of Whole Blood COHb by Study Product and Study Day (PP Populations)

		PP 28/29		PP 56/57		
Product	Statistic	Baseline	Day 28	Baseline	Day 28	Day 56
A	n	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX
	CV(%)	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX

Note: Product X: < >

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

Programmer Notes: Footnotes to include under the table, as appropriate: < . = Value missing or not reportable. >
Products B through E will also be presented in the table. For Change from baseline and percent change from baseline, Baseline timepoint will not be presented in the table.

Statistical comparison tables will be in the following format:

Page 1 of X

Table 14.2.2.1.2.1 Statistical Comparison of Whole Blood COHb Change From Baseline Between myblu™ and Continuous Smoking by Study Day (ITT Population)

Day	Comparison	LS Means: Test (n)	LS Means: Reference (n)	LS Mean Difference (Test − Reference)	95% Confidence Interval	p-value
28	Product A vs Product E	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product B vs Product E	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product C vs Product E	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product D vs Product E	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
56	Product A vs Product E	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product B vs Product E	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product C vs Product E	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product D vs Product E	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX

Note: Test = First product in the comparison; Reference = Product E
n = Number of observation used in the analysis; Least-squares means (LS Means) are calculated from the model.

Product X: < >

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

A table should also be presented for PK population for the following biomarkers: NNAL, NNN, 3-HPMA, CEMA, HMPMA, S-PMA; this table shall include Day 3.

Table 14.2.2.1.2.2 Statistical Comparison of Whole Blood COHb Change From Baseline Between myblu™ and Continuous Smoking by Study Day (PP Population)

Day	Comparison	LS Means Test (n)	LS Means Reference (n)	LS Mean Difference (Test – Reference)	95% Confidence Interval	p-value
28	Product A vs Product E	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product B vs Product E	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product C vs Product E	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product D vs Product E	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
56	Product A vs Product E	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product B vs Product E	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product C vs Product E	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product D vs Product E	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX

Note: Test = First product in the comparison; Reference = Product E
n = Number of observation used in the analysis; Least-squares means (LS Means) are calculated from the model.
Day 28 results are from the Day 28/29 PP Population
Day 56 results are from the Day 56/57 PP Population
Product X: < >

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

Statistical Tables 14.2.2.1.3.1 (ITT) and 14.2.2.1.3.2 (PP) will be in the following format:

Table 14.2.2.1.3.1 Statistical Comparison of Whole Blood COHb Change From Baseline Between Day 28 and Day 56 in the myblu™ Groups (ITT Population)

Product	LS Means Day 28 (n)	LS Means Day 56 (n)	LS Mean Difference (Day 28 – Day 56)	95% Confidence Interval	p-value
A	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
B	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
C	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
D	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX

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

Product X: < >

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

Statistical Table 14.2.2.1.4.1 (ITT) will be in the following format:

Table 14.2.2.1.4.1 Statistical Comparison of Whole Blood COHb Change From Baseline Between myblu™ Groups by Study Day (ITT Population)

Day	Comparison	LS Means Test (n)	LS Means Reference (n)	LS Mean Difference (Test – Reference)	95% Confidence Interval	p-value
28	Product A vs Product B	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product A vs Product C	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product A vs Product D	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product B vs Product C	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product B vs Product D	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product C vs Product D	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
56	Product A vs Product B	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product A vs Product C	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product A vs Product D	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product B vs Product C	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product B vs Product D	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product C vs Product D	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX

Note: Test = First product in the comparison; Reference = Second product in the comparison
n = Number of observation used in the analysis; Least-squares means (LS Means) are calculated from the model.

Product X: < >

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

Statistical Table 14.2.2.1.4.2 (PP) will be in the following format:

Table 14.2.2.1.4.2 Statistical Comparison of Whole Blood COHb Change From Baseline Between myblu™ Groups by Study Day (PP Population)

Day	Comparison	LS Means Test (n)	LS Means Reference (n)	LS Mean Difference (Test – Reference)	95% Confidence Interval	p-value
28	Product A vs Product B	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product A vs Product C	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product A vs Product D	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product B vs Product C	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product B vs Product D	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product C vs Product D	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
56	Product A vs Product B	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product A vs Product C	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product A vs Product D	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product B vs Product C	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product B vs Product D	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX
	Product C vs Product D	X.XX (X)	X.XX (X)	XXX.XX	XX.XX – XXX.XX	X.XXXX

Note: Test = First product in the comparison; Reference = Second product in the comparison
n = Number of observation used in the analysis; Least-squares means (LS Means) are calculated from the model.

Day 28 results are from the Day 28/29 PP Population
Day 56 results are from the Day 56/57 PP Population
Product X: < >

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

14.2.3 Physiologic Assessments Tables

Physiologic assessments tables (ITT population only), will be similar to Whole Blood COHb (blood biomarker) tables.

14.2.4 Pharmacokinetic Tables and 14.2.5 Urge to Smoke Tables

Tables 14.2.4.1.1.1 through 14.2.4.1.6.2 for unadjusted and Tables 14.2.4.2.1.1 through 14.2.4.2.6.2 for baseline-adjusted concentration data and Tables 14.2.5.1 through 14.2.5.6 for UTS data will be in the following format:

Table 14.2.4.1.1.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Controlled Use of myblu™ closed system with CF Cosmic Fog Tobacco Chill flavor, nicotine salt liquid 2.5 % (Product A) (PK Population)

Subject Number	Product Use Sequence	Product	Sample Times (min) 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 each product use (Controlled and *ad libitum*)
Please also present the geometric mean and 95% CI around the geometric mean for all concentration tables
Delete the Product Use Sequence column and Product Column as not applicable for parallel studies

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 14.2.4.3.1.1 through 14.2.4.3.6.2 (PK) and Tables 14.2.5.7 through 14.2.5.12 (UTS) will be in the following format:

Table 14.2.4.3.1.1: Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Controlled Use of myblu™ Closed System With CF Cosmic Fog Chilled Tobacco Flavor (25 mg With Lactic Acid) (Product A) (PK Population)

			Parameters Following <Controlled OR *Ad Libitum*> Use					
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)
- 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.
- CV% and Geom CV% for all parameters will be presented with 1 decimal
- Delete the Product Use Sequence column and Product Column as not applicable for parallel studies.

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

Tables 14.2.4.4.1.1 and 14.2.4.4.1.2 (PK) and Table 14.2.5.13 (UTS) will be in the following format:

Table 14.2.4.4.1.1: Statistical Comparisons of Baseline-Adjusted Plasma Nicotine PK Parameters AUC0-t and Cmax Between myblu™ Products and Continuous Smoking or JUUL Following Controlled Use (PK 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 E	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 E	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 E	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 D vs Product E	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 F	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 F	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 F	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 D vs Product F	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 = myblu™ closed system with CF Cosmic Fog Tobacco Chill flavor, nicotine salt liquid 2.5 %
Product B = myblu™ closed system with CF Cosmic Fog Tobacco Chill flavor, nicotine salt liquid 4.0%
Product C = myblu™ closed system with CF Cosmic Fog Honeymoon flavor, nicotine salt liquid 2.5 %
Product D = myblu™ closed system with CF Cosmic Fog Honeymoon flavor, nicotine salt liquid 4.0%
Product E = Subject's usual brand combustible cigarette
Product F = JUUL® system with Virginia Tobacco Flavor JUULpod, 5.0% nicotine

The mixed model includes product arm, study day, and product arm by study day interaction as fixed effect and subject as a random effect. 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

Tables 14.2.4.4.2.1 and 14.2.4.4.2.2 will be in the following format:

Table 14.2.4.4.2.1: Nonparametric Statistical Comparisons of Baseline-Adjusted Plasma Nicotine PK Parameter Tmax Between myblu™ and Continuous Smoking or JUUL Following Controlled Use (PK Population)

		Product		Difference Test-Reference		
Comparison	Parameter	Test	Reference	95% CI	Median	p-Value
Product A vs Product E	Tmax	X.XX	X.XX	X.XX - X.XX	X.XX	X.XXXX
Product B vs Product E	Tmax	X.XX	X.XX	X.XX - X.XX	X.XX	X.XXXX
Product C vs Product E	Tmax	X.XX	X.XX	X.XX - X.XX	X.XX	X.XXXX
Product D vs Product E	Tmax	X.XX	X.XX	X.XX - X.XX	X.XX	X.XXXX
Product A vs Product F	Tmax	X.XX	X.XX	X.XX - X.XX	X.XX	X.XXXX
Product B vs Product F	Tmax	X.XX	X.XX	X.XX - X.XX	X.XX	X.XXXX
Product C vs Product F	Tmax	X.XX	X.XX	X.XX - X.XX	X.XX	X.XXXX
Product D vs Product F	Tmax	X.XX	X.XX	X.XX - X.XX	X.XX	X.XXXX

Test = The first product in the comparison; Reference = The second product in the comparison

Product A = myblu™ closed system with CF Cosmic Fog Tobacco Chill flavor, nicotine salt liquid 2.5 %
Product B = myblu™ closed system with CF Cosmic Fog Tobacco Chill flavor, nicotine salt liquid 4.0%
Product C = myblu™ closed system with CF Cosmic Fog Honeymoon flavor, nicotine salt liquid 2.5 %
Product D = myblu™ closed system with CF Cosmic Fog Honeymoon flavor, nicotine salt liquid 4.0%
Product E = Subject's usual brand combustible cigarette
Product F = JUUL® system with Virginia Tobacco Flavor JUUL pod, 5.0% nicotine

p-values are from Wilcoxon rank sum test.

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

14.2.6 Questionnaires Tables

Tables 14.2.6.1.1-2, 14.2.6.3.1-2, 14.2.6.4.1-2, 14.2.6.5.1-2, 14.2.6.6.1-2, 14.2.6.7.1-2, and 14.2.6.8.1-2 will be in the following format:

Table 14.2.6.1.1 Summary of PSCDI or PSECDI Total Score by Study Product and Study Visit (ITT Population)

		Product					
Study Visit	Statistic	A	B	C	D	E	F
XXXXXXXX	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
XXXXXXXX	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

Product A = myblu™ closed system with CF Cosmic Fog Tobacco Chill flavor, nicotine salt liquid 2.5 %
Product B = myblu™ closed system with CF Cosmic Fog Tobacco Chill flavor, nicotine salt liquid 4.0%
Product C = myblu™ closed system with CF Cosmic Fog Honeymoon flavor, nicotine salt liquid 2.5 %
Product D = myblu™ closed system with CF Cosmic Fog Honeymoon flavor, nicotine salt liquid 4.0%
Product E = Subject's usual brand combustible cigarette
Total scoring: 0 - 3 = not dependent, 4 - 8 = low dependence, 9 - 12 = medium dependence, 13+ = high dependence

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

Programmer note: A table should also be presented for PK population; this table shall include Day 3

Programmer note: When there are multiple scores in a questionnaire to be summarized, an additional column for score category will be added to the table.

Tables 14.2.6.2.1-2 will be in the following format:

Table 14.2.6.1.1 Frequency Count of Cough Questionnaire by Study Product and Study Visit (ITT Population)

			Product					
Study Visit	Question	Response	A	B	C	D	E	F
XXXXXXXX	XXXXXXX	XXXX	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
		XXXX	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
		XXXX	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
	XXXXXXX	XXXX	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
		XXXX	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
		XXXX	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)

Product A = myblu™ closed system with CF Cosmic Fog Tobacco Chill flavor, nicotine salt liquid 2.5 %
Product B = myblu™ closed system with CF Cosmic Fog Tobacco Chill flavor, nicotine salt liquid 4.0%
Product C = myblu™ closed system with CF Cosmic Fog Honeymoon flavor, nicotine salt liquid 2.5 %
Product D = myblu™ closed system with CF Cosmic Fog Honeymoon flavor, nicotine salt liquid 4.0%
Product E = Subject's usual brand combustible cigarette
Product F = JUUL® system with Virginia Tobacco Flavor JUUL pod, 5.0% nicotine

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

Table 14.3.1.1 Product Use-emergent Adverse Event Frequency by Study Product – Number of Subjects Reporting the Event (% of Subjects Who Used Study Product) (Safety Population)

		Product						
Adverse Event*	Product Trial#	A	B	C	D	E	F	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%)
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 21.0.
Only include the adverse events occurred during the product trial period.
^ Adverse events occurred during the product trial period are excluded from Overall summary.
Product X: < >

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

Table 14.3.1.2 Product Use-emergent Adverse Event Frequency by Study Product – Number of Adverse Events (% of Total Adverse Events) (Safety Population)

Adverse Event*	Product Trial#	Product A	B	C	D	E	F	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 21.0.
Only include the adverse events occurred during the product trial period.
^ Adverse events occurred during the product trial period are excluded from Overall summary.
Product X: < >

Program: /CAXXXXX/sas_prg/stsas/tab cdash_tblae2a_auto.sas DDMMMYYYY HH:MM

Table 14.3.1.3 Adverse Event Frequency by Study Product, Intensity, and Relationship to Study Product - Number of Subjects Reporting Events (Safety Population)

Adverse Event*	Study Product	Number of Subjects with Adverse Events	Intensity			Relationship to Study Product		
			Mild	Moderate	Severe	Unrelated	Possibly	Probably
Abdominal pain	X	X	X	X	X	X	X	X
Constipation	X	X	X	X	X	X	X	X
Dry throat	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
Product Trial#		X	X	X	X	X	X	X
Study Product A		X	X	X	X	X	X	X
Study Product B		X	X	X	X	X	X	X
Study Product C		X	X	X	X	X	X	X
Study Product D		X	X	X	X	X	X	X
Study Product E		X	X	X	X	X	X	X
Study Product F		X	X	X	X	X	X	X
Overall^		X	X	X	X	X	X	X

Note: * Adverse events are classified according to MedDRA Version 21.0.
Only include the adverse events occurred during the product trial period.
^ Adverse events occurred during the product trial period are excluded from Overall summary.
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

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

Tables 14.3.4.1 to 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 HN				XX HN
		X	X	XX.XX	DDMMMYYYY	HH:MM:SS	XX LY^	XX LN		XX LYR+	

Note: # Age is calculated from the date of the first product use. F = Female, M = Male
H = Above normal range, L = Below normal range
Computer: N = Not clinically significant, Y = Clinically significant
PI Interpretation: - = Not clinically significant, R = Recheck requested, ^ = Will be retested later, + = Clinically significant

Programmer Notes: 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. Tables 14.3.4.2 and 14.3.4.3 will resemble 14.3.4.1.

Programmer Notes: Clinically significant lab values generally will be captured as AEs, some of which the PI may indicate in Appendix 16.2.8.1.5 lab comments (as per GPG.03.0028 sections 2.9 and 2.10). Derive an additional CS flag for PI flag (+) based on positive comments (i.e. CS/Clinically Significant). Present this derived 4th column in all tables, and list only subjects/tests which are PI-determined clinically significant lab values in Table 14.3.4.4.

Program: /CAXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMMYYYY HH:MM

Table 14.3.4.4 will be in the following format:

Page 1 of X

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	Normal Range	Unit
X	XX/X	X	X	X.X	DDMMMYYYY	HH:MM	XXXXXXXXXXXXXXX	XXXXXXXXXXX	XXX HYR+	X – X	mg/dL
			X	X.X	DDMMMYYYY	HH:MM	XXXXXXXXXXXXXXX	XXXXXXXXXXX	XXX	X – X	mg/dL

< All time points for a subject/test with at least one value deemed as CS by the PI will be presented in this table. >

Note: # Age is calculated from the date of the first product use. F = Female, M = Male
H = Above normal range
Computer: Y = Clinically significant
PI Interpretation: R = Recheck requested, + = Clinically significant

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

Programmer Note: If no event meet this criteria then include a statement as follows: “There were no clinical laboratory results documented as clinically significant by the PI.”

Tables 14.3.5.2 and 14.3.5.3 will resemble Table 14.3.5.1

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

Laboratory Test (units)	Normal Range	Time Point	Statistic	Product A	B	C	D	E	F
Testname (unit)	< - >#	Screen	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
		Check-in	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: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.
* Above Normal Range, ^ Below Normal Range
Product X: < >

< Similar for remaining laboratory tests. >

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

Table 14.3.5.4 Vital Sign Summary Vital Sign Summary at Screening, Check-in, and Prior to Discharge (Safety Population)

Vital Sign (units)	Time Point	Statistic	Product A	B	C	D	E	F
Testname (unit)	Screen	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
	Check-in	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

< Similar for remaining vital signs and time points. >

Note: Product X : < >

Program: /CAXXXXX/ECR/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	Gender	Age Category	Normal Range	Unit
Serum Chemistry	Test Name	<>	<>	XX – XX	units
	Test Name	<>	<>	XX – XX	units
	Test Name	<>	<>	XX – XX	units
	Test Name	<>	<>	XX – XX	units
	Test Name	<>	<>	XX – XX	units
	Test Name	<>	<>	XX – XX	units
Hematology	Test Name	<>	<>	XX – XX	units
	Test Name	<>	<>	XX – XX	units
	Test Name	<>	<>	XX – XX	units
	Test Name	<>	<>	XX – XX	units
	Test Name	<>	<>	XX – XX	units

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

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

Appendix 16.2.1 Subject Discontinuation

Subject Number	Date	Product	Completed Study?	Reason for Discontinuation	Specify
X	DDMMMYYYY	X	Yes		
X	DDMMMYYYY	X	Yes		
X	DDMMMYYYY	X	Yes		
X	DDMMMYYYY	X	Yes		
X	DDMMMYYYY	X	No	Personal Reason	
X	DDMMMYYYY	X	Yes		
X	DDMMMYYYY	X	Yes		
X	DDMMMYYYY	X	Yes		

Note: Product X: < >

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

Appendix 16.2.4.1.1 Subject Information (Safety Population)

Subject Number	Informed Consent Date	Protocol Version	Randomization Number	Randomization Date	Study Product	Subject Previously Screened?	Previous Subject Number	Re-consent Version	Re-consent Date
X	DDMMMYYYY	X	XX	DDMMMYYYY	X	XX			
X	DDMMMYYYY	X	XX	DDMMMYYYY	X	XX			

\- - -

Note: Product X: < >

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

Appendix 16.2.4.1.2 Demographics (Safety Population)

Subject Number	Age (yrs)	Sex	Race	Reproductive Status	Ethnicity	Height (cm)	Weight (kg)	BMI (kg/m^2)
X	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX
X	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX
X	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX
X	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX
X	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX
X	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX
X	XX	XXXX	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XX.X	XXX.X	XX.XX

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

Appendix 16.2.4.1.3 Additional Demographics Questionnaire (Safety Population)

Subject Number	Income*	Grade*	Marital Status	Identity*
X	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX
X	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX
X	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX
X	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX
X	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX
X	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX
X	XXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX	XXXXXXXXXXX

Note: * Income = What was your annual household income from all sources over the past year?
Grade = What was the highest grade or year of school you completed?
Identity = Which of the following options do you identify with?

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

Appendix 16.2.4.2.1 Physical Examination – Full (Safety Population)

Subject Number	Study Visit	Date	Was PE Performed?	Reason for Not Done	Body System	If Other, Specify	Result	Specify if Abnormal or Not Done
X	Screening	DDMMMYYYY	XXX		XXXXXXXX		XXXX	

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

Appendix 16.2.4.2.2 Physical Examination - Symptom-driven (Safety Population)

Subject Number	Study Visit	Date	Report Symptom?	Was PE Performed?	Reason for Not Done	Abnormal Findings?	Body System	If Other, Specify	Result	Specify if Abnormal
X	XXX	DDMMMYYYY	XXX	XXX	XXXXXXXX	XXX	XXXX			

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

Appendix 16.2.4.3 Medical and Surgical History (Safety Population)

Subject Number	Any History?	Study Visit	MH Number	Category	Body System	Report term	Onset Date	Ongoing	End Date
X	XXX	Screening	X	XXXXXXX	XXXXXX	XXXXX XXXXXXXXXXX	DDMMMYYYY	Yes	
			X	XXXXXXX	XXXXXX	XXXXX XXXXXXXXXXX	DDMMMYYYY	No	DDMMMYYYY

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

Appendix 16.2.4.4.1 Tobacco/Nicotine Product Use History Questionnaire (Safety Population)

Subject Number	Study Visit	Questionnaire Completed?	Date
X	Screening	XXX	DDMMMYYYY

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

Appendix 16.2.4.4.2 Smoking History (Safety Population)

Subject Number	Study Visit	Number of Years Smoked Cigarettes?	Average Number of Cigarettes Smoked During the Past Year
X	Screening	XXX	XX

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

Appendix 16.2.4.4.3 Usual Brand Documentation (Safety Population)

Subject Number	Study Visit	Usual Brand Changed?*	Color Photocopy?*	Brand	If Other, Specify	Brand Style	Flavor	Length
X	XXXXX	XXXXXX	XXX	XXXXXX		XXXXXXXX	XXX	XXXXX

Note: * Usual Brand Changed? = Has subject's usual brand changed since last reported?
* Color Photocopy? = Was a color photocopy of subject's usual brand cigarette package obtained?

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

Appendix 16.2.5.1 Inclusion / Exclusion Criteria Not Met (Safety Population)

Subject Number	Study Visit	Did subject meet all eligibility criteria?	Criterion Identifier	Inclusion/Exclusion Category	Did the Subject Enroll?
X	Screening	No	EXCLUSION X	XXXXXXXXXXXXXX XXXX	XXX
X	Screening	Yes			
X	Screening	Yes			

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

Appendix 16.2.5.2.1 myblu™ Product Preference Questionnaire (Safety Population)

Subject Number	Study Visit	Product	Rank
X	XXX	Tobacco Chill - low nicotine	X
		Tobacco Chill - high nicotine	X
		Honeymoon - low nicotine	X
		Honeymoon - high nicotine	X

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

Appendix 16.2.5.2.2 Product Selection (Safety Population)

Subject Number	Study Visit	Initial Product Selected	Switch?*	Product Selected To Continue
X	XXX	X	XXX	X

Note: Product X: < >
* = Indicate how subject would like to continue

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

Appendix 16.2.5.2.3 Staff-Recorded In-Clinic Product Use (Safety Population)

Subject Number	Study Day	Product	Date	Number of Cigarettes Smoked	Number of New Pods Started	FAS Flag	PP28/29 Flag	PP56/57 Flag
X	X	X	DDMMMYYYY	X	X	X	X	X

Note: . = Missing or not reportable, NA = Not applicable, Y = Included, N = Excluded
Product X = < >

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

Programmer Note: Puff and cartridge categories apply only to subjects using myblu™ products

Appendix 16.2.5.2.4 Self-Reported Product Use (Safety Population)

Subject Number	Study Day	Product	Date	Number of Cigarettes Smoked	Number of New Pods Started	Take More Than 50 Puffs From myblu™ Today?	FAS Flag	PP28/29 Flag	PP56/57 Flag
X	X	X	DDMMMYYYY	X	X	X	X	X	X

Note: . = Missing or not reportable, NA = Not applicable, Y = Included, N = Excluded
Product X = < >

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

Programmer Note: Puff and cartridge categories apply only to subjects using myblu™ products

Appendix 16.2.5.2.5 Product Use - Nicotine PK Assessment (Safety Population)

Subject Number	Study Visit	Pro-duct	Is Session Data Available?	Reason for Not Done	Session Date	Start Time	Missing Puffs?	Reason for Missing?	Pod Number	Start Weight(g)	Start Time	End Weight(g)	End Time	Number of Puffs Taken
	-													
X	XXX	X	XXXX		DDMMMYYYY	HH:MM			X	X.XXXX	HH:MM	X.XXXX	HH:MM	XX
									X	X.XXXX	HH:MM	X.XXXX	HH:MM	XX
									X	X.XXXX	HH:MM	X.XXXX	HH:MM	XX

Note: Product X: < >

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

Appendix 16.2.5.3.1 Pharmacokinetics Blood Sampling (Safety Population)

Subject Number	Study Visit	Study Product	Was Blood Sample Collected?	Reason for Not Done	Bioassay	Scheduled Timepoint	Date	Actual Time	Comments
X	X	X	XXX		XXXXX	XXXXXXXXXXXXXXXXX	DDMMMYYYY	HH:MM	
					XXXXX	XXXXXXXXXXXXXXXXX	DDMMMYYYY	HH:MM	
					XXXXX	XXXXXXXXXXXXXXXXX	DDMMMYYYY	HH:MM	
					XXXXX	XXXXXXXXXXXXXXXXX	DDMMMYYYY	HH:MM	

Note: Product X: < >

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

Appendix 16.2.5.3.2 24-Hour Urine Collection (Safety Population)

Subject Number	Study Visit	Study Product	Was Urine Sample Collected?	Reason for Not Done	Start Date	Start Time	End Date	End Time	Total Urine Weight (g)	Any Missed Void?	Reason for Missing Void
X	X	X	XXX		DDMMMYYYY	HH:MM	DDMMMYYYY	HH:MM	XXXX	XX	

Note: Product X: < >

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

Appendix 16.2.5.3.3 24-Hour Urine Collection - Pod Weight Documentation (Safety Population) (Safety Population)

Subject Number	Study Visit	Study Product	Number of Pods Used During 24-hour Urine Collection	Pod Number	Pod Starting Weight (g)	Pod End Weight (g)
X	X	X	XXX	X	X.XXXX	X.XXXX
				X	X.XXXX	X.XXXX
				X	X.XXXX	X.XXXX

Note: Product X: < >

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

Appendix 16.2.5.3.4 Carboxyhemoglobin Blood Collection (Safety Population)

Subject Number	Study Visit	Study Product	Were Blood Sample for COHb Collected?	Reason for Not Done	Collection Date	Collection Time
X	X	X	XXX		DDMMMYYYY	HH:MM

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

Appendix 16.2.5.3.5 Biomarkers and Bio-Banking Blood Collection (Safety Population)

Subject Number	Study Visit	Study Product	Were Blood Sample for Biomarkers and Biobanking Collected?	Reason for Not Done	Collection Date	Collection Time
X	X	X	XXX		DDMMMYYYY	HH:MM

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

Appendix 16.2.5.4 Prior and Concomitant Medications (Safety Population)

Subject Number	Study Visit	Study Product	Any Med?	Medication (WHO* Term)	Dosage	Route	Start Date	Stop Date	Frequency	Indication	MH Term	AE Term	Ongoing?
X	XXXX	X	XXX	XXXXXXXXXXX (XXXXXXXXXXX)	620 mg	ORAL	DDMMMYYYY	DDMMMYYYY	Once	Toothache			No

Note: * Concomitant medications are coded with WHO Dictionary Version DDMMMYYYY.
Product X: < >

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

Appendices for blood biomarkers will have the following format:

Page 1 of X

Appendix 16.2.6.2.1 Whole Blood COHb (Outcomes Population)

Subject Number	Product	Planned Visit	Study Day	COHb (% Saturation)	Change From Baseline (% Saturation)	% Change From Baseline	FAS Flag	PPS 5/6 Flag	PPS 29/30 Flag	PPS 59/60 Flag
X	X	Day -1	-X	X.X	NA	NA	Y	X	X	X
		Day 5	X	X.X	X.X	XX.XX	Y	X	X	X
		Day 29	XX	X.X	X.X	XX.XX	Y	NA	X	X
		Day 59	XX	X.X	X.X	XX.XX	Y	NA	NA	X

Note: Product X: < >

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

Appendices for urine biomarkers will have the following format:

Page 1 of X

Appendix 16.2.6.2.2 Urine NNAL (Outcomes Population)

Subject Number	Product	Day	Creatinine (mg/L)	NNAL (pg/mL)	NNAL (ng/g Cr)	-------NNAL------- ----(ng/g Cr)----- Change	% Change	Urine Weight (g)	Amount Excreted (ng/24hrs)	---NNAL Amount--- ----Excrreted---- Change	% Change	FAS Flag	PPS 5/6 Flag	PPS 29/30 Flag	PPS 59/60 Flag
03-0010	X	-X	XXX	XXX	XXX	NA	NA	XXXX	XXXX	NA	NA	Y	Y	Y	Y
		X	XXX	XXX	XXX	XXX	XXX	XXXX	XXXX	XXX	XXX	Y	Y	Y	Y
		XX	XXX	XXX	XXX	XXX	XXX	XXXX	XXXX	XXX	XXX	Y	N	Y	Y
		XX	XXX	XXX	XXX	XXX	XXX	XXXX	XXXX	XXX	XXX	Y	N	N	Y

Note: Product X: < >

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

Appendix 16.2.6.3.1 PSCDI, PSECDI Questionnaire (ITT 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 16.2.6.3.2 PSCDI, PSECDI Questionnaire Responses (ITT Population)

Subject Number	Product	Time Point	Question 1	2	3	4	5	6	7	8	9	10	Total Score
XXXXXX	X	XXXX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX

Note: Product X: < >
Refer to Appendix 16.2.6.3.1 for the description of questions.

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

Appendix 16.2.6.4.1 Cough Questionnaire (ITT Population)

1. Did you have a cough during the last 5 days?
2. How would you rate the intensity of your cough during the last 5 days?
3. How often did you cough up phlegm during the last 5 days?
4. How often did your cough disturb your sleep during the last 5 days?
5. How often did you have coughing bouts during the day, during the last 5 days?

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

Appendix 16.2.6.4.2 Cough Questionnaire Responses (ITT Population)

Subject Number	Product	Time Point	Question 1	2	3	4	5
XXXXXX	X	XXXX	XXXXXXXXXX	XXXXXXXXXX	XXXXXXXXXXXX	XXXXXXXXXX	XXXXXXXXXXX

Note: Product X: < >
Refer to Appendix 16.2.6.4.1 for the description of questions.

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

Appendix 16.2.6.5.1 MTWS-R Questionnaire (ITT 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 16.2.6.5.2 MTES-R Questionnaire Responses (ITT Population)

Subject Number	Product	Time Point	Question 1	2	3	4	5	6	7	8	Total Score
XXXXXX	X	XXXX	X	X	X	X	X	X	X	X	XX

Note: Product X: < >
Scale: 0 = none, 1 = slight, 2 = mild, 3 = moderate, 4 = severe
Refer to Appendix 16.2.6.5.1 for the description of questions.

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

Appendix 16.2.6.6.1 QSU-brief Questionnaire (ITT Population)

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

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

Appendix 16.2.6.5.2 MTES-R Questionnaire Responses (ITT Population)

Subject Number	Product	Time Point	Question 1	2	3	4	5	6	7	8	9	10	Factor Score 1	2
XXXXXX	X	XXXX	X	X	X	X	X	X	X	X	X	X	X	X

Note: Product X: < >
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 16.2.6.6.1 for the description of questions.

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

Appendix 16.2.6.7.1 PES Questionnaire (ITT 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 16.2.6.7.2 PES Questionnaire Responses (ITT Population)

Subject Number	Product	Time Point	Question 1	2	3	4	5	6	7	8	9	10	…….	21
XXXXXX	X	XXXX	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 16.2.6.7.1 for the description of questions.

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

Appendix 16.2.6.7.3 PES Questionnaire Subscales (ITT Population)

Subject Number	Product	Time Point	Question: Satisfaction	Question: Psychological Reward	Question: Aversion	Question: Relief
XXXXXX	X	XXXX	X	X	X	X

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

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

Appendix 16.2.6.8 Product Liking Questionnaire Responses (ITT Population)

Subject Number	Product	Time Point	Question	VAS Score
XXXXXX	X	XXXX	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX

Note: Product X: < >

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

Appendix 16.2.6.9 Future Intent to Use Questionnaire Responses (ITT Population)

Subject Number	Product	Time Point	Question	VAS Score
XXXXXX	X	XXXX	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX
			XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX
		XXXX	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX
			XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX

Note: Product X: < >

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

Appendix 16.2.6.10 Product and Health Effect Perceptions Questionnaire Responses (ITT Population)

Subject Number	Product	Time Point	Question	VAS Score
XXXXXX	X	XXXX	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX
			XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX
		XXXX	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX
			XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	XX

Note: Product X: < >

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

Appendix X Urge to Smoke Assessments (PK Population)

Subject Number	Product	Time Point	Question	VAS Score
XXXXXX	X	XXXX	How strong is your urge to smoke right now?	XX
		XXXX	How strong is your urge to smoke right now?	XX

Note: Product X: < >

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

Programmer Note: This listing also can be presented as horizontal format. It will only be presented for the sub-study.

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

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

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 Preferred Term Classification (Safety Population)

Subject Number	Study Visit	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 16.2.8.1.3 will have the following format.

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

Subject Number	Age/ Sex	Study Visit	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	DDMMMYYYY	XX HN	XX	XX	XX	XX HN	XX

Note: H = Above Reference Range, L = Below Reference Range
PI flag: CS = Clinically significant, NCS = 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 16.2.8.1.4 Serology (Safety Population)

Subject Number	Study Visit	Was the Sample Collected?	Reason for Not Done	Date of Collection
X	Screening	XXX		DDMMMYYYY

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

Appendix 16.2.8.1.5 Urine Drug Screen (Safety Population)

Subject Number	Study Visit	Was the Urine Sample Collected?	Reason for Not Done	Date of Collection	Test Name	Result
X	Screening	XXX		DDMMMYYYY	XXXXXXX	XXXXXX
					XXXXXXX	XXXXXX
					XXXXXXX	XXXXXX
					XXXXXXX	XXXXXX

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

Appendix 16.2.8.1.6 Alcohol Breath Test (Safety Population)

Subject Number	Study Visit	Was the Alcohol Breath Test Performed?	Reason for Not Done	Date of Test	Result
X	Screening	XXX		DDMMMYYYY	XXXXXX

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

Appendix 16.2.8.1.7 Urine Cotinine Screen (Safety Population)

Subject Number	Study Visit	Was the Urine Cotinine Sample Collected?	Reason for Not Done	Date of Collection	Result
X	Screening	XXX		DDMMMYYYY	XXXXXX

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

Appendix 16.2.8.1.8 Pregnancy Test (Safety Population)

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

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

Appendix 16.2.8.1.9 Serum FSH (Safety Population)

Subject Number	Study Visit	Was the Sample Collected?	Reason for Not Done	Date of Collection	Was Post-menopausal Status Confirmed?
X	Screening	XXX		DDMMMYYYY	XXX

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	Was VS Measured?	Reason for Not Done	Date	Time	Blood Pressure (mmHg) Systolic/Diastolic	Pulse (bpm)	Respiration (rpm)	Temperature (°C)	Weight (kg)
X	Screening		XXX		DDMMMYYYY	X:XX	XXX/ XX	XX	XX	XX.X	XXX.X
	X	X	XXX		DDMMMYYYY	XX:XX	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 Visit	ECG Done?	Reason for Not Done	Date	Time	Result	Heart Rate (bpm)	PR (msec)	QRS (msec)	QT (msec)	QTcB* (msec)	If Abnormal	
												Specify	Action Taken
X	Screening	XXX		DDMMMYYYY	X:XX:XX	Normal	XX	XXX.X	XX.X	XXX.X	XXX.X		

Note: QTCB* = QTc corrected using Bazett's correction.

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

Appendix 16.2.8.4 Carbon Monoxide Breath Test (Safety Population)

Subject Number	Study Visit	Were Exhaled CO Levels Measured	Reason for Not Done	Date	Time	Result (ppm)
X	Screening	XXX		DDMMMYYYY	HH:MM	XXX

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

Appendix 16.2.8.5 FeNO Measurement (Safety Population)

Subject Number	Study Visit	Were FeNO Measurements Collected?	Reason for Not Done	Date	Time	FeNO (ppb)	Comment
X	Screening	XXX		DDMMMYYYY	HH:MM	XXX	

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

Appendix 16.2.8.6 Spirometry (Safety Population)

Subject Number	Study Visit	Event*	Test Done?	Reason for Not Done?	Date	Time	FVC		FEV1		FVC:FEV1 Ratio		FEF 25-75%	
							M#(L)	P#(%)	M#(L)	P#(%)	M#	P#	M#	P#
X	Screening	Pre	XXX		DDMMMYYYY	HH:MM	XX	XX	XX	XX	XX	XX	XX	XX
		Alb	XXX			HH:MM								
		Post	XXX		DDMMMYYYY	HH:MM	XX	XX	XX	XX	XX	XX	XX	XX

Note: * pre = pre-bronchodilator, Alb = Albuterol administration, post = post-bronchodilator
M = Measured, P = Predicted

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